ORIGINAL

UNITED STATES OF AMERICA
FEDERAL TRADE COMMISSION

In the Matter of	)	
	)	
POM WONDERFUL LLC and	)	
ROLL INTERNATIONAL CORP.,	)	
companies and	)	**Docket No. 9344**
	)	**PUBLIC**
STEWART A. RESNICK,	)	
LYNDA RAE RESNICK, and	)	
MATTHEW TUPPER, individually and	)	
as officers of the companies.	)	
	)	

RESPONDENTS' PROPOSED FINDINGS OF FACT AND CONCLUSIONS OF LAW

POM Wonderful LLC
Roll Global LLC, successor in interest to Roll International Corp.,
Stewart A. Resnick,
Lynda Rae Resnick, and
Matthew Tupper

Kristina M. Diaz, Esq.
Alicia Mew, Esq.
Johnny Traboulsi, Esq.
Brooke Hammond, Esq.
Roll Law Group P.C.
11444 West Olympic Blvd., 10th Floor
Los Angeles, CA, 90064
Tel: 310.966.8400
Fax: 310.966.5758
Email: kdiaz@roll.com

John Graubert, Esq.
Skye Perryman, Esq.
Covington & Burling LLP
1201 Pennsylvania Avenue, NW
Washington, DC 20004
Tel: 202.662.6000
Fax: 202.662.6291
Email: jgraubert@cov.com

Bertram Fields, Esq.
Greenberg Glusker Fields
Claman & Machtinger, LLP
1900 Avenue of the Stars, Suite 2100
Los Angeles, CA 90067
Tel: 310.553.3610
Fax: 310.553.0687
Email: bfields@greenbergglusker.com

UNITED STATES OF AMERICA
FEDERAL TRADE COMMISSION

In the Matter of	)	
	)	
POM WONDERFUL LLC and	)	
ROLL INTERNATIONAL CORP.,	)	
companies and	)	**Docket No. 9344**
	)	**PUBLIC**
STEWART A. RESNICK,	)	
LYNDA RAE RESNICK, and	)	
MATTHEW TUPPER, individually and	)	
as officers of the companies.	)	
_____	)	

RESPONDENTS' PROPOSED FINDINGS OF FACT AND CONCLUSIONS OF LAW

POM Wonderful LLC
Roll Global LLC, successor in interest to Roll International Corp.,
Stewart A. Resnick,
Lynda Rae Resnick, and
Matthew Tupper

Kristina M. Diaz, Esq.
Alicia Mew, Esq.
Johnny Traboulsi, Esq.
Brooke Hammond, Esq.
Roll Law Group P.C.
11444 West Olympic Blvd., 10th Floor
Los Angeles, CA, 90064
Tel: 310.966.8400
Fax: 310.966.5758
Email: kdiaz@roll.com

John Graubert, Esq.
Skye Perryman, Esq.
Covington & Burling LLP
1201 Pennsylvania Avenue, NW
Washington, DC 20004
Tel: 202.662.6000
Fax: 202.662.6291
Email: jgraubert@cov.com

Bertram Fields, Esq.
Greenberg Glusker Fields
Claman & Machtinger, LLP
1900 Avenue of the Stars, Suite 2100
Los Angeles, CA 90067
Tel: 310.553.3610
Fax: 310.553.0687
Email: bfields@greenbergglusker.com

TABLE OF CONTENTS

RESPONDENTS' PROPOSED FINDINGS OF FACT

I. CASE BACKGROUND

A. Summary of Complaint and Answer

1. The FTC's Complaint

1. The Federal Trade Commission ("FTC") issued the Complaint in this matter on September 24, 2010 against POM, Roll Global, Stewart A. Resnisck, Lynda Rae Resnick and Matthew Tupper (collectively "Respondents"). (CX1426_0002).

2. The Complaint challenges POM's advertising of their POM Wonderful 100% Pomegranate Juice ("POM Juice"), POMx Pills, containing pomegranate extract, and POMx Liquid, a liquid form of the POMx Pills. (CX142_0003).

3. The FTC alleges that Respondents have disseminated or have caused to be disseminated deceptive and misleading advertising which violates Sections 5 and 12 of the Federal Trade Commission Act ("FTCA"). (CX1426_0020).

4. The FTC has taken the position, as stated by David Vladeck, Director of the FTC's Bureau of Consumer Protection, that "Any consumer who sees POM Wonderful products as a silver bullet against disease has been misled." (PX0449_0001; Press Release, *FTC Complaint Charges Deceptive Advertising by POM Wonderful*, Federal Trade Commission, Sept. 9, 2010, *at* http://www.ftc.gov/opa/2010/09/pom.shtm).

5. More specifically, Complaint Counsel alleges that POM's advertisements at issue have represented that, expressly or by implication, clinical studies, research and/or trials "prove" that drinking eight ounces of POM Juice, or taking one POMx Pill or one teaspoon of POMx Liquid, daily, is clinically proven to prevent or treat: 1) heart disease, including by (a) decreasing arterial plaque, (b) lowering blood pressure, and/or (c) improving blood flow; 2) prostate cancer, including by prolonging prostate-specific antigen doubling time; and 3) erectile dysfunction. (CX1426_0017-0019).

2. The Respondents' Answer

6. Respondents filed their Answer on October 18, 2010. (PX0364).

7. In their Answer, Respondents assert that the Complaint fails to state a claim upon which relief can be granted under Section 5 of the FTC Act, 15 U.S.C. §45. (PX0364-0007).

8. Respondents assert that the FTC lacks authority to impose all or part of the relief sought under the FTC Act, the Administrative Procedure Act, and the First and Fifth Amendments of the U.S. Constitution. (PX0364-0007).

9. Respondents further assert that the Complaint and the FTC's contemplated relief improperly seek to restrict consumers' access to valuable information about the potential health benefits of Respondents' products and therefore are contrary to public interest. (PX0364-0007).

10. Respondents also assert by that taking this enforcement action the FTC has, without adequate justification, changed its position with respect to the dissemination of such information and is seeking to impose new and unwarranted standards for the advertising of food products without adequate notice to the public, in particular to consumers and the business community. (PX0364-0007).

11. Respondents admit that POM disseminated the advertising and promotional materials attached to the Complaint as Exhibits A through N. (PX0364-0003).

12. However, Respondents deny any inference, characterization, suggestion or legal argument concerning those materials caused by selective quotation or comment added by the Complaint Counsel in the Complaint or attached exhibits. (PX0364-0003).

13. Respondents deny the dissemination dates alleged in the Complaint. (PX0364-0003).

14. Respondents deny that their advertisements conveyed the messages alleged by Complaint Counsel and assert all messages conveyed by any of the advertisements were supported and/or that Respondents had a reasonable basis for any claims made. (PX0364-0003-0006).

15. Respondents deny the allegations that they, in any way, engaged in deceptive acts or practices. (PX0364-0003-0006).

16. Respondents affirmatively maintain that they possessed and relied upon substantial scientific research indicating the health benefits of their products and substantiating their advertising and promotional materials. (PX0364-0003-0006).

B. Procedural Background

17. An unusually large body of scientific evidence was presented at trial and is part of this record.

18. Between December 3, 2010 and April 28, 2011, twenty-six percipient witness and fourteen expert witness depositions were taken.

19. The final pre-hearing conference was held on May 19, 2011, with trial commencing on May 24, 2011.

20. Complaint Counsel concede this case is different from previous cases brought before the Commission and they are not claiming Respondents are selling "snake oil." (Tr., 69).

21. Over nineteen hundred exhibits, containing approximately sixty-five thousand pages, were designated prior to the hearing, over 1,500 of which were admitted into evidence. (*See*, JX2 Attachment A).

22. Respondents submitted into evidence more than ninety scientific studies and reports sponsored by Respondents. (See PX Exhibit Nos. 2-12, 14-23, 38-41, 49-51, 53-66, 68-71, 73-77, 81-130, 136-148, 174-175).

23. A total of twenty-four live witnesses testified at trial, including fourteen experts.

24. The testimonial portion of the trial concluded on November 4, 2011 after nineteen days of trial.

25. The hearing record was closed on November 18, 2011, pursuant to Commission Rule 3.44(c), by Order dated November 18, 2011.

26. On January 11, 2012, the parties filed concurrent post-trial briefs, proposed findings of fact, and findings of law.

C. Evidence Before This Court

These findings of fact are based on the exhibits properly admitted into evidence, the transcripts of testimony at trial, and the briefs submitted by the parties. References to the record are abbreviated as follows:

CX – Complaint Counsel's Exhibit

PX – Respondents' Exhibit

RX – Respondents' Exhibit

JX1- Joint Stipulations of Law and Facts dated May 24, 2011

JX2 – Joint Stipulations on Admissibility of Exhibits dated May 24, 2011

JX2 Attachment A – Joint Exhibits Admitted Without Objection dated May 24, 2011

JX2 Attachment B – Conditionally Admitted Exhibits Subject to Objection dated May 24, 2011

JX3- Joint Stipulations dated November 14, 2011

Tr. – Transcript of Testimony before the ALJ

Dep. – Transcript of FTC Deposition

Tropicana Dep. – Transcript of Deposition taken in *POM Wonderful v. Tropicana*

Coke Dep. – Transcript of Deposition taken in *POM Wonderful v. Minute Maid*

Welch's Dep. – Transcript of Deposition taken in *POM Wonderful v. Welch Foods*

Ocean Spray Dep. – Transcript of Deposition taken in *POM Wonderful v. Ocean Spray*

Tropicana Tr. –Transcript of *POM Wonderful v. Tropicana*

II. SUMMARY OF KEY FINDINGS

A. Key Findings Regarding the Advertisements

27. Complaint Counsel is not alleging that any advertisements of POM convey the message that the challenged products "cure" any disease or condition. Complaint Counsel did not provide any expert testimony, or extrinsic evidence that consumers cannot and do not distinguish between a health message that a product is healthy for you, or of assistance in maintaining the health of a particular area of the body (erectile, heart, prostrate) and a message that the product has an effect, like a drug in preventing or treating a particular condition of the body. Yet, Complaint Counsel asks this court to adopt this significant premise fundamental to its claims.

28. Complaint Counsel did not provide any expert opinion or competent extrinsic evidence on what messages the ads actually conveyed, including whether the ads conveyed "clinically proven" claims.

29. Complaint Counsel did not provide any expert opinion or extrinsic evidence on whether and to what extent consumers interpreted the ads to convey that the Challenged Products prevent or reduce your risk against disease, like broccoli or blueberries prevent or reduce your risk against disease, or whether the ads

conveyed "prevention" in more absolute and targeted sense, like a drug or drug treatment, even an over-the-counter treatment such as Tough Action Tenactin, that says on its bottle that it can "prevent" and "cure" athelete's foot.

30. Complaint Counsel did not provide any extrinsic evidence or expert opinion on whether and to what extent a consumer looks at the ads referring to a scientific study whose participant suffered from a condition or disease, and where the advertisement explicitly refers to the condition or the disease, and concludes that the consumption of the product will treat or prevent that disease or condition.

31. Complaint Counsel did not present any extrinsic evidence or expert testimony that consumers do not distinguish between claims that the product "prevents" a condition and claims that the product "treats" a condition.

32. Even if the Commission could conclude that the "treat" and "prevent" claims were implied by the advertisements, POM's survey expert responded to these assertions with a well-conducted survey of his own, which Complaint Counsel failed to rebut.

33. Professor David Reibstein, POM's survey expert, concluded from his survey that less than 1.9% of POM's consumers purchase the 100% juice product because they believe it will alleviate a disease condition. (PX0223-0020).

34. Complaint Counsel do not address Professor Reibstein's survey directly and instead refer to POM's internal surveys, consumer logs and creative briefs to identify an "intent" sufficient to respond to Professor Reibstein's conclusions, but these references are insufficient to rebut Professor Reibstein's conclusions.

35. Complaint Counsel failed to offer in this case evidence regarding the advertisements or the issue of materiality that they presented in previous cases before the Commission.

36. Complaint Counsel expert, Professor Michael Mazis, failed to prepare any survey or present any opinion, on the messages conveyed in POM's advertisements or on the subject of materiality.

37. Complaint Counsel expert, Professor David Stewart, also failed to present any opinion on the messages conveyed in POM's advertisements or on the subject of materiality.

38. Professor Mazis, however, did testify that at least 3 exposures of any given ad was necessary before that ad could impact purchasing behavior. (Stewart, Tr. 3228-29; Mazis, Tr. 2752).

39. Yet, Mazis, in stark contrast to his testimony given in previous cases before the Commission, never gave any opinion about the number of exposures of any ad on consumers in this matter.

40. Accordingly, the FTC failed to meet its burden of proof on this fundamental issue.

B. The Advertisements Do Not Convey the Messages That The FTC Claims and Respondents Have Competent and Reliable Science to Support the Actual Claims Made

41. Complaint Counsel has now, late in trial and afterwards, narrowed the universe of advertisements to approximately 70 ads, from hundreds and hundreds of ads. (PX0263-0002-0013; PX0267-0002-0030).

42. Complaint Counsel focuses on POM's ads with the most aggressive health benefit claims that ran years ago, were discontinued and have not been disseminated within the last 4 to 7 years. Respondents assert that these ads were accurate and substantiated. Because Complaint Counsel has not presented evidence that it is probable Respondents will disseminate these ads again, these "outlier" ads cannot form the basis for the injunctive relief sought by the commission. (*See infra* XVII(E)).

43. POM's advertisements do not convey or imply the message that their products are "clinically proven" to prevent, treat or reduce the risk of disease as claimed by Complaint Counsel. (CX01426_0017-0020; Appendix of Advertisements, attached hereto as Appendix B).

44. Complaint Counsel failed to present significant extrinsic evidence or expert opinion to support their interpretation of the claims allegedly made by POM's advertising. (Appendix of Advertisments).

45. Even assuming that Complaint Counsel is entitled to a presumption of materiality, Respondents' survey expert Professor Reibstein, through his testimony and survey evidence, successfully rebutted any such presumption. (*See infra* XVIII(A)).

46. Respondents have a rational basis, and competent and reliable scientific evidence to support the claims that were expressly and implicitly made. (*See* supra XII-IV; XVII; Appendix of Advertisments).

C. Key Findings Regarding the Science Supporting the Health Benefits of the Challenged Products

47. Complaint Counsel presented no opposing scientific studies or evidence conducted by others or FTC experts showing that Respondents' claims were affirmatively

false, i.e., that the challenged products do not, in fact, have the health benefits explicitly or implicitly conveyed in the advertisements.

48. Complaint Counsel did not present any expert opinion that the challenged products do not have the health benefits explicitly or implicitly conveyed in the advertisements.

49. At a minimum, Complaint Counsel failed to show, by a preponderance of the evidence, that the health benefit claims made in POM's advertisements were, in fact, false.

50. Both Respondents' and Complaint Counsel's experts opined that an absence of a "positive" result in a scientific study does not support, or prove, the negative or opposing conclusion. (Sacks, Tr. 1608-09; CX1352 (Heber, Dep. at 218); PX0361 (Sacks, Dep. at 223-24, 230, 238, 243); Goldstein, Tr. 2598-99; Heber, Tr. 1981).

51. The totality of the evidence includes all studies, positive and negative studies, large and small studies, unpublished and published studies and basic science, (test tube and animal), as well as human clinical trials. (Heber, Tr. 1948-50; 2056; 2086, 2149, 2166, 2182; PX0353 (Heber, Dep. at 178); CX1352 (Heber, Dep. at 243)). Ornish, Tr. 2327-31, 2354-55; Miller, Tr. 2194; PX0206-0007, 0015; PX0004, PX0005, CX0611, PX0014, PX0020, PX0021, PX0023, PX0038, PX0127, PX0139, PX0002, PX0007, PX0008, PX0009, PX0010, PX0015, CX0543, PX0017, PX0022, CX0053, PX0055, PX0056, PX0057, PX0058, PX0059).

52. RCTs are <u>not</u> required to make any claim of health benefits for a safe whole food or whole food product, such as the Challenged Products. (Miller, Tr. 2194, 2201; PX0206-0010-0015; Heber, Tr. at 1948-50, 2056, 2166; PX0149-0006-0007; Burnett, Tr. 2272-74, 2303; PX0189-0003; Goldstein, Tr. 2600-02, 2611, 2620); deKernion, Tr. 3060; PX0025-0007).

D. <u>Matthew Tupper Is Not Personally Liable and No Order Should Issue Against Him</u>

53. Matthew Tupper was the former President of POM Wonderful, but he retired from that position at the end of 2010. (Tupper, Tr. 2972-73).

54. Mr. Tupper will not be working for Roll Global or any other company owned by the Resnicks after his retirement from POM Wonderful. His involvement with POM Wonderful or any other Resnick related entity is over. (Tupper, Tr. 2974).

55. Mr. Tupper has never had an ownership interest or equity shares in POM Wonderful (and never has) and has no expectation of such interest. (CX1353 (Tupper, Dep. at 14); Tupper, Tr. 2973).

56. Although Mr. Tupper managed the day-to-day operations on behalf of the Resnicks and was involved in several aspects of POM Wonderful's operations, excluding the science program and the advertisements none were under his exclusive or even majority control. (CX1363 (S. Resnick, Coke, Dep. at 86); CX1348 (Perdigao, Dep. at 50, 60-61); CX1359 (L. Resnick, Dep. at 36); CX1362 (L. Resnick, Coke, Dep. at 103-04); Tupper, Tr. 2974).

57. In fact, Mr. Tupper had no more authority at POM than was delegated to him by Mr. Resnick. (S. Resnick, Tr. 1870).

III. THE RESPONDENTS

A. The Respondents

1. POM Wonderful LLC

58. POM Wonderful ("POM Wonderful" or "POM") is a limited liability company organized under the laws of the State of Delaware. (CX1426_0002); (CX1367 (S. Resnick, Welch's Dep. at 8); CX1437; PX0364-0001).

59. POM Wonderful's principal office or place of business is at 11444 West Olympic Boulevard, Los Angeles, California 90064. (CX1426_0002; PX0364-0001).

60. POM Wonderful is wholly owned by the Stewart and Lynda Resnick Revocable Trust, dated December 27, 1988 ("1988 Resnick Trust"). (CX1426_0002; PX0364-0001; CX1384_0008).

61. Respondent POM Wonderful is a member-managed company, and the 1988 Resnick Trust is the sole member. (CX1426_0002; PX0364-0001).

62. In 2002, POM first launched POM Wonderful 100% Pomegranate Juice, the first premium, all-natural pomegranate juice made from pomegranates grown from POM's orchards. (L. Resnick, Tr.146).

63. POM Wonderful is currently in the business of selling fresh pomegranates and pomegranate-related products, including 100% pomegranate juice ("POM juice") and pomegranate extract products known as POMx pills and POMx liquid ("POMx"). (S. Resnick, Tr.1630-31); CX1364 (Tupper, Coke Dep. at 20); CX1374 (Tupper, Ocean Spray Dep. at 26); CX1363 (S. Resnick, Coke Dep. at 45-46).

2. Respondent Roll Global LLC

64. Roll International Corporation is a separate corporation organized under the laws of the State of Delaware. (CX1426_0002; PX0364-0001).

65. Roll International was reorganized at the end of 2010 and is currently known as Roll Global ("Roll"). (S. Resnick, Tr.1629).

66. Roll is wholly owned by the 1988 Resnick Trust. (CX1426_002-003; PX0364-0001).

67. Roll is a privately held corporation. (S. Resnick, Tr. 1630).

68. POM Wonderful, FIJI Water, Suterra, Paramount Farms, Paramount Citrus, Teleflora, Neptune Shipping, Paramount Farming, and Justin Winery are among the separate operating business under Roll's umbrella. (CX1364 (Tupper, Coke Dep. at 16-17); CX1374 (Tupper, Ocean Spray Dep. at 36); Perdigao, Tr. 593-94).

69. Stewart and Lynda Resnick are the sole owners of Roll and its affiliated companies, including POM Wonderful. (S. Resnick, Tr. 1629; CX1360 (S. Resnick, Dep. at 15); PX1376 (S. Resnick, Ocean Spray Dep. at 13)).

70. Roll's affiliated companies pay Roll for certain provided services. (CX1376 (S. Resnick, Ocean Spray Dep. at 24-25); L. Resnick, Trial Tr. 89; CX1359 (L. Resnick, Dep. at 26); Perdigao Tr. 616-17; CX1384_0011, 0014).

71. For example, Firestation acts as Roll's in-house advertising agency. Firestation bills POM and other Roll entities separately, and each client pays for all advertising and marketing expenses incurred. (CX1376 (S. Resnick, Ocean Spray Dep. at 24-25); L. Resnick, Tr. 89; CX1359 (L. Resnick, Dep. at 26); Perdigao Tr.616-17; CX1384_0011, 0014).

3. Respondents Stewart and Lynda Resnick

72. Stewart Resnick is the Chairman and President of Roll. (S. Resnick, Tr. 1629; CX1363 (S. Resnick, Coke Dep. at 54-55)).

73. Stewart Resnick is the Chairman of POM Wonderful. (CX1426_0003; PX0364-0002).

74. Stewart A. Resnick has the ultimate authority at POM Wonderful. (S. Resnick, Tr. 1869); CX1372 (S. Resnick, Tropicana Dep. at 25-26); (S. Resnick, Tr.1631; CX1360 (S. Resnick, Dep. at 20-21).

75. Notwithstanding his co-ownership of POM Wonderful, Respondent Stewart Resnick has very little involvement in the marketing of POM Wonderful's pomegranate products. (S. Resnick, Tr.1869; CX1360 (S. Resnick, Dep. at 49); CX1363 (S. Resnick, Coke Dep. at 95); CX1376 (S. Resnick, Ocean Spray Dep. at 140-42)).

76. Stewart Resnick is not involved in the day-to-day decisions related to the advertising of POM Wonderful's products. (S. Resnick, Tr. 1869-70).

77. Stewart Resnick, in consultation with POM's legal advisors, nevertheless maintains the ultimate decision-making authority to advertise the health benefits of POM's pomegranate products. (Tupper, Tr. 2975).

78. Stewart Resnick had the ultimate ability to decide whther any advertisements would be fun. (S. Resnick, Tr. 1870; Tupper, Tr. 2975).

79. Lynda Resnick is involved in POM's marketing, branding, public relations, and product development. (CX1363 (S. Resnick, Coke Dep. at 41); (CX1364 (Tupper, Coke Dep. at 27); (CX1347 (Glovsky, Dep. at 36)).

80. Both Lynda and Stewart Resnick have the ultimate authority in developing POM's marketing strategies. (Tupper, Tr. 2974-75; CX1362 (L. Resnick, Coke Dep. at 47, 78)).

81. Lynda Resnick's involvement with POM Wonderful has decreased since 2007. (L. Resnick, Tr. 86; CX1359 (L. Resnick, Dep. at 22); CX1375 (L. Resnick, Tropicana Dep. at 20).

82. Lynda Resnick has the final approval authority in deciding POM's marketing and advertising content and concepts. (CX1368 (L. Resnick, Welch's Dep. at 9); L. Resnick, Tr. 93).

83. POM Wonderful is owned solely by Stewart and Lynda Resnick. (S. Resnick, Tr. 1629; CX1359 (L. Resnick, Dep. at 26); Perdigao Tr. 616-17; CX1384_0011, 0014).

4. Respondent Matthew Tupper

84. Mr. Tupper served as the Vice President of Strategy for Roll from 2001 to 2003. (CX1364 (Tupper, Coke Dep. at 24-25); CX1371 (Tupper, Tropicana Dep. at 9); CX1374 (Tupper, Ocean Spray Dep. at 32-33)).

85. Mr. Tupper was first employed by POM Wonderful in 2003 and originally held the title of Chief Operating Officer. (Tupper, Tr. 2972, CX1353 (Tupper, Dep. at 21); CX1364 (Tupper, Coke Dep. at 14)).

86. In 2005, Mr. Tupper's title changed to President of POM. (Tupper, Tr. 2972; CX1369 (Tupper, Welch Dep. at 10); CX1374 (Tupper, Ocean Spray Dep. at 13, 33); CX1353 (Tupper Dep. at 9); CX1364 (Tupper Coke Dep. at 14)).

87. Mr. Tupper was not engaged in the marketing piece of POM's science-marketing dialogue prior to 2007. (Tupper, Tr. 2976-77).

88. Prior to 2007 Mr. Tupper had only limited involvement in the relationship between science and marketing. (Tupper, Tr. 2976-77).

89. It was not until sometime in 2007 that Mr. Tupper first began to engage in connecting POM's science to its advertising. (Tupper, Tr. 2975-77).

90. Mr. Tupper has never had any ownership interest in POM Wonderful and has no expectation of ever having such an interest. (CX1353 (Tupper, Dep. at 14); Tupper, Tr. 2973).

91. Mr. Tupper reported directly to Stewart Resnick. (CX1364 (Tupper, Coke Dep. at 27-28, 107); CX1367 (S. Resnick Welch Dep. at 53).

92. Mr. Tupper had a "dotted line" reporting to Lynda Resnick. (CX1375 (L. Resnick, Tropicana Dep. at 23-24)).

93. On behalf of the Resnicks, Mr. Tupper managed the day-to-day operations of POM Wonderful, including the POM marketing team. (Tupper, Tr. 2974; CX1363 (S. Resnick Coke Dep., 42)).

94. Mr. Tupper was involved in several aspects of POM's operations, science, advertisements and general POM theme. However, none of these aspects of POM's business were under his ultimate control. (CX1363 (S. Resnick, Coke Dep. at 86); CX1348 (Perdigao, Dep. at 50, 60-61); CX1359 (L. Resnick, Dep. at 36); CX1362 (L. Resnick, Coke Dep. at 103-104)).

95. Mr. Tupper had no more authority at POM Wonderful than was delegated to him by Stewart Resnick. (S. Resnick, Tr. 1870).

96. Mr. Tupper was responsible for administering POM marketing and scientific research budgets but did not have the authority to set those budgets. (Tupper, Tr. 912-913).

97. In fact, Mr. Resnick set all budgets for POM Wonderful. (S. Resnick, Tr. 1631).

98. Mr. Tupper consulted Stewart Resnick or Lynda Resnick for any major restructuring or personnel decisions. (Tupper, Tr. 903; CX1364 (Tupper, Coke Dep. at 31)).

99. In Stewart Resnick's own words he, not Mr. Tupper, is the "ultimate sole decision-maker on everything." (CX1367 (S. Resnick, Welch Dep. at 55).

100. Mr. Tupper did not, independent of the Resnicks, develop the marketing direction or decide how the POM Products would be marketed. The Resnicks had the ultimate authority in developing the direction of POM marketing and how to market POM products, and Mr. Tupper merely implemented the direction, once it was decided upon by the Resnicks. (Tupper, Tr. 2974-2975).

101. Mr. Tupper did not have the final approval authority in deciding POM's marketing and advertising content, concepts and media plans. (CX1368 (L. Resnick Welch's Dep. at 9); L. Resnick, Tr. 93; PX1347 (Glovsky, Dep. at 36); CX1357 (Kuyoomjian, Dep. at 84)).

102. When there were disputes or issues to resolve regarding advertising decisions, the final authority was either Lynda or Stewart Resnick's, not Mr. Tupper's. (CX1365 (Perdigao, Coke Dep. at 36-37)).

103. Since 2007, Mr. Tupper sought to ensure that POM's marketers correctly portrayed and interpreted the science in the advertisements and that POM's advertisements were vetted by the legal department. (Tupper, Tr. 2975-76).

104. POM has funded many millions of dollars of scientific research by renowned scientists, resulting in over 70 peer-reviewed publications. (CX1360 (S. Resnick Dep. at 257); Liker, Tr. 1888).

105. Mr. Tupper personally believes that all of the ads that POM has run were adequately supported by the body of science conducted on the Challenged Products. (Tupper, Tr. 3015).

106. Mr. Tupper retired from POM Wonderful at the end of the 2011. Mr. Tupper knew he was leaving the company and informed Stewart and Lynda Resnick of his intentions in June 2011. (Tupper, Tr. 2973).

107. Mr. Tupper will not be working for Roll Global or any other company owned by the Resnicks after his retirement from POM Wonderful. (Tupper, Tr. 2974).

IV. THE RESPONDENTS' AND COMPLAINT COUNSEL'S PRESENTATION OF EXPERT EVIDENCE AT TRIAL

A. Respondents Experts

108. Respondents' experts testified to an extraordinary body of science demonstrating that Respondents possess competent reliable scientific evidence to substantiate any reasonable construction of POM's advertisements.

109. In many cases, Respondents' experts testified that the body of science on pomegranates support health benefit claims that far exceed what POM actually conveyed in its advertising.

1. Dr. Denis Miller

110. Dr. Denis Miller is a board certified pediatrician and pediatric hematologist and oncologist licensed to practice medicine in the state of New Jersey. (PX0206 at 1; PX0354 (Miller, Dep. at 16)).

111. Dr. Miller has, for over 40 years, directed clinical care, education, laboratory and clinical research, and administration, and led departments at some of the most prestigious hospitals in the world. (PX0206 at 2; Miller, Tr. 2190).

112. He directs one of the largest pediatric oncology/hematology programs in the world and holds an endowed chair. (PX0206 at 3).

113. Dr. Miller has designed, managed, and directed many different research studies calculated to develop new anti-cancer agents (PX0206 at 2-3).

114. Dr. Miller has authored or co-authored over 300 book chapters, peer-reviewed articles, and abstracts mostly on cancer and blood disorders. (PX0206 at 4; Miller, Tr. 2191).

115. Complaint Counsel have retained Dr. Miller on several matters, and he testified for Complaint Counsel previously in *Daniel Chapter One*. (PX0206 at 5, 18).

116. Dr. Miller testified at trial in this matter that, in his opinion and the consensus of the scientific opinion, Respondents do not need RCTs to substantiate their health claims because, among other weighted factors, the Challenged Products are harmless pure fruit products and Respondents never urged the Challenged Products as substitutes for proper medical treatment. (Miller, Tr. 2194).

117. Dr. Miller distinguished this case against Respondents from *Daniel Chapter One*, a case for which he served as a principal expert witness for the FTC. (Miller, Tr. 2193).

118. He opined that, in *Daniel Chapter One*, RCTs were required to substantiate the Respondents' claims because the product was recommended in place of conventional medical treatment, and the mixture had potentially toxic side effects. Above all else, the nature of the product and its safety are the linchpins in determining the level of substantiation required to support one's claim. (Miller, Tr. 2193).

2. Dr. David Heber

119. Dr. Heber received his Ph.D. in Physiology from UCLA, a MD from Harvard Medical School (top 10 percent of his class, Alpha Omega Alpha), and a B.S. (*summa cum laude* in Chemistry and Phi Beta Kappa) from UCLA. (PX0192-0005).

120. Dr. Heber is a treating physician with patients, and has been a member of the faculty of UCLA Medical School for 33 years. He is currently a Professor of Medicine in Public Health. (Heber, Tr. 1937; CX1407 (Heber, Tropicana Tr. 76)).

121. Dr. Heber is the founding director of the UCLA Center for Human Nutrition, which is a center for clinical research, education, and public health endeavors. (Heber, Tr. 1937).

122. He has co-authored over 200 peer-reviewed publications in the field of nutrition and its relation to various diseases and written 25 chapters in other scientific texts. (Heber, Tr. 1939-40).

123. He was the editor-in-chief of the leading text on nutritional oncology and has written a book on the importance of diet in maintaining health and resisting diseases. (Heber, Tr. 1939).

124. Dr. Heber summarized Respondents' basic research and science in the areas of heart, prostate, erectile function, and the bioavailability, absorption, and safety of the Challenged Products. (Heber, Tr. 1936-103).

125. Dr. Heber and Dr. Miller maintain that RCTs are not necessary to properly substantiate health claims for harmless, pure fruit products, like the Challenged Products. In fact, Dr. Heber opined that RCTs are both expensive and often unreliable in dealing with foods, as opposed to drugs. (Heber, Tr. 1949-50, 2166, 2179, 2182).

126. Experts in the nutrition field consider competent and reliable science to support health claims for pomegranate juice based on the totality of evidence, which does not necessarily include RCTs. (Heber, Tr. 2182).

127. Dr. Heber testified as to the basic mechanisms of action underlying the health benefit properties of pomegranate juice. (Heber, Tr. 1957, 2112-13; CX1407 (Heber, Tropicana Tr. 228-31).

128. He testified that pomegranate polyphenols have anti-oxidative and anti-inflammatory properties that have dramatic implications for multiple conditions affecting human health, including the prolongation of nitric oxide in the body,

aging, cancer, mental function, and heart disease. (Heber, Tr. 1957, 2112-13; CX1407 (Heber, Tropicana Tr. 228-31).

129. Dr. Heber testified that POM juice and POMx are completely safe. (Heber, Tr. 2009).

130. He also opined that the antioxidant effect measured in the laboratory has not been different in POM juice and POMx. Dr. Heber firmly believes that pomegranate juice and POMx have the same impact on oxidative stress. (Heber, Tr. 2186-87).

131. Dr. Heber also reviewed Respondents' body of cardiovascular research, including research done by Dr. Michael Aviram, Dr. Dean Ornish, and Dr. Michael Davidson. Dr. Heber concluded Respondents' science showed that the Challenged Products were likely to cause a significant improvement in cardiovascular health and help to reduce the risk of cardiovascular disease. (Heber, Tr. 2012).

132. Dr. Heber reviewed Respondents' body of prostate health research, including animal research, studies done in vitro, and the clinical research done by Dr. Allan Pantuck and Dr. Michael Carducci. Based on this body of research, he concluded that it is likely POM juice and POMx lengthen PSA doubling time for men who have prostate cancer and those men may experience a deferred recurrence of the disease or death from prostate cancer. (Heber, Tr. 2012).

133. He also opined, based on this body of research, that POMx and POM juice are likely to lower the risk of prostate problems for men who have not yet been diagnosed with prostate cancer. (Heber, Tr. 2012-13).

134. Dr. Heber also reviewed Respondents' studies on erectile function. Dr. Heber opined that the animal studies showed that pomegranate juice created a marked improvement in proper erectile function and would probably do so in humans due to the effect of pomegranate juice prolongation on the lifespan of nitric oxide in the body. (Heber, Tr. 1968-69; CX1407 (Heber, Tropicana Tr. 242)).

135. Dr. Heber opined that Dr. Forest's erectile study on humans showed that consumption of POM juice created a marked improvement in erectile function among men who had experienced erectile dysfunction, and it had major clinical significance in showing a benefit from pomegranate juice despite barely missing statistical significance. (Heber, Tr. 1830-31, 1979).

3. Dr. Dean Ornish

136. Dr. Dean Ornish is a medical doctor and Clinical Professor of Medicine at the University of California at San Francisco. (Ornish, Tr. 2314).

137. For over 34 years, Dr. Ornish directed clinical research on the relationship between diet and lifestyle and coronary heart disease. He was the first to prove by a series of RCTs that heart disease could be reversed by simply making changes in diet and lifestyle. (Ornish, Tr. 2316-17).

138. Dr. Ornish has written six published books on the subject of the effect of diet and lifestyle on heart disease and other diseases. (Ornish, Tr. 2318).

139. Dr. Ornish's research has been reported in many prestigious journals, and he has written numerous articles for distinguished peer-reviewed journals. (Ornish, Tr. 2318-19).

140. Dr. Ornish testified at trial that heart health claims for pomegranate juice need not be substantiated by expensive RCTs, and the totality of Respondents' scientific evidence must be considered. (Ornish, Tr. 2320-31).

141. Dr. Ornish responded to the criticisms of his studies by Complaint Counsel's expert, Dr. Frank Sacks and opined that, in a nutritional context, in vitro and animal studies may be more effective in testing the efficacy of a nutrient. (Ornish, Tr. 2327-30, 2331-55).

142. He testified that Complaint Counsel's position that only RCTs are good science is overly simplistic and runs the danger of depriving the public of important nutritional information by discouraging research on natural products. (Ornish, Tr. 2325-28).

143. Dr. Ornish testified that the totality of Respondents' scientific studies conducted on the cardiovascular system convinces him that pomegranate juice is effective in reducing the risk of cardiovascular problems, and even reversing, in come instaces, adverse conditions already present in the cardiovascular system (Ornish, Tr. 2354-55).

4. Dr. Arthur Burnett

144. Dr. Arthur Burnett is a Professor of Urology serving on the faculty of the Department of Urology at the Johns Hopkins University School of Medicine/Johns Hopkins Hospital. (PX0149-0001; Burnett, Tr. 2241).

145. Dr. Burnett obtained his medical degree from the Johns Hopkins University School of Medicine in Baltimore, Maryland and completed his internship, residency and fellowship at the Johns Hopkins Hospital. (PX0149-0001; Burnett, Tr. 2240 – 41).

146. Dr. Burnett holds a faculty appointment in the Cellular and Molecular Medicine Training Program of the Johns Hopkins University School of Medicine and is the

Director of the Basic Science Laboratory in Neuro-urology of the James Buchanan Brady Urological Institute and Director of the Male Consultation Clinic/Sexual Medicine Division of the Department of Urology at Johns Hopkins. (PX0149-0001; Burnett, Tr. 2241).

147. Dr. Burnett has authored and published over 180 original peer-reviewed articles and 40 book chapters. (PX0149-0003).

148. Dr. Burnett has treated between 10,000 and 15,000 patients for erectile dysfunction. (Burnett, Tr. 2244).

149. Dr. Burnett has conducted world renowned research on nitric oxide ("NO"). (PX0149-0003).

150. Complaint Counsel's erectile health expert, Dr. Arnold Melman, recognizes "[t]hat Dr. Burnett of Johns Hopkins is a man highly respected in his field." (Melman, Tr. 1166).

151. Dr. Burnett explained at trial that the basic scientific mechanisms by which pomegranate juice, through its high antioxidant content, aids and enhances the critical function of nitric oxide in improving vascular blood flow to the penis and promoting the vascular biological health of the penis. (PX0149-0004-07; PX0349 (Burnett, Dep. at 87-90, 103, 118, 137); Burnett, Tr. 2250-56, 2303).

152. Dr. Burnett reviewed the work on the unique nitric oxide effect found in pomegranate juice done by Nobel Laureate Dr. Louis Ignarro and confirmed that nitric oxide was the principal source of proper erectile function. (PX484; PX0149-004-005; Burnett, Tr. 2249-50, 2253-56; 2276; PX0058).

153. Dr. Burnett concluded that the Respondents' basic scientific and clinical evidence is sufficient to support the conclusion that it is likely that pomegranate juice has a beneficial effect on erectile function. (PX0149-0006-0007; PX0349 (Burnett, Dep. at 103, 118, 137); Burnett, Tr. 2255-56).

154. Dr. Burnett also opined that RCTs should not be required to substantiate such claims for harmless pure fruit products like pomegranates, before permitting this information to be given to the public. (PX0149-0006-0007; Burnett, Tr. 2272-74, 2303; PX0349 (Burnett, Dep. at 118, 137)).

5. Dr. Irwin Goldstein

155. Dr. Goldstein is a sexual medicine physician who has been practicing medicine since 1976 and has been involved in sexual medicine clinical practice, clinical research and basic science research since 1980. (PX0189-0001-0002; PX0352 (Goldstein, Dep. at 14)).

156. Dr. Goldstein has been certified by the American Board of Urology since 1982. (PX0189-0001).

157. He was a Professor of Urology and Professor of Gynecology at the Boston University School of Medicine from 1990-2005 and 2002-2005. (PX0189-0002-0003).

158. Dr. Goldstein has published over 250 original peer-reviewed manuscripts in male and female sexual medicine. (PX0189-0002-0003).

159. Dr. Goldstein was part of the original advisory board to Pfizer that engaged in an extensive drug development plan that developed sildenafil (Viagra), and was also on the advisory boards of Bayer and Eli Lilly for the development of vardenafil (Levitra) and tadalafil (Cialis). (Goldstein, Tr. 2590-91).

160. Complaint Counsel's designated erectile-health expert, Dr. Melman, also recognizes Dr. Goldstein as "highly regarded" in the field. (Melman, Tr. 1166-67).

161. Dr. Goldstein agreed that RCT studies were not required for substantiating claims that pomegranate juice can aid in erectile health. (Goldstein, Tr. 2601-02).

162. He testified that in vitro and animal studies showed a likelihood that pomegranate juice improves erectile health. (Goldstein, Tr. 2601-02, 2605; PX0352 (Goldstein, Dep. at 37-42)).

163. Dr. Goldstein opined that the consumption of pomegranate juice is a logical option for men who are not responsive to conventional drugs designed to treat erectile dysfunction and who are unwilling to consider invasive or mechanical therapies for treatment of their erectile dysfunction. (PX0189-0005; PX0352 (Goldstein, Dep. at 37-42); Goldstein, Tr. 2605, 2641).

164. Dr. Goldstein concluded that reasonable and competent scientific evidence shows that pomegranate produced a definite benefit to proper and effective erectile function. (Goldstein, Tr. 2605).

6. Dr. Jean deKernion

165. Dr. Jean deKernion is the Chairman of the Department of Urology and Senior Associate Dean for Clinical Affairs at the UCLA School of Medicine. (PX0160-0001).

166. He served as dean of the Department of Urology at the UCLA School of Medicine for twenty-six years. (deKernion, Tr. 3039).

167. Dr. deKernion is a practicing urologist certified by both the American Board of Surgery and the American Board of Urology. (deKernion, Tr. 3039-40).

168. Dr. deKernion has been involved in basic and clinical research and has published 228 papers in peer-reviewed journals. (PX0161-0001).

169. For six years, he was the associate editor of the prestigious Journal of Urology and acted as a reviewer for approximately twenty other peer-reviewed journals. (PX0161-0002).

170. Dr. deKernion testified that in the case of fruit juice such as POM juice, that has low or no toxicity, RCTs are not required. (deKernion, Tr. 3060).

171. Dr. deKernion testified that Respondents' *in vitro* and animal studies showed that pomegranate juice inhibited the growth of prostate cancer cells and actually killed them. (deKernion, Tr. 3044-45, 3120).

172. Dr. deKernion stated that the PSA doubling-time studies of Dr. Pantuck and Dr. Carducci both showed a dramatic lengthening of PSA doubling time, which Dr. deKernion opined was a valid and effective endpoint for recurrence and death from prostate cancer after a radical prostatectomy. (deKernion, Tr. 3061).

173. He opined that there is a high degree of probability that POM products inhibit the clinical development of prostate cancer cells even in men not diagnosed with prostate cancer. (deKernion, Tr. 3061, 3119, 3126).

174. Dr. deKernion also concluded there was a high degree of probability that POM products provide a special benefit to men with rising PSA after radical prostatectomy and that POM products lengthened PSA doubling time, thus, deferring death from prostate cancer. (deKernion, Tr. 3126).

7. Professor Ronald Butters

175. Professor Ronald Butters is an expert in the science of linguistics, which is the study of all forms of human language. (Butters, Tr. 2813, 2816).

176. He is a Professor Emeritus at Duke University and has been on faculty at Duke for over forty years. (Butters, Tr. 2812).

177. He served as the Chairman of the Linguistics Department at Duke and Chairman of Duke University's English Department. (Butters, Tr. 2812).

178. He is a member of the advisory board of the New Oxford American Dictionary and has served as editor and co-editor of multiple prestigious scientific and academic publications. He participates in numerous professional associations and

is the past president of the International Association of Forensic Linguistics. (Butters, Tr. 2812-13).

179. He has written many textbooks and books on the subjects of linguistics, semantics, and semiotics. (Butters, Tr. 2814-15).

180. Professor Butters viewed all of POM's advertisements listed in Complaint Counsel's complaint and all the advertisements admitted into evidence. (Butters, Tr. 2817).

181. He considered the advertisements in their totality and took into account the nature of the Challenged Products. (Butters, Tr. 2817).

182. Professor Butters based his opinion on the language used in the advertisements and the implied message as would be interpreted by a reasonable person. (Butters, Tr. 2818).

183. Professor Butters concluded that none of Respondents advertisements stated explicitly or implied that the Challenged Products actually prevented or cured any disease. (Butters, Tr. 2818-19).

184. He also testified that none of POM's advertisements stated explicitly or implied that the Challenged products "treated" disease in the sense that the Challenged Products were a form of medical treatment or a substitute for conventional medical treatment. (Butters, Tr. 2819).

185. He also explained that use of the term "may" would not cause a reasonable person to believe that the product will produce that result. (Butters, Tr. 2822).

8. Professor David Reibstein

186. Professor David Reibstein is a tenured member of the faculty of Wharton School at the University of Pennsylvania, one of the nation's most distinguished schools of business and finance, and has been on faculty for thirty-one years. (Reibstein, Tr. 2481).

187. Professor Reibstein has provided management education in the field of marketing to more than 300 companies. (Reibstein, Tr. 2485).

188. He has designed, executed, and supervised hundreds of market research studies for over thirty years, including surveys concerning consumer behavior. (Reibstein, Tr. 2485-86).

189. Professor Reibstein has written textbooks on the field of marketing, serves on the board of American Marketing Association, and is currently the Chairman-elect of that organization. (Reibstein, Tr. 2484; PX0356 (Reibstein, Dep. at 14)).

190. Professor Reibstein offered expert testimony on the subject of materiality. Professor Reibstein also reviewed the Bovitz survey, upon which Complaint Counsel relies to suggest that POM's advertisements convey disease claims. (Reibstein, Tr. 2508).

191. He concluded that the Bovitz survey did not address consumers' motivations for purchasing pomegranate juice. (Reibstein, Tr. 2509).

192. Among many other flaws, the Bovitz survey did not even ask any questions about purchasing motivations and was limited to billboard advertisements, which Complaint Counsel conceded are not at issue in this case. (Reibstein, Tr. 2509, 2574).

193. Professor Reibstein also reviewed the A&U Survey and the AccentHealth survey. The A&U survey was conducted to figure out why people purchase pomegranate juice. (Reibstein, Tr. 2517).

194. In Professor Reibstein's expert opinion, the A&U survey was invalid and not reliable for multiple reasons. (Reibstein, Tr. 2518-21).

195. Professor Reibstein also concluded that the AccentHealth survey, which surveyed persons in urologists' offices as they were leaving and showed them a print ad, was severely flawed and unreliable. (Reibstein, Tr. 2522).

196. Professor Reibstein prepared a survey for Respondents to understand the underlying motivations that consumers had for purchasing pomegranate juice and what those motivations might have been. (PX0356 (Reibstein, Dep. at 11, 39); Reibstein, Tr. 2487).

197. In particular, Professor Reibstein's survey looked at the influential power of POM's advertisements on consumer purchasing behavior and how those advertisements influenced consumer motivation in those that purchased pomegranate juice. (PX0356 (Reibstein, Dep. at 52).

198. Professor Reibstein stated in his report and testified at trial that his survey overwhelmingly shows that less than 1% of POM buyers purchase POM juice to prevent, cure, or treat any disease. (Reibstein, Tr. 2493).

199. Less than 1% of those surveyed even mentioned any disease in stating why they buy POM. (Reibstein, Tr. 2525).

B. Complaint Counsel's Experts

200. Unlike Respondents' experts, each of Complaint Counsel's experts was significantly impeached. (Stampfer, Tr. 813-14, 823-826, 830, 840; Melman, Tr. 1134, 153-55, 1158; PX0360 (Melman, Dep. at 59, 130-31); Eastham, Tr. 1339-40; PX0178-0001, 0006, 0009; Sacks, Tr. 1541-46; 1554, 1561, 1608-09; PX0361 (Sacks, Dep. at 142-43).

201. Complaint Counsel provided no expert testimony denying the safety of the Challenged Products.

202. Complaint Counsel provided no expert testimony regarding the bioavailability or absorbency of the Challenged Products.

203. Complaint Counsel provided no expert testimony denying equivalency between POM juice and POMx.

204. Complaint Counsel provided no expert opinion on what messages the advertisements conveyed or on materiality.

205. In addition, Professor Mazis, in stark contrast to how he has been utilized by Complaint Counsel in previous cases, provided (1) no factual analysis of the ads; and (2) provided no competing survey either on the ads or on the subject of materiality.

1. Professor Meir Stampfer

206. Professor Stampfer is not a cardiologist or urologist. (Stampfer, Tr. 868).

207. Professor Stampfer testified to an improper substantiation standard as a matter of law. He stated that there was "some evidence" supporting Respondents' claims, but the evidence is insufficient substantiation unless those claims are proven "beyond a reasonable doubt." (Stampfer, Tr. 797-98).

208. Professor Stampfer does not hold himself to this same high standard. Professor Stampfer conceded at trial that he has publicly made statements that food and beverage products lower the risk of certain diseases, in the absence of RCT studies and even where the product is not completely safe. (Stampfer, Tr. 801-02, 805, 810).

209. He also admitted to making a number of public health recommendations in the absence of RCT studies. (Stampfer, Tr. 813-14).

210. Professor Stampfer also agreed that RCTs have certain limitations in a nutritional context, such as the length of time required and the number of participants, and

also because RCTs are a "huge expense," even simple ones are "very expensive". (Stampfer, Tr. 823-26).

211. Professor Stampfer also agreed that where the risk of harm is slight and a potential benefit exists, he is a strong advocate of giving that information to the public. (Stampfer, Tr. 827-29).

212. He also conceded that it is appropriate to rely on evidence short of RCTs, and in vitro and animal research can both provide useful information. (Stampfer, Tr. 830, 840).

213. Professor Stampfer provided no opinion about the specific chemical structure of pomegranate antioxidants. (PX0362 (Stampfer, Dep. at 199)).

214. Professor Stampfer provided no opinion about how pomegranate antioxidants are metabolized in the human body (i.e. mechanisms of action). (PX0362 (Stampfer, Dep. 200).

215. Professor Stampfer provided no opinion about the antioxidant effect of pomegranate juice relative to POMx. (PX0362 (Stampfer, Dep. at 200, 203)).

216. Professor Stampfer provided no opinion about the extent to which the antioxidant effect of pomegranate juice on human health is attributable to anthocyanins as opposed to other forms of antioxidants. (PX0362 (Stampfer, Dep. at 203).

217. Professor Stampfer provided no opinion about the safety of pomegranate juice, apart from its being a sugary drink. (PX0362 (Stampfer, Dep. at 195-96)).

218. Professor Stampfer provided no opinion about whether there are additional safety concerns for POMx relative to pomegranate juice. (PX0362 (Stampfer, Dep. at 201)).

219. Professor Stampfer was not asked to and did not create a rebuttal to the Heber report. (PX0362 (Stampfer, Dep. at 187-88)).

2. Dr. Arnold Melman

220. Dr. Arnold Melman testified as Complaint Counsel's expert in urology and erectile health. (Melman, Tr. 1081).

221. Dr. Melman testified that he didn't know the meaning of "RCT" studies. (Melman, Tr. 1134).

222. Dr. Melman conflated orgasm with erectile function and testified that reaching orgasm is absolutely required to show improvement in erectile function even when erection is achieved. (Melman, Tr. 1141-47).

223. Dr. Melman conceded that in requiring RCTs, he was applying the FDA's standard for drugs. He also held the absurd position that pomegranate juice and water are drugs. (PX0360 (Melman, Dep. at 17-19); Melman, Tr. 1140-41, 1165).

224. Dr. Melman, like Professor Stampfer, holds his own conduct to a lower standard than he would apply to Respondents. Dr. Melman hopes to market a gene transfer therapy for erectile dysfunction, and, in an interview, Dr. Melman made overblown public statements that this therapy produced spontaneous normal erections in men suffering from erectile dysfunction, the therapy was "modifying the aging process", and it was the "fountain of youth". (Melman, Tr. 1148, 1153-55).

225. Dr. Melman made these statements based solely on animal research despite knowing that people have died and become very sick from gene transfer therapy and without the support of the elaborate clinical studies he testified were absolutely necessary. (Melman, Tr. 1155, 1158; PX0360 (Melman, Dep. at 59, 130-31)).

226. Dr. Melman also attempted to criticize the Forest/Padma-Nathan RCT for using the GAQ questionnaire, a widely used and commonly accepted questionnaire, that Dr. Melman knew nothing about prior to this case and had made no effort to familiarize himself with. (Melman, Tr. 1180-82; Goldstein, Tr. 2602, 2603; Burnett, Tr. 2304; PX0349 (Burnett, Dep. at 127); CX1337 (Forest, Dep. at 79)).

227. Not knowing that the quote was from the opinion of the United States Supreme Court, Dr. Melman, on cross-examination, stated that he completely disagreed with the statement "medical professionals and researchers do not limit the data they consider to statistically significant evidence." (Melman, Tr. 1178-80).

3. Dr. James Eastham

228. Dr. Eastham testified that RCTs are required for health claims and that disease prevention studies should involve ten to thirty thousand men, which are "incredibly expensive" and in the range of $600 million. (Eastham, Tr. 1322-28).

229. Despite his insistence that RCTs are necessary to support claims made about a harmless product, such as fruit juice, Dr. Eastham nonetheless has performed many prostatectomies, which carry the risk of very serious side effects, even in the absence of RCTs. (Eastham, Tr. 1329-32).

230. Dr. Eastham also insisted that no one accepts PSA doubling time as a surrogate for progression or death from prostate cancer. However, Dr. Eastham was impeached by his own article which characterizes PSA doubling time "as an important factor in the evaluation of men with newly diagnosed prostate cancer or prostate cancer that recurs after treatment", and that it "can be used as a surrogate marker for prostate cancer specific death." Other parts of that article cited studies showing that "only PSADT was a significant predictor of either systematic progression or local recurrence [of disease] and that "PSADT was the strongest predictor of eventual clinical recurrence." Dr. Eastham concluded in his article that "PSADT is an important prognostic marker in men with biochemical failure after local therapy for prostate cancer, and it predicts the probably response to salvage radiotherapy, progression to metastatic disease and prostate cancer specific death". (Eastham, Tr. 1339-40; PX0178-0001, 0006, 0009).

231. Dr. Eastham contended in defense of the article, that PSADT was a predictive surrogate only at the moment of treatment, and subsequent changes in PSADT were not predictive of disease recurrence or death. However, Dr. Eastham was unable to explain when it stopped being predictive. (Eastham, Tr. 1344).

4. Dr. Frank Sacks

232. Dr. Sacks insisted that RCTs, which can cost hundreds of millions of dollars, are required to substantiate health claims even where a product is safe and provides a benefit to the public. (Sacks, Tr. 1535-37).

233. However, Dr. Sacks agreed that we must weigh the risk that the product will do harm against the risk of keeping potentially beneficial information from the public. (Sacks, Tr. 1559).

234. He conceded that his requirement of two RCTs is the FDA standard for drugs, and he also admitted that in evaluating a natural food, RCTs are simply not necessary in all cases. (Sacks, Tr. 1541-46).

235. When discussing the DASH Diet recommendation, Dr. Sacks stated that fruits as a category, including pomegranates, should be held to a lower standard of evidence than that of a drug and RCTs are not necessary. (Sacks, Tr. at 1545-46, 1554; PX0361 (Sacks, Dep. at 142-43)).

236. Dr. Sacks also acknowledges that RCTs are not feasible because of logistical, financial, and ethical considerations. (Sacks, Tr. 1561).

237. Dr. Sacks also agreed that lack of statistical significance for a positive result is not proof of a negative or proof that pomegranate does not work. (Sacks, Tr. 1608-09).

5. Professor David Stewart

238. Complaint Counsel offered Professor David Stewart as a rebuttal witness to Professor Ronald Butters, even though Professor Stewart is not an expert in linguistics, the subject of Dr. Butters' testimony. (Stewart, Tr. 3168-69).

239. Professor Stewart conceded that he was not offering any opinion on how consumers would interpret POM's advertisements but was only criticizing Professor Butters' methodology. He stated that he did not even know if Complaint Counsel had any evidence on the meaning of the advertisements. (PX0357 (Stewart, Dep. at 52)).

240. Professor Stewart conceded that he was not an expert in the legal standards by which advertisements are judged. (PX0357 (Stewart, Dep. at 67)).

241. He also stated that headlines like "Amaze your Cardiologist" and "Floss Your Arteries" would not be taken literally by consumers. (Stewart, Tr. 3230) .

242. Professor Stewart testified that he did not know if any of the creative briefs had any effect on any advertisements and there was not any other evidence of any such effect. (Stewart, Tr. 3235).

243. Professor Stewart testified that his reliance on the creative briefs would be affected if they were typically modified, rejected, or ignored after they were written. (Stewart, Tr. 3196).

244. Professor Stewart testified as to the OTX and Bovitz Surveys. Professor Stewart conceded that at least "three good exposures" to an advertisement were necessary before a consumer would take away the advertisement's message and that it could require "many more exposures" to get "three good exposures." (Stewart, Tr. 3228-29).

245. A federal court has previously rejected Professor Stewart's expert opinions. (Stewart, Tr. 3255).

246. Professor Stewart conceded that neither he nor Professor Butters were opining on Respondents' intent. (Stewart, Tr. 3233; PX0357 (Stewart, Dep. at 120, 130)).

6. Professor Michael Mazis

247. Complaint Counsel offered Professor Michael Mazis as a rebuttal expert to Professor Reibstein. (CX1297_0002).

248. In stark contrast to previous work Professor Mazis has done for Complaint Counsel in other litigation, he did not (a) conduct any facial analysis of POM's ads

or offer any expert opinion on them; (b) conduct any surveys on the ads, or (c) provide any expert opinion on the exposure of the ads to consumers, despite testifying that such exposures were critical to having an effect on consumers.

249. Despite his testimony that the appropriate measure of materiality is the potential impact of the challenged claim on the purchase behavior to show materiality, Professor Mazis also conceded that, to his knowledge, there was no evidence that POM's advertisements did cause anyone to buy the Challenged Products because it prevented, cured or treated any disease or even that "POM ads were material to the purchase decision." (Mazis, Tr. 90, 95, 96, 2700).

250. Like Professor Stewart, Professor Mazis testified that for an advertisement to affect the purchasing behavior of a consumer, a consumer would need more than one exposure. (Mazis, Tr. at 2752; Stewart, Tr. 3228-29).

V. THE DEVELOPMENT OF POM WONDERFUL'S SCIENCE PROGRAM

A. Initiation of the Program

251. Respondents' interest in pomegranates first began in 1986 when Stewart and Lynda Resnick acquired approximately 100 acres of pomegranate trees as part of a larger agricultural purchase. (CX1363 (S. Resnick, Coke Dep. at 26-27); S. Resnick, Tr. 1852-53).

252. Rather than use the acreage for citrus, Stewart and Lynda Resnick decided to keep the acres of pomegranates and began increasing their pomegranate acreage in the early 1990s based upon the initial sales of fresh pomegranates. (CX1367 (S. Resnick, Welch Dep. at 15)).

253. Currently, Respondents Stewart and Lynda Resnick own approximately 18,000 acres of pomegranate orchards and are the largest growers of pomegranates in the United States. (CX1374 (Tupper, Ocean Spray Dep. at 29-30)).

254. Years before launching their pomegranate products, Respondents set out to establish the health benefits of the fruit. Dr. Leslie Dornfeld, who was a close personal friend of the Resnicks and Professor of Internal Medicine at UCLA, explained the rich ancient history of the pomegranate's health giving properties and the health benefits associated with higher intake of polyphenolic antioxidants. (L. Resnick, Tr. 150; CX1363 (S. Resnick, Coke Dep. at 61-63); CX0105_0003; CX1362 (L. Resnick, Coke Dep. at 71-72); S. Resnick, Tr. 1855-56); CX1359 (L. Resnick, Dep. at 82)).

255. Intrigued by the folklore surrounding the pomegranate's health giving properties, Respondents set out to decipher if there was any scientific truth to the history.

(CX1360 (S. Resnick, Dep. at 84-85); PX1372 (S. Resnick, Tropicana Dep. at 32); CX1362 (L. Resnick, Coke Dep. at 71-72)).

256. In addition to their intrigue with the fruit's history, the Resnicks motivation to fund the exploration of the health benefits of pomegranates also originated from a family history of cardiovascular problems, Stewart Resnick's own battle with multiple cancers, and a strong belief in the connection between good nutrition and health. (S. Resnick, Tr. 1853-55; CX1376 (S. Resnick, Ocean Spray Dep. at 30-31); (CX1360 (S. Resnick, Dep. at 84)).

257. In 1998, Respondents and Dr. Leslie Dornfeld collaborated with Dr. Michael Aviram, the Head of the Technion Lipid Research Laboratory at the Rambam Medical Center in Haifa, Israel, known for his groundbreaking work exploring the antioxidant properties of red wine, to understand the antioxidant power and potential cardiovascular benefits of pomegranate juice. (CX1374 (Tupper, Ocean Spray Dep. at 87); CX1358 (Aviram Dep. at 4); CX1363 (S. Resnick, Coke Dep. at 61-63, 65-66); CX1367 (S. Resnick, Welch Dep. at 15); CX0001_0010-0011; L. Resnick, Tr. 150; PX0004).

258. Dr. Aviram's initial research paper showed that pomegranate possessed remarkable anti-oxidative and anti-atherosclerotic properties. (CX1358 (Aviram, Dep. at 7); PX0004).

259. Based on this paper, Dr. Michael Aviram believed and represented to Stewart Resnick that the antioxidant properties found in the pomegranate were the most powerful he had ever researched. (CX1363 (S. Resnick, Coke Dep. at 66)).

260. Despite the impressive findings and enthusiasm from Dr. Aviram, Respondents did not go public with these findings at that time. Respondents instead embarked on further research to see if there was any truth to these initial findings and the folklore surrounding the fruit's medicinal properties. (Ornish, Tr. 2325); (CX1360 (S. Resnick, Dep. at 84-85); PX1372 (S. Resnick, Tropicana Dep. at 32); (CX1376 (S. Resnick, Ocean Spray Dep. at 31-32)).

261. Dr. Dornfeld initially oversaw the development of POM's research program until he was no longer able to do so for health-related reasons. (Liker, Tr. 1877).

262. Dr. Dornfeld recruited Dr. Harley Liker to be his successor as POM's Medical Director. (S. Resnick, Tr. 1858).

263. Dr. Liker is a practicing medical doctor and board certified medical internist with an extensive background in biomedical research and has authored published papers published in peer-reviewed journals. (Liker, Tr. 1873-75).

264. Harley Liker has been a member of the faculty at UCLA School of Medicine since 1995 and was promoted to Associate Clinical Professor of Medicine in 2010. (Liker Tr. 1873; CX1350 (Liker Dep. at 15)).

265. In 2001, Dr. Liker began working as POM's Medical Director. (Liker, Tr. 1876-77; CX1350 (Liker, Dep. at 27-28)).

266. Part of his duties as POM's Medical Director is to assist Respondents' in the development of their research program by ensuring that Respondents use the best researchers and the science is conducted in a rigorous manner. (Liker,Tr. 1878-80; CX1350 (Liker, Dep. at 32-33)).

267. After identifying the area of scientific interest, Dr. Liker determines the leading experts in that scientific field and reaches out to them to conduct the Respondents research. (Liker, Tr. 1878-80).

268. In over span of a decade, Respondents sponsored over a hundred studies at forty-four different institutions. (Liker, Tr. 1887-88).

269. More than seventy of the studies sponsored by the Respondents have been published in top peer-reviewed scientific journals. Seventeen of these published studies are human clinical trials. (Liker, Tr. 1888; PX0014; CX0908; PX0060; PX0061; PX0004; CX0611; PX0020; PX0021; PX0023; PX0073; PX0074; PX0075; PX0005; PX0127; PX0136; PX0139; PX0146; Trombold JR, Barnes JN, Critchley L, and Coyle EF, *Ellagitannin Consumption Improves Strength Recovery 2-3 d after Eccentric Exercise*, Med. Sci. Sports Exerc., Vol. 42, No. 3, pp. 493-498, 2010).

B. POM's Continued Investment In Its Research Program

1. Purpose

270. Despite Respondents' belief that they have sufficient scientific substantiation for any health claims made in POM Wonderful's advertising, Respondents continue to sponsor medical research to uncover the full spectrum of benefits of their pomegranate products. (S. Resnick, Tr. 1752, 1861-63).

271. The goal of the research program is to uncover the truth behind the health benefits of the pomegranate--not to make health benefit claims. (CX1363 (S. Resnick, Coke Dep. at 59); S. Resnick, Tr. 1752-53; CX1374 (Tupper, Ocean Spray Dep. at 87); Tupper, Tr. 3001; CX1360 (S. Resnick, Dep. at 145-46)).

272. Stewart Resnick was more interested in understanding whether a benefit would be shown and how the product worked rather than whether or not the findings

reached statistical significance. (S. Resnick, Tr. 1859; Liker, Tr. 1881-84; CX1336 (Davidson, Dep. at 142)).

273. Respondent Stewart Resnick told the scientists that his primary interest in conducting the research is to establish the truth. (CX1358 (Aviram, Dep. at 74)).

274. Respondents even chose to sponsor studies even when they were told by scientists that the study, for any number of reasons related to the study, will likely not show a health benefit from consuming pomegranate. (S. Resnick, Tr.1859).

275. They did so to uncover the truth; to see what might happen. (CX1363 (S. Resnick, Coke Dep. at 59); S. Resnick, Tr. 1752-53; CX1374 (Tupper, Ocean Spray Dep. at 87); Tupper, Tr. 3001; CX1360 (S. Resnick, Dep. at 145-46)).

276. Respondents, for example, chose to use study designs, including the Davidson BART study, even when researchers suggested and communicated to Respondents that the study would likely not yield positive results. (CX1336 (Davidson Dep. at 142)).

277. Respondents chose study designs after being told that that those designs would not yield positive results because Respondents' motivation was to uncover the truth and to see if real benefits exist—not to just use the studies in marketing. CX1363 (S. Resnick, Coke Dep. at 59); S. Resnick, Tr. 1752-53; CX1336 (Davidson Dep. at 142); CX1374 (Tupper, Ocean Spray Dep. at 87); Tupper, Tr. 3001; CX1360 (S. Resnick, Dep. at 145-46)).

278. Respondents have invested over $35 million dollars in their research program and continue to spend money to invest in further research. (S. Resnick, Tr. 1864; CX1363 (S. Resnick, Coke Dep. at 74; Tupper, Tr. 1015).

279. Respondents believe that their scientific inquiries have gone far beyond the depth of research typically sponsored or conducted by other food and supplement companies. (CX1353 (Tupper, Dep. at 212-13; Tupper, Tr. 1014).

280. Respondents have sponsored over a hundred studies at forty-four different institutions that have explored the effect of POM products on many different areas of health, including, the cardiovascular system, immunity, athletic performance, erectile health, prostate cancer, skin care, cognitive function, dental health, and urinary tract health. (CX1353 (Tupper, Dep. at 47-49); Tupper, Tr. 2979-81); Liker, Tr. 1887-88).

281. Respondents' research efforts branch in various directions in order to examine the role that oxidation and inflammation play in many seemingly unrelated diseases and conditions. Over time, additional characteristics of the Challenged Products and its derivatives have come to light expanding both the scope of the company's

research portfolio and the rationale that supports it. (CX1353 (Tupper, Dep. at 47-49); Tupper, Tr. 2979-81; Heber Tr. 1957, 2112-13, 2185).

2. Depth of the Research Program

282. Anti-inflammation and anti-oxidative tendencies have beneficial implications for many different areas of human health, such as aging, cancer, heart disease, diabetes, and dementia. (Tupper, Tr. 2999; deKernion, Tr. 3046; Heber Tr. 1957, 2112-13, 2185).

283. Pomegranate polyphenols' anti-inflammatory and anti-oxidative properties are the connecting characteristics establishing the interrelationship between all of POM's science whether or not the results were positive or negative, published or unpublished. (Tupper, Tr. 3000-02).

284. POM has sponsored published research that has shown positive results, including, immunity, cognitive function, dental health, and urinary tract health. Yet, POM has chosen to not publicly discuss or make advertising claims in many of these areas until the science is sufficiently developed. (Tupper, Tr. 2979-81).

285. Respondents' do not advertise every newly discovered health benefit property without much deliberation and thought. (Tupper, Tr. 2979-81; S. Resnick, Tr. 1860).

286. Respondents hold themselves to a higher standard than their competitors when it comes to having enough information to make an advertising statement about the benefits of pomegranates. (S. Resnick, Tr. 1866).

287. Respondents' competitors have advertised many more areas in which pomegranate juice provides a benefit. (S. Resnick, Tr. 1865-66).

288. One of Respondents' competitors put out an advertisement with seventeen different benefits from pomegranate juice. (S. Resnick, Tr. 1866).

289. Respondents advertise only about three of those seventeen benefits—heart, prostate, and erectile dysfunction. (S. Resnick, Tr. 1866).

290. Respondents believe that those seventeen benefits exist but do not advertise all the other fourteen benefits because Respondents don't feel that it meets their degree of adequate scientific information. (S. Resnick, Tr. 1866).

291. Stewart Resnick's stated policy on the relationship between scientific studies and POM's advertising requires that the advertisements accurately represent the scientific conclusions. (Tupper, Tr. 2979).

292. POM includes in its advertising references to its science only if it is published clinical research involving human subjects. (PX1353 (Tupper, Dep. at 134)).

293. Respondents continue to conduct research in areas where they have already seen ongoing positive results. (Tupper, Tr. 984-85, 994; PX0023; PX0014; PX0060; PX0061).

294. For example, POM currently has ongoing research in the areas of cardiovascular health and prostate health despite having previously sponsored human clinical research yielding positive results. (Tupper, Tr. 984-85, 994; PX0023; PX0014; PX0060; PX0061).

295. Respondents also have continued to conduct both basic research and animal studies in areas where the research has shown ongoing positive results in humans. (PX0009, PX0002, PX0125, PX0017, PX0010).

3. Current Focus of the Research Program

296. Respondents are currently seeking botanical drug approval for POMx from the FDA under two different health indications. (Tupper, Tr. 3006-08).

297. Respondents are seeking botanical drug approval not because they believe they ever advertised the POM products as drugs but in order to distinguish their products in the marketplace. (Tupper, Tr. 3006-08).

298. POM is not seeking botanical drug approval for POM Wonderful 100% juice from the FDA because the FDA has no provision or process to obtain drug approval for a juice. (Tupper, Tr. 3006).

299. As part of their internal preparation to potentially submit an application to the FDA for drug approval, Respondents conducted candid reviews of POM's entire science portfolio to examine whether and to what extent their research would meet the requirements of the FDA, with its current limited recognition of surrogate markers used in POM's research. (Tupper, Tr. 3011).

300. One of these summaries entitled "Medical Portfolio Review" was prepared by Respondent Matt Tupper and Mark Dreher for an internal meeting with POM's advisors, including Mr. Tupper, Mark Dreher, Dr. Harley Liker, Dr. David Kessler, and Dr. David Heber, and Mr. Resnick. (Tupper, Tr. 942, 939, 3008-09; CX1353 (Tupper, Dep. at 248-49); Dreher, Tr. 556).

301. However, the science was ranked this way, not because Respondents do not believe in the high quality and caliber of their science or that this is the legal standard by which their science should be judged. The rationale for the three on a

scale of ten refers to an assessment given by doctors oriented to drug approval. (Tupper, Tr. 3001).

302. That score is also due to the fact that POM has pursued using different endpoints than those used by the FDA to approve a drug for heart disease. (Tupper, Tr. 3011).

303. Putting aside the strict FDA requirements and FDA lens, Respondent Matt Tupper personally ranks POM's body of erectile, prostate, and cardiovascular science each as an eight on a scale of ten. (Tupper, Tr. 3012).

304. Furthermore, Mr. Dreher also stated that the assessment of POM's research science in the Medical Research Portfolio Review was done from a "drug perspective" or through the lens of FDA approval. (Dreher, Tr. 564)

305. For example, POM assessed in the Medical Research Portfolio Review that the required action would be two studies with 1000 plus patients. (CX1029_0004).

306. This observation was made due to the fact that the FDA does not recognize PSA as a valid end point. (Dreher, Tr. 564).

307. POM's chief science officers, Brad Gillespie and Mark Dreher, were regularly asked to provide research summaries that included the FDA perspective as part of the candid assessment to establish the viability of obtaining FDA drug approval. (Tupper, Tr. 3014).

308. Respondents do not believe this should be the legal standard their science should be held to in order to meet the FTC's substantiation requirements. Instead, Respondents contemplate that one day they could potentially seek FDA drug approval. (CX1265, CX1266, CX1268, CX1269, CX1270, CX1271, CX1272; Tupper, Tr. 3014).

309. Respondents' standard in reviewing its science is, at times, even more severe than what is required for FDA drug approval. (PX0206 at 8-9).

310. For example, in some instances the FDA has not required one or more RCTs to approve a drug for use in clinical practice. (PX0206 at 8-9).

311. The FDA has also approved anticancer agents based on open-label randomized controlled trials without a placebo arm. (PX0206 at 8-9).

VI. POM'S METHODOLOGY IN SPONSORING STUDIES

A. Respondents' Diligent Effort to Ascertain the Truth

312. Respondents did not design its research solely to market the results but ultimately to understand how the consumption of pomegranate works in the human body. (CX1360 (S. Resnick, Dep. at 145-46); (Tupper, Tr. 3001).

313. The goal of the research program is to uncover the truth behind the health benefits of the pomegranate and not to just market the results. (CX1363 (S. Resnick, Coke Dep. at 59); S. Resnick, Tr. 1752-53; CX1374 (Tupper, Ocean Spray Dep. at 87); Tupper, Tr. 3001; CX1360 (S. Resnick, Dep. at 145-46)).

314. Respondents' diligent search for the truth about the medicinal and healing properties of pomegranates is evidenced by their insistence on the sponsorship of the very best research. (Liker, Tr. 1878-80, 1887-89; CX1350 (Liker, Dep. at 32-33); S. Resnick, Tr.1857, 1860-61).

315. Respondents have sponsored studies designed with the highest level of scientific integrity, conducted by the best scientists at the best institutions in the world. (Liker, Tr. 1878-80, 1887-89; CX1350 (Liker, Dep. at 32-33); S. Resnick, Tr. 1857, 1860-61).

316. To eliminate the potential for bias, POM Wonderful does not conduct its own medical research. CX1364 (Tupper, Coke Dep. at 55-56); CX1374 (Tupper, Ocean Spray Dep. at 14); CX1353 (Tupper, Dep. at 46); CX1363 (S. Resnick, Coke Dep. at 58-59)).

317. Scientists conducting POM's research have not held any interest in Respondents' companies. (CX1364 (Tupper, Coke Dep. at 55-56); CX1374 (Tupper, Ocean Spray Dep. at 14); CX1353 (Tupper, Dep. at 46); CX1363 (S. Resnick, Coke Dep. at 58-59)).

318. Respondents, instead, chose to sponsor studies even when they were told by scientists that the study, for any number of reasons related to the study, will likely not show a health benefit from consuming pomegranate. (S. Resnick, Tr. 1859).

319. Respondents, for example, chose to use study designs, including the Davidson BART study, even where researchers suggested and communicated to Respondents that the study would likely not yield positive results. (CX1336 (Davidson, Dep. at 142)).

320. Respondents chose study designs after being told that that those designs would not yield positive results because Respondents had faith those designs would show if a benefit existed. (CX1363 (S. Resnick, Coke Dep. at 59); S. Resnick, Tr. 1752-53;

CX1336 (Davidson Dep. at 142); CX1374 (Tupper, Ocean Spray Dep. at 87); Tupper, Tr. 3001; CX1360 (S. Resnick, Dep. at 145-46)).

321. Respondents did not select studies merely because they thought it would obtain positive results or statistically significant results. (S. Resnick, Tr. 1859; Liker, Tr. 1881; CX1336 (Davidson, Dep. at 142)).

322. For example, Dr. Liker and Dr. Forest advised Mr. Resnick that Dr. Forest's erectile function study was not sufficiently powered to yield statistically significant findings. (Liker, Tr. 1886-87).

323. Mr. Resnick, because of cost, chose not to add more participants to Dr. Forest's study because he felt that the study as originally designed would sufficiently show whether or not there was a benefit to erectile function. (Liker, Tr. 1886-87; S. Resnick, Tr. 1716-18).

B. Respondents' Consultant Advisors

324. Respondents' approach in developing its research program was to listen to the advice of its scientific advisors and choose the studies that were more likely to show the real effects. (S. Resnick, Tr. 1859; Liker, Tr. 1881; CX1336 (Davidson, Dep. at 142)).

325. Respondents have relied heavily upon the advice and counsel of esteemed scientists and scientific advisers in connection with the conduct of POM's research program. (Liker, Tr. 1894).

326. Three groups of scientists advise Respondent Stewart Resnick about the findings and potential directions of POM's future research sponsorship—Respondents' internal scientific advisors, POM Research Summits, and POM's scientific advisory boards. (Liker, Tr. 1889-91).

327. Respondent Stewart Resnick had regular consultations with his scientific advisors, including Dr. Liker, Dr. David Heber, and Dr. Gillespie. (Liker, Tr. 1889-91; CX1374 (Tupper, Ocean Spray Dep. at 122); S. Resnick, Tr.1859).

328. Dr. Heber, Dr. Liker, and Dr. Gillespie helped oversee the progress and results of POM's research, and Dr. Liker and Dr. Gillespie, POM's head of science, informed Mr. Resnick of the status of the ongoing research. (Liker, Tr. 1889-91; CX1360 (S. Resnick Dep. at 32); CX1349 (Gillespie Dep. at 32-34, 36-37).

C. POM Research Summits

329. Respondents hold periodic meetings, known as research summits, and invited distinguished scientists from institutions throughout the country to discuss the

progress of the science and what additional studies should be undertaken. (Liker, Tr. 1890-92; Tupper, Tr. 1026-27; S. Resnick, Tr. 1858-59, 1872; CX1360 (S. Resnick, Dep. at 157-58)).

330. POM's research summits play a direct and integral part in both administering and developing POM's research program. (Liker, Tr. 1890-92; Tupper, Tr. 1026-27; S. Resnick, Tr. 1858-59, 1872; CX1360 (S. Resnick, Dep. at 157-58)).

331. At POM's research summits, the scientists conducting POM's research discuss the findings of their research and the potential areas of research that Respondents might consider. (Liker, Tr. 1890-91).

332. At the research summits, scientists are given an opportunity to present the findings of their research and to engage in a dialogue with Respondents guiding them as to the appropriate direction of future research. (Liker, Tr. 1890-92; Tupper, Tr. 1026-27; S. Resnick, Tr. 1858-59, 1872; CX1360 (S. Resnick, Dep. at 157-58)).

333. Participants and attendees of POM's research summits have included many esteemed and award winning scientists. (Liker, Tr. 1890-92; Tupper, Tr. 1026-27; S. Resnick, Tr. 1858-59, 1872; CX1360 (S. Resnick, Dep. at 157-58)).

334. Participants and attendees of POM's research summits have included Nobel Laureate Dr. Louis Ignarro, Dr. David Heber, Dr. Michael Carducci, and other scientists actively participating in POM's ongoing research. (Liker, Tr. 1890-92; Tupper, Tr. 1026-27; S. Resnick, Tr. 1858-59, 1872; CX1360 (S. Resnick, Dep. at 157-58)).

D. Respondents' Scientific Advisory Board

335. Respondent Stewart Resnick is also advised by members of POM's scientific advisory groups. (Liker, Tr. 1889-93).

336. Members of POM's scientific advisory boards are individuals who do not conduct the research for Respondents but who are experts in certain disease or health areas. (Liker, Tr. 1889-93).

337. Members of the advisory boards discuss the studies that are ongoing as well as those that have been completed. (S. Resnick, Tr. 1859).

338. Members of the advisory board also discuss what additional studies should be done and make recommendations. (Liker, Tr. 1892-93).

339. POM's scientific advisory boards are divided by group, and there is a cardiovascular advisory group and a prostate advisory group. (Liker, Tr. 1892-93).

340. Dr. Phillip Kantoff, Dr. David Kessler, and Dr. Carducci advise Respondents in the area of prostate cancer. (Liker, Tr. 1892-93).

341. Dr. Kantoff is employed at the Dana-Farber Cancer Institute at Harvard Medical School and runs the genitourinary oncology program. (Liker, Tr. 1892; Kantoff, Tr. 3257).

342. Dr. David Kessler is the former head of the FDA. (S. Resnick, Tr. 1859, 1872).

343. Dr. P.K. Shah, Dr. Gregg Fonarow, and Dr. Ben Ansell advise Respondents in the area of cardiovascular health. (Liker, Tr. 1892-93).

344. Dr. Shah from Cedars-Sinai Medical Center is a world renowned cardiologist. (Liker, Tr. 1893).

345. Dr. Fonarow runs the Congestive Heart Failure Program at UCLA. (CX1352 (Heber, Dep. at 236)).

E. The Economic and Scientific Considerations of RCTs

1. The Limited Scientific Effectiveness of RCTs for Nutrients

346. Requiring Respondents to conduct two large RCTs to support the advertising claims is unreasonable because RCTs have limited effectiveness in testing the properties of a nutrient. (Sacks, Tr. 823; Ornish Tr.2327-29; PX0192-0022).

347. RCTs are not as effective as in vitro and animal research in helping Respondents reach their goal of uncovering the truth as to the benefits of associated with pomegranates. (PX0192-0022; Sacks, Tr. 823; Ornish Tr.2327-29; (PX0361 (Sacks, Dep. at 89-91); Stampfer, Tr. 840).

348. Professor Meir Stampfer testified and Respondents' expert Dr. Dean Ornish agreed that in a nutritional research context, there are specific and unique limitations in conducting RCTs. (Sacks, Tr. 823; Ornish Tr.2327-29).

349. For example, unlike a drug, which can be identified and readily traced in the body, single nutrients enter the body and merge with others forming a milieu that does not lend itself to conclusive results in RCTs. (PX0192-0022; Sacks, Tr. 823; Ornish Tr. 2327-29).

350. Also, there is difficulty in designing a placebo that is sufficiently similar to the intervention. (Ornish Tr. 2328-29; PX0352 (Goldstein, Dep. at 84-85); PX0189-0003).

351. Further, Complaint Counsel's experts have testified in this case that, in some instances, animal and in vitro models are better suited to test a food or food derivative. (PX0361 (Sacks, Dep. at 89-91); Stampfer, Tr. 840).

352. For example, Dr. Frank Sacks and Professor Meir Stampfer conceded that animal studies may be more useful in safety testing than RCTs because it is easier to isolate mechanisms in highly controlled settings. (PX0361 (Sacks, Dep. at 89); Stampfer, Tr. 840).

353. Complaint Counsel's experts have also testified that *in vitro* research, can more effectively than an RCT, isolate particular mechanisms or biological effects in highly controlled settings. (PX0361 (Sacks, Dep. at 90-91); Stampfer, Tr. 840).

2. The High Cost of Conducting RCTs

354. Economics are a recognized factor to consider under *Pfizer et al*. *In re Pfizer, Inc.,* 81 F.T.C. 23, 30 (1972).

355. It is the opinion of Dr. Denis Miller that the cost of the science is a factor to be considered in determining whether proper substantiation exists. (PX0206 at 7-8).

356. It is an economically unreasonable requirement to hold Respondents to the same requirements that some drugs do not even meet. (PX0206 at 8-9).

357. The FDA, for example, has approved several anticancer agents without RCTs containing a placebo arm. (PX0206 at 8-9).

358. The FDA has also approved drugs for release under an accelerated program that have not been subject to RCTs. http://www.fda.gov/ForConsumers/ByAudience/ForPatientAdvocates/SpeedingAccesstoImportantNewTherapies/ucm128291.htm.

359. Also, even in connection with drugs subjected to RCTs, many have been found to be dangerous or ineffective. (PX0377-001; PX0381).

360. Respondents have made it clear that economics necessarily play a part in defining the parameters of the studies they sponsor. (Liker, Tr.1886-87; S. Resnick, Tr. 1716).

361. For example, Respondent Stewart Resnick chose not to add more participants to Dr. Forest's erectile study in order to power the study to reach statistical significance because doing so would cause Respondents to spend funds in excess of the study's original budget. (S. Resnick, Tr. 1716; Liker, Tr. 1886-87; CX0908).

362. Respondents also have adjusted protocols to keep the studies within budget. (CX1350 (Liker, Dep. at 37-38, 188-89)).

363. Respondents also stated that they have not sponsored a 30-year RCT on prostate cancer and the consumption of pomegranate juice because it would be incredibly expensive. (S. Resnick, Tr. 1863-64).

364. However, Respondents deny that any sacrifices to the studies' scientific integrity, soundness or reliability were made. Instead POM characterizes its economic decision as normal decisions necessary to moderate costs. (S. Resnick, Tr.1716-18; CX1360 (S. Resnick, Dep. at 228-29)).

365. Respondents' sponsorship of its scientific studies to obtain the information about the potential health benefits of their product has already cost Respondents $35 million. (S. Resnick, Tr. 1864; CX1363 (S. Resnick, Coke Dep. at 74; Tupper, Tr. 1015).

366. RCTs are often very large, expensive studies costing hundreds of millions of dollars. (Heber, Tr. 1949).

367. Complaint Counsel's expert, Professor Meir Stampfer, characterized RCTs as a "huge expense" and stated that even the very simple ones are "very expensive". (Stampfer, Tr. 824-25).

368. A single participant in an RCT can cost up to $10,000 per participant. (Liker, Tr. 1886-87).

369. RCTs can cost anywhere from 6 million to 600 million dollars each. (Sacks, Tr.1537-38).

370. Dr. James Eastham testified that prevention studies should include ten to thirty thousand men, and that such studies are "incredibly expensive" and in the range of $600 million. (Eastham, Tr. 1322-28).

371. Dr. Sacks testified in his deposition that it would be extremely costly to design a RCT study on cardiovascular disease because it would take years or decades to evaluate the effectiveness of an intervention. (PX0361 (Sacks, Dep. at 113)).

372. The well-known Women's Health Study cost $600 million and produced inconclusive results. (Heber, Tr. 1938; Ornish, Tr. 2329; CX1352 (Heber, Dep. 224)).

373. In the case of getting FDA approval of some drugs, companies have spent billions of dollars on research to get a new drug approved. (Ornish Tr. at 2324-25).

374. Due to the "huge expense" of conducting an RCT, Professor Stampfer conceded that even governments and major institutions lack interest in conducting them. (Stampfer, Tr. 825).

375. Further, unlike a drug, wherein the manufacturer receives patent protection and market exclusivity in return for cost intensive research, producers of natural food products, like Respondents, receive no comparable compensation for their investment. (Stampfer, Tr. 826-27).

376. And even if intellectual properties rights were available for POM juice, unlike some drugs which can drive a huge profit, Respondents sells its POM juice for only $4.00 to $5.00 on average. (Tupper, Tr. 982).

377. Notwithstanding this, POM has sponsored some RCT research. (PX0023; PX0014; PX0062; PX0064; CX0908).

VII. RESPONDENTS' REASONED RELIANCE ON SCIENTISTS

378. Respondent Stewart Resnick relies heavily on the advice of scientists and scientific advisors in connection with the conduct of POM's research program. (S. Resnick, Tr. 1662, 1859; Liker, Tr. 1881; CX1336 (Davidson, Dep. at 142)).

379. Yet, importantly, though relying upon scientist in crafting their research program, Mr. Resnick and Respondents did so in a reasoned manner that underscored their responsibilities in disseminating truthful information regarding the health benefits of pomegranates. (CX1360 (S. Resnick, Dep. at 200-01, 1693); (Liker, Tr. 1903-04); PX0023; S. Resnick, Tr. 1693).

380. Respondents' approach in developing its research program was to listen to the advice of its scientific advisors and choose the studies that were more likely to show the real effects from the consumption of pomegranate juice, rather than to select studies likely to show a positive benefit. (S. Resnick, Tr. 1662, 1859; Liker, Tr. 1881; CX1336 (Davidson Dep. at 142)).

381. Mr. Resnick told Dr. Michael Aviram that his primary interest in sponsoring research was to establish the truth. (CX1358 (Aviram, Dep. at 74)).

382. Dr. Ornish also recalled meeting Stewart Resnick in the late 90's. Mr. Resnick indicated to Dr. Ornish that he had some early studies showing that pomegranate juice may be more beneficial than anybody realized, but rather than going public and marketing, he said that he wanted to fund research to see if it was true or not. (Ornish, Tr. 2325).

383. Mr. Resnick depends on his experts and has no reason to believe they have told him anything but the truth. (S. Resnick, Tr. 1662).

384. Respondents held periodic meetings, known as research summits, and invited distinguished scientists from institutions throughout the country to discuss the progress of the science and what additional studies should be undertaken. (Liker, Tr. 1890-92; Tupper, Tr. 1026-27; S. Resnick, Tr. 1858-59, 1872; CX1360 (S. Resnick, Dep. at 157-58)).

385. Respondent Stewart Resnick held meetings on specific health areas such as cardiovascular and prostate health, with noted experts in those fields to discuss what studies should be done, as well as to evaluate the results of the completed studies. (Liker, Tr. 1889-93).

386. Respondents rely significantly upon scientists regarding the design of protocols, the meaning of the results of its sponsored studies, and the direction the research program should take. (Liker, Tr. 1894; (S. Resnick, Tr. 1732-33; CX1360 (S. Resnick, Dep. at 225-26); CX1376 (S. Resnick, Ocean Spray Dep. at 237-38; (CX1350 (Liker, Dep. at 186-87)).

387. Respondents' use of scientists to assist in structuring studies was absolutely appropriate if not critical to obtaining well-designed studies of significant scientific integrity. (Liker, Tr. 1894; (S. Resnick, Tr. 1732-33; CX1360 (S. Resnick, Dep. at 225-26); CX1376 (S. Resnick, Ocean Spray Dep. at 237-38; (CX1350 (Liker, Dep. at 186-87)).

388. For example, the GAQ instrument was chosen and used as the primary measure in the Forest Padma-Nathan erectile study at Dr. Padma-Nathan's suggestion. (CX1350 (Liker, Dep. at 186-87)).

389. Mr. Resnick followed Dr. Michael Davidson's suggestion that a subgroup analysis and re-reading of the results take place to alleviate their confusion as to the results of his CIMT Study. (Liker, Tr. 1896-97).

390. Further, many different medical doctors assured Respondent Stewart Resnick that a placebo was not necessary and PSA doubling time was an acceptable endpoint in prostate cancer studies. (S. Resnick, Tr. 1732-33; CX1360 (S. Resnick, Dep. at 225-26); CX1376 (S. Resnick, Ocean Spray Dep. at 237-38)).

A. Reliance Upon the Peer-Review Process

391. Respondents also relied, in part, on the peer-review process and the publication in peer-reviewed journals as an indication that the sponsored science was both good and reliable. (Liker, Tr. 1899-1900; *Daubert v. Merrell Dow Pharms*, 43 F.3d 1311, 1318 (9th Cir. 1995) "That the research is accepted for publication in a reputable scientific journal after being subjected to the usual rigors of peer review

is a significant indication that it is taken seriously by other scientists, i.e., that it meets at least the minimal criteria of good science.").

392. For example, when Respondents could not figure out the different results at twelve and eighteen months in the Davidson CIMT study, Respondents decided to turn the findings over to the peer-review process to decide whether or not the results were worthy of publication. (Liker, Tr. 1899-1900).

393. More than seventy of the studies sponsored by the Respondents have been published in peer-reviewed journals. (Liker, Tr. 1888) .

394. At the very least, the publication in Respondents' research studies in peer-review journal is some evidence that the scientists vetting the research considered the studies important enough to publish. (Liker, Tr. 1899-1900; CX1352 (Heber Dep. at 199-200; *Daubert v. Merrell Dow Pharms*, 43 F.3d 1311, 1318 (9th Cir. 1995) ("That the research is accepted for publication in a reputable scientific journal after being subjected to the usual rigors of peer review is a significant indication that it is taken seriously.").

B. Reliance Upon Doctors' Statements

395. Respondents reasonably relied, in part, upon statements by scientists that the findings in the research were dramatic and impressive. (CX1363 (S. Resnick, Coke Dep. at 57-58, 66, 77-78); S. Resnick, Tr. 1662, 1734, 1736; CX1372 (S. Resnick, Tropicana Dep. at 44); PX0484; CX0004_0012; (CX1376 (S. Resnick, Ocean Spray Dep. at 31-32, 289)).

1. Statements about Cardiovascular Research

396. After reviewing the findings of his initial antioxidant research, Dr. Michael Aviram represented to Stewart Resnick that the antioxidant properties found in the pomegranate were the most powerful he had ever researched. (CX1363 (S. Resnick, Coke Dep. at 57, 66)).

397. Dr. Davidson conveyed to Respondents and Dr. Liker that he was extremely enthusiastic about the results of his CIMT study and wanted the study published. (Liker, Tr. 1896; CX1350 (Liker, Dep. at 151)).

398. In an August 2008 email, Dr. Michael Aviram sent to Respondents Stewart and Lynda Resnick and Matt Tupper the statement "The use of Anti-oxidants, and Anti-inflammatory agents (POM WONDERFUL), could be of major importance in the protection against the other 70% cardiovascular events." (PX0476).

399. When asked by Respondent Lynda Resnick what the findings of his recent publication were, Dr. Aviram stated in a January 2008 email that pomegranate

juice and POMx were "very potent protectors against cardiovascular diseases." (PX0479-0001).

400. Dr. Ornish, in an email to Respondent Stewart Resnick and cc'ing Respondent Matt Tupper, announced the acceptance of his myocardial perfusion study. He stated, "As you know, this study showed, for the first time, that the progression of coronary heart disease may be reversed by drinking pomegranate juice as evidenced by improved blood flow to the heart measured by thallium scans." (PX0485-0001).

401. Dr. Aviram provided Respondents with a written statement that his research was the first to show that POMx polyphenols had similar cardio protective effects to those of pomegranate juice polyphenols in the reduction of atherosclerotic risks and promoting cardiovascular health. (PX0500-0003).

402. Dr. Aviram provided his opinion to Respondents that POMx "indeed promotes cardiovascular health." (PX0500-0003).

403. Dr. Dean Ornish characterized the health benefits of pomegranate juice as "extraordinary." (PX0511).

404. Many of the doctors and cardiovascular researchers who were deposed in this case made statements supporting their research having shown a benefit from consuming pomegranate juice. (CX1350 (Liker, Dep. at 222); CX1358 (Aviram, Dep. at 6).

405. For example, Dr. Michael Aviram stated that he is a great believer in pomegranate juice as an anti-atherosclerotic, and he believes that doctors and the public should be informed about those benefits. (CX1358 (Aviram, Dep. 48-49).

406. Based upon Dr. Aviram's research, Dr. Liker stated in his deposition that he believes that drinking POM Wonderful juice lowers other risk factors for heart disease. (CX1350 (Liker, Dep. at 221-22)).

407. Based upon Dr. Aviram's research, Dr. Liker stated in deposition that he believes that "One glass a day has been shown to drastically reduce heart artery plaque" is an accurate statement. (CX1350 (Liker, Dep. at 221-22)).

408. In deposition, Dr. Michael Aviram stated that after a year of studying the consumption of pomegranate juice, he concluded that pomegranate juice had greater antioxidant potencies than red wine. (CX1358 (Aviram, Dep. at 6)).

409. Dr. Michael Davidson told Mr. Resnick and Dr. Liker that he believed the data from his CIMT study shows a signal of a benefit in the subgroup and should be presented. (CX1336 (Davidson, Dep. at 182-83).

410. The cardiovascular researchers have not only made statements to Respondents about their belief in the benefits of pomegranates but have also made public statements to reputable newspapers to that same effect. (PX0423-0001).

411. For example, Dr. Michael Davidson was quoted in a 2004 article in the Chicago Tribune stating, "It is the concentration of polyphenols that appear to make [pomegranate juice] the most potent antioxidant in nature." (PX0423-0001).

412. After conducting research, some of the cardiovascular researchers began recommending POM products to their patients because of the benefits shown in the research. (CX1336 (Davidson, Dep. at 225-26)).

413. For example, Dr. Davidson stated in deposition that his data supports a possible cardiovascular health benefit from the consumption of pomegranate juice, and he has recommended pomegranate juice or POMx to some of his patients. (CX1336 (Davidson, Dep. at 225-26)).

414. POM's cardiovascular advisory panel, who advise Mr. Resnick, also believed that cardiovascular benefits have been shown by the research. (CX1336 (Davidson, Dep. at 224)).

415. For example, Dr. Davidson recalled that members of POM's cardiovascular advisory panel believed that the findings in his CIMT trial were a real, true signal of a benefit in the subgroup. (CX1336 (Davidson, Dep. at 224)).

2. Statements about Prostate Health Research

416. Some of the doctors who researched the prostate benefits from consuming the Challenged Products have also made statements about their own belief that a benefit to the prostate was shown. (CX1350 (Liker, Dep. at 174-75); S. Resnick, Tr. 1734, 1736).

417. At trial, Stewart Resnick recalled that doctors reviewing the results of basic and animal studies done on prostate health told him that the results were the best they had ever seen. (S. Resnick, Tr. 1734, 1736).

418. Dr. Harley Liker told Respondents that Pantuck's Phase II study proves that pomegranate juice slows down the progression PSA. (CX1350 (Liker, Dep. at 174-75)).

419. In a January 2007 email, Dr. Heber stated to Mark Dreher, "The prolongation of PSA doubling time is considered clinically significant by urologists and is being confirmed in large multicenter trials." (PX0494).

420. In deposition, Dr. Liker recalled that Dr. David Heber has shared his view that POM products could contribute to the prevention of prostate cancer. (CX1350 (Liker, Dep. at 174)).

421. Like the cardiovascular researchers, the prostate health researchers also made statements in their depositions supporting the research and the conclusion that some benefit to prostate health exists. (CX1341 (Pantuck Dep. at 108, 254-55, 264)).

422. For example, Dr. Pantuck, in deposition, stood behind the results of his research and selection of endpoints. (CX1341 (Pantuck Dep. at 108, 254-55).

423. In his deposition, Dr. Pantuck supported the findings of his study that PSA doubling time was prolonged for men with prostate cancer when they were given pomegranate juice. (CX1341 (Pantuck Dep. at 108)).

424. In his deposition, Dr. Pantuck stated that PSA doubling time is clinically important for prostate cancer treatment and one of the most important variables that you can discuss to characterize a prostate cancer patient. (CX1341 (Pantuck Dep. at 254-55)).

425. Dr. Pantuck stated in his deposition that from a patient care standpoint PSA doubling time is extremely important. (CX1341 (Pantuck Dep. at 255)).

426. Dr. Pantuck also stated in his deposition that he consumes POM Wonderful pomegranate juice a few times a week. (CX1341 (Pantuck, Dep. at 264)).

427. Like the cardiovascular researchers, the researchers looking at prostate health benefits have also made public remarks that the research shows a benefit. (PX0428-0001).

428. For example, Dr. Pantuck has publicly made positive remarks about the findings in his research done for Respondents. (PX0428-0001).

429. In connection with his follow-up research to his 2006 study, Dr. Pantuck publicly remarked that the increase in doubling time from 15 to 54 months was a "big increase." He said that he was "surprised to see such an improvement in PSA numbers." He also contributed, "In older men 65 to 70, who have been treated for prostate cancer, we can give them pomegranate juice and it may be possible for them to outlive their risk of dying from their cancer." He also commented, "The juice seems to be working." (PX0428-0001; CX1341 (Pantuck, Dep. at 270-71)).

430. Like some of the cardiovascular researchers, the researchers looking at prostate health discuss the findings of their results with their patients. (CX1341 (Pantuck, Dep. at 270-71)).

431. For example, Dr. Pantuck discusses the benefits of pomegranate juice with his patients. (CX1341 (Pantuck, Dep. at 270-71)).

3. Statements about Erectile Health Research

432. Scientists have also represented to Respondents and to Complaint Counsel in deposition that a benefit to erectile health exists. (CX1363 (S. Resnick, Coke Dep. at 77-78); CX1372 (S. Resnick, Tropicana Dep. at 44); PX0484; CX1350 (Liker, Dep. at 190-91)).

433. Nobel Laureate Louis Ignarro represented to Stewart Resnick that he strongly believes pomegranate juice was 40% as effective as Viagra in helping with erectile dysfunction. (CX1363 (S. Resnick, Coke Dep. at 77-78); CX1372 (S. Resnick, Tropicana Dep. at 44)).

434. Louis Ignarro also told Respondents, "Based on studies conducted in my laboratory, pomegranate juice was 20 times better than any other fruit juice at increasing nitric oxide. It's astonishing – I've been working in this field for 20 years and I have never seen anything like it. I drink it 3 times a day without fail." (PX0484).

435. Dr. Liker, in his deposition, stated that he, Dr. Padma-Nathan, and Mr. Forest concluded that the Forest Padma-Nathan erectile study showed a clinically significant benefit to erectile health. (CX1350 (Liker, Dep. at 190-91)).

C. Respondents' Insistence on Scientific Rigor and Integrity

436. Notwithstanding the enthusiasm for the research by the scientists, Stewart Resnick double-checks both positive and negative results. (CX1360 (S. Resnick, Dep. at 200-01); (Liker, Tr. 1903-04); Liker, Tr. 1903; (S. Resnick, Tr. 1693; Liker, Tr. 1904; PX0023).

437. Respondents independently verify research results to ensure the information is accurate before it was published or placed in the public realm. (CX1360 (S. Resnick, Dep. at 200-01); Liker, Tr. 1903-04).

438. For example, Respondents delayed the publication of Dr. Aviram's study that showed an amazing 30% reduction of arterial plaque in order to have the data re-read to ensure Dr. Aviram's conveyed a correct interpretation of the results. (Liker, Tr. 1903).

439. Respondents also delayed the publication of Dr. Ornish's study on myocardial perfusion, which showed a statistically significant benefit, so that an independent party could double-check the results. (S. Resnick, Tr. 1693; Liker, Tr. 1904; PX0023).

D. POM's Policy with Regard to Publishing the Research

440. Complaint Counsel have produced no evidence that the delay in the publication of the Davidson CIMT study was nefarious or motivated by a desire to hide the results. In fact, the evidence shows the exact opposite. (Liker, Tr. 1903); CX1372 (S. Resnick, Tropicana Dep. at 33); CX1360 (S. Resnick, Dep. at 75); CX1358 (Aviram Dep. at 76); CX1336 (Davidson, Dep. at 230)).

441. Respondent Stewart Resnick has never improperly interfered with the publication of any report or dictated the contents of a report. (CX1372 (S. Resnick, Tropicana Dep. at 33)).

442. Respondent Stewart Resnick has never asked or told any scientist or researcher not to publish a manuscript or report. (CX1360 (S. Resnick, Dep. at 75); CX1358 (Aviram, Dep. at 76); CX1339 (Ornish, Dep. at 85)).

443. The delay of the publication of Dr. Davidson's CIMT study was caused by confusion on the part of POM's internal scientific team. Specifically, the delay in publication was due to having the results of the study re-read by a blinded independent group. (Liker, Tr. 1895-96; CX1350 (Liker, Dep. at 146, 149-50, 163-64)).

444. Respondents did not grant Dr. Davidson permission to present the results of the CIMT study to the American Heart Association because they were still trying to make sense of the data and alleviate confusion. (CX1350 (Liker, Dep. at 151-52)).

445. Individuals at POM, including Matt Tupper and Stewart Resnick, collectively made the decision to go forward with the publication of Dr. Davidson's CIMT study. (CX1350 (Liker, Dep. at 165-66)).

446. Respondents did not try to hide the 18 month results of the Davidson CIMT study. (Liker, Tr. 190).

447. Both the 18 month and 12 month results of Dr. Davidson's CIMT study were ultimately published in the American Journal of Cardiology, which is one of the leading journals in cardiovascular medicine. (Liker, Tr. 1902; PX0014).

VIII. RESPONDENTS' CARE IN ADVERTISING AND CHANGES IN POM'S ADVERTISING OVER TIME

448. POM selected studies to discover the truth about the health benefits of the pomegranate. (S. Resnick, Tr. 1859).

449. POM did not select studies based on whether or not they would produce a positive result. (S. Resnick, Tr. 1860).

450. POM endeavored to sponsor high quality science and sought the best scientists in their respective fields. (S. Resnick, Tr. 1857).

451. POM has sponsored over one hundred scientific studies at 44 different institutions and universities with some of the best scientists throughout the world. (Liker, Tr. 1887-88).

452. Even though very encouraging research has been completed and published on many areas of science, such as immunity, cold and flu, cognitive function, skin and dental health, POM has been somewhat conservative and has chosen not to discuss those results in advertising. (Tupper, Tr. 2979-81)

453. Even when initial research results are positive, POM delays sharing the results with the public until the science is sufficiently developed. (Tupper, Tr. 2979).

454. POM's policy is that a body of science must be developed and the physiological effects of pomegranates on any studied structure or function must be well understood before Respondents will use such research results in advertising. (Tupper, Tr. 2981).

455. In its early years from 2003 through 2006, the language and graphics in POM's advertisements regarding the health benefits of POM Juice were more aggressive. (*See infra* (XVII(E)).

456. Since those early years, POM's advertisements have evolved and changed significantly, largely as a result of the NAD decisions in 2005 and 2006 described below. (L. Resnick, Tr. 162, 168).

457. In 2005, POM's advertising was the subject of an inquiry by the National Advertising Division ("NAD"). (CX0037_0001).

458. The NAD found that many of the advertisements promoting POM Juice could be deemed mere puffery. (CX0037_0006; Tupper, Tr. 2983).

459. There were, however, two advertisements that the NAD believed extended beyond puffery: 1) "Amaze your cardiologist" and 2) "Floss your arteries," both of which made quantified performance claims. (CX0037_0008; CX0034; CX0031).

460. Both advertisements cited Dr. Aviram's 2004 study titled Pomegranate juice consumption for 3 years by patients with carotid artery stenosis reduces common carotid intimamedia thickness, blood pressure and LDL oxidation. (CX0611).

461. The NAD found that Dr. Aviram's 2004 study was reliable, sufficiently powered and had produced encouraging results concerning the antioxidant attributes of POM Juice. (CX0037_0007).

462. The NAD further acknowledged the prominent role that the antioxidants found in pomegranate juice can play in reducing the risk of free radical-related diseases, and in particular, the reduction of artery-clogging plaque. (CX0037_0010).

463. The NAD, however, found that POM did not adequately qualify the science that was being described in the "Amaze your cardiologist" and "Floss your arteries" advertisements. (Tupper, Tr. 2983; CX0037_0010).

464. POM disagreed with the NAD's 2005 ruling. (Tupper, Tr. 2984; CX0037_011).

465. POM believes that it appropriately and accurately portrayed the results of the science on pomegranate juice in its advertisements. (Tupper, Tr. 2984-86; CX0037_0011).

466. Nevertheless, POM took the NAD's 2005 findings into account with respect to its future advertising. (CX0037_0011).

467. POM stopped running the "Floss your arteries" advertisement in 2004 and has not disseminated it since that time. (Tupper, Tr. 2996).

468. POM stopped running the "Amaze you cardiologist" advertisement in 2005 and has not disseminated it since that time. (Tupper, Tr. 2996-2997; CX1353 (Tupper, Dep. at 131).

469. Despite those changes, POM's advertising was the subject of an inquiry by the NAD in 2006. (CX0055).

470. As in 2005, the NAD found that many of POM's advertising headlines and imagery could be deemed puffery. (Tupper, Tr. 2983-84; CX0055_0047).

471. The NAD, however, did not make any findings about the validity of the underlying science that had been referenced in POM's advertising. (Tupper, Tr. 2983-2984; CX0055_0038-39).

472. The NAD did acknowledge, however, that numerous studies have touted the benefits of eating foods high in antioxidants and that POM produced a "high quality, healthful drink demonstrating a high level of antioxidants." (CX0055 at 0025).

473. The NAD further stated that POM Juice is an excellent source of antioxidants and did not dispute that antioxidants may be beneficial to one's health. (CX0055_0039).

474. The NAD found that the language "[POM] can help prevent premature aging, heart disease, stroke, Alzheimer's, even cancer. Eight ounces a day is all you

need," when discussing the benefits of POM Juice, was too general and/or overly broad, and that POM had not sufficiently qualified the results of the scientific studies. (CX0055_0039, 0047).

475. Notably, the NAD found that POM's scientific evidence on cardiovascular health might be sufficient to support more narrowly tailored qualified claims. (CX0055_0047).

476. POM disagreed with the NAD's ruling that its claims were too broad. (Tupper, Tr. 2984; CX0055_48).

477. POM believes that the scientific studies have been appropriately portrayed in advertisements. (Tupper, Tr. 2984-86; CX0055_0048).

478. Nevertheless, POM deferred to the NAD's ruling and discontinued and/or modified certain claims in its advertising that the NAD had taken issue with. (CX0055_0048; Tupper, Tr. 2984-85).

479. Beginning in 2006, largely as a result of the two NAD decisions, POM stopped making generalized statements in advertisements about the science it had done. (Tupper, Tr. 2986-87).

480. Since 2006, when discussing the benefits of its products, POM's policy has been to discuss and describe what research was done, where it was done and to summarize the results of the specific scientific studies described in its advertisements. (Tupper, Tr. 2986-87).

481. For example, POM now uses the following language, "A recently published preliminary medical study followed 46 men previously treated for prostate cancer, either with surgery or radiation. After drinking 8 ounces of POM Wonderful 100% Pomegranate Juice daily for two years, these men experienced significantly longer PSA doubling times" to describe the results of the Pantuck study and convey the qualified message that the results were "preliminary." (CX0471).

482. Additionally, as a result of the NAD's decisions, in some of their ads, Respondents would direct people back to their website to read the full scientific study. (Tupper, Tr. 2985).

483. Importantly, since 2007 POM has implemented a more formalized and well-defined vetting process for advertisements relating to the health benefits of its products. This process requires multiple stages of review that ultimately culminate in approval by the legal department before any advertisement is run. This formalized process ensures that accurate information is presented to the public. (Tupper, Tr. 2977-78).

484. Respondents' continued policy regarding the relationship between scientific studies and advertisements is to ensure that what is portrayed in the advertisements is consistent and accurate with results of the scientific studies themselves. (Tupper, Tr. 2979).

485. Respondents firmly believe that everything that has been said in any of their advertising regarding the health benefits of their products is more than adequately supported by published research that has been conducted over the past 10 to 15 years. (Tupper, Tr. 2986).

486. POM would never knowingly publish any advertisement that the company did not believe was adequately supported by the body of science. (Tupper, Tr. 3015).

487. Likewise, Dr. Dreher, who was formerly POM's VP of Scientific Affairs in charge of overseeing POM's research program, entered into a settlement agreement with the FTC. (Dreher, Tr. 527-28, 587).

488. Dr. Dreher's settlement agreement with the FTC does not in any way, shape, or for suggest that Dr. Dreher believes that he did anything wrong. (Dreher, Tr. 587).

489. Dr. Dreher did not enter into a settlement agreement with the FTC because he believed he did anything wrong. (Dreher, Tr. 587).

490. Two newsletters authored by Dr. Dreher are the basis for Dr. Dreher's settlement agreement. One discussed prostate health and the other heart health. (Dreher, Tr. 587).

491. Dr. Dreher does not believe that there is anything false or misleading about the newsletters that were the basis for his settlement agreement with the FTC. (Dreher, Tr. 588).

492. Dr. Dreher does not believe there is anything false or misleading about the newsletters despite the FTC's accusations against him in connection with those newsletters. (Dreher, Tr. 588). Dr. Dreher believes in the science supporting the health benefits of pomegranates despite the FTC's accusations against him. (Dreher, Tr. 588).

IX. THE MANUFACTURE AND SALE OF POM JUICE AND POMX EXTRACT AND LIQUID

A. 100% Pomegranate Juice And POMx Are Wholly Derived From The Fruit

493. 100% POM Juice is a 100% juice product derived from whole pomegranate fruits. (PX0353 (Heber, Dep. at 124) CX1362 (L. Resnick, Dep. at 85-86); CX1363 (S. Resnick, Dep. at 46-47)).

494. POMx is an extract from the pomegranate, made through a process by which POMx Liquid is first derived from the whole fruit, and then POMx is extracted from the POMx Liquid. (CX1363(S. Resnick, Dep. at 46-47)).

495. POM has never advertised its products as a drug. (Tupper, Tr. 3008).

496. POM has never intended to advertise its products as a drug. (Tupper, Tr. 3008).

497. POM Juice is sold in the refrigerated produce section of the grocery store. (CX1367 (S. Resnick Welch Dep. at 122); CX1374 (Tupper Ocean Spray Dep. at 56-57)).

498. POM Juice is not sold in the "drug" or "over the counter" section of any establishment, or advertised or marketed in conjunction with or in comparison to any drug product. (CX1362 (L. Resnick Coke Dep. at 135-136); CX1367 (S. Resnick Welch Dep. at 122; CX1374 (Tupper Ocean Spray Dep. at 56-57)).

499. Consumers must go to the fresh produce aisle of a store to purchase any POM Juice product. (CX1362 (L. Resnick Coke Dep. at 135-136).

500. The Challenged Products do not state on their face that they "treat" or "prevent" some disease or condition, like products in the drug aisles of a grocery store such as "Tough Actin' Tinactin," that states on the product that it "prevents" or "cures" most athlete's foot, or Bengay that says it "stops pain" and provides "fast relief from minor arthritis, backache, muscle & joint pain." (Appendix of Advertisments).

501. POMx caters to those consumers who want the benefits of the juice, without the calories or sugar to get, "The Power of Pom, now in a Pill." (CX0169_0001).

X. RESPONDENTS' GENUINE BELIEF IN THE HEALTH BENEFITS OF THE PRODUCTS AND ITS ADVERTISING

A. Respondents' Personal Belief in the Health Benefits

502. Respondents genuinely believe in the integrity of POM's research program and the health benefits of the Challenged Products. (CX1406 (Tupper, Tropicana Tr.182-83); CX1363 (S. Resnick, Coke Dep. at 83; CX1360 (S. Resnick, Dep. at 200, 229, 246); PX1372 (S. Resnick, Tropicana Dep. at 42-43); CX1371 (Tupper, Tropicana Dep. at 171); CX1362 (L. Resnick, Coke Dep. at 51, 80); CX1375 (L. Resnick, Dep. at 8, 209)).

B. Belief in the Research

503. Based upon his belief and knowledge gained from statements made by POM's consulting doctors and POM's research studies, Respondent Matt Tupper advised members of his families with prostate cancer to consume pomegranate. (CX1406 (Tupper, Tropicana Tr.182-83).

504. Respondent Stewart Resnick personally believes that the research supports the conclusion that pomegranate prevents certain people from getting prostate cancer and in others it may prolong life. (CX1363 (S. Resnick, Coke Dep. at 83; CX1360 (S. Resnick, Dep. at 229)).

505. Respondent Stewart Resnick personally believes that consuming pomegranate juice helps with erectile dysfunction and that POM's research supports his belief. (CX1376 (S. Ocean Spray Dep. at 162)).

506. Stewart Resnick personally believes that the consumption of pomegranate juice is beneficial in the fight against cardiovascular disease and POM's research supports his belief. (CX1360 (S. Resnick, Dep. at 246); CX1360 (S. Resnick, Dep. at 200); (CX1372 (S. Resnick, Tropicana Dep. at 42-43)).

507. Respondent Matt Tupper stated at trial that Respondents believe that the body of science undertaken in the area of prostate health is sufficiently rigorous to lower the amount of future research that would need to be undertaken in order to obtain FDA approval for a claim that POMx pills prevent or treat prostate cancer. (Tupper, Tr. 991-92).

508. Respondents have stated that they believe that PSA doubling time is a valid and appropriate endpoint in research whether its products prevent or treat prostate cancer. (Tupper, Tr. 991-92).

509. Respondent Matt Tupper personal belief in the integrity of the research is evidenced by the high grade that he attaches to the disputed areas of science. He

personally grades POM's erectile, prostate, and cardiovascular research each as eight-out-of-ten. (Tupper, Tr. 3012-14).

C. Belief in the Health of the Products

510. Despite the fact that POM as a company is losing money, Respondents have chosen to stay in business because they believe that the product does provide all the health benefits that have been advertised. (S. Resnick, Tr. 1867).

511. Respondents genuinely believe that pomegranates are, in fact, "good medicine," in the sense that broccoli and a generally healthy lifestyle are good medicine. (Tupper, Tr. 2991-92).

512. Respondent Matt Tupper testified that Respondents believe that pomegranate is "good medicine" much in the same way that Hippocrates believed that food is medicine. Mr. Tupper recited a Hippocrates quote and said, "Our food should be our medicine, and our medicine should be our food." (Tupper, Tr. 2992).

513. Respondent Matt Tupper testified that Respondents believe that pomegranate juice is "good medicine" in the same way that a quote that has been out in the press states that food is medicine—"the medicine chest of the 21st century can be found in the produce department of your local supermarket." (Tupper, Tr. 2992).

514. Mr. Tupper in other litigation matters stated that he passionately believes pomegranate juice is incredibly healthy and that the power of a good plant-based diet can have a dramatic effect on one's long term health. (CX1371 (Tupper, Tropicana Dep. at 171)).

515. Respondent Stewart Resnick has stated that he believes that pomegranates are a uniquely healthy food. (CX1363 (S. Resnick, Coke Dep. at 50-52)).

516. Respondent Lynda Resnick stated that she personally believes pomegranates and pomegranate juice have unique health-giving properties. (CX1362 (L. Resnick, Coke Dep. at 51, 80); CX1375 (L. Resnick, Dep. at 8, 209).

517. Respondent Lynda Resnick considers POM juice to be "health in a bottle" because of the medical benefits of the juice revealed by both Respondents' research and the 8,000 year history of pomegranates. (L. Resnick, Tr. 78; CX1362 (L. Resnick, Dep. at 50-51); (CX1375 (L. Resnick, Tropicana Dep. at 110)).

518. Respondent Lynda Resnick believes "with all her heart" that if you lead a healthy lifestyle and consume pomegranate juice, you will be healthier. (CX1362 (L. Resnick, Dep. at 51)).

519. Respondent Lynda Resnick believes that part of POM juice's intrinsic value is that it has been shown to reduce arterial plaque and have a powerful effect against prostate cancer. (L. Resnick, Tr. 76; PX1359 (L. Resnick Dep. at 18)).

520. Respondents genuinely believe that the consumption of pomegranate juice improves one's odds in combating disease. (Tupper, Tr. 3011-13; CX1363 (S. Resnick, Coke Dep. at 83; CX1360 (S. Resnick, Dep. at 229); CX1376 (S. Ocean Spray Dep. at 162); CX1360 (S. Resnick, Dep. at 246); CX1360 (S. Resnick, Dep. at 200); (PX1372 (S. Resnick, Tropicana Dep. at 42-43); CX1406 (Tupper, Tropicana Tr.182-83)).

D. Respondents Belief in the Science is Justified by the High Level of Scientific Integrity

521. Respondents are justified in their belief in the integrity of the research program, in part, because of the level of scientific rigor that they have insisted upon in sponsoring research. (Liker, Tr. 1887-89; (S. Resnick, Tr.1857; Liker, Tr. 1878-80; CX1350 (Liker, Dep. at 32-33)).

522. Respondents have sponsored research at the finest medical and research institutions, including, UCLA, Johns Hopkins, M.D. Anderson in Houston, the Mayo Clinic, the Cleveland Clinic, and UC San Francisco. (Liker, Tr. 1887-89).

523. Respondents have also sought out the very best researchers in their respective fields to guide them in their decisions to explore different health conditions and areas and to conduct the research. (S. Resnick, Tr.1857; Liker, Tr. 1878-80; CX1350 (Liker, Dep. at 32-33)).

E. Respondents Do Not Believe Their Advertisements Regarding the Challenged Products Are Deceptive or Misleading

1. The Individual Respondents Never Believed or Suggested That Their Advertisements Were Meant to Convey the Message That The Challenged Products Are or Should Be "Silver Bullet" Against Disease Or Substitute for Conventional Medical Treatment

524. Mr. Resnick never intended POM products to be a substitute for recommended medical treatment or anything else recommended by a doctor. (S. Resnick, Tr. 1870).

525. Mr. Resnick is not aware of anyone associated with POM or Roll who suggests that people should drink POM instead of following their doctor's advice. (S. Resnick, Tr. 1870-71).

526. If Mr. Resnick found out an employee was recommending that a consumer drink POM instead of following his or her doctor's advice, Mr. Resnick would first terminate the employee; and second; he would make clear to the consumer that such information is not correct, and that the employee lacked the authority to make such a statement and should not have done so. (S. Resnick, Tr. 1871).

527. Mr. Tupper testified that it is absolutely against company policy to say or suggest that POM products are a substitute for proper medical treatment. (Tupper, Tr. 3018).

528. Mr. Tupper is unaware of any instance in which any employee told anyone to drink pomegranate juice as a substitute for consulting with a doctor and taking his or her advice. (Tupper, Tr. 3018).

529. Mr. Tupper testified that it is absolutely against company policy for a POM employee, when responding to consumer health inquiries, to remain silent and not inform the consumer that he or she consult his or her doctor. (Tupper, Tr. 3018-19).

530. In responding to health-related inquires or a question about a medical condition, POM instructs its employees to tell consumers to consult with his or her physician and strongly encourage this recommendation. (CX0308; Tupper, Tr. 3019).

2. The Individual Respondents Never Believed or Suggested That Their Advertisements Were Meant To Convey the Message That the Challenged Products Could Treat or Prevent Any Disease

(a) Lynda Resnick

531. Mrs. Resnick never believed the "I'm off to save prostates" advertisement was intended to mean that POM Juice would treat prostate cancer. (L. Resnick, Tr. 217-18; CX 1426_0009).

532. With respect to the "cheat death" advertisement, Mrs. Resnick was told from scientists that pomegranate juice has more antioxidants than any other drink, can help prevent premature aging, heart disease, stroke, Alzheimer's, even cancer". (CX471_0002; L. Resnick, Tr. 152).

533. In her Tropicana deposition, Mrs. Resnick testified that she did not feel comfortable and confident telling consumers that POM can help prevent Alzheimer's in an ad because she does not think the research is exhaustive enough. (L. Resnick, Tr. 155-56).

534. At the time she gave an interview to Martha Stewart, Mrs. Resnick stated that she believed POM Juice was helpful for Alzheimer's – that is what she believed then and now. (L. Resnick, Tr. 156).

535. The purpose of the "Cheat death" advertisement is not to prevent heart disease, but rather is to make the reader laugh; it is puffery. (L. Resnick, Tr. 194; 196-97).

536. Although she states that POM did tell consumers in 2006 that POM Juice could prevent Alzheimer's, Mrs. Resnick believes the statement to be true and that POM would not have made the statement if there was no scientific evidence to support it. (L. Resnick, Tropicana, Dep. at 100-101).

537. Mrs. Resnick did not intend to use Dr. Pantuck's prostate study to communicate to consumers that POM Juice would treat prostate cancer. (L. Resnick, Tr. 218-19).

(b) Stewart Resnick

538. In his Coke deposition, Mr. Resnick testified that POM's marketing did not indicate that POM Juice could "prevent any health conditions." (S. Resnick, Coke, Dep. at 81).

539. By drinking POM Juice, Mr. Resnick does not believe that you can completely prevent getting prostate cancer, but you might be able to slow its recurrence. (S. Resnick, Coke, Dep. at 81-82).

540. During the time the NAD issued its decision, Mr. Resnick did not believe that POM's advertisements claimed that POM Juice prevented or treated heart disease. (S. Resnick, Ocean Spray, Dep. at 135).

541. Assuming the advertisements did communicate to consumers that POM can prevent or delay the onset of prostate cancer, Mr. Resnick is still comfortable with the scientific evidence. (S. Resnick, Ocean Spray, Dep. at 155-156).

542. Although Mr. Resnick testified that POM believes pomegranate juice is beneficial in preventing and treating coronary heart disease, he does not want consumers to share this belief, but rather to look at their science and make up their own mind. (S. Resnick, Tropicana, Dep. at 42-43).

543. POM publishes the results of its research because it believes in the effects of pomegranate juice and people should try to both prevent and cure disease as they can. It is up to the individual to make their own decisions. (S. Resnick, Tropicana, Dep. at 43).

544. POM believes that pomegranate juice is beneficial for prevention and treatment of prostate cancer. (S. Resnick, Tropicana, Dep. at 48).

545. POM is not attempting to influence consumers to believe that pomegranate juice prevents prostate cancer or making a drug claim, but rather letting them make their own decisions. (S. Resnick, Tropicana, Dep. at 52).

546. Mr. Resnick does not believe that POM has made prevention claims, other than for prostate cancer, but this "prevent" really means "prolong" in this context. (S. Resnick, Tropicana, Dep. at 56-57).

547. Mr. Resnick testified that POM's advertisements are not intended to convey the message that they can prevent or treat coronary heart disease. (S. Resnick, Tropicana, Dep. at 58-59).

(c) Matthew Tupper

548. POM would never market a drug without FDA approval, regardless of what the indication. (Tupper, Tr. 992).

549. In POM's advertising, Mr. Tupper testified that POM never claimed that POM Juice can prevent, treat, cure, or mitigate any diseases. (Tupper, Coke, Dep. at 297, 299).

550. Mr. Tupper believes that POM does not claim that POM cures, prevents, or treats disease and has not made any such representations to any office or department of the U.S. government. (Tupper, Ocean Spray, Dep. at 6).

XI. HOW TO EVALUATE THE SCIENCE BEHIND THE CHALLENGED PRODUCTS

A. In Evaluating the Potential Health Benefits of a Natural and Safe Food, the Totality of the Scientific Evidence Should Be Considered, Including Basic Science, Animal Research, and "Pilot" Studies

568. The totality of scientific evidence can and should be considered in determining what constitutes competent and reliable scientific evidence, to prove the health benefits of the Challenged Products, given that: (1) pomegranate juice and its extracts are safe; and (2) no one suggests that pomegranate juice or extracts should be offered in lieu of conventional medical treatment. (Heber, Tr. 1948-49, 2166, 2182; Miller, Tr. 2194; PX0206-0007, 15; Ornish, Tr. 2327-31).

1. Basic and Animal Science Provide Valuable Scientific Information

569. Basic scientific evidence provides powerful scientific support and should not be disregarded. (PX0349 (Burnett, Dep. at 116 -117); PX0352 (Goldstein, Dep. at 118, 133); Goldstein, Tr. 2644; Heber, Tr. 2086, 2149; CX1352 (Heber, Dep. at

243); Heber, Tr. 2086; 2149, 2182; CX1352 (Heber, Dep. at 243); PX192-0011,0037,0038,0047-0055).

570. Animal studies are very informative as it can characterize what's going on at the human level, and provide for some clinical insights. (PX0349 (Burnett, Dep. at 111); PX0352 (Goldstein, Dep. at 122-124); Goldstein, Tr. 2644; Heber, Tr. 2086, 2149; CX1352 (Heber, Dep. at 243); Heber, Tr. 2086; 2149, 2182; CX1352 (Heber, Dep. at 243); PX192-0011,0037,0038,0047-0055).

571. In some instances, basic science is enough to provide sufficient substantiation for a health claim. (PX0206-0010-0011, 0013; Miller Tr. 2194; Heber, Tr. 2086, 2149; CX1352 (Heber, Dep. at 243); Heber, Tr. 2086; 2149, 2182; CX1352 (Heber, Dep. at 243); PX192-0011,0037,0038,0047-0055).

572. Results from animal studies have some potential for benefit of therapy at the human level. (PX0349 (Burnett, Dep. at 112); Burnett, Tr. 2262-63; Heber, Tr. 2086, 2149; CX1352 (Heber, Dep. at 243); Heber, Tr. 2086; 2149, 2182; CX1352 (Heber, Dep. at 243); PX192-0011,0037,0038,0047-0055).

573. Dr. Burnett testified that "there are interventions that [he would] think have some potential benefit on the basis of animal studies or in vitro studies . . . ." (Burnett, Tr. 2262-63).

574. It is an extreme position to state that evidence from in vitro and animal studies should not be considered in determining the therapeutic value of an intervention. (PX0025-0007).

575. While there are limitations to extrapolating from in vitro and animal studies to human studies, it is false to say this research has no value in determining therapeutic efficacy. (PX0025-0007).

576. Complaint Counsel's cardio expert, Dr. Sacks, testified that in vitro studies can be competent and reliable evidence of an agent's effect on a particular mechanism. (Sacks, Tr. 1578; PX0361 (Sacks, Dep. at 123-124)).

577. Dr. Sacks admits there is value in conducting in vitro studies and animal studies because you can isolate mechanisms of action and accomplish toxicity or safety testing. (PX0361 (Sacks, Dep. at 89 -91)).

578. In an animal study, researchers can examine specific mechanisms by taking out their organs and cells, which you cannot do in humans. (PX0361 (Sacks, Dep. at 91).

579. Dr. Sacks considers all levels of science in issuing national guidelines for the prevention or treatment of cardiovascular disease. (PX0361 (Sacks Dep. at 71)).

580. Dr. deKernion testified that the in vitro and animal studies alone showed that pomegranate juice inhibited the growth of prostate cancer cells and actually killed them. (deKernion, Tr. 3044-45, 3120).

581. Dr. Burnett also concluded that the basic scientific evidence alone "has a likely beneficial effect on erectile function" and is sufficient to support the use of pomegranate juice as a potential benefit for vascular blood flow and the vascular health of the penis. (Burnett, Tr. 2255; PX0349 (Burnett, Dep. at 103, 116-118); PX0149-0006-0007).

582. Dr. Heber testified "that the scientific community believes that the research done by Dr. Ornish and Dr. Aviram and Dr. Davidson on the basis of the basic science does provide a significant scientific agreement" that pomegranate helps to reduce the risk of heart disease. (Heber, Tr. 2081).

2. "Pilot" or Small Studies Are Instructive

583. Pilot studies are generally considered by other scientists and clinicians in the scientific community to be perfectly valid, accurate, and reliable studies. (CX1336 (Davidson, Dep. at 232-233); CX1342 (Hill, Dep. at 48, 49, 53); CX1339 (Ornish, Dep. at 23)).

584. For example, although the NAD noted "the small size of the test population utilized" in a POM pilot study conducted by Dr. Aviram, it found that it "was satisfied that the study was sufficiently powered and did not find that the number of participants here rendered the results unreliable." (CX0037_0007).

585. A small number of participants, however, do not weaken the importance of the results, especially if they are in agreement with in vitro, mechanistical studies and in animal models. (CX1358 (Aviram, Dep. at 18)).

586. Dr. Heber testified that "sometimes small studies can be more informative than large studies." (Heber, Tr. 1963).

587. Dr. Aviram considers the term "pilot study" to be positive. (CX1358 (Aviram, Dep. at 17).

588. A study with a small number of participants, however, may make it more difficult to achieve overall statistical significance. (CX1338 (Padma-Nathan, Dep. at 108-109); PX0349 (Burnett, Dep. at 138-141); Ornish, Tr. 2352-53; Liker, Tr. 1884-86).

589. If an under-powered study does achieve statistical significance, however, then the results would be considered to be "fairly dramatic." (Liker, Tr. 1884-85).

590. Nonetheless, a study that is under-powered to achieve statistical significance should not be misconstrued to mean that the study was deficient. (CX1338 (Padma-Nathan, Dep. at 108-109).

591. In Dr. Ornish's Beverage Study Protocol II Study ("BEV II Study"), Dr. Ornish estimated that he would need at least 200 patients to show a statistically significant difference, but due to funding, he was only able to recruit 73 patients, of whom 56 ended up providing pre and post data on. (Ornish, Tr. 2351-52).

592. As a result, Dr. Ornish was able to show an improvement in the carotid artery significant to the 0.13 level as opposed to the 0.15 level. If that degree of change had occurred in the larger number of patients he had initially projected, "it would have been clearly at the 0.05 level or less and it would have been a strong study showing pomegranate juice affected the progression of carotid disease." (Ornish, Tr. 2352-53).

593. With the 73 patients, they showed a definite benefit but did not reach statistical significance. (Ornish, Tr. 2354).

594. Dr. Ornish was confident that had he recruited and tested the number of patients in the protocol he originally planned, he would have reached statistical significance because there is no reason to think the next 127 patients would have been different than the first 73. (Ornish, Tr. 2353-54).

595. Similarly, with regard to the Forest/Padma-Nathan RCT Study, which was a percentage point shy of being statistically significant, a larger number of participants may have helped with achieving overall statistical significance. (CX1338 (Padma-Nathan, Dep. at 108-109); PX0349 (Burnett, Dep. at 138 -141); CX1337 (Forest, Dep. at 76); Goldstein, Tr. 2598-99; Heber, Tr. 2001; CX0908_0001).

596. Further, conducting a trial on healthy participants will necessarily require more participants than a trial conducted on sick participants to show that an intervention has an effect. (CX1345 (deGroof, Dep. at 63-66); CX1336 (Davidson Dep. at 228-229)).

597. This is because if the participants tested are healthy it is more difficult to show an effect in a study on health conditions. (CX1345 (deGroof, Dep. at 65-66)).

598. A benefit or change effected by an intervention on sick patients may be more easily and timely identified. (CX1345 (deGroof, Dep. at 63-66); CX1336 (Davidson Dep. at 228-229)).

B. The Lack of a Statistically Significant Result Does Not Undermine the Value of the Study and Does Not Mean That Experts Cannot Rely Upon the Study to Infer a Casual Link

599. Complaint Counsel argues under-powered studies should be disregarded in their entirety. (CX1287_0012, 0014; CX1289_0004, 0008, 0010, 0012, 0015; CX1291_0012-0013, 0035, 0038; CX1293_0020-0021; Stampfer, Tr. at 710-11; Melman, Tr. at 1092; Eastham, Tr. at 1273; Sacks, Tr. at 1440).

600. "Statistical significance" occurs when the results of a study have a p-value of .05 or less, meaning that the results would occur by chance less than 5 times out of a hundred or that there is a 95 percent probability of validity as opposed to chance. (CX1342 (Hill, Dep. at 100); Ornish, Tr. at 2340)).

601. A "power calculation" occurs when one designs a clinical study to determine the number of participants required to show a statistically significant difference between the treatment group and control group. (Liker,Tr. 1884-85).

602. A study would require fewer participants in order to demonstrate a benefit in a statistically significant manner where that test is expected to produce dramatic results. (Liker, Tr. 1885).

603. Respondents dispute that under-powered studies should be disregarded in their entirety and have presented significant, contrary testimony and evidence that a benefit can be shown from a study without reaching statistical significance. (PX0352 (Goldstein, Dep. at 108-109); Goldstein, Tr. at 2599; PX0189-0013; PX0361 (Sacks, Dep. at 109); CX1350 (Liker, Dep. at 190-191); PX0149-0006; PX0161-0010; Heber, Tr. at 1979; Burnett, Tr. 2255-56; PX0349 (Burnett, Dep. at 138-139)).

604. A lack of statistical significance for a positive result is not proof of the opposite or that pomegranate juice has no beneficial effect. (Sacks, Tr. 1608-09; CX1352 (Heber, Dep. at 218); PX0361 (Sacks, Dep. at 223-224, 230, 238, 243); Goldstein, Tr. 2598-99)).

605. Using statistical significance as the primary gauge in the determination on whether or not pomegranate juice offers a beneficial health property is an arbitrary and unnecessary convention. (Ornish, Tr. at 2340).

606. A study may show clinically significant results even where statistical significance is not reached. (PX0352 (Goldstein, Dep. at 108-109); Goldstein, Tr. at 2599; PX0189-0013; PX0361 (Sacks, Dep. at 109); PX0349 (Burnett, Dep. at 138-139)).

607. While there is no evidence or argument suggesting that a p-value significantly greater than .05 can show a benefit, there is ample evidence presented that slight

variations off this number can still evidence a clinically meaningful benefit that is scientifically supportable. (PX0352 (Goldstein Dep. at 108-109); Goldstein, Tr. 2599; PX0189-0013; PX0361 (Sacks, Dep. at 109); (Sacks, Tr. at 1608-09).

608. A lack of statistically significant data does not mean that there is no reliable basis for inferring a causal link between the consumption of pomegranate juice and a beneficial effect. *Matrixx Initiatives, Inc. v. Siracusano*, 131 S.Ct. 1309, 1319 (2011) ("A lack of statistically significant data does not mean that medical experts have no reliable basis for inferring a causal link between a drug and adverse events."); *Pearson v. Shalala*, 130 F.Supp.2d 105, 130 (D.D.C 2001) ("The mere absence of significant affirmative evidence in support of a particular claim . . . does not translate into negative evidence "against" it.").

609. Evidentiary support for POM's advertising claims should not be so narrowly limited as to include only research whose end result reaches statistical significance. *Matrixx Initiatives, Inc. v. Siracusano*, 131 S. Ct. 1309, 1319-1320 (2011) ("Medical professionals and researchers do not limit the data they consider to the results of randomized clinical trials or to statistically significant evidence."); *Pearson v. Shalala*, 130 F.Supp.2d 105, 130 (D.D.C 2001) ("The mere absence of significant affirmative evidence in support of a particular claim . . . does not translate into negative evidence "against" it.").

C. <u>The Absence of a Statistically Significant or Positive Result Does Not Prove the Opposite Conclusion</u>

610. Complaint Counsel's experts dispute the health benefits of the Challenged Products because Respondents' scientific research did not produce statistically significant changes in certain and/or all of their studies. (Melman, Tr. 1130-31; Sacks, Tr. 1488-89, 1507, 1512-13, 1516-19).

611. Dr. Heber testified, however, that not finding a statistically significant positive result in a study does not prove the negative; or in other words, the absence of evidence is not evidence of absence. (Heber, Tr. 1981; Sacks, Tr. 1608).

612. If a hypothesis is not proven in a particular study, it does not mean the hypothesis is wrong; it just means that it was not proven in that study. (Heber, Tr. 1981).

613. In science, this is called a Type II error which means there may have been a statistically significant difference, but the sample size was not sufficiently large to detect it. (PX0025-0019; CX1339 (Ornish, Dep. at 70-71)).

614. Complaint Counsel's own expert, Dr. Sacks, concedes that the lack of statistical significance for a positive result is <u>not proof of a negative and does not suggest</u>

that pomegranate juice does not cause the intended result. (Sacks, Tr. 1608) (emphasis added).

615. Complaint Counsel allege that Respondents deliberately violated the FTCA by continuing to make false and misleading representations after studies by Dr. Davidson, Dr. Ornish, and others purportedly "showed no significant difference[s]" following the consumption of pomegranate juice. (CX1426_0017-0018).

616. Respondents, however, cannot have deliberately violated the FTCA merely because every study of POM's did not show a benefit, or a benefit by a statistically significant amount, when their scientific research on pomegranate juice and/or its extracts never showed the opposite hypothesis: that pomegranate juice and/or its extracts does not have a positive benefit. (Heber, Tr. 1981; PX0025-0019; Sacks, Tr. 1608-09).

617. Respondents position on this issue is consistent with case law on the subject. *Matrixx Initiatives, Inc. v. Siracusano*, 131 S. Ct. 1309, 1319-1320 (2011) ("Medical professionals and researchers do not limit the data they consider to the results of randomized clinical trials or to statistically significant evidence."); *Pearson v. Shalala*, 130 F.Supp.2d 105, 130 (D.D.C 2001) ("The mere absence of significant affirmative evidence in support of a particular claim . . . does not translate into negative evidence "against" it.").

D. RCTs Are Not Required to Substantiate the Health Benefits of Natural Foods Such as the Challenged Products

618. A harmless pure fruit juice, like pomegranate juice, which is not urged as a substitute for proper medical treatment, does not require RCTs to substantiate health claims. (Miller, Tr. 2194, 2201; PX0206-0010-0015; Heber, Tr. at 1948-50, 2056, 2166; PX0149-0006-0007; Burnett, Tr. 2272-74, 2303; PX0189-0003; Goldstein, Tr. 2600-02, 2611, 2620); deKernion, Tr. 3060; PX0025-0007).

619. The level and rigor of substantiation of a health claim is quite different for a food than it is for the approval of a new drug designed for a specific disease indication. (PX0206-0013-0015).

620. A food, like pomegranate juice, is not a drug or a concoction of other herbs and therefore does not require a RCT. (Miller, Tr. 2198-99).

621. In fact, a RCT is almost unheard of in the food industry. (CX1338 (Padma-Nathan, Dep. at 196); Goldstein, Tr. 2601-02, 2613-14).

622. There is widespread scientific agreement that you look to the totality of science, which does not require RCTs, when determining whether a health claim about a

food, like pomegranate juice, is supported by adequate scientific substantiation. (Miller, Tr. 2194; Heber, Tr. 1948-50, 2056, 2166, 2182; Ornish, Tr. 2327-31).

623. Complaint Counsel admitted in discovery responses that scientific research undertaken without the purpose or goal of obtaining drug approval from the FDA can be used to substantiate health claims. (PX0268-0016).

624. Complaint Counsel's own expert, Professor Stampfer, testified that it is appropriate to rely upon evidence short of RCTs for claims regarding nutrients in food. (Stampfer, Tr. 830; PX0362 (Stampfer, Dep. at 73-79)).

625. Professor Stampfer conceded in trial that scientific evidentiary support for nutritional or dietary claims will necessarily be based on observational studies rather than RCT trials. (Stampfer, Tr. 834; PX0362 (Stampfer, Dep. at 73)).

626. Professor Stampfer noted in deposition "[t]hat observational studies are superior to randomized trials depends on the context . . . . In principle, they would not be, if there is no limitation of resources, and feasibility issues . . . . There are feasibility limitations … in principle, the randomized trials are best, but as a practical matter, we have to rely on observational studies because of all the constraints that we discussed." (PX0362 (Stampfer, Dep. at 73-79)).

627. Professor Stampfer notes that randomized, double-blind, and placebo-controlled clinical trial is not required to conclude a causal link regarding a nutrient and disease. (PX0362 (Stampfer, Dep. at 98)).

628. In his expert report, Professor Stampfer conceded that he "believe[s] that it may be appropriate to use evidence short of randomized clinical trials for crafting public health recommendations regarding nutrient guidelines even when causality cannot be established, because everyone eats and the public should be given advice based on the best evidence available." (CX1293_0029-0030).

629. Professor Stampfer agreed that evidence-based medicine is not restricted to RCTs. (Stampfer, Tr. 837).

2. RCTs Are Sometimes Not Possible or Not Even Better in Evaluating the Health Benefits of a Food or Nutrient

630. Indeed, in a recently published article entitled "*Evidence-based criteria in the nutritional context*," Professor Stampfer opined that the general principles of evidence-based nutrition "can provide a sufficient foundation for establishing nutrient requirements and dietary guidelines in the absence of RCTs for every nutrient and food group." (Stampfer, Tr. 831; see RX5007 Appendix A hereto).

631. In the article, Professor Stampfer stated that "certain features of [evidence-based medicine] seem ill-suited to the nutrition context." (see RX5007 Appendix hereto).

632. Professor Stampfer noted that "[n]utrients are orders of magnitude less expensive than drugs and often exhibit a broader margin between efficacy and toxicity." (see RX5007 Appendix hereto).

633. Professor Stampfer specifically opined that RCTs may not be appropriate for nutrient recommendations to prevent disease, as distinguished from testing drugs used to treat disease. (see RX5007 Appendix hereto).

634. Professor Stampfer noted that some of the differences between the evaluation of drugs and nutrients are: "(i) medical interventions are designed to cure a disease *not* produced by their absence, while nutrients prevent dysfunction that would result from their inadequate intake; (ii) it is usually not plausible to summon clinical equipoise for basic nutrient effects, thus creating ethical impediments to many trials; (iii) drug effects are generally intended to be large with limited scope of action, while nutrient effects are typically polyvalent in scope and, in effect size, are typically within the "noise" range of biological variability; (iv) drug effects are tend to be monotonic, with response varying in proportion to dose, while nutrient effects are often of a sigmoid character, with useful response occurring only across a portion of the intake range; (v) drug effects can be tested against a non-exposed (placebo) contrast group, whereas it is impossible and/or unethical to attempt a zero intake group for nutrients; and (vi) therapeutic drugs are intended to be efficacious within a relatively short term while the impact of nutrients on the reduction of risk of chronic disease may require decades to demonstrate – a difference with significant implications for the feasibility of conducting pertinent RCTs." (see RX5007 Appendix hereto; PX0362 (Stampfer, Dep. at 78)).

635. Professor Stampfer also testified that another difference between nutrients and pharmaceutical drugs is that no exclusive intellectual property rights (like a pharmaceutical patent) will result from a trial. (PX0362 (Stampfer, Dep. at 78)).

636. Other constraints Professor Stampfer testified to include: (1) the difficulty to ensure that large numbers of participants adhere to an altered diet over long-term periods; and (2) that ethical principles do not permit randomizing individuals to diets that may have negative health effects. (PX0362 (Stampfer, Dep. at 75-76)).

637. For all these reasons, Professor Stampher indicated that "it seemed useful to suggest some ways to advance the current approach to [evidence-based nutrition in] ways which better reflect the unique features of nutrients and dietary patterns,

and which also recognize the need to deal with uncertainty in situations in which evidence from RCTs might never be obtained." (see RX5007 Appendix hereto).

638. In trial, Professor Stampfer testified that because of feasibility reasons, RCTs, will often not be reached for diet and nutritional substances. (Stampfer, Tr. 834).

639. In the article, Professor Stampfer further noted that "it is unlikely that RCT evidence could feasibly or appropriately be produced with respect to the role of a nutrient for many nonindex-disease endpoints. Therefore, the majority of the evidence with respect to nutrients and nonindex diseases will continue, of necessity, to be derived from observational studies." (see RX5007 Appendix hereto).

640. Professor Stampfer also testified that in a nutritional context, a hypothesis about disease causation can, rarely, if ever, be directly tested in humans using the RCT design. (Stampfer, Tr. 832-33; PX0362 (Stampfer, Dep. at 73, 98); see RX5007 Appendix hereto).

641. Professor Stampfer opined that because RCT study designs may not be "available" (economically or scientifically) for nutrients, "nutrient related decisions could be made at a level of certainty somewhat below that required for drugs." (see RX5007 Appendix hereto).

642. In the article, Professor Stampfer stated that "it seems clear that requiring RCT-level evidence to answer questions for which the RCT may not be an available study design will surely impede the application of nutrition research to public health issues." (see RX5007 Appendix hereto).

643. Professor Stampfer also noted that some of the intellectual fathers of evidence based medicine "stressed" that evidence based medicine was "'not restricted to randomized trials and meta-analyses.'" (see RX5007 Appendix hereto).

644. Moreover, in the article, Professor Stampfer further stated that "to fail to act in the absence of conclusive RCT evidence increases the risk of forgoing benefits that might have been achieved with little risk and at low cost." (see RX5007 Appendix hereto).

645. Professor Stampfer testified that when there is little risk and little cost involved and a potential benefit, that we should "definitely" make that information available to the public rather than withhold it. (Stampfer, Tr. 838).

646. Dr. Heber agrees with Complaint Counsel's expert, Professor Stampfer, that in dealing with nutrients, RCTs are often infeasible and too expensive and that the drug standard should not be applied. (Heber, Tr. 1950; see RX5007 Appendix hereto).

647. Also, Complaint Counsel's expert, Dr. Sacks, concedes that a causal influence can be demonstrated between an agent and its effect on humans without the use of RCTs. (PX0361 (Sacks, Dep. at 134-135)).

648. Dr. Sacks testified that you don't need RCT trials to test the benefit of food categories that are included in a diet already tested, like the DASH diet, which includes pomegranates. (Sacks, Tr. 1545-46).

649. Dr. Miller testified that if a fruit juice were claiming to prevent prostate cancer, and there was reliable scientific data to support that claim, you could make that claim without a RCT. (Miller, Tr. 2201).

650. Urologists who treat men with erectile health concerns would not require that pomegranate juice be subjected to RCTs before concluding that pomegranate juice has a beneficial effect on preserving erectile function. (PX0149-0006-0007; Burnett, Tr. 2272-74, 2303; PX0189-0003; Goldstein, Tr. 2600-02, 2611, 2620).

651. Urologists who treat men with erectile health concerns would not require that pomegranate juice be subjected to RCTs before concluding that pomegranate juice has a beneficial effect on erectile dysfunction. (Burnett, Tr. 2272-74, 2303).

652. Also, most experts in the field of nutrition consider competent and reliable science to support health claims for pomegranate juice based upon the totality of evidence, which does not necessarily include RCTs. (Heber, Tr. 1948-49, 2166, 2182).

653. In fact, most experts in the field of nutrition believe that RCTs have some significant drawbacks when it comes to the study of nutrient substances like pomegranates. (Heber, Tr. 1948-49).

654. Further, a study is not thrown out because it is does not have a placebo control. (PX0361 (Sacks, Dep. at 137); CX1342 (Hill, Dep. at 131)).

655. According to Dr. Hill, there are two ways to test an intervention. First, in what is called a "pre/post design," the effect of an intervention is measured on a person before and after he/she receives the intervention. In a second design, one group would receive the intervention while another group would receive a placebo. The results of both groups would then be compared. However, no one design is better than the other. (CX1342 (Hill, Dep. at 45)).

656. While there are some advantages to a placebo controlled trial, a pre/post design can be very powerful when you are convinced that you are assessing a steady-state at baseline, and that the differences are attributed to your intervention. (CX1342 (Hill, Dep. at 131)).

3. A Balancing of Factors Favors Disclosure of Potential Health Benefits to the Public in the Absence of RCTs

657. Respondent's expert, Dr. Miller, confirms that when a food product is absolutely a safe, and where the claim or advertisement does not suggest that the product be used as a substitute for conventional medical care or treatment, then it is appropriate to look at the totality of the science (and in some cases, only basic science), and not require only RCTs, to substantiate health claims. (Miller, Tr. 2194, 2201; PX0206-0010-0015; Heber, Tr. at 1948-50, 2056, 2166; PX0149-0006-0007; Burnett, Tr. 2272-74, 2303; PX0189-0003; Goldstein, Tr. 2600-02, 2611, 2620); deKernion, Tr. 3060; PX0025-0007).

(a) Dr. Miller's Qualifications

658. Dr. Miller has been practicing medicine for over 50 years. (Miller, Tr. 2189, 2217).

659. Dr. Miller is a board certified pediatrician and pediatric hematologist/oncologist and is licensed to practice medicine in the state of New Jersey. (PX0206-0001; PX0354 (Miller, Dep. at 16)).

660. Dr. Miller is a Clinical Professor of Pediatrics at Robert Wood Johnson School of Medicine in New Brunswick, New Jersey. (PX0206-0001; PX0354 (Miller, Dep. at 12); Miller, Tr. 2189).

661. Dr. Miller received his AB and MD degrees from Cornell University and completed his residency in Pediatrics and his research fellowship in Pediatric Hematology/Oncology at the Children's Hospital and Harvard Medical School in Boston. (PX0206-0001; Miller, Tr. 2189-90).

662. Dr. Miller was captain in the Air Force as a physician. (Miller, Tr. 2190).

663. Dr. Miller was a Fulbright Scholar and Exchange Registrar, St. Mary's Hospital Medical School and University of London, in London, England. (PX0206-0001).

664. Dr. Miller is an expert in the design of clinical research protocols. (Miller, Tr. 2218).

665. Dr. Millers has, for over 40 years, directed clinical care, education, laboratory and clinical research, and administration, and lead divisions or departments at University of Rochester Medical Center, New York Hospital-Cornell Medical Center, Memorial Sloan Kettering Cancer Center ("MSKCC"), and Northwestern University Medical School. (PX0206-0001; Miller, Tr. 2190).

666. Dr. Miller's major area of clinical and laboratory research when he was in academic medicine was focused on hematopoietic malignancies but clinically, he was directly involved in and cared for patients with both solid tumors and blood cancers. (PX0206-0002).

667. Dr. Miller was the recipient of research grants from the National Cancer Institute, private foundations, and other organizations. (PX0206-0002).

668. Dr. Miller, as Chairman of the Department of Pediatrics at MSKCC, directed one of the largest pediatric oncology/hematology programs in the world and held an endowed chair. (PX0206-0002).

669. Dr. Miller, as Chairman of the Department, was heavily engaged in the entire gamut of Phase I through Phase IV research and in non-clinical studies of mechanisms of action of new agents and the biology and molecular pathology of cancer. (PX0206-0002).

670. Many of those investigational agents are now cornerstones of anticancer therapy. (PX0206-0002).

671. Currently, Dr. Miller is the Global Therapeutic Area Leader of Oncology/Hematology at PAREXEL International, one of the world's leading contract research organizations ("CRO") where he leads a twenty member team of full-time oncologists and hematologists who work in clinical drug development, in cancer and in blood diseases. (PX0206-0001; PX0354 (Miller, Dep. at 12)).

672. CROs, and PAREXEL in particular, manage clinical research trials for the pharmaceutical and biotechnology industries and provide them with scientific and medical consultative services and technical and regulatory guidance to facilitate the successful development of new products to treat patients with a wide variety of illnesses and to facilitate the regulatory approval and marketing authorization of these new medications. (PX0206-0001; PX0354 (Miller, Dep. at 12)).

673. A large number of these clinical trials are focused on targeted therapy for prostate cancer, including men who have undergone prostatectomy or radiation therapy but who have "biochemical recurrence" with a rising PSA level. (PX0206-0004).

674. The objective of these studies is to delay the development of locally recurrent or metastatic disease, not necessarily to prolong survival. (PX0206-0004).

675. Dr. Miller served as Vice-Chairman of the Children's Cancer Group (CCG, now COG), the world's first and largest cooperative group organized to treat children with cancer and discover more effective and safer therapies for them. (PX0206-0002).

676. The marked improvement in the survival and cure of children with cancer is attributable in part to the endeavors of CCG/COG and was accomplished with randomized clinical trials. (PX0206-0002).

677. Randomized double-blind, placebo-controlled studies were not the standard, were not required by the NCI or other regulatory agencies, and were not performed to establish that a new regimen was superior to the old standard. (PX0206-0002).

678. From 1990 to 1996, Dr. Miller served as Associate Medical Director of Cancer Treatment Centers of America ("CTCA") and from 1993 to 1996 was the Scientific Director of CTCA's Cancer Treatment Research Foundation. (PX0206-0002-0003; Miller, Tr. 2191).

679. In both capacities, Dr. Miller was involved actively in designing clinical research protocols for adults with a wide variety of malignancies, including prostate, breast, colorectal, and lung cancer, the four most common cancers in humans. (PX0206-0002-0003; Miller, Tr. 2191).

680. Dr. Miller, as Scientific Director, supervised the clinical research program, chaired the Scientific Advisory Committee of the Institutional Review Board, and was principal investigator for a number of Phase I/II studies of cancer treatments, including the common malignancies mentioned above. (PX0206-0002-0003).

681. These Phase I/II studies included innovative treatment for a wide variety of solid tumors and hematologic malignancies, including new combinations of chemotherapy, immunotherapy, targeted therapy, supportive care to ameliorate the side effects of conventional anticancer therapy, nutritional and psychosocial support, and alternative and complementary medicine. (PX0206-0003).

682. Since joining the pharmaceutical/biotechnology industry, one of Dr. Miller's major responsibilities and activities has been to be familiar with the process of regulatory approval and post-approval fulfillment requirements. (PX0206-0003).

683. Dr. Miller has participated in meetings with the FDA and EMEA at each phase of the drug development process, including pre-IND (Investigational New Drug), protocol submission and review, end Phase II meetings, Special Protocol Assessment (SPA), submission of dossiers for approval of pivotal trials, and presentations to ODAC (Oncology Drug Advisory Committee) that advises the FDA regarding the approval of a new anticancer agent. (PX0206-0003).

684. Dr. Miller has presented progress reports and has participated in special informational advisory meetings with national regulatory authorities in the United Kingdom, Sweden, France, Denmark, and Germany at which specific questions

relating to a drug development strategy or a specific clinical trial are posed by the sponsor and discussed with an expert panel of regulators. (PX0206-0003).

685. Dr. Miller has performed or managed numerous studies in early (Phase I) and later (Phase II through Phase IV) clinical development of new agents for the treatment of cancer and blood diseases. (PX0206-0003).

686. For the past 10 years, Dr. Miller, has been involved in the clinical development of newer anticancer agents called "targeted therapies" because they are directed against receptors, growth factors, or signal transduction pathways that drive the oncogenic genotype and cause cancer cells to behave abnormally and independent of control mechanisms that keep normal cells normal. (PX0206-0003-0004).

687. Dr. Miller in his capacity as Therapeutic Area Leader of Oncology/Hematology at PAREXEL is involved in the entire process of testing and evaluating new agents designed to treat cancer and blood issues.

688. A large number of these clinical trials are focused on targeted therapy of prostate cancer, including mean who have undergone prostatectomy or radiation therapy but who have "biochemical recurrence" with a rising PSA level.

689. The objective of these studies is to delay the development of locally recurrent or metastatic disease, not necessarily to prolong survival.

690. Many of these targeted therapies that give cancer cells a survival advantage, increase their rates of proliferation, multiplication, local spread, and distant metastases, and render them resistant to anticancer therapy. (PX0206-0004).

691. Dr. Miller is currently a member of the American Society of Clinical Oncology, the American Association for Cancer Research, and the American Society of Hematology. (PX0206-0004).

692. Dr. Miller was founding member and past president of the American Society of Pediatric Hematology/Oncology. (PX0206-0004).

693. Dr. Miller was elected to the Society for Pediatric Research, and the American Pediatric Society, societies that recognize one's contributions to pediatric research. (PX0206-0004).

694. Dr. Miller served on the editorial boards of the British Journal of Haematology, the American Journal of Clinical Oncology (Associate Editor, Pediatric Oncology), and the American Journal of Pediatric Hematology/Oncology (co-founder and Associate Editor). (PX0206-0004; Miller, Tr. 2191).

695. Dr. Miller continues to review submitted manuscripts for the British Journal of Hematology. (PX0206-0004).

696. Dr. Miller has authored or co-authored over 300 book chapters, peer-reviewed articles, and abstracts mostly on cancer and blood disorders. (PX0206-0004; Miller, Tr. 2191).

697. Dr. Miller was senior editor to four editions of a classic textbook, *Blood Diseases of Infancy and Childhood*. (PX0206-0004).

698. Dr. Miller is familiar with pharmacology (pharmacokinetics, pharmacodynamics), mechanisms of action, safety, and therapeutic efficacy, including clinical benefit, of most, if not all, agents used to treat or provide supportive care in cancer and blood diseases. (PX0206-0005).

699. This knowledge comes from a professional life devoted to patient care and involvement in the various processes, phases, and stages of clinical drug development. (PX0206-0005).

700. Thus, based on his training, experience, and ongoing clinical activities, Dr. Miller is well qualified to offer expert opinion in this case. (PX0206-0005).

(b) Substantiation for Food Products

701. Dr. Miller offers his expert opinion, on what the standard of substantiation should be, based on his 50 years of practicing medicine and being involved in clinical research both from the academic side as well as from the industry side. (Miller, Tr. 2217).

702. It is Dr. Miller's expert opinion that the critical issue is whether a pure food and its derivative require the same standard of substantiation as a drug. (PX0206-0007).

703. The key question for that determination is safety. (PX0206-0007).

704. If the product is a whole food or a derivative of a whole food and it is obviously safe there should be a cost benefit analysis to determine whether it makes sense to report possible, or probable benefits of consumption and to err on the side of giving more information to the public and medical community, so long as the claim does not suggest (by use of absolutes or in other ways) that an individual should forgo conventional medical care or treatment based on the consumption of the product and the underlying science is valid. (PX0206-0007-0008).

705. It is Dr. Miller's expert opinion that in dealing with a food product, as opposed to a drug, flexibility should be the guiding principle in determining what is required

to comply with the term "sufficient substantiation" of claims of any health benefits. (PX0206-0008).

(c) Substantiation for Dietary Supplements

706. If a dietary supplement is derived from a pure food it should require the same level of substantiation as a food. (Miller, Tr. 2213).

707. In the alternative, if a dietary supplement is "a mixture of fifty different minerals and elements and vitamins" then it is different than a food and require as a different level of substantiation. (Miller, Tr. 2213).

(1) POM's Products Are Safe Whole Food Products

708. Pomegranate juice, (and its derivatives) are whole food products (like broccoli or apples) consisting of pure pomegranate juice made from pressing the whole pomegranate including the husk, flesh and the arils (seeds). (PX0206-0009-0010; PX0354 (Miller, Dep. at 136)).

709. POMx is an extract from the pomegranate. There are no biological or chemical components added to POMx. (PX0206-0010).

710. Man has eaten pomegranates since Biblical times with no reports of serious adverse medical consequences. (PX0206-0010).

711. Pomegranate juice has been used uneventfully in Persian medicine for thousands of years. There is no reason to believe that there is any material risk involved in consuming POM products. (PX0206-0010).

712. The lack of demonstrable health risk supports the appropriateness of a less rigorous requirement for substantiating claims that the products under discussion and at issue are healthy in some way. (PX0206-0010).

713. In Dr. Miller's expert opinion there are essentially no risks in consuming POM Wonderful 100% Juice or POMx. Alternatively virtually every anticancer agent causes adverse events, some of which are serious and life-threatening and require dose reduction or interruption which may cause disease recurrence or induce resistance to the therapy. (PX0206-0010).

714. The above statement is not offered to imply that POM's products can replace or be substitutes for conventional anticancer therapy but merely that the one size or standard does not fit all and that a less rigorous standard for making a health claim for a food is reasonable. (PX0206-0010).

715. However, once the claim is made that a food can replace a proven therapy, that claim should be substantiated by conventional and standard clinical testing, including randomized controlled clinical trials and follow the same arduous pathway of any anticancer agent with similar attributes. (PX0206-0010).

716. It is Dr. Miller's expert opinion that given the obvious safety of pomegranate consumption, and so long as POM's pomegranate products have never been claimed to be a substitute for conventional care or medical therapy, from both a clinical and research perspective, sound basic science is enough to provide sufficient substantiation for a health claim for this natural food product or its derivatives (wherein the consumer is not getting more of some active agent or an additional active agent than what the consumer could find in the fruit). (PX0206-0010-0011; Miller, Tr. 2194).

717. Dr. Miller testified that you don't need to go through the process of clinical testing and randomized trials to establish the safety and efficacy of a food when there is already reliable scientific evidence supporting that. (Miller, Tr. 2205-06).

(2) POM Does Not Claim That Its Products Are A Substitute For Medical Treatment And POM's Has Valid Science Supporting Its Health Claims

718. The science should be valid and peer-reviewed, and whether clinical science is necessary to substantiate a particular claim would vary according to the strengths of the basic science and the particular claim. (PX0206-0011).

719. For example, in the area of prostate cancer, an unqualified claim that the product has be shown to slow the progression of PSA doubling times should actually be supported by clinical evidence. (PX0206-0011).

720. A qualified claim that POM products may be effective for the treatment or prevention of prostate cancer (or reduce the risks of getting the disease) is reasonable if there is no suggestion that pomegranate alone can 1) absolutely prevent the disease; or 2) that it can serve as a replacement, as distinguished from an adjunct therapy (like exercise, vitamins, etc), in the treatment of a disease. (PX0206-0011).

721. A reasonable oncologist or urologist or any other treating physician would not use POM products instead of any approved drug, biological agent, or vaccine that has been approved to treat a given stage of prostate cancer (for those patients where drugs are an option) because the evidence for these specific indications is not available to support that level of claim or use of pomegranate. (PX0206-0011).

722. However, there may be some subcategory of patients, who do not have many or any alternatives, and for them a clinician may reasonably decide to recommend, among other things, the consumption of pomegranate. (PX0206-0011).

723. Based on the strength of the reported research, POM products, for example, have demonstrable beneficial effects that are relevant to carcinogenesis and cancer prevention. (PX0206-0011).

724. Critically important would be the demonstration that POM products did not enhance prostate cancer cell growth and progression of disease. (PX0206-0011-0012).

725. Thus, POM would meet the test of "primum non nocere" or first, do no harm. And there is solid evidence that should meet any "reasonable" standard, and that the products may do good, especially in prostate cancer. (PX0206-0012).

(3) A Cost/Benefit Analysis Supports a Finding That It Is in The Public's Best Interest to Be Informed About The Health Benefits of POM's Products

726. Practicing physicians, who have firsthand knowledge regarding the needs and risks faced by their patients, are in the best position to conduct the cost/benefit analysis. (PX0206-0008).

727. Dr. Miller firmly believes that the public should be aware of potentially beneficial foods that have a salutary effect on health and cause no harm. (PX0206-0012).

728. Informing the public empowers them to add a potentially beneficial, harmless food to their diet that may prevent prostate cancer (and other disorders). (PX0206-0012).

729. Dr. Miller notes that public health and other agencies urge the populace to eat fruits and vegetables because of their beneficial effects. (PX0206-0012).

730. Complaint Counsels' expert Professor Stampfer went as far as to say that it is appropriate to use evidence short of randomized clinical trials for crafting public health recommendations regarding nutrient guidelines even when causality cannot be established because everyone eats and the public has a right to be given advice based on the best evidence available. (PX0300 (Stampfer, Dep. at 29-30)).

731. When a specific food like POM products have been subjected to rigorous testing and consistently demonstrate potent anticarcinogenic properties, harm can result from recommending its use in men because it may prevent prostate cancer. (PX0206-0012).

732. More likely than not, if POM products are effective in men with biochemical recurrence, it may prevent prostate cancer in an otherwise healthy but at risk individual. (PX0206-0012).

733. It is Dr. Miller's expert opinion that claiming that a fruit juice is good for prostate health or that it may reduce the risk of developing prostate cancer is much more limited in scope than suggesting that it should be used to treat active prostate cancer, or that it be used instead of conventional therapy. (PX0206-0012).

734. Health professionals are or should be strong advocates of healthy life style practices just as they are or should be to warn the public about unhealthy practices (cigarettes, alcohol, unprotected sex, obesity). (PX0206-0013).

735. Dr. Miller states that claims publicizing general health benefits ("fish oils lower your cholesterol and may protect your heart") or even more specific health benefits ("broccoli may protect one from colorectal cancer")" are rarely, if ever based upon or substantiated by an equivalent body of basic science or non-clinical and clinical data that are available now and support the anticancer activity of POM products. (PX0206-0013).

736. In Dr. Miller's expert opinion few scientists or clinicians would deny, if presented with the published data, that POM is beneficial because of its inhibitory effect on such important mechanisms as oxidative stress, inflammation, apoptosis, signal transduction, cell proliferation, and angiogenesis. (PX0206-0013).

737. Dr. Miller's opinied that retrospective or prospective observational cohort or case-control studies are not feasible to study the benefits of a food. (PX0206-0014).

738. A double-blind, placebo controlled trial evaluating POM products as a prostate cancer protective agents would take decades and thousands of patients and would have to control for other naturally occurring, dietary antioxidants, anti-inflammatory, and anticancer agents as well as life-style activities (e.g. exercise, smoking, alcohol use, just to mention a few), genetic predisposition, racial and ethnic factors, benign prostatic hypertrophy, and other factors that might have an effect on carcinogenesis of prostate cancer. (PX0206-0014).

739. A food is not patentable and it is not reasonable to require the maker of a potentially beneficial foodstuff to conduct a prohibitively expensive RCT to claim that it is beneficial to health. (PX0206-0016; Heber, Tr. 1949).

740. Even Complaint Counsels' expert, Professor Stampfer, said that observational studies are often superior as the basis for nutritional recommendations because large RCTs are impractical for assessing nutritional benefits. (PX0362 (Stampfer, Dep. at 74-79)).

741. Yet few scientists or clinicians would deny, if presented with the published data, that POM is beneficial because of its inhibitory effect on key oncogenic mechanisms defined above. (PX0206-0014).

742. In fact, Dr. Miller states, that based on the solid nonclinical data, there should be no need to conduct two randomized well controlled trials to publicize that drinking POM products might decrease one's risk of developing prostate cancer. (PX0206-0014).

743. Such a statement is in the public's best interest and empowers individuals to take control of their own health by drinking and eating healthful foods, engaging in healthy activities, and avoiding potentially or known harmful ones. (PX0206-0014-0015).

(4) Dr. Miller Concludes That Basic Science Can Constitute Sufficient Substantiation for Health Claims For a Whole Food Product or Its Derivative and RCTs are not Necessarily Required

744. It is Dr. Miller's opinion that the consensus among competent and reliable scientists is that if you are talking a pure food product or its derivative, and that product is not offered as a substitute for proper medical treatment, you look may rely on basic science and RCTs are not required for substantiation. (Miller, Tr. 2194; PX0206-0007, 0015).

E. Public Health Recommendations Are Made and Clinical Practices Followed In the Absence of RCTs

745. Not surprisingly, much of what physicians provide patients in their clinical practices has not been proven to be beneficial in RCTs. (PX0025-0007; Sacks, Tr. 1559; PX0361 (Sacks Dep. at 111); CX1341 (Pantuck, Dep. at 276-277)).

746. For example, Complaint Counsel's own expert, Dr. Eastham, admitted he has performed over 200 radical prostatectomies per year for a number of years before there were any RCTs showing that it worked. (Eastham Tr. 1331-32; PX0358 (Eastham, Dep. at 154-155)).

747. Dr. Eastham performed these radical operations without RCTs despite the fact that the side-effects of this operation are significant and include impotence, incontinence, bleeding, embolisms, infection plus risks of general anesthetic. (Eastham, Tr. 1331-32).

748. Also, Dr. Pantuck stated that clinicians remove kidneys without a RCT showing the benefits of nephrectomy. (CX1341 (Pantuck, Dep. at 276-277)).

749. Dr. Ornish also notes that randomized controlled trials have shown that angioplasties and stents do not prevent heart attacks or prolong life, yet the number of these procedures performed is greater than ever. (PX0025-0007).

750. Dr. Miller indicated that although health professionals, third party insurance carriers, and health related agencies highly recommend that eating 5 portions of fresh fruits and vegetables may prevent cancer, it is accepted without requiring controlled non-clinical or clinical trials. (PX0206-0012-0013).

751. Further, Complaint Counsel's experts, Professor Stampfer and Dr. Sacks, admitted that they have made public health recommendations that were not supported by RCTs. (Stampfer, Tr. at 810, 813-14; PX0300 (Stampfer, Dep. at 173); PX0361 (Sacks, Dep. at 35-38, 130-131)).

752. Moreover, RCTs were not the standard nor required by the National Cancer Institute or other regulatory agencies. (PX0206-0002).

753. In fact, the success in treating children with cancer at the National Cancer Institute was achieved without RCTs. (PX0206-0002).

754. Also, certain research agencies of the United States government and internationally recognized academic institutions have participated in and publicized their research addressing some of the very same health benefit topics and diseases that Respondents have also explored using in vitro, animal, and small-scale human models as the bases for their scientific inquiries. (PX0301-PX0324).

755. For example, the Agricultural Research Service, which is the U.S. Department of Agriculture's chief scientific research agency, has investigated and funded research on fruits, vegetables, and nuts and publicized studies examining various foods and their potential impact on various human ailments based on in vitro, animal, and small-scale human models. (PX0301-PX0318).

756. Similarly, the National Institutes of Health ("NIH"), which is a component of the U.S. Department of Health and Human Services, has provided, and continues to provide, grants and funding to support basic, clinical and translational medical research, including for research pertaining to pomegranates, in order "to seek fundamental knowledge about the nature and behavior of living systems and the application of that knowledge to enhance health, lengthen life, and reduce the burdens of illness and disability." (PX0392-PX0418; http://www.nih.gov/about/ and http://www.nih.gov/about/mission.htm (last visited, January 8, 2012).

757. In many instances, even the FDA has approved pharmaceutical products without requiring the type of rigorous clinical trials the FTC would require of a safe food product. (PX0206-0008-0009).

758. Dr. Miller states that many cancer agents now used in clinical practice in the US and around the world were approved in open-label randomized controlled trials without a placebo control arm. (PX0206-0008).

759. The following table provides a few examples of new anticancer agents and their Phase III pivotal study design that led to regulatory approval in the US (FDA) and in Europe (EMEA) which were done without a placebo control arm. (PX0206-0008).

Indication [subtype, line]	Agent (class of agent)	Randomized Study Design
NHL, [diffuse large B-cell, 1st]	Rituximab (anti-CD20 monoclonal antibody)	R-CHOP vs CHOP
NHL, [follicular, 1st]	Rituximab	R-CVP vs CVP
NHL [indolent, relapsed]	Rituximab	Monotherapy
CLL [1st]	Rituximab	FCR vs FC
Pancreatic cancer [1st]	Gemcitabine	Gemcitabine vs 5-FU
Prostate cancer [stage 4, HRPC, 1st line]	Docetaxel	Docetaxel + prednisone vs mitoxantrone + prednisone
Renal cell carcinoma [stage 4, 2nd line)	Sunitinib	Sunitinib vs IL-2
NSCLC [2nd line, IIIb-IV]	Pemetrexed	Pemetrexed vs docetaxel
CRC [stage IV, 1st line]	Bevacizumab	Bevacizumab + FOLFOX vs FOLFOX

NHL=non-Hodgkin lymphoma; CLL=chronic lymphocytic leukemia; HRPC=hormone refractory prostate cancer; NSCLC=non small cell lung cancer; CRC=colorectal cancer.

760. To reach Phase III, successful Phase I and Phase II studies were also required, but rarely if ever are RCTs trials done in this early stage of drug development. (PX0206-0009; PX0354 (Miller Dep. at 0025-0026)).

761. In addition, from 1973 through 2006, the FDA approved 31 oncology drugs without a randomized trial using the Accelerated Approval and Priority Review Program ("Fast Track Program"). (http://jco.ascopubs.org/content/27/36/6243.abstract (last visited, January 8, 2012); http://www.fda.gov/drugs/resourcesforyou/consumers/ucm143534.htm (last visited, January 8, 2012) (FDA guidance explaining the Fast Track Program); http://www.fda.gov/forconsumers/byaudience/forpatientadvocates/speedingaccesstoimportantnewtherapies/ucm128291.htm (last visited, January 8, 2012).

(explaining that "Fast Track" drugs may receive approval based on "an effect on a surrogate, or substitute endpoint reasonably likely to predict clinical benefit"); 21 CFR § 314.510 (allowing approval based on a surrogate endpoint or on an effect on a clinical endpoint other than survival or irreversible morbidity).

XII. THE SCIENCE BEHIND THE NUTRITIONAL BENEFITS OF POMEGRANATE JUICE AND EXTRACTS

A. The Nutritional Benefits of the Challenged Products Are Associated with Their High Antioxidant Content and Ability to Neutralize Free Radicals

1. Free Radicals Play an Integral Role in Cardiovascular Disease, Cancer and Other Diseases Caused by Oxidative Stress

745. Normal cellular metabolism or oxidation produces as its by-product various highly reactive molecules, collectively termed "oxidants" or "free radicals." (PX0192-0019; Heber, Tr. 1956).

746. Free radicals are also produced in response to environmental stressor such as air pollution, tobacco smoke, chemicals, stress, ultraviolet light or other forms of ionizing radiation. (CX1293_0010; Stampfer, Tr. 727; PX0192-0020).

747. Free radicals can cause oxidation which initiates a series of damaging effects on tissue and cellular components, including DNA, proteins, cell membranes, carbohydrates and fats. (Heber, Tr. 1956; PX0192-0018-0019; Stampfer, Tr. 727; CX1293_0010).

748. Free radicals and oxidative stress have been implicated in a wide variety of degenerative processes and diseases, including aging and age-related diseases like cancer and cardiovascular disease. (Heber, Tr. 2185; PX0192-0019-0020; Stampfer, Tr. 727).

749. Free radicals are one of the key mechanisms that promote cancer. (Heber, Tr. 1957).

750. Free radicals are one of the key mechanisms that operate to create the cellular basis of atherosclerosis, the buildup of plaque in arteries. This is accomplished by the oxidation of LDL cholesterol that accelerates the inflammatory response which in turns leads to the development of atherosclerotic plaque. (Heber, Tr. 1957; CX1293_0010).

751. Humans are constantly exposed to oxidative stress caused by oxidation. (PX0192-0019).

752. Although the body has many mechanisms to prevent and repair free radical damage, the human body cannot eliminate all oxidative damage by relying on its own antioxidant defenses. (Heber, Tr. 2185; PX0192-0019-0020; Stampfer, Tr. 727; CX1293_0010).

753. When free radical levels rise significantly, the body's defenses can become overwhelmed and cellular damage can occur, leading to incidences of cardiovascular disease and cancer. (Heber, Tr. 2185; PX0192-0019-0020; Stampfer, Tr. 727; CX1293_0010).

754. Free radicals play an important role in cardiovascular disease, cancer and other disease caused by oxidative stress.

2. Antioxidants Protect Cells Against the Effects of Free Radicals

755. Antioxidants neutralize free radicals by inhibiting oxidation at a molecular, cellular and organ level. (PX0192-0015, 0023; CX1293_0010; Stampfer, Tr. 728).

756. The word "antioxidant" is an umbrella term that includes many chemicals which have the power to oppose the effects of oxidation. (PX0192-0023; Heber, Tr. 2003; Stampfer, Tr. 727-729).

757. Antioxidants either help the body repair the damage caused by oxidation or they prevent oxidation by absorbing the energy of free radicals. (Stampfer, Tr. 727; PX0192-0023).

758. The human body has evolved a large array of endogenous antioxidant defenses against oxidative stress, including antioxidant enzymes such as superoxide dismutase, catalase, and various peroxides, as well as the ability to use small molecules with antioxidant activity such as glutathione, the hormone melatonin, and uric acid. (PX0192-0020; Stampfer, Tr. 728-9).

759. Antioxidation is not a single "druggable target," but rather is a physiologically important variable characterizing a diet that is either rich or poor in antioxidant intake. Consuming foods with increased antioxidant potency (which also have varied physiological effects) promotes overall health in a number of organ systems by different mechanisms. (PX0192-0022).

760. Although there is some dispute about the extent of the benefits, it is well accepted within the scientific community that antioxidants are impactful to the body in a beneficial way. (Heber, Tr. 1956, 2003; PX0192-0015, 16-18; Stampfer, Tr. 728-29).

761. Consumption of antioxidant-rich foods is associated with a healthy heart and a reduced risk of cancer. (PX0192).

762. The few studies that have found antioxidants ineffective for improving human health have generally involved Vitamin C and Vitamin E supplements, not polyphenol antioxidants. (Heber, Tr. 2002-2003; CX1293_0012-0015).

3. Research Agencies of the United States Government Recognize the Health Benefits of Antioxidants in Fighting Free Radicals

763. A Center for Disease Control ("CDC") webpage about the dangers of smoking states that the "[t]he body produces antioxidants to help repair damaged cells." (http://www.cdc.gov/tobacco/data_statistics/sgr/2004/highlights/harm/).

764. A 2004 Surgeon General's Report, located on the CDC website, recognizes the healing properties of antioxidants. The webpage states "Normally, your body fights damaging oxygen molecules with antioxidants. It fights the destructive enzymes with defensive enzymes." (http://www.cdc.gov/tobacco/data_statistics/sgr/2004/pdfs/whatitmeanstoyou.pdf).

765. Several CDC website pages dealing with eye health recommend a diet rich in antioxidants. One such webpage states, "Additional modifiable factors that might lend themselves to improved overall ocular health include a diet rich in antioxidants…" (http://www.cdc.gov/visionhealth/basic_information/lifespan.htm.).

766. One CDC webpage lists the study "Chemoprotection by phenolic antioxidants: Inhibition of tumor mecrosis factor alpha induction in macrophages" as a winner of the 2003 Alice Hamilton Award. This study explores the effect of antioxidants on toxicity and cancer. (http://www.cdc.gov/niosh/awards/hamilton/aliceabs03.html).

767. The National Institute of Health ("NIH") website has a page dedicated to antioxidants. The NIH defines antioxidants as "substances that may protect your cells against the effects of free radicals. Free radicals are molecules produced when your body breaks down food, or by environmental exposures like tobacco smoke and radiation. Free radicals can damage cells, and may play a role in heart disease, cancer and other diseases." (http://www.nlm.nih.gov/medlineplus/antioxidants.html).

768. When clicking on the Start Here link of the previous webpage, the following webpage states that "Antioxidants are substances that may prevent potentially disease-producing cell damage that can result from natural bodily processes and

from exposure to certain chemicals." (http://nccam.nih.gov/health/antioxidants/introduction.htm).

769. The NIH website has a webpage that links to 548 open studies regarding antioxidants. (http://clinicaltrials.gov/search/open/intervention=antioxidants).

770. The National Cancer Institute page of the NIH website contains an antioxidant fact page which states: "Antioxidants are substances that may protect cells from the damage caused by unstable molecules known as free radicals. Free radical damage may lead to cancer. Antioxidants interact with and stabilize free radicals and may prevent some of the damage free radicals might otherwise cause." The webpage goes on to say "Considerable laboratory evidence from chemical, cell culture, and animal studies indicates that antioxidants may slow or possibly prevent the development of cancer." (http://www.cancer.gov/cancertopics/factsheet/prevention/antioxidants).

771. The Agricultural Research Service ("ARS") website features a webpage stating that the pomegranate is "good for you" because it is "high in healthful antioxidants." (PX0306).

772. An ARS webpage entitled "Eating is Stressful, But Antioxidants Can Help" states that antioxidants can help neutralize free radicals. The article goes on to say that "omitting antioxidant rich foods from meals could lead to cellular damage by free radicals. Such damage is thought to increase risk of atherosclerosis, cancer and other diseases." (PX0308).

773. An ARS webpage displays a scientific study that states that an antioxidant compound in oats "may help prevent the buildup of plaque in arteries and thus lessen the risk of heart disease." (PX0316).

774. Another ARS webpage discusses the beneficial antioxidant effects of eating almonds. (PX0318).

775. The ARS website features a study that explores antioxidants' role in protection against colon cancer. (http://www.ars.usda.gov/research/publications/publications.htm?seq_no_115=185492).

776. The ARS website contains pages about the high antioxidant content of different food such as strawberries, cocoa, and peanut plants. (PX0309).

777. The FDA has issued a Small Entity Compliance Guide in pursuant to section 212 of the Small Business Regulatory Enforcement Fairness Act (Public Law 104-121) that establishes guidelines for making antioxidant nutrient claims.

(http://www.fda.gov/Food/GuidanceComplianceRegulatoryInformation/GuidanceDocuments/FoodLabelingNutrition/ucm063064.htm).

778. The United States Department of Agriculture's website contains pages that feature links to articles discussing the health benefits of antioxidants, including, among other pages, (http://riley.nal.usda.gov/nal_display/index.php?info_center=11&tax_level=2&tax_subject=388&level3_id=0&level4_id=0&level5_id=0&topic_id=1668&&placement_default=0; and http://fnic.nal.usda.gov/nal_display/index.php?info_center=4&tax_level=3&tax_subject=358&topic_id=1610&level3_id=5947&level4_id=0&level5_id=0&placement_default=0).

779. Research agencies of the United States Government recognize the health benefits of antioxidants in fighting free radicals.

4. The Challenged Products Contain Potent Antioxidants that Fight Free Radicals

780. Pomegranate juice is high in polyphenol antioxidants. (PX0192).

781. The consumption of pomegranate juice and extracts containing polyphenols contribute to overall antioxidant intake in the diet. (PX0192-0014; CX1352 (Heber, Dep. at 61)).

782. The antioxidant properties of pomegranates are well understood to be derived from the polyphenols found in the fruit. (PX0192-0016; PX0059; Burnett, Tr. 2290).

783. The Challenged Products contain a diverse, complex mixture of antioxidant polyphenols, including hydrolyzable tannins, flavonols, anthocyanins and acids. The hydrolysable tannins include, among others, punicalagins, ellagitannins, punicalins and gallotannins. The acids include ellagic acid, gallic acid and gallagic acid. (PX0192-0016, 0024; PX0074-0002; Heber, Tr. 2001-2002).

784. Punicalagin is a unique compound and is the largest known polyphenol antioxidant molecule in any fruit or vegetable. (PX0192-0021).

785. The Challenged Products contain among the most potent naturally occurring polyphenol antioxidants found in foods. (PX0192-0021, 0024; PX0189-0011; Goldstein, Tr. 2594-2595; Heber, Tr. 1967; PX484; Burnett, Tr. 2254-2255; PX0058; (PX0021-0001).

786. Laboratory examination has demonstrated POM Juice had more polyphenol antioxidants and a higher level of antioxidant activity or potency than the juices of

concord grapes, blueberries and acai. (PX0192-0020-0023; CX1352 (Heber, Dep. at 136); PX0098_0001; PX0097-0002; PX0021-0001).

787. Laboratory examination has demonstrated that POM Juice had more polyphenol antioxidants and a higher level of antioxidant activity or potency than red wine or green tea. (PX0192-0020-0023; CX1352 (Heber, Dep. at 136); PX0098_0001; PX0097-0001).

788. Several *in vitro* studies demonstrated that the Challenged Products reduces the oxidation of LDL better than any other food or beverage tested. (PX0021-0001).

789. Several human clinical trials demonstrated that the consumption of POM Juice reduces oxidation of LDL cholesterol. (PX0192-0035-0036; Heber, Tr. 2113).

790. Several animal studies demonstrated that the consumption of POM Juice reduces both early and late stage plaque development. (PX0192-0035).

791. The polyphenols in pomegranate juice have antioxidant effects such as inhibiting the oxidation of LDL cholesterol. (Heber, Tr. 2113; PX0192-0035-0036).

792. Pomegranate juice has antioxidant and anti-atherosclerotic effects attributable to its high content of polyphenols including ellagitannins. (PX0075-0001, 0005).

793. The antioxidant potency of POMx has been measured by Brunswick Laboratories, and the results were reported as 2,571 total oxygen radical absorbance capacity ("ORAC"), 6,976 ferric reducing antioxidant power ("FRAP"), 9,824 Trolox equivalent antioxidant capacity ("TEAC"), and 9,506 free radical scavenging capacity by 2,2-diphenyl-1-picrylhydrazyl ("DPPH"), which was exceptionally high relative to other types of dietary supplements. (PX0192-0024).

794. Hydrolyzable tannins, rather than anthocyanins, are the major compounds contributing to the high antioxidant activity found in POM Juice, POMx Pills and POMx Liquid. (PX0192-0024; Heber, Tr. 2002, 2186; PX0073-0004; PX0107-0005; PX0199_0001).

795. The potent antioxidant effects measured for POMx are consistent with scientific research finding that hydrolysable tannins like punicalagin, rather than anthocyanins, are the major active antioxidant component of pomegranates. (PX0192-0024; PX0107-0005).

796. There is no significant correlation between anthocyanin levels and antioxidant activity. (Heber, Tr. 2186).

Seeram NP, Aviram M, Zhang Y, Henning SM, Feng L, Dreher M, Heber D, "*Comparison of antioxidant potency of commonly-consumed*

***polyphenol rich beverages in the United States*" J. Agric. Food Chem. 2008; 56:1415-22**

797. In 2008, in a study entitled "Comparison of antioxidant potency of commonly-consumed polyphenol rich beverages in the United States," by Seeram NP, Aviram M, Zhang Y, Henning SM, Feng L, Dreher M, Heber D, J. Agric. Food Chem. 2008; 56:1415-22, Dr. Heber and his colleagues examined the antioxidant potency of a number of commonly-consumed polyphenol rich beverages, including: apple juice (3), acai juice (3), black cherry juice (3), blueberry juice (3), cranberry juice (3), Concord grape juice (3), orange juice (3), red wines (3), and iced tea beverages. (PX0192-0023; PX0098_0001).

798. The antioxidant potency of the various juices were measured using TEAC, ORAC, DPPH, and FRAP; a test of antioxidant functionality (inhibition of low-density lipoprotein oxidation by peroxides and malondialdehyde); and an evaluation of the total polyphenol content. (PX0192-0023; PX0098_0001).

799. Pomegranate juice had the greatest antioxidant potency composite index among the beverages tested, and was at least 20% higher than the other beverages. (PX0192-0023; PX0098_0001).

800. This study demonstrates that pomegranate juice has higher antioxidant potency than apple juice, acai juice, black cherry juice, blueberry juice, cranberry juice, Concord grape juice, orange juice, red wine and iced tea beverages.

Gil M., Tomas-Barberan F, Hess-Pierce B, Holcroft D, Kader A, "*Antioxidant activity of pomegranate juice and its relationship with phenolic composition and processing*" J. Agric. Food Chem. 2000, 48:4581-4589

801. In 2000, in a study entitled "Antioxidant Activity of Pomegranate Juice and Its Relationship with Phenolic Composition and Processing," by Gil M., Tomas-Barberan F, Hess-Pierce B, Holcroft D, Kader A, J. Agric. Food Chem. 2000, 48:4581-4589, Dr. Gil and her colleagues examined the antioxidant activity of pomegranate juice in comparison with red wine and a green tea infusion. (PX0097-0001).

802. The study applied four methods to test the antioxidant activity of pomegranate juices; free radical scavenging capacity by 2,2'-azinobis (3-ethylbenzothiazoline)-6-sulfonic acid ("ABTS"), free radical scavenging capacity by DPPH, free radical scavenging by N,N-dimethyl-p-phenylenediamine ("DMPD") and FRAP, and then compared this to the antioxidant activity of red wine and a green tea infusion. (PX0097-0001).

803. Commercial pomegranate juices showed an antioxidant activity three times higher than those of red wine and green tea. Antioxidant activity was also higher in commercial juices extracted from whole pomegranates (such as POM Juice) than in experimental pomegranate juice obtained from arils only. (PX0097-0001).

804. This study demonstrates that POM Juice has higher antioxidant potency that red wine, green tea and experimental pomegranate juices.

Rosenblat M, Volkove N, Attias, J, Mahamid R, Aviram M, *"Consumption of polyphenolic-rich beverages (mostly pomegranate and black currant juices) by healthy subjects for a short term increased serum antioxidant status, and the serum's ability to attenuate macrophage cholesterol accumulation*" Food Function, 2010, 1:99-109

805. In 2010, in a study entitled "Consumption of polyphenolic-rich beverages (mostly pomegranate and black currant juices) by healthy subjects for a short term increased serum antioxidant status, and the serum's ability to attenuate macrophage cholesterol accumulation," by Rosenblat M, Volkove N, Attias, J, Mahamid R, Aviram M, Food Function, 2010, 1:99-109, Dr. Aviram and his colleagues compared the polyphenol content of 35 beverages, *in vitro*, then selected the top five and examined their effect on antioxidant status in health humans., *in vivo*. (PX0021-0001).

806. The *in vitro* study beverages tested included, among others, several brands of beverages as follows: pomegranate juice, Concord grape juice, black cherry juice, black currant juice and blends, blueberry juice, yumberry, acai juice blends, "superfruit" blends, green tea and red wines. The *in vivo* study tested five polyphenol rich-beverages; POM Juice, acai juice blend, Concord grape juice, black currant juice and red wine. (PX0021-0001).

807. Dr. Aviram found that after short-term consumption the POM Juice and 100% black currant juices were the most potent antioxidants *in vitro* and also had the greatest impact on measures of antioxidant status in humans. (PX0021-0001).

808. The antioxidant potency and activity was measured by total polyphenol concentration, free radical scavenging capacity, ability to inhibit LDL oxidation or decrease serum susceptibility to AAPH-induced lipid peroxidation, ability to increase paraoxonase 1 ("PON1"), and serum biochemical parameters and basal serum oxidative status. (PX0021-0001).

809. This study demonstrates that POM Juice higher antioxidant potency *in vitro* and the greatest antioxidant activity than the tested beverages.

810. In sum, the expert opinions and affirmative evidence presented by Respondents prove that the antioxidants in the Challenged Products protect cells against the free radicals which is beneficial to cardiovascular and erectile health and cancer prevention.

5. Complaint Counsel Failed to Rebut Respondents' Evidence on the Benefits of Antioxidants in Fighting Free Radicals; to the Contrary, Complaint Counsel's Experts Provided Opinions that Supported Respondents' Evidence on Antioxidants

811. Complaint Counsel have presented no expert opinion or competent affirmative evidence rebutting Respondents' evidence that antioxidants inhibit the oxidizing effects of free radicals. (CX1293; PX0362 (Stampfer, Dep. at 1-205); Stampfer, Tr. 689-885; CX1291; PX0361 (Sacks, Dep. at 1-273); Sacks, Tr. 1410-1625; CX1289; PX0360 (Melman, Dep. at 1-141); Melman, Tr. 1069-1197; CX1287; PX0358 (Eastham, Dep. at 1-158); Eastham, Tr. 1204-1351; CX1295; PX0357 (Stewart, Dep. at 1-194); Stewart, Tr. 3158-3242; PX0359 (Mazis, Dep. 1-242); Mazis, Tr. 2651-2761).

812. Complaint Counsel have presented no expert opinion or competent affirmative evidence rebutting Respondents' evidence that free radicals play a role in cardiovascular disease and cancer. (CX1293; PX0362 (Stampfer, Dep. at 1-205); Stampfer, Tr. 689-885; CX1291; PX0361 (Sacks, Dep. at 1-273); Sacks, Tr. 1410-1625; CX1289; PX0360 (Melman, Dep. at 1-141); Melman, Tr. 1069-1197; CX1287; PX0358 (Eastham, Dep. at 1-158); Eastham, Tr. 1204-1351; CX1295; PX0357 (Stewart, Dep. at 1-194); Stewart, Tr. 3158-3242; PX0359 (Mazis, Dep. 1-242); Mazis, Tr. 2651-2761).

813. Complaint Counsel have presented no expert opinion or competent affirmative evidence rebutting Respondents' evidence concerning the antioxidant activity or potency of the Challenged Products. (CX1293; PX0362 (Stampfer, Dep. at 1-205); Stampfer, Tr. 689-885; CX1291; PX0361 (Sacks, Dep. at 1-273); Sacks, Tr. 1410-1625; CX1289; PX0360 (Melman, Dep. at 1-141); Melman, Tr. 1069-1197; CX1287; PX0358 (Eastham, Dep. at 1-158); Eastham, Tr. 1204-1351; CX1295; PX0357 (Stewart, Dep. at 1-194); Stewart, Tr. 3158-3242; PX0359 (Mazis, Dep. 1-242); Mazis, Tr. 2651-2761).

814. Complaint Counsel have presented no expert opinion or competent affirmative evidence rebutting Respondents' evidence that the Challenged Products contain more antioxidants than comparative fruit juices or supplements. (CX1293; PX0362 (Stampfer, Dep. at 1-205); Stampfer, Tr. 689-885; CX1291; PX0361 (Sacks, Dep. at 1-273); Sacks, Tr. 1410-1625; CX1289; PX0360 (Melman, Dep. at 1-141); Melman, Tr. 1069-1197; CX1287; PX0358 (Eastham, Dep. at 1-158);

Eastham, Tr. 1204-1351; CX1295; PX0357 (Stewart, Dep. at 1-194); Stewart, Tr. 3158-3242; PX0359 (Mazis, Dep. 1-242); Mazis, Tr. 2651-2761).

815. Complaint Counsel's expert, Professor Meir Stampfer, offered no expert opinion that the Challenged Products do not provide nutritional benefits in regards to cardiovascular, prostate and erectile health. Rather he merely opines that based on the materials Complaint Counsel provided him and that he reviewed, there is no competent or reliable scientific evidence to support Respondents' health-benefit claims. (CX1293_0007, 0016-0024, 0027-0029; Stampfer, Tr. 769-70).

816. Complaint Counsel's expert, Dr. James Eastham, offered no expert opinion that the Challenged Products do not provide the health benefits Complaint Counsel alleges Respondents make about Challenged Products. Rather Dr. Eastham merely opines that based on the materials Complaint Counsel provided him and that he reviewed, there is no competent or reliable scientific evidence to support Respondents' health-benefit claims. (CX1287_0006).

817. Professor Stampfer admits that he is not an urologist or cardiologist. (Stampfer, Tr. 868).

818. Professor Stampfer has no opinion about the particular classes of antioxidant compounds within pomegranates. (PX0362 (Stampfer, Dep. at 199)).

819. Professor Stampfer has no opinion about the extent to which the antioxidant effect of pomegranate juice on human health is attributable to anthocyanins as opposed to other antioxidants. (PX0362 (Stampfer, Dep. at 203)).

820. Professor Stampfer was not asked by Complaint Counsel, and did not prepare, a rebuttal report to Dr. Heber's expert report. (PX0362 (Stampfer, Dep. at 187-88)).

821. Professor Stampfer in preparing his expert report, did not review the expert reports of any of Respondents' experts. (CX1293_0008).

822. Professor Stampfer admits that animal studies "can be very important to help learn about biology, metabolism, biological pathways for the impact of a nutrient." (Stampfer, Tr. 722).

823. Professor Stampfer offered no expert opinion that the compounds that work *in vitro* or in animal cannot work the same way in humans, he only opines that these compounds "often" do not work the same way in humans. (CX1293_, 0008, 0016, 0023). Thus, Professor Meir Stampfer admits that the results of animal studies "sometimes" correspond with what will occur in humans. (Stampfer, Tr. 723).

824. Professor Stampfer admits that observational studies enable investigators to conclude there is an association between the nutrient and disease of interest. (CX1293_0008).

825. Professor Stampfer did not opine on what is a "sufficient size" for a study to be able to conclude a causal link between a nutrient and disease of interest. (CX1293_0009; PX0362 (Stampfer, Dep. at 1-205); Stampfer, Tr. 689-885).

826. Professor Stampfer admits that antioxidant polyphenols have been associated with reduced risk of prostate cancer in various *in vitro* and observational studies. (CX1293_0015).

827. Professor Stampfer admits that Dr. Michael Aviram found that the Challenged Products reduce the size of atherosclerotic lesions in mice. (CX1293_0016; CX0541).

828. Professor Stampfer admits that Dr. Filomena de Nigris found that POM Juice *in vitro* decreases LDL oxidation and the size of plaques in mice. (CX1293_0016; PX0059).

829. Complaint Counsel failed to rebut Respondents' evidence on the benefits of antioxidants in fighting free radicals and, indeed, their experts often provided opinions that supported Respondents evidence on antioxidants effects in the body.

830. Therefore, Complaint Counsel have failed to present expert opinion or affirmative evidence on the benefits of the antioxidants in the Challenged Products in fighting free radicals.

B. Antioxidants Positively Impact the Level and Preservation of Nitric Oxide Which Is Beneficial to Cardiovascular And Erectile Health

1. Respondents Presented Substantial Evidence on the Beneficial Effects of the Challenged Products on Nitric Oxide

831. Antioxidants are well known to enhance the biological actions of nitric oxide ("NO") by virtue of their capacity to improve endothelial NO synthase ("eNOS"). (PX0055-0002; PX0056).

832. Antioxidants are well known to increase and prolong cellular concentrations of NO by protecting it from oxidation. (PX0056-0002; PX0059-001, 0004; PX0149-0005-0006). Antioxidants accomplish this task by neutralizing free radicals. (PX0055-0002; PX0056-0002; PX0057; PX0059-001, 0004; PX0190-0006; PX0149-0005-0006); PX0189-0004-0005; Goldstein, Tr. 2604-2605).

833. The negative effects on NO caused by shear stress (the force of friction caused by perturbed blood flow around atherosclerosis) and on the expression of oxidation-sensitive genes can be mitigated by antioxidants. (PX0055-0002; PX0056).

834. Dr. Louis Ignarro, who was awarded the 1998 Nobel Prize in Physiology for demonstrating the signaling properties of NO, demonstrated that POM Juice and POMx were able to attenuate the effects of perturbed shear stress and atherogenisis. However, POMx was significantly more effective at enhancing the expression of endothelial nitric oxide synthase (eNOS – an enzyme necessary for cellular NO production) decreasing oxygen-sensitive gene expression and reducing lesion size. (PX0056).

835. Antioxidants enhance the bioavailability of NO. (CX0908_0001, 0002; PX0058).

836. NO helps maintain healthy blood vessels, which improves blood flow to almost every organ in the body, including the heart. (Heber, Tr. 1816, 1969; Burnett, Tr. 2250).

837. NO plays a key role in inflammation, blood flow regulation, cell growth and smooth muscle relaxation, all of which offer protection against atherosclerosis. (Heber, Tr. 1816, 1969, 1999; PX0149-0004; Burnett, Tr. 2249-2250; PX0189; PX0190-0006; Melman, Tr. 1169).

838. Maintaining healthy blood vessels and the flow of blood to the heart and penis are important to cardiovascular health and erectile function. (PX0149 at ¶ 12; Burnett, Tr. 2249-2250; PX0189; PX0190-0006; Heber, Tr. 1999; Melman, Tr. 1169).

839. Competent and reliable basic scientific evidence and clinical evidence shows that the Challenged Products affect NO in that they increase and prolong cellular concentrations of NO by protecting it from oxidation. (Burnett, Tr. 2251-2256; PX0349 (Burnett, Dep. at 103, 116-119, 137); Heber, Tr. 2012; PX0149; PX0189-0011; PX0058; PX0059).

840. In sum, the expert opinions and affirmative evidence presented by Respondents prove that the antioxidants in the Challenged Products increase and prolong NO in the body which is beneficial to cardiovascular, prostate and erectile health.

2. Complaint Counsel Have Failed to Rebut Respondents' Evidence on the Challenged Products' Effect on Nitric Oxide

841. Complaint Counsel's experts provided no expert opinion that NO does not help maintain healthy blood vessels and blood flow. (CX1293; PX0362 (Stampfer, Dep. at 1-205); Stampfer, Tr. 689-885; CX1291; PX0361 (Sacks, Dep. at 1-273); Sacks, Tr. 1410-1625; CX1289; PX0360 (Melman, Dep. at 1-141); Melman, Tr. 1069-1197; CX1287; PX0358 (Eastham, Dep. at 1-158); Eastham, Tr. 1204-1351;

CX1295; PX0357 (Stewart, Dep. at 1-194); Stewart, Tr. 3158-3242; PX0359 (Mazis, Dep. 1-242); Mazis, Tr. 2651-2761).

842. Complaint Counsel's experts provided no expert opinion that antioxidants do not protect NO against oxidative destruction. (CX1293; PX0362 (Stampfer, Dep. at 1-205); Stampfer, Tr. 689-885; CX1291; PX0361 (Sacks, Dep. at 1-273); Sacks, Tr. 1410-1625; CX1289; PX0360 (Melman, Dep. at 1-141); Melman, Tr. 1069-1197; CX1287; PX0358 (Eastham, Dep. at 1-158); Eastham, Tr. 1204-1351; CX1295; PX0357 (Stewart, Dep. at 1-194); Stewart, Tr. 3158-3242; PX0359 (Mazis, Dep. 1-242); Mazis, Tr. 2651-2761).

843. Complaint Counsel's experts provided no expert opinion disputing that NO plays a role in cardiovascular and erectile health. (CX1293; PX0362 (Stampfer, Dep. at 1-205); Stampfer, Tr. 689-885; CX1291; PX0361 (Sacks, Dep. at 1-273); Sacks, Tr. 1410-1625; CX1289; PX0360 (Melman, Dep. at 1-141); Melman, Tr. 1069-1197; CX1287; PX0358 (Eastham, Dep. at 1-158); Eastham, Tr. 1204-1351; CX1295; PX0357 (Stewart, Dep. at 1-194); Stewart, Tr. 3158-3242; PX0359 (Mazis, Dep. 1-242); Mazis, Tr. 2651-2761).

844. Antioxidants positively impact the level and preservation of nitric oxide which is beneficial to cardiovascular and erectile health.

845. Therefore, Complaint Counsel have failed to present expert opinion on the Challenged Products effect on nitric oxide.

C. Antioxidants Lessen Inflammation Which Provides Health Benefits In Regard to Cardiovascular Health, Cancer and Erectile Function

1. Chronic Inflammation Leads to a Variety of Health Problems

846. It is well established in the scientific community that chronic inflammation is a characteristic prostate cancer. (deKernion, Tr. 3046-3047; Heber, Tr. 1957, 1992; CX1352 (Heber, Dep. at 257-258); PX0192-0029-0030, 0045; PX0337a21-0011).

847. It is well established in the scientific community that chronic inflammation plays a critical role in atherosclerosis, the narrowing of arteries caused by buildup of cholesterol-based plaques, which is the primary cause of heart disease. (Heber, Tr. 1957; PX0192-0029-0030, 0033, 0045; PX0298a41-0009; PX0337a21-0011).

848. Because atherosclerosis leads to restricted blood flow, it is a causative factor in erectile dysfunction. (Heber, Tr. 1958-1960; Melman, Tr. 1169).

849. Activation of nuclear factor-*K*B ("NF-*K*B"), the oxidative stress responsive transcription factor, has been linked with a variety of inflammatory diseases,

including prostate cancer and cardiovascular disease. (PX0192-0015, 0029-030, 0033-0034; CX1352 (Heber, Dep. at 258); PX0298a41-0009).

850. Inflammation itself causes oxidation in the body. (Heber, Tr. 1956-1957).

851. Oxidized LDL cholesterol tends to accumulate in the wall of blood vessels. (Heber, Tr. 1959).

852. Macrophages continuously consume the oxidized LDL cholesterol that accumulates in the blood vessels and become foam cells, resulting in inflammation. (Heber, Tr. 1960; PX0021-0001).

853. Atherosclerotic plaque forms as a result of damage to the blood vessel that begins with the oxidation of LDL cholesterol that accumulates in the vessels. (Heber, Tr. 1959-1960; PX0021-0001).

854. Unstable atherosclerotic plaque, which causes heart disease, contains oxidized LDL cholesterol and macrophages, reft with inflammation. (Heber, Tr. 1960, 2088).

855. High-density lipoprotein ("HDL") contains an antioxidant enzyme called PON1 that protects against oxidation. (Heber, Tr. 1961).

856. Many antioxidants inhibit inflammation in the body. (Heber, Tr. 1957, 2003).

857. It is well established within the scientific community that blocking inflammation or oxidation of cholesterol can stabilize plaque. (Heber, Tr. 1960; PX0192-0033).

858. It is well established within the scientific community that inflammation in the prostate can be reduced if NF-*K*B is inhibited. (deKernion, Tr. 3046-3047; Heber, Tr. 1992; CX1352 (Heber, Dep. at 257-258); PX0192-0029-0030, 0045).

859. It is well established within the scientific community that the pathway that activates NF-*k*B can be inhibited by phytochemicals, thus providing a beneficial effect against atherosclerosis. (PX0192-0015, 0031; PX0298a41-0009).

2. Respondents Presented Substantial Evidence of the Challenged Products' Anti-Inflammatory Capabilities

860. Competent and reliable scientific evidence shows that the antioxidants in the Challenged Products inhibit the pathway that activates NF-*k*B, thereby mediating atherosclerosis and improving blood flow to the penis. (PX0192-0015, 0031; PX0341 (Heber, Dep. at 257-258); PX0353 (Heber, Dep. at 122); PX0298a41-0009; Melman, Tr. 1169).

861. Competent and reliable scientific evidence shows that the antioxidants in the Challenged Products inhibit the pathway that activates NF-*k*B, thereby reducing inflammation which is beneficial to cardiovascular and prostate health. (PX0192-0015, 0031; CX1352 (Heber, Dep. at 257-258); PX0353 (Heber, Dep. at 122); PX0298a41-0009).

862. Competent and reliable scientific evidence shows that the antioxidants in the Challenged Products increases PON1 association with HDL, thereby reducing inflammation in coronary arteries which is beneficial to cardiovascular health and other inflammatory diseases. (PX0021-0001; PX0192-0038; Heber, Tr. 1961).

Shukla, M, Gupta K, Rasheed Z, Khan K, Haggi, T, "*Consumption of hydrolysable tannins-rich pomegranate extract suppresses inflammation and joint damage in rheumatoid arthritis,*" Nutrition 24 (2008) 733-743

863. In 2008, in a peer-reviewed study entitled Consumption of hydrolysable tannins-rich pomegranate extract suppresses inflammation and joint damage in rheumatoid arthritis," by Shukla, M, Gupta K, Rasheed Z, Khan K, Haggi, T, (Nutrition 24 (2008) 733-743), Drs. Rasheed and Haqqi and their colleagues evaluated the anti-inflammatory properties of POMx in arthritic mice. (PX0124-0001).

864. The consumption of POMx delayed the onset and reduced the incidence of arthritis in mice. It also significantly reduced the disease's severity. In those mice fed POMx, the number of inflammatory cells infiltrating the joints was reduced and there was no destruction of bone or cartilage. (PX0124-0001).

865. This study demonstrates that POMx has anti-inflammatory properties.

Rasheed Z, Akhtar N, Anbazhagan A, Ramamurthy S, Shukla M, Haqqi T, "*Polyphenol-rich pomegranate extract (POMx) suppresses PMACI-induced expression of pro-inflammatory cytokines by inhibiting the activation of MAP Kinases and NF-kB in human KU812 cells,*" J. of Inflammation 6:1-12 (2009)

866. In 2009, in a peer-reviewed study entitled, "Polyphenol-rich pomegranate extract (POMx) suppresses PMACI-induced expression of pro-inflammatory cytokines by inhibiting the activation of MAP Kinases and NF-kB in human KU812 cells," by Rasheed Z, Akhtar N, Anbazhagan A, Ramamurthy S, Shukla M, Haqqi T (J. of Inflammation 6:1-12 (2009), Drs. Rasheed and Haqqi examined the anti-inflammatory properties of POMx. (PX0125-0001).

867. The consumption of POMx inhibited the activation of both mast cells and of NF-kB, a transcription factor that is part of an important signaling pathway involved in inflammatory responses related to several cancers. (PX0125-0001).

868. This study demonstrates that POMx has anti-inflammatory properties.

869. In sum, the expert opinions and affirmative evidence presented by Respondents prove that the antioxidants in the Challenged Products lessen inflammation which is beneficial to cardiovascular health, cancer prevention and erectile function.

3. Complaint Counsel Have Failed to Rebut Respondents Evidence on the Challenged Products' Ability to Lesson Inflammation

870. Complaint Counsel's experts provided no expert opinion disputing the fact that antioxidants inhibit inflammation. (CX1293; PX0362 (Stampfer, Dep. at 1-205); Stampfer, Tr. 689-885; CX1291; PX0361 (Sacks, Dep. at 1-273); Sacks, Tr. 1410-1625; CX1289; PX0360 (Melman, Dep. at 1-141); Melman, Tr. 1069-1197; CX1287; PX0358 (Eastham, Dep. at 1-158); Eastham, Tr. 1204-1351; CX1295; PX0357 (Stewart, Dep. at 1-194); Stewart, Tr. 3158-3242; PX0359 (Mazis, Dep. 1-242); Mazis, Tr. 2651-2761).

871. Complaint Counsel's experts provided no expert opinion disputing the fact that antioxidants inhibit NF-*k*B activation. (CX1293; PX0362 (Stampfer, Dep. at 1-205); Stampfer, Tr. 689-885; CX1291; PX0361 (Sacks, Dep. at 1-273); Sacks, Tr. 1410-1625; CX1289; PX0360 (Melman, Dep. at 1-141); Melman, Tr. 1069-1197; CX1287; PX0358 (Eastham, Dep. at 1-158); Eastham, Tr. 1204-1351; CX1295; PX0357 (Stewart, Dep. at 1-194); Stewart, Tr. 3158-3242; PX0359 (Mazis, Dep. 1-242); Mazis, Tr. 2651-2761).

872. Complaint Counsel's experts provided no expert opinion disputing the role of inflammation in the incidences of cardiovascular disease and prostate cancer. (CX1293; PX0362 (Stampfer, Dep. at 1-205); Stampfer, Tr. 689-885; CX1291; PX0361 (Sacks, Dep. at 1-273); Sacks, Tr. 1410-1625; CX1289; PX0360 (Melman, Dep. at 1-141); Melman, Tr. 1069-1197; CX1287; PX0358 (Eastham, Dep. at 1-158); Eastham, Tr. 1204-1351; CX1295; PX0357 (Stewart, Dep. at 1-194); Stewart, Tr. 3158-3242; PX0359 (Mazis, Dep. 1-242); Mazis, Tr. 2651-2761).

873. Therefore, Complaint Counsel have failed to present expert opinion on the Challenged Products' ability to lessen inflammation.

D. The Antioxidants in the Challenged Products Are Bioavailable in Humans Because They Are Absorbed Into the Blood and Urine

1. Respondents Presented Overwhelming Evidence on the Bioavailability of the Antioxidants in the Challenged Products

874. The antixodiants in the Challenged Products are bioavailable in humans. (PX0073; PX0074; PX0075; PX0192, 0021, 0025; CX1352 (Heber, Dep. at 24)).

875. A substance is said to be "bioavailable" when it has been absorbed into the body and is present in the blood, urine, or other body tissue or fluid. (PX0192-0024-0025).

876. Ellagic acid, an antioxidant in pomegranate juice, is a biomarker for bioavailability because after consuming pomegranate juice or extract, studies show that ellagic acid is absorbed into the blood of humans. (CX1352 (Heber, Dep. at 24); PX0192-0021, 0025).

877. Hydroxyl-6H-benzopyran-6-one derivatives ("urolithins"), a metabolite of punicalagin, are biomarkers for bioavailability because after consuming pomegranate juice or extract, studies show the number of urolithins in the urine of humans increases. (PX0192-0015, 0025).

878. Dimethylellagic acid glucuronide ("DMEAG"), a metabolite of punicalagin, is a biomarker for bioavailability because after consuming pomegranate juice or extract, studies show DMEAG is detected in the urine of humans. (PX0192-0025).

879. Punicalagins contain within their molecular structure ellagic acid, an antioxidant found in pomegranates, which is released and absorbed into the blood over several hours and is metabolized to an even smaller molecule called urilithin. (PX0192-0015, 0021).

880. Molecules that are not absorbed into the blood in the intestine travel to the colon, where bacteria called microbiome break down some of the molecules. Urolithins are then absorbed into the blood and are biologically active. (CX1352 (Heber, Dep. at 26, 76)).

881. A great deal is known within the scientific community about the absorption and metabolism of the hydrolysable tannins in pomegranate juice. (PX0192-0024).

> **Seeram NP, Zhang Y, McKeever R, Henning S, Lee R, Suchard, M, Li Z, Chen S, Thames G, Zerline A, Nguyen M, Wang D, Dreher M, Heber D, "*Pomegranate juice and extracts provide similar levels of plasma and urinary ellagitannin metabolites in human subjects*" J. Medicinal Food 11(2) 2008, 390-394**

882. In 2008, in a peer-reviewed human clinical study entitled **"**Pomegranate juice and extracts provide similar levels of plasma and urinary ellagitannin metabolites in human subjects," by Seeram NP, Zhang Y, McKeever R, Henning S, Lee R, Suchard, M, Li Z, Chen S, Thames G, Zerline A, Nguyen M, Wang D, Dreher M, Heber D, J. Medicinal Food 11(2) 2008, 390-394, Dr. Heber and his colleagues

examined the bioavailability of antioxidant polyphenols of pomegranate juice, POMx Pills and POMx Liquid. (PX0073-0001, 0002).

883. In this study, sixteen healthy volunteers sequentially consumed, with a 1-week washout period between treatments, pomegranate juice (8 oz), POMx Liquid (5ml in 8 oz water) and POMx Pills (1,000 mg). (PX00730001, 0002).

884. The three POM products delivered 857, 776 and 755 mg polyphenols as gallic acid equivalents ("GAE"), respectively. (PX0073-0001).

885. Ellagic acid increased in similar levels in the plasma of all subjects following administration of the pomegranate juice or the pomegranate extract. (PX0073-0001, 0003).

886. Urolithin-A glucuronide, a urinary metabolite of ellagic acid, was detected in similar levels in urine samples of the test subjects, reaching a maximum concentration of approximately 1,000 ng/mL and remained elevated for over 48 hours after consumption of the pomegranate juice or the pomegranate extract. (PX0073-0001, 0004).

887. The pomegranate juice, POMx Pills and POMx Liquid had similar ellagitannin bioavailability. (PX0073-0001, 0004).

888. This study demonstrates that the consumption of pomegranate juice, POMx Pills and POMx Liquid resulted in absorption of ellagic acid in the blood and urolithin-A glucuronide in the urine of humans. (PX0073-0001, 0004).

Seeram NP, Henning SM, Zhang, Y, Suchard, M. Li Z, Heber D, "*Pomegranate juice ellagitannin metabolites are present in human plasma and some persist in urine for up to 48 hours*" J. Nutr. 2006 6:2481-5

889. In 2006, in a peer-reviewed study entitled **"**Pomegranate juice ellagitannin metabolites are present in human plasma and some persist in urine for up to 48 hours," by Seeram NP, Henning SM, Zhang, Y, Suchard, M. Li Z, Heber D (J. Nutr. 136:2481-2485 (2006), Dr. Heber and his colleagues examined the absorption of pomegranate ellagitannins in humans. (PX0074-0001; PX0192-0024).

890. In this study, 18 healthy human subjects were given 180 ml of pomegranate juice concentrate, and blood samples were obtained for 6 hours afterwards, and twenty-four hour urine collections were obtained on the day before, the day of, and the day after the study. (PX0074-0001, 0002; PX0192-0024).

891. The most abundant bioactive polyphenol in pomegranate juice are the hydrolysable tannins called ellagitannins formed when ellagic acid binds with a carbohydrate. (PX0074-0001, 0003; PX0075-0001).

892. Punicalagin, which occurs as isomers, is the predominant ellagitannin present in pomegranate juice. (PX0074-0001).

893. The metabolites of punicalagin are ellagic acid, DMEAG and urolithins. (PX0074-0002).

894. Ellagitannins belong to the chemical class of hydrolysable tannins, which release ellagic acid into the plasma on hydrolysis. (PX0074-0001, 0004).

895. In this study, ellagic acid was detected in the plasma of all subjects post-consumption. (PX0074-0001, 0003; PX0192-0025).

896. Ellagic acid metabolites, including DMEAG and urolithins, were detected in the plasma and urine of the subjects post-consumption in conjugated and free forms. (PX0074-0001, 0003; PX0192-0025).

897. DMEAG was found in the urine obtained from 15 of 18 subjects on the day of the study, but was not detected on the day before or day after the study, demonstrating its potential as a biomarker of intake of pomegranate juice. (PX0074-0001, 0003; PX0192-0025).

898. Urolithin A-glucuronide was found in the urine of 11 subjects on the day of the study and in the urine of 16 subjects the day after the study. (PX0074-0001, 0003; PX0192-0025).

899. Urolithin B-glucuronide was found in the urine of 3 subjects on the day of the study and in the urine of 5 subjects on the day after the study. (PX0074-0001, 0003; PX0192-0025).

900. Urinary ellagic acid metabolites, such as urolithins, arise from biotransformation by the intestinal microflora on ellagic acid. (PX0074-0004).

901. Urolithins, formed by intestinal bacteria, contribute to the biological effects of pomegranate juice as they persist in plasma and tissues and account for some of the health benefits noted after consuming pomegranates. (PX0074-0001, 0003; PX0192-0025).

902. This study demonstrates the bioavailability of the antioxidants found in pomegranate juice. (PX0074-0004; PX0192-0025).

Seeram NP, Lee R, Heber D, "*Bioavailability of ellagic acid in human plasma after consumption of ellagitannins from pomegranate (Punica granatum) juice*" Clinica Chimica Acta 348 (2004) 63-68

903. In 2004, in a peer-reviewed study entitled **"**Bioavailability of ellagic acid in human plasma after consumption of ellagitannins from pomegranate (Punica granatum) juice," by Seeram NP, Lee R, Heber D, Clinica Chimica Acta 348 (2004) 63-68, Dr. Heber and his colleagues examined the bioavailability ellagic acid from consumption of ellagtannins from pomegranate juice concentrate in humans. (PX0075-0001-0002).

904. In this study, a human subject orally consumed 180 ml (6 oz) of pomegranate juice containing 25 mg of ellagic acid and 318 mg of ellagitannins. Blood samples were collected before and at 0.5, 1, 2, 3, 4, and 6 hours after consumption of the concentrated pomegranate juice. (PX0075-0001, 0004-0005).

905. Ellagic acid was not detected in the subjects' blood pre-consumption. (PX0075-0005).

906. Ellagic acid was detected in the blood at 0.5, 1, 2 and 3 hours post-consumption. The maximum concentration occurred after 1 hour post-consumption. (PX0075-0001, 0005).

907. This was the first study to show the absorption of ellagic acid from concentrated pomegranate juice in the human body. (PX0075-0001, 0002, 0006).

908. This study demonstrates that ellagic acid is a biomarker for the bioavailability of ellagitannins in humans. (PX0075-0001, 0006).

909. In sum, the expert opinions and affirmative evidence presented by Respondents prove that the antioxidants in the Challenged Products are bioavailable in humans.

2. Complaint Counsel Have Failed to Rebut Respondents' Evidence on the Bioavailability of the Challenged Products

910. It was not within the scope of Complaint Counsel's experts' assignment, and none opined in their report, that credible and reliable scientific evidence shows that the antioxidants in the Challenged Products are not bioavailable in humans. (CX1287; CX1289; CX1291; CX1293; CX1295).

911. Complaint Counsel's experts provided no expert testimony rebutting Respondents' evidence on the bioavailability of the antioxidants in the Challenged Products. (PX0362 (Stampfer, Dep. at 1-205); Stampfer, Tr. 689-885; PX0361 (Sacks, Dep. at 1-273); Sacks, Tr. 1410-1625; PX0360 (Melman, Dep. at 1-141); Melman, Tr. 1069-1197; PX0358 (Eastham, Dep. at 1-158); Eastham, Tr. 1204-1351; PX0357

(Stewart, Dep. at 1-194); Stewart, Tr. 3158-3242; PX0359 (Mazis, Dep. 1-242); Mazis, Tr. 2651-2761).

912. Complaint Counsel's expert, Dr. David Sacks, admitted that the issue of the bioequivalence of POMx to POM Juice was not within the scope of his assignment as an expert in this case. (PX0361 (Sacks, Dep. at 77); CX1291_0008-0009).

913. Complaint Counsel's expert, Professor Stampfer, has no opinion on the way in which the antioxidant compounds in pomegranates are metabolized within the human body. (PX0362 (Stampfer, Dep. at 200)).

914. Therefore, Complaint Counsel have failed to present expert opinion or affirmative evidence that the Challenged Products are not bioavailable in humans.

E. POMx Is Equivalent to POM Juice in Providing Nutritional Benefits

1. Respondents Presented Overwhelming Evidence on the Equivalency of the Challenged Products

915. POMx Pills and POMx Liquid contain polyphenol antioxidants derived from pomegranates similar to those found in POM Juice. (Heber, Tr. 1993).

916. The Challenged Products contain a diverse, complex mixture of antioxidant polyphenols, including hydrolysable tannins, flavonols, anthocyanins and acids. The hydrolysable tannins include, among others, punicalagins, ellagitannins, punicalins and gallotannins. The acids include ellagic acid, gallic acid and gallagic acid. (PX0192-0016, 0024; PX0074-0002; Heber, Tr. 2001-2002).

917. The Challenged Products have a similar level of primary polyphenols, which are hydrolyzed tannins which make up over 85% of the polyphenol antioxidants in all these products. (Heber, Tr. 2001 – 2002).

918. Because 85% of the polyphenols in POMx Pills and POMx Liquid are hydrolyzable tannins, and because they play the primary role in antioxidant activity, the bioactive components of POM Juice are preserved in the POMx products. (Heber, Tr. 2001 – 2002).

919. The Challenged Products each deliver at least 650 mg polyphenols as gallic acid equivalent per serving. (Heber, Tr. 2186; PX0073-0001).

920. Based on basic scientific studies focusing on the hydrolysable tannins family, especially punicalagins and ellagitannins, show that POMx Pills and POMx Liquid are equivalent to POM Juice in providing health benefits to humans. (Heber, Tr. 2002).

921. The POMx Pill and POMx Liquid have equivalent bioavailablity as POM Juice. (PX0073-0001, 0004; PX0139-0001).

922. Animal studies indicate that the effects of pomegranate juice and POMx Pills on prostate cancer are equivalent. (CX1352 (Heber, Dep. at 336); Heber, Tr. 2002).

923. In a study entitled "*Safety and efficacy of pomx in men with prostate cancer: an 18-month, randomized, double-blind, dose-finding study of the effects of two (2) doses of pomegranate juice extract capsules (1 or 3 capsules/day) on rising prostate specific antigen levels in men following initial therapy for prostate cancer*," Dr. Michael Carducci at John Hopkins University obtained a similar result when studying the effect of POMx on PSADT as obtained by Dr. Pantuck in his study entitled "Phase II Study of Pomegranate Juice for Men With Rising Prostate-Specific Antigen following Surgery or Radiation for Prostate Cancer," where the effectiveness of pomegranate juice on PSADT was studied. (Heber, Tr. 2002; PX0196 at 23-24; CX1341a214-0001).

924. In 2009, in a study entitled "*Effects of pomegranate juice and extract polyphenols on platelt function*," Dr. Teresa Mattiello and her colleagues showed in an *in vitro* study that pomegranate juice and pomegranate extract have similar effects on inhibiting platelet aggregation, which is beneficial to cardiovascular health. (PX0192-0050; PX0017).

925. In laboratory studies conducted by Dr. Heber, he found no difference in the antioxidant effect between POM Juice and POMx products. (Heber, Tr. 2186-2187).

> **Seeram NP, Zhang Y, McKeever R, Henning S, Lee R, Suchard, M, Li Z, Chen S, Thames G, Zerline A, Nguyen M, Wang D, Dreher M, Heber D, "*Pomegranate juice and extracts provide similar levels of plasma and urinary ellagitannin metabolites in human subjects*" J. Medicinal Food 11(2) 2008, 390-394**

926. In this peer-reviewed human clinical study, POM Juice, POMx Pills and POMx Liquid were provided to test subjects in three separate interventions with a washout period. (PX0073-0001).

927. The level of ellagic acid detected in the blood of the subjects was equivalent between the POMx Pill, POMx Liquid and pomegranate juice interventions. (PX0073-0001, 0004).

928. The same level of urolithin-A glucuonide, a urinary metabolite of ellagic acid, was detected in the urine samples in all POM products and remained elevated for over

48 hours after consumption of the pomegranate polyphenols. (PX0073-0001, 0004).

929. This study demonstrates that the consumption of the Challenged Products results in similar absorption of ellagic acid in the blood and urolithin-A glucuronide in the urine of humans. (PX0073-0001, 0004; CX_0022-0024).

Heber D, Seeram N, Wyatt H, Henning S, Zhang Y, Ogden L, Dreher M, Hill J, "*Safety and antioxidant activity of a pomegranate ellagitannin-enriched polyphenol dietary supplement in overweight individuals with increased waist size*" J. Agric. Food and Chem. 2007; 55:-10050-10054

930. In 2007, in a peer-reviewed study entitled "*Safety and antioxidant activity of a pomegranate ellagitannin-enriched polyphenol dietary supplement in overweight individuals with increased waist size*," by Heber D, Seeram N, Wyatt H, Henning S, Zhang Y, Ogden L, Dreher M, Hill J (J Agric. Food Chem. 2007; 55:-10050-10054), Dr. Heber and his colleagues examined the antioxidant activity in POMx Pills. (PX0139-0001).

931. In the study, 22 overweight subjects were administered two POMx Pills per day providing 1000 mg (610 mg of gallic acid equivalents) of extract versus baseline measurements. (PX0139-0001-0003).

932. Measurement of antioxidant activity as evidenced by thiobarbituric acid reactive substances ("TBARS") in plasma was taken before and after POMx Pill supplementation. (PX0139-0001, 0003).

933. There was evidence of antioxidant activity through a significant reduction in TBARS in the test subjects between baseline and 4 weeks. (PX0139-0001, 0004).

934. TBARS are an important biomarker of oxidative stress, measuring harmful products of lipid (fat) oxidation found in the blood. (PX0139-0004).

935. In regard to coronary heart disease, the amount of TBARS circulating in the blood increases, indicating elevated oxidative stress levels. (PX0139-0004; PX0037-0001).

936. In 2002, in a report entitled "Pomegranate Juice is a Major Source of Polyphenolic Flavonoids and It is Most Potent Antioxidant Against LDL Oxidation and Atherosclerosis," by Dr. Michael Aviram, the research showed that 8 ounces of pomegranate juice resulted in significant reduction of TBARS. (PX0192).

937. This study demonstrates that POMx Pills, just like pomegranate juice, provide antioxidant power sufficient to reduce TBARS. (PX0139-0004).

Aviram M, Volkova N, Coleman R, Dreher M, Reddy M, Ferreira D, Rosenblat M, "*Pomegranate phenolics from the peels, arils, and flowers are antiatherogenic: studies in vivo in atherosclerotic apolipoprotein e-deficient (e) mice and in vitro in cultured macrophages and lipoproteins,*" J. Agric. And Food Chem. 2008; 56:-1148-1157

938. In 2008, in a peer-reviewed study entitled "*Pomegranate phenolics from the peels, arils, and flowers are antiatherogenic: studies in vivo in atherosclerotic apolipoprotein e-deficient (e) mice and in vitro in cultured macrophages and lipoproteins*," by Aviram M, Volkova N, Coleman R, Dreher M, Reddy M, Ferreira D, Rosenblat M, (J. Agric. And Food Chem. 2008; 56:-1148-1157), Dr. Aviram and his colleagues examined the anti-atherogenic properties and the mechanisms of action of POMx Pills, POMx Liquid and other pomegranate fruit parts as compared to pomegranate juice. (PX0008-0002).

939. In the study, after consuming pomegranate juice, POMx Liquid and POMx Pills (200 mg of gallic acid equivalents per mouse per day) for 3 months, the atherosclerosis lesion area on the mice was significantly reduced by 44, 38 and 39% compared to the placebo treated control group, and there was no significant difference between the three POM products. (PX0008-0001, 0003).

940. Consumption of the pomegranate juice, POMx Liquid and POMx Pills also reduced cellular total peroxide levels for 35-53% as compared to placebo-treated mice with no significant difference between the POM products. (PX0008-0001, 0004).

941. The study found that free radical scavenging capacity of the pomegranate juice, POMx Liquid and POMx Pills was similar, with the POMx products performing better at reducing oxidated LDL-C uptake by cells than pomegranate juice. (PX0008-0001).

942. This study demonstrates the bioequivalence *in vitro* and *in vivo* of POMx Pills, POMx Liquid and pomegranate juice when measured at the same polyphenol levels.

de Nigris F, et al., "*Effects of pomegranate fruit extract rich in punicalagin on oxidation-sensitive genes and enos activity at sites of perturbed shear stress and atherogenesis*" Cardiovascular Research 73 (2007) 414-423

943. In 2007, in a study entitled "*Effects of pomegranate fruit extract rich in punicalagin on oxidation-sensitive genes and enos activity at sites of perturbed shear stress and atherogenesis*," by de Nigris F, *et al. (*Cardiovascular Research 73 (2007) 414-423), Dr. de Nigris and his colleagues examined the effects of

pomegranate extract on the expression of oxidation-sensitive responsive genes (such as ELK-1 and p-CREB) induced by high shear stress *in vitro* and *in vivo*. (PX0056-0001).

944. The study found that the polyphenolic antioxidants contained in pomegranate juice and extract contributed similarly to the reduction in oxidative stress and atherogenesis during disturbed shear stress in the cultured human endothelial cells and in atherosclerosis-prone areas of hyperchlorestrerolemic mice used in the study. (PX0056-0001-0008).

945. This study demonstrates that POMx, like pomegranate juice, have comparable effects on health as they all stimulate the production of nitric oxide.

de Nigris F, et al., "*The influence of pomegranate fruit extract in comparison to regular pomegranate juice and seed oil on nitric oxide and arterial function in obese Zucker rats*" 17 Nitric Oxide 50-54 (2007)

946. In 2007, in a study entitled "*The influence of pomegranate fruit extract in comparison to regular pomegranate juice and seed oil on nitric oxide and arterial function in obese Zucker rats*," by de Nigris F, *et al. (*17 Nitric Oxide 50-54 (2007)), Dr. de Nigris and his colleagues examined *in vivo* and *in vitro* the effect of the POMx Pill in comparison to pomegranate juice on the arterial function and biological actions of NO in rats. (PX0057-0001).

947. The study found that supplementation of pomegranate extract significantly decreased the expression of vascular inflammation markers related to heart disease comparable to that of pomegranate juice. (PX0057-0001, 0003).

948. The study found that supplementation of pomegranate extract significantly increased NO levels comparable to that of pomegranate juice. (PX0057-0001, 0004).

949. This study demonstrates that POMx, like pomegranate juice, have comparable effects on health as they all stimulate the production of nitric oxide.

950. This study demonstrates that POMx and pomegranate juice are bioequivalent.

951. In sum, the expert opinions and affirmative evidence presented by Respondents prove that the Challenged Products are bioequivalent.

2. Complaint Counsel Have Failed to Rebut Respondents' Evidence on the Bioequivalency of the Challenged Products

952. It was not within the scope of Complaint Counsel's experts' assignment, and none opined in their report, that credible and reliable scientific evidence exists that

POM Juice is not bioequivalent to POMx. (CX1287; CX1289; CX1291; CX1293; CX1295).

953. Complaint Counsel's experts provided no testimony that credible and reliable scientific evidence shows that POM Juice is not bioequivalent to POMx. (PX0362 (Stampfer, Dep. at 1-205); Stampfer, Tr. 689-885; PX0361 (Sacks, Dep. at 1-273); Sacks, Tr. 1410-1625; PX0360 (Melman, Dep. at 1-141); Melman, Tr. 1069-1197; PX0358 (Eastham, Dep. at 1-158); Eastham, Tr. 1204-1351; PX0357 (Stewart, Dep. at 1-194); Stewart, Tr. 3158-3242; PX0359 (Mazis, Dep. 1-242); Mazis, Tr. 2651-2761).

954. Complaint Counsel's expert, Dr. David Sacks, admitted that the issue of the bioequivalence of POMx to POM Juice was not within the scope of his assignment as an expert in this case. (PX0361 (Sacks, Dep. at 77); CX1291_0008-0009).

955. Dr. Sacks admitted that he has no opinion about whether POM Juice is bioequivalent to POMx Liquid. (PX0361 (Sacks, Dep. at 75)).

956. Dr. Sacks admitted that he has no opinion about whether there is a difference between POM Juice and POMx, or between POM Juice and the pomegranate fruit from which it is derived. (PX0361 (Sacks, Dep. at 77)).

957. Complaint Counsel's expert, Professor Stampfer, admitted that he has no opinion about the antioxidant effect of POM Juice relative to POMx. (PX0362 (Stampfer, Dep. at 200, 203)).

958. Therefore, Complaint Counsel have failed to present expert opinion or affirmative evidence that POMx are not bioequivalent to POM Juice.

F. Dr. Heber Is Extremely Well Qualified To Provide the Opinions He Offered in this Case

959. Dr. Heber is a tenured Professor of Medicine and Public Health at the David Geffen School of Medicine at UCLA and the Director of the UCLA Center for Human Nutrition which he founded in 1996 within the UCLA School of Medicine. (PX0192-0005).

960. As a Professor of Medicine and Public Health, Dr. Heber counsels patients at UCLA within the Risk Factor Obesity Program and medical programs of the Department of Medicine. (PX0192-0005). Dr. Heber has seen thousands of patients and has been listed as one of Best Doctors in America multiple times in the last decade. (PX0192-0005).

961. Dr. Heber received his Ph.D. in Physiology from the UCLA, a MD from Harvard Medical School (top 10 percent of his class, Alpha Omega Alpha), and a B.S.

(*summa cum laude* in Chemistry and Phi Beta Kappa) from UCLA. (PX0192-0005).

962. From 1978 to 1982, Dr. Heber served as Associate Director of the Harbor-UCLA National Institutes of Health ("NIH")-funded General Clinical Research Center. (PX0192-0005). In 1983, Dr. Heber moved to the main UCLA campus where he founded the Division of Clinical Nutrition within UCLA's Center for Health Science. (PX0192-0005).

963. Dr. Heber has directed several NIH-funded research projects. From 1992 to 2007, he directed the NIH-funded Nutrition and Obesity Training Program where he supervised the training of 22 M.D. or Ph.D. postdoctoral fellows and from 1999 to 2006, he directed the NIH-funded UCLA Center for Dietary Supplements Research: Botanicals. (PX0192-0006). From 1991 to 2006, Dr. Heber was also the Director of the National Cancer Institute-funded UCLA Clinical Nutrition Research Unit. (PX0192-0006).

964. Dr. Heber is a member of many prestigious organizations. He has been a member of the American Society for Nutrition since and was elected as the first Chair of its Nutrition Council. (PX0192-0005-0006). Dr. Heber is a Fellow of the American College of Physicians and the American College of Nutrition. (PX0192-0005). In 2009, Dr. Heber became a member of the Certification Board for Nutrition Specialists. (PX0192-0006).

965. Dr. Heber has been a member of multiple National Institute of Health Study Sections which review research grant applications including the Metabolic Pathology Study Section from 1987 to 1992 and Special Study Sections which review large program projects as well as programs within the National Institutes of Health. (PX0192-0006).

966. Dr. Heber has served on a number of government nutrition advisory committees including the National Cancer Institute Nutrition Implementation Committee in 1985. (PX0192-0006).

967. Dr. Heber's personal laboratory and clinical research has been on the effects of pomegranate juice phytonutrients on prostate cancer prevention. Dr. Heber has conducted basis research on the mechanisms of the immune system effects on pomegranate phytonutrients, and on the bioavailability and antioxidant activity of pomegranate phytonutrients in humans. (PX0192-0015).

968. Dr. Heber is an expert in basic biology, clinical research, endocrinology, the interface of nutrition and prostate cancer, research on prostate treatment, including hormonal results of prostate cancer treatment, the basic mechanisms underlying erectile function and their interface with nutrition, and the basic mechanisms

underlying cardiovascular disease and their interface with nutrition. (Heber, Tr. 2034-2035; PX0353, (Heber, Dep. at 10-12)).

969. Based his research on congestive heart failure and cholesterol-lowering substances and is counseling of patients with heart disease, Dr. Heber is an expert in the biology and mechanisms around heart disease. (Heber, Tr. 2037).

970. Dr. Heber is an expert on the basic mechanisms of action of pomegranate phytochemicals as antioxidants, the potency of pomegranate phytochemicals, and how phytochemicals act in the body. (PX0353, Heber, Dep. at 9)).

971. Dr. Heber is an expert on the basic mechanisms related to erectile dysfunction, especially as related to the role of nitric oxide in erectile health. (Heber, Tr. 2039).

972. Dr. Heber's nutritional research experience spans the gamut from basic molecular, cellular, and animal model studies to human clinical trials. (PX0192-0008).

973. Basic molecular, cellular, and animal model studies are important in understanding the benefits of fruits and vegetables. (PX0192-0008).

974. Dr. Heber maintains an active research career, including Dr. Heber's areas of research interest encompass clinical nutrition, inflammation, phytonutrients, obesity, and cancer. (PX0192-0006). Dr. Heber has conducted numerous clinical research projects with implications for public health, including on the potential health benefits of a number of different phytonutrients found in fruits and vegetables. (PX0192-0005-007).

975. Dr. Heber is familiar with epidemiological research as it can inform placebo-controlled nutritional intervention trials in large numbers of subjects. (PX0192-0005).

976. Dr. Heber directs core laboratory services in Nutritional Biomarkers including measures of oxidant stress, analytical phytochemistry, gene-nutrient interaction, immune modulation by nutrients, and has interacted extensively with the biostatisticians at UCLA over the last 27 years in the design and analysis of clinical studies. (PX0192-0006).

977. Dr. Heber was Co-Investigator of the UCLA Clinical Site of the Women's Health Initiative, the largest women's health study in history, which examined the impact of low fat diet, calcium, and vitamin D on cardiovascular disease and cancer. (PX0192-0005).

978. Dr. Heber has directed the UCLA Risk Factor Obesity Program since 2001 which is a comprehensive multidisciplinary obesity treatment program which currently has over 100 active patients. (PX0192-0006).

979. In 2005, Dr. Heber chaired the NIH Special Study Section for Clinical Nutrition Research Units. (PX0192-0006) In 2003, Dr. Heber was the organizing chair of the NIH/NCCAM Center Director's Meeting. (PX0192-0006). In 2006, Dr. Heber gave testimony to the President's Cancer Panel on "Diet, Obesity, Inflammation, and Cancer." (PX0192-0006).

980. Dr. Heber has published extensively in peer-reviewed journals, including many articles relating to nutrition. (PX0192-0006). Dr. Heber also originated the concept of color groups linked to phytonutrient content. (PX0192-0007). In that regard, Dr. Heber authored the book "What Color Is Your Diet?" (Harper Collins, 2001), which was a national best seller and is available in eleven languages. (PX0192-0007).

981. Dr. Heber was editor-in-chief of Nutritional Oncology 2nd Edition (Academic Press, 2006), a professional text containing 50 chapters written by national and international experts in nutrition and cancer summarizing the synthesis of information from population studies, basic animal and cell culture studies, and the limited information available from human clinical studies. (PX0192-0006-0007).

982. Dr. Heber has written a number of scientific reviews, including Heber D, Bowerman S., "Applying science to changing dietary patterns," J Nutr. 2001; 131:3078S-81S, linked to the concept of color groups linked to phytonutrient from which he is generally recognized by the nutrition science community. (PX0192-0007).

983. Dr. Heber is a physician scientist expert in nutrition translational research. (PX0192-0008-0009).

984. Translational nutritional science examines the best available evidence, including *in vitro*, animal, population and limited clinical intervention studies in humans, as a totality, rather than just one type of clinical study. (PX0192-0013; (PX0353 (Heber, Dep. at 13-14)). Translational science includes the practice of translating bench science to bedside clinical practice or dissemination to population-based community interventions. (PX0192-0008-0009).

985. Dr. Heber has extensive experience in translational research on pomegranate phytonutrients extrapolating from cell culture and animal studies to humans. Dr. Heber's intimate knowledge of translational research on pomegranate phytonutrients extrapolating from cell culture and animal studies to humans enables him to communicate a firsthand understanding of scientific basis for an

understanding of the health benefits of pomegranate juice within the overall context of what is known about the role of colorful fruits and vegetables in the diet through effects on oxidant stress, inflammation, and the multiple processes underlying common age-related chronic diseases. (PX0192-0007).

986. The NIH is funding several Clinical Translation Science Centers, including one at UCLA which will replace the former General Clinical Research Centers. (PX0192-0013).

987. Dr. Heber counsels patients with prostate cancer on nutritional matters. (Heber, Tr. 2035; CX1352 (Heber, Dep. at 239)).

988. Because his obese patients who have heart disease want to be fully informed, Dr. Heber counsels them about the research on pomegranates. (CX1352 (Heber, Dep. at 239)).

989. Dr. Heber received no compensation for his work in this case. (PX0192-0008).

990. Therefore, Dr. Heber is extremely well qualified to provide the expert opinions he offered in this case.

XIII. THE CHALLENGED PRODUCTS ARE SAFE FOR HUMAN CONSUMPTION

A. Respondents Presented Overwhelming Evidence on Safety

991. Pomegranate juice is a traditional source of human nutrition. (PX0192-0018).

992. Pomegranates have been safely consumed as nutritious food by humans for thousands of years. (PX0192-0013, 0018).

993. Pomegranate juice has been safely consumed by humans for centuries. (PX0192-0042).

994. Pomegranate juice and pomegranate extract have a "high degree of safety." (PX0192-0013).

995. Pomegranate juice is safe for human consumption if consumed within the nutritional range. (PX0192-0018; PX0353 (Heber, Dep. at 129-131)).

996. POMx is safe for human consumption if consumed within the nutritional range. (PX0192-0018).

997. All fruits are assumed safe for human consumption if consumed within the nutritional range. (PX0353 (Heber, Dep. at 129)).

998. One reason fruits are safe for human consumption is because they induce their own metabolism rapidly in the body. (PX0353 (Heber, Dep. at 129)).

999. Unlike some drugs, pomegranate juice has no adverse side effects. (PX0192-0042).

1000. The FDA maintains a list of substances that are identified by the FDA as generally regarded as safe ("GRAS"). (Heber, Tr. 2008-2009).

1001. Before a substance can be GRAS identified, the FDA reviews the scientific literature and the traditional intake of the substance. (Heber, Tr. 2009).

1002. Both pomegranate juice and pomegranate extract are GRAS identified. (Heber, Tr. 2009; 32; 21 C.F.R. § 182.20).

1003. There have been no reported cases of persons being harmed by eating a pomegranate or drinking pomegranate juice. (Heber, Tr. 1947-1948).

1004. There have been no reported cases of toxicity where pomegranates or pomegranate juice have been consumed in nutritional amounts. (Heber, Tr. 1948).

1005. In all the studies that have been conducted on pomegranate juice and pomegranate extract, there has never been any reports of any material harm caused to the subjects by consuming the products. (Heber, Tr. 2007-2008; PX0353 (Heber, Dep. at 115)).

1006. None of the clinical studies conducted on pomegranate juice and pomegranate extract found any serious risk to human health from consuming the products. (PX0192-0018).

1007. No serious adverse events occurred and no subjects discontinued use due to adverse events during Dr. Padma-Nathan's study entitled "Efficacy and safety of pomegranate juice on improvement of erectile dysfunction in male patients with mild to moderate erectile dysfunction: A randomized, placebo-controlled, double-blind, crossover study," International J. of Impotence Research (2007), 1-4. (CX0908_0003).

1008. Pomegranate juice is a food. (PX0192-0011).

1009. Pomegranate extract is a food-based dietary supplement which has substances found in pomegranate juice at levels within the nutritional range. (PX0192-0011).

1010. Pomegranate juice is a natural fruit and documented for over 5,000 years, and as a result, urologist would not require RCTs to determine its safety. (Goldstein, Tr. 2600, 2620).

1011. The IND approvals that the FDA issued for the POMx Pill and POMx Liquid found that the proposed studies regarding POMx were reasonably safe. (PX0192-0018).

1012. There were no changes in blood levels of the routine things you check for regarding drug safety and the liver tests of the subjects were normal in the study entitled "Safety and Antioxidant Activity of a Pomegranate Ellagitannin-Enriched Polyphenol Dietary Supplement in Overweight Individuals with Increased Waist Size." (Heber, Tr. 2008).

1013. Pomegranate juice is no more unsafe for diabetics than any other fruit juice. (Heber, Tr. 2011).

1014. Fruit juice does not have a particular risk for type 2 diabetics as long as the individual's overall diet has the proper glycemic load. (Heber, Tr. 2010).

1015. A particular food is not unsafe simply because it has a high glycemic index. (Heber, Tr. 2011).

1016. The glycemic index of pomegranate juice is 50, which is a midlevel glycemic index. (Heber, Tr. 2011).

1017. Based on conversations with Dr. David Heber and a human study finding POM Juice did not cause drug interaction, Stewart Resnick believed that pomegranate juice did not trigger drug interactions in humans. (S Resnick, Tr. 1774-1775).

1018. Despite the occurrence of mild diarrhea in 7.7% of the patients in Dr. Michael Carducci's prostate-related study of POMx, it is not known whether the consumption of the POMx caused the mild diarrhea in the human subjects. (Heber, Tr. 2007-2008; PX0192-0028).

1019. Mild diarrhea is a common side effect in studies in general. (Heber, Tr. 2007).

1020. Complaint Counsel's expert, Professor Meir Stampfer, believes it is better to err on the side of giving the information to the public as opposed to withholding the information and, thus is an advocate of giving information to the public where the risk of harm of a product is slight and a potential benefit of the product exists. (Stampfer, Tr. 827-828).

Pomegranate Juice Does Not Impair Clearance of Oral or Intravenous Midazolam, a Probe for Cytochrome P450-3A Activity: *Comparison With grapefruit juice*, by Farkas D, Oleson L, Zhao Y, Harmatz, J, Zinny M, Court M, Greenblatt D, J Clin. Pharmocol 2007; 47:286-294

1021. In 2007, in a peer reviewed study entitled "Pomegranate juice does not impair clearance of oral or intravenous midazolam, a probe for cytochrome P450-3a activity: comparison with grapefruit juice," by Farkas D, Oleson L, Zhao Y, Harmatz, J, Zinny M, Court M, Greenblatt D (J Clin. Pharmocol 2007; 47:286-294), Dr. Greenblatt and his colleagues examined the effect of POM Juice and grapefruit juice on inhibiting enteric cytocrhome P450-3A activity in healthy human volunteers. (PX0136-0001).

1022. When a substance produces inhibition of enteric cytochrome P450-3A enzymes, it causes pharmacokinetic interactions with certain drugs. (PX0136-0001-0002).

1023. POM Juice was shown to not cause drug interaction humans. (PX0136-0008).

***Safety and antioxidant activity of a pomegranate ellagitannin-enriched polyphenol dietary supplement in overweight individuals with increased waist size*, by Heber D, Seeram N, Wyatt H, Henning S, Zhang Y, Ogden L, Dreher M, Hill J, J Agric. Food Chem. 2007; 55:-10050-10054**

1024. In 2007, in a peer reviewed study entitled **"**Safety and antioxidant activity of a pomegranate ellagitannin-enriched polyphenol dietary supplement in overweight individuals with increased waist size," by Heber D, Seeram N, Wyatt H, Henning S, Zhang Y, Ogden L, Dreher M, Hill J (J Agric. Food Chem. 2007; 55:-10050-10054), Dr. Heber and his colleagues examined the safety in humans of consuming POMx Pills. (PX0139-0001).

1025. In the study, 64 overweight individuals with increased waist size consumed either one or two POMx Pills per day for 4 week providing 710 mg and 1420 mg of extract containing 435 and 870 mg of gallic acid equivalents, respectively. (PX0139-0001, 0002).

1026. To maintain blinding, subjects in the 710 mg arm received one bottle of placebo and one bottle of POMx Pills. Subjects in the 1420 arm received two bottles of POMx Pills. In addition, 7 of the 64 subjects received only a placebo. (PX0139-0002, 0003).

1027. No adverse events related to the POMx Pill consumption or changes in blood count, serum chemistry, or urinalysis was observed in the subjects. (PX0139-0001, 0004).

1028. Although there were 11 minor adverse events reported by 9 of the 64 subjects, none of these minor adverse effects were deemed to be related to POMx Pills. (PX0139-0003).

1029. The study demonstrates the safety of POMx Pills in humans. (PX0139-0001, 0004).

***POM oil: subchronic toxicity study (90 day dietary study in rats)* by Merkel D**

1030. In 2007, in an unpublished study entitled "POM Oil: subchronic toxicity study (90-day dietary study in rates)," by Merkel D, Dr. Merkel examined the potential subchronic toxicity of POMx Oil in male and female rats likely to arise from continuous exposure to POMx oil over a 90-day test period. (PX0138-0008).

1031. There were no test substance-related mortalities. There were no ophthalmological, clinical observations, organ weight changes, gross finding clinical or histopathologic alterations that were considered to be of toxicological significance as result of the POMx Oil. (PX0138-0008, 0016, 0021).

1032. The study concluded that there were no safety or toxicology issues with POMx Oil in rats. (PX0138-0008).

B. Complaint Counsel Experts Failed To Rebut Respondents' Evidence on the Safety of the Challenged Products

1033. It was not within the scope of Complaint Counsel's experts' assignment, and none opined in their report, on the safety of the Challenged Products or the safety of pomegranate juice and extracts in general. (CX1287; CX1289; CX1291; CX1293; CX1295).

1034. Complaint Counsel's experts did not provide any testimony refuting Respondents' evidence on the safety of the Challenged Products. (PX0362 (Stampfer, Dep. at 1-205); Stampfer, Tr. 689-885; PX0361 (Sacks, Dep. at 1-273); Sacks, Tr. 1410-1625; PX0360 (Melman, Dep. at 1-141); Melman, Tr. 1069-1197; PX0358 (Eastham, Dep. at 1-158); Eastham, Tr. 1204-1351; PX0357 (Stewart, Dep. at 1-194); Stewart, Tr. 3158-3242; PX0359 (Mazis, Dep. 1-242); Mazis, Tr. 2651-2761).

1035. Complaint Counsel's expert, Professor Meir Stampfer, admitted that there are no safety concerns with consuming pomegranate juice apart from "the usual harm that comes with fruit juice, sugary beverages… but that is not specific to pomegranate juice." (PX0362 (Stampfer, Dep. at 195-196)).

1036. Complaint Counsel's expert, Professor Meir Stampfer, admitted he has no opinion about whether there are safety concerns regarding POMx Pills or POMx Liquid

relative to the pomegranate fruit that both are derived from. (PX0362 (Stampfer, Dep. at 201)).

1037. Complaint Counsel's expert, Dr. David Sacks, admitted that the issue of the safety of the Challenged Products was not within the scope of his assignment as in this case, that his expert report contains no opinions on the safety of the Challenged Products, and that he has "no opinion about whether [the Challenged Products are] safe or not." (PX0361 (Sacks, Dep. at 74, 76); CX1291_0008-0009).

1038. Complaint Counsel's expert, Dr. David Sacks, is unaware of any adverse side effects associated with consuming pomegranate juice. (PX0361 (Sacks, Dep. at 119)).

1039. Complaint Counsel's expert, Dr. Gerald Melman, is unaware of any adverse side effects associated with consuming pomegranate juice. (PX0360 (Melman, Dep. at 59)).

XIV. RESPONDENTS' HEART HEALTH CLAIMS ARE SUBSTANTIATED BY COMPETENT AND RELIABLE SCIENTIFIC EVIDENCE.

A. Complaint Counsel's Allegations Regarding Respondents' Heart Health Claims

1040. Complaint Counsel allege that Respondents have falsely represented, expressly or by implication, that clinical studies, research, and/or trials prove that:

A. Drinking eight ounces of POM Juice, or taking one POMx Pill or one teaspoon of POMx Liquid, daily, prevents or reduces the risk of heart disease, including by (1) decreasing arterial plaque, (2) lowering blood pressure, and/or (3) improving blood flow to the heart; and

B. Drinking eight ounces of POM Juice, or taking one POMx Pill or one teaspoon of POMx Liquid, daily, treats heart disease, including by (1) decreasing arterial plaque, (2) lowering blood pressure, and/or (3) improving blood flow to the heart.

(CX 1426_0017-0018).

1041. Complaint Counsel also allege that, in the area of heart health, there was no:

> significant difference between consumption of pomegranate juice and a control beverage in carotid intima-media thickness progression rates after 18 months; two smaller studies funded by POM

> Wonderful or its agents showed no significant difference between consumption of pomegranate juice and a control beverage on measures of cardiovascular function; and multiple studies funded by POM Wonderful or its agents did not show that POM Wonderful products reduce blood pressure.

(CX 1426_0018).

1042. Complaint Counsel also allege that:

> [R]espondents have represented, expressly or by implication, that:
>
> A. Drinking eight ounces of POM Juice, or taking one POMx Pill or one teaspoon of POMx Liquid, daily, prevents or reduces the risk of heart disease, including by (1) decreasing arterial plaque, (2) lowering blood pressure, and/or (3) improving blood flow to the heart;
>
> B. Drinking eight ounces of POM Juice, or taking one POMx Pill or one teaspoon of POMx Liquid, daily, treats heart disease, including by (1) decreasing arterial plaque, (2) lowering blood pressure, and/or (3) improving blood flow to the heart.

(CX 1426_0019).

B. Respondents Deny Complaint Counsel's Allegations that Their Advertisements Are False and Misleading

1043. Respondents deny Complaint Counsel's allegations that their advertising and promotional materials make the claim that Respondents' clinical studies, research, and/or trials prove that drinking eight ounces of POM Juice, or taking one POMx Pill or one teaspoon of POMx Liquid, daily, prevents or reduces the risk; or treats heart disease, including by (1) decreasing arterial plaque, (2) lowering blood pressure, and/or (3) improving blood flow to the heart. (Answer, ¶ 12).

1044. Respondents dispute Complaint Counsel's allegations or characterizations regarding Respondents' science and aver there is substantial scientific research indicating the health benefits of their products and substantiating their advertising and promotional materials. (Answer, ¶ 13).

1045. Respondents deny Complaint Counsel's allegations that their advertising and promotional materials make the claim that drinking eight ounces of POM Juice, or taking one POMx Pill or one teaspoon of POMx Liquid, daily, prevents or reduces the risk; or treats heart disease, including by (1) decreasing arterial plaque,

(2) lowering blood pressure, and/or (3) improving blood flow to the heart. (Answer, ¶ 19).

C. Overview of Cardiovascular Disease

1046. A heart attack occurs when there is a sudden rupture of an inflamed plaque which covers about 50 percent of the lumen of a coronary vessel. (Heber, Tr. 1959).

1047. Plaque is the end result of decades of damage to the blood vessel, which begins with oxidation. (Heber, Tr. 1959).

1048. The process begins when a protein called low-density lipoprotein ("LDL") or so-called "bad cholesterol," which circulates through the blood, becomes oxidized. (Heber, Tr. 1959).

1049. When the LDL cholesterol gets oxidized, the chemical nature of the protein changes, causing the protein to reside and deposit in the wall of the blood vessel, where it accumulates. (Heber, Tr. 1959; CX1348 (Aviram, Dep. at 5)).

1050. It is not only the quantity of cholesterol in the blood which determines the risk for heart attack and stroke, but also the quality. (CX1348 (Aviram, Dep. at 5)).

1051. Regular cholesterol passes in and out of the arteries, but the oxidized cholesterol remains there. (Heber, Tr. 1959-60).

1052. Macrophages (white blood cells that respond to inflammation by digesting cellular debris), come in and they eat up this oxidized cholesterol. (Heber, Tr. 1960).

1053. Macrophages have ravenous appetites which do not stop, and they continue to accumulate until they become what are called foam cells, which are full of cholesterol and actually burst into the area, bringing in more cells and more inflammation. (Heber, Tr. 1960).

1054. Basically, oxidation is followed by inflammation, which is followed by damage to the interior of the blood vessel. (Heber, Tr. 1960).

1055. This damage is detected as yellow streaks in the coronary arteries. (Heber, Tr. 1960).

1056. As this process progresses, plaque forms and begins to fill those lumen. (Heber, Tr. 1960).

1057. Plaque can have different characteristics; it can be stable or unstable. (Heber, Tr. 1960).

1058. Unstable plaque is full of oxidized cholesterol and macrophages, rift with inflammation. (Heber, Tr. 1960).

1059. By blocking that inflammation and oxidation, it is possible to stabilize the plaque. (Heber, Tr. 1960; PX0192-0033).

1060. Inhibitors of the oxidation process are called antioxidants. (CX1348 (Aviram, Dep. at 5)).

1061. Several studies have indicated that pomegranate juice has antioxidant and anti-atherosclerotic properties due to the presence of multiple polyphenols such as tannins, flavonols, anthocyanins and ellagic acid. (PX0025-0008).

1062. Punicalagin, an ellagitannin, is the most abundant polyphenol that accounts for more than 50% of the antioxidant activity. (PX0025-0008).

1063. The evidence suggests that pomegranate juice may be effective in reducing heart disease risk factors, including LDL oxidation, macrophage oxidative status, and foam cell formation, all of which are steps in atherosclerosis and cardiovascular disease. (PX0025-0008).

D. Respondents' Scientific Research on Cardiovascular Health Demonstrates Beneficial Effects on Arterial Plaque, Blood Pressure, and Blood Flow

1. Basic Science and Animal Studies

1064. Respondents have sponsored approximately 15 published studies in cellular and animal models evaluating the effects of pomegranate juice and/or its extracts on cardiovascular health. (PX0002, PX0007, PX0008, PX0009, PX0010, PX0015, CX0543, PX0017, PX0022, PX0055, PX0056, PX0057, PX0058, PX0059, and CX0053).

1065. The earliest heart studies on pomegranate juice were carried out by Dr. Aviram at the Technion Institute in Israel. (Heber, Tr. 1957).

1066. Dr. Aviram is a Professor at the Technion Faculty of Medicine, Rappaport Institute for Research in the Medical Sciences and Rambam Medical Center, in Haifa, Israel, which is a highly regarded institution where several Nobel prizes have been awarded. (Heber, Tr. 1957-58).

1067. Dr. Aviram is considered an internationally renowned researcher, pioneer, and one the leading experts in the world on cholesterol, lipid oxidation and the protective role of dietary antioxidants related to cardiovascular disease. (Heber, Tr. 1957-58).

1068. Dr. Frank Sacks, Complaint Counsel's expert on cardiovascular health, acknowledges that Dr. Aviram does good basic science and that Technion is a good research institution. (Sacks, Tr. 1571).

1069. For the last 30 years, Dr. Aviram's major research focus has been on dietary antioxidants and antioxidants in general, especially their role in cardiovascular disease. (CX1348 (Aviram, Dep. at 5)).

1070. Before studying pomegranates, Dr. Aviram examined a number of antioxidants from plants, including lycopene from tomatoes, green tea, citrus fruits, and then red wine. (Heber, Tr. 1958).

1071. Dr. Aviram published a red-wine study, which explained partially the "French paradox," that people in France, even though they eat fatty foods like the Finnish, they do not get heart attacks in France compared to Finland. It was shown epidemiologically that it has to do with drinking red wine, because red wine contains antioxidants from the skin of the grape. (CX1348 (Aviram, Dep. at 5)).

1072. Dr. Aviram was approached by POM and Les Dornfeld, who wanted him to do the same type of study that he did for red wine, and other fruits and vegetables, but now for pomegranates. (CX1348 (Aviram, Dep at 6)).

1073. After a year of studying in 1998 or 1999, Dr. Aviram concluded that pomegranate juice had greater antioxidant potencies than red wine. (CX1348 (Aviram, Dep. at 6)).

1074. Dr. Aviram knew that pomegranate could inhibit the oxidation of cholesterol from very basic test tube studies, but he also noticed that pomegranate juice could inhibit the uptake of that oxidized cholesterol into the macrophages. (Heber, Tr. 1960-61).

1075. High-density lipoprotein cholesterol ("HDL" or so called "good cholesterol") contains an antioxidant enzyme, called "paraoxonase" or "PON1" which acts to protect the body against oxygen radicals. (Heber, Tr. 1961).

1076. Dr. Aviram found that pomegranate juice benefits the activity of paraoxonase or PON1 by increasing its binding to HDL cholesterol. (Heber, Tr. 1961).

1077. Beginning in 2000 and continuing as recently as 2010, Dr. Aviram and others observed that pomegranate juice and/or POMx has beneficial effects on cardiovascular health in their cellular and animal research by resulting in, among other things, the following:

- reduction in oxidation of LDL cholesterol;

- lessening the uptake of oxidized and native LDL cholesterol by macrophage foam cells;
- diminishing the size of atherosclerotic lesions and foam cells;
- inhibition of macrophage cholesterol biosynthesis;
- decrease in macrophage oxidative stress;
- protection against cellular lipid peroxidation;
- reduction of serum lipids and glucose levels;
- improvement of PON1; and
- lessening of platelet aggregation.

(PX0002, PX0007, PX0008, PX0009, PX0010, PX0015, CX0543, PX0017, PX0022, and CX0053).

1078. Dr. Sacks acknowledges that some of Respondents' *in vitro* studies have shown pomegranate juice's favorable effects on the mechanisms involved in cardiovascular disease and that *in vitro* studies, like Dr. Aviram's, can be competent and reliable evidence of an agent's effect on a particular mechanism. (Sacks, Tr. 1578).

1079. For example, Dr. Sacks agrees that Dr. Aviram's *in vitro* studies showed that pomegranate juice inhibits macrophage uptake of oxidized LDL, which is one component of atherosclerosis, and a significant reduction in atherosclerotic vessels. (Sacks, Tr. 1572; 1579).

1080. Dr. Sacks also concedes that Dr. Aviram's animal studies have demonstrated favorable effects for pomegranate juice in promoting cardiovascular health. (Sacks, Tr. 1578-79).

1081. Respondents have also sponsored significant research in the area of nitric oxide and understanding its role in cardiovascular health. (PX0055, PX0056, PX0057, PX0058, PX0059).

1082. Nitric oxide is produced by the cells lining the heart blood vessels and by the cells lining the blood vessels of many organs around the body. (Heber, Tr. 1966).

1083. Nitric oxide is beneficial in that it improves blood flow to almost every organ in the body that is dependent upon blood flow. (Heber, Tr. 1969-70).

1084. Nitric oxide opens up tiny blood vessels and helps, among other things, preserve blood flow to the heart. (Heber, Tr. 1968).

1085. Pomegranate juice contains an extraordinary ability to enhance the effect of nitric oxide and inhibit oxidative stress. (Heber, Tr. 1967-68).

1086. To this end, Respondents have sponsored research by Dr. deNigris, Dr. Napoli, and, most notably, Dr. Louis Ignarro, winner of the 1998 Nobel Prize and Professor of Pharmacology at UCLA School of Medicine, to conduct basic research on the effects of pomegranate juice on nitric oxide in the human body. (PX0055, PX0056, PX0057, PX0058, PX0059).

1087. In their studies, Dr. deNigris, Dr. Napoli, Dr. Ignarro , and others found that pomegranate juice and/or POMx demonstrated, among other things, the following beneficial effects:

- increasing and preserving levels of nitric oxide and decreasing expression of genes associated with stress and progression of atherosclerosis;
- reducing LDL oxidation, size of atherosclerotic plaques, and formation of foam cells;
- reversing effects of shear stress, which can damage the endothelial cells or thin layer of cells that line the interior of blood vessels; and
- decreasing cellular production and release of oxygen radicals in the vascular wall;
- inhibiting activation of oxidation-sensitive genes; and
- improving biological activity of nitric oxide.

(PX0055, PX0056, PX0057, PX0058, PX0059).

1088. In short, Respondents' basic and animal science constitutes competent and reliable scientific evidence that pomegranate juice and/or its extract are beneficial toward cardiovascular health by, among other things, reducing the oxidation of LDL cholesterol and its uptake, diminishing the size and scope of atherosclerotic legions, macrophages, and foam cells, lessening platelet aggregation, and enhancing the presence of nitric oxide. (PX0002, PX0007, PX0008, PX0009, PX0010, PX0015, CX0543, PX0017, PX0022, CX0053, PX0055, PX0056, PX0057, PX0058, PX0059).

2. Respondents' Clinical Trials

1089. Respondents have sponsored approximately 10 published studies on humans evaluating the effect of pomegranate juice and/or its extracts on cardiovascular health. (PX0004, PX0005, CX0611, PX0014, PX0020, PX0021, PX0023, PX0038, PX0127, PX0139).

1090. In addition to enlisting the assistance of Dr. Aviram, Respondents also worked with two of the most pre-eminent research scientists in the field of cardiovascular health to better understand the potential benefits of pomegranate juice and/or its derivatives in humans: Dr. Dean Ornish and Dr. Michael Davidson. (PX0014, PX0023).

1091. Dr. Dean Ornish is the Founder and President of the non-profit Preventive Medicine Research Institute in Sausalito, California and Clinical Professor of Medicine at the University of California, San Francisco. (PX0025-0001).

1092. Dr. Ornish is considered a pioneer in cardiovascular health and human wellness and one of the most influential people in the world in this regard. (Heber, Tr. 1970).

1093. Dr. Ornish, who conducted a landmark study showing that the effects of lifestyle on heart health, is widely published and continues to do research. (Heber, Tr. 1970).

1094. Dr. Davidson is the Clinical Professor of Medicine and Director of Preventive Cardiology at the University of Chicago Medical Center, Medical Director of Radiant Research, Chicago, and a practicing physician who typically treats patients with cholesterol abnormalities, coronary artery disease, or clinical atherosclerosis. (JX3; CX1134_0001; CX 1336 (Davidson, Dep. at 218-220)).

1095. Dr. Davidson has been involved, in some manner, in over 700 clinical studies over the past 25 years. (JX 3; CX1336 (Davidson, Dep. at 220-221)).

1096. Dr. Davidson is a nationally recognized expert on statins, novel lipid-lowering drugs and the reduction of coronary artery disease risk through diet and exercise. (http://www.uchospitals.edu/physicians/michael-davidson.html)

1097. Dr. Frank Sacks regards Dr. Davidson as one of the foremost clinical researchers in the cardiovascular field with a superb reputation for top-quality clinical trial research in cardiovascular disease. (Sacks, Tr. 1490).

1098. In their studies, Dr. Aviram, Dr. Ornish, Dr. Davidson and others found that pomegranate juice and/or POMx had, among other things, the following beneficial effects in humans:

- decrease of LDL susceptibility to aggregation and retention;
- increase in PON1;
- protection against oxidation of LDL;
- reduction in the activity of angio-tensin converting enzyme ("ACE"), an enzyme which produces "angiotensin II", a protein that causes blood vessels to constrict;
- lowering of systolic blood pressure;
- reduction in intima-media thickness of the coronary artery ("CIMT"); and
- increase blood flow or myocardial perfusion.

(PX0004, PX0005, CX0611, PX0014, PX0020, PX0021, PX0023, PX0038, PX0127, CX0934).

1099. In conclusion, Respondents' human clinical studies confirm and support the benefits found in the basic and animal research and together, the totality of the evidence constitutes competent and reliable scientific evidence that pomegranate juice and/or its extracts promote cardiovascular health by, among other things, helping to reduce arterial plaque, lower blood pressure, and improve blood flow. (PX0004, PX0005, CX0611, PX0014, PX0020, PX0021, PX0023, PX0038, PX0127, CX0934, PX0002, PX0007, PX0008, PX0009, PX0010, PX0015, CX0543, PX0017, PX0022, CX0053, PX0055, PX0056, PX0057, PX0058, PX0059)).

1100. The following chart summarizes Respondents' basic, animal, and human science demonstrating the benefits of pomegranate juice and/or POMx on cardiovascular health:

RESPONDENTS' PUBLISHED CARDIOVASCULAR HEALTH STUDIES				
Respondents' Basic Science and Animal Studies				
Year	**Publication/Researcher**	**Product Tested**	**Method**	**Findings**
2001	Kaplan, *et al*., Pomegranate juice supplementation to atherosclerotic mice reduces macrophage lipid peroxidation, cellular cholesterol accumulation and development of atherosclerosis, 131 *J. Nutr.* 2082-89 (2001). <u>Researcher/Affiliation</u> Dr. Aviram The Lipid Research Laboratory,	POM Wonderful 100% pomegranate juice	Apo E-deficient mice	Pomegranate juice supplementation to Apo E mice with advanced atherosclerosis reduced the lesion size by 17% compared to placebo mice. This supplementation reduced macrophage oxidative stress.

RESPONDENTS' PUBLISHED CARDIOVASCULAR HEALTH STUDIES				
Respondents' Basic Science and Animal Studies				
Year	**Publication/Researcher**	**Product Tested**	**Method**	**Findings**
	Technion Faculty of Medicine, Rambam Medical Center (CX0543)			
2005	Fuhrman, *et al*., Pomegranate juice inhibits oxidized LDL uptake and cholesterol biosynthesis in macrophages, 16 *J. Nutr. Biochemistry* 570-6 (2005). Researcher/Affiliation Dr. Aviram The Lipid Research Laboratory, Technion Faculty of Medicine, Rambam Medical Center (PX0015)	POM Wonderful 100% pomegranate juice	*In vitro*	Pre-incubation of macrophages with juice resulted in a significant reduction in ox-LDL degradation by 40%. Macrophage cholesterol biosynthesis was inhibited by 50% after cell incubation with juice.
2005	de Nigris, *et.al*., Beneficial effects of pomegranate juice on oxidation-sensitive genes and eNOS activity at sites of perturbed shear stress, 102(13) *Proceedings of the National Academy of Sciences* 4896-4901 (2005). Researcher/Affiliation Drs. Napoli and Ignarro University of Naples and UCLA (PX0059)	POM Wonderful 100% pomegranate juice	*In vitro* and *in vivo*	Pomegranate juice significantly increased levels of nitric oxide in cell culture, as well as decreased the expression genes that are associated with stress and progression of atherosclerosis. These results were also seen in mice both when juice was used as a preventative and a therapeutic treatment. Furthermore, LDL oxidation, the size of the atherosclerotic plaques, and formation of foam cells were significantly decreased in mice.
2006	Rosenblat, *et al*., Pomegranate byproduct administration to apolipoprotein e-deficient mice attenuates atherosclerosis development as a result of decreased macrophage oxidative stress and reduced cellular uptake of oxidized low-density lipoprotein, J *Agric Food Chem*. 2006 Mar 8;54(5):1928-35 Researcher/Affiliation Dr. Aviram The Lipid Research Laboratory, Technion Faculty of Medicine, Rambam Medical Center (CX0053)	POMx	*In vitro* and Apo E-deficient mice	Consumption of POMx by atherosclerotic mice E-deficient mice resulted in a significant reduction in the mouse macrophage oxidative stress and in the atherogenic oxidized LDL uptake by the cells, and these effects were associated with a significant attenuation atherosclerotic lesion development. Thus, the results showed that POMx significantly attenuates atherosclerosis development by its antioxidant properties in vitro and in E-deficient mice.

RESPONDENTS' PUBLISHED CARDIOVASCULAR HEALTH STUDIES				
Respondents' Basic Science and Animal Studies				
Year	**Publication/Researcher**	**Product Tested**	**Method**	**Findings**
2006	Ignarro, *et al*., Pomegranate juice protects nitric oxide against destruction and enhances the biological actions of nitric oxide, 15 *Nitric Oxide* 93-102. Researcher/Affiliation Dr. Ignarro UCLA (PX0058)	POM Wonderful 100% pomegranate juice	*In vitro*	Pomegranate juice is more potent in preserving nitric oxide than red wine, concord grape and blueberry juice. Pomegranate polyphenols retard vascular smooth muscle growth.
2006	de Nigris, *et al*., Pomegranate juice reduces oxidized low-density lipoprotein down regulation of endothelial nitric oxide synthase in human coronary endothelial cells, 15 *Nitric Oxide* 259-263 (2006). Researcher/Affiliation Drs. Napoli & Ignarro University of Naples & UCLA (PX0055)	POM Wonderful 100% pomegranate juice	*In vitro*	Pomegranate juice can revert the potent down regulation of the expression of endothelial nitric oxide synthase induced by oxidized LDL cholesterol in human endothelial cells via a significant dose dependent pathway.
2006	Rozenberg, et al., Pomegranate juice sugar fraction reduces macrophage oxidative state whereas grape juice fraction increases it, 188 *Atherosclerosis* 68-76. Researcher/Affiliation Dr. Aviram The Lipid Research Laboratory, Technion Faculty of Medicine, Rambam Medical Center (PX0022)	POM Wonderful 100% pomegranate juice	Male balb/C mice	PJ sugar fraction decreases macrophage oxidative stress by up to 72% whereas white grape juice increases oxidative stress by up to 37% vs. control group.
2007	deNigris, *et al*., The influence of pomegranate fruit extract in comparison to regular pomegranate juice and seed oil on nitric oxide and arterial function in obese Zucker rats, *Nitric Oxide* 17 (2007) 50–54 Researcher/Affiliation Dr. Napoli University of Naples (PX0057)	POM Juice, POMx Pills, and POM seed oil	Zucker rats	POM Juice and POMx Pills significantly reduce the expression of vascular inflammatory markers as well as significantly increasing nitric oxide levels.
2007	de Nigris, *et al*., Effects of a	POM Wonderful	*In vitro*	Results showed that

RESPONDENTS' PUBLISHED CARDIOVASCULAR HEALTH STUDIES				
Respondents' Basic Science and Animal Studies				
Year	**Publication/Researcher**	**Product Tested**	**Method**	**Findings**
	Pomegranate Fruit Extract rich in punicalagin on oxidation-sensitive genes and eNOS activity at sites of perturbed shear stress and atherogenesis, *Cardiovascular Research* 73 (2007) 414–423 Researcher/Affiliation Dr. Napoli University of Naples (PX0056)	100% pomegranate juice and POMx Liquid		proartherogenic effects induced by perturbed sheer stress is reduced by POMx and POM Juice.
2007	Shiner, *et al*., Macrophage paraoxonase 2 expression is up-regulated by pomegranate juice phenolic antioxidants via PPARy and AP-1 pathway activation, 195 *Atherosclerosis* 313-321. Researcher/Affiliation Dr. Aviram The Lipid Research Laboratory, Technion Faculty of Medicine, Rambam Medical Center (PX0007)	POM Wonderful 100% pomegranate juice	*In vitro*	Pomegranate juice up-regulates arterial macrophage PON2 expression and protects against cellular lipid peroxidation.
2008	Aviram, *et al*., Pomegranate Phenolics from the Peels, Arils, and Flowers Are Antiatherogenic: Studies in Vivo and in Atherosclerotic Apolipoprotein Edeficient (E) Mice and in Vitro in Cultured Macrophages and Lipoproteins, *J. Agric. Food Chem*. (2008), 56, 1148-1157 Researcher/Affiliation Dr. Aviram The Lipid Research Laboratory, Technion Faculty of Medicine, Rambam Medical Center (PX0008)	POM Wonderful 100% pomegranate juice, POMx Liquid, POMx Pills, POM oil, POM seeds, POM flowers, POM arils	*In vitro* and *in vivo*	All POM extracts possess antioxidant activity in vitro. After consumption of PJ, POMxl, POMxp, POMf, or POM arils by Apo E mice, the atherosclerotic lesion area was significantly decreased by 44, 38, 39, 6 or 70%, respectively as compared to placebo, while POMo had no effect and POMf reduced serum lipids and glucose levels by 18-25%.
2009	Mattiello, *et al*., Effects of Pomegranate Juice and Extract Polyphenols on Platelet Function, *J. Medicinal Foods* 12 (2) (2009) Researcher/Affiliation Dr. Mattielo	POM Wonderful 100% pomegranate juice and POMx Pills	*In vitro*	POM Juice and POMx reduce all platelet responses studied. Results demonstrated that cardiovascular health benefits of pomegranate may in part be related to the ability of polyphenols to inhibit platelet function.

RESPONDENTS' PUBLISHED CARDIOVASCULAR HEALTH STUDIES				
Respondents' Basic Science and Animal Studies				
Year	**Publication/Researcher**	**Product Tested**	**Method**	**Findings**
	Sapienza University of Rome (PX0017)			
2010	Fuhrman, *et al*., Pomegranate juice polyphenols increase recombinant paraoxonase-1 binding to high-density lipoprotein: studies in vitro and in diabetic patients, *Nutrition*. 2010 Apr; 26(4):359-66 <u>Researcher/Affiliation</u> Drs. Avirom and Fuhrman The Lipid Research Laboratory, Technion Faculty of Medicine, Rambam Medical Center (PX0009, unpub. manuscript)	POM Wonderful 100% pomegranate juice	*In vitro*	Oxidative stress impairs binding of PON1 to HDL. POM Juice polyphenols increase the binding beyond their anti-oxidative effect. These effects could be related to a POM Juice-mediated reduction in oxidative stress and to a direct effect of POM Juice polyphenols on the HDL-PON1 association.
2010	Khateeb, *et al*., Paraoxonase 1 (PON1) expression in hepatocytes is upregulated by pomegranate polyphenols: a role for PPAR-gamma pathway, *Atherosclerosis*. 2010 Jan; 208(1):119-25 <u>Researcher/Affiliation</u> Dr. Aviram The Lipid Research Laboratory Technion Faculty of Medicine Rambam Medical Center (PX0002, unpub. manuscript)	POM Wonderful 100% pomegranate juice	*In vitro*	The anti-atherogenic characteristics of POM Juice polyphenols are modulated, at least in part, via PON1 upregulation and its subsequent release to the medium.
2011	Rosenblat, *et al*., Pomegranate Juice Protects Macrophages from Triglyceride Accumulation: Inhibitory Effect on DGAT1 Activity and on Triglyceride Biosynthesis, Ann. Nutr. Metab. (2011), 58:1-9 <u>Researcher/Affiliation</u> Dr. Aviram The Lipid Research Laboratory Technion Faculty of Medicine Rambam Medical Center (PX0010)	POM Wonderful 100% pomegranate juice	*In vitro*	When macrophages were treated with pomegranate juice or punicalagin, the content and formation of triglycerides were reduced by at least 30%. The accumulation of lipids, to include triglycerides, within macrophages has been linked to the formation of atherosclerotic plaques. The authors concluded that the ability of POM Juice polyphenols to protect against macrophage triglyceride accumulation is an important contributor to the anti-artherogenic properties of pomegranate.

Respondents' Human Clinical Trials				
Year	**Publication/Researcher**	**Product Tested**	**Method**	**Findings**
2000	Researcher/Affiliation Aviram, *et al*., Pomegranate juice consumption reduces oxidative stress, atherogenic modifications to LDL, and platelet aggregation: studies in humans and in atherosclerotic apolipoprotein E-deficient mice, 71(5) *Am. J. Clinical Nutrition* 1062-76 (2000) Researcher/Affiliation Dr. Aviram The Lipid Research Laboratory, Technion Faculty of Medicine, Rambam Medical Center (PX0004)	POM Wonderful 100% pomegranate juice	Humans (and Apo E-deficient mice)	This study demonstrates that antioxidant activity in the blood of 13 healthy male volunteers who drank POM Wonderful pomegranate juice for 2 weeks increased by 9%, and the amount of LDL cholesterol oxidation decreased by 20%. The study also measured similar effects on mice with abnormal fatty deposits in their arteries. It was found that plaque build-up was 44% less than these mice than in the mice who did not receive pomegranate juice.
2001	Aviram, *et al*., Pomegranate juice consumption inhibits serum angiotensin converting enzyme activity and reduces systolic blood pressure, 158 *Atherosclerosis* 195-98 (2001). Researcher/Affiliation Dr. Aviram The Lipid Research Laboratory, Technion Faculty of Medicine, Rambam Medical Center (PX0005)	POM Wonderful 100% pomegranate juice	Humans	Ten patients, ranging in age from 62 to 77, with an average blood pressure of over 155/83 drank 8 oz of POM Wonderful pomegranate juice each day for 2 weeks. This resulted in a 5% decrease in systolic blood pressure. ACE (angiotensin converting enzyme), which helps to lower blood pressure was also reduced by 36%.
2004	Aviram, *et al*., Pomegranate juice consumption for 3 years by patients with carotid artery stenosis reduces common carotid intima-media thickness, blood pressure and LDL oxidation, 23 *Clinical Nutrition* 423-33 (2004). Researcher/Affiliation Dr. Aviram The Lipid Research Laboratory, Technion Faculty of Medicine, Rambam Medical Center (CX0611)	POM Wonderful 100% pomegranate juice	Humans	Ten patients consumed 8 oz a day of POM Wonderful pomegranate juice for 1 year. Nine patients did not consume pomegranate juice (controls). The intima-media thickness (IMT) of the carotid artery wall was measured at 3 month intervals. After 1 year, those patients who did not consume pomegranate juice showed a 9% increase in IMT, while those consuming juice showed a decrease in IMT of up to 30%. Furthermore, those consuming juice had a significant reduction in systolic blood pressure and a reduction of LDL oxidation by 90%. Benefits were maintained in 5 patients that continued to drink juice for 2 additional years.

Respondents' Human Clinical Trials				
Year	**Publication/Researcher**	**Product Tested**	**Method**	**Findings**
2004	Esmaillzadeh, *et al*., Concentrated pomegranate juice improves lipid profiles in diabetic patients with hyperlipidemia, 7 *J. Med. Food* 3 (2004) Researcher/Affiliation Dr. Esmaillzadeh Shaheed Beheshti University of Medical Sciences Tehran, Iran (PX0038)	POMx Liquid	Humans	The authors concluded that concentrated pomegranate juice consumption may modify heart disease risk factors in hyperlipidemic patients, and its inclusion therefore in their diets may be beneficial.
2005	Sumner, *et al*., Effects of pomegranate juice consumption on myocardial perfusion in patients with coronary heart disease, 96 *Am. J. Cardiol.* 810-14 (2005). Researcher/Affiliation Dr. Ornish The Preventive Medicine Research Institute in Sausalito, California (PX0023)	POM Wonderful 100% pomegranate juice	Humans	After 3 months, the extent of stress-induced ischemia decreased in the pomegranate juice group but increased in the control group for a significant change.
2006	Rosenblat, *et al*., Anti-oxidant effects of pomegranate juice consumption by diabetic patients on serum and on macrophages, 187 *Atherosclerosis* 363-371. Researcher/Affiliation Dr. Aviram The Lipid Research Laboratory, Technion Faculty of Medicine, Rambam Medical Center (PX0020)	POM Wonderful 100% pomegranate juice	Humans	Pomegranate juice resulted in significant reduction in serum peroxides, TBAR levels by 56% and 28%, and cellular peroxides by 71% and increased glutathione levels by 141% in patients with diabetes. Juice resulted in significant antioxidant benefit for people with diabetes.
2007	Heber, *et al*., Safety and antioxidant activity of pomegranate ellagitannin-enriched polyphenol dietary supplement in overweight individuals with increased waist size, *J. Agric. Food Chem*. 2007, 55, 10050–10054 Researcher/Affiliation Drs. Heber and Hill UCLA & University of Colorado	POMx Pills	Humans	No adverse events related to POMx were observed. After one month, a significant 13% percent reduction in plasma TBARS compared to baseline was observed.

Respondents' Human Clinical Trials				
Year	**Publication/Researcher**	**Product Tested**	**Method**	**Findings**
	(PX00139)			
2008	Rock, *et al*., Consumption of wonderful variety pomegranate juice and extract by diabetic patients increases paraoxonase I association with high-density lipoprotein and stimulates its catalytic activities, 56 *J. Agric. Food Chem*. (2008) Researcher/Affiliation Dr. Aviram The Lipid Research Laboratory, Technion Faculty of Medicine, Rambam Medical Center (PX0127)	POM Wonderful 100% pomegranate juice and POM Liquid	Humans	After 4 weeks, there was a significant 30% improvement in HDL paraoxonase 1 (PON1) and an overall lowering of oxidative stress associated with reduced atherosclerosis risk. POM Juice and POMx had similar efficacy. The beneficial effects of pomegranate juice consumption on serum PON1 stability and activity could lead to retardation of atherosclerosis development in diabetic patients.
2009	Davidson, *et al*., Effects of Consumption of Pomegranate Juice on Carotid Intima-Media Thickness in Men and Women at Moderate Risk for Coronary Heart Disease, 104 Am. J. Cardiology 936 (2009) Researcher/Affiliation Dr. Davidson Radiant Research University of Chicago (PX0014)	POM Wonderful 100% pomegranate juice	Humans	A randomized, placebo-controlled, double-blind clinical trial followed 289 subjects at moderate risk for coronary heart disease. These subjects consumed 8 ounces per day of either Wonderful variety 100% pomegranate juice or a placebo beverage. After 18 months, there was no reduction in the progression of intima-media thickness of the carotid artery (CIMT) in the 100% pomegranate juice group as a whole. However, further analysis revealed that the rate of CIMT progression slowed in nearly one third of 100% pomegranate juice subjects, those with elevated cardiovascular disease risk factors.
2010	Rosenblat, *et al*., Consumption of polyphenolic-rich beverages (mostly pomegranate and black currant juices) by healthy subjects for a short term increased serum antioxidant status, and the serum's ability to attenuate macrophage cholesterol accumulation, Food Funct. 2010, 1, 99-109. Researcher/Affiliation Dr. Aviram	POM Wonderful 100% pomegranate juice		100% pomegranate juice and 100% black currant juice demonstrated the highest total polyphenol content and antioxidant potency in a comparative study of 35 U.S. beverages including red wine, green tea, and several deeply colored fruit juices. In addition, the blood serum of healthy subjects who drank 100% Wonderful-variety pomegranate juice and 100% black currant

Respondents' Human Clinical Trials				
Year	**Publication/Researcher**	**Product Tested**	**Method**	**Findings**
	The Lipid Research Laboratory Technion Faculty of Medicine Rambam Medical Center (PX0021)			juice for one week exhibited several measures of increased antioxidant activity.

3. Selected Cardiovascular Studies Sponsored by Respondents

(a) Aviram, et al., *Pomegranate juice consumption reduces oxidative stress, atherogenic modifications to LDL, and platelet aggregation: studies in humans and in atherosclerotic apolipoprotein E-deficient mice,* Am. J. Clin. Nutr. 2000: 71;1062-76. (PX0004).

1101. In 2000, in a study entitled "Pomegranate juice consumption reduces oxidative stress, atherogenic modifications to LDL, and platelet aggregation: studies in humans and in atherosclerotic apolipoprotein E-deficient mice" by Aviram M, Dornfeld L, Rosenblat M, Volkova N, Kaplan M, Coleman R, Hayek T, Presser D, and Fuhrman B (Am. J. Clin. Nutr. 2000: 71;1062-76), Dr. Aviram and his colleagues examined the effect of pomegranate juice consumption on the atherogensis process (the development of fatty plaques in the walls of arteries) in humans, animal models, and cells. (PX0004).

1102. In this study, 13 human subjects consumed pomegranate juice daily for two weeks with three subjects receiving increased doses for 10 weeks. A polipoprotein E-deficient mice also received pomegranate juice supplementation for a period of 11 weeks. (PX0004).

1103. In humans, Dr. Aviram found that pomegranate juice consumption decreased, by 20%, LDL susceptibility to aggregation and retention and increased, by 18%, the activity of PON1. (PX0004).

1104. In mice, pomegranate consumption reduced the oxidation of LDL by up to 90%, the uptake of oxidized and native LDL by macrophage foam cells (white blood cells that respond to inflammation by digesting cellular debris) by 20%, and the size of atherosclerotic lesions and foam cells by 44%. (PX0004).

1105. The authors concluded that the study "showed the antiatherogenic capabilities of PJ [pomegranate juice] in 3 related components of atherosclerosis, plasma lipoproteins, arterial macrophages, and blood platelets. The potent antioxidative capacity of PJ against lipid peroxidation may be the central link for the antiatherogenic effects of PJ on lipoproteins, macrophages, and platelets" (PX0004-0014).

1106. Dr. Aviram's study constitutes competent and reliable evidence that the consumption of pomegranate juice is beneficial to cardiovascular health by, among other things, decreasing the LDL oxidation process and increasing PON1 in humans. (PX0004).

(b) **Aviram*, et al.*, *Pomegranate juice consumption inhibits serum angiotensin converting enzyme activity and reduces systolic blood pressure*, Atherosclerosis 158 (2001) 195-198 (CX0005).**

1107. In 2001, in a study entitled "Pomegranate juice consumption inhibits serum angiotensin converting enzyme activity and reduces systolic blood pressure" by Aviram M and Dornfled L, (Atherosclerosis 158 (2001) 195-198), Dr. Aviram and his co-workers also demonstrated the effects of pomegranate juice on blood pressure via an action on ACE. (CX0005).

1108. In humans, after two weeks of pomegranate juice consumption, the study observed a 36% reduction in serum ACE activity and a 5% decrease in systolic blood pressure. A 31% decrease of was observed also *in vitro*, thus confirming the effect of pomegranate juice. (CX0005; CX1348 (Aviram, Dep. at 22-23)).

1109. The authors concluded: "the significant inhibitory effect of pomegranate juice on serum ACE activity and the minor attenuation in blood pressure in hypertensive patients, in addition to its potent inhibitory effect on lipid peroxidation, suggests that pomegranate juice consumption can offer a wide protection against cardiovascular disease." (CX0005_0003).

1110. Dr. Aviram's study constitutes competent and reliable evidence that the consumption of POM Juice is beneficial to cardiovascular health by, among other things, lowering blood pressure. (CX0005).

(c) **Aviram, et al.*, Pomegranate juice consumption for 3 years by patients with carotid artery stenosis reduces common carotid intima-media thickness, blood pressure and LDL oxidation*, Clin Nutr. 2004;23:423-33. (CX0611).**

1111. In 2004, in a study entitled "Pomegranate juice consumption for 3 years by patients with carotid artery stenosis reduces common carotid intima-media thickness, blood pressure and LDL oxidation" by Aviram M, Rosenblat M, Gaitini D, Nitecki S, Hoffman A, Dornfeld L, Volkova N, Presser D, Attias J, Liker H, Hayek T., Clin Nutr. 2004; 23:423-33, Dr. Aviram and his co-workers investigated, among other things, the effects of pomegranate juice consumption by patients with carotid artery stenosis. (CX0611).

1112. The carotid arteries are located on each side of the neck which provide the main blood supply to the brain. (JX3).

1113. Carotid artery stenosis ("CAS") is a narrowing of constriction of the inner surface (lumen) of the carotid artery, usually caused by atherosclerosis. (JX3).

1114. Stenosis occurs when a person has more than a 50 percent blockage in one of his or her carotid arteries. (Heber, Tr. 1963).

1115. To remove a blockage in the carotid artery, a person undergoes an operation called an endarterectomy, where the buildup is removed and a graft is placed in the artery. (Heber, Tr. 1963).

1116. Although originally believed these carotid lesions in the carotid arteries were a risk factor for stroke, carotid stenosis is actually a risk for heart disease. (Heber, Tr. 1963).

1117. In this study, 10 patients received pomegranate juice for one year and five of them continued for up to 3 years. (CX0611).

1118. In the control group that did not consume pomegranate juice, the patients' carotid intima-media thickness ("CIMT" or thickness of the carotid artery) increased by 9% during one year, whereas, pomegranate juice consumption resulted in a significant CIMT reduction, by up to 30%, after one year. (CX0611).

1119. There was a 39 percent comparative improvement comparing the pomegranate juice group to the placebo group. (Heber, Tr. 1964).

1120. Systolic blood pressure was reduced after one year of pomegranate juice consumption by 12%.

1121. In the study, Dr. Aviram was able to remove and examine portions of certain patients' carotid arteries and by doing so, found less oxidized LDL cholesterol in their plaque and importantly confirmed the effects of pomegranate juice on humans that he had previously shown in cellular studies. (Heber, Tr. 1963-64).

1122. Although this was a relatively small study, sometimes small studies can be more informative than large studies. (Heber, Tr. 1963).

1123. Dr. Aviram sent his material to an independent institution in the United States, to verify his results. (Heber, Tr. 1964).

1124. The results of this study concluded that pomegranate juice consumption by patients with CAS decreased CIMT which were related to the potent antioxidant characteristics of pomegranate juice polyphenols. (CX0611).

1125. Specifically, the authors wrote: "We thus conclude that, as previously shown in atherosclerotic mice, also in humans pomegranate juice consumption (by patients with carotid artery stenosis) possess anti-atherosclerotic properties, as it substantially decreased serum oxidative stress and, in parallel, reduced common carotid intima-media thickness." (CX0611-0009).

1126. Dr. Aviram's study constitutes competent and reliable evidence that the consumption of POM Juice is beneficial to cardiovascular health by, among other things, reducing arterial plaque and lowering blood pressure. (CX0611; Heber, Tr. 1962-64).

(d) **Sumner, et al., *Effects of pomegranate juice consumption on myocardial perfusion in patients with coronary heart disease*, 96 Am. J. Cardiology 810 (2005) (PX0023).**

1127. In 2005, Dr. Dean Ornish and colleagues investigated whether the daily consumption of pomegranate juice for three months would affect myocardial perfusion (or blood flow) in 45 patients who had coronary heart disease and myocardial ischemia (narrowing of the arteries) in a randomized, placebo-controlled, double-blind study. (PX0023).

1128. Dr. Ornish's randomized, double blinded, placebo controlled study measured the effect of pomegranate juice consumption on a patient's blood flow (or myocardial perfusion) at rest and under stress. (PX0023; Ornish, Tr. 2336; Heber, Tr. 1970-71).

1129. In this study, patients were randomly assigned into one or two groups: a pomegranate juice group (240 ml/day) or a placebo group that drank a beverage of similar caloric content, amount, flavor, and color. (PX0023).

1130. Dr. Ornish found that after only three months of patients drinking an eight ounce glass of pomegranate juice daily, those patients showed an 18 percent improvement in blood flow to their heart compared to the randomized, placebo control group, which experienced a 17 percent worsening. (PX0023; Ornish, Tr. 2337; Heber, Tr. 1970-71).

1131. The comparative benefit of the pomegranate juice group to the placebo group was about 35 percent. (PX0023; Ornish, Tr. 2337-38; Heber, Tr. 1972).

1132. Those differences were statistically significant and the results were published in the American Journal of Cardiology. (PX0023; Ornish, Tr. 2337-39); Heber, Tr. 1971-72).

1133. The finding of a 35 percent improvement in myocardial perfusion is likely to benefit a substantial number of people in the United States because it could reduce

the risk of coronary heart disease, which is a leading cause of death. (Ornish, Tr. 2338).

1134. In the study, Dr. Ornish concluded: "The results of this study demonstrates, for the first time, that daily consumption of pomegranate juice for 3 months may decrease myocardial ischemia and improve myocardial perfusion in patients who have ischemic CHD [coronary heart disease] as measured by the SOS." (PX0023-0004).

1135. Because the natural history of heart disease is to get worse over time and it is unusual for people to get better, especially in such a short period of time, Dr. Ornish discovered that the mechanisms that affect blood flow to the heart are more dynamic than he once realized and that his findings are real. (Ornish, Tr. 233).

1136. Dr. Ornish's finding is also consistent with his earlier studies in which he found that blood flow could be improved to the heart after just one month when people made intensive changes in diet and lifestyle. (Ornish, Tr. 2338).

1137. Dr. Ornish drinks POM Juice and takes POMx. (PX0355 (Ornish, Dep. at 72)).

1138. Dr. Ornish's myocardial perfusion study constitutes competent and reliable scientific evidence showing that pomegranate juice lessens the risk of cardiovascular problems by improving blood flow in people who already have heart disease and is likely to work even better in helping prevent them in the first place. (Ornish, Tr. 2354-55).

(e) **Davidson, et al.,** ***Effects of consumption of pomegranate juice on carotid intima-media thickness in men and women at moderate risk for coronary heart disease,*** **Am J Cardiol. 2009; 104:936-42. (PX0014).**

1139. In 2009, Dr. Davidson published the findings of his randomized, double-blinded, and placebo-controlled study on the effects of consuming pomegranate juice on CIMT thickness on patients at moderate risk for coronary heart disease. (PX0014).

1140. Dr. Davidson's study examined 289 participants who consumed pomegranate juice and placebos for 12 and 18 months. (PX0014).

1141. At 12 months, data showed a statistically significant reduction in CIMT in the group consuming pomegranate juice versus the placebo group in composite measurements, but statistical significance between the two groups was not demonstrated at 18 months. (PX0014; CX 1336 (Davidson, Dep. at 55)).

1142. In a post-hoc exploratory analysis of subjects with the highest risk factors of coronary heart disease, however, Dr. Davidson noted that those in the pomegranate juice group had significantly less anterior wall and/or composite CIMT progression versus control subjects. (PX0014).

1143. According to Dr. Davidson's study, the consumption of pomegranate juice resulted in a statistically significant improvement in CIMT after 12 months and, in those subjects with increased oxidative stress, significantly less anterior wall and/or composite CIMT progression versus control subjects. (PX0014; CX 1336 (Davidson, Dep. at 57)).

1144. Dr. Davidson, who has a very low HDL and high triglyceride levels and fits the subgroup population, has been consuming the POMx extract since his study came out. (CX1336 (Davidson, Dep. at 226)).

1145. Dr. Davidson recommends pomegranate juice to his patients who appear to fit the profile in the post hoc analysis. (CX1336 (Davidson, Dep. at 226)).

1146. Dr. Davidson's study constitutes competent and reliable evidence that the consumption of POM Juice is beneficial to cardiovascular health by, among other things, reducing arterial plaque. (PX0014; Heber Tr. 1979-86).

E. Respondents' Experts Confirm That Respondents' Scientific Research Constitutes Competent and Reliable Scientific Evidence of the Effect of Pomegranate Juice and/or Its Extracts on Arterial Plaque, Blood Pressure, and Blood Flow

1. Qualifications of Respondents' Experts on Cardiovascular Health and Nutrition and Cardiovascular Health

(a) Dr. Dean Ornish

1147. Dr. Dean Ornish is the Founder and President of the non-profit Preventive Medicine Research Institute in Sausalito, California. (PX0025-0001).

1148. He is also a medical doctor and also serves as a Clinical Professor of Medicine at the University of California, San Francisco. (PX0025-0001; Ornish, Tr. 2314 2321).

1149. In 1975, Dr. Ornish received a Bachelor of Arts (B.A.) degree in Humanities summa cum laude from the University of Texas in Austin, where he gave the baccalaureate address. (PX0025-0001; Ornish, Tr. 2314-15).

1150. In 1980, Dr. Ornish received a Doctor of Medicine (M.D.) degree from the Baylor College of Medicine in Houston, where he studied bypass surgery with Dr.

Michael DeBakey, who developed open heart surgery. (PX0025-0001; Ornish, Tr. 2315).

1151. From 1981-1984, Dr. Ornish was a Clinical Fellow in Medicine at Harvard Medical School and an Intern, Junior Assistant Resident in Medicine, and Senior Resident in Medicine at the Massachusetts General Hospital in Boston. (PX0025-0001; Ornish, Tr. 2315-16).

1152. For over 34 years, Dr. Ornish has directed clinical research on the relationship between diet and lifestyle and coronary heart disease demonstrating, for the first time, the landmark study that comprehensive lifestyle changes may begin to reverse even severe coronary heart disease, without drugs or surgery. (PX0025-0001; Ornish, Tr. 2316-17).

1153. Dr. Sacks credits Dr. Ornish for having proven that his overall lifestyle program, including diet, could reverse coronary artery disease and publishing his "landmark" study in the Lancet. (Sacks, Tr. 1480-81).

1154. Many of his studies have been on the subject of cardiovascular disease which has been the principal area of his research for over 35 years. (Ornish, Tr. 2319).

1155. In August 2010, Medicare agreed to provide coverage for his Program for Reversing Heart Disease, the first time that Medicare has covered a program of comprehensive lifestyle changes for reversing coronary heart disease. (PX0025-0001; Ornish, Tr. 2319).

1156. U.S. News and World Report rated his diet as number one for heart health, among all such diets. (Ornish, Tr. 2320-21).

1157. Dr. Ornish directed the first randomized controlled trial demonstrating that comprehensive lifestyle changes may affect the progression of early-stage prostate cancer, which was done in collaboration with the Chair of Urology at UCSF and the then-Chair of Urology and Urologic Oncology at Memorial Sloan-Kettering Cancer Center. (PX0025-0001; Ornish, Tr. 2318).

1158. Dr. Ornish's current research showed that these comprehensive lifestyle changes affect gene expression, "turning on" disease-preventing genes and "turning off" genes that promote prostate cancer, breast cancer and heart disease, as well as increasing telomerase, an enzyme that lengthens telomeres, the ends of our chromosomes which control aging (in collaboration with Dr. Elizabeth Blackburn, who was awarded the Nobel Prize in Medicine in 2009). (PX0025-0001).

1159. The research that Dr. Ornish and his colleagues conducted has been published in the Journal of the American Medical Association, The Lancet, Proceedings of the National Academy of Sciences, Circulation, the American Journal of Cardiology,

The Lancet Oncology, The New England Journal of Medicine, and elsewhere. (PX0025-0001; Ornish, Tr. 2318-19).

1160. Dr. Ornish has written numerous articles for peer-reviewed journals, as well as a chapter on the management of coronary heart disease in Harrison Principles of Internal Medicine and the companion to the Braunwald Cardiology textbooks. (Ornish, Tr. 2319).

1161. Dr. Ornish has been a reviewer of scientific and medical articles for several of the leading peer-reviewed journals. (PX0025-0003).

1162. A one-hour documentary of Dr. Ornish's work was broadcast on NOVA, the PBS science series, and was featured on Bill Moyers' PBS series, Healing & The Mind. Dr. Ornish's work has been featured in all major media, including cover stories in Newsweek, Time, and U.S. News & World Report. (PX0025-0003).

1163. Dr. Ornish has written a monthly column for Newsweek and Reader's Digest magazines and is currently Medical Editor of The Huffington Post. (PX0025-0003).

1164. Dr. Ornish is a member of the boards of directors of the non-profit San Francisco Food Bank and the nonprofit J. Craig Venter Institute and previously served on the board of directors of the United Nations High Commission on Refugees. (PX0025-0003).

1165. Dr. Ornish was appointed by President Clinton to the White House Commission on Complementary and Alternative Medicine Policy and elected to the California Academy of Medicine. He has consulted with food companies to make more healthful foods. Dr. Ornish also chaired the Google Health Advisory Council 2007-2009. (PX0025-0003).

1166. Dr. Ornish has written six published books on the subject of the effect of diet and lifestyle on heart disease and other diseases, including Dr. Dean Ornish's Program for Reversing Heart Disease; Eat More, Weigh Less; Love & Survival; and The Spectrum, and chapters in standard medicine and cardiology books by other people. (PX0025-0003; Ornish, Tr. 2318).

1167. Dr. Ornish has received several awards, including the 1994 Outstanding Young Alumnus Award from the University of Texas, Austin, the University of California, Berkeley, "National Public Health Hero" award, the Jan J. Kellermann Memorial Award for distinguished contribution in the field of cardiovascular disease prevention from the International Academy of Cardiology, a Presidential Citation from the American Psychological Association, the Beckmann Medal from the German Society for Prevention and Rehabilitation of Cardiovascular Diseases,

the "Pioneer in Integrative Medicine" award from California Pacific Medical Center, the Golden Plate Award from the American Academy of Achievement, the Linus Pauling Award from the Institute for Functional Medicine, the Glenn Foundation Award for Research, the Bravewell Collaborative Pioneer of Integrative Medicine award, and the Sheila Kar Health Foundation Humanitarian Award from Cedars-Sinai Medical Center (Los Angeles). (PX0025-0003-0004; Ornish, Tr. 2320).

1168. Dr. Ornish was selected as one of the "TIME 100" in integrative medicine, honored as "one of the 125 most extraordinary University of Texas alumni in the past 125 years," chosen by LIFE magazine as "one of the fifty most influential members of his generation" and by Forbes magazine as "one of the seven most powerful teachers in the world." (PX0025-0004; Ornish, Tr. 2320).

1169. Dr. Ornish has received many awards, including: the Kellerman Award for Distinguished Contribution to the Field of Cardiovascular Disease Prevention awarded by International Academy of Cardiology; recognized by the University of Texas as one of the most extraordinary alumni in the past 125 years; listed by Life Magazine as one of the 50 most influential people of his generation; recognized by Forbes as one of the most powerful teachers in the world. (Ornish, Tr. 2320).

1170. Dr. Ornish has been a physician consultant to President Clinton since 1993 and to several bipartisan members of the U.S. Congress, and has consulted with the chefs at The White House, Camp David, and Air Force One to cook more healthfully (1993-2000). (PX0025-0004).

1171. Dr. Ornish has served or is serving as principal investigator in several federally-funded studies relating to nutrition and coronary heart disease, including support from the National Heart, Lung, and Blood Institute of the National Institutes of Health and from the Department of Defense. (PX0025-0004; Ornish, Tr. 2317-18).

1172. Dr. Ornish is frequently invited to lecture on the role of nutrition and lifestyle in preventing and reversing coronary heart disease and other chronic illnesses, including recent lectures at Medical Grand Rounds at the Mayo Clinic, The Cleveland Clinic, UCSF, and the M.D. Anderson Cancer Center, and keynote presentations at the American College of Preventive Medicine and American College of Lifestyle Medicine annual meetings. (PX0025-0004; Ornish, Tr. 2321).

1173. Dr. Ornish has lectured on several occasions at the World Economic Forum in Davos and at the TED conferences and has given invited presentations at the annual scientific meetings of the American Heart Association, the American Dietetic Association, and the American College of Cardiology. (PX0025-0004).

1174. In 2009, Dr. Ornish was invited to give a keynote speech reviewing the science of integrative medicine at the Institute of Medicine's Summit on Integrative Medicine at the National Academy of Sciences. (PX0025-0004).

1175. Dr. Ornish is on reasonably good terms with the Resnicks even though they cut funding midway through one of his studies because he apparently was not recruiting patients as fast as initially projected. (Ornish, Tr. 2322-23).

1176. The Resnicks are not presently sponsoring any of Dr. Ornish's current research. (Ornish, Tr. 2323).

1177. As an expert witness, Dr. Ornish is only being compensated one dollar an hour. (Ornish, Tr. 2323-24).

1178. Although he has been asked to serve as an expert witness all of the time, Dr. Ornish has never done so. (Ornish, Tr. 2374).

1179. Dr. Ornish is serving as expert witness in this case because he believes this is a historic case and that liberties of the American public are at stake. (Ornish, Tr. 2324).

1180. Dr. Ornish testified that keeping valuable information from the American people could make a difference in the quality of their lives and possibly even be life-saving to them. (Ornish, Tr. 2324).

1181. Based upon his professional training, knowledge, and experience, Dr. Ornish is qualified as an expert in the evaluation of whether a food or product is beneficial in maintaining cardiovascular health and lessening the risk of cardiovascular disease, and also the analysis of clinical studies. (PX0025-0004; Ornish, Tr. 2321-22).

1182. In arriving at his expert opinions, Dr. Ornish relied upon and reviewed, among other things, the Expert Report of Dr. Sacks and supporting materials, Respondents' sponsored cardiovascular studies, and also relied upon peer-reviewed published literature in the field including human studies as well as basic animal and *in vitro* evidence of health benefits of pomegranate juice. (PX0025-0004-0007).

(b) Dr. David Heber

1183. Based upon his professional training, knowledge, and experience, Dr. Heber is qualified as an expert on the role of nutrition and cardiovascular health. (*See* RFF 959-990).

2. Standard for Evaluating Cardiovascular Research

1184. In evaluating whether a food, is beneficial in maintaining cardiovascular health and in lessening the risk of cardiovascular disease, the totality and preponderance of the evidence should be examined, given that: (1) pomegranate juice and its extract are safe; and (2) no one suggests that pomegranate juice or extract should be offered in lieu of conventional medical treatment or surgery studies. (PX0025-0007).

1185. It is a rather extreme position to state that only evidence from RCTs should be considered in evaluating the therapeutic efficacy. (PX0025-0007).

1186. The research of Complaint Counsel's own expert, Dr. Frank Sacks, would not meet this RCT standard and thus would not be clinically or scientifically relevant because most of his published studies have been epidemiological and observational in nature, rather than RCTs, and include relatively small numbers of patients. (PX0025-0007).

1187. Much of what physicians provide patients in their clinical practices has not been proven to be beneficial in RCTs. (PX0025-0007).

1188. It is an extreme position to state that evidence from *in vitro* and animal studies should not be considered in determining the therapeutic value of an intervention. (PX0025-0007).

1189. While there are limitations to extrapolating from *in vitro* and animal studies to human studies, it is false to say this research has no value in determining therapeutic efficacy. (PX0025-0007).

1190. RCTs, even when conducted perfectly, do not control for all sources of bias and may inject new ones unique to RCTs. (PX0025-0008).

1191. A more thoughtful way of analyzing therapeutic efficacy is to carefully examine the totality of scientific evidence, including but not limited to RCTs that are perfectly conducted. (PX0025-0008).

1192. It is an extreme position to state that the therapeutic efficacy of a fruit juice or extract of pomegranate juice should be held to the same standard of evidence as a new drug. (PX0025-0008).

1193. The benefits of pomegranates have been described since Biblical times over thousands of years. (PX0025-0008).

1194. Dr. Ornish is not aware of any studies showing any harmful effects of consuming pomegranates or pomegranate juice. (PX0025-0008).

1195. The study of pomegranates or pomegranate juice is different than studying a new drug, in which harmful side-effects, both short-term and long-term, are the rule rather than the exception. (PX0025-0008).

1196. A new drug needs to be held to a higher standard than a juice that has been around for thousands of years. (Ornish, Tr. 2340).

1197. Dr. Ornish understands that no one is suggesting that pomegranates, pomegranate juice, or pomegranate extract be an alternative to conventional treatments of heart disease such as drugs and surgery. (PX0025-0008).

1198. There is a world of difference between offering juice as a healthy lifestyle choice or as an *adjunct* to conventional treatments than offering it as a <u>replacement</u> for conventional medical care. (PX0025-0008).

1199. A beverage, which has been around since the Bible for thousands of years and whose side effects are good ones, should not be held to a drug standard, because then, in fact, no one can meet that standard, because drug companies spend literally billions of dollars to get a new drug approved. (Ornish, Tr. 2324-25).

1200. Pfizer got four drugs approved in the last 10 years at an average cost of one to four billion dollars each. (Ornish, Tr. 2325).

1201. No manufacturer would spend billions of dollars to test a fruit unless it is a drug like Lipitor, where you could make billions of dollars a year and it would be worthwhile to make such an investment. (Ornish, Tr. 2325).

1202. With all of the research done on pomegranates, if simple health claims cannot be made about the potential benefits, then no one will be able to make health claims except drug companies and that is to the detriment of the American people. (Ornish, Tr. 2326).

1203. There are literally hundreds of thousands of protective substances in predominantly fruits, vegetables, whole grains, legumes, and soy products, and it is important for manufacturers to be able to share science-based information with the American people so that they can decide whether or not they want to purchase these products, not to overstate the claims and not say that these are a substitute for conventional approaches. It is important for the American people to know about these benefits so they can make their own choices and not have the Government do it for them. (Ornish, Tr. 2326-27).

1204. From a preventive standpoint, in cardiac studies since there is a preponderance of evidence from RCTs (even if not perfectly conducted) as well as other clinical trials, animal studies, and *in vitro* studies indicating that pomegranate juice is likely beneficial, it would be unfortunate to say that these benefits should not be

communicated to the general public, including in advertising that is appropriately qualified, when the costs of pomegranate juice are relatively small (especially when compared to drugs) and the safety is clear. (PX0025-0008).

1205. In examining the totality of the evidence, it is important to look at many elements from different studies, such as inflammation, oxidation and related biomarkers, which are interconnected. (PX0353 (Heber, Dep. at 178)).

3. Summary of Conclusions

1206. Taken as a whole, the preponderance of the scientific evidence from basic scientific studies, animal research, and clinical trials in humans reveals that the pomegranate in its various forms (including POM Wonderful 100% Pomegranate Juice, POMx Pills, or POMx Liquid) is likely to be beneficial in maintaining cardiovascular health and is likely to help reduce the risk of cardiovascular disease. (PX0025-0005).

1207. The universe of existing science provides significant evidence that pomegranate juice is likely to, among other things, reduce arterial plaque, improve blood flow, and reduce blood pressure. (PX0025-0005; PX0355 (Ornish, Dep. at 42); Ornish, Tr. 2374-75).

1208. The consumption of pomegranate juice or its derivatives is not a "silver bullet" or a substitute for conventional treatments for heart disease, and Respondents do not suggest otherwise. (PX0025-0005).

1209. There is credible scientific evidence that pomegranate juice and pomegranate extracts have significant health benefits for human cardiovascular systems, including: (1) decreases in arterial plaque; (2) lowering of blood pressure; and (3) improvement of cardiac blood flow, based on the biological mechanism of prolonging the half-life of nitric oxide in vasculature. (PX0192-00045; PX0353 (Heber, Dep. at 76-80)).

1210. Drinking eight ounces of POM Juice, or taking one POMx Pill or one teaspoon of POMx Liquid, daily, is likely to help prevent or reduce the risk of heart disease by (1) decreasing arterial plaque; (2) lowering blood pressure, and/or (3) improving blood flow to the heart. (PX0025-0005; Ornish, Tr. 2374-75; PX0355 (Ornish, Dep. at 42); PX0192-0045; PX0353 (Heber, Dep. at 76-80)).

1211. Drinking eight ounces of POM Juice, or taking one POMx Pill or one teaspoon of POMx Liquid, daily, is likely to treat heart disease by reversing the progression of heart disease in people who already have severe heart disease.

F. Complaint Counsel's Expert on Cardiovascular Disease/Health, Dr. Frank Sacks, Fails to Rebut Dr. Ornish's and Dr. Heber's

Conclusions that Competent and Reliable Scientific Evidence Exists to Support Respondent's Alleged Claims on Arterial Plaque, Blood Pressure, and Blood Flow

1. Dr. Sacks Adopts a Flawed and Unsupported Drug Standard to Evaluate a Natural Food's Effects on Cardiovascular Health

(a) Dr. Sacks Requires RCTs In All Circumstances, Regardless of the Study Cost, Safety, or Potential Benefit of the Product

1212. Dr. Sacks testified that the type of evidence required to substantiate a claim that a product, including a conventional food or dietary supplement, can prevent or reduce the risk of heart disease would be only results of appropriately analyzed results of well-designed, well-conducted, double-blinded, controlled human clinical studies (or RCTs) demonstrating significant changes in valid surrogate markers of cardiovascular health. (Sacks, Tr. 1430-31).

1213. Dr. Sacks believes the same level of evidence is needed to show that clinical studies, research, or trials prove that a product prevents or reduces the risk of heart disease. (Sacks, Tr. 1430-31).

1214. Dr. Sacks, who did not previously disclose that he is a consultant to approximately 10 pharmaceutical companies, argues that a product can only be proven safe with large and expensive RCTs, some costing $6, $60 or $600 million, which are still required even if the product is completely safe. (Sacks, Tr. 1530-38).

1215. Dr. Sacks concedes that it would be extremely costly to design a RCT study on cardiovascular disease because it would take years or decades to evaluate the effectiveness of an intervention. (PX0361 (Sacks, Dep. at 113)).

1216. Dr. Sacks, however, admits that he is making a judgment on standard of evidence in this case regardless of the cost of RCTs, whether the product is safe, and irrespective of whether there is a potential (and even substantial) benefit. (Sacks, Tr. 1538-40; 1567).

(b) Dr. Sacks Contradicts Himself By Conceding That Health Benefit Claims Can Be Made for Food or Nutrients in the Absence of RCTs and Admits That the Potential Risk Against Possible Benefit Must Be Weighed in Making Such Claims

(1) Dr. Sacks Admits That You Do Not Need a RCT When Evaluating the Health Benefit Claims for a Fruit or Fruit Juice

1217. Dr. Sacks served as the Chair of the Design and Analysis Committee for the DASH ("Dietary Approaches to Stop Hypertension") diet sponsored by the National Heart, Lung and Blood Institute, part of the National Institute of Health. (PX0361a03).

1218. The DASH study was a multi-center study to look at the effect of fruits and vegetables in lowering blood pressure and the effect of a total dietary approach in lowering blood pressure, including the reduction of sodium intake. (PX0361 (Sacks, Dep. at 49)).

1219. The DASH diet showed that diets high in fruits and vegetables, among other things, substantially lowered blood pressure in subjects compared to the control group. (Sacks, Tr. 1418).

1220. As part of the DASH diet, fruits were tested and approved as a category. (Sacks, Tr. 1549).

1221. In the DASH diet, Dr. Sacks admits that fruits and fruit juices are treated as the same and participants can pick any one of the fruit juices listed. (Sacks, Tr. 1549-55).

1222. In allowing this flexibility, Dr. Sacks concedes that it is not necessary to conduct RCTs on all individual fruits that a person may decide to consume as part of the DASH diet, because the "category of fruit," including pomegranates, has previously been studied. (Sacks, Tr. 1541-1547).

1223. Dr. Sacks acknowledges that because the pomegranate is included in a "category of fruit" already tested, it would get a lower and more flexible standard of evidence. (Sacks, Tr. 1546; 1554; PX0361 (Sacks, Dep. at 142-143)).

1224. Dr. Sacks admits that pomegranates are like blueberries, considered to be in the category of being safe and part of a diet that is rich in fruits and vegetables, and thus has no problem including them in the DASH diet. (Sacks, Tr. 1567-68; PX 361 (Sacks, Dep. at 143)).

1225. When looking at the totality of the evidence, which may include RCTs, Dr. Sacks acknowledges that RCTs are not necessary when discussing the benefits of fruit juice or broccoli. (Ornish, Tr. 2331).

1226. Dr. Sacks concedes that it is possible to demonstrate a causal influence between an agent and its effect on humans without the use of RCTs, such as the treatment of infectious diseases. (PX036 (Sacks, Dep. at 135)).

(2) Dr. Sacks Has Made Dietary Health Recommendations in the Absence of a RCT or Scientific Agreement

1227. Dr. Sacks has made public health recommendations based on a standard of research that is less than a RCT. (PX0361 (Sacks, Dep. at 130-131)).

1228. Dr. Sacks would recommend to patient with heart failure to reduce his or her intake of sodium even though there are no RCTs proving any benefit. (PX0361 (Sacks, Dep. at 35-38)).

1229. Dr. Sacks would recommend fish oil or Omega-3, which is indicated to lower triglyceride levels, to a patient to help prevent or reduce the risk of coronary heart disease even though the scientific results are not settled. (PX0361 (Sacks, Dep. at 55-56)).

1230. In fact, Dr. Sacks has criticized Omega-3 trials, much like he criticizes Respondents' cardiovascular studies, but still relies upon the science. (Sacks, Tr. 1562-63).

1231. Dr. Sacks has informed the public that low sodium is an integral component of preventing cardiovascular disease, stroke and kidney disease, even though a previous study he conducted was not realistically blinded. (Sacks, Tr. 1561-62; 1587).

1232. Dr. Sacks concedes there are clinical practices and guidelines in place today that have not been proven by double-blind, placebo-controlled studies. (PX0361 (Sacks, Dep. at 111)).

1233. Dr. Sacks admits that it is appropriate to advise the public on the effect of an agent on human health as it relates to cardiovascular disease by using all evidence weighing the likelihood of the benefit against the likelihood of harm. (PX 361 (Sacks, Dep. at 137)).

1234. Dr. Sacks agrees that if a study has flaws, this does not disqualify it from consideration; the study may still have major strengths. (Sacks, Tr. 1564).

(3) Dr. Sacks Concedes that the Potential Risk of a Food Product Must Be Weighed Against Potential Benefit in Making Public Health Recommendations

1235. Dr. Sacks admits that the potential risk of the product must be weighed against the potential benefit and harm of keeping information from the public. (Sacks, Tr. 1530-40; 1558-59; RX 5007).

1236. Complaint Counsel's expert on nutrition, Professor Stampfer, authored an article entitled "Evidence-based criteria in the nutritional context," Nutr Rev. 2010 Aug; 68(8):478-84. (RX 5007).

1237. In establishing nutrient requirements and dietary guidelines, Dr. Sacks agrees with Professor Stampfer's statement that "it will be important to assess the balance between the potential harm of making any given recommendation and the potential harm of not making it." (Sacks, Tr. 1559; RX 5007).

1238. In an article entitled "The Importance of Population-Wide Sodium Reduction as a Means to Prevent Cardiovascular Disease and Stroke: A Call to Action From the American Heart Association" published in their journal (Circulation. 2011 Mar 15;123(10):1138-43), Dr. Sacks, as one of the authors, wrote: "Some scientists still question the evidence supporting population-wide sodium reduction. Common arguments include the absence of a major trial with hard clinical outcomes. It is well-known, however, that such trials are not feasible because of logistic, financial, and often ethical considerations." (Sacks, Tr. 1561; PX0361a03).

1239. In writing about "financial considerations" in this article, Dr. Sacks conceded that he meant the cost of conducting a major trial. (Sacks, Tr. 1561).

1240. Dr. Sacks concedes that it is appropriate to advise the public on the effect of an agent on human health as it relates to cardiovascular disease by using all evidence weighing the likelihood of the benefit against the likelihood of harm. (PX0361 (Sacks, Dep. at 137)).

(c) RCTs Are Not Perfect and Cannot Always Be Implemented in a Double-Blind, Placebo-Controlled Fashion

1241. Dr. Ornish observes, and Dr. Sacks agrees, that it is possible for RCTs to have their own biases. (Ornish, Tr. 2327-28; PX0361 (Sacks, Dep. at 100)).

1242. RCTs can be beneficial, but they are not perfect and, when dealing with nutrition, they have their own set of limitations as well. (Ornish, Tr. 2329).

1243. In studying a drug, RCTs are possible because placebos can be used and subjects, therefore, do not know if they are getting a drug or not. (Ornish, Tr. 2328).

1244. In studying a fruit or a food, however, it is very hard to do a RCT because the subjects know what they are consuming. (Ornish, Tr. 2328).

1245. In addition, in RCTs involving a food or juice, because the control group often knows the intervention, the subjects could begin taking the food or beverage

thereby contaminating the study, such is what occurred with diets during the Women's Health Initiative Study. (Ornish, Tr. 2328-29).

1246. In the DASH diet, researchers accepted the fact that the subjects would know of the sodium contents of their diets; this was a necessary limitation in the study design and illustrates that the intervention cannot be strictly blinded to the subjects. (PX0361 (Sacks, Dep. at 105-106)).

1247. Dr. Sacks concedes that blinding is one component of a good study design, but acknowledges, that in some instances, the blinding of patients is not possible and if a study becomes unblinded, it can still have value. (Sacks, Tr. 1435; PX0 361 (Sacks, Dep. at 104-105)).

1248. Dr. Sacks agrees that some studies cannot be conducted with a placebo, *i.e.* foods and nutrients, and a study is not thrown out because it does not have a placebo. (PX0361 (Sacks, Dep. at 111, 137)).

(d) Larger Studies Are Not Necessarily Better and Pilot Studies Can Provide Valid Scientific Evidence

1249. There is a common misconception that a larger study is a better study, but the opposite can be argued. (Ornish, Tr. 2362; PX1339 (Ornish, Dep. at 22-23)).

1250. When a study has a smaller number of patients, the treatment has to be that much more powerful and that much more consistent for it to be statistically significant. (Ornish, Tr. 2362-63; PX1339 (Ornish, Dep. at 22-23)).

1251. A pilot study simply means that a researcher is conducting a study that has not been done before, but that does not mean that it is not as scientifically valid as a larger study. (PX1339 (Ornish, Dep. at 23; 119-20)).

(e) Statistical Significance Defined as a P-Value of 0.05 Is an Arbitrary Convention in the Context of Studying Pomegranate Juice

1252. In evaluating scientific research related to a whole food, it is not necessary to reach statistical significance to have really important information about something like pomegranate juice as opposed to a prescription drug. (Ornish, Tr. 2340).

1253. The convention of a finding that there be a five percent or less likely due to chance finding is an arbitrary convention. (Ornish, Tr. 2340).

1254. There is nothing magical about the five percent threshold. (Ornish, Tr. 2368).

1255. When you have a p-value of 0.05, there is a 95 percent probability of validity as opposed to chance. (Ornish, Tr. 2340).

1256. When you have a p-value of 0.058, there is a 94 percent validity as opposed to chance. (Ornish, Tr. 2340).

(f) Dr. Sacks Concedes That "Treat" Can Include Nutrition and Exercise Recommendations, "Prevent" Does Not Mean Absolutely Prevent Something in All Cases, and "Prove" Does Not Mean Something Is Proven 100% in 100% of All Subjects

1257. Dr. Sacks agrees that a diet rich in fruits and vegetables protects against cardiovascular disease. (PX0361 (Sacks, Dep. at 141)).

1258. Doctors routinely recommend to their patients foods, such as spinach, for which there are no clinical trials, but where there are studies on categories of fruits or vegetables. (PX0361 (Sacks, Dep. at 147)).

1259. As a practicing clinician, in counseling patients on issues of cardiovascular health or disease, Dr. Sacks initially would emphasize nutritional and other nondrug treatment like exercise, weight loss, improving the quality of the diet. (PX0361 (Sacks, Dep. at 23-24)).

1260. The treatment of patients with a nutritional emphasis is the accepted sequence of treatment for prevention of cardiovascular disease and recurrent disease. (PX0361 (Sacks, Dep. at 25)).

1261. According to Dr. Sacks, the term "treat" does not translate into curing a disease, but rather means to ameliorate symptoms of people who have the disease or reduce the risk of a recurrent cardiovascular event. (PX0361 (Sacks, Dep. at 65-66)).

1262. Dr. Sacks defines the term "prevent heart disease," not to suggest that it can prevent heart disease absolutely in all cases, but instead to mean to lower the incidence of a cardiovascular event, like myocardial infarction or stroke, in proportion to the cases in the population. (PX0361 (Sacks, Dep. at 64-65)).

1263. Dr. Sacks understands the term "reduce the risk" of heart disease to mean that one would reduce the probability of getting heart disease over a given amount of time. (PX 361 (Sacks, Dep. at 65)).

1264. With respect to the meaning of "prove," Dr. Sacks concedes that this does not mean that a 100% of all patients all of the time are benefitted. (PX0361 (Sacks, Dep. at 81)).

(g) Dr. Sacks' Opinions Are Limited: He Cannot Offer Any Expert Opinion Regarding the Safety of the Challenged Products, or Any Alleged Differences of POM Juice Compared to POMx or POM Liquid

1265. Dr. Sacks has never done any studies on the effect of pomegranates, antioxidants, or nitric oxide on human health. (PX0361 (Sacks, Dep. at 57)).

1266. In preparing his expert report, Dr. Sacks does not know if he has reviewed all of Respondent's research studies on cardiovascular health. (PX0361 (Sacks, Dep. at 78)).

1267. Dr. Sacks is not offering any expert opinion regarding any differences between pomegranates and POM juice. (Sacks, Tr. 1547-48; PX0361 (Sacks, Dep. at 77)).

1268. Dr. Sacks is not offering any opinion in this case about the physical properties of pomegranates or pomegranate juice. (Sacks, Tr. 1548).

1269. In his report, Dr. Sacks did not offer any expert opinion on the issues of safety or bioequivalency and these subjects were not within the scope of his assignment in this case. (PX0361 (Sacks, Dep. at 76)).

1270. Dr. Sacks does not know the distinction between POMx Liquid and POM Juice. (PX0361 (Sacks, Dep. at 75)).

1271. Dr. Sacks has no idea how POM Juice or POMx are made. (Sacks, Tr. 1570; PX 0361 (Sacks, Dep. at 143-145)).

1272. Dr. Sacks does not know that pomegranates have been eaten safely for centuries. (Sacks, Tr. 1570).

1273. Dr. Sacks does not know if anybody has been harmed by eating pomegranates. (Sacks, Tr. 1570-71).

2. Studies by Dr. Michael Aviram and Colleagues

(a) In Vitro and Animal Studies

Aviram M, Dornfeld L, Rosenblat M, Volkova N, Kaplan M, Coleman R, Hayek T, Presser D, and Fuhrman B, *Pomegranate juice consumption reduces oxidative stress, atherogenic modifications to LDL, and platelet aggregation: studies in humans and in atherosclerotic apolipoprotein E-deficient mice,* Am. J. Clin. Nutr. 2000: 71;1062-76 (PX0004)

Fuhrman B, Volkova N, Aviram M, *Pomegranate juice inhibits oxidized LDL uptake and cholesterol biosynthesis in macrophages,* J. Nutrit. Biochem. 16 (2005) 570-576 (PX0015)

1274. Dr. Sacks attempts to dismiss Respondents' *in vitro* and animal science on the grounds that such research cannot predict what effect a treatment will have on humans. (CX1291_0015-0016).

1275. Dr. Ornish, notes, however, that is important not to generalize too broadly to suggest there are limitation to extrapolating from animal studies because it depends which part of the physiology is being studied. (Ornish, Tr. 2370).

1276. In some cases, animal physiology is identical to humans, but in other cases, it is different. (Ornish, Tr. 2370).

1277. A very well-designed animal study may actually provide a higher level of evidence than a poorly designed human study. (PX0355 (Ornish, Dep. at 65)).

1278. Dr. Sacks admits there is value in conducting *in vitro* studies and animal studies because it is possible to isolate mechanisms of action and accomplish toxicity or safety testing. (PX0361 (Sacks, Dep. at 89-91)).

1279. In an animal study, Dr. Sacks acknowledges that researchers can examine specific mechanisms by taking out their organs and cells, which you cannot do in humans. (PX0361 (Sacks, Dep. at 91)).

(b) Human Studies

Aviram M and Dornfeld L, *Pomegranate juice consumption inhibits serum angiotensin converting enzyme activity and reduces systolic blood pressure,* 158 Atherosclerosis 195 (2001) (CX 542)

1280. Dr. Sacks believes that CX 542 does not provide reliable evidence of an improvement of ACE or blood pressure because it was not blinded or placebo-controlled, involved a small sample size, and lasted two weeks. (Sacks, Tr. 1453; CX 1291_0017).

1281. Dr. Ornish, however, responds that Dr. Aviram's study should be viewed in the larger context of other studies in this area, as its findings are congruent with and supportive of other research. (PX0025-0009).

1282. Dr. Aviram explains that the use of each patient as his or her own control and without a placebo represents another method to conduct an animal or human study, but is not a less appropriate method. (CX1348 (Aviram, Dep. at 12-13)).

1283. If a pilot study is preceded by good mechanistic studies, including *in vitro*, cell culture, test tube, or animal studies, then a subsequent study on a small number of human subjects is simply called a "pilot" study. (CX1348 (Aviram, Dep. at 17)).

1284. Dr. Aviram considers pilot studies to be positive and disputes that a pilot study cannot be good enough to substantiate a claim. (CX1348 (Aviram, Dep. at 17)).

1285. A study with a small number of subjects or conducted without a placebo does not weaken the importance of the result, especially if the results are in agreement with previously published, findings conducted through *in vitro*, mechanistic, and animal models. (CX1348 (Aviram, Dep. at 18)).

1286. Dr. Davidson also confirms that RCTs are not the only kinds of studies considered to be valid. (CX1336 (Davidson, Dep. at 232)).

1287. Pilot studies and non-double blind, placebo-controlled studies are valid, accurate, and reliable studies and generally considered by other scientists and clinicians in the scientific community to be valid. (CX1336 (Davidson, Dep. at 232-33)).

Aviram M, Rosenblat M, Gaitini M, Nitecki S, Hoffman A, Dornfeld L, Volkova N, Presser D, Attias J, Liker H, and Hayek T, *Pomegranate juice consumption for 3 years by patients with carotid artery stenosis reduces common carotid intima media thickness, blood pressure and LDL oxidation,* 23 Clin. Nutr. 423 (2004) (CX 611)

1288. Dr. Sacks disagrees with Dr. Aviram's conclusion that pomegranate juice had a favorable effect in reducing cholesterol in carotid artery lesions because (a) there was no randomized, placebo, control group to compare effects; and (b) people who had been drinking pomegranate juice had deterioration in their atherosclerosis which required them to have surgery, so no claim of benefit can be made. (Sacks, Tr. 1455-56; 1459-60).

1289. Dr. Sacks' statement that no conclusions can be drawn from the study is extreme. (PX0025-0011).

1290. This was the first study ever published indicating that pomegranate juice may affect the progression of carotid atherosclerosis. (PX0025-0011).

1291. Science usually progresses when someone publishes a study of a series of patients with a non-randomized control group that shows an unprecedented finding which is then replicated by one or more subsequent randomized controlled trials, such as the one published by Dr. Davidson. (PX0025-0011).

1292. The study reported significant reductions in carotid IMT decreased systolic blood pressure, and a substantial inhibition of lipid peroxidation in serum and in LDL. (PX0025-0011).

1293. Dr. Sacks ignores the value of Dr. Aviram's analysis of carotid lesions in a subgroup of patients who underwent carotid endartherectomy, in which the lesions were surgically removed from the carotid artery. (PX0025-0011).

1294. In two out of the ten patients on pomegranate juice (after 3 and 12 months) due to clinical deterioration, carotid endartherectomy operation was performed and their carotid lesions were analyzed and compared to lesions obtained from seven patients that did not consume pomegranate juice (not the patients of the placebo group). (PX0025-0011).

1295. The cholesterol content in carotid lesions from the two patients that consumed pomegranate juice was lower by 58% and 20%, respectively, in comparison to lesions obtained from carotid artery stenosis patients that did not consume pomegranate juice. (PX0025-0011).

1296. Similarly, the lipid peroxides content in lesions obtained from the patients after pomegranate juice consumption for 3 or 12 months was significantly reduced by 61% or 44%, respectively, as compared to lesions from patients that did not consume pomegranate juice. (PX0025-0011).

1297. These findings suggests that oxidative stress, including oxidation of LDL to a form that makes it more likely to cause arterial blockages and cause foam cell production in macrophages (macrophage-derived foam cells play integral roles in all stages of atherosclerosis) may have been reduced by pomegranate juice consumption in these patients. (PX0025-0011).

1298. Although he complains this study lacked a control group, Dr. Sacks admits that a group taking nothing can serve as a control. (Sacks, Tr. 1585-86).

1299. Dr. Sacks concedes that he has no basis to disagree with Dr. Aviram's numbers. (Sacks, Tr. 1589-90).

1300. Dr. Sacks confirms that the CIMT test is "a worthy test" and is relevant to cardiovascular health. (Sacks, Tr. 1589-90).

1301. According to Dr. Sacks, CIMT is an indicator that the treatment may be beneficial and, in this case, the treatment was pomegranate juice. (Sacks, Tr. 1590).

1302. If the study design was not good enough, no peer-reviewed journal, such as the American Journal of Clinical Nutrition, would have published Dr. Aviram's study. (CX1348 (Aviram, Dep. at 28)).

3. Studies by Dr. Ornish and Colleagues

(a) Sumner M, Elliott-Eller M, Weidner G, Daubenmier JJ, Chew MH, Marlin R, Raisin CJ, and Ornish D, *Effects of pomegranate juice consumption on myocardial perfusion in patients with coronary heart disease*, 96 Am. J. Cardiology 810 (2005) (PX0023)

(1) Myocardial Perfusion (or Blood Flow to the Heart) Is the "Bottom-Line" in Evaluating Cardiovascular Health and Better Predictor and/or Surrogate for Cardiac Events

1303. Dr. Sacks believes that myocardial perfusion is a biologically and clinically interesting process, but is not used as the primary outcome in studies of drug treatment in coronary heart disease or recognized as surrogate marker of therapeutic effects on coronary heart disease. (CX 1291_0020-0021; Sacks, Tr. 1464).

1304. Dr. Sacks also complains that: (1) even where blood flow is shown to be improved, it will not necessarily result in improved cardiovascular health, such as reductions in heart attack and stroke; and (2) myocardial perfusion is a measurement that is not commonly used in studies of treatment efficacy. (CX 1291_0021).

a. Myocardial Perfusion Is the Bottom Line in Cardiovascular Health

1305. Blood flow is essential to life, an important measure of heart disease, and the bottom line in coronary heart disease. (Ornish, Tr. 2331).

1306. How much blood flow the heart receives is really the "bottom line" in coronary heart disease (along with how well the heart is pumping blood, called the ejection fraction). (PX0025-0012).

1307. Blood carries oxygen and nutrients that feed the heart. (PX0025-0012).

1308. If the blood flow to the heart (perfusion) is reduced, then the heart is no longer receiving enough blood flow to maintain itself. (PX0025-0012).

1309. Coronary heart disease, which is the most common form of heart disease, occurs when the heart does not get enough blood to fuel itself and blood carries oxygen, which is the fuel for the heart. (Ornish, Tr. 2331-32).

1310. Dr. Sacks concedes that if blood flow is reduced, then this is not desirable. (PX0361 (Sacks, Dep. at 179)).

1311. If this is temporary, then the person often experiences angina, or chest pain. (PX0025-0012).

1312. If this reduction in blood to the heart lasts more than a few hours, then that portion of the heart that is underperfused may die and turn in to scar tissue—this is commonly referred to as a "heart attack." (PX0025-0012).

1313. If this scar tissue is small, then the person may live; if this scar tissue is large or affects a critical part of the heart (e.g., the conduction system), then the person may die. (PX0025-0012).

1314. Any increase in myocardial perfusion would reduce the risk of cardiovascular or coronary problems and improve heart health because, even with a blockage of a minor artery, a patient could have a stent inserted at a hospital or allow him or her to survive the ride in the ambulance, and in the case of a blockage in a major blood vessel, there would be an increased chance of recovery. (Heber, Tr. at 1972-73).

1315. A surrogate is either a sign or a symptom that is associated along the pathway to a disease. (Heber, Tr. 1973).

1316. The FDA approves of LDL cholesterol as surrogate for cardiovascular disease. (Ornish, Tr. 2334).

1317. Dr. Ornish testified, however, that LDL cholesterol is really a risk factor for heart disease, and because it is not actually heart disease, it cannot be a valid surrogate. (Ornish, Tr. 2334).

1318. While the FDA for the purposes of drug registration and testing only accepts a limited number of surrogate markers, such as LDL cholesterol and blood pressure, the number of indicators that physicians and scientists use are much greater and can be at many points along the pathway of heart disease. (Heber, Tr. 1973).

1319. Clinical decisions are made, the health of the patient assessed and certain procedures are undertaken based on things that are surrogate markers, but may not be officially accepted by the FDA. (Heber, Tr. 1973).

1320. Doctors want a surrogate marker to be something as closely related as possible to the actual disease, so that studying the surrogate may allow us to predict the likelihood of the disease or its progression. (Heber, Tr. 1973-74).

1321. In comparing myocardial perfusion and LDL cholesterol, myocardial perfusion is more closely connected as a surrogate for cardiovascular disease. (Ornish, Tr. 2334).

1322. When a person has a biomarker like high LDL cholesterol which increases his or her risk, that is very distal or far away from the actual event of a heart attack which may be affected by many other factors, such as inflammation and oxidation. (Heber, Tr. 1974).

1323. There are a number of people who have low cholesterol levels, but get heart disease. (Ornish, Tr. 2334-35).

1324. About 50 percent of the people who die from a heart attack actually have cholesterol in the normal range. (Heber, Tr. 1974).

1325. There are people who have high cholesterol levels who do not have heart disease, and the same is true blood pressure. (Ornish, Tr. 2334-35).

1326. When measuring myocardial perfusion, researchers are actually measuring what matters most, which is how much blood flow the heart is getting. (Ornish, Tr. 2334-35).

1327. Dr. Sacks concedes that proper blood flow from the coronary artery and to the heart is fundamental to lowering the risk of cardiovascular disease. (Sacks, Tr. 1593).

b. Myocardial Perfusion Is a Better Scientific Test Than Coronary Angiography

1328. Dr. Ornish explains that for many years, it has been recognized that change in myocardial perfusion (blood flow to the heart) is actually a better predictor of cardiac events (thus a better surrogate marker) than coronary angiography. (PX0025-0012).

1329. Coronary angiography measures how much blockage is in the coronary arteries that feed the heart. (PX0025-0012).

1330. However, the degree of blockage is only one of several mechanisms that affect perfusion, or blood flow to the heart. (PX0025-0012).

1331. These include changes in vasomotor tone (how dilated or constricted the coronary arteries are), platelet aggregation (how sticky the platelets are that can form blood clots which may partially or complete occlude the flow of blood to the heart), and collateral blood flow (the heart can grow new blood vessels that provide additional blood flow around partial or even completely blocked arteries if the blockage occurs slowly overtime). (PX0025-0012).

1332. In addition, conventional coronary angiography (the most commonly performed type in clinical practice) provides only a two-dimensional view of the inside of the lumen of the coronary artery. (PX0025-0012).

1333. In a study a entitled "Compensatory enlargement of human atherosclerotic coronary arteries," N Engl J Med. 1987 May 28;316(22):1371-5, Dr. Glagov and others demonstrated that the majority of the coronary atherosclerosis (blockage) is inside the vessel wall and cannot be visualized using conventional coronary angiography—somewhat analogous to only being able to view the tipoff an iceberg but not the bulk of it below the surface of the ocean. (PX0025-0012).

1334. In a major study directly comparing the value of thallium 201-scintigraphy (the test used in Dr. Ornish's study to measure the effects of pomegranate juice on blood flow to the heart) and coronary angiography, the authors found measures of blood flow were more predictive of subsequent clinical events (e.g., heart attacks) than coronary angiography, and both were equivalent in predicting subsequent mortality. (PX0025-0012 *citing* Gibson RS, Watson DD, Craddock GB, *et al*. Prediction of cardiac events after uncomplicated myocardial infarction: a prospective study comparing predischarge exercise thallium-201 scintigraphy and coronary angiography. Circulation. 1983;68(2):321-336).

1335. The authors wrote: "Scintigraphy predicted low-risk status better than exercise testing ($p = .01$) or angiography ($p = .05$). Each predicted mortality with equal accuracy. However, scintigraphy was more sensitive in detecting patients who experienced reinfarction or who developed class III or IV angina….the overall sensitivity of angiography was lower than that of scintigraphy (71% vs. 94%; $p < .01$)." (PX0025-0012-13).

1336. This study was published in *Circulation*, the American Heart Association's lead scientific journal. (PX0025-0013).

1337. A more recent study that compared perfusion (blood flow) studies with an extensive variety of other cardiac measures, including coronary angiography, concluded: "Myocardial perfusion abnormalities at rest and after stress are still the best predictors of cardiac event–free survival in patients with known or suspected IHD, even when compared with an extensive diagnostic work-up." (PX0025-0012-13 *quoting* Gimelli A, Rossi G, Landi P, et al. Abnormalities by Gated

SPECT: Still the Best Predictor of Cardiac Events in Stable Ischemic Heart Disease. J Nucl Med 2009; 50:546–553).

1338. Thus, studies have shown that measures of myocardial perfusion or blood flow to the heart are actually not only as predictive, but are often more predictive of who is going to get a subsequent heart attack or dies than the blockages alone. (Ornish, Tr. 2333-34).

(2) Measures of SSS, SDS, and SRS

1339. In his myocardial perfusion study, Dr. Ornish examined three measures: (1) the sum of the segmental scores at stress ("SSS") (amount of infarcted, ischemic, or jeopardized myocardium); (2) the sum of the segmental scores at rest ("SRS") (amount of infarcted or hibernating myocardium); and (3) the sum difference score ("SDS") (the difference between SRS and SSS or amount of ischemic or jeopardized myocardium). (Ornish, Tr. 2341; PX0025-0013).

1340. "Ischemia" and "jeopardized" mean that part of the heart muscle (myocardium) is not receiving enough blood flow. (PX0025-0014).

1341. "Infarcted" means part of the heart muscle has died and turned into scar tissue and is nonfunctioning. (PX0025-0014).

1342. "Hibernating" means part of the heart muscle is also nonfunctioning and on the way to becoming infarcted. (PX0025-0014).

1343. SDS is considered a valid surrogate for coronary heart disease. (Ornish, Tr. 2341-42).

1344. Dr. Sacks complains, however, that Dr. Ornish's study shows significant changes in only one of the three measures at the end of the study –SDS, but not in SRS or SSS. (CX1291_0021).

1345. Dr. Sacks also argues the protocol for the study did not identify whether the primary endpoint would be SSS, SRS, or SDS or some other measurement calculated from the imaging data. (Sacks, Tr. 1475).

1346. Dr. Ornish observes, however, that the study protocol made it clear that the primary endpoint measure of the study was improvements in reversible ischemia as measured by exercise or pharmacologic perfusion studies (this is why one of the primary selection criteria for patients enrolled in this study was that they needed to have a reversible perfusion defect at baseline). (PX0025-0013).

1347. The primary end point, stated *a priori*, was how much blood flow the heart is getting when compared to rest and stress, which is what SDS measures. (Ornish, Tr. 2341).

1348. While SRS is a good predictor of who is likely to die earlier from heart disease since it measures dead or scarred heart tissue, this was not the question that Dr. Ornish attempt to answer in his myocardial perfusion study. (Ornish, Tr. 2342).

1349. Instead, Dr. Ornish was trying to determine whether areas of the heart that were not getting enough blood flow during peak exercise improve blood flow after drinking pomegranate juice, which is what he found. (Ornish, Tr. 2342-43)

1350. In other words, the SDS measures what Dr. Ornish stated *a priori* that he was most interested in: in plain English, would parts of the heart that were not receiving enough blood flow at baseline improve in patients who drank pomegranate juice compared to those in the randomized control group who drank a placebo? (PX0025-0014).

1351. While Dr. Ornish did not specify that changes in SDS would be the primary endpoint measure, it was not necessary to do so since SDS is a measure of how much of the heart was not receiving enough blood flow. (PX0025-0014).

1352. Because SDS is derived by subtracting SRS from SSS, it is a way of factoring out the amount of infarcted or hibernating myocardium so Dr. Ornish could focus on what he was most interested in: SDS. (PX0025-0014).

1353. Dr. Michael Sumner, who authored the study with Dr. Ornish, confirmed, through literature and discussions with a number of cardiologists, that SDS was the key variable to study. (CX1344 (Sumner, Dep. at 181)).

1354. Dead heart muscle does not get better, so the condition was not going to improve from pomegranate juice or from any other intervention. (PX0025-0014).

1355. Pomegranate juice improves blood flow to the heart but it does not bring dead tissue back to life. (PX0025-0014).

1356. Dr. Ornish did not expect to find any changes in either SSS or SRS, since these are measures of infarction, and that is just what he found. (PX0025-0014).

1357. Dr. Ornish, therefore, did not cherry-pick the data, and he did not ignore the SSS and SRS measures which were reported in the *American Journal of Cardiology* manuscript. (PX0025-0014).

1358. An improvement in myocardial perfusion is associated with decreased cardiac events (heart attacks, strokes, etc.) whether or not accompanied by improvements in angina or other clinical symptoms, which are much more subjective and less predictive than changes in myocardial perfusion. (PX0025-0014).

(3) Alleged Differences at Baseline for SRS and SSS Did Not Affect the Outcome of Dr. Ornish's Study

1359. Dr. Sacks critiques Dr. Ornish's study on the grounds that apparently there was a discrepancy in the baseline values of SRS and SSS, the two components of the SDS. (CX1291_0022; Sacks, Tr. 1461-62).

1360. Dr. Sacks, as a result, complains that it could be predicted that the control group, having worse coronary perfusion than the pomegranate group at baseline, would have a more accelerated form of the disease and show worsening on follow-up. (CX1291_0022; Sacks, Tr. 1469-70).

1361. Dr. Ornish explains, however, there was no difference in SRS and SDS at baseline, only a difference in SSS. (Ornish, Tr. 2343; PX0025-0015).

1362. Although there was a difference in SSS at baseline, Dr. Ornish employed an "analysis of variance," which took into account any baseline differences. (Ornish, Tr. 2343).

1363. Even if there had been a difference in SSS at baseline, this would not have undermined the validity of the study, particularly since it was not Dr. Ornish's primary end point measure. (Ornish, Tr. 2343; PX0025-0015).

1364. When researchers recruit randomly and look at a number of different measures, it is not uncommon that one difference may be statistically significant in the group. (Ornish, Tr. 2343-44).

1365. In his myocardial perfusion study, there were no differences between the groups in their cholesterol, blood pressure, blood sugar, and weights levels at baseline. (Ornish, Tr. 2344-45).

1366. The statistical phenomenon called "regression to the mean," holds that if someone is measured more than once, the outliers tend to come towards the middle, and any differences between the groups would be narrowed. (Ornish, Tr. 2344; PX0025-0015).

1367. As a result, if someone were sicker, all other things equal, if there was no effective intervention, it would be expected for the subsequent measures to show that the subjects were a little better, not that they were necessarily worse. (Ornish, Tr. 2344).

1368. As Dr. Sacks concedes out, "in any study involving a large number of variables, it is likely that some will be positive, simply due to chance." (PX0025-0015).

1369. In his study, Dr. Ornish reported: "To test for the effects of experimental condition and time (and their interaction) on medical characteristics, 2 (experimental vs. placebo) X 2 (baseline vs 3 months) analyses of variance for repeated measurements were run." (PX0025-0015).

1370. Thus, controlling for baseline differences is built into this analysis. (PX0025-0015; Ornish, Tr. 2394).

1371. In other words, it is concerned with whether the change over time is different between groups, so the groups do not have to start at the same place. Therefore, "statistical adjustment" is not necessary and could easily introduce bias. (PX0025-0015).

(4) Any Purported Omission of Patient Data Did Not Alter the Results of Dr. Ornish's Study

1372. Dr. Sacks attempts to discredit Dr. Ornish's study for only providing data on 39 patients although 45 persons planned to be enrolled in the study. (CX1291_0022).

1373. Dr. Sacks concedes that Dr. Ornish's study provides some rationale for removing four patients' data, but still argues the study offers no explanation for why the remaining two original patients were not included in the final data analysis. (CX1291_0022).

1374. According to Dr. Sacks, alterations in the original sample size may be critical when there is a borderline "p" value. (CX1291_0022).

1375. Dr. Sacks argues that Dr. Ornish's study did not follow the "intention-to-treat" analysis, which he regards as the standard for clinical trial analysis, to include data on all patients originally randomized to treatment or control, even data on dropouts. (CX1291_0022; Sacks, Tr. 1469).

1376. The basic principle of intention to treat is that participants in the trials should be analyzed in the groups to which they were randomized, regardless of whether they received or adhered to the allocated intervention. (PX0025-0016 *citing* Hollis S, Campbell F. What is meant by intention to treat analysis? Survey of published randomised controlled trials. BMJ 1999; 319 : 670).

1377. Dr. Ornish agrees that a mistake was made in not reporting data on the remaining 41 patients. (PX0025-0015).

1378. However, when data on all 41 patients were analyzed, the difference in SDS remained statistically significant and, therefore, the conclusions of the study remain valid. (PX0025-0015; Ornish, Tr. 2347-48).

1379. If anything, the results were more statistically significant and even stronger because the sample size was slightly larger. (Ornish, Tr. 2347-48; 2394).

1380. The idea that clinical trials must use the intention to treat analysis or they are not valid is a rather extreme position, especially because this is a randomized, double-blind, placebo-controlled trial, which is considered to be the most rigorous experimental design. (PX0025-0015-0016).

1381. A published survey shows that per-protocol was the basis of at least 50 percent of the studies published by four of the top-tier scientific journals: the New England Journal of Medicine, the Journal of the American Medical Association, Lancet, and British Medical Journal and less than half of the studies were even randomized, controlled trials, much less using intention-to-treat method. (Ornish, Tr. 2350-51; PX0025-0016).

1382. Dr. Sacks' assertion that it was not a RCT and therefore is not good science, is not borne out by the top-tier journals who publish these studies all the time. (Ornish, Tr. 2350-51).

1383. Most of Dr. Sacks' own research would not meet this standard. (PX0025-0016).

1384. Dr. Ornish used the intention-to-treat method in reporting all available data. (Ornish, Tr. 2349).

1385. In this case, if Dr. Ornish used the last value carried forward, *i.e*. baseline values of patients who did not receive the intervention, that would mean there would be no change and that would be introducing a negative bias. (Ornish, Tr. 2349).

1386. The "last observation carried forward" analysis is not appropriate when only baseline measurements are available in dropouts, as imputing missing data may introduce its own set of biases. (PX0025-0016 *citing* Julious SA, Mullee MA. Issues with using baseline in last observation carried forward analysis. Pharmaceut. Statist. 2008; 7: 142–146.).

1387. If studying a new drug, such as a chemotherapy agent that has major toxicities, it would be appropriate to use the most conservative method of analysis before you release that information to the American public. (Ornish, Tr. 2349).

1388. But when evaluating a fruit juice, it is not necessary to go to the extreme of biasing against showing the effect. (Ornish, Tr. 2349-50).

1389. Dr. Ornish also used the per-protocol method as well and reported all available data. (Ornish, Tr. 2350).

(5) The Unblinding of Patients or Lack of Placebo Does Not Diminish the Validity of Dr. Ornish's Study

1390. Dr. Sacks challenges Dr. Ornish's study on the grounds that seven or eight of the patients in the placebo group were unblinded before their three-month data was collected. (CX1291_0023; Sacks, Tr. 1476-77).

1391. Dr. Sacks also complains that two other patients in the placebo group did not, in fact, receive a placebo treatment. (CX1291_0023; Sacks, Tr. 1476-77).

1392. Dr. Ornish agrees with Dr. Sacks that the fact that a few participants became unblinded is a "demerit," but this does not affect the outcome of the study. (Ornish, Tr. 2345).

1393. The expectation that an intervention is beneficial has the potential for confounding the outcome of a study, but such an outcome was unlikely to have occurred in this study. (PX0025-0016).

1394. At the time that the study was conducted, there was not an awareness in the general population that pomegranate juice was beneficial or even that the subjects were drinking pomegranate juice (the study was entitled a "beverage study"). (PX0025-0016; (CX1339 (Ornish, Dep. at 148-149)).

1395. At the time of the unblinding, people did not know that pomegranate juice might even be beneficial to them and if they found they were drinking Gatorade, there was a greater likelihood that that they would have thought that was the intervention. (Ornish, Tr. 2345-46; (CX1339 (Ornish, Dep. at 148-149)).

1396. The real issue or reason studies are blinded is the expectation that something might have a positive benefit can sometimes be self-fulfilling, but in this case, there is no reason why the subjects would have necessarily thought that, even if they knew they were drinking pomegranate juice that was likely to provide them a benefit, because this was before people even knew what pomegranate juice was other than an exotic juice. (Ornish, Tr. 2346; (CX1339 (Ornish, Dep. at 148-149)).

1397. It would be a stretch to say that subjects simply thinking they were getting something beneficial could affect blood flow to the heart, but even if one assumed that were true, they might just as well thought that the Gatorade would be as beneficial as the pomegranate juice. (Ornish, Tr. 2347).

1398. Although these minor discrepancies were not optimal, they do not undermine the validity of the study or its conclusions. (PX0025-0016).

(6) The Results of Dr. Ornish's Study Remain Valid Despite a Three-Month Testing Period

1399. Dr. Sacks notes that Dr. Ornish's study originally was designed to last for 12 months, with measurements at baseline, three months, and 12 months, but was halted after three months due to funding shortfalls. (CX1291_0023).

1400. Dr. Sacks speculates that the study was terminated under unusual circumstances because, according to correspondence, at the time, the p-value was considered significant rather than at the time the trial was originally set to end. (CX1291_0023-0024).

1401. Dr. Sacks suggests the shortened study period and failure to report the planned duration is inconsistent with widely-accepted standards for conduct of clinical trials and undermines any confidence in the findings. (CX1291_0024; Sacks, Tr. 1474-75).

1402. Dr. Ornish explains that study was terminated after three months only because the Resnicks did not provide the funding that they had previously committed to this study, not because the p-value was statistically significant at three months. (PX0025-0017).

1403. Dr. Ornish originally planned to study these patients at three months and at one year, but because he did not have the funding to do it for one year, he only measured patients for three months. (PX0025-0017; Ornish, Tr. 2351-52).

1404. Dr. Ornish clearly intended to do a twelve-month follow-up which is why nine of the patients completed their 12-month testing before the funding was cut. (PX0025-0017).

1405. The only reason Dr. Ornish did not test all of the patients at 12 months is that the funding was no longer available to do so for reasons beyond his control. (PX0025-0017).

1406. While Dr. Ornish did not have 12 months of follow-up data, this does not undermine the confidence in the three-month findings, which stand on their own. (PX0025-0017).

1407. Bias is not an issue because outside factors precluded obtaining twelve-month data. (PX0025-0017).

(7) The Results of Dr. Ornish's Myocardial Perfusion Study Remain Valid Despite Dr. Sacks' Overall Criticisms

1408. Dr. Sacks is not a cardiologist and not even an expert on technique Dr. Ornish used. (Sacks, Tr. 1591).

1409. Despite his criticisms, Dr. Sacks nevertheless concedes that the concerns he raises regarding the unblinding of patients, the change in duration of the study, or the use of per protocol analysis are just demerits, none of which are fatal to the study. (Sacks, Tr. 1602-03; PX0361 (Sacks, Dep. at 201-202)).

1410. Dr. Sacks also tries to discredit Dr. Ornish's study on the grounds that other factors, such as blood pressure, cholesterol, inflammatory biomarkers, and oxidative stress were not improved. (CX1291_0024).

1411. The fact that other factors such as blood pressure and cholesterol did not improve does not in any way provide evidence that pomegranate juice was not beneficial, as its effects may have been mediated via other pathways. (PX0025-0017-0018).

1412. Indeed, Dr. Sacks concedes the lack of statistical significance for a positive result is not proof of a negative. (Sacks, Tr. 1608).

1413. No single study is perfect and virtually all studies have limitations. (PX0025-0005).

1414. Dr. Ornish explains that an unbiased doctor could not throw out his positive myocardial perfusion study because of the criticisms raised by Dr. Sacks. (Ornish, Tr. 2351).

(b) The Unpublished Beverage Study II, June 21, 2003 ("Bev II") (CX 754)

1415. Dr. Sacks complains that Dr. Ornish's unpublished Bev II Study, designed to measure CIMT in 200 patients for a period of one year, showed no statistically significant changes to CIMT, elasticity, blood pressure, body mass index, cholesterol, HDL, and TG at the end of the trial. (CX 754; Sacks, Tr. 1484-1486).

1416. In preparing his power analysis for this study, and based on earlier studies in the field, Dr. Ornish estimated that he would need at least 200 patients to show a statistically significant difference in CIMT and budgeted his study accordingly. (Ornish, Tr. 2352).

1417. During the Bev II study, however, because recruitment took longer than anticipated (since most patients with heart disease ended up having angioplasty,

stents, and/or bypass surgery at a much higher rate than anticipated), the funding was cut, so Dr. Ornish was only able to recruit 73 patients, from which 56 patients pre and post data was collected. (Ornish, Tr. 2352).

1418. In his findings, Dr. Ornish nevertheless observed an improvement in the carotid artery significant to the 0.13 level as opposed to the 0.15 level. (Ornish, Tr. 2352-54).

1419. Dr. Sacks agrees that the Bev II Study concept and study design were fine and the measurements read by good institutions. (Sacks, Tr. 1603).

1420. If that degree of change had occurred in the larger number of patients he had projected (i.e. 200 instead of 73), it would have been clearly at the 0.05 level or less and it would have been a strong study showing pomegranate juice affected the progression of carotid disease. (Ornish, Tr. 2352-54).

1421. In the Bev II Study, Dr. Ornish also found a similar, almost statistically significant improvement in the elasticity of the arteries. (Ornish, Tr. 2353).

1422. If he recruited and tested the number of patients in the protocol, Dr. Ornish would have reached statistical significance because there is no reason to think the next 127 patients would have been different than the first 73. (Ornish, Tr. 2353-54).

1423. It would have been inaccurate to report that pomegranate juice did not affect the progression of carotid atherosclerosis, since the study was underpowered for this purpose, and it would have been what is known as a type II error: that there may have been a statistically significant difference but the sample size was not sufficiently large to detect it. (PX0025-0019; (CX1339 (Ornish, Dep. at 70-71; 81-82).

1424. While Dr. Sacks states that this study proved that pomegranate juice had no effect on carotid IMT, it would be more accurate to see this study as a validation of the Dr. Aviram and Dr. Davidson studies since the differences in CIMT would have been statistically significant if the findings we measured in 73 patients were found in the 200 patients that we originally planned to enroll. (PX0025-0019).

1425. Although he disputes Dr. Ornish's suggestion that this study was underpowered, Dr. Sacks admits that the Bev II Study was indeed "underpowered" and concedes it is possible there could have been statistically significant differences if the sample size were larger. (Sacks, Tr. 1607-08; PX0361 (Sacks, Dep. at 210)).

1426. Dr. Sacks admits that the lack of statistical significance for a positive result in Bev II Study is not proof of a negative and does not mean pomegranate juice is not beneficial. (Sacks, Tr. 1608-09).

4. Studies by Dr. Davidson and Colleagues

(a) Davidson MH, Maki KC, Dicklin MR, Feinstein SB, Witchger MS, Bell M, McGuire DK, Provost JC, Liker H, and Aviram M, Effects of consumption of pomegranate juice on carotid intima-media thickness in men and women at moderate risk for coronary heart disease, 104 Am. J. Cardiology 936 (2009) (PX0014)

(1) Dr. Sacks Cannot Dismiss Dr. Davidson's Findings Because the Composite Measure of CIMT Was Allegedly Not Listed as the Primary Outcome Endpoint in the Original Protocol

1427. Dr. Sacks criticizes Dr. Davidson's study because it reports a statistically significant change in the composite measurements of the IMT at 12 months (and statistically significant changes in the anterior and composite measurements in a certain subgroup of patients at 18 months), not the posterior wall measurements as purportedly identified in the study protocol. (CX1291_0027; Sacks, Tr. 1498; CX 716_0028; CX1336 Davidson Dep. at 10-11, 16)).

1428. Although Dr. Sacks acknowledges that the composite rate for all measured carotid artery walls demonstrated a significantly smaller value at 12 months in the pomegranate juice group, he discounts the importance of this finding because (a) it was not the primary endpoint measure, and (b) "this difference was no longer significant at the end of the study." (Sacks, Tr. 1498-99; CX1291_0028; PX0025-0019).

1429. Dr. Ornish explains, however, that the composite rate for all measured carotid artery walls should have been the primary endpoint measure in Dr. Davidson's study because it includes all measurements of CIMT, not just the posterior wall. (PX0025-0020).

1430. In his deposition, Dr. Davidson believed that the primary outcome was modified to be the composite of the anterior and posterior wall measurements and this decision was made before unblinding of the study. (CX1336 (Davidson, Dep. at 24-25)).

1431. Another secondary outcome measure identified in the protocol was the composite CIMT, combining the common and internal carotid artery and carotid bifurcation. (CX1336 (Davidson, Dep. at 17); CX1291_0027).

1432. Here, Dr. Davidson's composite measure was clearly stated *a priori* as a secondary hypothesis in the study protocol: "The secondary outcome variables will include the difference between placebo and POM Wonderful juice groups in

the composite measure, which combines the measurements of the common and internal carotid artery and the carotid bifurcation (Smilde 2001), in mm/year." (PX0025-0020; CX0716_0028).

1433. Dr. Sacks concedes that secondary outcome variables are included in a clinical trial because they are often considered to be an important secondary manifestation of disease secondary to what is declared as primary. (PX0361 (Sacks, Dep. at 212).

1434. Dr. Sacks confirms that the use of secondary outcome variables are generally accepted method in conducting clinical trials. (PX0361 (Sacks, Dep. at 213).

1435. Dr. Sacks admits that when a secondary outcome variable is stated in advance, this increases the credibility of the result because it eliminates the chance of cherry picking results that are later found to be positive. (PX0361 (Sacks, Dep. at 213).

1436. As such, Dr. Davidson's finding at 12 months is not likely to be just a chance finding of having measured lots of different parameters; it is the most clinically meaningful. (PX0025-0020).

1437. Because Dr. Davidson's composite measure was listed as a secondary outcome, Dr. Sacks cannot conclude that the findings were somehow "due to chance." (PX0025-0020).

1438. Dr. Sacks also admits that one reason that the posterior wall CIMT was chosen as the primary endpoint initially was not because it was the best measure, but because it was easier to obtain: "One reason to use posterior wall measurements as the primary outcome is that they do not require injection of a contrast agent like anterior wall measurements do." (CX1291_0029; PX0025-0020).

1439. Because the investigators were successful in obtaining anterior wall measurements on a larger group of patients than expected, it would be extreme to say that this finding was not important or clinically relevant simply because it was not stated as the primary endpoint measure *a priori* but was stated as a secondary endpoint measure a priori. (PX0025-0020).

1440. By examining the composite measurement, Dr. Davidson did not believe this calculation would be the most likely to present a positive result, but simply that it would give him more walls and more power to seen an effect if there was one. (CX1336 (Davidson, Dep. at 142)).

(2) The Lack of a Statistical Significance Finding at 18 months Does Not Diminish Dr. Davidson's Study or the Conclusion that Pomegranate Juice Can Affect Arterial Plaque

1441. Dr. Sacks complains there was no significant effect of pomegranate juice on CIMT of the anterior, posterior, or composite carotid artery at the end of the trial. (Sacks, Tr. 1491).

1442. The fact that differences in the composite measurement of CIMT were not statistically significant at 18 months does not change the fact that these differences were statistically significant after 12 months. (PX0025-0020; PX0014-0005).

1443. Dr. Davidson's protocol called for measurements at both 12 months and 18 months. (Heber, Tr. 1980-81).

1444. A likely explanation for the difference in the CIMT progression rate for the intervention group could be that compliance for drinking pomegranate juice declined significantly after the first year. (PX0025-0020; PX0014-0005).

1445. In his 34 years of directing RCTs, Dr. Ornish notes that it is very challenging to motivate patients to continue following any intervention for more than one year. (PX0025-0020).

1446. Dr. Ornish further observes that is not unusual for patients to be less than honest in describing their compliance as patients often describe that it is embarrassing and even humiliating to report that they have not done what they were supposed to do. (PX0025-0020).

1447. It is also possible that patients in the control group may have started drinking pomegranate juice after one year. (PX0025-0020).

1448. Although there was not objective evidence of noncompliance, Dr. Davidson believes the fact that the antioxidant measures were positive at 52 weeks, but not positive at the end of the study, suggests that the subjects may have not been taking the pomegranate juice at the end of the study. (CX1336 (Davidson, Dep. at 174-75)).

1449. The indeterminate result at 18 months is not proof of the negative; it does not prove that pomegranate juice does not have an effect. (Heber, Tr. 1981).

1450. If a hypothesis is not proved in a particular study, it does not mean the hypothesis is wrong; it just means the researcher did not prove it in that study. (Heber, Tr. 1981).

(3) The Lack of Statistical Significance re other Biomarkers

1451. Dr. Sacks complains there were no significant effects of pomegranate juice compared to the control group on measures of inflammation and oxidative stress, including blood pressure and TBARS. (Sacks, Tr. 1492-93; CX1291_0028).

1452. Dr. Sacks also speculates that Dr. Davidson's study did not replicate improvement in LDL oxidation, increase in paraoxonase activity, and decrease in TBARS found in Dr. Aviram's studies. (Sacks, Tr. 1507).

1453. The fact that certain biomarkers did not reflect a statistically significant change does not invalidate the statistically significant improvements in both the composite CIMT as well as in the subgroup of patients who were at highest risk. (PX0025-0021).

1454. The absence of evidence is not evidence of absence, so merely the fact that a research has not found something in a particular study does not mean the result does not exist. (Heber, Tr. 1981).

1455. Dr. Sacks concedes that the absence of positive results with respect to indicators of inflammation of oxidative stress, fasting lipoproteins, or blood pressure does not prove the negative. (PX0361 (Sacks, Dep. at 223-24)).

(4) Post Hoc or Subgroup Analyses Like Dr. Davidson's, Are Commonly Done and Provide Useful Information

1456. Dr. Sacks challenges Dr. Davidson's post hoc analysis, in which Dr. Davidson found a statistically significant lower anterior and/or composite IMT progression rates at the end of the study in a certain subgroup of patients, because it was not "pre-planned" and because patients with metabolic syndrome within that subgroup did not show a benefit. (CX1291_0028-30).

1457. While a post hoc analysis is not as rigorous as one stated *a priori*, it does provide supporting evidence that there was statistically significant lower CIMT progression rates for pomegranate versus control subjects in those with higher cardiovascular disease risk factors. (PX0025-0021).

1458. Dr. Davidson's post hoc analysis is clinically important, as other studies, including RCTs, also showed that subpopulations of patients who are sicker often are more likely to show improvement. (PX0025-0021).

1459. Dr. Davidson's finding was appropriately qualified in his study, but it would be extreme to dismiss this finding as being irrelevant simply because it was not stated *a priori*. (PX0025-0021).

1460. In scientific research, post-hoc analysis is routine. (Heber, Tr. 1984).

1461. Although the exploratory analysis was not called for by the protocol, such analyses, including those on subgroups, are commonly done. (CX1336 (Davidson, Dep. at 57, 221)).

1462. Dr. Davidson commonly performs subgroup analyses in the studies in which he is the lead investigator. (CX1336 (Davidson, Dep. at 221)).

1463. In Dr. Davidson's view as a clinician, important information might be available in subgroup analysis that could be ultimately very clinically beneficial to patients. (CX1336 (Davidson, Dep. at 221)).

1464. In the Women's Health Initiative study, for example, the largest women's health study in history, the overall effects of a low fat diet on breast cancer were indeterminate, but many of its important findings, however, were so-called post hoc analyses. (Heber, Tr. 1984).

1465. In many studies, researchers often go back and look at the data in the two groups and try to find additional leads for future studies, generate additional information to clarify the findings of that study, so it is a method that is routinely done. (Heber, Tr. 1984).

1466. Dr. Sacks admits that it is certainly fine to conduct a post hoc analysis of some groups and concedes that he has done so in his own studies because he was interested in understanding whether a treatment affected all of the different patient groups or subgroups in the study. (PX0361 (Sacks, Dep. at 221-23)).

1467. Dr. Sacks does not discount Dr. Davidson's subgroup analysis. ((PX0361 (Sacks, Dep. at 268)).

1468. If there is a positive result in the subpopulation, the post hoc analysis does not undermine the results of the research on the population as a whole. (CX1352 (Heber, Dep. at 223)).

1469. It is not necessary to wait for a subsequent study before telling the public of the likely benefit arising from a subgroup analysis. (Heber, Tr. 1984-85).

1470. There could be tens of millions of people in the United States in Dr. Davidson's high risk subgroup shown to be helped by pomegranate juice who are unaware of their health risks. (Heber, Tr. 1985).

1471. If there is a 5 percent improvement in health measure and it affected tens of millions of people in the United States, a 5 percent change would not be too small to consider as an important finding, especially if there no toxicities associated with it. (Heber, Tr. 2007).

1472. The post hoc analysis done in Dr. Davidson's study has clinical relevance because it is consistent with the potential benefits of antioxidant treatment with pomegranate juice. (CX1336 (Davidson, Dep. at 221)).

1473. The subgroup in which a benefit was found is a group having more oxidative stress, so there was more likely to see a benefit in that subgroup. (CX1336 (Davidson, Dep. at 222)).

1474. The benefits occurred at a composite endpoint, but they also appeared directionally in the same way for both the anterior and posterior wall, which means there are two artery walls showing the same consistent effect. (CX1336 (Davidson, Dep. at 222)).

1475. There was also a benefit on the inflammatory marker of CRP, which is a surrogate for cardiovascular disease. (CX1336 (Davidson, Dep. at 222)).

1476. There were two independent biomarkers showing an effect in the same subgroups, which leads Dr. Davidson to believe the benefit in these subgroups are real and need to be verified with further research. (CX1336 (Davidson, Dep. at 221-22)).

1477. Dr. Davidson also notes that when researchers try to look at an effect of a treatment, they have to make sure they are using it in the patients that are having a problem that the treatment can address. (CX1336 (Davidson, Dep. at 222-23)).

1478. Dr. Davidson has presented his post hoc analysis to members of the scientific community who believed his finding was a real, true signal of benefit in the subgroup that would be supported in a future trial. (CX1336 (Davidson, Dep. at 224)).

1479. Looking at the whole set of data in totality and at multiple subgroups showing a benefit, Dr. Davidson's study was convincing to panel members there was a potential benefit in the subgroup population. ((CX1336 (Davidson, Dep. at 225)).

(5) Correcting for Multiple Comparisons Was Not Necessary

1480. Dr. Sacks critiques Dr. Davidson's study on the grounds that no correction for multiple comparisons were made. (Sacks, Tr. 1504-05).

1481. According to Dr. Davidson, it was not appropriate to make any corrections for multiple comparisons because he already stated in the study that these were hypothesis-generating findings. (CX1336 (Davidson, Dep. at 81)).

1482. Dr. Sacks concedes that many researchers do not correct for multiple comparisons in their studies. (PX0361 (Sacks, Dep. at 228)).

(6) Dr. Sacks Cannot Challenge a Benefit to the High-Risk Subgroup Based on Data from the Metabolic Syndrome Group

1483. In Dr. Davidson's study, a subgroup of patients demonstrated a 4 to 9 percent statistically significant improvement in CIMT at the end of the study, depending on whether one looked at the anterior or posterior wall of the artery in terms of thickness. (Heber, Tr. 1982).

1484. Dr. Sacks complains, however, that the pomegranate juice subjects with metabolic syndrome were not among the sub-populations who had significantly lower CIMT values after treatment. (CX1291_0028).

1485. Metabolic syndrome is an umbrella term, which probably affects 50 percent of people between the ages of 45 and 65, and includes anyone with three of the five criteria, such as increased waist circumference, high blood sugar, high blood pressure, high triglycerides, and low HDL. (Heber, Tr. 2006).

1486. The subgroup in Dr. Davidson's study included people with high triglycerides and low HDL cholesterol. (Heber, Tr. 2006).

1487. Individuals with these factors typically have metabolic syndrome, suffering from high triglyceride and low HDL, and meeting one other criteria like a large waist circumference, a high blood sugar, an intermediate range or high blood pressure. (Heber, Tr. 2006).

1488. The measure of high triglyceride is the most sensitive index of increased oxidative stress, so a high triglyceride/low HDL population would make sense as the group that would have increased oxidative stress and would benefit more from the consumption of pomegranate juice. (Heber, Tr. 2006).

1489. In criticizing Dr. Davidson, Dr. Sacks contradicts himself: although he claims post hoc analyses are not reliable, he must think that post hoc analyses have scientific value even if not at the same level of rigor as endpoint measures declared *a priori*, so he undercuts his earlier, more extreme argument that the statistically significant improvements in composite rate for all measured carotid artery walls should not be considered as valid evidence. (PX0025-0022).

1490. The finding that pomegranate juice did not significantly reduce CIMT in metabolic syndrome patients does not detract from the fact that there were significantly lower CIMT progression rates for pomegranate versus control subjects at the end of the study in certain subpopulations with higher CVD risk factors, such as those in the highest tertiles for apolipoprotein B, TG, TG to HDL ratio, total cholesterol to HDL ratio, as well as a purported marker of antioxidant function, PD-AAPH. (PX0025-0022).

1491. In addition, the fact that pomegranate juice did reduce carotid artery blockages in subgroups with these cardiac risk factors is not diminished by the fact that it did not reduce carotid artery blockages in all subgroups of risk factors, such as those with metabolic syndrome. (PX0025-0022).

1492. These are of interest more from the standpoint of having a better understanding of the mechanisms by which pomegranate juice may be beneficial than on whether or not pomegranate juice is beneficial in reducing carotid artery blockages (atherosclerosis). (PX0025-0022).

1493. The "bottom line" is improvements (reductions) in carotid artery blockages from drinking pomegranate juice, which were statistically significant in composite rate for all measured carotid artery walls in these patients. (PX0025-0022).

1494. Dr. Sacks concedes that subgroup benefited in Dr. Davidson's study could include millions of people in the United States alone, but still takes the extreme position that such information cannot be disseminated. (Sacks, Tr. 1613-16).

(7) Conclusions

1495. Dr. Sacks' overall criticisms of the Davidson study are without merit. (PX0025-0019-0021; *infra* RFF 1427-1494).

1496. Dr. Davidson's study was conducted and evaluated in an objective manner by people qualified to do so. (CX1336 (Davidson, Dep. at 227)).

1497. Dr. Davidson has recommended pomegranate juice or POMx to patients who fit the high-risk profile. (CX1336 (Davidson, Dep. at 225)).

1498. There are no adverse risks of taking pomegranate juice. (CX1336 (Davidson, Dep. at 226)).

1499. To see the effect of an antioxidant therapy like pomegranate juice, the intervention needs to be used in a population with high oxidative stress, and the more oxidative stress present, the more likely it will be to see a benefit with the treatment. (CX1336 (Davidson, Dep. at 228-29)).

1500. Testing an intervention in populations with higher levels of oxidative stress has been in a theme in Dr. Davidson's findings and it is consistent with other research. (CX1336 (Davidson, Dep. at 228-29)).

1501. Dr. Davidson's study does not suggest in any way that pomegranate juice affirmatively does not benefit the heart. (CX1336 (Davidson, Dep. at 229)).

1502. Nobody at POM or Roll ever suggested anything to Dr. Davidson regarding this study that he thought was scientifically unsound or inappropriate. (CX1336 (Davidson, Dep. at 230)).

1503. Dr. Davidson's study was approved and published in a reputable journal, which meant that editors were satisfied with the responses to the reviewers comments. (CX1336 (Davidson, Dep. at 230)).

1504. A peer-reviewed journal would have only published Dr. Davidson's study if it believed the data was worth publishing and significant. (CX1352 (Heber, Dep. at 199-200)).

(b) Dr. Davidson's Unpublished "BART" (or Flow-Mediated Vasolidation) Study

1505. Brachial artery reactivity testing or "BART" is a measurement of how much the brachial artery dilates (enlarges) after a blood pressure cuff is inflated, and then released. This is also called flow mediated dilation ("FMD") testing. (JX 3; CX1336 (Davidson, Dep. at 34-35)).

1506. The brachial artery is a major blood vessel of the arm. (JX 3).

1507. Flow mediated dilation (or "FMD") is the amount by which the brachial artery dilates (gets larger) after the blood pressure cuff is deflated. (JX 3).

1508. Dr. Davidson studied the effect of POM pomegranate juice on 45 patients (from his IMT study) for 13 weeks using the BART measurement. (PX0019; CX1336 (Davidson, Dep. at 37)).

1509. At the end of 13 weeks, no statistically significant differences were observed between or within the treatment groups. (PX0019; Sacks, Tr. 1510; CX1336 (Davidson, Dep. at 87)).

1510. Although he acknowledges that Dr. Davidson's BART study was carefully designed and did not have any critical problems, Dr. Sacks complains that BART is not a reliable marker of heart health, although of interest, is not a valid or generally recognized surrogate marker of coronary heart disease. (1291_0031; Sacks, Tr. 1510-11).

1511. Dr. Sacks also suggests that Dr. Davidson's BART study showed no effect on blood pressure or ACE, which is somehow inconsistent with Dr. Aviram's prior research. (Sacks, Tr. 1512-13).

1512. In response, if Dr. Sacks believes that "brachial artery reactivity, although of interest, is not a valid or generally recognized surrogate marker of coronary heart disease," then the study's findings that there were no statistically significant differences between the groups is irrelevant. (PX0025-0024).

1513. Dr. Sacks concedes that just because the BART study does not show statistically significant changes with respect to blood pressure and ACE, among other measurements, that the absence of such evidence is proof there is no effect. (PX0361 (Sacks, Dep. at 230)).

5. The Overweight Study Conducted by Dr. Heber and Dr. Hill Demonstrates POMx's Safety and Antioxidant Effect and Does Not Contradict Respondents' Previous Scientific Research

1514. In 2007, in a study entitled "Safety and Antioxidant Activity of Pomegranate Ellagitannin-Enriched Polyphenol Dietary Supplement in Overweight Individuals with Increased Waist Size" by Dr. Heber, et al., J. Agric. Food Chem. 2007, 55, 10050–10054, Dr. Heber and Dr. Hill, at the University of Colorado, examined the safety and antioxidant activity of POMx on overweight individuals with increased waist size. (CX0934).

1515. At the San Diego site, where the authors conducted the safety part of the study, 64 overweight individuals received one or two POMx capsules per day for four weeks. (CX0934).

1516. With respect to the safety of POMx, Dr. Heber found that "[t]here were no serious adverse events reported," "no qualitative or quantitative differences between treatment groups or by comparison placebo," "no apparent treatment-related changes of clinical significance, and no laboratory results were outside the normal range in any of the chemistry, hematology, or urinalysis laboratory testing." (CX0934_0003).

1517. At the Denver site, where antioxidant activity was measured, 22 overweight subjects received two POMx capsules per day for four weeks. (CX0934_0003).

1518. With respect to antioxidant activity, Dr. Hill found a statistically significant reduction in "TBARS" (thiobarbituric acid reactive substances), which is an important biomarker of oxidative stress in humans and strongly predictive of cardiovascular events in people with stable coronary artery disease, independent of traditional risk factors and inflammatory markers. (CX0934_0003-0004).

1519. In conducting this study, Dr. Hill decided that TBARS (would be the best measure of antioxidant activity after reviewing literature and consulting with colleagues, specifically researchers at the National Jewish Hospital who have expertise in antioxidant activity. (CX 1342; Hill, Dep. at 41-42))

1520. A higher level of TBARS is bad while a lower level of TBARS is good. (CX 1342; Hill, Dep. at 42)).

1521. Together, the authors concluded that POMx is safe and effective in reducing oxidative stress in humans through the measure of TBARS. (CX0934_0004).

(a) Dr. Sacks' Complaints Regarding the Denver Site Study Lack Merit

1522. Although he acknowledges there was a decrease in TBARS, Dr. Sacks complains the change in TBARS was of only borderline significance and that the analysis was not adjusted for the number of comparisons being made. (Sacks, Tr. 1514; CX1291_0033).

1523. Dr. Sacks also complains that at the Denver site, the other factors measured – including diastolic and systolic blood pressure, TG, HDL, LDL, CRP, and PON – did not change during the trial. (CX1291_0033).

1524. Dr. Sacks further points to a preliminary data report which suggests the researchers "did not detect any effect of POMx on inflammation but identification of better biomarker assays for inflammation is needed.. . . [T]his pilot project suggests that a larger trial is warranted in abdominally obese subjects who may be at risk for development of metabolic diseases." (CX1291_0033).

1525. Finally, Dr. Sacks suggests that the lack of a control group renders the study's finding unreliable. (CX1291_0035).

(1) Even If Considered a "Pilot" Study, the Results Are Still Valid

1526. The reason a researcher conducts a "pilot" study is because he or she is not certain how many subjects it will take to adequately power the study. (CX1342 (Hill, Dep. at 48)).

1527. If it turns out that a researcher has adequately powered his or her study, then statistics confirm that it does not matter if it was a "pilot" study. (CX1342 (Hill, Dep. at 48)).

1528. If there is no effect shown, then this allows the investigators to address any concerns regarding the study. (CX1342 (Hill, Dep. at 46-47)).

1529. In short, there is no difference between a pilot study and regular study if there is statistical significance. (CX1342 (Hill, Dep. at 49)).

1530. In Dr. Hill's study, the effect was large enough that he saw a statistically significant difference. (CX1342 (Hill, Dep. at 47)).

1531. If he received a difference that was not significant, then Dr. Hill would not have been able to publish his results. (CX1342 (Hill, Dep. at 47)).

1532. A "pilot" study does not mean that it is not as scientifically valid as a larger study. (PX1339 (Ornish, Dep. at 23; 119-20).

(2) The Lack of a Placebo Control Group Does Not Render the Results Unreliable

1533. In a pre/post test design, the effect of an intervention is measured on a person before and after he/she receives the intervention. (CX1342 (Hill, Dep. at 45)).

1534. In a control group design, one group would receive the intervention while another group would receive a placebo, and the results of both groups would then be compared. (CX1342 (Hill, Dep. at 45)).

1535. Neither the pre/post nor control group design is a better than the other. (CX1342 (Hill, Dep. at 45)).

1536. The two approaches are apples and oranges: each provides different information, both are very fair and reasonable designs, and some questions lend themselves more to a between group analysis, while some lend themselves to a within group analysis. (CX1342 (Hill, Dep. at 100-101, 133)).

1537. A placebo-controlled trial is more costly and requires a lot more effort to conduct. (CX1342 (Hill, Dep. at 45)).

1538. Given that Dr. Hill did not have information that would allow him to adequately power this trial, the pre/post trial design was the most efficient approach and would provide the outcome needed. (CX 1342 (Hill, Dep. at 45-46)).

1539. While there are some advantages to a placebo controlled trial, a pre/post design can be very powerful when you are convinced that you are assessing a steady-state at baseline, and that the differences are attributed to your intervention. (CX 1342 (Hill, Dep. at 131)).

1540. To suggest that "the lack of a control group render its findings unreliable" is to belie the premise of a pilot study, which is to generate preliminary findings that

can be used to justify doing a larger, more expensive intervention with a control group. (PX0025-0024)

(3) Adjusting for the Number of Comparisons Made Is Not Common Among the Scientific Community

1541. The analysis or adjustment for comparisons made is a very conservative approach and not always made. (CX 1342 (Hill, Dep. at 102-103, 141)).

1542. In fact, it is probably more frequently not made, than made. (CX 1342 (Hill, Dep. at 102-103, 141)).

1543. An adjustment for comparisons made is less important where your study is hypothesis driven, such as here, versus an open-ended fishing approach. (CX 1342 (Hill, Dep. at 103)).

(4) The Absence of Statistically Significant Changes in Certain Lipids, Which Are Not Primary Endpoints, Does Not Prove the Negative

1544. At the Denver site, as a safety issue, heart rate and blood pressure were measured just to make sure there were no problems among the patients. (CX 1342 (Hill, Dep. at 71-72)).

1545. If there was a subject who had a very high heart rate, then he or she would be tested. (CX 1342 (Hill, Dep. at 71-72)).

1546. Similarly, if someone had an elevated blood pressure, he or she would be sent to a doctor and not used in the study. (CX 1342 (Hill, Dep. at 71-72)).

1547. In his deposition and at trial, Dr. Sacks repeatedly conceded that the absence of positive information of change, does prove the negative. (RFF 1455, 1513, 1553).

(5) Dr. Sacks' Criticisms Regarding the San Diego Site Study Should Be Dismissed

1548. Although he concedes that Dr. Heber's San Diego study is "well-designed" and "there is no evidence of problems with its conduct," Dr. Sacks complains that the study measured the markers of oxidized phospholipids, oxidized LDL/HDL, serum nitric oxide, PON, and others, none of which, according to Dr. Sacks, are valid surrogate marker of cardiovascular disease or response of disease to treatment. (CX1291_0034-0035).

1549. Dr. Sacks also argues that Dr. Heber's San Diego study did not show (or include) any statistically significant changes in nitric oxide measures, blood pressure, inflammatory or antioxidant markers. (Sacks, Tr. 1516-29).

1550. Dr. Heber, however, properly qualified his safety findings when he wrote: "This study demonstrates in *preliminary* fashion that a pomegranate ellagitannin enriched polyphenol (POMx) dietary supplement is safe when ingested by healthy human subjects in amounts up to 1420 mg/day providing a total of 870 mg of GAEs/day for 28 days. No adverse events related to the dietary supplement consumption or changes in hematology, serum chemistry, or urinalyses were observed." (PX0025-0025; CX0934_0004).

1551. In this context, Dr. Heber's comments about this study are appropriately qualified and accurate. (PX0025-0025).

1552. Contrary to Dr. Sacks' assertions, the study did evaluate the biomarker of TBARS, which as Dr. Heber wrote, is "strongly predictable of cardiovascular events in people with stable coronary artery disease, independent of traditional risk factors and inflammatory markers." (PX0025-0025; CX0934_0004).

1553. With respect to the lack of significantly significant changes with respect to blood pressure and other biomarkers, such as TG, HDL, LDL, CRP, and PON, Dr. Sacks concedes the absence of information does not prove the negative. (PX0361 (Sacks, Dep. at 238; 243)).

6. Dr. Sacks Cannot Summarily Dismiss Respondents' Diabetes Studies on the Grounds That They Are Not RCTs

1554. Respondents have sponsored numerous studies evaluating the effect of pomegranate juice and/or its derivatives on persons with diabetes. (PX0038; PX0127; PX0128; CX 0765; CX1055).

1555. The antioxidant effect of pomegranate juice is likely to be observed in persons with diabetes because they have the highest level of oxidative stress among all cardiovascular patients. (CX1348 (Aviram, Dep. at 54)).

1556. Dr. Sacks attempts to discredit the value of three of Respondents' diabetes studies—PX0038 (Concentrated Pomegranate Juice Improves Lipid Profiles in Diabetic Patients with Hyperlipidemia); PX0127 (Consumption of Wonderful Variety Pomegranate Juice and Extract by Diabetic Patients Increases Paraoxonase 1 Association with High-Density Lipoprotein and Stimulates Its Catalytic Activities); CX0765 (Anti-oxidative effects of pomegranate juice (P J) consumption by diabetic patients on serum and on macrophages)—on the grounds

that they are not RCTs, the study size is too small, and duration is too limited in scope. (CX1291_036-37; Sacks, Tr. 1521-1523).

1557. Dr. Sacks suggests that a qualified scientist cannot conclude that changes reported in these studies were due to pomegranate juice or POMx consumption because, without a control group, one does not know if the observed changes are due to the pomegranate agent or just would have happened that way. (Sacks, Tr. 1523).

1558. In conclusion, Dr. Sacks suggests that none of the published studies on pomegranate products by diabetics provide scientific support for claims that POM juice or POMx prevents, reduces the risk of, or treats heart disease. (Sacks, Tr. 1524).

1559. Dr. Aviram, Dr. Ornish, and Dr. Heber all disagree on the necessity of an RCT to demonstrate the efficacy of pomegranate juice and/or its derivatives on humans. (RFF 1184-1205; 1274-1279).

7. Respondents' Scientific Research on Cardiovascular Health Is Not Inconsistent

(a) The Findings by Dr. Aviram and Dr. Davidson on IMT Are Not Contradictory

1560. Dr. Davidson's finding of a 4 to 9% improvement in a subgroup of high risk patients without significant plaque is consistent with Dr. Aviram's 30% improvement in people with significant plaque and stenosis. (Heber, Tr. 1975-76; 1983-84).

1561. In the Dr. Aviram's study, the subjects had thickened plaque, whereas, in the Dr. Davidson's study, his patients had less plaque to the point where it was not significant. (Heber, Tr. 1975-76; 1983-84).

1562. The general definition of plaque is 1.5 millimeters in thickness of the CIMT. (Heber, Tr. 1980).

1563. The average thickness of the CIMT in Dr. Davidson's his patients in the study was .85 millimeters. (Heber, Tr. 1980)

1564. Dr. Davidson's protocol actually excluded people with significant stenosis or plaque from his study. (Heber, Tr. 1819).

1565. As a result, Dr. Aviram and Dr. Davidson's studies are really apples and oranges: they used the same surrogate (CIMT) in a different group of patients. (Heber, Tr. (Heber, Tr. 1975-76).

1566. Dr. Aviram's and Dr. Davidson's studies are two different studies, so basically there is one group of patients who have very significant disease and the other group where it was just at risk. (Heber, Tr. 1983-84).

1567. As a result, seeing a smaller result in the at-risk group than in the carotid artery stenosis group is not that surprising. (Heber, Tr. 1983-84).

1568. Dr. Aviram's and Dr. Davidson's results are also consistent with one another because Dr. Aviram examined a group of patients with high oxidative stress which is similar to the high-risk subgroup in Dr. Davidson's study and the trend can be observed in both studies. (CX_1348 (Aviram, Dep. at 74)).

1569. Dr. Davidson does not believe that his findings contradict any of the previous studies conducted by Dr. Aviram, Dr. Sumner, Dr. Ornish, Dr. Ignarro, Dr. Kaplan, or Dr. Rosenblat and he believes his findings are consistent. (CX1336 (Davidson, Dep. at 227-228)).

(b) Dr. Aviram's Positive Findings on Blood Pressure Are Not Contradicted by Subsequent Research Sponsored by Respondents

1570. In any clinical study, it is routine to take a blood pressure, pulse, body temperature, among others, to make sure patients are healthy. (Heber, Tr. 2101).

1571. Although blood pressure is measured in many studies, a specific claim on blood pressure requires a very specific study involving special equipment and personnel. (Heber, Tr. 2040).

1572. In Dr. Ornish's myocardial perfusion study, the primary endpoint was blood flow, not blood pressure, so one cannot conclude there was no effect of pomegranate juice on blood pressure in his study. (Heber, Tr. 2101-02; PX0353 (Heber, Dep. at 173)).

1573. In Dr. Davidson's BART study, the primary endpoint was flow-mediated dilation, not blood pressure, and therefore any results for blood pressure cannot be relied upon as negative evidence to the contrary. (Heber, Tr. 2106-07; PX0353 (Heber, Dep. at 173)).

XV. RESPONDENTS' PROSTATE HEALTH CLAIMS ARE SUBSTANTIATED

1577. Competent and reliable scientific evidence supports the conclusion that the consumption of pomegranate juice and pomegranate extract supports prostate health, including by prolonging PSA doubling time in men with rising PSA after primary treatment for prostate cancer. (PX0161; PX0353 (Heber, Dep. at 84-85); deKernion, Tr. 3126; PX0351 (deKernion, Dep. at 41-42); Heber, Tr. 2012).

1578. Additionally, competent and reliable scientific evidence supports the conclusion that the same mechanism shown in the *in vitro* and animal studies and in the Pantuck and Carducci human studies also showed with a high degree of probability that the Challenged Products inhibit the clinical development of prostate cancer cells in men who have not been diagnosed. (deKernion, Tr. 3126; PX0351 (deKernion, Dep. at 76-77); PX0206 at 12; Heber, Tr. 2156).

1579. Further, because pomegranate juice is a fruit and not a pharmaceutical drug, physicians who treat patients concerned with prostate health would not hold pomegranate juice to the standards of safety and efficacy traditionally required by the FDA for approval of a pharmaceutical (performance of a large, randomized, double-blind, placebo controlled clinical trial ("RCT")) before recommending pomegranate juice to their patients. (PX0206).

A. Summary of Complaint Counsel's Allegations Regarding Respondents Prostate Health Advertisements

1580. Complaint Counsel allege that Respondents have falsely represented, expressly or by implication, that clinical studies, research, and/or trials prove that:

A. Drinking eight ounces of POM Juice, or taking one POMx Pill or one teaspoon of POMx Liquid, daily, prevents or reduces the risk of prostate cancer, including by prolonging prostate-specific antigen doubling time ("PSADT"); and

B. Drinking eight ounces of POM Juice, or taking one POMx Pill or one teaspoon of POMx Liquid, daily, treats prostate cancer, including by prolonging PSADT. (CX1426_0018-0020).

B. Respondents Deny Complaint Counsel's Allegations That Their Advertisements Are False and Misleading

1581. Respondents deny Complaint Counsel's allegations that their advertising and promotional materials make the claim that (1) Respondents' clinical studies, research, and/or trials prove that drinking eight ounces of POM Juice, or taking one POMx Pill or one teaspoon of POMx Liquid, daily, prevents or reduces the risk of prostate cancer and (2) treats prostate cancer. (PX0364-0004-0006).

1582. Respondents dispute Complaint Counsel's allegations or characterizations regarding Respondents' science and aver there is substantial scientific research indicating the health benefit of their products and substantiating their advertising and promotional materials. (PX0364-0004-0006).

1583. Respondents deny Complaint Counsel's allegations that their advertising and promotional materials make the claim that drinking eight ounces of POM Juice, or

taking one POMx Pill or one teaspoon of POMx Liquid, daily (1) prevents or reduces the risk of prostate cancer, including by prolonging PSADT; (2) treats prostate cancer, including by prolonging PSADT. (PX0364-0004-0006).

C. Competent and Reliable Scientific Evidence Supports Respondents' Claims

1. Overview of Pomegranates and its Effects on Prostates

(a) Prostate Function and Prostate Cancer

1584. The prostate is a gland that's located in the male pelvis that is an organ of sexual function and fertility. (Eastham, Tr. 1236).

1585. Prostate cancer occurs when cells of the prostate, typically the glandular cells, become cancerous, which means they have uncontrolled cell growth. (Eastham, Tr. 1236).

1586. Last year about 220,000 men were diagnosed with prostate cancer in the United States. (Eastham, Tr. 1237).

1587. Approximately one in six men over the age of 60 will be diagnosed with prostate cancer each year. (Eastham, Tr. 1238-39).

1588. The average age of prostate cancer diagnosis is in the sixties. (Eastham, Tr. 1239).

1589. About 30,000 men die from prostate cancer each year. (Eastham, Tr. 1239).

1590. Although there has been a trend toward improved survival, prostate cancer remains the second most common cause of cancer death in men in the United States, accounting for 11% of all cancer deaths. (PX0061).

1591. Prostate cancer does not have a typical course. (Eastham, Tr. 1236).

1592. There are many prostate cancers that, while they are seen under the microscope they do not represent a threat to the life expectancy or the quality of life of the patient. (Eastham, Tr. 1236).

1593. Blood levels of prostate specific antigen (PSA) are measured in healthy men to assess their risk of prostate cancer. (Stampfer, Tr. 774).

1594. PSA is a protein that's derived almost exclusively from the prostate and is widely used for screening for the risk of prostate cancer. (Stampfer, Tr. 774).

1595. PSA is also used after diagnosis of prostate cancer to monitor the progression of disease. (Stampfer, Tr. 774).

1596. For men that have low or intermediate-risk prostate cancer or even some high-risk patients, patients that have clinically localized disease, meaning, based on a clinical evaluation of the man that the cancer is only in the area of the prostate, but it's of a risk that is beyond monitoring, those men are candidates for potentially curative therapies. (Eastham, Tr. 1237).

1597. The two mainstays of cure are either radical prostatectomy, surgical removal of the prostate, or radiation therapy to the prostate. (Eastham, Tr. 1237; PX0061-0001).

1598. Although this is adequate for permanent disease control in many patients, a significant number of patients relapse and ultimately develop metastatic disease. (PX0061-0001).

1599. However, approximately one third of prostate cancer patients with clinically confined cancer that are treated with radical prostatectomy will develop a biochemical recurrence. (PX0061-0001).

1600. There are limited treatment options for patients who have undergone primary therapy with curative intent and who have progressive elevation of their PSA without documented evidence of metastatic disease. (PX0061-0002).

1601. Early initiation of hormonal ablation is associated with significant morbidity and effect on quality of life, including fatigue, hot flashes, loss of libido, decreased muscle mass, and osteoporosis with long-term use. (PX0061-0002).

1602. Strategies to delay clinical prostate cancer progression and prolong the interval from treatment failure to hormonal ablation would be of paramount importance. (PX0061-0002).

1603. A combination of epidemiologic and basic science evidence strongly suggests that diet and plant-derived phytochemicals may play an important role in prostate cancer prevention or treatment. (PX0061-0002).

1604. Epidemiologic studies suggest that a reduced risk of cancer is associated with the consumption of a phytochemical-rich diet that includes fruits and vegetables. (PX0061-0002).

1605. Fresh and processed fruits and food products contain high levels of a diverse range of phytochemicals of which polyphenols, including hydrolyzable tannins (ellagitannins andgallotannins) and condensed tannins (proanthocyanidins), and anthocyanins and other flavonoids make up a large proportion. (PX0061- 0002).

1606. Several phytochemicals have been proposed as potential chemoprevention agents based on animal and laboratory evidence of antitumor effects. (PX0061-0002).

1607. Suggested mechanisms of anticancer effects of polyphenols include the inhibition of cancer cell growth by interfering with growth factor receptor signaling and cell cycle progression, promotion of cellular differentiation, modulation of phosphodiesterase/ cyclooxygenase pathways, inhibition of kinases involved in cell signaling, and inhibition of inflammation. (PX0061-0002).

(b) Mechanism of Action of Pomegranates in the Prostate

1608. The pomegranate (Punica granatum L.) fruit has been used for centuries in ancient cultures for its medicinal purposes. (PX0061-0002).

1609. Pomegranate fruits are widely consumed fresh and in beverage forms as juice and wines. Commercial pomegranate juice shows potent antioxidant and antiatherosclerotic properties attributed to its high content of polyphenols, including ellagic acid in its free and bound forms (as ellagitannins and ellagic acid glycosides), gallotannins, and anthocyanins (cyanidin, delphinidin, and pelargonidin glycosides) and other flavonoids (quercetin, kaempferol, and luteolin glycoside). (PX0061-0002).

1610. The most abundant of these polyphenols is punicalagin, an ellagitannin implicated as the bioactive constituent responsible for >50% of the potent antioxidant activity of the juice. Punicalagin is abundant in the fruit husk and, during processing, is extracted into pomegranate juice in significant quantities reaching levels. (PX0061-0002).

1611. Ellagic acid and tannins have been shown previously to exhibit in vitro and in vivo anticarcinogenic properties, such as induction of cell cycle arrest and apoptosis, as well as the inhibition of tumor formation and growth in animals. (PX0061-0002).

(1) In Vivo Research Has Demonstrated That POM Reduces Inflammation in Prostate Tumors (Inflammation in the Human Is A Key Step in Prostate Cancer Progression)

1612. For centuries, pomegranates have been used in traditional Chinese medicine as anti-inflammatory agents. (PX01929-0016, 0018).

1613. A large body of literature has linked inflammation to prostate carcinogenesis at all stages of the development of prostate cancer from normal tissue to advanced cancer. (PX0192 at 0029; PX0070-0001).

1614. Inflammation in the human is a key step in prostate cancer progression. (CX1352 (Heber, Dep. at 257-258); PX0070-0001).

1615. Areas of chronic inflammation are almost universally present in pathologic specimens of the prostate, including biopsy cores in men prior to the diagnosis of prostate cancer, transurethral resection chips, and total prostatectomy specimens. (PX0192-0029).

1616. 98 percent of prostate tumors removed at surgery for cancer have evidence of inflammation. (CX1352 (Heber, Dep. at 257-258); PX0192-0029-0030).

1617. In vivo research has demonstrated that POM reduces inflammation in the prostate tumor. (CX1352 (Heber, Dep. at 257-258); Heber, Tr. 1992).

(2) In Prostate Cancer Tumors Treated with POM, Nuclear Factor Kappa B Decreased Causing a Decrease in Tumor Growth

1618. One of the most well-established signaling pathways mediating inflammatory responses relevant to cancer is the nuclear factor-κB (NF-κB) pathway. (PX0192-0030; deKernion, Tr. 3046-47; Heber, Tr. 1992; PX0070-00001).

1619. This unique protein was the subject of Nobel Prize-winning research by Dr. David Baltimore who identified the protein's unique ability to both receive a signal from the outside of a cell and translate that signal into genetic programming of inflammatory proteins that secreted by cells. (PX0192-0030; Heber, Tr. 1992).

1620. The activity of NF-κB is regulated by another protein inhibitor called IκB, which binds to and sequesters NF-κB family members in the fluid part of the cell away from DNA called the cytoplasm. (PX0192-0030; PX0070-0001).

1621. When the NF-κB pathway is activated, IκB is chemically modified by an enzyme called IκB kinase, which adds a phosphorus atom at specific amino acids on the IkB protein (serine residues 32 and 36). (PX0192-0030; PX0070-0001).

1622. Once altered the inhibitory protein IκB is degraded and NF-κB is free to move to the nucleus, where it functions to activate genetic mechanisms after binding to DNA resulting in the secretion of proinflammatory signaling proteins. (PX0192-0030; PX0070- 0001).

1623. While normal activation of NF-κB is temporary in response to a stimulus meant to activate immune function, constant or constitutive activation has been observed in breast cancer, liver cancer, melanoma, Hodgkin's disease, and cervical cancer. (PX0192 -0030; PX0070-0001).

1624. Direct genetic evidence in mouse models of colon and liver cancer have established that NF-κB activation within tumor cells or infiltrating inflammatory cells is required for tumor initiation or promotion. (PX0192-0030; PX0070-0001).

1625. Importantly, activation of NF-κB is observed in primary prostate cancer specimens as evidenced by its presence in the nucleus of cells where the genes reside and represents an independent risk factor for recurrence of prostate cancer after radical prostatectomy. (PX0192-0030; PX0070-0001).

1626. Pomegranate extract (PE) has been shown to inhibit NF-κB in normal human cells, including chondrocytes, epidermal keratinocytes, and vascular endothelial cells. (PX0192 -0031; PX0070-0002).

1627. Pomegranate extract inhibits both continuous (constitutive) and stimulated (cytokineinduced)NF-κB activity in prostate cancer cells *in vitro*. Importantly, the NF-κB-inhibitory effect of pomegranate extract was necessary for the maximal cell killing effects of PE. (PX0192-0031; Heber, Tr. 1993; PX0070-0002).

1628. In tumors treated with pomegranate extract the NF-kappaB decreased, therefore causing decrease of tumor growth. (deKernion, Tr. 3046-47; Heber, Tr. 1993).

1629. There is an absolute linear connection between the polyphenol mechanisms in pomegranate extract and the decrease in tumor growth. (deKernion, Tr. 3046-47; Heber, Tr. 1993).

1630. NF-Kappa B is not the only mechanism of action of pomegranate polyphenols, but it is one of the major ones accounting probably anywhere from 70 to 85 percent of the inhibition of prostate cancer cell growth in cell culture. (PX0353 (Heber, Dep. at 122)).

1631. The mechanisms of action of the Challenged Products on inflammation and nuclear factor kappa B, contributes to the total body of research constituting competent and reliable scientific evidence that the Challenged Products, supports prostate health and could play a role in prevention. (PX0161 at 0011-0012; PX0353 (Heber, Dep. at 84-91); PX0192 -0031; PX0206-0012; PX0070).

D. Brief Summary of Basic Science Studies and Prostate Health

1632. Pre-clinical laboratory studies, including in vitro and in-vivo mouse models are critical to a preliminary assessment of a new treatment. (PX0161-0008-0009).

1633. The pre-clinical laboratory evidence to support an effect of POM on prostate cancer is robust. (PX0161-0009).

1634. Preclinical research and studies involved in vitro growing of human tumor cells in petri dishes in laboratories, adding POM and POM products and determining the effect on the human tumor cells. (deKernion, Tr. 3044).

1635. These initial studies (further outlined below) showed a significant decrease in growth, increase in apoptosis, (programmed tumor death), decrease in inflammation, factors which are all related to cancer. (deKernion, Tr. 3044-45).

1636. Subsequent research involved in vivo study. A human tumor is grown in immune deficient mice, an environment, which behaves as though it were in a human. In these studies which used LAPC4, a particular prostate tumor line, researchers demonstrated that when a prostate tumor is grown in mice and pomegranate extract and pomegranate products are added, the tumors markedly decrease. (deKernion, Tr. 3045).

1637. These were not studies of animal glands but were studies of human prostate tissue put in animals. All of these studies showed that POM had an antitumor effect on human tumors. (deKernion, Tr. 3049).

1638. In 2001, Agensys, a biotech company, performed early preclinical research for POM investigating the effect of pomegranate juice and prostate cancer. (deKernion, Tr. 3115; Tupper Tr. 1034; PX0065).

1639. Agensys found that *in vitro* pomegranate juice consumption "substantially inhibits prostate cancer cells." (PX0065-0036).

1640. Agensys *in vivo* research found that pomegranate juice consumption "retards the growth of subcutaneous and orthotopic prostate tumors in mice." (PX065-0037).

1641. In a study entitled, "Pomegranate Ellagitannin-Derived Metabolites Inhibit Prostate Cancer Growth and Localize to the Mouse Prostate Gland" Dr.'s Navindra Seeram, Arie Belledegrum, David Heber, and colleagues evaluated the effects of pomegranate extract on prostate cancer growth in severe combined immunodeficient mice injected with human prostate cancer cells. (PX0069).

1642. The study showed that pomegranate extract significantly inhibited prostate cancer in the mice as compared to the control. (PX0069).

1643. Researchers also found that ellagic acid and synthesized urolithins from the pomegranate extract were shown to inhibit the growth of human prostate cancer cells in vitro. (PX0069).

1644. The researchers further concluded that the chemopreventive potential of pomegranate ellagitannins and localization of their bioactive metabolites in mouse prostate tissue suggest that the pomegranate may play a role in prostate cancer treatment and chemoprevention. (PX0069).

1645. In a study entitled, "Pomegranate polyphenols down-regulate expression of androgen-synthesizing genes in human prostate cancer cells overexpressing the

androgen receptor", Doctors Hong, Seeram, and Heber examined the effects of pomegranate polyphenols from POMx Pill and POM Wonderful 100% pomegranate juice on the expression of androgen enzymes and androgen receptors. (PX0068).

1646. Recurrent prostate tumors advance to an androgen- independent state where they progress in the absence of circulating testosterone leading to advanced cancer. (PX0068).

1647. During the development of the androgen-independent state, prostate cells are known to increase intracellular testosterone synthesis which maintains cancer cell growth in the absence of significant amounts of circulating testosterone. Over expression of androgen receptor to produce testosterone occurs in androgen-independent prostate cancer. (PX0068).

1648. POM polyphenols from either POMx Pill or POM Wonderful 100% pomegranate juice significantly inhibited gene expression and androgen receptors as a potential mechanism for maintaining healthy prostate cells. (PX0068).

1649. The researchers concluded that, "these results suggest that pomegranate polyphenols may be particularly helpful in the subgroup of patients with androgen-independent prostate cancer." (PX0068).

1650. A study by Doctors Rettig, Heber, et al., entitled, "Pomegranate extract inhibits androgen-independent prostate cancer growth through a nuclear factor-kappaB-dependent mechanism" evaluated POMx Pill and POM Wonderful 100% pomegranate juice and found that their consumption was linked to reduction in cancer growth and decreased plasma PSA levels. (PX0070).

1651. As discussed above, one of the most well-established signaling pathways mediating inflammatory responses relevant to cancer is the NF-kB pathway, which serves as a predictor for recurrence of prostate cancer after radical prostatectomy. (PX0070).

1652. POMx inhibited NF kB and cancer cell viability in a dose response fashion in vitro and Human LAPC4 prostate cancer xenograft mouse model, and this was similar to juice. (PX0070).

1653. Based on the results reported, the researchers concluded "that pomegranate juice could have potential as a dietary agent to prevent the emergence of androgen-independence," thus potentially prolonging life expectancy of prostate cancer patients, and suggested "that this may be a high priority area for future clinical investigation." (PX0070).

1654. In a study by Dr. Sartippour, et al., entitled, "Ellagitannin-Rich Pomegranate Extract Inhibits Angiogenesis In Prostate Cancer In Vitro And In Vivo" the in vivo results showed that POMx Pill inhibits prostate tumor growth compared to control in immunodecifient mice injected with human prostate cancer cells. (PX0071).

1655. The mice were given a dose comparable, using caloric demand scaling, to that found in POMx and taken by humans. (PX0071).

1656. POMx was shown to significantly decrease the overall blood vessel density in mouse tumors or angiogenesis, which is important to slow prostate cancer cell growth linked directly to PSA doubling time. (PX0071).

1657. In vitro results showed that POMx pill significantly inhibited proliferation of human prostate cancer cells at low ug/ml concentrations. (PX0071).

1658. The researchers concluded, "these findings strongly suggest the potential of pomegranate ellagitannins for prevention of the multi-focal development of prostate cancer as well as to prolong survival in the growing population of prostate cancer survivors of primary therapy." (PX0071).

1659. The findings from Respondents pre-clinical research, which has demonstrated an effect of pomegranates on prostate cancer tumors, contributes to the total body of research constituting competent and reliable scientific evidence that the Challenged Products, supports prostate health and could play a role in prevention. (PX0161- 0011-0012; PX0353 (Heber, Dep. at 84-91).

E. Respondents Human Clinical Trials and Prostate Health

1. In 2006, Dr. Allan Pantuck, of the UCLA Medical School, Published the Results of the First Human Clinical Trial on Pomegranate Juice With Men With Rising PSA Doubling Time Following Radical Prostatectomy and Found That Pomegranate Juice Consumption Produced a Dramatic Lengthening of PSA Doubling Time, an Effective Marker for Recurrence and Death From Prostate Cancer

1660. After successful preclinical trials, research on prostate health with POM progressed to human clinical trials. (deKernion, Tr. 3050).

1661. In a study entitled, "Phase II Study of Pomegranate Juice for Men with Rising Prostate-Specific Antigen following Surgery or Radiation for Prostate Cancer," Dr. Allan Pantuck and his colleagues of UCLA Medical School found that through the consumption of pomegranate juice, the mean PSA doubling time significantly

increased with treatment from a mean of 15 months at baseline to 54 months post-treatment. (PX0060).

1662. Patients were treated with 8 oz per day of POM Wonderful 100% pomegranate juice until disease progression end points. (PX0060).

1663. Clinical end points were effect on serum PSA, serum-induced proliferation and apoptosis of prostate cancer cells, serum lipid peroxidation, and serum nitric oxide levels. (PX0060).

1664. Mean PSA doubling time significantly increased with treatment from a mean of 15 months at baseline to 54 months post treatment. (PX0060).

1665. PSA doubling time is a mathematical expression of the rapidity with which the prostate specific antigen (PSA) is rising, and is an expression of the rapidity of growth and number of prostate tumor cells. (deKernion, Tr. 3050).

1666. The doubling time for PSA is a measure of the likelihood of recurrence of the tumor after a man has had his prostate removed. (deKernion, Tr. 3051).

1667. The presence of detectable PSA after radical prostatectomy or other radical treatment usually indicates cancer is present. (deKernion, Tr. 3051).

1668. PSA doubling time provides an expression of how those tumor cells are going to behave. (deKernion, Tr. 3051-52).

1669. The longer the PSA doubling time, the less dangerous the growth of the cancer (deKernion, Tr. 3052).

1670. In vitro assays comparing pretreatment and post treatment patient serum on the growth of the prostate cancer line LNCaP showed a 12% decrease in cell proliferation and a 17% increase in apoptosis, a 23% increase in serum nitric oxide, and significant reductions in oxidative state and sensitivity to oxidation of serum lipids after versus before pomegranate juice consumption. (PX0060).

1671. The study was the first clinical trial of pomegranate polyphenol antioxidants in patients with prostate cancer. (PX0060).

1672. The statistically significant prolongation of PSA doubling time, coupled with corresponding laboratory effects on prostate cancer in vitro cell proliferation and apoptosis as well as oxidative stress, provides good indication of a relationship between pomegranate polyphenol antioxidants and prostate health. (PX0060).

1673. Dr. Pantuck's study was published in the Journal of Clinical Cancer Research an extremely well regarded peer reviewed journal. It is considered one of if not the finest clinical cancer journals. (CX1352 (Heber Dep. at 268-269); (PX0060).

1674. The process and rigor for being published in the Journal of Clinical Cancer Research is very high. (CX1352 (Heber, Dep. at 268)).

1675. Dr. Heber testified that Dr. Pantuck's study is considered, "a very highly esteemed paper." (CX1352 (Heber, Dep. at 268)).

(a) Dr. Allan Pantuck Long's Term Follow-Up Study demonstrated that for those who continued on pomegranate juice maintained a lengthening of their PSA doubling time compared to men who did not continue on pomegranate juice

1676. In 2008 Dr. Pantuck presented a report of an abstract to the American Society of Clinical Oncology entitled, "Long Term Follow Up of Pomegranate Juice for Men with Prostate Cancer and Rising PSA Shows Durable Improvement in PSA Doubling Time." (PX0061).

1677. Dr. Pantuck and his colleagues found a durable increase in PSA doubling time from men who continued to take pomegranate juice following the Phase II trial. (PX0061).

1678. Mean PSA doubling time for the entire cohort continued to show a significant increase following treatment, from a mean of 15.4 at baseline to 60 months post-treatment, while the median PSA slope decreased 60% from 0.06 to 0.024. (PX0061).

1679. Patients remaining on study ("active") were compared to those no longer on study ("non-active"). (PX0061).

1680. At baseline, mean PSA doubling times were similar between Active and Non-Active patients. However, post-treatment PSA DT prolongation was greater and the decline in median PSA slope was larger in Active compared to Non-Active patients. (PX0061).

1681. The study demonstrated that for those who continued on pomegranate juice maintained a lengthening of their PSA doubling time compared to men who did not continue on pomegranate juice. (PX0061; Eastham, Tr. 1305; CX1341 (Pantuck, Dep. at 136).

(b) Dr. Allan Pantuck Supports the Findings of His Pomegranate Research That PSA Doubling Time Was

Prolonged for Men With Prostate Cancer When They Were Given Pomegranate Juice

1682. Dr. Pantuck's deposition was taken in this matter on December 15, 2010. (CX1341).

1683. Dr. Pantuck attended college at Columbia University and medical school at Robert Woods Johnson Medical School. (CX1341 (Pantuck Dep. at 20-21)).

1684. Dr. Pantuck also has a Masters Degree in Clinical Research from UCLA Medical School. (CX1090_0001).

1685. Dr. Pantuck is an associate professor of Urology at UCLA Medical School and maintains a clinical practice at UCLA. (CX1341 (Pantuck Dep. at 22)).

1686. Dr. Pantuck's clinical appointments include: Attending Urologist at Harbor-UCLA Medical Center, Attending Urologist Wadsworth Veterans Affairs Medical Center, and Attending Urologist, UCLA Medical Center. (CX1090_0004).

1687. Dr. Pantuck's professional societies and memberships include the American Society of Clinical Oncology, American Urological Association, Jonsson Comprehensive Cancer Center, and the Society of Urologic Oncology. (CX1090_0002).

1688. Dr. Pantuck served as editor of Advances in the Management of Renal Cell Carcinoma. Proceedings of the Irish Society of Surgical Oncology. (2003) (CX1090_0003).

1689. Dr. Pantuck has been a reviewer for journals such as the British Journal of Urology International, The Journal of Urology, Clinical Cancer Research, and Urologic Oncology. (CX1090_0003).

1690. In deposition testimony, Dr. Pantuck supported the findings of his study that PSA doubling time was prolonged for men with prostate cancer when they were given pomegranate juice. (CX1341 (Pantuck Dep. at 108)).

1691. Dr. Pantuck, stated that the design of the study was for subjects to serve as their own control. Patients had a specific PSA doubling time prior to treatment; patients would then be treated and measured for any change in their doubling time after treatment. (CX1341 (Pantuck, Dep. at 78)).

1692. Dr. Pantuck further testified that the study showed evidence that the growth of the cancer had been altered by POM. (CX1341 (Pantuck, Dep. at 119)).

1693. Dr. Pantuck stated that the feedback from the scientific community with regard to the peer-reviewed published Phase II study has primarily been favorable, and that some doctors have discussed the findings with patients. (CX1341 (Pantuck, Dep. at 268)).

1694. Dr. Pantuck stated that there are categories of patients with whom he has discussed the benefits of pomegranate juice. (CX1341 (Pantuck, Dep. at 270-271)).

2. Dr. Michael Carducci, of Johns Hopkins School of Medicine, Conducted a Clinical Trial on Pomegranate Extract with Men With Rising PSA Doubling Time Following Primary Therapy And Found that POMx Demonstrated Antitumor Effects in Prostate Cancer and Significantly Increased PSA Doubling Time

1695. In 2011 Dr. Michael Carducci presented the abstract of his clinical research study entitled, "A Phase II Study of Pomegranate Extract for Men with Rising Prostate-specific Antigen Following Primary Therapy" at the disease specific meeting of the American Society of Clinical Oncology. (PX0175).

1696. Dr. Carducci and colleagues found that pomegranate extract (POMx) demonstrated antitumor effects in prostate cancer. (PX0175).

1697. The study was a multi-center, double blind Phase II randomized trial that studied men with rising PSA and without metastases. They were given either high or low dose POMx, stratified by baseline PSADT and Gleason score, and with no restrictions for PSADT and no upper limit PSA value. (PX0175).

1698. Men were treated until progression or for 18 months. PSA levels were obtained every 3 months. (PX0175).

1699. The clinical trial showed that POMx treatment significantly increased the PSA doubling time by over 6 months in both treatment arms. (PX0175).

1700. The study confirmed slowing of PSADT after treatment with POMx as was found with POM Juice in Dr. Pantuck's study. (PX0175; CX1340 (Carducci, Dep. at 178)).

(a) Dr. Michael Carducci Supports the Findings of His Pomegranate Research That PSA Doubling Time Was Prolonged for Men with Prostate Cancer When They Were Given Pomegranate Extract

1701. Dr. Michael Carducci's deposition was taken in this matter on December 13, 2010. (CX1340).

1702. Dr. Carducci is a graduate of Georgetown University and Wayne State University Medical School. (CX1340 (Carducci, Dep. at 13-14)).

1703. Dr. Carducci did a residency in internal medicine at the University of Colorado in Denver. (CX1340 (Carducci, Dep. at 14)).

1704. After completing a year as chief resident at the University of Colorado he accepted a fellowship in oncology at Johns Hopkins University. (CX1340 (Carducci, Dep. at 14)).

1705. Dr. Carducci is currently a professor of oncology and urology at the Johns Hopkins School of Medicine, in Baltimore, Maryland. (CX1340 (Carducci, Dep. at 14-15)).

1706. Within the Cancer Center, he leads two programs, the prostate cancer/genitourinary cancer program and chemical therapeutics. (CX1340 (Carducci, Dep. at 14-15)).

1707. Dr. Carducci has conducted 40-50 clinical trials relating to prostate cancer. (CX1340 (Carducci, Dep. at 15)).

1708. He has published approximately 80 articles related to prostate cancer. (CX1340 (Carducci, Dep. at 15-16)).

1709. In his deposition Dr. Carducci testified that POM Wonderful did not look at or manipulate the data analysis of his study. (CX1340 (Carducci, Dep. at 43)).

1710. He stated that the use of PSA doubling time as a primary endpoint to determine if POMx has an effect on the disease was scientifically valid. (CX1340 (Carducci, Dep. at 181-182)).

1711. He stated that his study was not designed to use endpoints that were "drug-like" but specifically designed for a natural product. (CX1340 (Carducci, Dep. at 50-51)).

1712. Dr. Carducci stated that researchers were looking at safety and whether POMx had an effect on rising PSA. (CX1340 (Carducci, Dep. at 51)).

1713. He confirmed that the study results as designed and planned were statistically significant. (CX1340 (Carducci, Dep. at 183)).

1714. Dr. Carducci was selected to present the results of his study on POMx at a disease specific meeting of the American Society of Clinical Oncology, the American Society of Therapeutic Radiation Oncology and the Society of Urologic Oncology. (CX1340 (Carducci, Dep. at 176)).

1715. 1500 to 2000 people typically attend this meeting. (CX1340 (Carducci, Dep. at 177)).

1716. Dr. Carducci's abstract was peer reviewed prior to being selected for presentation. (CX1340 (Carducci, Dep. at 176)).

1717. Only 10 of the highest ranking abstracts or with the most relevance to the audience (out of 500 submitted) are generally selected for an oral presentation. (CX1340 (Carducci, Dep. at 61–62)).

1718. The findings from Respondents human clinical research, which has demonstrated an effect of pomegranates on prostate cancer including by extending PSA doubling time, contributes to the total body of research constituting competent and reliable scientific evidence that the Challenged Products, support prostate health and could play a role in prevention. (PX0161-0011-0012; PX0353 (Heber, Dep. at 84-91); PX0060; PX0061; PX0175).

F. Respondents' Expert Confirms That Respondents' Substantiation Constitutes Competent and Reliable Scientific Evidence

1. Respondents' Proffered Expert

(a) Dr. Jean Dekernion Has for Over 30 Years Been One of The Foremost Leaders in Urological Research and Clinical Practice

1719. Respondents have presented the expert report and expert testimony of Dr. Jean deKernion, a practicing clinician in the field of prostate cancer and prostate health. (PX0161; PX0351; deKernion, Tr. 3039-3127).

1720. Dr. Jean deKernion is a Doctor of Medicine and obtained his medical degree in 1965 from Louisiana State University School of Medicine in New Orleans, Louisiana. (deKernion, Tr. 3040).

1721. Dr. deKernion did his residencies in surgery and urology at the university hospitals of Cleveland and the National Cancer Institute. (deKernion, Tr. 3040).

1722. Dr. deKernion has been a visiting professor at 50 different medical institutions including M.D. Anderson in Houston, Stanford, University of Pennsylvania, and the Cleveland Clinic. (deKernion, Tr. 3041-42).

1723. Dr. deKernion has been certified by the American Board of Urology since 1975. (PX0161-0002).

1724. Dr. deKernion was from 1981 until his retirement in 2011 Chairman of the Department of Urology and Senior Associate Dean for Clinical Affairs (2001 – 2011) at the David Geffen UCLA School of Medicine. (deKernion, Tr. 3039; PX0161-0001).

1725. Dr. deKernion's responsibilities included the urological clinical and research education of students, residents, and fellows at all levels; a busy practice in urologic oncology, primarily related to prostate cancer but also bladder and kidney cancer; growth and oversight of large and diverse research programs; and administration of programs for the Dean's office and hospital. (PX0161-0001).

1726. Dr. deKernion served as an advisor to a number of university research programs, and served on a Data and Safety Monitoring Committee (DSMC) for a bladder cancer project. (PX0161-0002).

1727. During Dr. deKernion's tenure as Chair of the Department of Urology at UCLA, he built a multidisciplinary research portfolio, which ranks among the largest and best in the United States. (PX0161-0003).

1728. In the role as Chair of the Department of Urology at UCLA, Dr. deKernion had general oversight of funded research projects, as well as mentoring responsibilities for faculty, residents, PhD faculty and PhD students. (PX0161-0003).

1729. Dr. deKernion's career in urologic oncology has involved both clinical and basic/translational research. (PX0161-0001).

1730. He co-authored the first book on urologic oncology and has co-authored 133 chapters since. (PX0161-0002; deKernion, Tr. 3042).

1731. His research has involved both basic laboratory research and clinical research publishing 228 papers to date in peer-reviewed journals and many other invited manuscripts. (PX0161-0002; deKernion, Tr. 3043).

1732. For 6 years Dr. deKernion was the associate editor of the Journal of Urology and has been a reviewer for approximately 20 other peer-reviewed journals. (deKernion, Tr. 3041; PX0161-0002).

1733. Dr. deKernion served on a number of national committees and was a founding member of the Society of Urologic Oncology. (PX0161-0002).

1734. Dr. deKernion was elected as a trustee of the American Board of Urology, and numerous committees of national urological societies. (PX0161-0002).

1735. Dr. deKernion was appointed to the National Cancer Advisory board by President Bush. (deKernion, Tr. 3040).

1736. At the National Cancer Institute, Dr. deKernion was a member of the NCI Clinical Trials Advocacy Committee and the SPORE Leadership Committee. (PX0161-0002).

1737. Dr. deKernion served as the chair of the Department of Defense prostate cancer integration and research panel. (deKernion, Tr. 3040).

1738. Among the awards and prizes that he has received are the Jonsson Prize for Research awarded by the Jonsson Cancer Foundation and the Hugh Hampton Young Award of the American Urological Association. (deKernion, Tr. 3043; PX0161-0014).

2. Summary of Dr. deKernion's Opinions

(a) POM's In Vitro and Animal Studies Showed That the Challenged Products Inhibited the Growth Of Prostate Cancer Cells and Actually Killed Them

1739. In addition to the publications attached to Dr. deKernion's expert report upon which he relied, Dr. deKernion has also extensively relied upon his education, years of experience and knowledge of developments in the field of urology and prostate health, including the promotion of prostate heath and treatment of prostate cancer in forming his opinions on Respondents' prostate health research. (PX0351 (deKernion, Dep. at 26); PX0351a02-0001; PX0351a04-0001-PX0351a04-0002; PX0351a05-0001; PX0161).

1740. Dr. deKernion testified that Respondents' *in vitro* and animal studies showed that pomegranate juice inhibited the growth of prostate cancer cells and actually killed them. (deKernion, Tr. 3044-45, 3120; PX0351 (deKernion, Dep. at 110).

1741. Dr. deKernion testified that while we cannot always extrapolate from *in vitro* and animal results to what the results would be in humans, these pre-clinical studies indicated a strong likelihood that, in humans, pomegranate juice would at least inhibit the growth of prostate cancer cells. (deKernion, Tr. 3063; PX0161-0011-0012).

1742. Dr. deKernion, noted that Respondents animal studies were on human prostate tissue inserted in the animals and were not merely a study of animal glands. (deKernion, Tr. 3049).

(b) PSA Doubling Time Is a Valid Surrogate Marker for Prostate Cancer Recurrence and Death

1743. Dr. deKernion opined in his expert report as well as during deposition and trial testimony on the validity of PSA doubling time as a surrogate marker in clinical trials. (PX0161; PX0351; deKernion, Tr. 3039-3127).

1744. He stated that PSA doubling time is used to determine success or failure of prostate cancer treatment and that multiple studies have associated PSA doubling time with not only the risk of clinical recurrence but also death. (PX0161-0004, 0007; deKernion, Tr. 3050-58).

1745. He testified that there are different risk profiles based on the length of the PSA doubling time, with less than 3 months in the highest risk and those of 12 to 15 months and above in a lower risk category. (PX0351 (deKernion, Dep. at 96); deKernion, Tr. 3084-85).

1746. Dr. deKernion stated that PSA doubling time is clearly a useful marker in determining risk or outcome in patients following prostate cancer treatment. (deKernion, Tr. 3055).

1747. Dr. deKernion testified that given the understanding of PSA doubling time in predicting risk of clinical recurrence and to some extent survival, it is not only permissible and logical to use changes in PSADT as indicative of an intervention's effectiveness regarding prostate tumor behavior, but it is particularly compelling when coupled with the previous science, including in vivo, and in vitro, using POM and adjudging its usefulness as to prostate health. (PX0161-0007, 0011-0012).

1748. If PSA doubling time is used as predictive of risk of clinical recurrence and death, it is simply illogical that radical changes to PSADT due to intervention would not be informative of the intervention's effectiveness—particularly when you see such large and statistically significant changes in PSADT following consumption of POM. (PX0161-0007, 0011-0012).

1749. Dr. Heber also opined that PSA doubling time was a valid surrogate for prostate cancer recurrence and death and that this was now widely recognized by doctors in the field. (Heber, Tr. 1996-97).

1750. Dr. Heber stated that there is a lot of "enthusiasm for the PSA doubling time" among clinical urologists because it could likely predict clinical benefit and was utilized in clinical decision making. (CX1352 (Heber, Dep. at 314)).

1751. Dr. Heber testified that PSA doubling time is a, "very important clinically utilized marker of clinical status." (CX1352 (Heber, Dep. at 314)).

1752. Dr. Liker testified that most experts believe that there is a relationship between PSA going up and the progression of prostate cancer. (CX1350 (Liker, Dep. at 175)).

1753. Dr. Heber testified that there is a lot of support from the urological community to get the FDA to accept PSA as a surrogate endpoint. (CX1352 (Heber, Dep. at 316)).

1754. Dr. Heber testified that there is, "a lot of feeling in the urological community and scientific agreement that [the] rate of rise of PSA is an important biomarker." (CX1352 (Heber, Dep. at 316-317)).

1755. Dr. Heber also opined that, "PSA doubling time is an accepted variable by the vast majority of the urological community, including members of the American Urological Association and all the leading experts in prostate cancer research in the United States. This is not in dispute." (Heber, Tr. 2151).

(c) From a Patient Care Standpoint PSA Doubling Time Is Extremely Important

1756. Dr. deKernion stated that level of comfort, quality of life, avoidance of more drastic invasive and potentially complicated treatments, all are very important and PSA doubling time serves as a good marker in addressing these points. (PX0161-0010; deKernion Tr. 3065).

1757. Dr. Pantuck stated that PSA doubling time is clinically important for prostate cancer treatment and one of the most important variables that you can discuss to characterize a prostate cancer patient. (CX1341 (Pantuck Dep. at 254-255)).

1758. Dr. Pantuck stated that from a patient care standpoint PSA doubling time is extremely important. (CX1341 (Pantuck, Dep. at 255)).

1759. Dr. Carducci testified that the potential benefits from a clinical or patient point of view of extending PSA doubling time include delaying more aggressive therapy and living longer. (CX1340 (Carducci, Dep. at 182)).

(d) POM's Clinical Studies Showed, With a "High Degree of Probability" That POM and POMx Lengthened PSA Doubling Time and Thus at Least Deferred Death from Prostate Cancer

1760. The fact that the Carducci and Pantuck studies were published and survived the peer review process is significant evidence that the research was scientifically valid. (Eastham, Tr. 1224).

1761. Dr. deKernion testified that in order to show an effect of POM on cancer, the best way to do that research is on patients whose prostate had been removed because the presence of PSA elevation is almost always indication of remaining cancer. This is how the Pantuck and Carducci studies were conducted. (deKernion, Tr. 3057).

1762. Dr. deKernion testified that the study population of Dr. Pantuck and Dr. Carducci's study were people who should have been cured of prostate cancer except their PSA was detectable, which indicated they had microscopic cancer. (deKernion, Tr. 3057).

1763. In each of the studies, they then treated the subjects with POM Juice (Pantuck study) or POMx (Carducci study), and showed that it slowed down the growth of the tumor cells as expressed by the longer time it took for those tumor cells to double. (deKernion, Tr. 3057).

1764. Dr. deKernion testified that in each of the Dr. Pantuck and Dr. Carducci studies the control was the previous doubling time prior to treatment. (deKernion, Tr. 3058).

1765. The researchers measured the doubling time before patients took POM Juice or POMx and then measured doubling time afterwards comparing one to the other. (deKernion, Tr. 3058).

1766. This was done in lieu of a separate placebo group. (deKernion, Tr. 3058).

1767. Dr. deKernion testified that the use of a placebo group is more important when you have a subjective reporting as opposed to an objective reporting. (deKernion, Tr. 3059).

1768. A control arm is not necessary for an objective Phase II study which is exploratory in nature. Many studies on food and many other categories in science are observational type studies without use of a control—a control is important when there is a high risk that the observed effect could be attributed to something other than the substance being tested. (deKernion, Tr. 3059-60; PX0351 (deKernion, Dep. at 97-99); PX0161- 0007).

1769. A control is often used to control for the placebo effect—in POM's clinical studies on prostate health, the researchers are looking and testing objective blood results—there is no evidence to suggest the placebo effect plays any role in modulating the PSADT of the subject. (deKernion, Tr. 3059-3060; PX0351 (deKernion, Dep. at 97-99).

1770. Dr. deKernion testified that patients in a placebo-group often want and sometimes seek the treatment being tested. (deKernion, Tr. 3083).

1771. Dr. Heber also testified that one of the reasons that there was no placebo group was the difficulty in recruiting prostate cancer patients for a placebo arm, after being aware of the benefits of pomegranate juice. (PX0353 (Heber, Dep. at 155-156)).

1772. Dr. deKernion testified that the PSA doubling time studies of Drs. Pantuck and Carducci both showed a dramatic lengthening of PSA doubling time, which Dr. deKerinon opined was a valid and effective marker (i.e. surrogate) for recurrence and death from prostate cancer after radical prostatectomy. (deKernion, Tr. 3052-58).

1773. Dr. deKernion stated that it is standard practice among researchers to qualify studies with language such as "further studies are required" regardless of how exciting or ground breaking the results may be. (deKernion, Tr. 3103-04).

1774. Dr. deKernion testified that based on all of the science it is likely that POM or POMx will improve the chances of avoiding or deferring the recurrence of prostate cancer in men who have had a radical prostatectomy. (deKernion, Tr. 3061).

1775. Dr. Heber testified that competent and reliable science showed that POM and POMx lengthens the PSA doubling time for men who have had prostate cancer. (Heber, Tr. 2012).

1776. Dr. Heber testified that POM and POMx lengthened PSA doubling time and thus at least deferred recurrence or death from prostate cancer. (Heber, Tr. 2012).

(e) The Evidence Is Compelling That POM Promotes Prostate Health and May Help Prevent Prostate Cancer, Including for Healthy Undiagnosed Persons

1777. Dr. deKernion opined that, while such things could never be subject to 100% proof, the same mechanism shown in the in vitro and animal studies and in the Pantuck and Carducci human studies also showed, with a "high degree of probability" that POM and POMx would inhibit the clinical development of prostate cancer in men who have not been diagnosed with that disease. (deKernion, Tr. 3119-20).

1778. Dr. deKernion opined that in healthy men, who have never been diagnosed with prostate cancer POM could possibly play a role in preventing them from getting prostate cancer. (PX0351 (deKernion, Dep. at 76-77)).

1779. Dr. Heber also testified that there is competent and reliable science showing that POMx and POM are likely to lower the risk of prostate problems for men who have not yet been diagnosed with prostate cancer. (Heber, Tr. 2012-13).

1780. Dr. deKernion stated that the data has shown that the POM products and especially specific polyphenols have an impact on the inflammatory half-ways in the prostate and that is evidence that it could prevent prostate cancer. (PX0351 (deKernion, Dep. at 76-77).

1781. In Dr. Miller's expert opinion it is more likely than not, if POM Wonderful is effective in men with biochemical recurrence, it may prevent prostate cancer in an otherwise healthy but at risk individual. (PX0206-0012).

1782. Dr. Heber stated that he would not exclude from the realm of possibility that, based on what we have scientifically, that pomegranate, ellagitannins in a supplement or juice form could contribute to the prevention of prostate cancer. (CX1352 (Heber, Dep. at 329)).

1783. Dr. Heber further opined that, "there's a significant body of scientific evidence to indicate that both pomegranate fruit juice and pomegranate extract can help to prevent or reduce the risk or help to treat prostate cancer." (Heber, Tr. 2156).

(f) RCTs Are Not Necessary in the Context of a Food Like Pomegranate Juice

1784. Dr. deKernion testified that in the case of fruit juice such as POM Juice, that has low or no toxicity, it is not necessary to have a RCT, placebo-controlled test. (deKernion, Tr. 3060).

1785. Dr. Miller opined that a double-blind, placebo controlled trial evaluating the Challenged Products as a prostate cancer protective agent would take decades and thousands of patients and would have to control for other naturally occurring, dietary antioxidants, anti-inflammatory, and anticancer agents as well as life-style activities (e.g. exercise, smoking, alcohol use, just to mention a few), genetic predisposition, racial and ethnic factors, benign prostatic hypertrophy, and other factors that might have an effect on carcinogenesis of prostate cancer. (PX0206-0014).

1786. Dr. Miller stated that, "based on the solid nonclinical data, there should be no need to conduct two randomized well controlled trials to publicize that drinking POM Wonderful might decrease one's risk of developing prostate cancer. Such a statement is in the public's best interest and empowers individuals to take control of their own health by drinking and eating healthful foods, engaging in healthy activities, and avoiding potentially or known harmful ones." (PX0206-0013).

1787. Dr. Miller testified that if a fruit juice were claiming to prevent prostate cancer and there was reliable scientific data to support that you could make that claim without a RCT. (Miller, Tr. 2201).

1788. As a practicing clinician, Dr. Pantuck believed, that the level of certainty required of a study before he relies on it for clinical practice, is not necessarily based on Phase III placebo controlled studies, but based on a clinical judgment of what the risks and benefits and level of evidence are to suggest that some treatment might be good for some patient. (CX1341 (Pantuck, Dep. at 26)).

1789. Dr. Pantuck further testified that there is no study to show that radiation and surgery are equivalent in terms of a cure for prostate cancer but every week he makes recommendations to patients about whether they should have radiation or surgery. (CX1341 (Pantuck, Dep. at 267-268)).

1790. In clinical practice Dr. Pantuck guessed that significantly less than 50 percent of his clinical decisions are based on results of randomized placebo controlled Phase III studies as there are very few in urology that have been done. (CX1341 (Pantuck, Dep. at 276)).

1791. Dr. Pantuck stated that clinicians remove kidneys without a randomized placebo controlled Phase III trial showing the benefits of nephrectomy. (CX1341 (Pantuck, Dep. at 276-277)).

1792. Dr. Pantuck opined that clinicians base recommendations on the best estimates of the safety and benefits of treatments that are available at the time. (CX1341 (Pantuck, Dep. at 277)).

(g) Clinicians Currently Recommend Pomegranate Juice Consumption as an Adjunct to Traditional Medical Care for Some Categories of Patients with Prostate Cancer

1793. Dr. deKernion testified that POM products are a reasonable adjunct, meaning in addition to and not a substitute, for medical care for prostate cancer patients and recommends POM to some of his patients. (deKernion, Tr. 3104; PX0161-0012).

1794. Dr. deKernion stated that POM is a reasonable adjunct for a patient who wishes to help their general health and help avoid a clinical recurrence of prostate cancer. (PX0161- 0011-0012).

1795. Dr. deKernion opined that a food can be used as a treatment for prostate cancer if there is evidence that it might treat it and if there's no toxicity. (PX0351 (deKernion, Dep. at 83)).

1796. Dr. Pantuck testified that there are categories of patients that he recommends pomegranate juice. (CX1341 (Pantuck, Dep. at 269-271)).

1797. Dr. Pantuck also testified that he is aware of doctors who have discussed the findings of his research with their patients. (CX1341 (Pantuck, Dep. at 268)).

1798. Dr. Pantuck, himself, consumes POM Wonderful pomegranate juice a few times a week. (CX1341 (Pantuck, Dep. at 264)).

1799. Dr. deKernion, testified that he consumes pomegranate extract. (deKernion, Tr. 3117).

1800. Dr. Heber testified that he informs prostate cancer patients about the research on pomegranate juice and pomegranate extract. (CX1352 (Heber, Dep. at 239)).

1801. Dr. Miller opined that, there may be some subcategory of patients, who do not have many or any alternatives, and for them a clinician may reasonably decide to recommend, among other things, the consumption of pomegranate. Based on the strength of the reported research. (PX0206-0011).

(h) Premiere Hospitals in America Reference Information about the Health Benefits of the Pomegranate and Prostate Health in Their Publications and Websites

1802. The University of Texas MD Anderson Cancer Center, ranked by U.S. News & World Report as the best cancer hospital in America includes pomegranates in its" Glossary of Caner Terms." (U.S. News & World Report, *Best Hospitals Rankings*, *available at* http://health.usnews.com/best-hospitals/rankings/cancer (last visited Jan. 3, 2012)).

1803. MD Anderson Cancer Center defines pomegranate as "Punica granatum. A subtropical shrub or tree. Juice from the fruit may contain substances that decrease or slow the rise of prostate-specific antigen (PSA) levels. It is being studied for its ability to delay or prevent recurrent prostate cancer." (MD Anderson Cancer Center, Glossary of Cancer Terms, P, *available at* http://www.mdanderson.org/patient-and-cancer-information/cancer-information/glossary-of-cancer-terms/p.html (last visited Jan. 3, 2012)).

1804. Inside Integrative Medicine a newsletter published by MD Anderson Cancer Center's Integrative Medicine Center too has cited the "Anticancer Effects of Pomegranate" stating that it may have preventative effects against prostate cancer. (MD Cancer Center, Inside Integrative Medicine (February/March 2010), *available at* http://www.mdanderson.org/publications/inside-integrative-medicine/issues/issue-15-febmarch2-010.pdf (last visited Jan. 3, 2012)).

1805. Memorial Sloan-Kettering Cancer Center in New York, is ranked second on U.S. News and World Reports list of best cancer hospitals. (U.S. News & World Report, *Best Hospitals Rankings*, *available at* http://health.usnews.com/health-news/best-hospitals/articles/2011/07/18/best-hospitals-2011-12-the-honor-roll (last visited Jan. 3, 2012)).

1806. Memorial Sloan-Kettering Cancer Center is also the hospital of Complaint Counsel's prostate expert Dr. James Eastham. (Eastham Tr. 1207).

1807. On the website of Memorial Sloan-Kettering Cancer Center, information about the pomegranate is included on their Cancer Care Integrative Medicine web page. (Memorial Sloan-Kettering Cancer Center, Pomegranate, *available at* http://www.mskcc.org/cancer-care/herb/pomegranate (last visited Jan. 3, 2012)).

1808. The webpage includes a clinical summary of the pomegranate stating that pomegranate juice has been shown to "suppress inflammatory cell signaling, inhibit prostate tumor grown, and lower serum PSA levels." (Memorial Sloan-Kettering Cancer Center, Pomegranate, *available at* http://www.mskcc.org/cancer-care/herb/pomegranate (last visited Jan. 3, 2012)).

1809. The clinical summary also states that pomegranate juice was "found to benefit patients with carotid artery stenosis, in those with hypertension, hyperlipdemia, mild to moderate erectile dysfunction." (Memorial Sloan-Kettering Cancer Center, Pomegranate, *available at* http://www.mskcc.org/cancer-care/herb/pomegranate (last visited Jan. 3, 2012)).

1810. The webpage cites many POM sponsored studies including the Pantuck (prostate) study. (Memorial Sloan-Kettering Cancer Center, Pomegranate, *available at* http://www.mskcc.org/cancer-care/herb/pomegranate (last visited Jan. 3, 2012)).

1811. Johns Hopkins Hospital in Baltimore, Maryland is consistently ranked at the top or near the top of hospitals in America. U.S. News & World Report currently ranks Johns Hopkins as the number one overall hospital in America and as the third best cancer hospital in the country. (U.S. News & World Report, *Best Hospitals Rankings*, *available at* http://health.usnews.com/health-news/best-hospitals/articles/2011/07/18/best-hospitals-2011-12-the-honor-roll (last visited Jan. 3, 2012)).

1812. On the Johns Hopkins Prostate Cancer webpage for the Sidney Kimmel Comprehensive Cancer Center under the section New Treatments and Research, information about pomegranate research is provided under the heading, "Alternative Medicine/Natural Product Therapies." (New Treatments and Research: The Johns Hopkins Kimmel Cancer Center, *available at* (http://www.hopkinsmedicine.org/kimmel_cancer_center/types_cancer/prostate_cancer/new_treatments.html) (last visited Jan. 3, 2012)).

1813. Dr. Carducci's study on pomegranate extract which slowed PSA doubling time by more than six months in men with rising PSA levels following treatment for prostate cancer is cited. (New Treatments and Research: The Johns Hopkins Kimmel Cancer Center, *available at*

(http://www.hopkinsmedicine.org/kimmel_cancer_center/types_cancer/prostate_cancer/new_treatments.html) (last visited Jan. 3, 2012)).

1814. The May 29, 2008 Johns Hopkins Health Alert Newsletter notes that pomegranates and pomegranate juice has been found to cause prostate cancer cells to "self-destruct." (Johns Hopkins Health Alerts, *Prostate Disorder Special Report: Simple Steps to Protect Yourself Against Prostate Cancer*, *available at* http://www.johnshopkinshealthalerts.com/reports/prostate_disorders/2016-1.html (last visited Jan. 3, 2012)).

1815. The May 29, 2008 Johns Hopkins Health Alert Newsletter further states that, "among men with prostate cancer, daily glasses of pomegranate juice have slowed the increase in PSA levels after treatment." (Johns Hopkins Health Alerts, *Prostate Disorder Special Report: Simple Steps to Protect Yourself Against Prostate Cancer*, *available at* http://www.johnshopkinshealthalerts.com/reports/prostate_disorders/2016-1.html (last visited Jan. 3, 2012)).

1816. The Mayo Clinic in Rochester, Minnesota, is according to U.S. News & World Report the third best hospital in America.(U.S. News & World Report, *Best Hospitals Rankings*, *available at* http://health.usnews.com/health-news/best-hospitals/articles/2011/07/18/best-hospitals-2011-12-the-honor-roll (last visited Jan. 3, 2012)).

1817. On the expert answers portion of the Mayo Clinic website the question is posed whether pomegranate juice is a cure for prostate cancer. (Mayo Clinic, Pomegranate juice: A cure for prostate cancer? *available at* http://www.mayoclinic.com/health/pomegranate-juice/AN01477 (last visited Jan. 3, 2012)).

1818. In response to whether pomegranate juice is a cure for prostate cancer, Mayo Clinic urologist Dr. Erik Castle, responds by stating that, "some research suggests that drinking pomegranate juice may slow the progression of prostate cancer." (Mayo Clinic, Pomegranate juice: A cure for prostate cancer?, *available at* http://www.mayoclinic.com/health/pomegranate-juice/AN01477 (last visited Jan. 3, 2012)).

1819. In response to whether pomegranate juice is a cure for prostate cancer, Mayo Clinic urologist Dr. Erik Castle cites the POM sponsored Allan Pantuck study where PSA doubling time was extended after drinking pomegranate juice. (Mayo Clinic, Pomegranate juice: A cure for prostate cancer? *available at* http://www.mayoclinic.com/health/pomegranate-juice/AN01477 (last visited Jan. 3, 2012)).

1820. In response to whether pomegranate juice is a cure for prostate cancer, Mayo Clinic urologist Dr. Erik Castle, states that, "a longer PSA doubling time indicates cancer may be progressing less rapidly." (Mayo Clinic, Pomegranate juice: A cure for prostate cancer? *available at* http://www.mayoclinic.com/health/pomegranate-juice/AN01477 (last visited Jan. 3, 2012)).

G. Complaint Counsel's Expert Offered Opinions That Are Insufficient to Undermine Respondents' Showing of Substantiation

1. Dr. Eastham's Positions Are Extreme

1821. Dr. James Eastham testified that RCT studies are required for health claims. (Eastham, Tr. 1327-30).

1822. He testified that studies of disease prevention should involve 10,000 to 30,000 mean and that such studies are "incredibly expensive" and in the range of $600 million. (Eastham, Tr.1328).

1823. Dr. Eastham testified that even if a product is safe and might create a benefit, like fruit juice, he would still require an expensive randomized control trial before he would consider it. (Eastham, Tr. 1329-31).

1824. Dr. Eastham has performed over 200 radical prostatectomies per year for a number years without a randomized control trial proving a benefit. (Eastham, Tr.1331-32).

1825. He performed operations without RCTs despite the fact that the side-effects of this operation are significant and include impotence, incontinence, bleeding, embolisms, infection plus risks of general anesthetic. (Eastham Tr. 1331-32).

1826. Pomegranate juice consumption on the other hand has none of these side effects. (PX0352 (Goldstein, Dep. at 44); CX1341 (Pantuck, Dep. at 270).

1827. Dr. Eastham conceded that he cut out hundreds of prostates despite all those risks and without RCT substantiation, yet he would not consider pomegranate juice unless supported by RCTs. (Eastham, Tr. 1332).

2. Dr. Eastham Agrees That the Pantuck and Carducci Studies Are Good Well Conducted Studies

1828. Dr. Pantuck's study was a Phase II study. Dr. Eastham agreed that the Pantuck study as a Phase II study could not be blinded. He agrees that blinding is not important in such a study. (Eastham, Tr. 1327).

1829. Dr. Eastham admits that the Carducci and Pantuck studies were well-designed, good studies. (Eastham, Tr. 1339).

1830. They were well designed in how they selected patients, how they did their statistics and calculations. (Eastham, Tr. 1339).

3. Dr. Eastham Incorrectly Asserts That Changes in PSA Doubling Time as a Surrogate For Progression or Death from Prostate Cancer Are Not Accepted

1831. In his testimony, Dr. Eastham stated that no one accepts modulation of or change in PSADT as a surrogate for progression or death from prostate cancer. (Eastham, Tr. 1340-41).

1832. He testified that at baseline, PSADT is a prognostic marker – a predictor of clinical progression and death but does not know when after baseline it stops being a predictor. (Eastham, Tr.1342-44).

1833. Dr. Eastham could not say when or why it stopped being predictive. (Eastham, Tr.1344-45).

1834. Dr. Eastham insisted that no one would propose that changes in PSA doubling time are a prognostic factor. However Dr. deKernion and Dr. Heber did. Which is consistent with many articles (further illustrated below) that have used PSA doubling time as a surrogate and predictor of disease and death. (Eastham, Tr. 1345).

1835. Complaint counsel's expert, Dr. Meir Stampfer opined that PSA doubling time was a "predictor of disease and mortality" and that, if the extension of PSA doubling time is true, it would substantially prolong lives. (Stampfer, Tr. 869, 873).

1836. Complaint counsel's expert, Dr. Sacks also testified that if something is considered a surrogate for a particular illness or death (as is PSA doubling time), it necessarily follow that changes in that surrogate predict the likelihood of illness or death. (Sacks, Tr. 1613).

1837. Dr. Eastham testified that he would not use the word "surrogate" for PSA doubling time but used it in his article, "Prostate-specific antigen doubling time as a prognostic marker in prostate cancer" published in Nature Clinical Practice October 2005. (PX0178; Eastham, Tr. 1342).

1838. In his article, Dr. Eastham wrote that, "PSA doubling time has emerged as an important factor in the evaluation of men with newly diagnosed prostate cancer or prostate cancer that recurs after treatment. PSA doubling time can be used as a

surrogate marker for prostate cancer specific death." (emphasis added) (PX0178-0001).

1839. Dr. Eastham cites studies showing that "only PSADT was a significant predictor of either systematic progression or local recurrence" of disease, that "PSADT was the strongest predictor of eventual clinical recurrence" and that authors, "suggest that PSADT might serve as a possible surrogate for prostate-cancer-specific death." (PX0178 -0006-0008).

1840. In his article, Dr. Eastham concludes that "PSADT is an important prognostic marker in men with biochemical failure after local therapy for prostate cancer, and it predicts the probable response to salvage radiotherapy, progression to metastatic disease and prostate cancer specific death." (PX0178-0009).

4. A Number of Published Studies Have Demonstrated the Now Widespread Acceptance of PSA Doubling Time as a Valid Surrogate and Predictor of Disease and Death

1841. In a study entitled, "Does PSADT After Radical Prostatectomy Correlate With Overall Survival?" Dr. Anna Teeter and her colleagues wrote in the January 2011 edition of the Journal of Urology of the "widespread acceptance" that PSADT after radical prostatectomy predicts prostate cancer mortality and that this has been "well established" and that PSADT is "a powerful predictor of overall survival." (PX0167).

1842. In the Teeter study the researchers examined the correlation between prostate-specific antigen doubling time and overall survival among men undergoing radical prostatectomy. The authors concluded that a PSADT of less than three months was associated with poorer overall survival than a PSADT of equal to or greater than 15 months. (PX0167).

1843. The authors also concluded that their study validated previous findings that PSADT is a "useful tool for identifying men at increased risk of all-cause mortality early in their disease course." (PX0167).

1844. Dr. Tollefson and colleagues wrote in the April 2007 issue of Mayo Clinic Proceedings in a study entitled, "Stratification of Patient Risk Based on Prostate-Specific Antigen Doubling Time after Radical Retropublic Prostatectomy" that PSADT was "a highly significant and reliable test" to determine the likelihood of disease recurrence and death, an "excellent indicator of clinical disease recurrence" and the only significant factor that predicts clinical progression." (PX0166)(emphasis added).

1845. In the Tollefson study, researchers sought to "assess the risk of local recurrence, systemic progression, and death from cancer among patients who experience biochemical relapse after radical retropubic prostatectomy and to stratify those patients by prostate-specific antigen doubling time." (PX0166).

1846. The researchers concluded that, "prostate-specific antigen doubling time is an independent predictor of clinical disease recurrence and mortality after surgical biochemical failure." (PX0166).

1847. In a study entitled, "Risk of Prostate Cancer-Specific Mortality Following Biochemical Recurrence After Radical Prostatectomy" Dr. Freedland and colleagues used PSADT to "define risk factors for prostate cancer death following radical prostatectomy and to develop tables to risk stratify for prostate cancer-specific survival." (PX0165).

1848. Dr. Freedland et al., found that patients with a PSADT in less than 3 months had a median survival of 6 years. Patients with a PSADT in less than 3 months, biochemical recurrence 3 years or less after surgery, and a pathological Gleason score of 8-10 has a median survival of 3 years. Patients with a PSADT of 15 or more months and a biochemical recurrence more than 3 years after surgery had a 100% cause–specific survival. (PX0165).

1849. The researchers found that clinical parameters such as PSADT can help risk stratify patients for prostate cancer-specific mortality following biochemical recurrence after radical prostatectomy. (PX0165).

1850. In a study entitled, "Recurrence Patterns After Radical Retropubic Prostatectomy: Clinical Usefulness of Prostate Specific Antigen Doubling Times and Log Slope Prostate Speicfic Antigen" published in the October 1997 edition of the Journal of Urology, Drs. Patel, deKernion, et al. studied the correlation between prostate specific antigen doubling time and clinical recurrence in patients with detectable PSA after radical retropubic prostatectomy. (PX0162).

1851. The researchers concluded that, after PSA became detectable PSA doubling time was a better indicator of the risk and time to clinical recurrence after radical retropubic prostatectomy than other factors including preoperative PSA. (PX0162).

5. Dr. Eastham's Opinions Do Not Rebut Respondents Pre-Clinical, and Clinical Research Showing a Benefit for Pomegranates and Prostate Health

1852. Dr. Eastham's opinions on PSA doubling time were impeached by his own article. (PX0178).

1853. Dr. Eastham himself has performed over 200 radical prostatectomies per year for a number of years when no RCT had been done showing that the operation provided a benefit for the treatment of prostate cancer. (Eastham, Tr. 1331; PX0358 (Eastham, Dep. at 154-155).

1854. Dr. Eastham testified that Dr. Pantuck's study was a well-designed Phase II study and that in the grouping of patients that were examined, PSA doubling time was prolonged. (PX0358 (Eastham, Dep. at 88)).

H. In Addition to the Science, Research, and Expert Testimony Discussed Above, Respondents Offered Into Evidence Additional Research That Provides Substantiation for the Challenged Products

1. Research Not Sponsored by POM Wonderful, But on Similar Extracts, Supports Findings That the Challenged Products Support Prostate Health

1855. In a study by Malik, et al., *Pomegranate Fruit Juice for Chemoprevention and Chemotherapy of Prostate Cancer*, Proc. Natl. Acad. Sci. USA, 2005 Oct 11; 102(41): 14813-8, pomegranate fruit extract was shown to have an effect on prostate cancer cells. (PX0173).

1856. In the Malik study, pomegranate fruit extract with acetone and water (Fruit Juice Extract or FJE) known to be rich in pomegranate ellagitannins similar to POM Wonderful juice, POMx, and POMx Liquid were shown to have potent prostate cancer reducing effects when consumed by mice implanted with androgen-sensitive CWR22Rvl cells. (PX0173).

1857. The research showed significant inhibition in tumor growth concomitant with a significant decrease in serum prostate-specific antigen levels. (PX0173).

1858. FJE (pomegranate ellagitannins) consumption resulted in a significant drop in PSA levels or doubling time in direct relationship to prostate cancer tumor volume. (PX0173).

1859. FJE (pomegranate ellagitannins) inhibited PSA, a marker for prostate cancer progression. (PX0173).

1860. Also, in vitro results demonstrated that FJE (10-100 ug/ml) treatment of highly aggressive human prostate cancer PC3 cells resulted in a dose dependent inhibition of cell growth/cell viability and induction of apoptosis. (PX0173).

1861. Also, FJE decreased PSA expression in human prostate cancer cells. (PX0173).

1862. The researchers concluded that "the fruit pomegranate and its associated antioxidants may possess a strong potential for development as a chemopreventive and possible therapeutic agent against CaP (prostate cancer)." (PX0173).

1863. In a study by, Albrecht M, Jiang W, Kumi-Diaka J, et al., *Pomegranate extracts potently suppress proliferation, xenograft growth, and invasion of human prostate cancer cells*. J Med Food 7: 274-283, 2004, pomegranate extract was shown to have anti-tumor activity. (PX0207).

1864. In this study, pomegranate juice and pericarp (extract from peel) polyphenols were studied on human prostate cancer cell xenograft growth (in vivo) and the proliferation, cell cycle distribution, apoptosis, and gene expression (in vitro). (PX0207).

1865. The juice and pericarp polyphenols demonstrated similar and significant anti-tumor activity against human cancer cells (LNCaP, PC-3 and DU 145). (PX0207).

1866. Pericarp polyphenols demonstrated potent inhibition of PC-3 xenograft growth in mice. (PX0207).

1867. The researchers concluded that pomegranate juice and extract have similar anti-cancer effects. (PX0207).

1868. Respondents have also offered into evidence further research not sponsored by POM Wonderful supporting the Challenged Products and prostate health. (PX0382).

2. Additional Research Contributing to the Total Body Of Science Supporting the Challenged Products and Prostate Health

1869. Seeram NP, Aronson WJ, Zhang Y, Henning SM, Moro A, Lee R, Sartippour M, Harris DM, Rettig M, Suchard MA, Pantuck AJ, Belldegrun A, and Heber D, *Pomegranate Ellagitannin-Derived Metabolites Inhibit Prostate Cancer Growth and Localize to the Mouse Prostate Gland*, J. Agric. Food Chem.2007, 55, 7732-7737. (PX0069).

1870. Rettig MB, Heber D, An J, Seeram NP, Rao JY, Liu H, Klatt T, Belldegrun A, Moro A, Henning SM, Mo D, Aronson WJ, and Pantuck A, *Pomegranate extract inhibits androgen-independent prostate cancer growth through a nuclear factor-κB-dependent mechanism*, Molecular Cancer Therapy 7 (9): 2662-2671 (2008). (PX0070).

1871. Sartippour MR, Seeram NP, Rao JY, Moro A, Harris DM, Henning SM, Firouzi A, Rettig MB, Aronson WJ, Pantuck AJ, and Heber D, *Ellagitannin-rich*

pomegranate extract inhibits angiogenesis in prostate cancer in vitro and in vivo, International Journal of Oncology 32: 475-480, 2008. (PX0071).

1872. Koyama, et al., *Pomegranate Extract Induces Apoptosis in Human Prostate Cancer Cells by Modulation of the IGF-IGFBP Axis*, Growth Horm IGF Res. 2010 Feb; 20(1): 55-62. (PX0183).

1873. Agensys, *Investigation of the Effect of Pomegranate Juice (PJC) on Human Prostate Cancer* (Unpublished Study Results, 2001) (PX065).

1874. Agensys, *Investigation of the Effect of Pomegranate Juice (PJC) on Human Prostate Cance*r, Final Power Point Presentation (2003) (PX0066).

1875. Agensys, *PJC Reduces Subcutaneous Growth of Prostate Tumors* (11/20/2001) (PX0067)

1876. Hong MY, Seeram NP, and Heber D, *Pomegranate polyphenols down-regulate expression of androgen synthesizing genes in human prostate cancer cells overexpressing the androgen receptor*, Journal of Nutritional Biochemistry 19 (2008) 848-855. (PX0068).

1877. Carducci MA, Safety and Efficacy of POMx in Men with Prostate Cancer: An 18-Month, Randomized, Double-Blind, Dose-Finding Study of the Effects of Two (2) Doses of Pomegranate Juice Extract Capsules (1 or 3 capsules/day) on Rising Prostate Specific Antigen Levels in Men Following Initial Therapy for Prostate Cancer (unpublished clinical study report, 2007) (PX0063).

1878. Beer, et al., Double-Blinded Randomized Study of High-Dose Calcitriol Plus Docetaxel in Androgen-Independent Prostate Cancer: A Report From the ASCENT Investigators, J. Clin. Oncol. 2007 Feb 20; 25(6): 669-74 (PX0186).

1879. Andriole, et al., Treatment With Finasteride Following Radical Prostatectomy for Prostate Cancer, Urology, March 1995, Volume 45, Number 3. (PX0177).

1880. Carducci, et al., A Phase II Study of Pomegranate Extract for Men with Rising Prostate-Specific Antigen Following Primary Therapy, J. Clin. Oncol. 29: 2011 (suppl 7; abstr 11). (PX0175).

1881. Carmody, et al., A dietary Intervention for Recurrent Prostate Cancer after Definitive Primary Treatment: Results of a Randomized Pilot Trial, Urology 2008 December; 72(6): 1324-8. (PX0168).

1882. deNigris et al., Beneficial Effects of Antioxidants and L-arginine on Oxidation-Sensitive Gene Expression and Endothelial NO Synthase Activity at Sites of Disturbed Shear Stress, PNAS 2003 100: 1420-1425. (PX0174).

1883. Freedland, et al., Risk of Prostate Cancer-Specific Mortality Following Biochemical Recurrence After Radical Prostatectomy (Abstract), JAMA, 2005; 294(4): 433-439. (PX0165).

1884. Giovacchini, et al., PSA Doubling Time for Prediction of [(11)C]choline PET/CT Findings in Prostate Cancer Patients with Biochemical Failure after Radical Rrostatectomy (Abstract), Eur. J. Nucl. Med. Mol. Imaging, 2010 June; 37(6): 1106-16. (PX0164).

1885. Leung, et al., Exercise Alters the IGF Axis In Vivo and Increases P54 Protein in Prostate Tumor Cells In Vitro, J. Appl. Physiol. 96: 450-454, 2004; 10.1152/japplphysiol.00871.203 (PX0176).

1886. Pantuck AJ, Leppert JT, Zomorodian N, Aronson W, Hong J, Bardnard RJ, Seeram N, Liker H, Wang J, Elashoff R, Heber D, Aviram M, Ignarro L, Belldegrun A, Phase II Study of Pomegranate Juice for Men with Rising Prostate-Specific Antigen following Surgery or Radiation for Prostate Cancer, Clin. Cancer Research 12 (13): 4018-4026 (2006). (PX0060).

1887. Pantuck AJ, Zomorodian N, Rettig M, Aronson WJ, Heber D, Belldegrun AS, Long Term Follow Up of Phase 2 Study of Pomegranate Juice for Men with Prostate Cancer Shows Durable Prolongation of PSA Doubling Time, J. of Urology Vol. 181 No. 4, Supplement (2009). (PX0061).

1888. Patel, et al., Recurrence Patterns After Radical Retropubic Prostatectomy: Clinical Usefulness of Prostate Specific Antigen Doubling Times and Log Slope Prostate Specific Antigen, Journal of Urology, Vol. 158, 1441-1445, October 1997. (PX0162).

1889. Pound, et al., Natural History of Progression After PSA Elevation Following Radical Prostatectomy (Abstract), JAMA 1999; 281(17): 1591-1597. (PX0163).

1890. Schroder, et al., Randomized, Double-Blind, Placebo-Controlled Crossover Study in Men with Prostate Cancer and Rising PSA: Effectiveness of a Dietary Supplement, Eur. Urol. 2005 December; 48(6): 922-30. (PX0169).

1891. Smith MR, et al., Rosiglitazone versus Placebo for Men with Prostate Cancer and a Rising Serum Prostate Specific Antigen after Radical Prostatectomy and/or Radiation Therapy, Cancer, 2004 October 1; 101(7): 1569-74. (PX0172).

1892. Teeter, et al., Does PSADT after Prostatectomy Correlate with Overall Survival?—A Report from the SEARCH Database Group, Urology. 2011 January; 77(1): 149-53. (PX0167).

1893. Tollefson, et al., Stratification of Patient Risk Based on Prostate-Specific Antigen Doubling Time after Tadical Retropubic Prostatectomy (Abstract), Mayo Clin. Proc. 2007 Apr; 82(4): 422-7. (PX0166).

1894. Trapasso, et al, The Incidence and Significance of Detectable Levles of Serum Prostate Specific Antigen After Radical Prostatectomy, Journal of Urology, Vol. 152, 1821-1825, November 1994. (PX0171).

1895. Zhang, et al., Effect of Lycopene on Androgen Receptor and Prostate-Specific Antigen Velocity, Chin. Med J. (Engl) 2010 August; 123(16): 2231-6. (PX0170).

1896. Benchikh El Fegoun, et al., PSA and Follow-up after Treatment of Prostate Cancer, Prog. Urol. 2008 Mar; 18(3): 137-44. (PX0187).

1897. Danella, et al., Detectable Prostate Specific Antigen Levels Following Radical Prostatectomy: Relationship of Doubling Time to Clinical Outcome, Presented at the American Urological Association 88th Annual Meeting, San Antonio, Texas, May 1993. (PX0180).

1898. Eastham, Prostate Specific Antigen Doubling Time as a Prognostic Marker in Prostate Cancer, Nat. Clin. Pract. Urol. 2005 Oct: 2(10): 482-91. (PX0178).

1899. Finley, et al., The Natural History of Ultrasensitive PSA Following Radical Prostatectomy, Unpublished. (PX0179).

1900. Oudard, et al., Prostate Specific Antigen Doubling Time before Onset of Chemotherapy as a Predictor of Survival for Hormone-refractory Prostate Cancer Patients, Ann Oncol. 2007 Nov; 18(11): 1828-33. (PX0181).

1901. Petrylak, et al., Evaluation of Prostate-Specific Antigen Declines for Surrogacy in Patients Treated on SWOG 99-16, J. Natl Cancer Inst. Volume 98 Issue 8: pp. 516-521. (PX0185).

1902. Roberts, et al., PSA Doubling Time as a Predictor of Clinical Progression after Biochemical Failure Following Radical Prostatectomy for Prostate Cancer, Mayo Clin. Proc. 2001 Jun; 76(6): 576-81. (PX0188).

1903. Trock, et al., Prostate Cancer-Specific Survival Following Salvage Radiotherapy vs Observation in Men with Biochemical Recurrence after Radical Prostatectomy, JAMA 2008; Jun 18; 299(23): 2760-9. (PX0182).

I. Researchers Communicated to Respondents the Prostate Health Benefits of the Challenged Products

1904. Doctors reviewing the results of basic and animal studies done on prostate health represented to Respondent Stewart Resnick that the results were the best they had ever seen. (S. Resnick, Tr. 1734, 1736).

1905. Many different medical doctors assured Respondent Stewart Resnick that PSA doubling time was an acceptable endpoint in prostate cancer studies and a placebo was not necessary. (S. Resnick, Tr. at 1732-1733; CX1360 (S. Resnick, Dep. at 225-226); CX1376 (S. Resnick, Ocean Spray Dep. at 237-238)).

1906. Dr. Harley Liker told Respondents that Pantuck's Phase II study proves that pomegranate juice slows down the progression PSA. (CX1350 (Liker, Dep. at 174-175)).

1907. In a January 2007 email, Dr. Heber stated to Mark Dreher, "The prolongation of PSA doubling time is considered clinically significant by urologists and is being confirmed in large multicenter trials." (PX0494).

1908. Dr. David Heber has shared his view with Dr. Liker that POM products could contribute to the prevention of prostate cancer. (CX1350 (Liker, Dep. at 174)).

1909. In a January 2007 email, Dr. Heber stated to Mark Dreher, "The prolongation of PSA doubling time is considered clinically significant by urologists and is being confirmed in large multicenter trials." (PX0494).

1910. In a January 2007, Dr. Heber stated to Mark Dreher that there was justification for the statement that "pomegranate extract promotes prostate health." (PX0494).

1911. Dr. Heber attended meetings with Respondents about prostate cancer research attended by Allan Pantuck, Phil Kantoff, and Michael Carducci. (Heber, Tr. 2157-58).

1912. Dr. Heber testified that at meetings with Respondents about prostate cancer research there was a discussion of the scientific data which included comments to Respondents that the Challenged Products, considering the studies done to date, could help prevent prostate cancer. (Heber, Tr. 2157-58).

1913. Dr. Heber testified that there was enthusiasm from everyone including Dr. Phillip Kantoff of Harvard Medical School. (Heber, Tr. 2157-58).

1914. Dr. Heber stated that ultimately there, "was substantial agreement on the body of evidence there that it could help to prevent in the correct setting." (Heber, Tr. 2157-58).

1915. Dr. Heber further testified that prevent would not mean absolutely prevent nor a substitute for a pharmaceutical prevention. (Heber, Tr. 2157-58).

1916. Researchers looking at prostate health benefits have also made public remarks that the research shows a benefit. (PX0428_0001).

1917. For example, Dr. Pantuck has publicly made positive remarks about the findings in his research done for Respondents. (PX0428_0001).

1918. In connection with his follow-up research to his 2006 study, Dr. Pantuck publicly remarked that the increase in doubling time from 15 to 54 months was a "big increase." He said that he was "surprised to see such an improvement in PSA numbers." He also contributed, "In older men 65 to 70, who have been treated for prostate cancer, we can give them pomegranate juice and it may be possible for them to outlive their risk of dying from their cancer." He also commented, "The juice seems to be working." (PX0428_0001) (CX1341 (Pantuck, Dep. at 270-271)).

J. Summary of Prostate Health Claims Supported By the Evidence

1919. Research on the Challenged Products has gone through the rigorous peer review process by respected journals, performed by thought leading researchers and performed at prestigious institutions. (Liker, Tr. 1887-1888; CX1352 (Heber Dep. at 268-269; CX1340 (Carducci, Dep. at 176).

1920. Respondents' research has involved *in vitro*, animal studies and successful human clinical trials all showing prostate health benefits. (PX0065; PX0068; PX0069; PX0070; PX0071; PX0060; PX0061; PX0175).

1921. Competent and reliable scientific evidence supports the conclusion that the consumption of pomegranate juice and pomegranate extract supports prostate health, including by prolonging PSA doubling time in men with rising PSA after primary treatment for prostate cancer. (PX0161; PX0353 (Heber Dep. at 84-85); deKernion Tr. 3126; PX0351 (deKernion, Dep. at 41-42); Heber, Tr. 2012).

1922. Competent and reliable scientific evidence supports the conclusion that the same mechanism shown in the *in vitro* and animal studies and in the Pantuck and Carducci human studies also showed with a high degree of probability that the Challenged Products inhibit the clinical development of prostate cancer cells in men who have not been diagnosed. (deKernion, Tr. 3126; PX0351 (deKernion, Dep. at 76-77); PX0206 at 12; Heber, Tr. 2156).

XVI. RESPONDENTS' ERECTILE HEALTH CLAIMS ARE SUBSTANTIATED

A. Respondents' Erectile Health Claims Are Substantiated

1923. It is "[w]ithout a question" that competent and reliable scientific evidence demonstrates that pomegranate juice in its various forms (including POM Juice, POMx, and POM Pills) provides a positive benefit to erectile health and erectile function. (Goldstein, Tr. 2605; PX0189-0014; PX0149-0006-0007; Burnett, Tr. 2255-56; PX0349 (Burnett, Dep. at 103, 116-118, 137; Heber, Tr. 2012).

1924. The mechanism by which this fruit promotes erectile health and function is via its potent antioxidant components and its impact on nitric oxide ("NO"), which is of "paramount importance" to good erectile health and function and is the key molecule that governs penile erections. (PX0149-0004-0006; Burnett, Tr. 2249-51, 2276; PX0190-0006; Melman, Tr. 1169; PX0189-0011).

1925. Additionally, because pomegranate juice is a fruit and not a pharmaceutical drug, physicians who treat patients concerned with erectile health would not hold pomegranate juice to the standards of safety and efficacy traditionally required by the FDA for approval of a pharmaceutical (i.e., performance of a large, randomized, double-blind, placebo controlled clinical trial ("RCT")) before recommending pomegranate juice to their patients. (PX0149; PX0189; Heber, Tr. 2182).

B. POM's Advertising Claims Regarding Erectile Health

1926. Complaint Counsel's Complaint identifies four purported advertisements for the Challenged Products in which Respondents allegedly made health-benefit claims regarding erectile dysfunction. (CX1426_0027, 0031-0035).

1927. Paragraph 9.A and Ex. A of the Complaint identify a POM Wonderful juice bottle "hangtag" that incorporates (in pertinent part) the following text:

> 100% PURE POMEGRANATE JUICE
>
> It's 100% pure! It's heroically healthy! It's The Antioxidant Superpower, POM Wonderful 100% authentic pomegranate juice. Backed by $25 million in medical research. Proven to fight for cardiovascular, prostate and erectile health. Committed to keeping you healthy for a good, long time!

1928. Paragraph 9.D and Ex. E-1 of the Complaint identify a *screen capture* from Respondents' pomegranatetruth.com website, which allegedly contained (in pertinent part) the following text as of April 28, 2009:

> Backed by science.
>
> POM is the only pomegranate juice backed by $25 million in medical research. To date, numerous published clinical studies have documented the benefits of drinking pomegranate juice, benefits that include improved heart and prostate health and better erectile function. **All of the studies featured patients who drank POM Wonderful 100% Pomegranate Juice, not any other brands**. . . . Read more.

1929. Paragraph 9.G and Ex. F of the Complaint identify a *Newsweek* article consisting of an *interview* of Respondent Lynda Resnick. Paragraph 9.G of the Complaint selectively quotes the following language from the interview, ignoring the several preceding pages in which Mrs. Resnick discusses the economy, politics, and business philosophy:

> * * *
>
> **Should I take vitamins?**
>
> I don't know your family history. How's your father?
>
> **He's in good health. Had a bout of prostate cancer, but that's–**
>
> You have to be on pomegranate juice. You have a 50 percent chance of getting it. Listen to me. It is the one thing that will keep your PSA normal. You have to drink pomegranate juice. There is nothing else we know of that will keep your PSA in check. Ask any urologist—your father should be on it. Your father should be on it. I'm sorry to do this to you, but I have to tell you. We just did a study at UCLA, on 43 men . . . it arrested their PSA. How old are you, 28?
>
> **Twenty-six.**
>
> Get a base line now. [*Pause, wink*] It's also 40 percent as effective as Viagra. Not that you need it. But—couldn't hoit!

1930. Paragraph 9.H and Ex. E-2 of the Complaint identify a *screen capture* from Respondents' pomwonderful.com "POM Truth – Backed by Science" web page, which allegedly contained (in pertinent part) the following text as of April 29, 2009:

> **Backed by Science**
>
> Only POM Wonderful products are backed by $32 million in medical research. Actually, we are the only pomegranate juice backed by any medical research at all.
>
> There has been a lot of talk lately about the role of pomegranates in promoting heart health, prostate health and proper erectile function. . . .
>
> * * *
>
> **Erectile Function**
>
> A pilot study released in the International Journal of Impotence Research in 2007 examined 61 male subjects with mild to moderate erectile dysfunction. Compared to participants taking a placebo, **those men drinking 8oz [sic] of POM Wonderful 100% Pomegranate Juice daily for four weeks were 50% more likely to experience improved erections**.

1931. In addition to advertisements identified in their Complaint, Complaint Counsel also identified in discovery a print ad for POMx capsules, which contains (in pertinent part) the following text regarding erectile function:

> **$32 million in research.**
>
> **We're not just playing doctor.**
>
> POMx is made from the only pomegranates backed by $32 million in medical research at the world's leading universities. Not only has this research documented the unique and superior antioxidant power of pomegranates, it has revealed promising results for erectile, prostate and cardiovascular health.
>
> **Is that POMx in your pocket?**

> Our POMx pills are made from the same pomegranates we use to make our POM Wonderful 100% Pomegranate Juice, on which each of the following medical studies was conducted:
>
> In a preliminary study on erectile function, men who consumed POM juice reported a 50% greater likelihood of improved erections as compared to placebo. "As a powerful antioxidant, enhancing the actions of nitric oxide in vascular endothelial cells, POM has potential in the management of ED… further studies are warranted." *International Journal of Impotence* Research[1, 2, 3]
>
> [1]pompills.com/research. [2]These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure or prevent any disease. [3]53 men with mild/moderate erectile dysfunction drank 8oz. 100% pomegranate juice daily for one month.

1932. Based on these representations, Complaint Counsel alleges, that Respondents "have represented, expressly or by implication, that clinical studies, research, and/or trials prove that: [¶] A. Drinking eight ounces of POM Juice daily prevents or reduces the risk of erectile dysfunction; and [¶] B. Drinking eight ounces of POM Juice daily treats erectile dysfunction." (CX1426_0019).

C. Respondents Deny Complaint Counsel's Allegations That Their Advertisements Are False and Misleading

1933. Respondents deny Complaint Counsel's allegations that their advertising and promotional materials make the claim that: "A. Drinking eight ounces of POM Juice daily prevents or reduces the risk of erectile dysfunction; and B. Drinking eight ounces of POM Juice daily treats erectile dysfunction." (PX0364-0005).

1934. Respondents dispute Complaint Counsel's allegations or characterizations regarding Respondents' science and aver there is substantial scientific research indicating the health benefit of their products and substantiating their advertising and promotional materials. (PX0364-0005).

1935. Respondents deny Complaint Counsel's allegations that their advertising and promotional materials make the claim that "A. Drinking eight ounces of POM Juice daily prevents or reduces the risk of erectile dysfunction; and B. Drinking eight ounces of POM Juice daily treats erectile dysfunction." (PX0364-0005).

D. Substantiation for Respondents' Erectile Health Claims

1. Competent and Reliable Scientific Evidence Supports The Conclusion That The Consumption of Pomegranate Juice Has Positive Effects On Erectile Function

(a) *In Vitro* and *In Vivo* Studies on the Challenged Products Specifically

(1) Dr. Aviram and Colleagues Found that Pomegranate Juice Had Potent Anitatherogenic Effects in Humans and Atherosclerotic Mice That May be Attributable to its Antioxidative Properties

1936. Dr. Aviram, is a distinguished professor of biochemistry and researcher at the Technion Faculty of Medicine and the Rambam Medical Center in Haifa, Israel, and head of the Lipid Research Laboratory. (PX0004; CX1358 (Aviram, Dep. at 7-8)).

1937. Complaint Counsel's designated erectile function expert, Arnold Melman, described Technion Institute in Haifa, Israel as a "terrific" institution. (Melman, Tr. 1168).

1938. For over 30 years, Dr. Aviram's major research focused on antioxidants in general, and on its dietary role in cardiovascular disease. (CX1358 (Aviram, Dep. at 5)).

1939. Dr. Aviram's Study, entitled *Pomegranate juice consumption reduces oxidative stress, atherogenic modifications to LDL and platelet aggregation: Studies in humans and in atherosclerotic apolipoprotein e-deficient mice*, reported that dietary supplementation with nutrients rich in antioxidants was associated with inhibition of atherosclerosis. (PX0189-0012; PX0004).

1940. Dr. Aviram and colleagues studied in healthy male volunteers (and in atherosclerotic apolipoprotein E-deficient mice) the effect of consumption of pomegranate juice on such outcomes as lipoprotein oxidation, aggregation and retention, macrophage atherogenicity, platelet aggregation and atherosclerosis. (PX0189-0012; PX0004).

1941. Dr. Aviram and colleagues found that in humans, pomegranate juice consumption decreased low-density lipoprotein ("LDL") susceptibility to aggregation and retention and increased an high-density lipoprotein ("HDL") associated esterase that can protect against lipid peroxidation. (PX0189-0012; PX0004).

1942. Similar positive anti atherosclerosis effects were seen in the E-deficient mice. (PX0189-0012; PX0004).

1943. Dr. Aviram and colleagues concluded that pomegranate juice had potent antiatherogenic effects in humans (and atherosclerotic mice) that may be attributable to its antioxidative properties. (PX0189-0012; PX0004).

1944. Dr. Goldstein noted that Dr. Aviram's study is "a very fascinating and very important piece of information." (PX0352 (Goldstein, Dep. at 127)).

(2) Dr. Azadzoi and Colleagues Found That Pomegranate Juice Possesses Potent Antioxidants, and That Long Term Intake of Pomegranate Juice Increased Intracavernosal Blood Flow, Improved Erectile Responses, Improved Smooth Muscle Relaxation, and Decreased Erectile Tissue Fibrosis

1945. Dr. Azadzoi is a distinguished research professor of urology and pathology at the Boston University School of Medicine and Director of Urology Research at the Veterans Affairs Boston Healthcare System. (PX0051).

1946. Dr. Azadzoi, along with Dr. Goldstein developed an atherosclerotic animal model for erectile dysfunction. (Goldstein, Tr. 2595).

1947. Dr. Azadzoi has published extensively on studies using atherosclerotic animal models with erectile dysfunction. (Goldstein, Tr. 2595).

1948. Dr. Azadzoi's Study entitled *Oxidative stress in arteriogenic erectile dysfunction: Prophylactic role of antioxidants*, studied the anti-oxidant properties of various fruit juices, such as orange juice, blueberry juice, and cranberry juice, and other known antioxidant beverages such as green tea and red wine, and reported that pomegranate juice possessed the highest free radical scavenging capacity. (PX0189-0011-0012; PX0051; PX0352 (Goldstein, Dep. at 123-124); Goldstein, Tr. 2595).

1949. Dr. Azadzoi and colleagues examined that effect of various antioxidant beverages on atherogenic erectile dysfunction in rabbits that demonstrated decreased intracavernous blood flow, erectile dysfunction, loss of smooth muscle relaxation, decreased endothelial nitric oxide synthase, and neuronal nitric oxide synthase, diffuse cavernosal fibrosis and increased cavernous levels of the oxidative product isoprostane 8 – epi – prostaglandin F 2 alpha. (PX0189-0011-0012; PX0051).

1950. Animal studies are very informative as it can characterize what's going on at the human level. (PX0349 (Burnett, Dep. at 111); PX0352 (Goldstein, Dep. at 122-124); Goldstein, Tr. 2644). Work from animal studies have some potential for

benefit of a therapy at the human level. (PX0349 (Burnett, Dep. at 112); Burnett, Tr. 2262-63).

1951. Dr. Azadzoi and colleagues found that long term pomegranate juice intake increased intracavernosal blood flow, improved erectile responses, improved smooth muscle relaxation, and decreased erectile tissue fibrosis. (PX0189-0011-0012; PX0051; PX0352 (Goldstein, Dep. at 123); Goldstein, Tr. 2595-97).

1952. Dr. Azadzoi and colleagues concluded that arteriogenic erectile dysfunction accumulates oxidative products in erectile tissues and that oxidative stress is an important pathophysiologic factor of erectile dysfunction. (PX0189-0011-0012; PX0051).

1953. Dr. Azadzoi and colleagues found antioxidant therapy may be useful as a prophylactic for preventing smooth muscle dysfunction and fibrosis in erectile dysfunction. (PX0189-0011-0012; PX0051).

(3) Dr. de Nigris and Colleagues Showed that Polyphenolic Antioxidants Contained in Pomegranate Juice Can Contribute to the Reduction of Oxidative Stress and Atherogenesis Both *In Vitro* in Cultured Human Coronary Endothelial Cells and *In Vivo* in Hypercholesterolemic Mice

1954. Dr. de Nigris, of the Department of General Pathology and Excellence Research Center on Cardiovascular Diseases of the 1st School of Medicine at the II University of Naples, Italy, and colleagues, including Dr. Louis Ignarro, evaluated the effects of intervention with pomegranate juice on oxidation-sensitive genes and endothelial nitric oxide synthase expression induced by high shear stress *in vitro* and *in vivo*. (PX0059). The study was entitled *Beneficial effects of pomegranate juice on oxidation-sensitive genes and endothelial nitric oxide synthase activity at sites of perturbed shear stress*. (PX0059).

1955. Cultured human coronary artery endothelial cells exposed to high shear stress *in vitro* and hypercholesterolemic mice were used in the study. (PX0059).

1956. Dr. de Nigris and colleagues found that pomegranate juice concentrate reduced the activation of redox-sensetive genes and increased endothelial nitric oxide synthase expression in cultured human coronary artery endothelial cells and hypercholesterolemic mice. (PX0059; Burnett, Tr. 2290).

1957. Dr. de Nigris and colleagues also found that oral administration of pomegranate juice to hypercholesterolemic mice at various stages of disease reduced significantly the progression of atherosclerosis. (PX0059).

1958. This study indicates that polyphenolic antioxidants contained in pomegranate juice can contribute to the reduction of oxidative stress and atherogenesis. (PX0059; Burnett, Tr. 2290).

(4) Dr. de Nigris and Colleagues Found that Prolonged Supplementation with Pomegranate Fruit Extract or Pomegranate Juice Can Largely Correct the Perturbed Shear Stress-Induced Proatherogenic Di4sequilibrium by Increasing Endothelial Nitric Oxide Synthase and cGMP and Decreasing Redox-Sensitive Transcription Factors Both *In Vitro* in Cultured Human Coronary Endothelial Cells and *In Vivo* in Hypercholesterolemic Mice

1959. In a study entitled *Effects of a pomegranate fruit extract rich in punicalagin on oxidation-sensitive genes and eNOS activity at sites of perturbed shear stress and atherogenesis*, Dr. de Nigris and her esteemed colleagues showed that atherosclerosis is enhanced in arterial segments exposed to perturbed shear stress as a result of increased expression of oxidation-sensitive responsive genes. (PX0189-0010-0011; PX0056).

1960. The authors studied the effect of pomegranate fruit extract and pomegranate juice antioxidant activity on reduction of oxidative stress and atherogenesis during disturbed shear stress flow using cultured human coronary artery endothelial cells. (PX0189-0010-0011; PX0056).

1961. Their study showed that pomegranate fruit extract and pomegranate juice reduced the activation of oxidation-sensitive genes and increased endothelial nitric oxide synthase expression. (PX0189-0010-0011; PX0056).

1962. Their study also showed that pomegranate fruit extract and pomegranate juice increased cyclic GMP levels. (PX0189-0010-0011; PX0056).

1963. Their study further showed that administration of pomegranate juice reduced the progression of atherosclerosis in hypercholesterolemic mice. (PX0189-0010-0011; PX0056).

1964. The authors concluded that the proatherogenic effects of perturbed shear stress can be reversed with chronic administration of pomegranate fruit extract. (PX0189-0010-0011; PX0056).

(5) Nobel-Prize-Winner Dr. Louis Ignarro Found that Pomegranate Juice Possesses Potent Antioxidant Activity that Results in Marked Protection of Nitric Oxide Against Oxidative Destruction in Vascular Endothelial Cells

1965. Nobel-prize-winner Dr. Louis Ignarro for his discoveries concerning nitric oxide, conducted an *in vitro* study, entitled *Pomegranate juice protects nitric oxide against oxidative destruction and enhances the biological actions of nitric oxide*, to evaluate pomegranate juice's capacity to protect nitric oxide against oxidative destruction. (PX0189-0011; PX0058; Goldstein, Tr. 2593-95; Heber, Tr. 1995-96; Burnett, Tr. 2252-53).

1966. Dr. Ignarro found that pomegranate juice was found to possess more antioxidant activity than grape juice, blueberry juice, red wine, and ascorbic acid. (PX0189-0011; PX0058).

1967. Based on a series of studies that were performed on vascular endothelial cells, Dr. Ignarro concluded that pomegranate juice possesses potent antioxidant activity that results in marked protection of nitric oxide against oxidative destruction, thereby augmenting the biologic actions of nitric oxide. (PX0189-0011; PX0058).

1968. Dr. Goldstein testified that the "Ignarro study is another part of the sequence of evidence that supports that a nutraceutical, specifically pomegranate juice, has incredible vascular-sparing properties that ultimately, when you follow this path leads to the improvement of erectile function in men with erectile health issues." (PX0352 (Goldstein, Dep. at 133)).

1969. Complaint Counsel's erectile health expert, Dr. Arnold Melman, recognizes that Dr. Ignarro is highly respected. (Melman, Tr. 1167).

1970. Dr. Melman also agrees that UCLA School of Medicine, where Dr. Ignarro is a professor in molecular and medical pharmacology, has a good reputation. (Melman, Tr. 1168; PX0058; Goldstein, Tr. 2593-94).

(b) Clinical Trial

(1) Dr. Padma-Nathan's Study is Clinically Significant in That it Suggests a Likely Beneficial Effect of Pomegranate Juice on Erectile Tissue Physiology and Health and Supports the Conclusion That The Positive Results in The Basic Science Are Borne Out in Human Function

1971. Dr. Padma Nathan received the first fellowship from the American Foundation for Urologic Disease that was awarded in the area of erectile dysfunction. The prestigious fellowship is awarded to two urologists annually. His work involved two years of basic lab and in vitro scientific research in smooth muscle pharmacology cosponsored by the Department of Urology and the Department of Cardiology at Boston University. (CX1338 (Padma-Nathan, Dep. at 32-33)).

1972. Dr. Padma-Nathan is a man of repute in the field of urology. (Heber, Tr. 2000).

1973. Dr. Padma-Nathan and colleagues performed a randomized, double-blind, placebo-controlled cross-over design trial of Wonderful variety pomegranate juice versus placebo. (PX0189-0012-0013; CX0908; Goldstein, Tr. 2598).

1974. The study, entitled *Efficacy and safety of pomegranate juice on improvement of erectile dysfunction in male patients with mild to moderate erectile dysfunction: A randomized, placebo-controlled, double-blind, crossover study*, was published in the International Journal of Impotence Research in 2007, a very reputable journal. (Hereinafter referred to as the "*Forest/Padma-Nathan RCT Study*"). (PX0189-0012-0013; CX0908; CX1337 (Forest, Dep. at 225)).

1975. Dr. Goldstein, Respondent's expert, indicated that as editor in chief of the International Journal of Impotence Research, the *Forest/Padma-Nathan RCT Study* "is the first and only nutraceutical clinical trial that is randomized and double-blind that [he has] ever come across in [the] field." (Goldstein, Tr. 2598).

1976. The *Forest/Padma-Nathan RCT Study* engaged 53 completed subjects with mild-to-moderate erectile dysfunction who underwent two four-week treatment periods separated by a two-week washout. (PX0189-0012-0013; CX0908).

1977. The *Forest/Padma-Nathan RCT Study* had all the same scientific rigors of any study, including drug studies. (CX1337 (Forest, Dep. at 220-221); CX1338 (Padma-Nathan, Dep. at 195-197)).

1978. Such a scientifically rigorous study is almost unheard of in the food industry. (CX1338 (Padma-Nathan, Dep. at 196); Goldstein, Tr. 2601-02, 2613-14)).

1979. A total of 42 subjects demonstrated improved Global Assessment Question (GAQ) scores, 25 after drinking pomegranate juice. (PX0189-0012-0013; CX0908).

1980. In the pomegranate juice–placebo sequence, 56% demonstrated improvement of GAQ score versus 33% in placebo. (PX0189-0012-0013; CX0908).

1981. In the placebo—pomegranate juice sequence, 38% versus 29% reported improvement in GAQ score. (PX0189-0012-0013; CX0908).

1982. The *Forest/Padma-Nathan RCT Study* achieved a probability value ("p-value") of 0.058 which was a hair above a statistical significance measure of 0.050. (PX0189-0012-0013; CX0908; Heber, Tr. 1978; Goldstein, Tr. 2598).

1983. This means the study had a 94%, rather than 95%, probability of being valid and not the result of chance. (Heber, Tr. 1978; Goldstein, Tr. 2599; Burnett, Tr. 2305).

1984. Dr. Goldstein testified that choosing a significance level is technically an arbitrary task, and although a p-value of 0.050 was agreed upon in the *Forest/Padma-Nathan RCT Study*, "in specific situations a different value could be utilized." (Goldstein, Tr. 2598-99).

1985. Overall, the GAQ scores demonstrated that pomegranate juice drinkers enjoyed a nearly 50% better improvement in erections over placebo drinkers. (CX0908-0003; PX0352 (Goldstein, Dep. at 109, 144); CX1338 (Padma-Nathan, Dep. at 191-192)).

1986. Although the p-value was a few thousandths of a percentage point shy of an arbitrary 95% threshold, the study has major clinical significance in showing a benefit from pomegranate juice on erectile tissue physiology and health, and supporting the conclusion that the positive results in the basic science are borne out in human function. (PX0189-0013; PX0149-0006; CX0908; Heber, Tr. 1979, 2001; Goldstein, Tr. 2598-99; PX0352 (Goldstein, Dep. at 108-109); Burnett, Tr. 2256; PX0349 (Burnett, Dep. at 138-139); CX1350 (Liker, Dep. at 190-191)).

1987. The *Forest/Padma-Nathan RCT Study* also demonstrates pomegranate juice is "a potential treatment for ED." (PX0349 (Burnett, Dep. at 142)).

(c) Testing On The Mechanisms Of Action Generally

1988. In addition to studies specifically evaluating the Challenged Products, a significant body of scientific literature supports the validity of the mechanisms of action by which pomegranate juice promotes erectile function. (PX0352 (Goldstein, Dep. at 100-101)).

1989. Clinical trials demonstrate that the Mediterranean Diet, with which pomegranate juice consumption is consistent, promotes healthy erectile function. (PX0189-0013; PX0190).

1990. For example, Dr. Esposito's study entitled "Dietary Factors, Mediterranean Diet and Erectile Dysfunction" showed that the adoption of the Mediterranean diet for two years by obese men with erectile dysfunction had statistically significant improvement in their erectile dysfunction score compared to men in the control group. (PX0190; Goldstein, Tr. 2641-42; PX0352 (Goldstein, Dep. at 134-135); PX0189-0013).

1991. Significant scientific evidence and published studies also exists to support the general proposition that antioxidants "have the ability to improve the erectile function of those people that take the antioxidant." (Goldstein, Tr. 2604-2605; PX0352 (Goldstein, Dep. at 100-104)). Some of that evidence includes the following studies:

- Javier Angulo, PhD, et al., *The novel antioxidant, AC3056 (2,6-di-t-butyl-4-((Dimethyl-4-Methoxyphenylsilyl)Methyloxy)Phenol), reverses erectile dysfunction in diabetic rats and improves NO-mediated responses in penile tissue from diabetic men*, J. Sex. Med. (2009); 6:373-387. (PX0352 (Goldstein, Dep. at 100));

- Alessandra Barassi, MD, *et al.*, *Oxidative stress and antioxidant status in patients with erectile dysfunction*, J. Sex. Med. (2009); 6:2820-2825. (PX0352 (Goldstein, Dep. at 100));

- Sekar Suresh, PhD, *et al.*, *Effect of mucuna pruriens (Linn.) on oxidative stress-induced structural alteration of corpus cavernosum in streptozotocin-induced diabetic rat*, J. Sex. Med. (PX0352 (Goldstein, Dep. at 100-101));

- Rita C. Tostes, PhD, *et al.*, *Cigarette smoking and erectile dysfunction: focus on NO bioavailability and ROS generation*, J. Sex. Med. (2008); 5:1284-1295. (PX0352 (Goldstein, Dep. at 101));

- Enzo Vicari, MD, *et al.*, *Endothelial antioxidant administration ameliorates the erectile response to PDE5 regardless of the extension of the atherosclerotic process*, J. Sex. Med. (2010); 7:1247-1253. (PX0352 (Goldstein, Dep. at 81-82, 100)).

E. Tools For Evaluating Erectile Function

1. The GAQ

1992. The global assessment questionnaire ("GAQ") is a single question designed to assess the individual self-evaluation of the study treatment (e.g., pomegranate juice consumption versus placebo consumption) effect on the patient's sexual health concern. (PX0189-0009).

1993. The GAQ is a yes/no question. (Goldstein, Tr. 2603).

1994. The GAQ is a very easy evaluation and written for a high school educated person to understand. (Goldstein, Tr. 2603; CX1337 (Forest, Dep. at 151-152)).

1995. The GAQ is informative. (Burnett, Tr. 2294; PX0349 (Burnett, Dep. at 131-132)).

1996. The GAQ is widely used. (Goldstein, Tr. 2602, 2603; Burnett, Tr. 2304; PX0349 (Burnett, Dep. at 127)).

1997. The GAQ is valuable to use in clinical studies. (Burnett, Tr. 2294).

1998. The GAQ is commonly accepted as a standardized instrument among those conducting erectile dysfunction research. (CX1337 (Forest, Dep. at 79)).

1999. The GAQ is used on all sexual medicine trials. (Goldstein, Tr. 2603; PX0352 (Goldstein, Dep. at 57)).

2000. The GAQ was used by Pfizer in testing sildenafil (Viagra). (Burnett, Tr. 2304; Goldstein, Tr. 2602).

2001. The GAQ was also used in every vardenafil (Levitra) and tadalafil (Cialis) trial. (Goldstein, Tr. 2602; PX0352 (Goldstein, Dep. at 57)).

2002. The GAQ is a very "acceptable," informative," and "valuable" tool to use for testing pomegranate juice. (Burnett, Tr. 2294, 2304).

2. The IIEF

2003. The International Index of Erectile Function ("IIEF") is a 15 question psychometrically validated instrument designed to assess a man's overall erectile and sexual function via the individual domains of erectile function, orgasmic function, sexual desire, intercourse satisfaction and overall satisfaction. (PX0189-0009).

2004. Although validated, the IIEF also has its deficiencies as it requires patient recall and involves patients' subjective interpretation of their erection physiology. (Burnett, Tr. 2294).

2005. The IIEF was designed for evaluating pharmaceuticals, not natural botanical products. (Goldstein, Tr. 2604).

2006. The erectile function domain relates only to erectile performance and does not evaluate orgasm or ejaculation. (Goldstein, Tr. 2604).

F. Respondents' Experts Confirm That Respondents' Substantiation Constitutes Competent and Reliable Scientific Evidence

1. Qualifications of Respondents Proffered Experts

(a) Arthur L. Burnett, M.D.

2007. Dr. Burnett is a Doctor of Medicine and obtained his medical degree in 1988 from the Johns Hopkins University School of Medicine in Baltimore, Maryland. (PX0149-0001).

2008. From 1988 to 1993, he completed an internship in general surgery and residencies in general surgery and urology at the Johns Hopkins Hospital. From 1993 to 1996, he completed fellowships in urology and reconstructive urology & urodynamics also at the Johns Hopkins Hospital. (PX0149-0001; Burnett, Tr. 2240-41).

2009. Dr. Burnett completed a master's degree in business administration with a concentration in medical services management in 2009 from the Johns Hopkins University Carey Business School. (PX0149-0001).

2010. Dr. Burnett is board certified in urology and is a practicing urological surgeon specializing in sexual medicine, major pelvic reconstruction, voiding dysfunction, female urology, and prostate cancer. (PX0149-0001).

2011. He has treated between 10,000 and 15,000 patients for erectile dysfunction ("ED"). (Burnett, Tr. 2244).

2012. Dr. Burnett is also the Patrick C. Walsh Professor of Urology within the faculty of the Department of Urology at the Johns Hopkins University School of Medicine/Johns Hopkins Hospital in Baltimore, Maryland. (PX0149-0001; Burnett, Tr. 2241; PX0349 (Burnett, Dep. at 19)).

2013. Dr. Burnett also holds a faculty appointment in the Cellular and Molecular Medicine Training Program of the Johns Hopkins University School of Medicine. (PX0149-0001; PX0349 (Burnett, Dep. at 20)).

2014. Dr. Burnett also is the Director of the Basic Science Laboratory in Neuro-urology of the James Buchanan Brady Urological Institute and Director of the Male Consultation Clinic/Sexual Medicine Division of the Department of Urology at Johns Hopkins. (PX0149-0001; Burnett, Tr. 2241; PX0349 (Burnett, Dep. at 19)).

2015. Dr. Burnett has had a number of visiting professorships in urology nationally and internationally. (Burnett, Tr. 2241-42).

2016. Dr. Burnett has served in many journal editorial capacities including as an Assistant Editor of The Journal of Urology; Co-Editor-in-Chief of The Journal of Andrology; Reviews and Associate Editor of The Journal of Sexual Medicine, and Administrative Editor of Practical Reviews in Urology. (PX0149-0002-0003; Burnett, Tr. 2242).

2017. Dr. Burnett has authored and published over 180 original peer-reviewed articles and 40 book chapters, along with numerous editorials, books and reviews relating

to his biomedical research and clinical activities. His work has appeared in many prominent journals, including *Science, Nature Medicine, Proceedings of the National Academy of Sciences, The Journal of Urology, Urology, The Journal of Andrology, and The Journal of Sexual Medicine*. (PX0149-0003; Burnett, Tr. 2243).

2018. Dr. Burnett has received multiple investigator-initiated research awards at federal, foundation sponsored and industry-related levels. (PX0149-0003). He has continuously been funded by the National Institutes of Health since 1998 holding project titles such as "Nitric Oxide Regulatory System in the Penis" and "Endothelial Nitric Oxide Synthase Regulatory Mechanisms in Penile Vascular Function", which have enabled his research group to advance the science of erection disorders related to nitric oxide biology. (PX0149-0003; Burnett, Tr. 2243).

2019. Dr. Burnett's research on nitric oxide ("NO") is world renowned. (PX0149-0003).

2020. Dr. Burnett's lab was instrumental in describing NO as a physiologic mediator of penile erection and the mechanism of NO-dependent penile erection. (PX0149-0005; PX0349 (Burnett, Dep. at 89)). Their research work established neuronal NO as the physiologic initiator of penile erection and further clarified the molecular mechanisms involved in neurogenic stimulation of the erectile response. (PX0149-0005).

2021. Dr. Burnett's lab further described blood flow endothelial NO-dependent forces in the penis, which promote and sustain the erectile response, and described the new science of penile erections involving combined roles of neuronal and endothelial NO mechanisms. (PX0149-0005).

2022. Dr. Burnett's lab also refined the understanding of PDE5 (type 5 phosphodiesterases) function in the penis, which varies with different medical conditions (diabetes, cardiovascular diseases, aging, cigarette smoking, sickle cell disease) and accordingly accounts in varying ways for erectile dysfunction problems. (PX0149-0005; PX0349 (Burnett, Dep. at 89)).

2023. Dr. Burnett's lab also contributed research work that has clarified the interaction between NO and other major opposing regulatory mediators of penile erection including agents that cause penile vasoconstriction (anti-erectile mediators) and oxidative stress factors (reactive oxygen species/molecules that cause tissue damage). (PX0149-0005).

2024. Complaint Counsel's purported erectile health expert, Dr. Melman, recognizes "[t]hat Dr. Burnett of Johns Hopkins is a man highly respected in his field." (Melman, Tr. 1166).

(b) Irwin Goldstein, M.D.

2025. Dr. Goldstein is a sexual medicine physician and has been practicing medicine since 1976. (PX0189-0001; PX0352 (Goldstein, Dep. at 14)).

2026. Dr. Goldstein has been involved in sexual medicine clinical practice, clinical research and basic science research since 1980. (PX0189-0002).

2027. Dr. Goldstein obtained his medical degree in 1975 from McGill University in Montreal, Quebec, Canada. (PX0149-0001).

2028. From 1975-1976, Dr. Goldstein completed an internship at the Royal Victoria Hospital in Montreal, Canada. (PX0149-0001).

2029. From 1976-1977, Dr. Goldstein completed a first year surgical residency at the Boston University School of Medicine at University Hospital in Boston. (PX0149-0001).

2030. From 1977-1980, Dr. Goldstein completed a urology residency at the Boston University School of Medicine at University Hospital in Boston. (PX0149-0001).

2031. From 1981-1984, Dr. Goldstein completed a Urology Fellowship and was awarded the Clinical Investigator Award from the NIAMDDK which allowed him to do research in the field of sexual medicine. (PX0189-0001; Goldstein, Tr. 2588-89).

2032. Dr. Goldstein has been certified by the American Board of Urology since 1982. (PX0189-0001).

2033. Dr. Goldstein was Professor of Urology and Professor of Gynecology at the Boston University School of Medicine from 1990-2005 and 2002-2005, respectively. (PX0189-0001).

2034. Dr. Goldstein was the Director/Co-Director of the Laboratory for Sexual Medicine Research at the Boston University School of Medicine from 1981-2005. (PX0189-0002).

2035. From 2002-2005, Dr. Goldstein also served as Director of the Institute for Sexual Medicine at the Boston University School of Medicine. (PX0189-0001).

2036. Since 2007, Dr. Goldstein has served as the Director of San Diego Sexual Medicine, APC and as the Director of Sexual Medicine at Alvarado Hospital, San Diego, California. (PX0189-0001; PX0352 (Goldstein, Dep. at 11)).

2037. Dr. Goldstein also serves as Clinical Professor of Surgery, University of California, San Diego, and has held this position since 2007. (PX0189-0001; PX0352 (Goldstein, Dep. at 11)).

2038. In his clinical practice, Dr. Goldstein manages male and female patients with varying types of sexual health complaints, including numerous male patients who have had normal erectile function and desired enhanced sexual performance due to issues of sexual confidence, erection quality and better sexual performance, and also numerous men with erectile dysfunction who have had limited responses to traditional first-line therapies such as phosphodiesterase type 5 inhibitors ("PDE5 inhibitors" or "PDE5i"s), including Viagra, and who do not wish to consider invasive or mechanical treatments for their erectile health complaint. (PX0189-0001-0002; PX0352 (Goldstein, Dep. at 13)).

2039. Dr. Goldstein also established the first sexual medicine clinic in a Veterans Administration Hospital in the United States. (Goldstein, Tr. 2591).

2040. Dr. Goldstein is currently a member of, and has been involved in, numerous sexual medicine societies including serving as Board Member and Editor-in-Chief of The Journal of Sexual Medicine since 2004, and serving as Editor-in-Chief of The International Journal of Impotence Research from 2002-2003. (PX0189-0002).

2041. Dr. Goldstein was part of the original advisory board to Pfizer that engaged in a very extensive drug development plan that developed sildenafil (Viagra). (Goldstein, Tr. 2590-91).

2042. Dr. Goldstein was also on the advisory boards of Bayer and Eli Lilly for the development of vardenafil (Levitra) and tadalafil (Cialis), respectively. (Goldstein, Tr. 2591).

2043. For 25 consecutive years, Dr. Goldstein has received funding from the NIH to study physiology of erectile function and pathophysiology of erectile dysfunction. (Goldstein, Tr. 2591-92).

2044. Dr. Goldstein has published over 250 original peer-reviewed manuscripts in male and female sexual medicine. (PX0189-0002-0003).

2045. Complaint Counsel's designated erectile-health expert, Dr. Melman, also recognizes Dr. Goldstein as "highly regarded" in the field. (Melman, Tr. 1166-67).

2046. In addition to the publications attached to Exhibit 3 of Drs. Goldstein and Burnett's expert reports upon which they relied upon, both experts have also extensively relied upon their education, years of experience and knowledge of developments in the field of urology and sexual medicine, including the promotion

of erectile heath and treatment of erectile dysfunction. (PX0149-0004; PX0349 (Burnett, Dep. at 21-22); PX0189-0005; PX0352 (Goldstein, Dep. at 10)).

2. Opinions

(a) Erectile Health and Erectile Dysfunction

2047. Erectile health is having a healthy erectile mechanism. (PX0189-0008).

2048. Erectile health is promoted when the male practices strategies that encourage endothelial health. (PX0352 (Goldstein, Dep. at 148); PX0189-0008).

2049. Erectile health is distinguished from erectile dysfunction. (PX0189-0008).

2050. Erectile dysfunction, which has a clinical connotation, is very different from the concept of something that has a potential beneficial effect on erectile tissue function and health. (Burnett, Tr. 2256-57).

2051. Erectile dysfunction is the consistent or persistent inability to obtain and/or sustain an erection adequate for sexual intercourse. (PX0189-0008-0009).

2052. Erectile dysfunction has been estimated to affect up to 30 million men in the United States. (PX0189-0008-0009).

2053. The most common cause of erectile dysfunction is cardiovascular disease. (PX0189-0009).

2054. "Subjects with ED seem to have a vascular mechanism similar to that seen in atherosclerosis [] and therefore, a diagnosis of ED may be seen as a sentinel event that should prompt investigation for coronary heart disease (CHD) in asymptomatic men." (PX0190-0002).

2055. Cardiovascular disease is strongly associated with endothelial cell dysfunction. (PX0189-0009).

2056. Endothelial cell dysfunction may act to adversely affect the structure and function of the critical arterial inflow mechanism, the critical expandability of the erectile tissue and the critical integrity of the veno-occlusive mechanism. (PX0189-0009).

2057. Risk factors for cardiovascular disease, erectile dysfunction and endothelial dysfunction are shared and include such concerns as hypertension, diabetes, hypercholesterolemia, obesity, aging, and metabolic syndrome. (PX0189-0008).

2058. Health care providers may recommend to a patient with a sexual health concern prophylactic strategies that encourage the long-term health of the erectile mechanism. (PX0189-0008).

2059. The erectile mechanism is largely dependent on the health, integrity, structure and function of the arterial vascular and corporal erectile tissue systems. (PX0189-0008).

2060. Erectile health is promoted, in particular, when the man practices strategies that encourage endothelial health, such as exercise, use of the Mediterranean diet, and use of endothelial-healthy medications (such as aspirin, statins, and PDE5-inhibitors). (PX0189-0008; PX0190).

(b) Physiology of Human Penile Erection

2061. The penis consists of two corpora cavernosa or erectile chambers and a corpus spongiosum or erectile tissue surrounding the urethra. The corpora cavernosa erectile tissue are contained by a thick and strong fibrous lining called the tunica albuginea that stretches to some extent during penile erection but also acts as a container to provide axial rigidity to the erect penis. (PX0189-0006; Burnett, Tr. 2245).

2062. The erectile tissue includes numerous interconnecting lacunar spaces that fill with blood during erection, and are lined by vascular endothelial cells. The lacunar spaces are surrounded by vascular smooth muscle and connective tissue such as collagen and elastin. (PX0189-0006).

2063. Arterial blood enters the corpora cavernosa via the right and left cavernosal arteries. There are numerous small regulatory arteries off the cavernosal artery called helicine arterioles that open into the lacunar spaces. At the peripheral edge of the erectile tissue, underneath the tunica albuginea, there are small veins called sub-tunical venules that drain blood from the peripheral lacunar spaces through the tunica into draining veins at the side of the penis to eventually return blood back to the heart. (PX0189-0006; Burnett, Tr. 2245-46).

2064. In the flaccid state, smooth muscle in the helicine arterioles and surrounding the lacunar spaces are contracted allowing only small amounts of blood to enter the erectile chambers. Relaxation of the vascular smooth muscle of the corpora cavernosa leads to penile erection. Dilation of the helicine arterioles increases perfusion of high pressure arterial blood into the lacunar spaces. Relaxation of the smooth muscle surrounding the lacunar spaces results in engorgement of the erectile tissue and expansion of the erectile tissue against the tunca albuginea. This erectile tissue expansion results in compression of the sub-tunical venules that restricts blood outflow from the corporal erectile chambers. This venous trapping mechanism is the corporal veno-occlusive mechanism. Due to the hydraulic nature of increasing blood inflow and perfusion pressure and restricting blood outflow, there is an increase in intracavernosal pressure to a value approximating the mean systemic arterial blood pressure. The containment of

pressure within the tunica albuginea leads to axial rigidity and penile hardness that enables functional penile penetration. (PX0189-0006-0007; Burnett, Tr. 2246-48).

(c) The Role of Nitric Oxide In Human Penile Erection

2065. Nitric oxide ("NO") was proclaimed "molecule of the year". (Heber, Tr. 1970).

2066. NO has a beneficial effect on blood flow. (Heber, Tr. 1969, 2140; Burnett, Tr. 2250).

2067. Blood vessels and the flow of blood to the penis are important to erectile function. (Melman, Tr. 1169).

2068. NO is "known to be of paramount importance in the maintenance of good erectile function" and is the key molecule that governs penile erection. (PX0149-0004; Burnett, Tr. 2249-50, 2276; PX0190-0006).

2069. Complaint Counsel's own erectile expert, Dr. Melman, testified that NO employs a critical role in the erectile process. (Melman, Tr. 1169).

2070. The physiologic mechanism of penile erection involves release of NO in the corpus cavernsosum during sexual stimulation. (PX0149-0004-0005; PX0189-0007).

2071. The NO is released from shear stress off the endothelial cells in the lacunar spaces within the corpora cavernosa and from autonomic nerves that innervate the erectile tissue and are activated during sexual stimulation. (PX0189-0007; Burnett, Tr. 2248-49; PX0349 (Burnett, Dep. at 88-90)).

2072. Upon its synthesis and release from their cellular sources, NO diffuses to neighboring vascular and trabecular smooth muscle cells lining the lacunar spaces. (PX0149-0004-0005; PX0189-0007; PX0349 (Burnett, Dep. at 87-90)).

2073. The NO activates the enzyme guanylate cyclase within the vascular smooth muscle cells that results in increased levels of cyclic guanosine monophosphate (cGMP), an effector of smooth muscle relaxation via protein kinase G (PKG) actions. (PX0149-0004-0005; PX0189-0007; PX0349 (Burnett, Dep. at 87-90)).

2074. NO, cGMP and PKG mediates the relaxation of the cavernous smooth muscle and vasodilation of blood vessels. (PX0149-0004; PX0189-0007).

2075. Persistent smooth muscle relaxation leads to tissue engorgement within the corpora cavernosa and penile erection. (PX0189-0007).

2076. Cyclic guanosine monophosphate is hydrolyzed by the phosphodiesterases, predominantly type 5 ("PDE5"), to inactive 5'-GMP, terminating penile erection. (PX0149-0004-0005; PX0349 (Burnett, Dep. at 92-93)).

2077. PDE5 inhibitors such as sildenafil (Viagra), vardenafil (Levitra) and tadalafil (Cialis) inhibit PDE5, thereby augmenting cGMP levels. (PX0149-0004-0005; PX0349 (Burnett, Dep. at 93)).

2078. Endothelial nitric oxide function is fundamental to the vascular process. (Burnett, Tr. 2290).

2079. The vascular function of vessels in various parts of the body behave similarly. (Burnett, Tr. 2290).

(d) Pomegranate Juice Enhances The Production and Preservation of Nitric Oxide

2080. Oxidative stress molecules in the body, which are produced by various kinds of conditions of inflammatory change, disease states, etc., have deleterious effects throughout the body in the vasculature and in the penis that actually counter-effect the body's nitric oxide regulatory mechanism, not just for transient effects to bring about erection, but also to maintain the wellness of the erectile tissue. (PX0349 (Burnett, Dep. at 90); Burnett, Tr. 2251; Goldstein, Tr. 2604-05; PX0190-0006).

2081. Antioxidants are well known to enhance the biological actions of NO by virtue of their capacity to stabilize NO by protecting against the oxidative destruction of NO by oxidative stress molecules. (PX0056-0002; PX0059-0001,0004; PX0190-0006; PX0149 at ¶ 14; PX0189 at ¶¶ 13, 14; Goldstein, Tr. 2604-2605).

2082. This antioxidant effect results in much higher and more prolonged cellular concentrations of NO, leading to markedly increased biological actions of NO. (PX0056-0002; PX0059-0001, 0004; PX0149-0005-0006).

2083. Pomegranate juice possesses potent flavonoid antioxidants. (PX0149-0005-0006; Burnett, Tr. 2250-51; PX0189-0011; PX0056; PX0058; PX0051; PX0004).

2084. Dr. Aviram concluded that based on his medical research, pomegranate juice had greater antioxidant potencies than red wine, which he believed, at the time, possessed the most potent antioxidant. (CX1358 (Aviram, Dep. at 5-6)).

2085. Based on his studies, Dr. Aviram represented to Stewart Resnick that the antioxidant properties found in the pomegranate were the most powerful he had ever researched. (CX1363 (S. Resnick, Coke Dep. at 57, 66)).

2086. Dr. Louis Ignarro, a Nobel Prize winner for his work on nitric oxide, and who published an article in the New England Journal describing nitric oxide as the neurotransmitter of penile erection, also found that pomegranate juice possesses more antioxidant activity than grape juice, blueberry juice, red wine and ascorbic acid. (PX0189-0011; Goldstein, Tr. 2594-95).

2087. Not surprisingly, Dr. Ignarro found that pomegranate juice was around 5,000 times more potent than the other antioxidants he has tested. (Heber, Tr. 1967).

2088. Dr. Ignarro, has tested pomegranate juice for its capacity to protect nitric oxide against oxidative destruction. (PX0189-0011; Burnett, Tr. 2253; PX0058).

2089. After a series of studies, Dr. Ignarro concluded that pomegranate juice possesses potent antioxidant activity that results in marked protection of nitric oxide against oxidative destruction thereby augmenting the biologic actions of nitric oxide. (Burnett, Tr. 2256; PX0058).

2090. Pomegranate juice enhances the production of endothelial nitric oxide formation by suppressing the oxidative stress molecules that oppose the endothelial nitric oxide synthase function. (PX0149-0005-0006; PX0349 (Burnett, Dep. at 103, 119); Burnett, Tr. 2251-54).

2091. Based on his research, Dr. Ignarro concluded that "pomegranate juice was 20 times better than any other fruit juice at increasing nitric oxide." (PX484; Burnett, Tr. 2254-55; PX0484).

2092. As a result of these findings, Dr. Ignarro told Respondents that – "It's astonishing – I've been working in this field for 20 years and I have never seen anything like it. I drink it 3 times a day without fail." (PX0484).

2093. Pomegranate juice's anti-oxidative molecular effects activate endothelial nitric oxide mechanisms in vasculature which serve potential beneficial effects on vascular blood flow and promote vascular biologic health of the penis. (PX0149-0005-0006).

(e) Pomegranate Juice Promotes Erectile Health and Function

2094. Antioxidants play a potential role in preserving erectile tissue health. (Burnett, Tr. 2285-86; Goldstein, Tr. 2604-05).

2095. Antioxidants also play a potential role in promoting one's likelihood of preserving their erection function. (Burnett, Tr. 2285-86; Goldstein, Tr. 2604-05; PX0190-0006).

2096. The mechanism by which consuming pomegranate juice promotes erectile health may be shown through the data that pomegranate juice possesses antioxidant properties, antioxidants help maintain endothelial health, endothelial health is strongly associated with erectile health, and therefore, pomegranate juice helps to maintain erectile health. (PX0189-0003, 0008-0009; PX0190-0006).

2097. The competent and reliable scientific evidence demonstrates that pomegranate juice provides a benefit to erectile health and erectile function. (Goldstein, Tr. 2605; PX0189-0014; PX0149-0006; Burnett, Tr. 2255-56; PX0349 (Burnett, Dep. at 103, 116-118, 137); Heber, Tr. 2012).

2098. Dr. Goldstein concluded "that competent and reliable scientific evidence exists upon which clinicians who treat men with erectile health concerns would rely in concluding that pomegranate juice promotes erectile health." (PX0189-0014).

2099. Dr. Goldstein also testified that "without a question" there is competent and reliable science showing that pomegranate juice provides a benefit to erectile function. (Goldstein, Tr. 2605).

2100. Dr. Burnett concluded "that the basic scientific and clinical evidence is sufficient to support the use of pomegranate juice as a potential benefit for vascular blood flow and the vascular health of the penis. (PX0149-0006).

2101. Dr. Burnett also testified that based on POM's *in vitro* and *in vivo* studies and *Forest/Padma-Nathan RCT Study*, pomegranate juice has a likely beneficial effect on erectile function. (Burnett, Tr. 2255-56).

2102. Moreover, Dr. Burnett testified that that he thinks "there's good basic science support that pomegranate juice is a very effective agent . . . in vascular function." (PX0349 (Burnett, Dep. at 103, 116-118).

2103. Dr. Burnett further testified that the basic science only "support[s] the potential benefit at the human level to [sic] improve the physiology of erectile tissue preserving erect tissue health." (PX0349 (Burnett, Dep. at 103, 116-118).

2104. Dr. Burnett testified that he thinks "work from animal studies do [sic] have some potential for benefit of a therapy at the human level." (PX0349 (Burnett, Dep. at 112).

2105. Dr. Burnett further testified that the basic science only "support[s] the potential benefit at the human level to [sic] improve the physiology of erectile tissue preserving erect tissue health." (PX0349 (Burnett, Dep. at 103, 116-118).

2106. Dr. Burnett testified that the in vitro and in vivo studies alone "provide powerful support for pomegranate juice, extracts and related sort of agents here and

pomegranate effects here as antioxidants; that they work with very potent effects on the nitric oxide regulatory mechanism; that there's evidence that they do demonstrate antioxidant effects on genes that have to do with the oxidative stress mechanisms and the nitric oxide release mechanisms; that there is evidence that these agents do reduce some of the pathophysiologic effects at the tissue level including structural changes on the tissue in terms of atherosclerosis, that is, hardening of vessels that leads to the functional changes where the tissue is not able to properly relax and is consistent with how the blood vessels have to dilate and allow blood flow to occur within target organs." (PX0349 (Burnett, Dep. at 116).

2107. Dr. Heber testified that there is competent and reliable science showing that pomegranate juice and its derivative are likely to lessen the risk of erectile disease and enhance erectile function. (Heber, Tr. 2012).

2108. Dr. Liker, in his deposition, stated that he, Dr. Padma-Nathan and Forest concluded that the *Forest/Padma-Nathan RCT Study* showed a clinically significant benefit to erectile health. (CX1350 (Liker, Dep. at 190-191)).

2109. The *Forest/Padma-Nathan RCT Study* has major clinical significance in showing a benefit from pomegranate juice on erectile tissue physiology and health, and also supports the conclusion that the positive results in the basic science are borne out in human function. (PX0189-0013; PX0149-0006; CX0908; Heber, Tr. 1979, 2001; Goldstein, Tr. 2598-99; PX0352 (Goldstein, Dep. at 108-109); Burnett, Tr. 2256; PX0349 (Burnett, Dep. at 138-139)).

2110. Dr. Goldstein opined that he would recommend pomegranate juice as a management tool to promote erectile health in men who are aware that their erectile function is declining but who do not yet meet the clinical definition of ED under the IIEF and therefore do not qualify for pharmacologic treatment. (PX0189-0014-0015; PX0352 (Goldstein, Dep. at 42-45); Goldstein, Tr. 2609).

2111. The validity of the existence of this subpopulation is corroborated by the existence of a robust market for the recreational use of PDE5 inhibitors like Viagra. (PX0189-0014; PX0352 (Goldstein, Dep. at 43-44)).

2112. Dr. Goldstein also testified that men who have been diagnosed with clinical ED but who have an insufficient response to PDE5 inhibitors (like Viagra) and who are unwilling to consider invasive or mechanical therapies (such as injecting needles into the penis, inserting urethral suppositories, using vacuum pumps, or having surgically implanted prostheses), the suggestion to utilize the Mediterranean diet, which the pomegranate fruit is part of, to improve endothelial function and erectile health, is logical and rational given the risk-benefit ratio.

(PX0189-0004-0005, 0014-0015; PX0352 (Goldstein, Dep. at 37-42); Goldstein, Tr. 2605, 2641; PX0190-0006-0007).

2113. Improving ones erectile function may also help improving ones erectile dysfunction. (Burnett, Tr. 2303).

2114. The *Forest/Padma-Nathan RCT Study* demonstrates pomegranate juice is "a potential treatment for ED." (PX0349 (Burnett, Dep. at 137-139, 142)).

2115. Dr. Heber has testified that "[t]he body of research on pomegranate juice and extract revealing how they react on the body provides support for potential health benefits for erectile dysfunction." (CX2007 (Heber, Dep. at 85)).

2116. Nobel Laureate Louis Ignarro indicated that he strongly believed pomegranate juice was 40% as effective as Viagra in helping with erectile dysfunction. (CX1363 (S. Resnick, Coke Dep. at 77-78); CX1372 (S. Resnick, Tropicana Dep. at 44)).

2117. Inside Integrative Medicine, a newsletter published by University of Texas MD Anderson Cancer Center, published an article entitled the "Anticancer Effects of Pomegranate" which provided that "early research also suggests that pomegranate may be beneficial as a treatment for erectile dysfunction . . . ." (MD Cancer Center, Inside Integrative Medicine (February/March 2010), available at http://www.mdanderson.org/publications/inside-integrative-medicine/issues/issue-15-febmarch2-010.pdf. (last visited Jan. 3, 2012)).

2118. On the website of Memorial Sloan-Kettering Cancer Center in New York, information about the pomegranate is included on their Cancer Care Integrative Medicine web page which provides a clinical summary of the pomegranate, stating that pomegranate juice was "found to benefit patients with carotid artery stenosis, in those with hypertension, hyperlipdemia, mild to moderate erectile dysfunction." (Memorial Sloan-Kettering Cancer Center, Pomegranate, available at http://www.mskcc.org/cancer-care/herb/pomegranate. (last visited Jan. 3, 2012)).

(f) Pomegranate Juice Reduces the Risk of ED in Some Population of Men

2119. Dr. Goldstein testified that reasonable and competent science shows that pomegranate juice reduces the risk of, or ameliorates erectile dysfunction in men caused by endothelial dysfunction or blood flow impairment or oxidative stress. (Goldstein, Tr. 2605).

(g) Substantiation Standard

2120. Pomegranate juice is a natural fruit with health promoting characteristics, and documented for over 5,000 years, and as a result, urologist would not require RCTs for its safety. (PX0189-0003; Goldstein, Tr. 2601-02, 2611, 2620; Miller, Tr. 2194, 2201; PX0206-0010; Heber, Tr. at 1948-1950, 2056, 2166; PX0149-0006-0007; (Burnett, Tr. 2272-2274, 2303); PX0189-0003; Goldstein, Tr. 2600-02, 2611, 2620); deKernion, Tr. 3060; PX0025-0007).

2121. Moreover, urologist would not require RCTs to substantiate health benefit claims for harmless pure fruit products like pomegranate juice. (PX0149-0006-0007; (Burnett, Tr. 2272, 2303); PX0189-0003; Goldstein, Tr. 2600-02, 2611, 2620).

2122. Urologists who treat men with erectile health concerns would not require that pomegranate juice or its derivatives be subjected to RCTs before concluding that pomegranate juice has a beneficial effect on preserving erectile function. (PX0149-0006-0007; Burnett, Tr. 2272-74, 2303; PX0189-0003; Goldstein, Tr. 2600-02, 2611, 2620).

2123. Urologists who treat men with erectile health concerns would not require that pomegranate juice or derivatives be subjected to RCTs before concluding that pomegranate juice has a beneficial effect on erectile dysfunction. (Burnett, Tr. 2272-74, 2303).

2124. In the context of treating ED, "there may be a conclusion made that a therapy has a potential benefit in that treatment, even if it does not meet statistical significance." (Burnett, Tr. 2270).

2125. A clinical treatment for ED is different than the concept of something having a potential beneficial effect on erectile tissue function and health. (PX0349 (Burnett, Dep. at 56-57)).

(h) Information Of Pomegranate Juice's Potential Erectile Health Benefits May Be Communicated to Consumers

2126. A recommendation to consider using antioxidants to benefit one's erectile health does not have to be made exclusively by a clinician or physician. (Burnett, Tr. 2288).

2127. Because pomegranate juice creates no material risk of harm and assuming that drinking pomegranate juice is not advocated as an alternative to following medical advice, information of pomegranate juice's likely benefit may be communicated to consumers. (PX0149-0006-0007; PX0206-0010-0011).

2128. The *Forest/Padma-Nathan RCT Study*, which achieved a probability value of 0.058 still has 94% validity and therefore "is important information with likely benefits" that should be communicated to consumers. (Burnett, Tr. 2306).

2129. Dr. Burnett testified that "[a] product could be potentially clinically significant and not meet statistical significance and it still be informative and really valuable to know and worth communicating and potentially having a role for patients out there." (PX0349 (Burnett, Dep. at 67); PX0352 (Goldstein, Dep. at 108-109)).

2130. When talking about consuming pomegranate juice rather than clinical treatment for ED, it is not necessary for a study to reach statistical significance in order for the study to convey important information. (Burnett, Tr. 2305).

2131. Dr. Goldstein testified that the *Forest/Padma-Nathan RCT Study* although falling short of statistical significance was nonetheless "absolutely" clinically significant. (PX0352 (Goldstein, Dep. at 108); PX0189-0013).

2132. Dr. Goldstein indicated that the results showed that "there were 50 percent more people than the placebo who thought that there was erectile benefit from using this drug. And I will call that clinically significant in conjunction with the fact that there are no deaths, no priapisms, no heart attacks, no strokes, no flushing, no nasal congestion, none of the traditional side effects seen by PDE5 inhibitors. No need for stents, drug-eluting stints, no need for surgery. No need for penile prosthetic procedures." (PX0352 (Goldstein, Dep. at 109)).

2133. Dr. Burnett believes that the current scientific and clinical evidence about pomegranate juice's potential erectile health benefits "can be put out in the public domain." (PX0349 (Burnett, Dep. at 118, 137); PX0149-0006-0007)).

G. Complaint Counsel's Erectile Expert Offered Extreme Opinions That Are Insufficient to Undermine Respondents' Showing of Substantiation

1. Dr. Melman's Opinions Are Motivated by Bias

(a) Dr. Melman Is Currently Engaged In Developing His Own Erectile Dysfunction Product, Which He Hopes To Market And Make Money From, And That He Has Described As The "Fountain of Youth"

2134. Dr. Melman is the CEO and co-founder of Ion Channel Innovations, which is developing a gene-transfer therapy for erectile dysfunction called hMaxi-K. (Melman, Tr. 1148).

2135. Dr. Melman hopes to market hMaxi-K and make money from doing so. (Melman, Tr. 1153-54).

2136. Dr. Melman has 17 patents on his gene transfer therapy. (Melman, Tr. 1153).

2137. hMaxi-K is injected into the penis. (Melman, Tr. 1192).

2138. Dr. Melman convinced a patient of his, who was a school teacher, to invest one million dollars into Ion Channel Innovations. (Melman, Tr. 1159-60).

2139. Dr. Melman announced to the public, in an interview with the New York Observer, that his hMaxi-K produced spontaneous normal erections in men suffering from erectile dysfunction. (Melman, Tr. 1154).

2140. Dr. Melman also told the New York Observer reporter that the men who tried it became like they were young again. (Melman, Tr. 1154).

2141. Dr. Melman told the reporter that he was talking about "modifying the aging process." (Melman, Tr. 1155).

2142. Dr. Melman told the reporter that his product was the "the fountain of youth." (Melman, Tr. 1154 -55).

2143. Dr. Melman's public claim regarding his hMaxi-K product was based on an animal study. (Melman, Tr. 1155).

2144. There are severe health risks associated with gene-transfer therapy. (Melman, Tr. 1158).

2145. Dr. Melman acknowledged people have died and gotten very sick from gene-transfer therapy. (Melman, Tr. 1158).

2146. Dr. Melman admits that pomegranate juice is safe. (PX0360 (Melman, Dep. at 59, 130-131)).

2147. Nevertheless, Dr. Melman contends that "the standards . . . for substantiating a claim for fruit juice are the same as for substantiating a claim for gene transfer therapy." (Melman, Tr. 1148-49).

2148. Dr. Melman further testified that if a patient with ED was unresponsive to PDE5 inhibitors like Viagra and did not want to undergo invasive therapies, like penile injections (required by his competing hMaxi-K product), that he would still not recommend pomegranate juice and that he'd tell his patients to "stop having intercourse." (Melman, Tr. 1192-94; PX0360 (Melman, Dep. at 31)).

(b) **Dr. Melman Always Sides With the FTC**

2149. Dr. Melman has testified on behalf of the FTC on three or four prior occasions. (Melman, Tr. 1161).

2150. Dr. Melman always testified in favor of the FTC, i.e., that the respondent lacked adequate substantiation. (Melman, Tr. 1161).

2. Dr. Melman's Positions Are Extreme

(a) Dr. Melman's Position Regarding Claims That Help With Erectile Function Are Extreme

2151. Dr. Melman testified that the only kind of science to support claims to help erectile function are two double-blind placebo based randomized trials. (Melman, Tr. 1138-39).

2152. Dr. Melman also testified that there has to be a trial done in two separate institutions. (Melman, Tr. 1138-39).

2153. Dr. Melman testified there must also be a large group, and the two studies must reach statistical significance. (Melman, Tr. 1139).

2154. Dr. Melman testified that the trials must be held in multiple locations. (Melman, Tr. 1137-39).

2155. Dr. Melman testified that the men's sexual partners must also confirm the result. (Melman, Tr. 1139-40).

2156. Dr. Melman testified that for a study to claim any improvement in participants, the men must have reached orgasm. (Melman, Tr. 1141-43).

2157. Dr. Melman testified that for a study to claim any improvement in participants, the sexual partner must reach sexual satisfaction. (Melman, Tr. 1142-43).

2158. Dr. Melman testified that you cannot properly make public claims that a product helps with erectile function in absence of such trials. (Melman, Tr. 1138-39).

2159. Dr. Melman agreed that, with respect to such requirements, he was applying the FDA standard for drugs being submitted to the FDA. (Melman, Tr. 1140).

2160. Dr. Melman testified that even if Dr. Burnett did a proper RCT at Johns Hopkins, who he deems to be a very distinguished man in the field, and the RCT came out positive, it is still not enough to support a public claim. (Melman, Tr. 1139).

(b) Dr. Melman Insists Pomegranate Juice Is a Drug

2161. Dr. Melman takes the extreme position that "pomegranate juice is a drug." (PX0360 (Melman, Dep. at 17-19); Melman, Tr. 1141).

2162. He even goes so far as to suggest that water is a drug because it is composed of hydrogen and oxygen molecules. (Melman, Tr. 1141).

2163. On cross-examination, Dr. Melman testified that everything is a drug. (Melman, Tr. 1165).

2164. Dr. Goldstein testified, however, that pomegranate juice is a nutraceutical (a naturally occurring botanical product with health-promoting characteristics) and not a drug. (PX0352 (Goldstein, Dep. at 134); PX0189-0003).

(c) Dr. Melman Insists That If a Study Doesn't Show Statistical Significance, It Is Not a Difference

2165. Dr. Melman testified that pomegranate juice "doesn't work" because the *Forest/Padma-Nathan RCT Study* did not reach statistical significance. (Melman, Tr. 1171-78).

2166. Dr. Melman insisted that if a difference doesn't reach statistical significance, it's not a difference. (Melman, Tr. 1176-78).

3. Dr. Melman's Opinions Are Uninformed

(a) Dr. Melman Had Never Heard of the Ubiquitous GAQ

2167. Even though the GAQ is widely used—including in virtually every published study of Viagra, Cialis, and Levitra (Goldstein, Tr. 2602, 2603; Burnett, Tr. 2304)—Dr. Melman testified that he had never heard of it before his involvement in this case. (Melman, Tr. 1180).

2168. Indeed, Dr. Melman claims that he tried to research the GAQ but was unable to find anything about it—he "tried but failed." (Melman, Tr. 1181-82).

2169. Dr. Melman conceded that he doesn't "know whether it's widely used or not." (Melman, Tr. 1187-88).

2170. Dr. Melman was even unaware that Pfizer had used the GAQ questionnaire in their studies on Viagra. (Melman, Tr. 1187-88).

2171. Dr. Goldstein testified that for Dr. Melman to not know the GAQ is widely used "is a little embarrassing." (Goldstein, Tr. 2602).

2172. Regardless, Dr. Melman called the GAQ questionnaire a "lousy test". (Melman, Tr. 1174, 1182).

2173. Although Dr. Melman had no experience with the GAQ questionnaire prior to this case, he insisted that pomegranate juice "doesn't work" because the *Forest/Padma-Nathan RCT Study* used the GAQ questionnaire (in addition to the study not reaching statistical significance). (Melman, Tr. 1171-74).

(b) Dr. Melman's Doesn't Know The Meaning Of "RCT"

2174. Dr. Melman doesn't know the meaning of the term "RCT" which is commonly used by researchers to indicate randomized double-blind, placebo-based trial. (Melman, Tr. 1134-35).

(c) Dr. Melman Believed the FTC Had to Give Approval In Advance to Market a Product

2175. Dr. Melman testified that he thought the FTC "has to give approval in advance to market a product." (Melman, Tr. 1138).

(d) Dr. Melman's Opinions Are Contrary to Recent Supreme Court Precedent

2176. The Supreme Court held in *Matrix Initiatives, Inc. v. Siracusano*, 131 S.Ct. 1309, 1319 (2011), that "medical professionals and researchers do not limit the data they consider to the results of randomized clinical trials or to statistically significant evidence." Dr. Melman disagrees with this statement of the law. (Melman, Tr. 1178-80).

(e) Dr. Melman Has Never Studied a Food Product

2177. Dr. Melman concedes that he has never conducted any clinical work on a food product. (Melman, Tr. 1165).

2178. Dr. Melman testified that he has never done any testing on pomegranate juice. (Melman, Tr. 1164).

2179. Dr. Melman testified he has not written about the oral treatment of ED. (Melman, Tr. 1164).

2180. Most of Dr. Melman's current research is on gene transfer therapy and overactive bladder condition. (Melman, Tr. 1164-65).

(f) Dr. Melman Requires That a Patient Have an Orgasm Before His ED Is Deemed Treated

2181. Dr. Melman testified that in the hypothetical case of "a man [that] hasn't been able to have an erection for five years, then he tries [a] product and he now has an erection and he can penetrate his wife and bring her to sexual satisfaction, but he doesn't have an orgasm himself," the maker of the product "can't tell the public about what [the product has] done." (Melman, Tr. 1146-47).

2182. Dr. Goldstein testified that he "couldn't disagree more" with Dr. Melman's statement. (Goldstein, Tr. 2604).

2183. Dr. Goldstein testified that Dr. Melman's statement was contrary to the IIEF. (Goldstein, Tr. 2604).

2184. This opinion imposing an orgasm prerequisite to the treatment of ED is unsupported by the erectile function domain of the IIEF for which Dr. Melman advocates, as that domain gathers no information regarding a patient's orgasm. (Goldstein, Tr. 2604).

(g) Dr. Melman Blindly Critiqued the Forest/Padma-Nathan RCT Study's Placebo

2185. Dr. Melman criticizes the *Forest/Padma-Nathan RCT Study* for not having an identical placebo match, but admits that he "ha[s] no idea" whether any test subject knew he was drinking placebo. (Melman, Tr. 1190).

2186. In fact, any potential limitation arising from pomegranate juice's unique appearance and taste "was minimized for the study by taste and color matching the placebo beverage as well as providing a 2-week washout so that it would be difficult for subjects to discern any subtle difference in taste or appearance between the study beverages." (CX0908).

(h) Dr. Melman's Characterization of the Davidson Study as Being a Negative ED Study Is Misplaced as the Baseline IIEF Data Collection Was Admittedly Flawed from the Outset

2187. Dr. Melman characterized the Davidson Study as having negative ED findings. (Melman, Tr. 1130).

2188. The Davidson study, however, was primarily a cardiovascular study and therefore the protocols did not include any of the type of inclusion or exclusion criteria one would expect to see in even a basic ED clinical trial. (CX0716; PX0019; Melman, Tr. 1092).

2189. In fact, the ED findings in the Davidson Study were flawed as one of the two study sites was unable to collect any data for the baseline IIEF measurement. (CX0654_0001 – "IIEF data not collected on most subjects at site 2; Mary Sue was aware of this and site staff reported that subjects are uncomfortable completing this questionnaire in the office (close quarters) so they tried to send it to them prior to their visit for them to bring in completed, yet it still was incomplete. Unfortunately, this baseline data will be missing.")

4. Dr. Melman's Opinions Are Hypocritical

(a) Dr. Melman Critiques Respondents' Studies Even Though He Has Conducted Studies Similarly

2190. Dr. Melman criticizes the *Forest/Padma-Nathan RCT Study* for studying a population with a mean age of 46 years old, even though Dr. Melman himself conducted a study in which the mean age of study participants was 40. (Melman, Tr. 1190-92).

(b) Dr. Melman Holds Respondents to a Higher Standard Than That to Which He Holds Himself

2191. While Dr. Melman claims that Respondents must have two RCTs before they can publicize the positive effects of pomegranate juice on men with ED, he publicized preliminary results of studies on his gene-transfer therapy based only on the results of an animal study. (Melman, Tr. 1149-55).

H. Summary of Erectile Health Claims That Respondents Can Support

2192. The competent and reliable scientific evidence demonstrates that pomegranate juice provides a benefit to erectile health and erectile function. (Goldstein, Tr. 2605; PX0189-0014; PX0149-0006; Burnett, Tr. 2255-56; PX0349 (Burnett, Dep. at 103, 116-118, 137); Heber, Tr. 2012).

2193. Pomegranate juice would be recommended as a management tool to promote erectile health in men who are aware that their erectile function is declining but who do not yet meet the clinical definition of ED under the IIEF and therefore do not qualify for pharmacologic treatment. (PX0189-0014-0015; PX0352 (Goldstein, Dep. at 42-45); Goldstein, Tr. 2609; CX2007 (Heber, Dep. at 85)).

2194. Improving ones erectile function may also help improving ones erectile dysfunction. (Burnett, Tr. 2303).

2195. The suggestion to utilize the Mediterranean diet, which the pomegranate fruit is part of, to improve endothelial function and erectile health, is logical and rational in men who have been diagnosed with clinical ED but who have an insufficient response to PDE5 inhibitors (like Viagra) and who are unwilling to consider invasive or mechanical therapies (such as injecting needles into the penis, inserting urethral suppositories, using vacuum pumps, or having surgically implanted prostheses), (PX0189-0005, 0014-0015; PX0352 (Goldstein, Dep. at 37-42); Goldstein, Tr. 2605, 2641; PX0190-0006-0007).

2196. Reasonable and competent science shows that pomegranate juice reduces the risk of, or ameliorates erectile dysfunction in men caused by endothelial dysfunction or blood flow impairment or oxidative stress. (Goldstein, Tr. 2605).

XVII. POM'S ADVERTISEMENTS

A. Overview of Respondents' Contentions Regarding the Advertisements

2197. Complaint Counsel has now, late in trial and afterwards, narrowed the universe of advertisements to approximately 70 ads and more than a dozen website captures, from hundreds and hundreds of ads. (*See infra* XVII(F)).

2198. Of these, approximately eight are the much older ads that have not run in several years, on which Complaint Counsel concentrated on at trial. These eight ads, while accurate and truthful, were "outliers" at POM, using more aggressive language and graphics regarding the health benefits of POM's pomegranate juice. (*See infra* XVII(E)).

2199. The rest of the ads fall into three categories, all of which are qualified claims and are substantiated by competent and reliable scientific evidence. (*See infra* XVII(G)).

2200. Unlike other cases, such as *In re Telebrands Corp.*, 140 F.T.C. 278 (2005), Complaint Counsel failed to present significant extrinsic evidence or expert opinion on the meaning of the ads to support their claims. Contrary to Complaint Counsels' contentions, such extrinsic evidence is necessary because the implied claims they assign to the challenged ads are not "conspicuous, self-evident, or reasonably clear" so that they can be "determined with confidence" from the face of the ads that the claims can be ascertained without extrinsic evidence. (Appendix of Advertisements; Mazis, Tr. 2752).

2201. The audience for POM products includes men and women, spanning all levels of age and income, who want to take an active approach to health, via good nutrition, to live vibrant and healthy lives. (Tupper, Tr. 3017-18).

2202. Typical consumers of POM products are affluent and health conscious. (CX1375 (L. Resnick, Tropicana Dep. at 131); CX1357 (Kuyoomjian, Dep. at 102).

2203. POM consumers understand that the Challenged Products are 100 percent derived from a fruit (which is a fact heavily emphasized in POM's advertising), and no reasonable consumer would reasonably take away the message from Respondents' advertising that the Challenged Products can treat their diseases or that they should disregard conventional medical treatment if they were to consume the Challenged Products. (Butters Tr. 2817-18; Appendix of Advertisements).

2204. Instead, POM consumers view Respondents' advertising through the lens that the Challenged Products are wholly derived from pomegranates and perceive the Challenged Products the way they perceive any other whole food, like broccoli or blueberries, which may help or improve your odds against disease. (Butters Tr. 2817-18; Appendix of Advertisements).

2205. As set forth in the further detail below, the implied claims on which Complaint Counsel base their claims are very aggressive and unreasonable interpretations on what messages the ads convey.

B. The Dispute Regarding the Advertisements

1. Complaint Counsel Claim That POM's advertisements Make "Clinically Proven" Disease Claims

2206. The FTC claims that, in its advertising, POM contended that the Challenged Products were "clinically proven" to prevent or treat heart disease, prostate cancer, and erectile dysfunction, and that POM products were a "silver bullet against disease." (FTC Press Release: FTC Complaint Charges Deceptive Advertising by POM Wonderful (9/27/2010), available at http://www.ftc.gov/opa/2010/09/pom.shtm (quoting David Vladek, Director of the FTC's Bureau of Consumer Protection)).

2207. The FTC claims that Respondents' "clinically proven" disease claims are false and misleading because Respondents' clinical studies, research and/or trials did not prove the challenged benefits claimed. (CX1426 at 0017-0020).

2208. The FTC further claims that Respondents' "clinically proven" disease claims are material to the purchasing decisions of POM's consumers. (Compl. Pretrial Br. at 30).

2. Respondents' Deny That They Make "Clinically Proven" Disease Claims

2209. As described in the paragraphs below, Complaint Counsels' contentions that POM's ads make "clinically proven" disease claims are wrong for many reasons. (*See infra* ¶ 2210).

2210. First, POM's advertising do not convey the disease messages that Complaint Counsel assert are expressly made in the advertisements.

(a) Nowhere do Respondents expressly (*i.e.*, unequivocally and directly) state that the Challenged Products are "clinically proven" to "prevent," "treat," or "reduce the risk" of heart disease, prostate cancer and erectile dysfunction. (Appendix of Advertisements); and

(b) Nowhere do Respondents expressly (*i.e.*, unequivocally and directly) state that the Challenged Products "prevent," "treat," or "reduce the risk" of heart disease, prostate cancer and erectile dysfunction. (Appendix of Advertisements).

2211. Second, POM's advertising does not convey the disease messages that Complaint Counsel assert are impliedly made in the advertisements.

(c) Respondents assert that the Commission may rely on its own reasoned analysis to determine what implied claims are conveyed, absent reference to extrinsic evidence, only if those claims are "conspicuous, self-evident, or reasonably clear on the face of the ad." (*Kraft, Inc. v. F.T.C.*, 970 F.2d 311, 320 (7th Cir. 1972) *cert. denied*, 507 U.S. 909 (1993));

(d) In this case, however, it is impossible for Complaint Counsel to "conclude with confidence" that POM's advertisements convey the "clinically proven" claims to prevent or treat disease, as alleged, on the face of the challenged ads. (see *In re Thompson Medical Co.*, 104 F.T.C. 648, 789 (1984), *aff'd*, 791 F.2d 189 (D.C. Cir. 1986), *cert. denied*, 479 U.S. 1086 (1987));

(e) POM's advertising, viewed as a whole, does not clearly and conspicuously convey to a reasonable consumer that the Challenged Products prevent, treat or reduce the risk of heart disease, prostate cancer and erectile dysfunction under Complaint Counsels' "net impression" analysis or any analysis for implied claims. (Appendix of Advertisements);

(f) POM's advertising, viewed as a whole, does not clearly and conspicuously convey to a reasonable consumer that the Challenged Products are "clinically proven" to prevent, treat or reduce the risk of heart disease, prostate cancer and erectile dysfunction under Complaint Counsels' "net impression" analysis or any analysis for implied claims. (Appendix of Advertisements);

(g) To the extent a "proven" claim can be implied from any of POM's advertising (which it cannot), the overall impression of any ad is not that the Challenged Products are "proven" to be 100% effective in preventing, treating or reducing the risk of heart disease, prostate cancer or erectile dysfunction because "proven" in science means the "average person in the study benefitted." "Proven" does not mean that "everyone in the study necessarily benefitted." (Heber, Tr. 2011; Butters, Tr. 2893-94; PX0361 (Sacks, Dep. at 81)));

(h) To the extent a "treat" claim can be implied from any of POM's advertising (which it cannot), the overall net impression of any ad is not that the Challenged Products are a substitute for conventional medical treatment. (Butters, Tr. 2821-22; Appendix of Advertisements); and

(i) To the extent a "reduce the risk" claim can be implied from any of POM's advertising, the overall net impression of any ad is not that the Challenged Products "reduce the risk" of heart disease, prostate cancer or erectile dysfunction, like a drug with a single target of action, but "reduce the risk" like a healthy diet of fruits and vegetables and exercise "reduce the risk" of disease. (Butters Tr. 2817-18).

2212. Third, because the challenged implied claims may not be determined with confidence from the face of the challenged advertisements, extrinsic evidence must be examined, including consumer surveys and expert testimony. (*See* Appendix of Advertisements; *In re Stouffer Food Corp.*, 118 F.T.C. 746, 777 (1994) (citing Kraft, 970 F.2d at 318)).

2213. Here, Complaint Counsel failed to present any reliable extrinsic evidence or expert opinion:

(a) on the meaning of POM's ads, or on consumers' expectations or perceptions on the ads;

(b) that POM's ads conveyed that the Challenged Products are "clinically proven" to prevent, treat or reduce the risk of heart disease, prostate cancer or erectile dysfunction;

(c) that POM's ads conveyed that the Challenged Products prevent, treat or reduce the risk of heart disease, prostate cancer or erectile dysfunction; or

(d) of Respondents' intent to convey such messages to prove that POM's advertising made the alleged implied disease claims or "clinically proven" disease claims. (CX1287; CX1289; CX1291; CX1293; CX1295; Mazis, Tr. 2752).

2214. Fourth, Complaint Counsel failed to present any reliable extrinsic evidence or expert opinion rebutting the fact that many of the ads were meant to be hyperbolic, puffery and humorous. (*See, e.g.*, *Sterling Drug, Inc. v. F.T.C.*, 741 F.2d 1146, 1150 (9th Cir. 1984)). Indeed, most of the statements in the majority of the ads were not meant to be taken literally and cannot be objectively verified, and thus constitute puffery. (*In re Thompson Medical*, 104 F.T.C. 648, 788-89 n.6).

2215. Furthermore, as set forth in detail below, to the extent the challenged advertisements do not rely on puffery or hyperbole, POM's advertisements contain

carefully qualified statements that convey accurate messages about the health benefits of the Challenged Products, the results of the scientific studies and related information. (Appendix of Advertisements).

2216. Indeed, the overall net impressions of POM's advertising were as follows:

(a) Some of the ads conveyed general health messages, such as the Challenged Products are healthy for your body or promote a healthy heart or a healthy prostate. (Appendix of Advertisements);

(b) Other ads conveyed more specific qualified messages – *e.g.*, the Challenged Products "reduce the risk" of heart disease, prostate cancer or erectile dysfunction, like a healthy diet of fruits and vegetables and exercise "reduce the risk" of disease. (Appendix of Advertisements); and

(c) Others fall somewhere in between. (Appendix of Advertisements).

3. POM's advertisements Are Substantiated by Rigorous, Competent and Reliable Scientific Evidence

2217. Each of the health-related messages conveyed by POM's advertising, as described above, are truthful and not misleading because Respondents had rigorous, competent and reliable scientific evidence to support the messages conveyed in those advertisements. (*See infra* (XVII(G)).

2218. Even assuming *arguendo* that POM's advertising do expressly or impliedly convey the "clinically proven" disease messages that Complaint Counsel assign to them, all POM's advertising claims about the Challenged Products are truthful and not misleading because Respondents also had rigorous, competent and reliable scientific evidence to support those representations. (*See infra* (XVII(G)).

4. Respondents' Survey Evidence Demonstrates That Their Advertising Claims Are Not Material to Consumers

2219. Additionally, assuming *arguendo* that the presumption of materiality applies in favor of the Commission, such presumption was successfully rebutted by Respondents' expert witness, David Reibstein, a marketing professor at The Wharton School of the University of Pennsylvania. His survey demonstrated that, even if the ads conveyed the messages that Complaint Counsel assign to them, any alleged disease claims made by Respondents were not material to the purchasing decisions of POM consumers. (*See infra* (XVIII(A)).

2220. Thus, the presumption of materiality has disappeared here. (*See infra* XVIII; *In the Matter of Novartis Corp.*, 127 F.T.C. 580, 686 (1999), citing *St. Mary's Honor Ctr. v. Hicks*, 509 U.S. 502, 506 (1993)).

2221. The Administrative Law Judge ("ALJ") now weighs the evidence on materiality presented by each side, as with any other factual issue, to decide if Complaint Counsel have met their burden of providing a preponderance of evidence on the issue. *In the Matter of Novartis Corp.*, 127 F.T.C. 580, 686 (1999), citing *St. Mary's Honor Ctr. v. Hicks*, 509 U.S. 502, 506 (1993).

2222. Complaint Counsel have presented no reliable evidence to rebut Professor Reibstein's survey findings.

2223. Specifically, Complaint Counsels' own rebuttal expert to Professor Reibstein, Professor Mazis, in contrast to previous work he has done for Complaint Counsel in other litigation, did not (a) conduct any facial analysis of POM's ads or offer any expert opinion on them; (b) conduct any surveys on the ads or (c) provide any expert opinion on the exposure of the ads to consumers (and testified that he was aware of no such evidence), despite testifying that such exposures were critical to having an effect on consumers. (*See infra* (XVIII(B)). ; Mazis, Tr. 2752).

C. Complaint Counsels' Initial Allegations and Complaint

2224. Complaint Counsel claim that in certain of POM's advertising and promotional materials for POM Juice and POMx Pills and POMx Liquid (hereinafter "POMx") (collectively, the "Challenged Products"), described in the paragraphs below, Respondents have represented, expressly or by implication, that clinical studies, research, and/or trials prove to consumers that the Challenged Products will prevent, treat or reduce the risk of heart disease, prostate cancer and erectile dysfunction. (CX1426 at 0017-0020).

2225. Specifically, in their Complaint, Complaint Counsel take an aggressive position regarding what POM's ads convey and allege generally that Respondents make the following claims in their advertising:

(a) Drinking eight ounces of POM Juice, or taking one POMx Pill or one teaspoon of POMx Liquid, daily, prevents or reduces the risk of heart disease, including by (1) decreasing arterial plaque, (2) lowering blood pressure, and/or (3) improving blood flow to the heart;

(b) Drinking eight ounces of POM Juice, or taking one POMx Pill or one teaspoon of POMx Liquid, daily, treats heart disease, including by (1) decreasing arterial plaque, (2) lowering blood pressure, and/or (3) improving blood flow to the heart;

(c) Drinking eight ounces of POM Juice, or taking one POMx Pill or one teaspoon of POMx Liquid, daily, prevents or reduces the risk of prostate cancer, including by prolonging PSADT;

(d) Drinking eight ounces of POM Juice, or taking one POMx Pill or one teaspoon of POMx Liquid, daily, treats prostate cancer, including by prolonging PSADT;

(e) Drinking eight ounces of POM Juice daily prevents or reduces the risk of erectile dysfunction; and

(f) Drinking eight ounces of POM Juice daily treats erectile dysfunction.

(CX1426 at 0017-0020).

2226. Complaint Counsel complain that POM's advertising, website and promotional materials are false and misleading because Respondents did not have a reasonable basis to substantiate the representations set forth in the paragraph above at the time the representations were made – *i.e.*, that Respondents' clinical studies, research, and/or trials did not prove the challenged benefits claimed. (CX1426 at 0017-0020).

2227. Complaint Counsel claim that in order to have a reasonable basis that substantiates the allegedly express or implied product claims at issue and for the allegedly express or implied claims to be truthful and non-misleading, Respondents needed "competent and reliable scientific evidence" substantiating those claims at the time they were made. (PX0267-0031, 0054).

D. The Changing Universe of the Challenged Advertisements

2228. Since POM's inception in 2001, POM published at least hundreds and hundreds of health-oriented advertisements in various media, including print, "out-of-home" ("OOH") (*e.g.*, billboards, gym posters and bus shelters), Internet and television. (CX135 (Tupper, Dep. at 63:9-22) (types of media); PX0267 at 0002-00035 (identifying hundreds of ads by Bates number); CX0364 (VMS search results listing hundreds of ads)).

2229. Even Complaint Counsel admit that POM disseminated "thousands" of ads in various media. (PX0267 at 0030, 0033).

2230. Complaint Counsel initially based their allegations on the hundreds and hundreds of print, OOH and Internet advertisements going as far back as 2003 that Respondents produced in discovery. (PX0263-0002-0013; PX0267-0002-0030).

2231. Indeed, during discovery and throughout most of trial, Complaint Counsel refused to pare down the advertisements at issue from the hundreds and hundreds of ads that POM produced in discovery. (PX0263 at 0003, 0015; PX0267 at 0029-0030; 0033-0034).

2232. However, during and throughout trial, Complaint Counsel narrowed the universe of advertisements they are challenging. (*See infra* (XVII(D)).

1. During Trial, Complaint Counsel, Through Their Experts and Lawyers, Narrowed the Universe of Advertisements "at Issue" by Excluding Billboards, POM Juice Advertisements Disseminated After December 2008 and POM Juice Website Entries After August 2009

2233. During trial, Complaint Counsels admitted, through their lawyers and experts, that Complaint Counsel were not challenging (a) POM's billboard advertisements, (Reibstein, Tr. 2540); (b) any POM juice advertisements disseminated after December 2008; or (c) POM juice website entries after August 2009. (*See infra* (XVII(D)).

2234. First, during the cross-examination of Professor Reibstein, Complaint Counsel admitted that Complaint Counsel were not challenging Respondents' billboards as violating Sections 5 and 12 of the FTC Act. (Reibstein, Tr. 2540.)

2235. Billboards contain only pictures and headlines. There is no accompanying text or body copy. (CX1359 (L. Resnick, Dep. at 199)).

2236. In the advertising industry, billboards are generally referred to as OOH advertisements, which include other outdoor advertising such as gym posters, subway posters and bus shelters. (CX1353 (Tupper, Dep. at 63)). As with billboards, all OOH advertisements contain only pictures and headlines without any accompanying text or body copy.

2237. Based on their own admissions, Complaint Counsel ostensibly do not contend that any of Respondents' billboards or OOH ads that contain only pictures and headlines without any accompanying text or body copy violate Sections 5 and 12 of the FTC Act. (*See infra* (XVII(D)).

2238. Second, Complaint Counsel further narrowed the universe of ads at issue through evidence presented by their own survey expert, Professor Mazis. Professor Mazis testified that Complaint Counsel informed him that the FTC was only challenging POM Juice print advertisements that ran at least twenty-two months before the execution of the Reibstein Survey and POM Juice website entries that were disseminated in the fourteen months before the execution of the Reibstein Study. (PX0296 at 0010; Mazis, Tr. 2753-54).

2239. Professor Mazis used this concession to show that the reason for this was because the participants in the Reibstein Survey have forgotten the ads. (Mazis, Tr. 2712-13). Indeed, in his expert report Professor Mazis said that "[e]ven if consumers

could recall POM juice advertising, they would be expected to recall more advertising, which is not being challenged by the FTC." (PX0296 at 0010).

2240. Professor Reibstein testified that he put his survey in the field around the end of October 2010. (Reibstein, Tr. 2541).

2241. Twenty-two months before the execution of the Reibstein Survey is December 2008; and fourteen months before execution of Reibstein Survey is August 2009. (*See infra* (XVIII(B)).

2242. After having sought an advantage against Professor Reibstein's survey by arguing that his survey would not reflect the only ads at issue, which were disseminated years before his survey, Complaint Counsel have effectively narrowed the universe of POM Juice ads at issue to those disseminated prior to December 2008. (*See infra* (XVIII(B)).

2243. Similarly, Complaint Counsel have effectively narrowed the universe of POM Juice website ads to those disseminated prior to August 2009. (*See infra* (XVIII(B)).

2. After the Conclusion of Live Witness Testimony and Days Before the ALJ Closed the Evidentiary Record, Complaint Counsel Again Narrowed the Universe of Advertisements at Issue By Proposing a Stipulation Re: Challenged Advertisements

2244. After the conclusion of live witnesses and at the urging of the ALJ, on or about November 9, 2011 - just nine days before the evidentiary record closed, (11/18/11 Order Closing Hearing Record) - Complaint Counsel proposed a stipulation purporting to narrow the universe of hundreds and hundreds of ads to approximately 43 exhibits, some of which included multiple ads or website entries (hereinafter, "11/9/11 Proposed Ad Stipulation"). (11/9/11 email from Mary Johnson to Counsel for Respondents re POM Wonderful et al., Dkt 9344 -- proposed stips re: challenged ads/misreps (hereinafter "11/9/11 Johnson email"), attached hereto as Exhibit 1; Complaint Counsels' Proposed Stipulations, dated 11/8/11 (hereinafter, "Proposed Stipulations"), attached hereto as Exhibit 2).

2245. These are the ads Respondents believe are now at issue, which Complaint Counsel identified in the 11/9/11 Proposed Ad Stipulation as: CX0013; CX0016; CX0029; CX0031; CX0033; CX0034; CX0036; CX0044; CX0065; CX0103; CX0109; CX0120; CX0122; CX0128; CX0169; CX0180; CX0188; CX0192; CX0251; CX0260; CX0274; CX0279; CX0280; CX0314; CX0328; CX0331; CX0336; CX0337; CX0342; CX0348; CX0350; CX0351; CX0353; CX0355; CX0372; CX0379; CX0380; CX0463; CX0466; CX0468; CX0472; CX0473; CX1426 Exhs. A-N. (11/9/11 Johnson email; Proposed Stipulations).

2246. Complaint Counsel did not, however, specify what was false and misleading or unsubstantiated about any of the identified advertisements, websites or promotional materials. (11/9/11 Johnson email).

2247. Additionally, many of the ads identified in the 11/9/11 Proposed Ad Stipulation included those ads which Complaint Counsels' expert, Professor Mazis, admitted were not being challenged. (*See infra* XVIII(B)).

3. Because Complaint Counsel Failed to Present Evidence That Respondents Disseminated Some of the Ads, the Universe of Ads Identified In The 11/9/11 Proposed Ad Stipulation Should Be Further Narrowed to Those That Were Actually Disseminated

2248. Even prior to addressing whether POM's advertisements are false, within the meaning of Section 12 of the FTC Act, the ALJ must determine as a preliminary matter whether the materials constitute: (1) the dissemination of advertisements; (2) for the purpose of inducing, or which are likely to induce, purchases in or affecting commerce; (3) of "food" or "drugs."

2249. Respondents represent that the chart below summarizes the dissemination information for each exhibit, to the extent such dissemination information is available in the evidentiary record.

2250. Where Complaint Counsel failed to present any specific evidence of dissemination, those exhibits are listed under the heading "No Dissemination Evidence Presented."

2251. Complaint Counsel cannot now challenge those ads because they have not proven that Respondents disseminated them, thus narrowing the universe of ads "at issue."

4. Based On Complaint Counsels' Own Representations and Failings, a Much Smaller Universe of the Advertisements Listed In the 11/9/11 Proposed Ad Stipulation Remain "At Issue"

2252. In summary, based on (a) Complaint Counsels' own admissions during the cross-examination of Professor Reibstein regarding billboards, (b) the trial testimony of Professor Mazis regarding POM Juice print and website ads and (c) Complaint Counsels' failure to establish that certain ads were disseminated, the chart below summarizes the ads that remain "at issue":

Trial Exh. No.	Headline/Description	Dissemination Date	Reference to Evidentiary Record

Trial Exh. No.	Headline/Description	Dissemination Date	Reference to Evidentiary Record
POM Juice and POMx Pill Ads Disseminated From October 2003 Through December 2008 ("At Issue")			
CX0016	Drink and be healthy	10/12/2003	VMS[1]
CX0029	Studies Show That 10 Out of 10 People Don't Want To Die	11/01/04	VMS
CX0031	Floss your arteries. Daily.	12/01/2004	VMS
CX0033	Life support	12/30/04	VMS
CX0034	Amaze your cardiologist	02/01/2005	VMS
CX0036	Cheat death.	03/10/2005	VMS
CX0103	Decompress	03/01/2007	VMS
CX0109	Heart therapy	04/01/2007	VMS
CX0120	One small pill for mankind	05/28/2007	VMS
CX0122	Science, not fiction	06/01/2007	VMS
CX1426, Exh. M	Your Partner in Promoting Lifelong Health, Volume 1, Issue 1: For Your Heart (hereinafter, "Dreher Heart Newsletter")	Summer 2007	Written on Exhibit
CX1426, Exh. N	Your Partner in Promoting Lifelong Health, Volume 1, Issue 2: Prostate Health (hereinafter, "Dreher Prostate Newsletter")	Fall 2007	Written on Exhibit
CX0169	The power of POM in one little pill	01/06/2008	VMS
CX0180	The antioxidant superpill	02/03/2008	VMS
CX0188	Cheat death.	04/01/2008	Grid Below Ad: Date Out
CX0192	What gets your heart pumping?	05/01/2008	VMS
CX0314_0003	Drink to prostate health	09/09/08	Grid Below Ad: Date Out
CX0314_0004	POM Wonderful and Prostate Health	09/09/08	Grid Below Ad: Release Date
CX0314_0005	The proof is in the POM	09/09/2008	Grid Below

[1] The VMS run date stamped on the face of the ad reflects the dissemination date. (CX0474)

Trial Exh. No.	Headline/Description	Dissemination Date	Reference to Evidentiary Record
			Ad: Date Out
CX0314_0006	The Antioxidant Superpower	09/09/2008	Grid Below Ad: Date Out
CX0314_0008	POM Wonderful and Prostate Health	10/23/08	Written on Exhibit
CX0314_0009	The proof is in the POM	10/23/08	Written on Exhibit
CX0251	Imitation may be sincere. But is it pure?	11/01/2008	VMS
CX0260	Drink to prostate health	12/01/2008	VMS
CX1426, Exh. I	Antioxidant Superpill	Not available, but there is evidence that it ran.	(L. Resnick, Tr. 177:18-178:18; Leow, Dep. At 178-179)
POMx Pill Ads Disseminated Between January 2009 Through Present ("At Issue")			
CX0279	Science, Not Fiction	03/01/2009	VMS
CX0280	Live Long Enough To Watch your 401(k) Recover.	03/12/2009	VMS
CX0331	Healthy, ~~Wealthy~~ & Wise	09/27/2009	VMS
CX0328	Your New Health Care Plan	11/08/2009	VMS
CX0337	The First Bottle You Should Open in 2010	01/03/2010	VMS
CX342	Take Out a Life Insurance Supplement	02/22/2010	VMS
CX0348	24 Scientific Studies Now In One Easy-To-Swallow Pill	04/01/2010	VMS
CX0350	24 Scientific Studies Now In One Easy-To-Swallow Pill	04/26/2010	VMS
CX0351	The Only Antioxidant Supplement Rated X	06/01/2010	VMS
CX0353	Take Out a Life Insurance Supplement	06/14/2010	VMS
CX0355	The Only Antioxidant Supplement Rated X	07/01/2010	VMS
Website Materials			

Trial Exh. No.	Headline/Description	Dissemination Date	Reference to Evidentiary Record
("At Issue")			
CX1426, Exh. E-1	Website captures from www.pomegranatetruth.com	04/28/2009	Time stamp from website capture
CX1426, Exh. E-2	Website captures from Health Benefits section of www.pomwonderful.com, including "Real Studies" webpage	04/29/2009	Time stamp from website capture
CX1426, Exh. E-3	7 POM Video Ads	4/30/2009	Time stamp from website capture
CX1426, Exh. E-4	Website captures re POM Products from www.pomwonderful.com	04/30/2009	Time stamp from website capture
CX1426, Exh. E-8	Website captures from www.pompills.com	04/29/2009	Time stamp from website capture
CX1426, Exh. E-9	Website captures from www.pompills.com	01/27/2010	Time stamp from website capture
CX0463_0001	Heart Therapy Flash Video	None	N/A
CX0466_0001	Hurry Prostates Everywhere are in Danger Flash video	None	N/A
CX0473	Rushton CD	N/A	N/A
CX472_0001	Roll International Website Video	None	N/A
Press Releases ("At Issue")			
CX0013_0001-0005	Press Release – Consumer Demand for POM Wonderful's Refrigerated All-Natural Pomegranate Juice Grows as the Health Benefits of Pomegranate Juice Become Recognized	01/09/03	CX0013_0001-0005
CX044_0001-0003	Pomegranate Juice May Affect the Progression of Coronary Heart Disease	09/16/2005	CX044_0001-0003
CX0065_0001-0004	Press Release - POMx, a Highly Concentrated Form of Healthy Pomegranate Antioxidants,	07/10/06	CX0065_0001-0004

Trial Exh. No.	Headline/Description	Dissemination Date	Reference to Evidentiary Record
	Becomes Available to Consumers for the First Time		
CX0128_0001-0004	Press Release - POM Wonderful 100% Pomegranate Juice May Improve Mild to Moderate Cases of Erectile Dysfunction	06/27/07	CX0128_0001-0004
POM Juice Ads Disseminated Between January 2009 Through Present (Not "At Issue" Per Professor Mazis)			
CX0274	I'm off to save prostates!	02/01/2009	
CX0379_0001	Lucky I have super HEALTH POWERS	08/20/2009	Grid Below Ad: Date Out CX0379_0001
CX0379_0002	Holy Health! $32 million in medical research.	08/20/2009	Grid Below Ad: Release Date CX0379_0002
CX379_0003	KA-POM!	08/20/2009	Grid Below Ad: Release Date CX379_0003
CX0379_0004	Risk your health in this economy? NEVER!	08/20/2009	Grid Below Ad: Date Out CX0379_0004
CX0372_0001	Lucky I have super HEALTH POWERS	09/10/2009	Grid Below Ad: Release Date CX0372_0001
CX372_0002	Holy Health! $32 million in medical research.	09/10/2009	Grid Below Ad: Release Date CX372_0002
CX0372_0003	KA-POM!	09/10/2009	Grid Below Ad: Release Date CX0372_0003
CX0372_0004	100% PURE Pomegranate Juice to the Rescue	09/10/2009	Grid Below Ad:

Trial Exh. No.	Headline/Description	Dissemination Date	Reference to Evidentiary Record
			Release Date CX0372_0004
CX0380_0001	Lucky I have super HEALTH POWERS	09/10/2009	Grid Below Ad: Release Date CX0380_0001
CX00380_0002	Holy Health! $32 million in medical research	09/10/2009	Grid Below Ad: Release Date CX00380_0002
CX380_0003	KA-POM!	09/10/2009	Grid Below Ad: Release Date CX380_0003
CX0380_0004	Have no health fear… POM IS HERE!	09/10/2009	Grid Below Ad: Release Date CX0380_0004
POM Juice Website Ads Disseminated Between September 2009 Through Present (Not "At Issue" Per Professor Mazis)			
CX0336_0001-0019	POM Health Benefits: Fact or Fiction (multiple press releases in Exhibit)	12/2009	CX0336_0001-0019
CX1426, Exh. E-5	Website Excerpt from www.pomwonderful.com	01/27/2010	CX1426, Exh. E-5[1]
No Specific Dissemination Evidence Presented (Not "At Issue")			
CX0314_0010	Ingredients: pomegranates, $25 million in medical research	None in record	N/A
CX 1426, Exh. A	Super HEALTH Powers! (Hangtag)	None in record	N/A
CX1426, Exh. B	Drink to prostate health	None in record	N/A
CX1426, Exh. C	I'm off to save PROSTATES!	None in record	N/A
CX1426,	Holy Health! $25 million in	None in record	N/A

[1] Date information based on the name of the file and the 2010 copyright on the website.

Trial Exh. No.	Headline/Description	Dissemination Date	Reference to Evidentiary Record
Exh. D	medical research.		
CX1426, Exh. G CX0468	Amaze your urologist	None in record	N/A
CX1426, Exh. H	I'm off to save PROSTATES!	None in record	N/A
CX1426 Exhibit J	Healthy, ~~Wealthy~~, and Wise	None in record	N/A
CX1426, Exh. K	The Antioxidant Superpill	None in record	N/A
CX1426, Exh. L	The power of POM in one little pill	None in record	N/A
CX0314_0007	Drink to prostate health	None in record	N/A
CX0380_0005	Lucky I have super HEALTH POWERS	None in record	N/A
CX0380_0006	100% PURE pomegranate juice to the rescue!	None in record	N/A
CX0380_0007	Lucky I have super HEALTH POWER	None in record	N/A
Interviews/Discussions (Not "At Issue" Because Not Advertising)			
CX1426, Exh. E-7	Tupper Interview on FOX Business	06/17/08	CX1426, Exh. E-7
CX1426, Exh. E-6	L. Resnick Interview on *The Martha Stewart Show*	11/20/2008	CX1426, Exh. E-6[2]
CX472_0003	Lynda Resnick on the Early Show	02/19/09	CX472_0003[3]
CX1426 Exhibit F	Newsweek Interview with Lynda Resnick	03/20/2009	CX1426 Exhibit F
CX0472_0002	Lynda Resnick Presentation at USC	04/09/09	CX0472_0002

[2] The YouTube video was uploaded the following date on 11/21/2008.

[3] The video file is titled 3.25.10 and was uploaded on 2/19/2009.

2253. Nevertheless, despite the fact that the evidentiary record reflects that Complaint Counsel have represented that a smaller universe of ads is at issue, out of an abundance of caution, Respondents will analyze in the sections below and in the Appendix of Advertisements, attached hereto, each of the advertisements identified in Complaint Counsels' 11/9/11 Proposed Ad Stipulation.

E. Out of Hundreds and Hundreds of Ads Respondents Disseminated, Complaint Counsel Focuses On Only Eight "Outlier" Ads Run During the Very Early Years (2003-2006). These Ads, Although Non-Misleading And Substantiated, Have Not Run In Several Years, and There Is No Evidence That It Is Probable That Respondents Would Run These Type of Ads Again

2254. Out of the hundreds and hundreds of ads disseminated by Respondents since POM's inception and the full universe of ads now identified by Complaint Counsel in their 11/9/11 Proposed Ad Stipulation, Complaint Counsel focuses on eight "outliers" from POM's ads. (*See supra* XVII(A-D)).

2255. Respondents refer to these eight ads as "outliers," although non-misleading and substantiated, because the images in the ads and the language in the body copy regarding the health benefits of POM Juice were more aggressive than was typical of Respondent, especially in the later years. (*See supra* XVII(D)).

2256. Eight "outliers" is an extremely miniscule percentage, given the hundreds, maybe even thousands, of ads disseminated by Respondents. (*See supra* XVII(A-D)).

2257. The eight "outliers" are as follows:

(a) Cheat death. (CX CX0036_0001);

(b) Drink and be healthy. (CX0016_0001);

(c) Decompress. (CX0103_0001; CX0459_0001);

(d) Floss your arteries. Daily. (CX0031-0001);

(e) Amaze your cardiologist. (CX0034_0001;CX0471_0012);

(f) Imitation may be sincere. But is it pure? (CX0251_001);

(g) Ingredients: pomegranates, $25 million in medical research. (CX314_010); and

(h) pomwonderful.com "Real Studies" webpage (CX1426, Exh. E-2).

2258. With the exception of the inadvertent blood pressure reference on POM's website, the eight "outlier" ads were disseminated in the early years of POM or at least six years ago (and some of them eight years ago). (*See supra* XVII(E.1-8)).

2259. As described below, a few of these ads were primarily issued as the result of staff mistakes and they immediately ceased being run when the mistake was discovered. (*See supra* XVII(E.1-8)).

2260. Such mistakes are not likely to occur in the future because Respondents' current advertising review policy is a formalized process, which includes a checklist of individuals who review and sign off on the health-related advertisements, culminating ultimately in legal review. (L. Resnick, Tr. 248; Tupper Tr. 2977-78).

2261. Complaint Counsel have presented no evidence to the contrary or nor have they presented any evidence that it is probable that Respondents will run these type of "outlier" ads, although non-misleading and substantiated, again.

2262. Complaint Counsel also have not presented any evidence that any of the eight "outlier" ads, although non-misleading and substantiated, were the result of Respondents' intentionally false or misleading conduct.

2263. Because the "outlier" ads were discontinued so long ago and there is no evidence that Respondents would run these types of ads again, the eight "outliers," although non-misleading and substantiated, pose no real threat that Respondents will violate the FTC Act in the future and cannot form the basis for injunctive relief. (*See supra* XVII(E.1-8)).

1. Cheat Death

2264. According to Complaint Counsel, POM ran an advertisement with the headline "Cheat death" with this body copy:

> **Cheat death**.
>
> Dying is so dead. Drink to life with POM Wonderful Pomegranate Juice, the world's most powerful antioxidant. It has more antioxidants than any other drink and can help prevent premature aging, heart disease, stroke, Alzheimer's, even cancer. Eight ounces a day is all you need. The sooner you drink it, the longer you will enjoy it.
>
> **POM Wonderful Pomegranate Juice. The Antioxidant Superpower**.

(CX0036_0001) (emphasis in original).

2265. Complaint Counsel contend that this "Cheat death" headline and exact body copy ran on March 10, 2005. (CX0036_0001).

2266. Complaint Counsel have presented no other definitive dissemination information regarding this particular ad.

2267. Mr. Tupper testified that although this early "Cheat death" ad indicated a benefit regarding Alzheimer's, the Alzheimer's references were stopped early on because, although POM had some early preliminary research on Alzheimer's and the formation of plaques in the brain that are ultimately the cause of Alzheimer's, POM decided to focus its advertising on the areas of science that were farther along. (Tupper, Tr. 2994).

2268. Mr. Tupper further testified that this "Cheat death" ad, with the above-quoted body copy that POM "can help prevent" certain diseases stopped running five or six years ago and believes that POM stopped this body copy from running in connection with an NAD ruling. (Tupper, Tr. 2987-90).

2269. While Mr. Tupper stated that POM has since used the "Cheat death" headline and imagery, those ads contained no body copy or different body copy which contained no reference to POM helping to prevent any diseases. (Tupper, Tr. 2989).

2270. Complaint Counsel have presented no evidence to contradict Mr. Tupper's testimony that this "Cheat death" ad has not run in over five or six years.

2271. Moreover, Complaint Counsel have presented no evidence that it is probable that Respondents would run this type of ad again.

2272. Because this ad ceased running more than five or six years ago and there is no evidence that Respondents are likely to run this ad in the future, the ad provides no basis for injunctive relief.

2273. Nowhere in this ad do Respondents expressly (*i.e.*, unequivocally and directly) state that (a) POM Juice "prevents," "treats," or "reduces the risk" of heart disease, prostate cancer and erectile dysfunction; or (b) POM Juice is "clinically proven" to "prevent," "treat," or "reduce the risk" of heart disease, prostate cancer and erectile dysfunction. (CX0036_0001).

2274. Complaint Counsels' assertion that the ad conveys the message that (a) POM Juice "prevents," "treats," or "reduces the risk" of heart disease, prostate cancer and erectile dysfunction; or (b) POM Juice is "clinically proven" to "prevent," "treat," or "reduce the risk" of heart disease, prostate cancer and erectile dysfunction is not conspicuous, self-evident, or reasonably clear from the face of the ad. (CX0036_0001). Consequently, extrinsic evidence must be examined.

2275. Respondents' linguistics expert, Professor Butters, opined that no reasonable consumer could interpret this ad to communicate that drinking eight ounces of POM juice prevents or reduces the risk of heart disease. (PX0350 (Butters, Dep. at 101-103).

2276. Several of Respondents' witnesses also testified that some of the "Cheat death" ad, including the headline and some words, was meant to be hyperbolic, puffery and humorous. (*See infra* ¶¶ 2278-2280.)

2277. Mr. Perdigao testified that the "Cheat death" execution was meant to be edgy and provocative with the unusual visual of a broken noose around the neck of a POM juice bottle. (CX1348 (Perdigao, Dep. 125-28)).

2278. Mr. Perdigao further testified that headline, graphics and line "Dying is so dead" were meant to be humorous, hyperbole and puffery. He said "it's going to extreme puffery in terms of the fact that our product is so healthy that this bottle was able to cheat death." (CX1348 (Perdigao, Dep. at 125-28)).

2279. Mr. Tupper also testified that much of the "Cheat death" advertisement was not meant to be interpreted literally, but was an example of puffery. (Tupper, Tr. 2987-90).

2280. Mrs. Resnick agreed that much of the "Cheat death" ad is puffery and stated that the headline is meant to convey the fact that the product is good for you. (CX1362 (L. Resnick, Dep. at 283-84)). She further testified that the idea of the ad is to make you laugh. "And what we're saying here essentially with puffery is that you'll live longer if you -- you can cheat death, which we all know you can't." (L. Resnick, Tr. 194).

2281. The overall net impression of this "Cheat death" ad is not that (a) drinking eight ounces of POM Juice prevents, treats or reduces the risk of certain diseases, such as heart disease or prostate cancer; or (b) drinking eight ounces of POM Juice is "clinically proven" to prevent, treat or reduce the risk of certain diseases, such as heart disease or prostate cancer. (CX0036_0001). Even, the language of the ad, itself, uses the qualifier "can help." (CX0036_0001).

2282. To the extent a "<u>may</u> reduce the risk" claim can be implied from this ad, the overall net impression is not that drinking eight ounces of POM Juice "reduces the risk" of certain diseases, such as heart disease or prostate cancer, like a drug with a single target of action, but "<u>may</u> reduce the risk," like a healthy diet of fruits and vegetables and exercise "may reduce the risk" of disease. (CX0036_0001).

2283. To the extent a "treat" claim can be implied from this ad (which it cannot), the overall net impression of any ad is not that POM Juice is a substitute for

conventional medical treatment. (Butters, Tr. 2821-22; Appendix of Advertisements); and

2284. To the extent a "proven" claim can be implied from this ad (which it cannot), the overall impression of "Cheat Death" is not that POM Juice is "proven" to be 100% effective in preventing, treating or reducing the risk of heart disease, prostate cancer or erectile dysfunction because "proven" in science means the "average person in the study benefitted." "Proven" does not mean that "everyone in the study necessarily benefitted." (Heber, Tr. 2011; Butters, Tr. 2893-94; PX0361 (Sacks, Dep. at 81)).

2285. Moreover, Complaint Counsel has presented no extrinsic evidence or expert opinion on the meaning of this "Cheat death" ad or of consumer perceptions or interpretations of the ad. ((PX0357 (Stewart Dep. at 49, 52); Mazis, Tr. 2752).

2286. Complaint Counsel also have presented no evidence that this "Cheat death" ad conveyed that POM Juice is "clinically proven" to prevent, treat or reduce the risk of any disease.

2287. Even assuming *arguendo* that this "Cheat death" ad conveys the message Complaint Counsel assigns to it, Professor Reibstein's survey effectively demonstrates that any alleged disease claims made by Respondents were not material to the purchasing decisions of POM consumers. (*See infra* (XVIII(A)(1)).

2288. Indeed, the NAD has found that the tagline "Cheat Death" to be in the realm of puffery and hyperbole. (CX0037; CX0055).

2289. Complaint Counsel have presented no reliable evidence to rebut Professor's Reibstein's survey findings or to show that any alleged disease claims made in POM's ads were material to the purchasing decisions of POM consumers.

2290. Complaint Counsel failed to present any evidence regarding the number of exposures consumers had to this ad or any particular POM advertisement.

2. Drink And Be Healthy

2291. According to Complaint Counsel, POM ran an advertisement with the headline "Drink and be healthy" with this body copy:

> **Drink and be healthy**.
>
> **100% all-natural pomegranate juice.**
> **The delicious, refreshing antioxidant superpower**.

> • **More naturally occurring antioxidant power than any other drink**, including red wine, blueberry juice, cranberry juice, orange juice and green tea.
>
> • **Antioxidants guard your body against harmful free radicals** that can cause heart disease, premature aging, Alzheimer's disease even cancer.
>
> [comparative chart omitted]
>
> • **Medical studies have shown that drinking 8oz. of POM Wonderful** pomegranate juice daily minimizes factors that lead to atherosclerosis (plaque buildup in the arteries), a major cause of heart disease.
>
> **In the refrigerated produce section of your grocer. www.pomwonderful.com**

(CX0016) (emphasis in original).

2292. Complaint Counsel contend that this "Drink and be healthy" headline and exact body copy ran on October 12, 2003. (CX0016_0001).

2293. Complaint Counsel have presented no other definitive dissemination information regarding this particular ad.

2294. The "Drink and be healthy" advertisement featured the image of a POM 100% Pomegranate Juice glass bottle, (CX0016_0001; Tupper, Tr. 2995), which Mr. Tupper testified that POM stopped using in the beginning of 2004. (Tupper, Tr. 2995).

2295. Mr. Tupper further testified that this advertisement ran in 2003 as part of the original launch of POM's 100% pomegranate juice and has not been disseminated since 2003. (Tupper, Tr. 2995).

2296. Mrs. Resnick also testified that this ad was one of the first ads Respondents ever ran. (L. Resnick, Tr. 157).

2297. Complaint Counsel have presented no evidence to contradict Mr. Tupper's testimony that this "Drink and be healthy" ad has not run in over nine years.

2298. Moreover, Complaint Counsel have presented no evidence that it is probable that Respondents would run this type of ad again.

2299. Because this ad stopped running more than nine years ago and there is no evidence that Respondents are likely to run this ad in the future, the ad provides no basis for injunctive relief.

2300. Nowhere in this ad do Respondents expressly (*i.e.*, unequivocally and directly) state that (a) POM Juice "prevents" or "treats" heart disease, prostate cancer and erectile dysfunction; or (b) POM Juice is "clinically proven" to "prevent," "treat," or "reduce the risk" of heart disease, prostate cancer and erectile dysfunction. (CX0016).

2301. Complaint Counsels' assertion that the ad conveys the message that (a) POM Juice "prevents," "treats," or "reduces the risk" of heart disease, prostate cancer and erectile dysfunction; or (b) POM Juice is "clinically proven" to "prevent," "treat," or "reduce the risk" of heart disease, prostate cancer and erectile dysfunction is conveyed in this "Drink and be healthy" ad is not conspicuous, self-evident, or reasonably clear from the face of the ad. (CX0016). Consequently, extrinsic evidence must be examined. (Mazis, Tr. 2752).

2302. Respondents' linguistics expert, Professor Butters, opined that it was unlikely that a reasonable consumer would conclude that drinking eight ounces of POM Juice would treat atherosclerosis. (Butters, Tr. 2930).

2303. The overall net impression of this "Drink and be health" ad is not that (a) drinking eight ounces of POM Juice prevents or treats certain diseases, such as heart disease or prostate cancer; or (b) drinking eight ounces of POM Juice is "clinically proven" to prevent, treat or reduce the risk of certain diseases, such as heart disease or prostate cancer. (CX0016). Even, the language of the ad, itself, uses the qualifier "can help." (CX0016).

2304. To the extent a "reduce the risk" claim can be implied from this ad, the overall net impression is not that drinking eight ounces of POM Juice "reduces the risk" of certain diseases, such as heart disease or prostate cancer, like a drug with a single target of action, but "reduces the risk," like a healthy diet of fruits and vegetables and exercise "reduces the risk" of disease. (CX0016).

2305. To the extent a "treat" claim can be implied from this ad (which it cannot), the overall net impression of any ad is not that POM Juice is a substitute for conventional medical treatment. (Butters, Tr. 2821-22; Appendix of Advertisements); and

2306. To the extent a "proven" claim can be implied from this ad (which it cannot), the overall impression of "Drink and be healthy" is not that POM Juice is "proven" to be 100% effective in preventing, treating or reducing the risk of heart disease, prostate cancer or erectile dysfunction because "proven" in science means the

"average person in the study benefitted." "Proven" does not mean that "everyone in the study necessarily benefitted." (Heber, Tr. 2011; Butters, Tr. 2893-2894; PX0361 (Sacks, Dep. at 81));

2307. Complaint Counsel have presented no extrinsic evidence or expert opinion on the meaning of this "Drink and be healthy" ad or of consumer perceptions or interpretations of the ad. (Mazis, Tr. 2752).

2308. Complaint Counsel also have presented no evidence that this "Drink and be healthy" ad conveyed that POM Juice is "clinically proven" to prevent, treat or reduce the risk of heart disease.

2309. The claim that POM Juice has more naturally occurring antioxidant power than red wine, blueberry juice, cranberry juice, orange juice and green tea is true, (Goldstein, Tr. 2595; PX0051), and Respondents had competent and reliable scientific evidence to support this representation at the time it was made. (*See infra* XVII(G)(3)).

2310. The statement that "Antioxidants guard your body against free radicals that can cause heart disease, premature aging, Alzheimer's disease even cancer" is also true, (*see infra* XVII(G)(3)), and Respondents had competent and reliable scientific evidence to support this representation at the time it was made. (*See infra* XVII(G)(3)).

2311. The statement "Medical studies show that drinking 8 oz. of POM Wonderful pomegranate juice daily minimizes factors that lead to atherosclerosis (plaque buildup in the arteries), a major cause of heart disease" also was true, and Respondents had competent and reliable scientific evidence to support this representation at the time it was made, including the Aviram Study (2004). (*See infra* XVII(G)(3)).

2312. Even assuming *arguendo* that this "Drink and be healthy" ad conveys the message Complaint Counsel assign to it, Professor Reibstein's survey effectively and powerfully demonstrates that any alleged disease claims made by Respondents were not material to the purchasing decisions of POM consumers. (*See infra* XVIII(A)).

2313. Complaint Counsel have presented no reliable evidence to rebut Professor's Reibstein's survey findings or to show that any alleged disease claims made in POM's ads were material to the purchasing decisions of POM consumers.

2314. Complaint Counsel failed to present any evidence regarding the number of exposures consumers had to this ad or any particular POM advertisement.

3. Decompress

2315. According to Complaint Counsel, POM ran an advertisement with the headline "Decompress" with this body copy:

> **Decompress**.
>
> Amaze your cardiologist. Drink POM Wonderful Pomegranate Juice. It helps guard your body against free radicals, unstable molecules that emerging science suggests aggressively destroy and weaken healthy cells in your body and contribute to disease. POM Wonderful Pomegranate Juice is supported by $20 million of initial scientific research from leading universities, which has uncovered encouraging results in prostate and cardiovascular health. Keep your ticker ticking and drink 8 ounces a day.
>
> **POM Wonderful Pomegranate Juice. The Antioxidant Superpower.**

(CX0103_0001; CX0459_0001) (emphasis in original).

2316. Complaint Counsel contend that this "Decompress" headline and exact body copy ran on March 1, 2007. (CX0103_0001).

2317. Complaint Counsel have presented no other definitive dissemination information regarding this particular ad.

2318. Mr. Tupper testified that Respondents has not disseminated this advertisement since at least 2008. (Tupper, Tr. 3004).

2319. Complaint Counsel have presented no evidence to contradict Mr. Tupper's testimony that this "Decompress" ad has not run in over four years.

2320. Moreover, Complaint Counsel have presented no evidence that it is probable that Respondents would run this type of ad again.

2321. Because this ad ceased running more than four years ago and there is no evidence that Respondents are likely to run this ad in the future, the ad provides no basis for injunctive relief.

2322. Nowhere in this ad do Respondents expressly (*i.e.*, unequivocally and directly) state that (a) POM Juice "prevents," "treats," or "reduces the risk" of heart disease, prostate cancer and erectile dysfunction; or (b) POM Juice is "clinically proven" to "prevent," "treat," or "reduce the risk" of heart disease, prostate cancer and erectile dysfunction. (CX0103_0001; CX0459_0001).

2323. The "Decompress" advertisement featured the image of a POM Juice bottle with a blood pressure cuff wrapped around it. (CX0103_0001; CX0459_0001).

2324. Complaint Counsels' assertion that the ad conveys the message that (a) POM Juice "prevents," "treats," or "reduces the risk" of heart disease, prostate cancer and erectile dysfunction; or (b) POM Juice is "clinically proven" to "prevent," "treat," or "reduce the risk" of heart disease, prostate cancer and erectile dysfunction is not conspicuous, self-evident, or reasonably clear from the face of the ad. (CX0103_0001; CX0459_0001). Consequently, extrinsic evidence must be examined. (See supra ¶ 2348).

2325. The overall net impression of this "Decompress" ad is not that (a) drinking eight ounces of POM Juice prevents, treats or reduces the risk of certain diseases, such as heart disease or prostate cancer; or (b) drinking eight ounces of POM Juice is "clinically proven" to prevent, treat or reduce the risk of certain diseases, such as heart disease or prostate cancer. (CX0103_0001; CX0459_0001). Even the language of the ad itself uses the qualifiers "helps guard", "emerging science suggests," "initial scientific research," and "encouraging results." (CX0103_0001; CX0459_0001).

2326. To the extent a "reduce the risk" claim can be implied from this ad, the overall net impression is not that drinking eight ounces of POM Juice "reduces the risk" of certain diseases, such as heart disease or prostate cancer, like a drug with a single target of action, but "reduces the risk," like a healthy diet of fruits and vegetables and exercise "reduces the risk" of disease. (CX0103_0001; CX0459_0001).

2327. To the extent a "treat" claim can be implied from this ad (which it cannot), the overall net impression of any ad is not that POM Juice is a substitute for conventional medical treatment. (Butters, Tr. 2821-22; Appendix of Advertisements).

2328. To the extent a "proven" claim can be implied from this ad (which it cannot), the overall impression of "Decompress" is not that POM Juice is "proven" to be 100% effective in preventing, treating or reducing the risk of heart disease, prostate cancer or erectile dysfunction because "proven" in science means the "average person in the study benefitted." "Proven" does not mean that "everyone in the study necessarily benefitted." (Heber, Tr. 2011; Butters, Tr. 2893-2894; PX0361 (Sacks, Dep. at 81)).

2329. The body copy of the ad itself does not use the words "blood pressure" or say anything about "blood pressure." (CX0103_0001; CX0459_0001).

2330. Several of Respondents' witnesses also testified that the intended message of the "Decompress" ad was not related to blood pressure. (*See infra* ¶¶ 2331-2336).

2331. Mr. Tupper expressly stated that Respondents did not intend to convey a message about blood pressure with the "Decompress" headline and image. (Tupper, Tr. 3004).

2332. Mr. Tupper testified that the ad was intended to let people know that POM juice is a healthy and natural product, as well as that it is backed by serious science indicating encouraging results for prostate and cardiovascular health. (Tupper , Tr. 3004-05).

2333. Mr. Tupper further testified that the blood pressure cuff coupled with the word "Decompress" was intended to convey a meaning of relaxation, de-stressing and general health. (Tupper, Tr. 3005). Indeed, the image of the blood pressure cuff image was intended to be a visual cue or a symbol that you would associate with cardiovascular health. (Tupper, Tr. 3005).

2334. Ms. Leow also testified that POM used the blood pressure cuff imagery to show or suggest that pomegranate juice may be healthy for the heart. (Leow, Tr. 489).

2335. Similarly, Mr. Resnick testified that the "Decompress" advertisement is a tongue-in-cheek way to show that POM is healthy and it will help your heart. (CX1376 (S. Resnick, Ocean Spray Dep. at 163-64)).

2336. Dr. Butters testified that it would be a gross exaggeration for anybody to think that the image of a blood pressure cuff around the POM Juice bottle and the headline "Decompress" could literally mean drink a glass of pomegranate juice and your blood pressure will go down. (Butters, Tr. 2933).

2337. Viewing the "Decompress" ad as a whole, including the interaction of the words and visual imagery, the overall net impression of the ad is that POM Juice is healthy, healthy for your heart and good for cardiovascular health. (*See supra* ¶¶ 2331-2336; CX0103_0001; CX0459_0001).

2338. In contrast, Complaint Counsel failed to provide any expert opinion on the meaning of this "Decompress" ad or of consumer perceptions or interpretations the "Decompress" ad with body copy referenced above.

2339. Complaint Counsel also have presented no reliable evidence that this "Decompress" ad conveyed that POM Juice is "clinically proven" to prevent, treat or reduce the risk of heart disease.

2340. Instead, Complaint Counsel have presented a conclusion from a 2009 survey of health-focused individuals conducted by the Bovitz Research Group (hereinafter "Bovitz Survey"), that found that approximately 14% of respondents who were shown only the "Decompress" billboard ad – i.e., an ad with the "Decompress"

headline and image but no body copy - thought that the billboard indicated that POM Juice could help/lower blood pressure. (PX0225; Reibstein, Tr. 2515).

2341. As testified to by Professor Reibstein, the Bovitz Survey is methodologically flawed, *see infra* (XVIII(C)(1)(b)), and substantively only relates to the "Decompress" ad without body copy. (*See* PX0223-0412).

2342. Complaint Counsel accordingly have presented no survey evidence or other evidence that anyone who viewed the "Decompress" headline and imagery with the body copy quoted above would construe that POM Juice is "clinically proven" to prevent, treat or reduce the risk of heart disease by lowering blood pressure.

2343. Moreover, as set forth above, because Respondents stopped running this ad in 2008, which was a year before the Bovitz Survey was even conducted, (*see supra* (XVIII(C)(1)(b)), Complaint Counsel has not presented any evidence that it is probable that Respondents would run this type of ad again.

2344. Moreover, even assuming *arguendo* that Complaint Counsel contend that other portions of the ad are false and misleading, the advertisement's reference that POM can help guard your body against free radicals is true, (*see* i*nfra* (XVII(G)(3)), and was substantiated by competent and reliable scientific evidence at the time it was made. (*See infra* (XVII(G)(3))).

2345. The advertisement's statement that POM Juice "is supported by $20 million of initial scientific research from leading universities" is also true. (*See infra* (XVII(G)(2))(emphasis added)).

2346. The advertisement's statement that "initial scientific research . . . has uncovered encouraging results in prostate and cardiovascular health" is also true, and was substantiated by competent and reliable scientific evidence, including the studies by Drs. Aviram, Ornish, Heber, Pantuck, Carducci and DeKernion. (*See infra* (XVII(G)(2))(emphasis added).

2347. The words "can help," "initial" and "encouraging" also qualified the health-related message contained in the ad. (CX0103_0001; CX0459_0001).

2348. Complaint Counsel have to present any evidence regarding the number of exposures consumers had to this ad or any particular POM advertisement. (Mazis, Tr. 2752).

4. Floss your arteries. Daily

2349. According to Complaint Counsel, Respondents ran an advertisement with the headline "Floss your arteries. Daily" with this body copy:

Floss your arteries. Daily.

Clogged arteries lead to heart trouble. It's that simple. That's where we come in. Delicious POM Wonderful Pomegranate Juice has more naturally occurring antioxidants than any other drink. Theses antioxidants fight free radicals - - molecules that are the cause of sticky, artery clogging plaque. Just eight ounces a day can reduce plaque up to 30%! So every day: wash your face, brush your teeth, and drink your POM Wonderful.

POM Wonderful Pomegranate Juice. The Antioxidant Superpower.

(CX0031_001) (emphasis in original).

2350. In contrast to future ads which specifically described Respondents' scientific studies on the Challenged Products, the "Floss your arteries" ad included a quantified performance claim. (CX0031_001; CX0055_0011-0012).

2351. Complaint Counsel contend that this "Floss your arteries" headline and exact body copy ran on December 1, 2004. (CX0031_0001).

2352. Complaint Counsel have presented no other definitive dissemination information regarding this particular ad.

2353. Mr. Tupper testified that POM first ran this advertisement in 2004 and stopped running it that same year. The "Floss your arteries" headline, image and body copy thus have not run as part of any advertisement for more than seven years. (Tupper, Tr. 2996).

2354. Complaint Counsel have presented no evidence to contradict Mr. Tupper's or Mrs. Resnick's testimony that this "Floss your arteries" ad has not run in more than seven years.

2355. Moreover, Complaint Counsel have presented no evidence that it is probable or likely that Respondents would run this type of ad again.

2356. Because this ad ran over seven years ago and there is no evidence that Respondents are likely to run this ad in the future, the ad provides no basis for injunctive relief.

2357. Moreover, at the time the "Floss your arteries" ad was run in 2004, the phrase "a glass a day can reduce plaque by up to 30%" was supported by competent and reliable scientific evidence, including the Aviram Study (2004), which found a

35% decrease in CIMT in people that had severe carotid stenosis and significant plaque build-up (i.e., a baseline IMT more than 1.5 mm). (Tupper, Tr. 954; (*see supra* XVII(G))).

2358. Additionally, the use of the phrase "up to" and the word "can" instead of "will" qualifies the statement "A glass a day can reduce plaque by up to 30%". (Butters, Tr. 2913).

2359. Moreover, the advertisement's statement that "antioxidants fight free radicals that cause plaque is true and substantiated by competent and reliable scientific evidence. (*see supra* XVII(G)).

2360. Nowhere in this ad do Respondents expressly (*i.e.*, unequivocally and directly) state that (a) POM Juice "prevents," "treats," or "reduces the risk" of heart disease; or (b) POM Juice is "clinically proven" to "prevent," "treat," or "reduce the risk" of heart disease. (CX0031).

2361. Complaint Counsels' assertion that the ad conveys the message that (a) POM Juice "prevents," "treats," or "reduces the risk" of heart disease; or (b) POM Juice is "clinically proven" to "prevent," "treat," or "reduce the risk" of heart disease is not conspicuous, self-evident, or reasonably clear from the face of the ad. (CX0031). Consequently, extrinsic evidence must be examined. (Mazis, Tr. 2752).

2362. The overall net impression of this "Floss your arteries" ad is not that (a) drinking eight ounces of POM Juice prevents, treats or reduces the risk of certain diseases, such as heart disease; or (b) drinking eight ounces of POM Juice is "clinically proven" to prevent, treat or reduce the risk of certain diseases, such as heart disease. (CX0031).

2363. Indeed, in 2005, the NAD found that the statement "A glass a day can reduce plaque by up to 30%" was not an establishment claim (*i.e.*, a "clinically proven" claim). (CX0037_0006-0007).

2364. The "Floss your arteries daily" advertisement featured the image of a POM 100% Pomegranate Juice bottle on a shelf next to, among other things, a toothbrush and a tube of tooth paste. (CX0031_0001). As such, the headline "Floss your arteries" is hyperbolic and humorous. (Butters, Tr. 2914-15).

2365. Viewing the "Floss your arteries" ad as a whole, including the interaction of the words and visual imagery, the overall net impression of the ad is that POM Juice is healthy and good for you. (CX0031). Mr. Butters testified that no reasonable person would take this ad literally. (Butters, Tr. 2914).

2366. In contrast, Complaint Counsel have presented no extrinsic evidence or expert opinion on the meaning of this "Floss your arteries" ad or of consumer perceptions or interpretations of the ad. ((PX0357 (Stewart Dep. at 49, 52); (Mazis, Tr. 2752)).

2367. To the extent a "may reduce the risk" claim can be implied from this ad, the overall net impression is not that drinking eight ounces of POM Juice "reduces the risk" of heart disease, like a drug with a single target of action, but "may reduce the risk," like a healthy diet of fruits and vegetables and exercise "may reduce the risk" of heart disease. (CX0031).

2368. To the extent a "treat" claim can be implied from this ad (which it cannot), the overall net impression of any ad is not that POM Juice is a substitute for conventional medical treatment. (Butters, Tr. 2821-22; Appendix of Advertisements).

2369. To the extent a "proven" claim can be implied from this ad (which it cannot), the overall impression of "Floss your arteries" is not that POM Juice is "proven" to be 100% effective in preventing, treating or reducing the risk of heart disease because "proven" in science means the "average person in the study benefitted." "Proven" does not mean that "everyone in the study necessarily benefitted." (Heber, Tr. 2011; Butters, Tr. 2893-2894; PX0361 (Sacks, Dep. at 81)).

2370. Complaint Counsel have presented no evidence that this "Floss your arteries" ad conveyed that POM Juice is "clinically proven" to prevent, treat or reduce the risk of any disease.

2371. Even assuming *arguendo* that this "Floss your arteries" ad conveys the message Complaint Counsel assigns to it, Professor Reibstein's survey effectively demonstrates that any alleged disease claims made by Respondents were not material to the purchasing decisions of POM consumers. (*See infra* (XVIII(A)(1)).

2372. Complaint Counsel have presented no reliable evidence to rebut Professor's Reibstein's survey findings or to show that any alleged disease claims made in POM's ads were material to the purchasing decisions of POM consumers.

2373. Complaint Counsel failed to present any evidence regarding the number of exposures consumers had to this ad or any particular POM advertisement.

5. Amaze your cardiologist

2374. According to Complaint Counsel, Respondents ran an advertisement with the headline "Amaze your cardiologist" with this body copy:

Amaze your cardiologist.

Ace your EKG: just drink 8 ounces of delicious POM Wonderful Pomegranate juice a day. It has more naturally occurring antioxidants than any other drink. Antioxidants fight free radicals . . . nasty little molecules that can cause sticky, artery clogging plaque. A glass a day can reduce plaque by up to 30%! Trust us, your cardiologist will be amazed.

POM Wonderful Pomegranate Juice. The Antioxidant Superpower.

(CX0034_0001;CX0471_0012) (emphasis in original).

2375. Complaint Counsel contend that this "Amaze your cardiologist" headline and exact body copy ran on February 1, 2005. (CX0034_0001).

2376. Complaint Counsel have presented no other definitive dissemination information regarding this particular ad.

2377. As with the "Floss your arteries" ad described above, which has similar body copy, Mr. Tupper testified that this advertisement stopped running in 2005 and has not been disseminated in more than six years. (Tupper, Tr. 2996-97; CX1353 (Tupper. Dep. at 131)).

2378. Complaint Counsel have presented no evidence to contradict Mr. Tupper's testimony that this "Amaze your cardiologist" advertisement has not run in more than six years.

2379. Moreover, Complaint Counsel has presented no evidence that it is probable that Respondents would run this type of ad again.

2380. Because this ad has not run for eight years and there is no evidence that Respondents are likely to run this ad in the future, the ad provides no basis for injunctive relief.

2381. At the time the "Amaze your cardiologist" ad was run in 2004, the phrase "a glass a day can reduce plaque by up to 30%" was supported by competent and reliable scientific evidence, including the Aviram Study (2004), which found a 35% decrease in CIMT in people that had severe carotid stenosis and significant plaque build-up (i.e., a baseline IMT more than 1.5 mm). (Tupper, Tr. 954; (*see supra* XVII(G)).

2382. Additionally, the use of the phrase "up to" and the word "can" instead of "will" qualifies the statement "A glass a day can reduce plaque by up to 30%". (Butters, Tr. 2913).

2383. Moreover, the advertisement's statement that "Antioxidants fight free radicals" is true and substantiated by competent and reliable scientific evidence. (*See supra* XVII(G)).

2384. Nowhere in this ad do Respondents expressly (*i.e.*, unequivocally and directly) state that (a) POM Juice "prevents," "treats," or "reduces the risk" of heart disease; or (b) POM Juice is "clinically proven" to "prevent," "treat," or "reduce the risk" of heart disease. (CX0034).

2385. Complaint Counsels' assertion that the ad conveys the message that (a) POM Juice "prevents," "treats," or "reduces the risk" of heart disease; or (b) POM Juice is "clinically proven" to "prevent," "treat," or "reduce the risk" of heart disease is not conspicuous, self-evident, or reasonably clear from the face of the ad. (CX0034). Consequently, extrinsic evidence must be examined. (Mazis, Tr. 2752).

2386. In 2005, the NAD found that the statement "A glass a day can reduce plaque by up to 30%" was not an establishment claim (*i.e.*, a "clinically proven" claim). (CX0037_0006-0007).

2387. The "Amaze your cardiologist" advertisement featured the image of a POM Wonderful 100% Pomegranate Juice bottle attached with EKG sensors. (CX0034_0001;CX0471_0012).

2388. The overall net impression of this "Amaze your cardiologist" ad is not that (a) drinking eight ounces of POM Juice prevents, treats or reduces the risk of certain diseases, such as heart disease; or (b) drinking eight ounces of POM Juice is "clinically proven" to prevent, treat or reduce the risk of certain diseases, such as heart disease. (CX0034_0001;CX0471_0012).

2389. To the extent a "<u>may</u> reduce the risk" claim can be implied from this ad, the overall net impression is not that drinking eight ounces of POM Juice "reduces the risk" of heart disease, like a drug with a single target of action, but "may reduce the risk," like a healthy diet of fruits and vegetables and exercise "may reduce the risk" of heart disease. (CX0034_0001;CX0471_0012).

2390. To the extent a "treat" claim can be implied from this ad (which it cannot), the overall net impression of any ad is not that POM Juice is a substitute for conventional medical treatment. (Butters, Tr. 2821-22; Appendix of Advertisements).

2391. To the extent a "proven" claim can be implied from this ad (which it cannot), the overall impression of "Amaze your cardiologist" is not that POM Juice is "proven" to be 100% effective in preventing, treating or reducing the risk of heart disease because "proven" in science means the "average person in the study benefitted." "Proven" does not mean that "everyone in the study necessarily benefitted." (Heber, Tr. 2011; Butters, Tr. 2893-2894; PX0361 (Sacks, Dep. at 81)).

2392. The image in the advertisement, the headline "Amaze your cardiologist," and the phrases "ACE your EKG" and "your cardiologist will be amazed" were intended as puffery. Dr. Butters testified that the headline "Amaze your cardiologist" is hyperbolic. (Butters, Tr. 2914-15). Even Dr. Stewart, Complaint Counsels' own expert, testified that the headline "Amaze your cardiologist" is not to be taken literally. (Stewart, Tr. 3230).

2393. Mr. Tupper testified that POM did intend for the image of the bottle with little EKG sticks on it to be a visual cue drawing attention to the encouraging research about pomegranate juice and cardiovascular health. (Tupper, Tr. 3005).

2394. Viewing the "Amaze your cardiologist" ad as a whole, including the interaction of the words and visual imagery, the overall net impression of the ad is that POM Juice is healthy and good for you. (CX0034_0001;CX0471_0012; Tupper, Tr. 3005).

2395. In contrast, Complaint Counsel have presented no extrinsic evidence or expert opinion on the meaning of this "Amaze your cardiologist" ad or of consumer perceptions or interpretations of the ad. (PX0357 (Stewart Dep. at 49, 52); (Mazis, Tr. 2752)).

2396. Complaint Counsel also have presented no evidence that this "Amaze your cardiologist" ad conveyed that POM Juice is "clinically proven" to prevent, treat or reduce the risk of heart disease.

2397. Even assuming *arguendo* that this "Amaze your cardiologist" ad conveys the message Complaint Counsel assigns to it, Professor Reibstein's survey effectively demonstrates that any alleged disease claims made by Respondents were not material to the purchasing decisions of POM consumers. (*See infra* (XVIII(A)(1)).

2398. Complaint Counsel failed to present any evidence regarding the number of exposures consumers had to this ad or any particular POM advertisement.

2399. Complaint Counsel have presented no reliable evidence to rebut Professor's Reibstein's survey findings or to show that any alleged disease claims made in POM's ads were material to the purchasing decisions of POM consumers.

6. Imitation May Be Sincere. But Is It Pure?

2400. According to Complaint Counsel, Respondents ran an advertisement with the headline "Imitation may be sincere. But is it pure?" with this body copy:

> **Imitation may be sincere. But is it pure?**
>
> There are a lot of pomegranate juices on the market, but only one is guaranteed to be 100% pure pomegranate juice: the original POM Wonderful. It's the only pomegranate juice that's actually quality-controlled from tree to bottle. The only one that doesn't add sugar, colorants or cheap filler juices. And, perhaps most importantly, the only one that's backed by $25 million in published medical research. So be aware of what's in your pomegranate juice. Beware of impostors. **Trust in POM**.

(CX0251_001) (emphasis in original).

2401. Complaint Counsel contends that this "Imitation may be sincere ad" and exact body copy ran on November 1, 2008. (CX0251_0001).

2402. Complaint Counsel has presented no other dissemination information regarding this particular ad.

2403. Mr. Tupper testified that the ad ran only once in 2008, over three years ago. Mr. Tupper testified that the reference to a number of "published studies" was simply an inadvertent mistake because some of the studies had not been "published". The ad should have said "backed by $25 million in medical research" and when the mistake was discovered, the word "published" was quickly eliminated. (Tupper, Tr. 1041, 3003).

2404. Complaint Counsel have presented no evidence to contradict Mr. Tupper's testimony that this ad has not run again.

2405. Moreover, Complaint Counsel have presented no evidence that it is probable that Respondents would run this type of ad again.

2406. Because this ad last ran more than three years ago, it was the result of an inadvertent, one-time mistake and there is no evidence that Respondents are likely to run this ad in the future, the ad provides no basis for injunctive relief.

2407. Nowhere in this ad do Respondents expressly (*i.e.*, unequivocally and directly) state that (a) POM Juice "prevents," "treats," or "reduces the risk" of heart disease, prostate cancer and erectile dysfunction; or (b) POM Juice is "clinically proven" to "prevent," "treat," or "reduce the risk" of heart disease, prostate cancer and erectile dysfunction. (CX0251).

2408. Complaint Counsels' assertion that the ad conveys the message that (a) POM Juice "prevents," "treats," or "reduces the risk" of heart disease, prostate cancer and erectile dysfunction; or (b) POM Juice is "clinically proven" to "prevent," "treat," or "reduce the risk" of heart disease, prostate cancer and erectile dysfunction is not conspicuous, self-evident, or reasonably clear from the face of the ad. (CX0251). Consequently, extrinsic evidence must be examined. (Mazis, Tr. 2752).

2409. The overall net impression of this ad is not that (a) drinking eight ounces of POM Juice prevents, treats or reduces the risk of certain diseases, such as heart disease, prostate cancer or erectile dysfunction; or (b) drinking eight ounces of POM Juice is "clinically proven" to prevent, treat or reduce the risk of certain diseases, such as heart disease, prostate cancer or erectile dysfunction. (CX0251).

2410. To the extent a "reduce the risk" claim can be implied from this ad, the overall net impression is not that drinking eight ounces of POM Juice "reduces the risk" of certain diseases, such as heart disease, prostate cancer or erectile dysfunction, like a drug with a single target of action, but "reduces the risk," like a healthy diet of fruits and vegetables and exercise "reduces the risk" of disease. (CX0251).

2411. To the extent a "treat" claim can be implied from this ad (which it cannot), the overall net impression of any ad is not that POM Juice is a substitute for conventional medical treatment. (Butters, Tr. 2821-22; Appendix of Advertisements).

2412. To the extent a "proven" claim can be implied from this ad (which it cannot), the overall impression of ad is not that POM Juice is "proven" to be 100% effective in preventing, treating or reducing the risk of heart disease, prostate cancer or erectile dysfunction because "proven" in science means the "average person in the study benefitted." "Proven" does not mean that "everyone in the study necessarily benefitted." (Heber, Tr. 2011; Butters, Tr. 2893-2894; PX0361 (Sacks, Dep. at 81)).

2413. Complaint Counsel, however, have presented no extrinsic evidence or expert opinion on the meaning of this "Imitation may be sincere" ad or of consumer perceptions or interpretations of the ad. (PX0357 (Stewart Dep. at 49, 52) (Mazis, Tr. 2752)).

2414. Complaint Counsel also have presented no evidence that this "Imitation may be sincere" ad conveyed that POM Juice is "clinically proven" to prevent, treat or reduce the risk of any disease.

2415. Even assuming *arguendo* that this "Imitation may be sincere" ad conveys the message Complaint Counsel assigns to it, Professor Reibstein's survey effectively demonstrates that any alleged disease claims made by Respondents were not material to the purchasing decisions of POM consumers. (*See infra* (XVIII(A)(1))).

2416. Moreover, because Professor Reibstein's uncontroverted survey showed that none of the respondents bought POM because of the number of "published" studies versus "unpublished" studies, it is not likely that any significant number of consumers bought POM because of the numerous studies that had been "published". (PX0223-0006-0007, 00020).

2417. Complaint Counsel have presented no reliable evidence to rebut Professor's Reibstein's survey findings.

2418. Complaint Counsel failed to present any evidence regarding the number of exposures consumers had to this ad or any particular POM advertisement.

7. Ingredients: Pomegranates, $25 Million In Medical Research.

2419. Complaint Counsel has presented no definitive evidence that Respondents ran an advertisement with the headline "Ingredients: pomegranates, $25 million in medical research." (CX314_010).

2420. Complaint Counsel accordingly cannot challenge this ad because they have not proven that Respondents disseminated it, thus narrowing the universe of ads "at issue."

2421. According to CX0314_0010, the body copy of the ad read, in pertinent part:

> **Ingredients: pomegranates, $25 million in medical research.**
>
> What goes into our POM Wonderful bottle goes into you – 100% authentic Wonderful variety pomegranate juice, your daily dose of free-radical fighting antioxidants, $25 million in published medical research and proven health benefits. Nothing else. That means no cheap filler juices. No sweeteners. And no added colorants. So read the label. And drink to your health. **Trust in POM**.

(CX314_010) (emphasis in original).

2422. Assuming the advertisement did run, Mr. Tupper testified with respect to a very similar ad - the "Imitation may be sincere" ad. Specifically, Mr. Tupper testified that the phrase "$25 million in published medical research" was simply an inadvertent mistake that word "published" was used in the phrase "backed by $25 million in published medical research." (Tupper, Tr. 1041, 3003).

2423. Nowhere in this ad do Respondents expressly (*i.e.*, unequivocally and directly) state that (a) POM Juice "prevents," "treats," or "reduces the risk" of heart disease, prostate cancer and erectile dysfunction; or (b) POM Juice is "clinically proven" to "prevent," "treat," or "reduce the risk" of heart disease, prostate cancer and erectile dysfunction. (CX000314_0010).

2424. Complaint Counsels' assertion that the ad conveys the message that (a) POM Juice "prevents," "treats," or "reduces the risk" of heart disease, prostate cancer and erectile dysfunction; or (b) POM Juice is "clinically proven" to "prevent," "treat," or "reduce the risk" of heart disease, prostate cancer and erectile dysfunction is not conspicuous, self-evident, or reasonably clear from the face of the ad. (CX000314_0010). Consequently, extrinsic evidence must be examined. (Mazis, Tr. 2752).

2425. The overall net impression of this ad is not that (a) drinking eight ounces of POM Juice prevents, treats or reduces the risk of certain diseases, such as heart disease, prostate cancer or erectile dysfunction; or (b) drinking eight ounces of POM Juice is "clinically proven" to prevent, treat or reduce the risk of certain diseases, such as heart disease, prostate cancer or erectile dysfunction. (CX000314_0010).

2426. To the extent a "reduce the risk" claim can be implied from this ad, the overall net impression is not that drinking eight ounces of POM Juice "reduces the risk" of certain diseases, such as heart disease, prostate cancer or erectile dysfunction, like a drug with a single target of action, but "reduces the risk," like a healthy diet of fruits and vegetables and exercise "reduces the risk" of disease. (CX000314_0010).

2427. To the extent a "treat" claim can be implied from this ad (which it cannot), the overall net impression of any ad is not that POM Juice is a substitute for conventional medical treatment. (Butters, Tr. 2821-22; Appendix of Advertisements).

2428. To the extent a "proven" claim can be implied from this ad (which it cannot), the overall impression of ad is not that POM Juice is "proven" to be 100% effective in preventing, treating or reducing the risk of heart disease, prostate cancer or erectile dysfunction because "proven" in science means the "average person in the study benefitted." "Proven" does not mean that "everyone in the study necessarily

benefitted." (Heber, Tr. 2011; Butters, Tr. 2893-2894; PX0361 (Sacks, Dep. at 81)).

2429. Complaint Counsel, however, have presented no extrinsic evidence or expert opinion on the meaning of this "Ingredients: pomegranates, $25 million in medical research" ad or of consumer perceptions or interpretations of the ad. (PX0357 (Stewart Dep. at 49, 52); (Mazis, Tr. 2752)).

2430. Complaint Counsel also have presented no evidence that this "Ingredients: pomegranates, $25 million in medical research" ad conveyed that POM Juice is "clinically proven" to prevent, treat or reduce the risk of any disease.

2431. Even assuming *arguendo* that this "Ingredients: pomegranates, $25 million in medical research" ad conveys the message Complaint Counsel assigns to it, Professor Reibstein's survey effectively demonstrates that any alleged disease claims made by Respondents were not material to the purchasing decisions of POM consumers. (*See infra* (XVIII(A)(1)).

2432. Moreover, because Dr. Reibstein's uncontroverted survey showed that none of the respondents bought POM because of the number of "published" studies versus "unpublished" studies, it is not likely that any significant number of consumers bought POM because of the numerous studies that had been "published." (PX0223-0006-0007, 00020).

2433. Complaint Counsel have presented no reliable evidence to rebut Professor's Reibstein's survey findings.

2434. Complaint Counsel failed to present any evidence regarding the number of exposures consumers had to this ad or any particular POM advertisement.

8. pomwonderful.com "Real Studies" Web Page

2435. Paragraph 9.F of the Complaint and Exh. E-2, attached thereto, (CX1426, Exh. E-2) identify a screen capture from POM's pomwonderful.com "Real Studies" web page, which allegedly contained the following text as of April 29, 2009:

> ACE and Systolic Blood Pressure.
>
> With hypertension, or high blood pressure, the heart works harder. Arteries are under pressure and the chances of a stroke or heart attack are greater. [footnote omitted] ACE (or angiotensin converting enzyme) is an enzyme that the body produces which may lead to high blood pressure resulting in atherosclerosis. [footnote omitted] In a preliminary research study, ten elderly patients with hypertension drank 8 oz. of

> POM Wonderful 100% Pomegranate Juice a day for just two weeks. After those two weeks, in those patients drinking POM Wonderful ACE activity was significantly decreased by 36%, and, they also saw their systolic blood pressure drop by 5%. [footnote omitted]

(CX1426, Exh. E-2).

2436. Complaint Counsel have presented no other definitive dissemination information regarding this particular ad.

2437. Historically, Respondents ran advertisements that mentioned blood pressure among a list of other health conditions for which pomegranate juice may have some benefit. (Tupper, Tr. 2992). POM, however, never ran advertisements that explicitly focused on blood pressure. (Tupper, Tr. 2992).

2438. Any very early ads that referred to blood pressure benefits were supported by competent and reliable scientific evidence, including the Aviram Study (2001) that found a 5% decrease in systolic blood pressure and the Aviram Study (2004) that found a 12% decrease in systolic blood pressure. (*See infra* XIV(F)).

2439. When subsequent studies did not a show a similar result, although they did not use the specialized equipment needed for an accurate blood pressure study, (Heber, Tr. 2040), and Mr. Resnick did not receive a satisfactory explanation, Mr. Resnick requested that Respondents stop mentioning blood pressure in any advertisements. Mr. Resnick's view was that the science was too ambiguous to justify any claim. Mr. Tupper testified that this occurred in 2007, if not even sooner. (Tupper, Tr. 2993).

2440. All references to blood pressure should have been removed when the website was updated between 2006 and 2007 to conform to Respondents' change in policy about how Respondents discuss scientific findings with the public. (Tupper, Tr. 2977, 2986-87, 2993).

2441. After 2007, any lingering reference to blood pressure on any of the POM Wonderful web pages was an inadvertent mistake, (Tupper, Tr. 2993), including the short reference to blood pressure in POM's pomwonderful.com "Real Studies" web page quoted above. (Tupper, Tr. 3006). These lines have since been deleted from POM's webpage. (Tupper, Trial Tr. 3006).

2442. Nowhere on this web page do Respondents expressly (*i.e.*, unequivocally and directly) state that (a) POM Juice "prevents," "treats," or "reduces the risk" of heart disease by lowering blood pressure; or (b) POM Juice is "clinically proven" to "prevent," "treat," or "reduce the risk" of heart disease. (CX1426, Exh. E-2).

2443. Complaint Counsels' assertion that the ad conveys the message that (a) POM Juice "prevents," "treats" or "reduces the risk of heart disease; or (b) POM Juice is "clinically proven" to "prevent," "treat," or "reduce the risk" of heart disease is not conspicuous, self-evident, or reasonably clear from the face of the ad. (CX1426, Exh. E-2). Consequently, extrinsic evidence must be examined. (Mazis, Tr. 2752).

2444. The overall net impression of this web page is not that (a) drinking eight ounces of POM Juice prevents or treats heart disease by lowering blood pressure; or (b) drinking eight ounces of POM Juice is "clinically proven" to prevent, treat or reduce the risk of heart disease. (CX1426, Exh. E-2).

2445. To the extent a "reduce the risk" claim can be implied from this ad, the overall net impression is not that drinking eight ounces of POM Juice "reduces the risk" of heart disease, like a drug with a single target of action, but "reduces the risk," like a healthy diet of fruits and vegetables and exercise "reduces the risk" of heart disease. (CX1426, Exh. E-2).

2446. To the extent a "treat" claim can be implied from this ad (which it cannot), the overall net impression of any ad is not that POM Juice is a substitute for conventional medical treatment. (Butters, Tr. 2821-22; Appendix of Advertisements).

2447. To the extent a "proven" claim can be implied from this ad (which it cannot), the overall impression of this web page is not that POM Juice is "proven" to be 100% effective in preventing, treating or reducing the risk of heart disease because "proven" in science means the "average person in the study benefitted." "Proven" does not mean that "everyone in the study necessarily benefitted." (Heber, Tr. 2011; Butters, Tr. 2893-2894; PX0361 (Sacks, Dep. at 81)).

2448. Complaint Counsel, however, have presented no extrinsic evidence or expert opinion on the meaning of these website lines or of consumer perceptions or interpretations of the website lines. (PX0357 (Stewart Dep. at 49, 52); (Mazis, Tr. 2752)).

2449. Complaint Counsel also have presented no evidence that this "Real Studies" web page conveyed that POM Juice is "clinically proven" to prevent, treat or reduce the risk of any disease.

2450. Even assuming *arguendo* that this "Real Studies" web page conveys the message Complaint Counsel assigns to it, Professor Reibstein's survey effectively demonstrates that any alleged disease claims made by Respondents were not material to the purchasing decisions of POM consumers. (*See infra* (XVIII(A)(1)).

2451. Complaint Counsel have presented no reliable evidence to rebut Professor's Reibstein's survey findings or to show that any alleged disease claims made in POM's ads were material to the purchasing decisions of POM consumers.

2452. Complaint Counsel failed to present any evidence regarding the number of exposures consumers had to this website material or any particular POM advertisement.

F. POM's advertisements Changed Significantly Throughout the Later Years From 2006 to 2011, Largely As a Result of the NAD Decisions in 2005 and 2006

2453. POM's ads have changed significantly over time since the early years when the "outlier" ads ran. (L. Resnick, Tr. 162, 168).

2454. In 2005 and 2006, the NAD issued two decisions. Notably, the NAD agreed with Respondents that the images and headlines in their ads constituted puffery. The following headlines, for example, were deemed to be in the realm of puffery and hyperbole: "Outlive Your Spouse," "Cheat Death," "Life Preserver," "Life Guard," "Relax You'll Live Longer," "Forever Young," and "The New Shape of Protection". (CX0037; CX0055).

2455. And, although, the NAD took issue with some of the language used to describe and qualify the science in the body copy of the advertisements, the NAD did not take issue with whether the science itself was significantly strong, valid or substantive. (Tupper, Tr. 2983-2984). Moreover, for some of the ads such as "Amaze your cardiologist" and "Floss your arteries," the NAD simply recommended that Respondents modify their claims. (CX0037).

2456. In response to those NAD decisions, starting in 2006, Respondents shifted the focus of their ads away from general statements and quantified performance claims, like those made in the "Floss your arteries" and "Amaze your cardiologist" ads. (Tupper, Tr. 2985-87; *see supra* (XVIII)).

2457. Instead, when Respondents wanted to advertise the science behind the Challenged Products, Respondents would summarize and describe the specific results of studies that were completed using appropriate language to qualify the description of the studies. (Tupper, Tr. 2985-87, 3026).

2458. Also, as a result of the NAD's decisions, Respondents would direct people back to their website to read the full study in some of their ads. (Tupper, Tr. 2985).

G. Respondents' Later Advertisements (2006 To 2011) Generally Fall Into Three Major Categories, All of Which are Truthful and Not

Misleading and Which Were Substantiated by Competent and Reliable Scientific Evidence

2459. The vast majority of POM's ads from 2006 through 2010 fall into three general categories: (a) specific study; (b) "backed by" and (c) antioxidant.

2460. The first category of ads, "specific study" ads, summarized some of Respondents' scientific studies on the Challenged Products in the areas of cardiovascular, prostate and erectile health.

2461. The second category, "backed by" ads, stated that Respondents spent a particular amount of money on their scientific studies on the Challenged Products to back-up Respondents' healthy claims.

2462. The third category, "antioxidant" ads, includes general antioxidant ads, comparative antioxidant ads, antioxidant benefits ads and multi-step ads. Generally, these antioxidant ads discussed the potential benefits of antioxidants and stated that the Challenged Products contained antioxidants.

2463. The ads in each of the three categories are qualified and substantiated by competent and reliable scientific evidence. (*See supra* (XIV, XV, XVI)).

2464. As analyzed in detail below, some ads fall into multiple and overlapping categories.

(a) For example, one ad may summarize a specific study and may make reference to a number of dollars spent on research. (*See, e.g.*, CX0328 (Your New Health Care Plan); CX0331 (Healthy, Wealthy, and Wise.); CX0337 (The First Bottle You Should Open in 2010); CX0280 (Live Long Enough to Watch your 401(k) Recover); CX0355 (The Only Antioxidant Supplement Rated X); CX0279 (Science, not fiction.); CX0180 (The antioxidant superpill); CX1426, Exh. J (Healthy, Wealthy, and Wise.); CX1426, Exh. K (The antioxidant superpill); CX0342 (Take Out a Life Insurance Supplement); CX0353 (Take Out a Life Insurance Supplement); CX0350 (24 Scientific Studies Now in One Easy-To-Swallow Pill); CX0348 (24 Scientific Studies Now in One Easy-To-Swallow Pill); CX0351 (The Only Antioxidant Supplement Rated X); CX0169 (The power of POM, in one little pill); CX1426, Exh. L (The power of POM, in one little pill); CX1426, Exh. M (Dreher Heart Newsletter); CX1426, Exh. I (Antioxidant Superpill); CX0122 (Science, not fiction); CX0372_0002 (HOLY HEALTH! $32 million in medical research); CX0379_0002 (HOLY HEALTH! $32 million in medical research); and CX0380_0002 (HOLY HEALTH! $32 million in medical research);

(b) Another ad may reference a specific study and also discuss the benefits of antioxidants found in pomegranate juice. (*See, e.g.*, CX0328 (Your New Health Care Plan);); CX0331 (Healthy, Wealthy, and Wise.); CX0337 (The First Bottle You Should Open in 2010);); CX0280 (Live Long Enough to Watch your 401(k); CX0355 (The Only Antioxidant Supplement Rated X); CX0279 (Science, not fiction.); CX0180 (The antioxidant superpill); CX1426, Exh. K (The antioxidant superpill); CX0120 (One small pill for mankind); CX0122 (Science, not fiction); CX1426, Exh. J (Healthy, Wealthy, and Wise); CX0342 (Take Out a Life Insurance Supplement); CX0353 (Take Out a Life Insurance Supplement); CX0350 (24 Scientific Studies Now in One Easy-To-Swallow Pill); CX0348 (24 Scientific Studies Now in One Easy-To-Swallow Pill); CX0351 (The Only Antioxidant Supplement Rated X); CX0169 (The power of POM, in one little pill); CX1426, Exh. L (The power of POM, in one little pill); CX1426, Exh. M (Dreher Heart Newsletter); CX0029 (Studies Show That 10 Out of 10 People Don't Want to Die); CX1426, Exh. I (Antioxidant Superpill); and CX1426, Exh. N (Dreher Prostate Newsletter); and

(c) Another ad may describe a specific study, describe the benefits of antioxidants and also state the number of dollars Respondents spent on scientific research. (See, e.g., CX0328 (Your New Health Care Plan); CX0331 (Healthy, Wealthy, and Wise.); CX0337 (The First Bottle You Should Open in 2010); CX0280 (Live Long Enough to Watch your 401(k) Recover); CX0355 (The Only Antioxidant Supplement Rated X); CX0279 (Science, not fiction.); CX0180 (The antioxidant superpill); CX1426, Exh. J (Healthy, Wealthy, and Wise); CX1426, Exh. K (The antioxidant superpill); CX0342 (Take Out a Life Insurance Supplement); CX0353 (Take Out a Life Insurance Supplement); CX0350 (24 Scientific Studies Now in One Easy-To-Swallow Pill); CX0348 (24 Scientific Studies Now in One Easy-To-Swallow Pill); CX0351 (The Only Antioxidant Supplement Rated X); CX0169 (The power of POM, in one little pill); CX1426, Exh. L (The power of POM, in one little pill); CX1426, Exh. M (Dreher Heart Newsletter); CX0122 (Science, not fiction); CX1426, Exh. I (Antioxidant Superpill); and CX1426, Exh. N (Dreher Prostate Newsletter).

2465. No matter how the ads are categorized, the overarching commonality among all the ads is that they used qualified language to describe the health-related benefits of the Challenged Products. (*See infra* (XVII(G)(1-3)).

2466. For example and as described in detail below and in the attached Appendix of Advertisements, POM's ads generally conveyed the restrained and qualified message that scientific studies show results that are merely "promising," "encouraging" or "hopeful" for prostate, cardiovascular and erectile health or

stated that POM "may" help with a particular condition or that POM is "fighting" for better health in a particular area. (*See* Appendix of Advertisements).

2467. Nowhere in the three categories of ads do Respondents expressly (*i.e.,* unequivocally and directly) state that the Challenged Products "prevent," "treat" or "reduce the risk" of heart disease, prostate cancer and erectile dysfunction. (*See* Appendix of Advertisements).

2468. Nowhere in the three categories of ads do Respondents expressly (*i.e.,* unequivocally and directly) state that the Challenged Products are "clinically proven" to "prevent," "treat" or "reduce the risk" of heart disease, prostate cancer and erectile dysfunction. (*See* Appendix of Advertisements).

2469. The overall net impression of POM's ads that use qualified language, such as "promising," "encouraging" or "hopeful", is not that the Challenged Products are a "silver bullet against disease" or "clinically proven" to "prevent," "treat" or "reduce the risk" of heart disease, prostate cancer or erectile dysfunction. (*See* Appendix of Advertisements).

2470. POM's advertising, viewed as a whole, do not clearly and conspicuously convey to a reasonable consumer that the Challenged Products prevent, treat or reduce the risk of heart disease, prostate cancer and erectile dysfunction under Complaint Counsels' "net impression" analysis or any analysis for implied claims. (*See* Appendix of Advertisements);

2471. POM's advertising, viewed as a whole, do not clearly and conspicuously convey to a reasonable consumer that the Challenged Products are "clinically proven" to prevent, treat or reduce the risk of heart disease, prostate cancer and erectile dysfunction under Complaint Counsels' "net impression" analysis or any analysis for implied claims. (*See* Appendix of Advertisements);

2472. To the extent a "proven" claim can be implied from any of POM's advertising (which it cannot), the overall impression of any ad is not that the Challenged Products are "proven" to be 100% effective in preventing, treating or reducing the risk of heart disease, prostate cancer or erectile dysfunction because "proven" in science means the "average person in the study benefitted." "Proven" does not mean that "everyone in the study necessarily benefitted." (Heber, Tr. 2011; Butters, Tr. 2893-2894; PX0361 (Sacks, Dep. at 81)).

2473. To the extent a "treat" claim can be implied from any of POM's advertising (which it cannot), the overall net impression of any ad is not that the Challenged Products are a substitute for conventional medical treatment. (Butters, Tr. 2821-22; Appendix of Advertisements); and

2474. To the extent a "reduce the risk" claim can be implied from any of POM's advertising, the overall net impression of any ad is not that the Challenged Products "reduce the risk" of heart disease, prostate cancer or erectile dysfunction, like a drug with a single target of action, but "reduce the risk" like a healthy diet of fruits and vegetables and exercise "reduce the risk" of disease. (Butters Tr. 2817-18).

2475. Moreover, as set for the below and in the attached Appendix of Advertisements, Complaint Counsel failed to present any reliable extrinsic evidence or expert opinion (a) on the meaning of POM's ads or of consumers' expectations or perceptions or the ads, (b) that POM's ads conveyed that they are "clinically proven" to prevent, treat or reduce the risk of heart disease, prostate cancer or erectile dysfunction; (c) that POM's ads conveyed that the Challenged Products prevent, treat or reduce the risk of heart disease, prostate cancer or erectile dysfunction; or (d) of Respondents' intent to convey such messages to prove that POM's advertising made the alleged implied "clinically proven" disease claims. (*See* Appendix of Advertisements; Mazis, Tr. 2752).

2476. Additionally, Complaint Counsel have presented no reliable evidence to rebut Professor's Reibstein's survey findings or to show that any alleged disease claims made in POM's ads were material to the purchasing decisions of POM consumers.

2477. Complaint Counsel also failed to present any evidence regarding the number of exposures consumers had to this ad or any particular POM advertisement.

1. Respondents Disseminated "Specific Study" Ads That Are Not False and Misleading Because They Accurately and Truthfully Summarized Respondents' Scientific Studies on the Challenged Products and Described the Studies Using Qualified Language

2478. The first category, "specific study" ads, summarized some of the Respondents' scientific studies on the Challenged Products and described the results of the studies using qualified language. (*See, e.g.*, CX0328); CX0331 (Healthy, ~~Wealthy~~, and Wise.); CX0337 (The First Bottle You Should Open in 2010); CX0280 (Live Long Enough to Watch your 401(k) Recover); CX0355 (The Only Antioxidant Supplement Rated X); CX0279 (Science, not fiction.) CX0180 (The antioxidant superpill); CX1426, Exh. J (Healthy, ~~Wealthy~~, and Wise.); CX1426, Exh. K (The antioxidant superpill); CX0342 (Take Out a Life Insurance Supplement); CX0353 (Take Out a Life Insurance Supplement); CX0350 (24 Scientific Studies Now in One Easy-To-Swallow Pill); CX0348 (24 Scientific Studies Now in One Easy-To-Swallow Pill); CX0351 (The Only Antioxidant Supplement Rated X); CX0169 (The power of POM, in one little pill); CX1426, Exh. L (The power of POM, in one little pill); CX1426, Exh. M (Dreher Heart

Newsletter); CX0120 (One small pill for mankind); CX0122 (Science, not fiction); CX1426, Exh. B (Drink to prostate health); CX0260 (Drink to prostate health); CX1426 Exh. I (Antioxidant Superpill); CX1426, Exh. N (Dreher Prostate Newsletter);CX0372_0002 (HOLY HEALTH! $32 million in medical research); CX0379_0002 (HOLY HEALTH! $32 million in medical research); CX0380_0002 (HOLY HEALTH! $32 million in medical research); CX0314_0004 (POM Wonderful and Prostate Health); and CX0314_0008 (POM Wonderful and Prostate Health)

2479. While Respondents have sponsored at least one hundred scientific studies on the Challenged Products conducted in forty-four different and renowned medical institutions, sixty-seven of which were published in peer-reviewed journals and seventeen of which were human clinical studies, (*see supra* V), Respondents only specifically described four of these studies in the areas of prostate, cardiovascular and erectile health in their ads.

2480. These four studies include:

Prostate Health

(a) Pantuck AJ, Leppert JT, Zomorodian N, Aronson W, Hong J, Bardnard RJ, Seeram N, Liker H, Wang J, Elashoff R, Heber D, Aviram M, Ignarro L, Belldegrun A, *Phase II Study of Pomegranate Juice for Men with Rising Prostate-Specific Antigen following Surgery or Radiation for Prostate Cancer*, Clin. Cancer Research 12 (13): 4018-4026 (2006) (hereinafter "Pantuck Study (2006)"). (PX0060);

Cardiovascular Health

(b) Aviram M, Rosenblat M, Gaitini M, Nitecki S, Hoffman A, Dornfeld L, Volkova N, Presser D, Attias J, Liker H, and Hayek T, *Pomegranate juice consumption for 3 years by patients with carotid artery stenosis reduces common carotid intimamedia thickness, blood pressure and LDL oxidation*, 23 Clin. Nutr. 423-33 (2004). Erratum in 27 Clin. Nutr. 671 (2008) (hereinafter, "Aviram Study 2004") (CX0611);

(c) Sumner M, Elliott-Eller M, Weidner G, Daubenmier JJ, Chew MH, Marlin R, Raisin CJ, and Ornish D, *Effects of pomegranate juice consumption on myocardial perfusion in patients with coronary heart disease*, 96 Am. J. Cardiology 810 (2005) (hereinafter "Bev I Coronary Perfusion Study") (PX0023);

Erectile Health

(d) CP Forest, H Padma-Nathan and HR Liker, Efficacy and safety of pomegranate juice on improvement of erectile dysfunction in male patients with mild to moderate erectile dysfunction: a randomized, placebo-controlled, double-blind, crossover study, 19 Int J Impot Res. 564-67 (2007) (hereinafter "Forest/Padma-Nathan RCT Study") (CX908).

2481. As described below, the "specific study" ads on prostate, cardiovascular and erectile health ads are not false and misleading.

2482. They accurately and truthfully summarize the scientific studies in question. (*See supra* XVI(D)).

2483. Moreover, as detailed below, each "specific study" ad uses qualified language to describe the studies and other claims in the ads.

(a) Prostate Health - Pantuck Study (2006)

2484. In the Pantuck Study (2006), Dr. Pantuck and his colleagues at UCLA Medical School found that through the consumption of pomegranate juice, the mean PSA doubling time significantly increased with treatment from a mean of 15 months at baseline to 54 months post-treatment. (PX0060). Forty-six men with recurrent prostate cancer following radical prostatectomy treatment, were given 8 ounces of pomegranate juice. The consumption of POM was associated with statistically significant prolongation of PSADT. (CX06110).

2485. When describing the results of the Pantuck Study (2006) in their advertisements, Respondents' used the following body copy:

(a) A recently published preliminary medical study followed 46 men previously treated for prostate cancer, either with surgery or radiation. After drinking 8 ounces of POM Wonderful 100% Pomegranate Juice daily for at least two years, these men experienced significantly longer PSA doubling times. (CX_0260 and CX1426, Exh. B (Drink to prostate health));

(b) A recently published preliminary medical study followed 46 men previously treated for prostate cancer either with surgery or radiation. After drinking eight ounces of POM Wonderful 100% Pomegranate Juice daily for at least two years, these men experienced significantly longer PSA doubling times. PSA (Prostate-Specific Antigen) is a biomarker that indicates the presence of prostate cancer. "PSA doubling time" is a measure of how long it takes for PSA levels to double. A longer doubling time may indicate slower progression of the disease. At the beginning of

the study, PSA levels doubled on average every 15 months. By the end of the study, doubling time had slowed to 54 months – nearly a four-fold improvement. "This is a big increase. I was surprised when I saw such an improvement in PSA numbers," said Dr. Allan Pantuck, lead author of the UCLA Study. In addition, in vitro testing using blood serum from the patients who drank pomegranate juice showed a 17% increase in prostate cancer cell death and a 12% decrease in cancer cell growth. . . . Results from this study were so promising that many of the original patients continued to drink pomegranate juice daily, and their PSA doubling times remained suppressed. Three more clinical studies are not underway to further investigate the effects of POM on prostate health. (CX314_0008 and CX314_0004 (Time Wrap – POM Wonderful and Prostate Health));

(c) A preliminary UCLA medical study involving POM Wonderful 100% Pomegranate Juice revealed promising news. 46 men who had been treated for prostate cancer with surgery or radiation were given 8 oz. of POM Wonderful 100% Pomegranate Juice to drink daily. A majority of the patients experienced a significantly extended PSA doubling time. Doubling time is an indicator of prostate cancer progression – extended doubling time may indicate slower disease progression. Before the study, the mean doubling time was 15 months. After drinking 8 oz. of pomegranate juice daily for two years, the mean PSA doubling time increased to 54 months. Testing on patient blood serum showed a 12% decrease in cancer cell proliferation and a 17% decrease in cancer cell death (apoptosis). In another study, in vitro laboratory testing at UCLA showed that POMx significant decreased human prostate cancer cell growth and increased cancer cell death. (CX1426, Exh. N and CX1426_0049-0051 (Dreher Prostate Newsletter));

(d) An initial UCLA medical study on POM Wonderful 100% Pomegranate Juice showed hopeful results for men with prostate cancer. (CX0120 (One Small Pill for Mankind); CX0122 (Science, Not Fiction));

(e) "Findings from a small study suggest that pomegranate juice may one day prove an effective-weapon against prostate cancer." *The New York Times* (July 4, 2006) … According to a UCLA study of 46 men age 65 to 70 with advanced prostate cancer, drinking an 8 oz glass of POM Wonderful 100% Pomegranate Juice every day slowed their PSA doubling time by nearly 350%. 83% of those who participated in the study showed a significant decrease in their cancer regrowth rate. (CX1426, Exh. I and CX1426_0038-0042(Antioxidant Superpill));

(f) After drinking eight ounces of POM Wonderful 100% Pomegranate Juice daily for at least two years, these men experience significantly slower

average PSA doubling times. PSA (Prostate-Specific Antigen) is a biomarker that indicates the presence of prostate cancer. PSA doubling time is a measure of how long it takes for PSA levels to double. A longer doubling time may indicate slower progression of the disease. At the binning of the study, PSA levels doubled on average every 15 months. By the end of the study, doubling time had slowed to 54 months – nearly four-fold improvement, *"This is a big increase. I was surprised when I saw such an improvement in PSA numbers," said Dr. Allen Pantuck, lead author of the UCLA study*. … Results from this study were so promising that many of the original patients continued to drink pomegranate juice daily, and their PSA doubling times remained suppressed. Three more clinical studies are not underway to further investigate the effects of POM on prostate health. (CX0372_0002, CX0379_0002, CX0380_0002 (Holy Health! $32 million in medical research));

(g) An initial UCLA study on our juice found hopeful results for prostate health, reporting "statistically significant prolongation of PSA doubling times," according to Dr. Allen J. Pantuck in *Clinical Cancer Research, '06*. (CX0328 (Your New Healthcare Plan); CX0331 (Healthy, ~~Wealthy~~ & Wise); CX0337 (The First Bottle You Should Open in 2010); CX0280) (Live Long Enough to Watch Your 401(k) Recover); CX0355 (The Only Antioxidant Supplement Rated X); CX0279 (Science, not fiction); CX0180 (The Antioxidant Superpill); CX1426, Exh. K (The Antioxidant Superpill); CX0342 (Take Out a Life Insurance Supplement); CX0353 (Take Out a Life Insurance Supplement); CX0350 (24 Scientific Studies Now In One Easy-To-Swallow Pill); CX0348 (24 Scientific Studies Now In One Easy-To-Swallow Pill); CX0351 (The Only Antioxidant Supplement Rated X)); and

(h) An initial UCLA MEDICAL STUDY on POM Wonderful 100% Pomegranate Juice found *hopeful results for prostate health.* "Pomegranate juice delays PSA doubling time in humans," according to AJ Pantuck, et al, in Clinical Cancer Research, 2006. (CX0169 and CX1426, Exh. L (The power of POM in one little pill)).

(i) In a clinical study involving 46 men with rising PSA after prostate cancer treatment (surgery or radiation) who consumed 8 ounces of POM Wonderful 100% Pomegranate Juice daily over two years, PSA doubling time increased from 15 to 54 months ($p<0.001$).5 A longer term (6-year) continued evaluation of active sub-group patients showed a further increase

in PSA doubling time to 88 months. (CX1426, Exh. E-1_0006[4], Rushton_006[5])

(j) Recently, the American Association for Cancer Research published research that indicates that a daily pomegranate regimen has a positive effect for men with prostate cancer. Specifically, drinking 8 ounces of POM Wonderful pomegranate juice daily prolonged post-prostate surgery PSA doubling time from 15 to 54 months (*Clinical Cancer Research*, July 1, 2006). PSA is a protein marker for prostate cancer and the faster PSA levels increase in the blood of men after treatment, the greater their potential for dying of prostate cancer. David Heber, MD, PhD, Professor Medicine and Director, UCLA Center for Human Nutrition, provided additional commentary on POMx as it relates to prostate cancer. "Basic studies indicate that the effects of POMx and POM Wonderful pomegranate juice on prostate cancer are the same. The most abundant and most active ingredients in pomegranate juice are also found in POMx." (CX0065 (Press Release – POMx, a Highly Concentrated Form of Healthy Pomegranate Antioxidants, Becomes Available to Consumers for the First Time)).

2486. As described in the findings of fact related to Respondents' studies on prostate health, the language quoted above accurately summarized the Pantuck Study (2006). (*See supra infra* XV(B)).

2487. Moreover, as further described in the findings of fact related to Respondents' studies on prostate health, at the time the representations were made, Respondents had competent and reliable scientific evidence to support the statements made above. (*See supra infra* XV(B)).

(b) Cardiovascular Health

(1) Aviram Study (2004)

2488. In the Aviram Study (2004), Dr. Aviram and his co-workers investigated, among other things, the effects of pomegranate juice consumption by patients with CAS

---

[4] Complaint Counsel attached several POM website captures to their complaint as Exhibit E. For ease of reference, Respondents sequentially numbered the pages discussed herein beginning with CX1426, Exh. E_001.

[5] Complaint Counsel marked a CD containing POM website captures as Exhibit 2 to Mr. Rushton's deposition on December 21, 2010. For ease of reference, Respondents sequentially numbered the pages discussed herein beginning with Rushton_001.

or the narrowing of the inner surface of the carotid artery. (CX0611). In the study, ten patients received pomegranate juice for one year and five of them continued for up to three years. In the control group that did not consume pomegranate juice, CIMT increased by 9% during one year, whereas, pomegranate juice consumption resulted in a significant CIMT reduction, by up to 30%, after one year. (CX0611). The results of this study indicated that pomegranate juice consumption by patients with CAS decreased CIMT which were related to the potent antioxidant characteristics of pomegranate juice polyphenols. (CX0611).

2489. When describing the results of the Aviram Study (2004) in their advertisements, Respondents' used the following body copy:

(a) And a clinical pilot study shows that an 8 oz. glass of POM Wonderful 100% Pomegranate Juice, consumed daily, reduces plaque in the arteries up to 30%. (CX0029 (Studies Show That 10 Out Of 10 People Don't Want To Die));

(b) And preliminary human research suggests that our California-grown pomegranate juice also promotes heart health. (CX0120 (One small pill for mankind); CX0122 (Science, not fiction));

(c) "Pomegranate juice consumption resulted in significant reduction in IMT (thickness of arterial plaque) by up to 30% after one year," said Dr. Michael Aviram in Clinical Nutrition, '04. (CX0328 (Your new healthcare plan); CX0331 (Healthy, Wealthy & Wise); CX0337 (The First Bottle You Should Open in 2010); CX0280 (Live Long Enough to Watch Your 401(k) Recover); CX0355 (The Only Antioxidant Supplement Rated X); CX0279 (Science, Not Fiction); CX0180 (The Antioxidant Superpill); CX1426, Exh. K (The Antioxidant Superpill));

(d) Two additional preliminary studies on our juice showed promising results for heart health. … "Pomegranate juice pilot research suggests anti-atherosclerosis benefits," according to M. Aviram, et al, in Clinical Nutrition, 2004. (CX0169 and CX1426, Exh. L(The power of POM in one little pill));

(e) In two groundbreaking preliminary studies, patients who drank POM Wonderful 100% Pomegranate Juice experienced impressive cardiovascular results. A pilot study at the Rambam Medical Center in Israel included 19 patients with atherosclerosis (clogged arteries). After a year, arterial plaque decreased 30% for those patients who consumed 8 oz of POM Wonderful 100% Juice daily… "POM Wonderful Pomegranate Juice has been proven to promote cardiovascular health, and we believe that POMx may have the

same health benefits." Dr. Michael Aviram quote. (CX1426, Exh. I and CX1426_0038-0042 (Antioxidant Superpill)); and

(f) A randomized, placebo-controlled, double-blind clinical trial followed 289 subjects at moderate risk for coronary heart disease. These subjects consumed 8 ounces per day of either POM Wonderful 100% Pomegranate Juice or a placebo beverage. After 18 months, there was no reduction in the progression of intima-media thickness of the carotid artery (CIMT) in the group as a whole. However, further analysis revealed an indication that the rate of CIMT progression slowed in nearly one third of patients, those with elevated cardiovascular disease risk factors. Read the Study. (CX1426, Exh. E-1_0004, Rushton_004).

2490. As described in the findings of facts related to Respondents' studies on heart health, the language quoted above accurately and truthfully summarized the Aviram Study (2004), which showed a comparative improvement in CIMT of 39% (CX0611). (*See infra* XIV(D)).

2491. Moreover, as further described in the findings of fact related to Respondents' studies on cardiovascular health, at the time the representations were made, Respondents had competent and reliable scientific evidence to support the statements made above. (*See infra* XIV(D)).

2492. Complaint Counsel, however, claim that certain ads disseminated after May 2007 are false and misleading because these ads purportedly did not take into the accounts the results of the Davidson CIMT Study, which became available in May 2007. (Compl., ¶ 11). This is an erroneous view because Dr. Heber and Mr. Tupper both testified that the Dr. Davidson CIMT study was not inconsistent with Dr. Aviram's 2004 clinical study. Indeed, Dr. Davidson's CIMT Study was not a plaque study at all because he did not study anyone with significant plaque or stenosis. The subjects in Dr. Davidson's CIMT Study had a baseline IMT of .84/.78 mm, which were significantly below the 1.5 mm baseline in Dr. Aviram's 2004 study. This differences at baseline show that the participants in Dr. Aviram's study were at significant cardiovascular risk to the point of stenosis, while the participants in Dr. Davidson's were not. In fact, Dr. Davison excluded from his study anyone with significant plaque or stenosis. Accordingly, because Dr. Davidson's findings are in no way inconsistent with Dr. Aviram's, it was not false or misleading for POM to continue describing the results of Dr. Aviram's plaque study. (*See supra* XVI).

2493. Complaint Counsel are incorrect. As described at length, Respondents have proffered substantial evidence that (a) the Davidson CIMT study was not inconsistent with the Aviram Study (2004). (*See infra* XIV(F)).

(3) Bev I Coronary Perfusion Study

2494. In the Bev I Study, Dr. Ornish and colleagues investigated whether the daily consumption of pomegranate juice for three months would affect myocardial perfusion (or blood flow) in forty-five patients who had coronary heart disease and myocardial ischemia (narrowing of the arteries) in a randomized, placebo-controlled, double-blind study. (PX0023). After three months, the extent of stress-induced ischemia (restriction of blood flow) decreased in the pomegranate group, but increased in the control group. (PX0023). In conclusion, the authors found that the daily consumption of pomegranate juice may improve stress-induced myocardial ischemia in patients who have coronary heart disease. (PX0023).

2495. When describing the results of the Bev I Coronary Perfusion Study, POM's ads used the following body copy:

(a) Two additional preliminary studies on our juice showed promising results for heart health. "Stress induced ischemia (restricted blood flow to the heart) decreased in the pomegranate group," Dr. Dean Ornish reported in the American Journal of Cardiology, '05. (CX0328 (Your New Healthcare Plan); CX0331 (Healthy, Wealthy & Wise); CX0337 (The First Bottle You Should Open in 2010); CX0280 (Live Long Enough To Watch Your 401(k) Recover); CX355 (The Only Antioxidant Supplement Rated X); CX279 (Science, not fiction); CX0180 (The Antioxidant Superpill); CX1426, Exhs. J Healthy, Wealthy & Wise) and K (The Antioxidant Superpill));

(b) Additional preliminary study on our juice showed promising results for heart health. "Stress induced ischemia (restricted blood flow to the heart) decreased in the pomegranate group," Dr. Dean Ornish reported in the American Journal of Cardiology, '05. (CX0342 (Take Out a Life Insurance Supplement); CX0353 (Take Out a Life Insurance Supplement); CX0350 (24 Scientific Studies Now In-One-Easy to Swallow Pill); CX0348));

(c) A preliminary study on our juice showed promising results for heart health. "Stress induced ischemia (restricted blood flow to the heart) decreased in the pomegranate group," Dr. Dean Ornish reported in the American Journal of Cardiology, '05. (CX0351 (The Only Antioxidant Supplement Rated X));

(d) Two additional preliminary studies on our juice showed promising results for heart health. "Pomegranate juice improves myocardial perfusion in coronary heart patients," per D. Ornish, et al, in the American Journal of Cardiology, 2005. (CX0169 and CX1426, Exh. L(The power of POM in one little pill));

(e) And preliminary human research suggests that our California-grown pomegranate juice also promotes heart health. (CX0120 (One small pill for mankind); CX0122 (Science, not fiction);

(f) In two groundbreaking preliminary studies, patients who drank POM Wonderful 100% Pomegranate Juice experienced impressive cardiovascular results… An additional study at the University of California, San Francisco included 45 patients with impaired blood flow to the heart. Patients who consumed 8 oz of POM Wonderful 100% Pomegranate Juice daily for three months experienced a 17% improvement in blood flow. Initial studies on POMx share similar promise for heart health, and our research continues. (CX1426, Exh. I and CX1426_0038-0042 (Antioxidant Superpill); and

(g) Men and women with coronary heart disease who drink one glass of pomegranate juice daily may improve blood flow to their heart, according to a new study. This research is the first randomized, double-blind, placebo-controlled trial showing that pomegranate juice may affect the progression of coronary heart disease, which is the #1 cause of death in the U.S. and in most of the world. Promising results from this research will be published in the September 16th issue of the American Journal of Cardiology, one of the leading peer-reviewed cardiology journals (www.ajconline.org). Researchers from the non-profit Preventive Medicine Research Institute, University of California, San Francisco, and California Pacific Medical Center studied patients with coronary heart disease who had reduced blood flow to the heart. These 45 patients were randomly assigned into one of two groups: one group who drank a glass of pomegranate juice each day (240 ml/day, which is approximately 8.5 oz/day) or to a placebo group, who drank a beverage of similar caloric content, amount, flavor and color. After only three months, blood flow to the heart improved approximately 17% in the pomegranate juice group but worsened approximately 18% in the comparison group (i.e., a 35% relative between-group difference). These differences were statistically significant. This benefit was observed without changes in cardiac medications or revascularization in either group. Also, there were no negative effects on lipids, blood glucose, hemoglobin Alc, body weight or blood pressure…. "Although the sample in this study was relatively small, the strength of the design and the significant improvements in blood flow to the heart observed after only three months suggest that pomegranate juice may have important clinical benefits in those with coronary heart disease," said senior author, Dean Ornish, M.D., who is founder of the Preventive Medicine Research Institute and clinical professor of medicine at UCSF. "Also, it may help to prevent it." (CX0044 (Press Release – Pomegranate Juice May Affect the Progression of Coronary Heart Disease)).

2496. As described in the findings of fact related to Respondents' studies on heart health, the language quoted above accurately and truthfully summarized the Bev I Coronary Perfusion Study. (*See supra* XIV(D)).

2497. Moreover, as further described in the findings of fact related to Respondents' studies on heart health, at the time the representations were made, Respondents had competent and reliable scientific evidence to support the statements made above. (*See supra* XIV(D)).

(4) Aviram Study (2006)

2498. In an article entitled, "Pomegranate byproduct administration to apolipoprotein e-deficient mice attenuates atherosclerosis development as a result of decreased macrophage oxidative stress and reduced cellular uptake of oxidized low-density lipoprotein, J Agric Food Chem. 2006 Mar 8;54(5):1928-35, Dr. Aviram and colleagues found that the consumption of POMx by atherosclerotic mice E-deficient mice resulted in a significant reduction in the mouse macrophage oxidative stress and in the atherogenic oxidized LDL uptake by the cells, and these effects were associated with a significant attenuation atherosclerotic lesion development. The authors concluded that POMx significantly attenuates atherosclerosis development by its antioxidant properties in vitro and in E-deficient mice. (CX0053).

2499. The only alleged "ad" that summarized the Aviram Study (2006) was a July 2006 Press Release - POMx, a Highly Concentrated Form of Healthy Pomegranate Antioxidants, Becomes Available to Consumers for the First Time, which used the following body copy:

> According to Michael Aviram, DSc, Professor of Biochemistry and Head Lipid Research Laboratory, Technion Faculty of Medicine and Rambam Medical Center, Haifa, Israel, who was at the forefront of the initial research on pomegranates, the research on POMx looks very promising. In 2006, Aviram led a study on POMx which was recently published (*Journal of Agriculture and Food Chemistry*, 2006 54:1928-1935). Commenting on this research, Professor Aviram remarks, "The results showed that POMx is as potent an antioxidant as pomegranate juice and just like pomegranate juice may protect against cardiovascular as well as other diseases." (CX0065)

2500. As described in the findings of fact related to Respondents' studies on heart health, the language quoted above accurately and truthfully summarized the Aviram Study (2006). (*See supra* XIV(F)).

2501. Moreover, as further described in the findings of fact related to Respondents' studies on heart health, at the time the representations were made, Respondents had competent and reliable scientific evidence to support the statements made above. (*See supra* XIV(D)).

(c) Erectile Health – Forest/Padma-Nathan RCT Study

2502. The Forest/Padma-Nathan RCT Study engaged 53 completed subjects with mild-to-moderate erectile dysfunction who underwent two four-week treatment periods separated by a two-week washout. (PX0189 at ¶ 32; CX0908). A total of 42 subjects demonstrated improved Global Assessment Question (GAQ) scores, 25 after drinking pomegranate juice. (PX0189 at ¶ 32; CX0908). Overall, the GAQ scores demonstrated that pomegranate juice drinkers enjoyed a nearly 50% better improvement in erections over placebo drinkers. (CX0908-0003; PX0352 (Goldstein, Dep. at 109, 144); CX1338 (Padma-Nathan, Dep. at 191 – 192)).

2503. When describing the results of the Forest/Padma-Nathan Study, POM's ads used the following body copy:

(a) In a preliminary study on erectile function, men who consumed POM Juice reported a 50% greater likelihood of improved erections as compared to placebo. "As a power antioxidant, enhancing the actions of nitric oxide in vascular endothelial cells, POM has potential in the management of ED… further studies are warranted." International Journal of Impotence Research, '07. (CX0351 (The Only Antioxidant Supplement Rated X));

(b) A pilot study released in the International Journal of Impotence Research in 2007 examined 61 male subjects with mild to moderate erectile dysfunction. Compared to participants taking a placebo, those men drinking 8oz [sic] of POM Wonderful 100% Pomegranate Juice daily for four weeks were 50% more likely to experience improved erections. (CX1426, Exh. E-2 (POM Wonderful website)); and

(c) According to a pilot study released in the International Journal of Impotence Research (http://www.nature.com/ijir), POM Wonderful 100% Pomegranate Juice was found to have beneficial effects on erectile dysfunction (ED) … This randomized, placebo-controlled, double-blind, crossover pilot study examined the efficacy of pomegranate juice versus placebo in improving erections in 61 male subjects. To qualify, participants had to experience mild to moderate ED for at least 3 months;

be in a stable, monogamous relationship with a consenting female partner, and be willing to attempt sexual intercourse on at least one occasion per week during each study period. … For the first four weeks of the study, the subjects were assigned to drink either 8 oz of POM Wonderful Pomegranate Juice or 8 oz. or placebo beverage daily with their evening meal or shortly after. After a two-week washout period during which the subjects did not consume any study beverage nor utilize any ED treatment, they were assigned to drink 8 oz. of the opposite study beverage every evening for another four weeks. … Forty seven percent of the subjects reported that their erections improved with POM Wonderful Pomegranate Juice, while only 32% reported improved erections with the placebo (p=0.058). … Although the study did not achieve overall statistical significance, the authors conclude that additional studies with more patients and longer treatment periods may in fact reach statistical significance. The strong directional results of this pilot study are encouraging because almost half of the test subjects experienced a benefit simply by adding pomegranate juice to their daily diet, without the use of ED drugs. Researchers believe that the results might be due to the potent antioxidant content of pomegranate juice, which can prevent free radical molecules from disrupting proper circulatory function. … According to study co-author Harin Padma-Nathan, MD, FACS, FRCS, Clinical Professor of Urology at the Keck School of Medicine, University of Southern California, "These findings are very encouraging as they suggest there is a non-invasive, non-drug way to potentially alleviate this qualify of life issue that affects so many men. For men with ED, it is important to maintain a healthy diet and exercise. Drinking pomegranate juice daily could be an important addition to the diet in the management of this condition." (CX0128 (Press Release – POM Wonderful 100% Pomegranate Juice May Improve Mild to Moderate Cases of Erectile Dysfunction)).

2504. As described in the findings of fact related to Respondents' studies on erectile health, the language quoted above accurately and truthfully summarized the Forest/Padma-Nathan Study. (*See supra* XVI).

2505. Moreover, as further described in the findings of fact related to Respondents' studies on erectile health, at the time the representations were made, Respondents had competent and reliable scientific evidence to support the statements made above. (*See supra* XVI).

(d) Each Category Of "Specific Study" Ads Are Also Qualified

2506. Each of the "specific study" ads discussed above describes the results of the studies using very qualified language.

(a) For example, the science was described as being "emerging science". (CX0328 (Your New Healthcare Plan); CX0331 (Healthy, Wealthy & Wise); CX0280 (Live Long Enough to Watch Your 401(k) Recover); CX0355 (The Only Antioxidant Supplement Rated X); CX1426, Exh. I (Antioxidant Superpill), J (Healthy, Wealthy & Wise), and L (The power of POM in one little pill); CX0342 (Take Out a Life Insurance Supplement); CX0353 (Take Out a Life Insurance Supplement); CX0350 (24 Scientific Studies Now In One Easy-To-Swallow Pill); CX0348 (24 Scientific Studies Now In One Easy-To-Swallow Pill); CX0351 (The Only Antioxidant Supplement Rated X); CX0169 (The power of POM in one little pill));

(b) The research results were described using qualified language such as being either "promising", "hopeful" or encouraging. ((CX0328 (Your New Healthcare Plan); CX0331 (Healthy, Wealthy & Wise); CX0280 (Live Long Enough to Watch Your 401(k) Recover); CX0355 (The Only Antioxidant Supplement Rated X); CX0180 (The Antioxidant Superpill); CX1426, Exhs. J (Healthy, Wealthy & Wise), K (The Antioxidant Superpill), L (The power of POM in one little pill), and M (Dreher Heart Newsletter); CX0342 (Take Out a Life Insurance Policy); CX0353 (Take Out a Life Insurance Policy) ; CX0350 (24 Scientific Studies Now In One Easy-To-Swallow Pill); CX0348 (24 Scientific Studies Now In One Easy-To-Swallow Pill); CX0351 (The Only Antioxidant Supplement Rated X); CX0169 (The power of POM in one little pill); CX0120 (One small pill for mankind); CX0314_0008 (POM Wonderful and Prostate Health); CX0314_0004 (POM Wonderful and Prostate Health); CX0372_0002 (Holy Health! $32 million in medical research); CX0379_0002 (Holy Health! $32 million in medical research); CX0380_0002 (Holy Health! $32 million in medical research) ; CX0128 (Press Release – POM Wonderful 100% Pomegranate Juice May Improve Mild to Moderate Cases of Erectile Dysfunction); CX0065 (Press Release – POMx, a Highly Concentrated Form of Healthy Pomegranate Antioxidants, Becomes Available to Consumers for the First Time); CX0044 (Press Release – Pomegranate Juice May Affect the Progression of Coronary Heart Disease));

(c) Likewise, the benefits from the research only "suggest" or "may indicate" benefits. (CX0169 (The power of POM in one little pill0; CX1426, Exh. L (The power of POM in one little pill) and N (Dreher Prostate Newsletter); CX0314_0008 (POM Wonderful and Prostate Health); CX0314_ 0004 (POM Wonderful and Prostate Health); CX0372_0002 (Holy Health! $32 million in medical research); CX0379_0002 (Holy Health! $32 million in medical research); CX0380_0002 (Holy Health! $32 million in medical

research); CX0120 (One small pill for mankind); CX0122 (Science, not fiction));

(d) And the studies were either "initial" or "preliminary". (CX0328 (Your New Healthcare Plan); CX0331 (Healthy, Wealthy & Wise); CX0280 (Live Long Enough To Watch Your 401(k) Recover); CX0355 (The Only Antioxidant Supplement Rated X); CX0279 (Science, not fiction); CX0180 (The Antioxidant Superpill); CX1426, Exh. B (Drink to prostate health), I (Antioxidant Superpill), J (Healthy, Wealthy & Wise), K (The Antioxidant Superpill), L (The power of POM in one little pill), M (Dreher Heart Newsletter) and N (Dreher Prostate Newsletter); CX0342 (Take Out a Life Insurance Supplement); CX0353(Take Out a Life Insurance Supplement); CX0350 (24 Scientific Studies Now In One-Easy-To Swallow Pill); CX0348 (24 Scientific Studies Now In One-Easy-To Swallow Pill); CX0351 (The Only Antioxidant Supplement Rated X); CX0169 (The power of POM in one little pill); CX 0120 (One small pill for mankind); CX0260 (Drink to prostate health); CX0122 (Science, not fiction); CX0128 (Press Release – POM Wonderful 100% Pomegranate Juice May Improve Mild to Moderate Cases of Erectile Dysfunction));

(e) Rather than a definitive statement, the ads stated that "pomegranate juice may help" and that the juice "promotes" health. (CX1426, Exh. M (Dreher Heart Newsletter)); and

(f) Similarly, the ads stated that antioxidants are "helping to prevent". (CX0029 (Studies Show That 10 Out of 10 People Don't Want to Die); CX1426, Exhs. I (Antioxidant Superpill) and M (Dreher Heart Newsletter)).

2. <u>POM Disseminated "Backed By" Ads That Are Not False and Misleading Because They Accurately and Truthfully Represented Respondents' Expenditures on Scientific Studies on the Challenged Products and Conveyed Qualified Messages</u>

2507. The second category, "backed by" ads, stated that Respondents spent a particular amount of money on their scientific studies on the Challenged Products to back-up Respondents' healthy claims.

2508. Examples of the body copy used in the "backed by" ads read, in pertinent part:

(a) POM Wonderful Pomegranate Juice is supported by $20 million of initial scientific research from leading universities, which has uncovered encouraging results in prostate and cardiovascular health. (CX0109 (Heart therapy));

(b) POM Wonderful 100% Pomegranate Juice is supported by $23 million of initial scientific research from leading universities, which has uncovered encouraging results in prostate and cardiovascular health. (CX0188 (Cheat death); CX0192 (What gets your heart pumping?));

(c) Backed by $25 million in medical research. (CX1426, Exh. A (Super HEALTH Powers!); CX0314_0009 (The proof is in the POM); CX0314_0005 (The proof is in the POM); CX1426_0027 (Super HEALTH Powers!));

(d) Backed by an unheard of $25 million in medical research. (CX1426, Exh. D (Holy Health! $25 million in medical research));

(e) Backed by $25 million in vigilant medical research. (CX0274 (I'm off to save prostates));

(f) Only POM products are backed by $32 million in medical research conducted at the world's leading universities, primarily in the areas of cardiovascular, prostate and erectile function. (CX0372_0003 (KA-POM!); CX0379_0003 (KA-POM!); CX0380_0003 ((KA-POM!));

(g) Can POM products $32 million in medical research truly make a difference in the current state of your health? (CX0380_0006 and CX0372_0004 (100% PURE pomegranate juice to the rescue)); and

(h) One of the POM products backed by $32 million in medical research. (CX0379_0004 (Risk your health in this economy? NEVER!); CX1426, Exh. C (I'm off to save PROSTATES!));

(i) POM is the only pomegranate juice backed by $25 million in medical research. (CX1426, Exh. E-003, Rushton_003 (POM Truth website); and

(j) POM Wonderful 100% Pomegranate Juice is the only pomegranate juice backed by $25 million in medical research. (CX1426, Exh. E-1_0001, Rushton_001) POM Truth website)).

2509. The following ads also fall into the "backed by" category and contain body copy that is similar or almost identical to the ads described above: CX0251 (Imitation may be sincere. But is it pure?); CX0314_0010 (Ingredients: pomegranates, $25 million in medical research) CX0103 (Decompress); CX0328 (Your New Health Care Plan); CX0331 (Healthy, ~~Wealthy~~, and Wise.); CX0337 (The First Bottle You Should Open in 2010); CX0280 (Live Long Enough to Watch your 401(k) Recover); CX0355 (The Only Antioxidant Supplement Rated X); CX0279 (Science, not fiction.); CX0180 (The antioxidant superpill); CX1426, Exh. J (Healthy, ~~Wealthy~~, and Wise.); CX1426, Exh. K (The antioxidant superpill);

CX0342 (Take Out a Life Insurance Supplement); CX0353 (Take Out a Life Insurance Supplement); CX0350 (24 Scientific Studies Now in One Easy-To-Swallow Pill); CX0348 (24 Scientific Studies Now in One Easy-To-Swallow Pill); CX0351 (The Only Antioxidant Supplement Rated X); CX0169 (The power of POM, in one little pill); CX1426, Exh. L (The power of POM, in one little pill); CX1426, Exh. M (Dreher Heart Newsletter); CX0122 (Science, not fiction); CX1426, Exh. I (Antioxidant Superpill); CX1426, Exh. N (Dreher Prostate Newsletter); CX0372_0002 (HOLY HEALTH! $32 million in medical research); CX0372_0003 (KA-POM!); CX0372_0004 (100% PURE pomegranate juice to the rescue!); CX0379_0002 (HOLY HEALTH! $32 million in medical research); CX0379_0003 (KA-POM!) CX0379_0004 (Risk your health in this economy? NEVER!) CX0380_0002 (HOLY HEALTH! $32 million in medical research); CX0380_0003 (KA-POM!); CX0380_0006 (100% PURE pomegranate juice to the rescue!); CX0314_0005 (The proof is POM); CX0314_0009 (The proof is POM); CX0109 (Heart therapy); CX0188 (Cheat death); CX0192(What gets your heart pumping?); CX1426, Exh. A (Super HEALTH POWERS!); CX1426, Exh. D (HOLY HEALTH! $25 million in medical research); CX0274 (I'm off to save PROSTATES!); and CX1426, Exh. C (I'm off to save PROSTATES!))

2510. Respondents' "backed by" ads described above are not false or misleading because they accurately represented the dollars spent by Respondents on the totality of the science on the Challenged Products, including basic, animal and human studies, at the time the representations were made. (S*ee supra* XVII(G)(2)).

2511. The studies done concerning one disease or condition, such as the effect of antioxidants or of nitric oxide, are sufficiently interrelated to other diseases and conditions that it is not misleading to treat all of Respondents' scientific expenditures – now approximately $34 million – as "backing" Respondents' health claims. (CX1276)

2512. Even the fact that POM's ads listed an amount of money spent on Respondents' scientific studies that had a null or even negative result is not false or misleading. (S*ee supra* XI(B),(C)).

2513. Mr. Tupper testified that Respondents learned a great deal even from the unsuccessful studies and, in a very real way, all of Respondents' studies were important sources of knowledge that allowed them to make informed decisions. (Tupper, Tr. 3000-30001).

2514. In fact, Respondents' substantially understated the dollars spent on research in their advertising because they excluded all overhead items, such as rent and salaries very significant added costs. (Tupper, Tr. 2999-3000).

2515. Moreover, Complaint Counsel has presented no evidence that any significant number of consumers bought POM Juice because they thought Respondents spent a certain amount of money in a particular area of research.

2516. Indeed, Professor Reibstein's uncontroverted survey showed that no one bought POM Juice because of the amount of money spent on science. (PX0223-0006)

2517. Each of the "backed by" ads discussed above conveyed qualified messages.

(a) For example, the ads stated that the juice is "committed" to keeping you healthy or that it would "help guard" or "help fight". (CX0109 (Heart therapy); CX0188 (Cheat death); CX0192 (What gets your heart pumping?); CX0274 (I'm off to save PROSTATES!); CX1426, Exh. A (Super HEALTH Powers!0; CX1426, Exh. C (Drink to prostate health));

(b) The science was described as being "emerging science". (CX0109 (Heart therapy); CX0188 (Cheat death); CX0192 (What gets your heart pumping?));

(c) The research results were described using qualified language such as being either "encouraging". (CX0109 (Heart therapy); CX0188 (Cheat death); CX0192 (What gets your heart pumping?)); and

(d) Likewise, the scientific research was described as being "initial". (CX0109 (Heart therapy); CX0192 (What gets your heart pumping?)).

3. POM Disseminated "Antioxidant" Ads That Are Not False or Misleading Because They Are Supported By Competent and Reliable Scientific Evidence and Conveyed Qualified Messages

2518. The third category, "antioxidant" ads, discussed the potential benefits of antioxidants and stated that the Challenged Products contained antioxidants. (*See* Appendix of Ads).

2519. The "antioxidant" ads can be grouped into four sub-categories: (a) general antioxidant; (b) comparative antioxidant, (c) antioxidant benefits and (d) multi-step.

(a) General Antioxidant

2520. The first sub-category, "general antioxidant", described POM Juice as the "Antioxidant Superpower" and/or full of antioxidants and POMx Pills as the "Antioxidant Superpill" and/or a concentrated and potent source of antioxidants. (*See* Appendix of Ads).

2521. Examples of the body copy used in POM's "general antioxidant" ads include the following:

(a) The Antioxidant Superpower. (CX1426, Exh. A (Super HEALTH Powers); CX1426, Exh. C (I'm off to save PROSTATES!); CX1426, Exh. D (Holy Health $25 million in medical research); CX1426, Exh. H (I'm off to save PROSTATES!); CX1426, Exh. G (Amaze your urologist); CX0468 (Amaze your urologist); CX0314_0005 (The Proof is in the POM); CX0314_0006 (The Antioxidant Superpower); CX0314_0009 (The proof is in the POM); CX0380_0001 (Lucky I have super HEALTH POWERS!); CX0380_0003 (KA-POM!); CX0380_0004 (Have no health fear… POM IS HERE!); CX0380_0005 (Lucky I have HEALTH POWERS!); CX0380_0006 (100% PURE pomegranate juice to the rescue); CX0380_0007 (Lucky I have super HEALTH POWERS!); CX0372_0001 (Lucky I have super HEALTH POWERS!); CX0372_0003 (KA-POM!); CX0372_0004 (100% PURE pomegranate juice to the rescue); CX0379_0001 (Lucky I have super HEALTH POWERS!); CX0379_0003 (KA-POM!); CX0379_0004 (Risk your health in this economy? NEVER!); CX0036 (Cheat death); CX0031 (Floss your arteries. Daily); CX0034 (Amaze your cardiologist); CX0103 (Decompress); CX0109 (Heart therapy); CX0192 (What gets your heart pumping?) ; CX0274 (I'm off to save PROSTATES!));

(b) The Antioxidant Superpill. (CX0328 (Your New Health Care Plan); CX0331 (Healthy, Wealthy, and Wise); CX0337 (The First Bottle You Should Open in 2010); CX0280 (Live Long Enough to Watch your 401(k) Recover); CX0355 (The Only Antioxidant Supplement Rated X); CX1426, Exh. K (The Antioxidant Superpill); CX0342 (Take Out a Life Insurance Supplement); CX0353 (Take Out a Life Insurance Supplement); CX0350 (24 Scientific Studies Now In One Easy-To-Swallow Pill); CX0348 (24 Scientific Studies Now In One Easy-To-Swallow Pill); CX0351 (The Only Antioxidant Supplement Rated X); CX0169 (The power of POM, in one little pill); CX1426, Exh. L (The power of POM, in one little pill); CX1426, Exh. I (Antioxidant Superpill));

(c) We only grow "Wonderful" variety pomegranates, renowned for their superior antioxidants and delicious taste. (CX0314_0005 (The proof is in the POM); CX0314_0009 (The proof is in the POM); CX0372_0003 (KA-POM!); CX0379_0003 (KA-POM!); CX0380_0003 (KA-POM!);

(d) Pomegranate contains powerful antioxidants. (CX1426, E-3 (POM Wonderful Video Ads));

(e) POMx is an all-natural, ultra potent antioxidant extract. Containing a full spectrum of pomegranate polyphenols, POMx is so concentrated that a single capsule has the antioxidant power of a full glass of POM Wonderful 100% Pomegranate Juice. (CX0328 (Your New Health Care Plan); CX0331 (Healthy, Wealthy, and Wise); CX0337 (The First Bottle You Should Open in 2010); CX0355 (The Only Antioxidant Supplement Rated X); CX1426, Exh. J (Healthy, Wealthy, and Wise); CX0342 (Take Out a Life Insurance Supplement); CX0353 (Take Out a Life Insurance Supplement); CX0350 (24 Scientific Studies Now In One Easy-To-Swallow Pill); CX0348 (24 Scientific Studies Now In One Easy-To-Swallow Pill); CX0351 (The Only Antioxidant Supplement Rated X));

(f) The unique and superior antioxidant power of pomegranates. (CX0328 (Your New Health Care Plan); CX0331 (Healthy, Wealthy, and Wise); CX0337 (The First Bottle You Should Open in 2010); CX0280 (Live Long Enough to Watch your 401(k) Recover); CX0355 (The Only Antioxidant Supplement Rated X); CX1426, Exh. J (Healthy, Wealthy, and Wise); CX0342 (Take Out a Life Insurance Supplement); CX0353 (Take Out a Life Insurance Supplement); CX0350 (24 Scientific Studies Now In One Easy-To-Swallow Pill); CX0348 (24 Scientific Studies Now In One Easy-To-Swallow Pill); CX0351(The Only Antioxidant Supplement Rated X));

(g) Ready to take on free radicals? Put up your POMx and fight them with a mighty 1000mg capsule – that's more concentrated pomegranate polyphenol antioxidants than any other 100% pomegranate supplement. (CX0120 (One small pill for mankind); CX0122 (24 Scientific Studies Now In One Easy-To-Swallow Pill)); and

(h) POMx is a highly concentrated, powerful blend of polyphenol antioxidants made from the very same pomegranates as POM Wonderful 100% Pomegranate Juice … just 100% pomegranate polyphenol antioxidants . . . . (CX0169 (The power of POM, in one little pill); CX1426, Exh. L (The power of POM, in one little pill)).

2522. The following ads also fall into the "general antioxidant" category and contain body copy that is similar or almost identical to the ads described above: CX0016; CX1426, Exh. I; CX0280; CX0279; CX0180; CX1426, Exh. K; CX0120; and CX0122.

2523. As exemplified in the body copy quoted above, the overall net impression of "general antioxidant" category of ads is not that the Challenged Products are "clinically proven" to prevent, treat or reduce the risk of heart disease, prostate cancer or erectile dysfunction. (*See* Appendix of Advertisements).

2524. Dr. Butters testified that these "superpower" ads were intended to be "a work of fiction" in that they are personifying the pomegranate bottle by comparing the bottle to a superhero. (Butters, Tr. 2906).

2525. Moreover, POM's ads in this category are truthful and adequately supported by competent and reliable scientific evidence. (*See supra* XII, XIV, XV, XVI).

(b) Comparative Antioxidant

2526. The second sub-category, "comparative antioxidant", described POM Juice as surpassing other drinks in its antioxidant capacity. (*See* Appendix of Ads).

2527. Examples of the body copy used in POM's "comparative antioxidant" ads include the following:

(a) [W]ith more naturally occurring antioxidant power than any other drink . . . Since our bodies don't produce enough antioxidants to do the job on their own, we need a little outside help. POM Wonderful Pomegranate Juice, with a higher level of antioxidants than any other drink, is a real Antioxidant Superpower. (CX0029 (Studies Show That 10 out of 10 People Don't Want To Die)); and

(b) Sip for sip, POM Wonderful 100% Pomegranate Juice has more polyphenol antioxidants than red wine, green tea and other juices. (CX0314_0005 (The proof is in the POM); CX0314_0009 (The proof is in the POM); CX0372_0003 (KA-POM!); CX0379_0003 (KA-POM!); CX0380_0003 (KA-POM!)).

2528. The following ads also fall into the "comparative antioxidant" category and contain body copy that is similar or almost identical to the ads described above: CX0314_0006 (The Antioxidant Superpower), CX0031 (Floss your artery).

2529. As exemplified in the body copy quoted above, POM's ads in the "comparative antioxidant" category, the overall net impression of "comparative antioxidant" category of ads is not that the Challenged Products are "clinically proven" to prevent, treat or reduce the risk of heart disease, prostate cancer or erectile dysfunction. (*See* Appendix of Advertisements).

2530. Moreover, POM's ads in this category are truthful and adequately supported by competent and reliable scientific evidence. (*See supra* XII, XIV, XV, XVI).

(c) Antioxidant Benefits

2531. The third sub-category, "antioxidant benefits" state that POM Juice and/or POMx Pills contain abundant antioxidants and that antioxidants can help fight or neutralize free radicals. (*See* Appendix of Ads).

2532. Examples of the body copy used in POM's "antioxidant benefits" ads include the following:

(a) Not all antioxidants are created equal. POMx fights free radicals with a mighty 1000 mg in every pill. That's more concentrated antioxidants than any other pomegranate antioxidant supplement. There are antioxidants, and then there are POMx antioxidants. (CX0169 (The power of POM, in one little pill); CX1426, Exh. L (The power of POM, in one little pill));

(b) Emerging science suggests that antioxidants are critically important to maintaining good health because they protect you from free radicals, which can damage your body. Taking one POMx pill a day will help protect you against free radicals and keep you at your healthy best. (CX0328 (Your New Health Care Plan); CX0331 (Healthy, ~~Wealthy~~, and Wise); CX0337 (The First Bottle You Should Open in 2010); CX0280 (Live Long Enough to Watch your 401(k) Recover); CX0355 (The Only Antioxidant Supplement Rated X); CX1426, Exh. J (Healthy, ~~Wealthy~~, and Wise); CX0342 (Take Out a Life Insurance Supplement); CX0353(Take Out a Life Insurance Supplement); CX0350 (24 Scientific Studies Now In One Easy-To-Swallow Pill); CX0348 (24 Scientific Studies Now In One Easy-To-Swallow Pill); CX0351(The Only Antioxidant Supplement Rated X)); and

(c) With uniquely high levels of powerful antioxidants, POM Wonderful 100% Pomegranate Juice has demonstrated superior ability to neutralize harmful free radicals and to inhibit excess inflammation. (CX0314_0005 (The proof is in the POM); CX0314_0009 (The proof is in the POM); CX0372_0003 (KA-POM!); CX0379_0003 (KA-POM!); CX0380_0003 (KA-POM!)).

2533. These ads also fall into the "antioxidant benefits" category and contain body copy that is similar or almost identical to the ads described above: CX1426, Exh. M (Dreher Heart Newsletter); CX0034 (Amaze your cardiologist); and CX314_005 (The proof is in the POM).

2534. Many of the "antioxidant benefit" ads discussed above conveyed a qualified message.

(a) For example, the science behind the antioxidant claims was described as "emerging science". (CX0328 (Your New Health Care Plan); CX0331 (Healthy, ~~Wealthy~~, and Wise); CX0337 (The First Bottle You Should Open

in 2010); CX0280 (Live Long Enough to Watch your 401(k) Recover); CX0355 (The Only Antioxidant Supplement Rated X); CX1426, Exh. J (Healthy, ~~Wealthy~~, and Wise); CX0342 (Take Out a Life Insurance Supplement); CX0353 (Take Out a Life Insurance Supplement); CX0350 (24 Scientific Studies Now In One Easy-To-Swallow Pill); CX0348 (24 Scientific Studies Now In One Easy-To-Swallow Pill); CX0351 (The Only Antioxidant Supplement Rated X); CX0188 (Cheat death)); and

(b) Similarly, the ads stated that one POMx Pill "will help protect" against free radicals. (CX0328 (Your New Health Care Plan); CX0331 (Healthy, Wealthy, and Wise); CX0337 (The First Bottle You Should Open in 2010); CX0280 (Live Long Enough to Watch your 401(k) Recover); CX0355 (The Only Antioxidant Supplement Rated X); CX1426, Exh. J (Healthy, Wealthy, and Wise); CX0342 (Take Out a Life Insurance Supplement); CX0353 (Take Out a Life Insurance Supplement); CX0350 (24 Scientific Studies Now In One Easy-To-Swallow Pill); CX0348 (24 Scientific Studies Now In One Easy-To-Swallow Pill); CX0351 (The Only Antioxidant Supplement Rated X); CX0188 (Cheat death)).

2535. As exemplified in the body copy quoted above, the overall net impression of "antioxidant benefit" category of ads is not that the Challenged Products are "clinically proven" to prevent, treat or reduce the risk of heart disease, prostate cancer or erectile dysfunction. (*See* Appendix of Advertisements).

2536. Moreover, POM's ads in this category are truthful and adequately supported by competent and reliable scientific evidence. (*See supra* XII, XIV, XV, XVI).

(d) Multi-Step

2537. The fourth sub-category, "multi-step" antioxidant ads, states that (a) emerging science suggests that free radicals may be damaging to health and may be implicated in a number of diseases; (b) POM Juice is high in antioxidants and have more antioxidants than other drinks; (c) antioxidants may help protect your body against free radicals; and therefore (d) POM Juice is beneficial and good for your health. (*See* Appendix of Ads).

2538. Examples of the body copy used in POM's "antioxidant benefits" ads include the following:

(a) What's it like to have a personal superhero? Find out by drinking delicious and refreshing POM Wonderful 100% Pomegranate Juice. It has more naturally occurring antioxidants than other drinks. Antioxidants fight free radicals, villainous little molecules that may cause premature aging, heart

disease, stroke, Alzheimer's, even cancer. (CX0314_0006 (The Antioxidant Superpower));

(b) You need antioxidants. And POM Wonderful 100% Pomegranate Juice is loaded with them. It helps guard your body against free radicals, unstable molecules that emerging science suggests aggressively destroy healthy cells in your body and contribute to disease. (CX0188 (Cheat death)); and

(c) On top of being refreshing and delicious, this amazing juice has more naturally occurring antioxidants than any other drink. These antioxidants fight hard against free radicals that can cause heart disease, premature aging, Alzheimer's, even cancer. (CX0033 (Life support)).

2539. The following ads also fall into the "multi-step" category and contain body copy that is similar or almost identical to the ads described above: CX0016.

2540. Some of the "multi-step" ads are also accompanied by humorous, comical and frivolous images. For example, the "Life support" ad has an intravenous line ("IV") with a pomegranate bottle in place of IV solution. (CX0033).

2541. Dr. Butters testified that the image is a "frivolous exaggeration" and that it is not possible that the IV imagery was conveying drugs and medicine. (Butters, Dep. at 165).

2542. Many of the "multi-step" ads discussed above also conveyed qualified messages.

(a) For example, the science behind the antioxidant claims was described as being "emerging science" and that such science "suggests" that free radicals destroy healthy cells. (CX0188 (Cheat death)); and

(b) The ads stated that antioxidants fight free radicals and that free radicals "may cause" certain diseases, (CX0314_0006 (The Antioxidant Superpower)), or "can cause" certain diseases" (CX0033 (Life support)), not that free radicals affirmatively do cause diseases.

2543. As exemplified in the body copy quoted above, the overall net impression of "multi-step" antioxidant category of ads is not that the Challenged Products are "clinically proven" to prevent, treat or reduce the risk of heart disease, prostate cancer or erectile dysfunction. (*See* Appendix of Advertisements).

2544. Moreover, POM's ads in this category are truthful and adequately supported by competent and reliable scientific evidence. (*See supra* XII, XIV, XV, XVI).

H. The Handful of Media Interviews and/or Presentations Given By Respondents, Mrs. Resnick And Mr. Tupper, Are Not Actionable Advertising

2545. In the 11/9/11 Proposed Ad Stipulation, Complaint Counsel contend that four media interviews, three given by Mrs. Resnick (CX1426, Exhs. E-6 and F, CX472_0003) and one given by Mr. Tupper (CX1426, Exh. E-7), as well as a discussion with Mrs. Resnick at the University of Southern California ("USC") Annenberg School of Communication (CX472_0002), violate Section 5 and 12 of the FTC Act. (11/9/11 Johnson email).

2546. The four media interviews and one discussion include:

(a) Mrs. Resnick's November 2008 television appearance on *The Martha Stewart Show* ("*Martha Stewart*") in which she shared personal recipes for a POMtini cocktail and Thanksgiving stuffing, (CX1426, E-6);

(b) Mrs. Resnick's February 2009 television appearance on *The Early Show* in which she shared some marketing ideas for POM and FIJI Water, (CX472_0003);

(c) an interview of Mrs. Resnick in *Newsweek* magazine, dated March 20, 2009, discussing the economy, her business acumen, and her book, *Rubies in the Orchard*, (CX1426, Exh. F);

(d) an April 2009 discussion with Mrs. Resnick at USC's Annenberg School of Communication with Dean Ernest J. Wilson III on "How to Uncover the Hidden Gems in Your Business", (CX472_0002); and

(e) a June 2008 television interview of Mr. Tupper on FOX Business discussing the newest "hot" wave in foods - the pomegranate - and the pomegranate juice industry, (CX1426, Exh E-7).

2547. As discussed below, neither Mrs. Resnick nor Mr. Tupper can be held liable under Section 5 and 12 of the FTC Act for these statements.

2548. First, the statements by Mrs. Resnick and Mr. Tupper are not advertising as defined by the FTC in *In the Matter of R.J. Reynolds Tobacco Co., Inc.,* 9206, 1988 WL 490114 (F.T.C. Mar. 4, 1988). (*See infra* XVII(H)(1-5)).

2549. Second, the "main purposes" or "primary motivations" for the interviews given by Mrs. Resnick and Mr. Tupper were not to sell POM products. (*See infra* XVII(H)(1-5)).

2550. Third, the challenged statements by Mrs. Resnick and Mr. Tupper were their honest opinions in response to unsolicited questions posed by the interviewers and, therefore, are protected by the First Amendment. (*See infra* XVII(H)(1-5)).

2551. Last, Complaint Counsel has failed to introduce any evidence whatsoever that any of the statements by Mrs. Resnick or Mr. Tupper were material to consumers' decisions to purchase POM Juice. (*See infra* XVIII(A)).

1. Lynda Resnick's Appearance on the Martha Stewart Show

2552. On November 20, 2008, Mrs. Resnick appeared on *Martha Stewart*. (CX1426, Exh. E-6). The substance of the interview, itself, makes clear that Mrs. Resnick's interview primarily focused on pomegranates, the company, POM, and the POMtini. (CX1426, Exh. E-6).

2553. Although the first segment of the two-part interview is set forth in a video marked as CX1426, Exh. E-6, the Complaint quoted the following 35 second transcription from the six minute and 15 second interview:

> **Mrs. Resnick:** . . . But, the Wonderfuls are [the pomegranates] ones that we grow because they're the sweetest and they have the health benefits.
>
> ***
>
> **Ms. Stewart:** But, the medical benefits even outweigh the mythical benefits?
>
> **Ms. Resnick:** Oh, they do, they do. I mean, it's the magic elixir of our age and of all ages, and we know that it helps circulation, it helps Alzheimer's, it helps all sorts of things in the body—
>
> **Ms. Stewart:** Antioxidants.
>
> **Ms. Resnick:** Antioxidants. Polyphenol antioxidants off the chart.
>
> **Ms. Stewart:** Right.
>
> **Ms. Resnick:** And if you know a man that you care about or you are a man, make him drink eight ounces of pomegranate juice a day because what it does for prostate cancer is amazing.

(CX1426, Exh. E-6).

2554. At the end of the first segment, Martha Stewart states that when they return from the commercial break that she and Mrs. Resnick are going to make an amazing pomegranate cornbread stuffing. (CX1426, Exh. E-6.) That next segment in which Mrs. Resnick and Martha Stewart make the stuffing and continue the interview is 6 minutes and 17 seconds. (Lynda Resnick Interview on *Martha Stewart* (November 20, 2008), available on You Tube at http://www.youtube.com/watch?v=IBejxwUTGAQ). The total length of Mrs. Resnick's interview on *Martha Stewart* is over 12 minutes.

2555. Complaint Counsel has presented no evidence that Mrs. Resnick or the other Respondents paid any money to *Martha Stewart* or anyone else for her participation in the interview or to allow her to speak about pomegranate juice.

2556. Complaint Counsel has presented no evidence that Mrs. Resnick's "main purpose" or "primary motivation" for participating in an interview on *Martha Stewart* was to sell POM.

2557. During the interview, Ms. Resnick's reference to the health benefits of pomegranate juice was very, very short - only about 35 seconds out of the two segment interview, which lasted 12 minutes and 30 seconds. (CX1426, Exh. E-6; Lynda Resnick Interview on *Martha Stewart* (November 20, 2008), available on You Tube at http://www.youtube.com/watch?v=IBejxwUTGAQ).

2558. Mrs. Resnick's reference to the "medical benefits" of pomegranate juice during the course of her interview was strictly "reactive" and was directly in response to a question posed by Martha Stewart. (CX1426, Exh. E-6).

2559. Ms. Resnick's responses to questions concerning the "medical benefits" of pomegranate juice were purely statements of her opinion, which are protected under the First Amendment. (L. Resnick, Tr. 156; CX1375 (L. Resnick, Tropicana Dep. at 101)).

2560. Mrs. Resnick staunchly believes that the opinions she expressed in her interview are completely true. (L. Resnick, Tr. 156; CX1375 (L. Resnick, Tropicana Dep. at101). Indeed, at the time of the *Martha Stewart* interview, Mrs. Resnick believed that POM juice is helpful for Alzheimer's and she still believes that today. (L. Resnick, Tr. 153-56).

2561. The substance of the interview, itself, evidence that neither Ms. Resnick's statements on *Martha Stewart* nor even her specific opinions on the benefits of pomegranate juice "proposed a commercial transaction." (CX1426, Exh. E-6).

2562. During her appearance, Mrs. Resnick made no mention of the then-upcoming release of her book, *Rubies in the Orchard*. (CX1426, Exh. E-6).

2563. Although POM provided each audience member with a free, fresh pomegranate, (Lynda Resnick Interview on *Martha Stewart* (November 20, 2008), available on You Tube at http://www.youtube.com/watch?v=IBejxwUTGAQ).

2564. Moreover, even assuming *arguendo* that Mrs. Resnick's *Martha Stewart* interview constitutes "advertising", Complaint Counsel has presented no evidence that showed any causal relationship between this interview and consumer purchasing decisions.

2565. The Reibstein Survey shows that no mention of disease in Mrs. Resnick's interview was material to consumers' purchase decisions because less than 1.5% of the hundreds of survey respondents even mentioned disease as a reason for buying POM Juice. (Reibstein, Tr. at 2493; PX02223-0020).

2566. No liability can be based on Mrs. Resnick's appearance on *Martha Stewart* because (a) it was not advertising; (b) it is constitutionally protected speech; and (c) her opinions were not material to the consumer purchasing decisions.

2. Lynda Resnick's Appearance on the Early Show

2567. On February 19, 2009, Mrs. Resnick appeared on CBS' *The Early Show* in a segment titled "Cashing in on Ideas". (CX472_0003). The substance of the interview, itself, makes clear that the interview primarily focused on the history and story behind the company, POM, and Mrs. Resnick's marketing secrets. (CX472_0003).

2568. Although the entire 3 minute and 52 second interview is set forth in a video marked as CX472_0003, the interview is not an exhibit to or excerpt in the Complaint. (*See* CX1426).

2569. Respondents' therefore surmise that Complaint Counsel challenge the following 20 second transcription:

> **Julie Chen:** And how did you start marketing [POM]? Because, like I see that bottle and I just want to drink it.
>
> **Mrs. Resnick:** I know. I know. . . And we decided to see if that was true. We started doing scientific, peer-reviewed research. And we found out, indeed, that the pomegranate has all these health-giving properties. There isn't a man

> in America that shouldn't drink 8oz. a day. Because it keeps you from getting prostate cancer or your PSA from rising. It's really an, amazing, amazing thing. And good for circulation too.

(CX472_0003).

2570. Complaint Counsel has proffered no evidence that Mrs. Resnick or the other Respondents paid any money to *The Early Show* or anyone else for her participation in the interview or to allow her to speak about pomegranate juice.

2571. Ms. Resnick's reference to the "health-giving properties" of pomegranates during the interview was very small, only about 20 seconds out of a 3 minute and 52 second segment. (CX472_0003).

2572. Mrs. Resnick's reference to the "health-giving properties" of pomegranates was strictly "reactive" and directly in response to an unsolicited inquiry by the interviewer, Mrs. Chen, asking "how did [she] start marketing POM?" (CX472_0003).

2573. Mrs. Resnick staunchly believes that the opinions she expressed in her interview are completely true. (CX1375 (L. Resnick, Tropicana Dep. at101)).

2574. Complaint Counsel has presented no evidence that Mrs. Resnick's "main purpose" or "primary motivation" for participating in an interview on *The Early Show* was to sell POM or her book, *Rubies in the Orchard*.

2575. The substance of the interview, itself, evidences that the "main purpose" of the interview was to share with the viewer her successful marketing ideas and to provide tips on how to turn ideas into cash. (CX472_0003).

2576. The substance of the interview, itself, further evidence that neither Ms. Resnick's statements on *The Early Show* nor even her specific opinions on the benefits of pomegranate juice "proposed a commercial transaction." (CX472_0003).

2577. The Reibstein Survey shows that no mention of disease in Mrs. Resnick's interview was material to consumers' purchase decisions because less than 1.5% of the hundreds of survey respondents even mentioned disease as a reason for buying POM Juice. (Reibstein, Tr. at 2493; PX02223-0020).

2578. Even assuming *arguendo* that Mrs. Resnick's interview on *The Early Show* constitutes "advertising", Complaint Counsel has presented no evidence that showed any causal relationship between this interview and consumer purchasing decisions.

2579. Moreover, Ms. Resnick's responses to questions concerning pomegranate juice were purely statements of her opinion, which are protected under the First Amendment. (CX1375 (L. Resnick, Tropicana Dep. at 101)).

2580. No liability can be based on Mrs. Resnick's *The Early Show* interview because (a) it was not advertising; (b) it is constitutionally protected speech; and (c) her opinions were not material to the consumer purchasing decisions.

3. Lynda Resnick's Newsweek Interview

2581. On March 20, 2009, *Newsweek* published on its website two pages of excerpts from an interview with Mrs. Resnick titled "Striking Out On Your Own. Is now a good time to start a business?" (CX1426, Exh. F).

2582. The content of the *Newsweek* publication, itself, evidences that the primary focus of the article was Mrs. Resnick's business acumen and marketing strategies, as embodied in her book *Rubies in the Orchard*, as well as commentary on the economy and Bush administration. (CX1426, Exh. F).

2583. Although the entire 2-page, 1500-word article is set forth in CX1426, Exh. F, the Complaint quoted, out of context, the following 150 words:

[Interviewer:]	Should I take vitamins?
[L. Resnick:]	I don't know your family history. How's your father?
[Interviewer:]	He's in good health. Had a bout of prostate cancer, but that's—
[L. Resnick:]	You have to be on pomegranate juice. You have a 50 percent chance of getting it. Listen to me. It is the one thing that will keep your PSA normal. You have to drink pomegranate juice. There is nothing else we know of that will keep your PSA in check. Ask any urologist—your father should be on it. Your father should be on it. I'm sorry to do this to you, but I have to tell you. We just did a study at UCLA, on 43 men … It arrested their PSA. How old are you, 28?

[Interviewer:] Twenty-six.

[L. Resnick:] Get a base line now. [*Pause, wink*] It's also 40 percent as effective as Viagra. Not that you need it. But—couldn't hoit!

(CX1426, Exh. F).

2584. Mrs. Resnick staunchly believes that the opinions she expressed in her interview are completely true. (CX1375 (L. Resnick, Tropicana Dep. at 101)).

2585. Complaint Counsel has presented no evidence that Mrs. Resnick or the other Respondents paid any money to *Newsweek* or anyone else for her participation in the interview or to allow her to speak about pomegranate juice.

2586. Complaint Counsel has presented no evidence that Mrs. Resnick's "main purpose" or "primary motivation" for participating in an interview with *Newsweek* was to sell POM or her book, *Rubies in the Orchard*.

2587. The content of the *Newsweek* article, itself, evidences that the "main purpose" of the interview was to provide the viewer or reader with a wide-ranging discussion of herself and her views, interests and accomplishments. (CX1426, Exh. F).

2588. Ms. Resnick's references to the health benefits of pomegranate juice were very small, only about 150 words out of a 1500-word article. (CX1426, Exh. F).

2589. Mrs. Resnick's references to health benefits of pomegranate juice during the course of her interview were strictly "reactive" and in direct response to the unsolicited question, "Should I take vitamins?" posed by the interviewer. (CX1426, Exh. F).

2590. Ms. Resnick's responses to questions concerning pomegranate juice were purely statements of her opinion, which are protected under the First Amendment. (CX1375 (L. Resnick, Tropicana Dep. at 101)).

2591. The content of the *Newsweek* article, itself, further evidence that neither Ms. Resnick's statements during the interview nor even her specific opinions on the benefits of pomegranate juice "proposed a commercial transaction." (CX1426, Exh. F).

2592. Indeed, Complaint Counsel has presented no evidence that the *Newsweek* interview was solely related to the economic interests of Mrs. Resnick and her audience.

2593. The Reibstein Survey shows that no mention of disease in Mrs. Resnick's interview was material to consumers' purchase decisions because less than 1.5% of the hundreds of survey respondents even mentioned disease as a reason for buying POM Juice. (Reibstein, Tr. at 2493; PX02223-0020).

2594. Moreover, even assuming *arguendo* that Mrs. Resnick's interview with *Newsweek* constitutes "advertising", Complaint Counsel has presented no evidence that showed any causal relationship between this interview and consumer purchasing decisions.

2595. No liability can be based on Mrs. Resnick's *Newsweek* interview because (a) it was not advertising; (b) it is constitutionally protected speech; and (c) her opinions were not material to the consumer purchasing decisions.

4. Discussion With Lynda Resnick at USC's Annenberg School of Communication

2596. On April 9, 2009, Mrs. Resnick joined Dean Ernest J. Wilson III at the USC Annenberg School of Communication for a discussion titled "How to Uncover the Hidden Gems in Your Business" (hereinafter, "Dean's Forum"). The substance of discussion, itself, makes clear that it was focused on entrepreneurship, the secrets of Mrs. Resnick's success with the Roll family of companies and demystifying the marketing and creative process. (CX472_0002).

2597. Although the entire Dean's Forum was almost an hour and is set forth in a video marked as CX472_0002, the discussion is not an exhibit to or excerpt in the Complaint. (See CX472_0002).

2598. Respondents' therefore speculate that Complaint Counsel challenge the following 10 seconds excerpted below:

> [Speaker:] I have one question I'd like to ask you . . . I wonder if you could share your thoughts a little bit especially with this audience about what you mean by the term communication. How does that fit into the picture?
>
> **[**L. Resnick:] Well, we are really everywhere . . . We had some pretty horrible PR nightmares. . . So the PETA decided that we were bad because I order for us to do our medical research, first you do the research in the test tube and then you test

> on animals. And then you go to humans. It's just the protocol. And we did some testing on our juice on rats and mice. And one rabbit study. But they were happy because that was because we were testing the Viagra quality of POM juice which is 40% as effective as Viagra . . . .

(CX472_0002).

2599. Complaint Counsel, however, has presented no evidence that Mrs. Resnick did not believe that that the opinions she expressed during the "Question and Answer" portion of the Dean's Forum or any portion of the Dean's Forum were not completely true.

2600. Complaint Counsel has presented no evidence that Mrs. Resnick or the other Respondents paid any money to USC or anyone else for her participation at the Dean's Forum to allow her to speak about pomegranate juice.

2601. Complaint Counsel has presented no evidence that Mrs. Resnick's "main purpose" or "primary motivation" for participating in the Dean's Forum was to sell POM or her book, *Rubies in the Orchard*.

2602. The content of the Dean's Forum, itself, evidences that the "main purpose" of the discussion was to provide the audience with a discussion regarding marketing, public relations and building successful brands. (CX472_0002).

2603. Ms. Resnick's references to the health benefits of pomegranate juice were very, very small, only about 10 seconds out of an hour-long discussion. (CX472_0002).

2604. Ms. Resnick's statements regarding the health benefits of pomegranate juice were purely statements of her <u>opinion</u>, which are protected under the First Amendment.

2605. The content of the Dean's Forum, itself, further evidence that neither Ms. Resnick's statements during the forum nor even her specific opinions on the benefits of pomegranate juice "proposed a commercial transaction." (CX472_0002).

2606. Indeed, Complaint Counsel has presented no evidence that the Dean's Forum was solely related to the economic interests of Mrs. Resnick and her audience.

2607. The Reibstein Survey shows that no mention of disease in Mrs. Resnick's discussion was material to consumers' purchase decisions because less than 1.5%

of the hundreds of survey respondents even mentioned disease as a reason for buying POM Juice. (Reibstein, Tr. at 2493; PX02223-0020).

2608. Moreover, even assuming *arguendo* that Mrs. Resnick's discussion at the Dean's Forum constitutes "advertising", Complaint Counsel has presented no evidence that showed any causal relationship between this discussion and consumer purchasing decisions.

2609. No liability can be based on Mrs. Resnick's discussion at the Dean's Forum because (a) it was not advertising; (b) it is constitutionally protected speech; and (c) her opinions were not material to the consumer purchasing decisions.

5. Matt Tupper's Interview on Fox Business

2610. On June 17, 2008, Mr. Tupper appeared on FOX Business. The substance of the interview, itself, makes clear that the interview primarily focused on pomegranates - the newest super food, POM, and pomegranate product applications. (CX1426, Exh. E-7).

2611. Although the entire 6 minute and 5 second interview is set forth in a video marked as CX1426, Exh. E-7, Complaint Counsel appear to challenge the 100 second excerpt quoted in the Complaint:

* * *

Brian Sullivan: Alright, well, talk to us about the claims, heavy in anti-oxidants, credited with reducing heart disease. How much of a real benefit though are we talking about? And what's, you now, some of this food, you know we're showing some of your bottles here, but some of this food you say, well it will reduce your risk if you ingest , you know, 7 lbs. of it a day or something unnatural like that. How much do you have to have?

Mr. Tupper: With pomegranate, the dose that's been shown to be effective is eight ounces a day… pomegranate is the one fruit that's actually been tested in human beings by dozens of researchers across the globe. There's actually been a study published recently on prostate cancer. Men suffering

from advanced stages of prostate cancer drinking eight ounces a day saw the progression of the prostate cancer actually slow dramatically. In addition, there have been a number of studies published on cardiovascular disease in which sick patients again consuming eight ounces of pomegranate juice every day saw dramatic improvements in things like atherosclerosis, which is plaque in the arteries, the amount of blood flow delivered to the heart.

* * *

Brian Sullivan: There's a lot of different pomegranate things. How many more products can you put out there, and how much of it is just hooey,.., you know, pomegranate pills, et cetera?

Mr. Tupper: The products that we put into the market, though, all stem from the fundamental science of the pomegranate, and everything that we put into the market, whether it's juice, whether it's tea, whether it's the supplements that we sell, are all backed by an enormous investment in science. We've actually funded more than $25 million of scientific research worldwide since we started the business. And, therefore, every product that we sell is backed by that science. Every product that we sell contains those unique antioxidants. We don't do things for scents and flavors. We do them for the health benefits and for the science.

* * *

(CX1426, Exh. E-7).

2612. Complaint Counsel has presented no evidence that Mr. Tupper did not believe that the opinions he expressed during his interview by Brian Sullivan were not completely true.

2613. Complaint Counsel has proffered no evidence that Mr. Tupper or the other Respondents paid any money to FOX Business or anyone else for his participation in the interview or to allow him to speak about pomegranate juice.

2614. Complaint Counsel has presented no evidence that Mr. Tupper's "main purpose" or "primary motivation" for participating in an interview with FOX Business was to sell POM.

2615. Mr. Tuppers's references to the health benefits of pomegranate juice during the interview were very small, only about 100 seconds out of a 6 minute and 5 second interview. (CX1426, Exh. E-7)

2616. Mr. Tupper's references to the health benefits of pomegranate juice during the course of his interview were strictly "reactive" as opposed to proactive. For example, Mr. Tupper's statement that "the dose that's been shown to be effective is 8 oz. a day" was in direct response to Brian Sullivan's question, "How much do you have to have?" (Tupper, Tr. 1061-62).

2617. Mr. Tupper's responses to questions concerning pomegranate juice were purely statements of his opinion, which are protected under the First Amendment.

2618. The substance of the interview, itself, further evidence that neither Mr. Tupper's statements on FOX Business nor even his specific opinions on the benefits of pomegranate juice "proposed a commercial transaction." (CX1426, Exh. E-7).

2619. The Reibstein Survey shows that no mention of disease in Mr. Tupper's interview was material to consumers' purchase decisions because less than 1.5% of the hundreds of survey respondents even mentioned disease as a reason for buying POM. (Reibstein, Tr. at 2493; PX02223-0020).

2620. Moreover, even assuming *arguendo* that Mr. Tupper's interview on FOX Business constitutes "advertising", Complaint Counsel has presented no evidence that showed any causal relationship between this interview and consumer purchasing decisions.

2621. No liability can be based on Mr. Tupper's appearance on FOX Business because (a) it was not advertising; (b) it is constitutionally protected speech; and (c) his opinions were not material to the consumer purchasing decisions.

I. Summary of the Evidentiary Record Regarding POM's advertisements

2622. In conclusion, Respondents summarize their factual findings regarding their advertisements as follows:

(a) Complaint Counsel, from their own actions, admissions, and from the testimony of their expert, Professor Mazis, have repeatedly narrowed the scope of the ads at issue to POM juice prints ads disseminated before December 2008 and POM juice website ads disseminated before August 2009. (*See supra* XVII(D)).

(b) Consequently, those ads remaining at issue, many of which Complaint Counsel focused heavily on at trial, were disseminated three to seven years ago and have not been disseminated since then. (*See supra* XVII(E)).

(c) Complaint Counsel has presented no evidence whatsoever that it is probable or likely that POM would disseminate these "older" types of advertisements again. (*See supra* XVII(E)).

(d) Moreover, there have been significant changed in POM's advertising since 2006 and Respondents' later advertisements convey qualified claims that are substantiated by competent and reliable scientific evidence. (*See supra* XVIII).

(e) Accordingly, Complaint Counsel failed to meet their burden of showing that Respondents' past wrongs are ongoing or likely to recur. As a general rule, "[p]ast wrongs are not enough for the grant of an injunction"; an injunction will issue only if the wrongs are ongoing or likely to recur. *F.T.C. v. Evans Products Co.*, 775 F.2d 1084, 1087 (9th Cir. 1985).

(f) Respondents assert that the Commission may rely on its own reasoned analysis to determine what claims, including implied ones, are conveyed only if those claims are "conspicuous, self-evident or reasonably clear from the face of the ad." (*Kraft*, 970 F.2d 311, 320 (7th Cir. 1972) *cert. denied*, 507 U.S. 909 (1993)).

(g) In this case, however, it is impossible for Complaint Counsel to "conclude with confidence" that POM's advertisements convey the "clinically proven" claims to prevent or treat disease, as alleged. (*See In re Thompson Medical Co.*, 104 F.T.C. 648, 789 (1984), *aff'd*, 791 F.2d 189 (D.C. Cir. 1986), *cert. denied*, 479 U.S. 1086 (1987)).

(h) Consequently, because the challenged implied claims may not be determined with confidence from the face of the challenged advertisements, extrinsic evidence must be examined, including consumer surveys and expert testimony. (*See* Appendix of Advertisements; *In re Stouffer Food Corp.*, 118 F.T.C. 746, 777 (1994) (citing *Kraft*, 970 F.2d at 318)).

(i) Here, even if the ALJ were to allow Complaint Counsel to proceed on a broader number of ads and statements, the net impression of POM's ads do not convey to a reasonable consumer the "clinically proven" claims that Complaint Counsel asserts are implied in the advertisements under Complaint Counsels' "net impression" analysis or any analysis. (*See* Appendix of Advertisements).

(j) Moreover, Complaint Counsel have failed to present any reliable extrinsic evidence or expert opinion on the challenged ads. (Mazis, Tr. 2752).

(k) Additionally, assuming *arguendo* that the presumption of materiality applies in favor of the Commission, such presumption was successfully rebutted by Respondents' expert witness, Professor Reibstein. His survey demonstrated that, even if the ads conveyed the messages that Complaint Counsel assign to them, any alleged disease claims made by Respondents were not material to the purchasing decisions of POM consumers. (*See infra* XVIII(A)).

(l) Additionally, Complaint Counsels' own rebuttal survey expert, Professor Mazis, in stark contrast to work he has performed previously for Complaint Counsel, (a) did not conduct any facial analysis of the ads or offer any expert opinion on them; (b) did not conduct any surveys on the ads and (c) did not provide any expert opinion on the exposure of the ads to consumers, despite testifying that such exposures were critical to having an effect on consumers. (*See infra* XVIII(B)).

(m) The statements made by individual respondents, Mrs. Resnick and Mr. Tupper, during media interviews, on which Complaint Counsel rely, do not constitute "advertisements" and were not intended to market the Challenged Products. (*See infra* XVII(H)).

(n) Consequently, Complaint Counsel cannot rely on these statements to the media to prove its case against POM. (*See infra* XVII(H)).

(o) The Challenged Advertisements are truthful and supported by competent reliable science. (*See infra* XIV, XV, XVI).

(p) None of the Challenged Advertisements convey that a Challenged Product is a substitute for conventional medical treatment. (Butters, Tr. 2819).

XVIII. THE ASSERTED IMPLIED CLAIMS WERE NOT MATERIAL TO CONSUMERS

A. Any Presumption of Materiality Was Successfully Rebutted By Respondents' Exert Witness Professor David Reibstein

1. The Reibstein Survey Proves that Consumers Purchase POM Juice For Reasons Other Than Disease-Related Advertising Claims

2623. Only 1.48% (6 out of 406) of POM Juice buyers (i) bought, (ii) would buy again, or (iii) would recommend to a friend POM Juice because they believe that it cures or prevents any specific disease. (PX0223-0020).

2624. Only 1.74% (6 out of 344) of non-POM Juice buyers (i) bought, (ii) would buy again, or (iii) would recommend to a friend POM Juice because they believe that it cures or prevents any specific disease. (PX0223-0020).

2625. Based on Questions E and H "Why Did You Purchase," less than 1% (7 out of 750) of pomegranate juice buyers (POM and non-POM) bought the juice because they believe it cures or prevents any specific disease. (Reibstein, Tr. 2493, 2495; PX0223-0010-0011, 0020).

2626. Based on Questions F1a and I1a "Why Would You Buy Again," less than 1% (2 out of 755) of pomegranate juice buyers who mentioned that they would buy pomegranate juice (any brand) again stated they would do so because they believe that pomegranate juice cures or prevents any specific disease. (Reibstein, Tr. 2493, 2495; PX0223-0011, 0020).

2627. Based on Questions G1a and J1a "Why Would You Recommend," less than 1% (4 out of the 750) of pomegranate juice buyers who mentioned that they would recommend pomegranate juice (any brand) to a friend stated they would do so because they believe pomegranate juice cures or prevents any specific disease. (Reibstein, Tr. 2493, 2495; PX0223-0012, 0020).

2628. Based on the results of Questions E, F1, G1, H1, I1 and J1, very few pomegranate juice buyers POM or non-POM bought, would buy again or would recommend pomegranate juice because they believe the juice cures or prevents any specific disease. (PX0223-0012; Reibstein, Tr. 2499, 2501).

2629. Based on the results of Questions E, F1, G1, H1, I1 and J1, there is no significant difference in the perception of whether pomegranate juice can cure or prevent disease between POM Juice buyers and non-POM Juice buyers. (Reibstein, Tr. 2499, 2501; PX0223-0010-0012, 0020).

2630. A summary of the results of Questions E-J were set forth by Professor Reibstein in Figure 5 in his expert report. Figure 5 is set forth below:

Question	Percentage of POM Wonderful Juice Buyers whose response mentions a specific disease reference n=406	Percentage of Pomegranate Juice Buyers whose response mentions a specific disease reference n=344
E/H (Why did you purchase?)	1.0% (4/406)[6]	9% (3/344)[7]
F/I (Why would you purchase/not purchase again?)	5% (2/406)[8]	0% (0/344)
G/J (Why would/would not recommend?)	.3% (1/406)[9]	9% (3/344)[10]
NET	**1.48% (6/406)[11]**	**1.74% (6/344)**

2631. In response to Question E "Why Did You Purchase," only 1% of the 406 POM Juice buyers bought the product because they believe it cures or prevents any specific disease. (Reibstein, Tr. 2493, 2495; PX0223-0006, 0011; PX0233-0007, 0008).

2632. In response to Question E "Why Did You Purchase," less than 1% of the 344 non-POM Juice buyers bought the juice because they believe it cures or prevents any specific disease. (Reibstein, Tr. 2493, 2495; PX0223-0006, 0011; PX0233-0008).

2633. In response to Question E "Why Did You Purchase," 43.6% of the POM Juice buyers bought the juice because of "Taste." (Reibstein, Tr. 2496, 2553; PX0223-0006; PX0233-0008).

2634. In response to Question E "Why Did You Purchase," approximately 35% of POM Juice buyers bought the juice because they thought the product was "Healthy"

---

[6] 4 respondents – 1200046, 1200183, 1200349, 1200618

[7] 3 respondents – 1200175, 1200543, 1201150

[8] 2 respondent – 1200284, 1200618

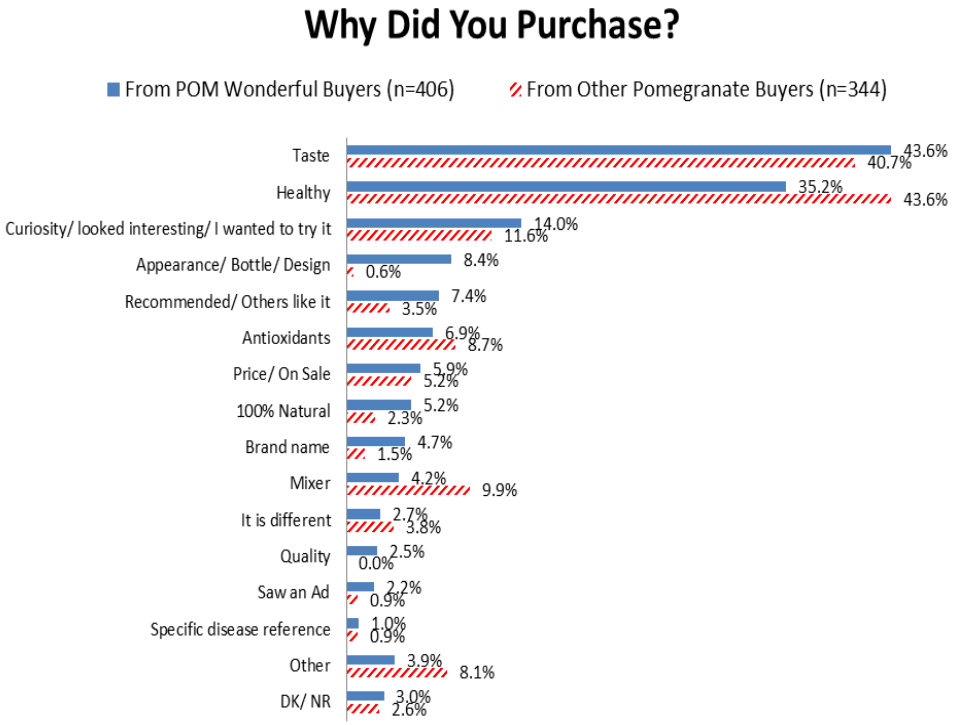
[9] 1 respondent - 1200229

[10] 3 respondents – 1200687, 1200836, 1200543

[11] Respondent 1200618 appears twice. In the NET he/she is only counted once.

versus 43.6% of non-POM Juice buyers. (Reibstein, Tr. 2496, 2553; PX0223-0006; PX0233-0008).

2635. The results of Question E "Why Did You Purchase" were set forth by Professor Reibstein in Figure 1 in his expert report. Figure 1 is set forth below:



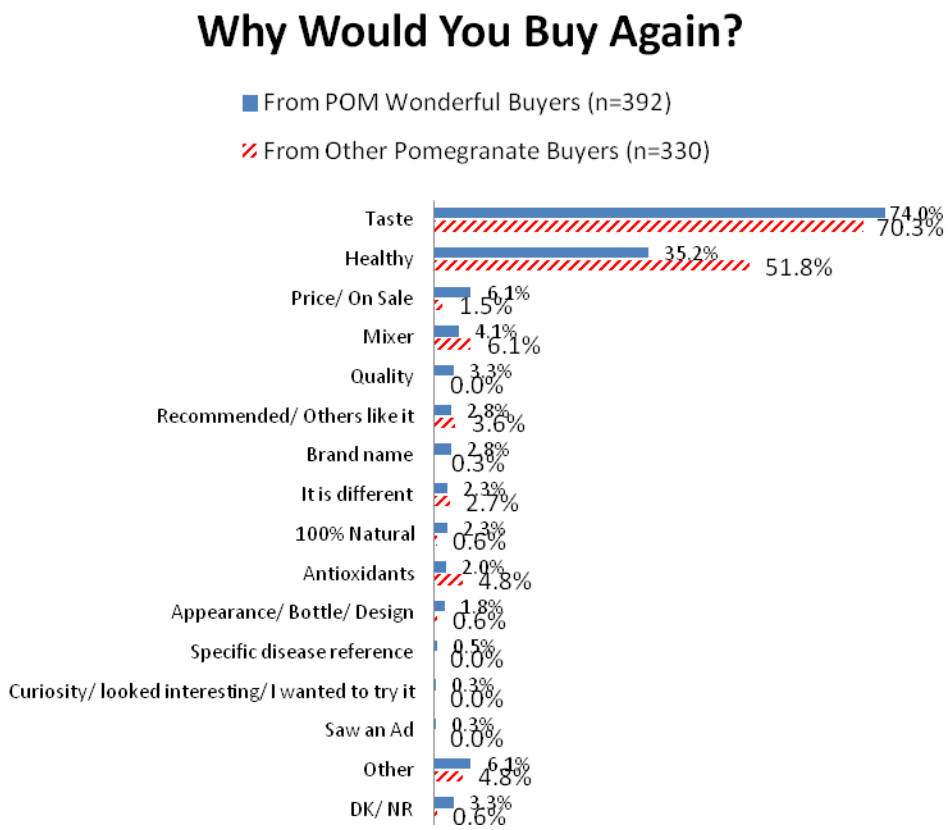
2636. In response to Question F1a "Why Would You Buy Again," only 0.5% of the POM Juice buyers would buy again because they believe it cures or prevents any specific disease. (Reibstein, Tr. 2497-98; PX0223-0007, 0011; PX0233-0012).

2637. In response to Question F1a "Why Would You Buy Again," 0% of non-POM Juice buyers would buy again because they believe it cures or prevents any specific disease. (Reibstein, Tr. 2497-98; PX0223-0007; PX0233-0012).

2638. In response to Question F1a "Why Would You Buy Again," 74% of the POM Juice buyers would buy again because of "Taste." (PX0223-0006; PX0233-0012).

2639. In response to Question F1a "Why Would You Buy Again," 35.2% of POM Juice buyers would buy again because they thought the product was "Healthy" versus 51.8% of non-POM Juice buyers. (PX0223-0007; PX0233-0012).

2640. The results of Question F1a "Why Would You Buy Again" were set forth by Professor Reibstein in Figure 2 in his expert report. Figure 2 is set forth below:



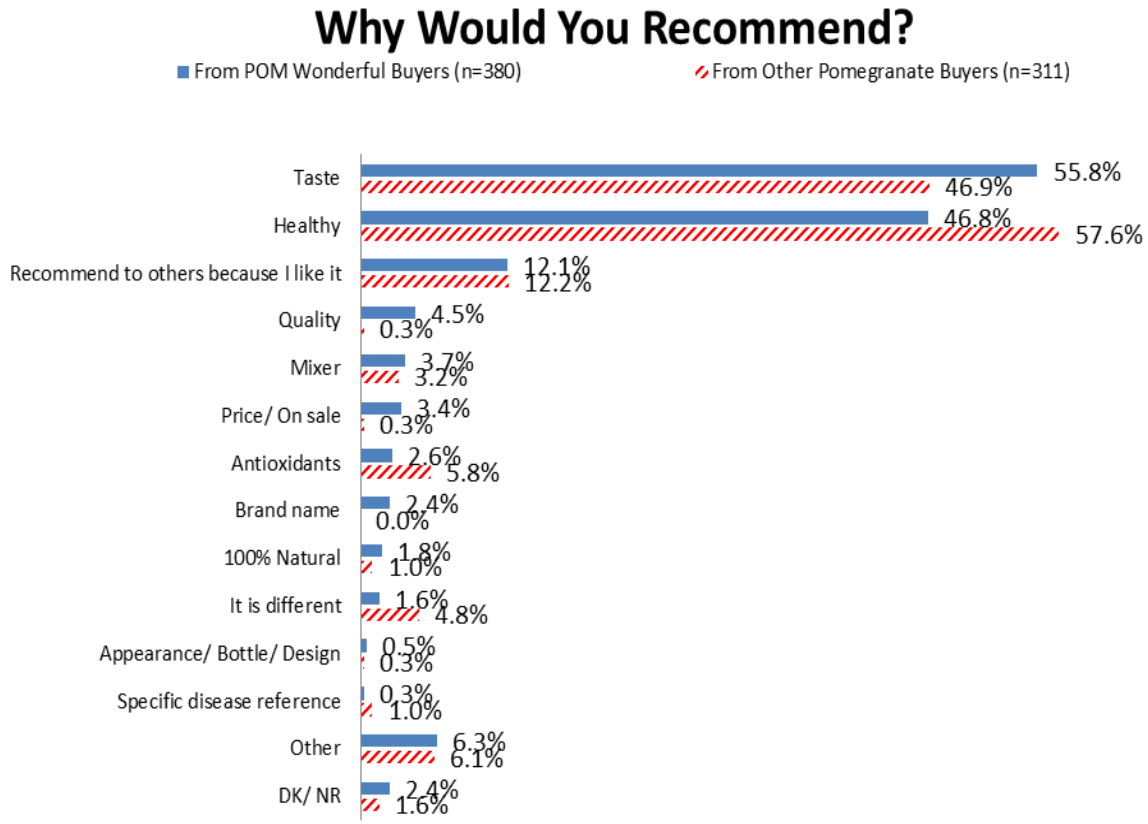
2641. In response to Question G1a "Why Would You Recommend," only 0.3% of the POM Juice buyers would recommend the juice because they believe it cures or prevents any specific disease. (Reibstein, Tr. 2498-99; PX0223-0008, 0012; PX0233-0018).

2642. In response to Question G1a "Why Would You Recommend," only 1% of the non-POM Juice buyers would recommend the juice because they believe it cures or prevents any specific disease. (PX0223-0008, 0012; Reibstein, Tr. 2498-99; PX0233-0018).

2643. In response to Question G1a "Why Would You Recommend," 55.8% of the POM Juice buyers would recommend the juice because of "Taste." (PX0223-0008; PX0233-0018).

2644. In response to Question G "Why Would You Recommend," 46.8% of POM Juice buyers would recommend the juice because they thought the product was "Healthy" versus 57.6% of non-POM Juice buyers. (PX0223-0008; PX0233-0018; Reibstein, Tr. 2499).

2645. The results of Question G1a "Why Would You Recommend" were set forth by Professor Reibstein in Figure 3 in his expert report. Figure 3 is set forth below:



2. The Reibstein Survey Proves That POM's Advertisements Had No Impact on Buyers Beliefs In the Curative or Preventive Attributes of Pomegranate Juice

2646. From the results of Questions E-K, POM's advertisements had no impact on buyers' beliefs that pomegranate juice can or will cure or prevent disease. (PX0223-0016-0020). A total of 12 unique respondents out of 750 total respondents, including non-POM Juice buyers, mentioned a specific disease as a reason for purchasing or recommending pomegranate juice. Among these respondents, only 4 of them have seen a POM advertisement at some point and 8 never have. (PX0223-0016-0020).

2647. The data from the Reibstein Survey shows that the small portion of pomegranate juice buyers who believe in the curative or preventive attributes of pomegranate juice is very similar between the group of respondents who had seen a POM advertisement and ones who have not. (PX0223-0016-0020).

2648. Based on Question K1 "Have You Seen a POM Ad," 41.9% of POM Juice buyers, 36.9% of the non-POM Juice buyers, and 39.6% of people (297 out of 750) who consumed pomegranate juice in the last 6 months had ever seen a POM advertisement. (PX0223-0009, 0016; PX0233-0028; Reibstein, Tr. 2536).

2649. Based on Question K1a, none of the respondents who saw a POM advertisement responded that they remember the advertisement making a specific disease claim. (PX0223-0009; PX0233-0029).

2650. Based on Questions E and H "Why Did You Purchase," among the respondents who bought pomegranate juice and who have seen a POM advertisement, only 0.7% (2 out of 297 total) bought the juice because they believe it cures or prevents any specific disease whereas 42.8% (127 out of 297 total) bought the juice because they think it is "Healthy." (PX0223-0016-0017; Reibstein, Tr. 2507).

2651. Based on Questions E and H "Why Did You Purchase," among the respondents who bought pomegranate juice and who did not see a POM advertisement, less than 2% bought the juice because they believe it cures or prevents any specific disease whereas approximately 36% bought the juice because they think it is "Healthy." (PX0223-0016-0017.).

2652. Based on Questions F1a and I1a "Why Would You Buy Again," among the respondents who bought pomegranate juice and stated they would purchase pomegranate juice again and who have seen a POM advertisement, only 0.4% (1 out of 285 total) would purchase the juice again because think it cures or prevents any specific disease and 46.3% (132 out of 285 total) said they would purchase again because they think it is "Healthy." (PX0223-0017-0018; PX0233-0012).

2653. Based on Questions F1a and I1a "Why Would You Buy Again," among the respondents who bought pomegranate juice and who did not see a POM advertisement, only 0.3% (1 out of 349 total) said they would purchase the juice again because think it cures or prevents any specific disease whereas 37.8% (132 out of 349 total) said they would purchase again because they think it is "Healthy." (PX0223-0017-0018; PX0233-0012).

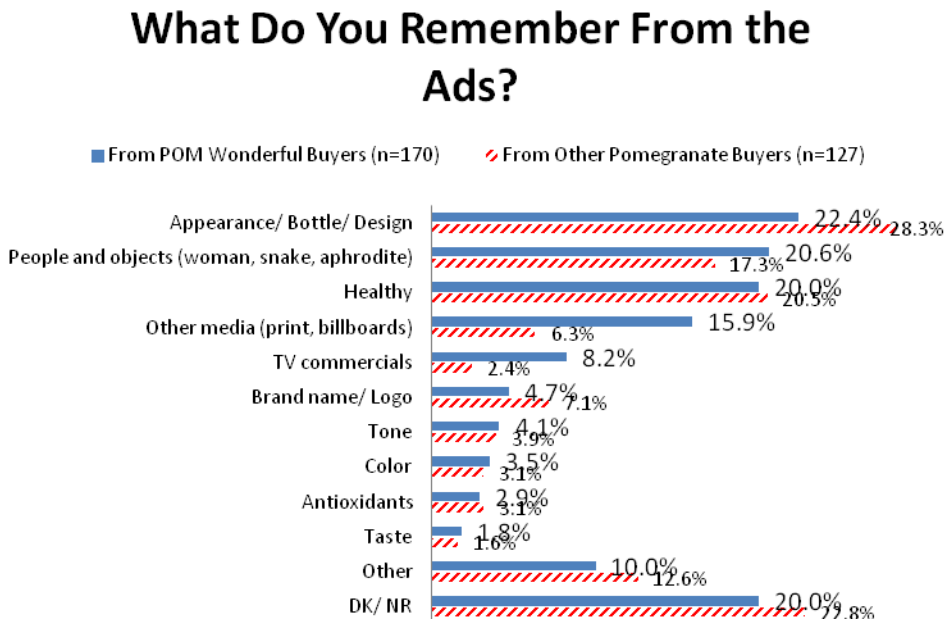
2654. Based on Questions G1a and J1a "Would you Recommend," among the respondents who bought pomegranate juice and stated that they would recommend pomegranate juice to a friend and who have seen a POM advertisement, only 0.4% (1 out of 279 total) said they would recommend the juice because they think it cures or prevents any specific disease whereas 55.6% (155 out of 279 total) said they would recommend the juice because they think it is "Healthy." (PX0223-0018-0019; PX0233-0012).

2655. Based on Questions G1a and J1a "Would you Recommend," among the respondents who bought pomegranate juice and stated that they would recommend pomegranate juice to a friend and who have not seen a POM advertisement, only 0.9% (3 out of 328 total) said they would recommend the juice because think it cures or prevents any specific disease whereas 47.3% (155 out of 328 total) said

they would recommend the juice because they think it is "Healthy." (PX0223-0019; PX0233-0012).

2656. The amount of money POM spent on its research was not a factor in why respondents purchased POM Juice. (Reibstein, Tr. 2508).

2657. A summary of the results of Questions K1a were set forth by Professor Reibstein in Figure 4 in his expert report. Figure 4 is set forth below:



3. The Methodology of the Reibstein Survey Is Scientifically Valid

2658. The Reibstein Survey was conducted by an independent market research company, Horizon Consumer Science ("HCS") under Professor Reibstein's direction. (PX0223-0003).

2659. HCS maintains an on-line panel of over one million subjects. From this population, a stratified sample of 2,164 was drawn from the U.S. population. (PX0223-0004).

2660. The Reibstein Survey was designed to reveal (i) a buyer's motivation for purchasing pomegranate juice; (ii) whether having previously seen POM Juice advertisements in the normal sequence of view ads, and not in an artificial setting, the ads affected the buyer's motivations for buying pomegranate juice; and (iii) whether the buyer's awareness of the legal issues around the case might have affected their motivation for buying pomegranate juice. (PX0223-0005; Reibstein, Tr. 2487; PX0356 (Reibstein Dep. at 11, 39, 51)).

2661. To qualify for the survey, respondents had to meet the following criteria: (i) purchased pomegranate juice in the last 6 months; (ii) had not completed any online survey within the past 3 months for any beverage products; (iii) did not work in any of the following industries: advertising, public relations, beverages, marketing or market research; and (iv) was over 18 years old. This was accomplished through a serious of screening questions. (PX0223-0004; PX0237-0001-0002; PX0356 (Reibstein, Dep. at 50, 57-58)).

2662. The 2,164 chosen panelists completed the online survey and 750 of them met the qualification criteria and actually conducted the survey. (PX0223-0004).

2663. The Reibstein Survey surveyed two groups, 406 respondents who purchased POM Juice in the past 6 months and 344 respondents who purchased brands of pomegranate juice other than POM in the past 6 months. (PX0223-0004; Reibstein, Tr. 2494).

2664. In order to find out what motivated the sample of 406 POM Juice consumers to buy POM Juice, the Reibstein Survey asked three primary open-ended questions as set forth in Questions E through G. (PX0223-0005).

2665. Question E asked "Why did you purchase POM Wonderful 100% Pomegranate Juice? *Please include as many specific details*." (PX0237-0002; PX0223-0006).

2666. Question F asked "Would you consider purchasing POM Wonderful 100% Pomegranate Juice again? (SELECT ONE ONLY) 1. Yes a. Why? *Please include as many specific details as to why you would?* 2. No. a. Why not? *Please include as many specific details as to why you would not?* 3. Don't know." (PX0237-0002; PX0223-0007).

2667. Question G asked "Would you recommend POM Wonderful 100% Pomegranate Juice to a friend? (SELECT ONE ONLY) 1. Yes a. Why? *Please include as many specific details as to why you would?* 2. No. a. Why not? *Please include as many specific details as to why you would not?* 3. Don't know." (PX0237-0002; PX0223-0008).

2668. In order to find out what motivated the sample of 344 non-POM Juice pomegranate juice consumers to buy POM Juice, the Reibstein Survey asked three primary open-ended questions as set forth in Questions H through J. (PX0223-0005).

2669. Question H asked "You indicated that you have purchased pomegranate juice. *Please include as many specific details* as to why you purchased it. *Please be as detailed as possible.*" (PX0237-0002; PX0223-0006).

2670. Question I asked "Would you consider purchasing pomegranate juice again? (SELECT ONE ONLY) 1. Yes a. Why? *Please include as many specific details as to why you would again*? 2. No. a. Why not? *Please include as many specific details as to why you would not again*? 3. Don't know." (PX0237-0003).

2671. Question J asked "Would you recommend pomegranate juice to a friend? (SELECT ONE ONLY) 1. Yes a. Why? *Please include as many specific details as to why you would?* 2. No. a. Why not? *Please include as many specific details as to why you would not?* 3. Don't know." (PX0237-0003).

2672. Questions E-J were asked in open-ended format, which reduces any biasing of the respondents. (PX0223-0005; PX0356 (Reibstein Dep. at 84-85)).

2673. Question K asked respondents "Have you ever seen a POM Wonderful 100% Pomegranate Juice advertisement? (SELECT ONLY ONE) 1. Yes. A. Please include as many specific details as to what you remember about the ad. *Please be as detailed as possible*. 2. No 3. Don't know." (PX0237-0003; PX0223-0016; Reibstein, Tr. 2507, 2567).

2674. The Reibstein Survey employed two types of controls. The first control was to draw a sample of non-POM Juice buyers and ask them the same questions as the POM Juice buyers to see if these buyers had different motivations for purchasing pomegranate juice. The second control was to compare the responses of people who had seen POM advertisements against those who had not seen any POM advertisement. (PX0223-0004, 0005; Reibstein, Tr. 2488-89, 2493; PX0356 (Reibstein, Dep. at 73-74)).

2675. Respondents to the Reibstein survey were not shown any POM advertisements because there is no need to show respondents advertisements to determine what motivated them to purchase pomegranate juice. (Reibstein, Tr. 2494, 2525).

2676. The Reibstein Survey included in the category "Specific disease reference" responses such as pomegranate juice is good for bowel movements or helpful in fighting urinary tract infections. (Reibstein, Tr. 2505; PX0223-0011).

2677. The Reibstein Survey was conducted in or about October 2010. (PX0356 (Reibstein Dep. at 12); Mazis, Tr. 2759).

2678. The results of the Reibstein Survey are statistically significant because there were more than 300 respondents in each group. (PX0223-0004; Reibstein, Tr. 2495-96).

2679. The survey respondents were compensated solely by the provision of contributions to a charity for their participation in the Reibstein Survey. (PX0223-0004).

B. Complaint Counsel's Survey Expert Failed to Rebut Respondents' Credible Evidence Disproving the Materiality of the Challenged Claims

1. Professor Michael Mazis Offered No Opinion on the Materiality of the Challenged Claims But Concedes That a Claim is Material Only If It Affects a Consumer Purchasing Decisions

2680. It was not within the scope of Professor Mazis' assignment to examine the materiality of the Challenged Claims. (PX0296).

2681. Professor Mazis offered no expert opinion on the materiality of the Challenged Claims in his export report, deposition or trial testimony. (PX0296; Mazis, Tr. 2651-2761; PXO359 (Mazis, Dep. at 1-242)).

2682. Professor Mazis was only asked by Complaint Counsel to evaluate the "scientific adequacy" of the Reibstein Survey. (PX0296-0002; PX0359 (Mazis, Dep. at 119)).

2683. Professor Mazis' expert opinions offered in this case were limited solely to the "scientific adequacy" of the Reibstein Survey. (PX0296-0002).

2684. Professor Mazis was neither asked by Complaint Counsel nor did he design or conduct a consumer survey regarding the Challenged Claims or any POM advertising. (PX0359 (Mazis, Dep. at 128, 232; Mazis, Tr. 2736).

2685. Professor Mazis provided no expert opinion based on a facial analysis of POM's advertisements. (PX0296; Mazis, Tr. 2651-2761; PX0359 (Mazis, Dep. at 1-242).

2686. Professor Mazis provided no expert opinion on the impact of POM's advertisements on consumers. (PX0296; Mazis, Tr. 2651-2761; PX0359 (Mazis, Dep. at 1-242).

2687. Professor Mazis provided no expert opinion on the "indirect effects" of POM's advertisements. (PX0296; Mazis, Tr. 2651-2761; PX0359 (Mazis, Dep. at 1-242).

2688. Professor Mazis provided no expert opinion on POM's advertisements based on the psychological and consumer behavior theory of "categorization." (PX0296; Mazis, Tr. 2651-2761; PX0359 (Mazis, Dep. at 1-242).

2689. Professor Mazis conceded that there is no evidence in the record in this case regarding whether "it's probable that any POM Juice or POMx advertisement was likely to affect anyone's belief about POM." (Mazis, Tr. 2753).

2690. Professor Mazis agreed that a statement is material if it is likely to affect a consumer's choice to purchase a product. (PX0296-0008; Mazis, Tr. 2699-2700, 2727).

2691. According to Professor Mazis, "the appropriate measure of materiality" is "the potential impact of the challenged claim on purchase or usage behavior." (Mazis, Tr. 2700).

2692. Professor Mazis testified that "an advertising claim may involve information important to consumers, but to be material is has to be important to their decision to buy." (Mazis, Tr. 2672-2673, 2700-2701, 2727).

2693. Professor Mazis testified that a product may have a certain effect but that may not be the reason the consumer purchases the product. (Mazis, Tr. 2700-2701).

2694. Professor Mazis testified that a survey on materiality does not need to show the survey participants actual advertisements. (Mazis, Tr. 2725).

2695. Professor Mazis has never done a materiality survey on behalf of the FTC or any federal agency. (PX0359 (Mazis, Dep. at 99); Mazis, Tr. 2721).

2. There is No Evidence in the Record Showing that Consumers Were Exposed to POM's Advertisements on Multiple Occasions

2696. The general rule is that it takes three good exposures to an advertisement for the message of the advertisement to be effective on consumers. And it takes many exposures to constitute three good exposures. (Stewart, Tr. 3228-3229).

2697. Professor Mazis testified that a "couple of exposures to an ad" are "probably . . .not going to affect people's belief about a product." (Mazis, Tr. 2752).

2698. Professor Mazis testified that he has no idea how many times any POM Juice or POMx advertisements were run by POM. (Mazis, Tr. 2752).

2699. Professor Mazis testified that no surveys have been introduced to show how many times any POM Juice or POMx advertisements were run by POM. (Mazis, Tr. 2752).

2700. There is no evidence in the record regarding the number of exposures consumers had to any particular POM advertisement. (Mazis, Tr. 2752).

2701. There is no evidence in the record regarding whether any POM advertisement making a disease claim of any kind had more than a single run. (Mazis, Tr. 2752).

2702. Complaint Counsel informed Professor Mazis that the FTC was only challenging POM Juice print advertisements that ran at least 22 months prior to the execution of the Reibstein Survey and POM Juice website entries in the 14 months prior to the execution of the Reibstein Study. (PX0296-0010; Mazis, Tr. 2753-2754). This is because the participants in the Reibstein Survey may have forgotten the advertisements. In his expert report, Professor Mazis said that "[e]ven if consumers could recall POM Juice advertising, they would be expected to recall more recent advertising, which is not being challenged by the FTC." (PX0296-0010).

3. Professor Mazis Was Repeatedly Impeached at Trial

2703. Professor Mazis admitted that he wrote an article called the Use of Consumer Surveys in FTC Advertising Cases. (Mazis, Tr. 2754). He testified that, in that article, he suggested, as one way of proving that ads were not material, a survey asking why the participants buy the advertised product, using three open-ended questions. The open-ended questions Professor Mazis used as examples of how to prove non-materiality were: (1) "what are the reasons you buy cheese?"; (2) "what are the reasons for your buying individually wrapped cheese food slices?"; and (3) what are "'all the reasons you can think of as to why you buy Kraft singles?'" (Mazis, Tr. 2755-56). Professor Mazis stated that, while these open-ended questions might understate the importance of calcium in selecting cheese, they would nevertheless have "probative value" in showing that the ads in question were not material. (Mazis, Tr. 2756).

2704. Professor Mazis' testimony at the hearing was inconsistent with what he said in his deposition. In his deposition, Professor Mazis testified that Dr. Reibstein concluded that a very small percentage of POM Juice buyers believed the product was beneficial to any disease and that "the statement is true because Dr. Reibstein found that in his study. So I'm not disagreeing with what he found. I'm just disagreeing with the methodology he used to find that out." (PX0359 (Mazis, Dep. at 66)). At the hearing, however, Professor Mazis claimed that when he testified in his deposition that Dr. Reibstein's "statement" that only a tiny percentage of POM Juice buyers believe the product helps a disease "is true," he really meant that the statement isn't true, but that Dr. Reibstein only "said it was true." (Mazis. Tr. 2703-04).

2705. Professor Mazis' testimony at the hearing was inconsistent with what he said in his deposition. At the hearing, Professor Mazis criticized Dr. Reibstein for using six months as the period in which participants bought the product. He testified that, "if he were Dr. Reibstein" he would never have divided the survey participants into two groups - those that bought POM pomegranate juice in the last six months and those that did not. (Mazis, Tr. 2719-20). In his deposition, however, Professor Mazis said exactly the opposite. He said "from

Dr. Reibstein's point of view" and "if I were Dr. Reibstein", the relevant universe for the survey would be "people who purchased pomegranate juice in the last six months," which would be divided into two subgroups – "people who purchased POM Juice and people who didn't purchase POM Juice." (PX0359 (Mazis, Dep. at 230-31)). Confronted with his inconsistent deposition testimony, at the hearing, Professor Mazis testified that, in his deposition, he was only speaking "from Dr. Reibstein's point of view" and "based on Dr. Reibstein's approach." He further testified that when he testified at the hearing that he would never divide the participants into the two six month groups, he was not speaking from Dr. Reibstein's point of view, but only from his own point of view. [Mazis, Tr. 2724-25).

4. Professor Mazis Is Biased Against Respondents Because of His Long Employment and Consulting Relationship with Complaint Counsel

2706. Over the years, Professor Mazis has served as a paid consultant for numerous federal government agencies, including the FTC, FDA, Consumer Product Safety Commission, Department of Justice, Federal Deposit Insurance Corporation, Bureau of Alcohol, Tobacco and Firearms and U.S. Mint. (PX0296 at 0003; Mazis, Tr. 2656, 2697).

2707. Professor Mazis was employed by the FTC from July, 1977 through August, 1979. (PX096a001 at 0001; Mazis, Tr. 2653). During that time he was Chief of Marketing and Consumer Research in the Office of Policy and Planning. (Mazis, Tr. 2696).

2708. Beginning in the mid 1990's, Professor Mazis worked a day-a-week for the FTC, at its offices in Washington D.C., for five to six years. (PX0359 (Mazis, Dep. at 22-24).

2709. Professor Mazis served as the FTC's principal marketing witness in several cases, including *FTC v. Novartis* in 1997, *FTC v. Trans Union* in 1998, *FTC v. Mercury Marketing* in 2003 and *FTC v. Telebrands* in 2004. (PX096a at 0012).

2710. In the past four years, Professor Mazis has been a testifying expert witness in 24 legal proceedings. (PX096a002 at 0001-0002; Mazis, Tr. 2697-98).

5. Professor Mazis' Objections to the Reibstein Survey Are Baseless

2711. Professor Mazis' two principal criticisms of the Reibstein Survey were that Dr. Reibstein's questions were not relevant to either the issues of advertising communication or the FTC's standard regarding materiality and that

Dr. Reibstein's methodology was flawed because he asked only open-ended questions with no follow-up questions probing further the respondents' answers. (Mazis, Tr. 2720; PX0296-0004,0007,0009).

2712. Professor Mazis does not consider himself an expert on what the FTC considers material, how the FTC determines materiality or what survey evidence the FTC considers relevant in assessing materiality. (Mazis, Tr. 2720-21; PX0359 (Mazis, Dep. at 98)).

2713. Professor Mazis wrote an article called the Use of Consumer Surveys in FTC Advertising Cases. (Mazis, Tr. 2754). He testified that, in that article, he suggested, as one way of proving that ads were not material to consumers, a survey asking why the participants buy the advertised product, using three open-ended questions. The open-ended questions Professor Mazis used as examples of how to prove non-materiality were: (1) "what are the reasons you buy cheese?"; (2) "what are the reasons for your buying individually wrapped cheese food slices?"; and (3) what are "'all the reasons you can think of as to why you buy Kraft singles?'" (Mazis, Tr. 2755-56). No follow up questions were asked. Professor Mazis stated that, while these open-ended questions might understate the importance of calcium in selecting cheese, they would nevertheless have "probative value" in showing that the ads in question were not material. (Mazis, Tr. 2756).

2714. Professor Mazis is not an attorney trained in the legal concepts governing materiality.

2715. Professor Mazis agreed that open-ended questions make it "significantly less likely that the respondents will be led into giving a particular answer." (Mazis, Tr. 2732).

2716. Professor Mazis testified that in his opinion the Reibstein Survey was not a "causal study" (Mazis, Tr. 2734-36, 2741). But Professor Mazis also testified that non-causal studies do not need a control. (PX0359 (Mazis, Dep. at 207)). Despite this fact, Professor Mazis criticized the Reibstein Survey for not allegedly having a "true" control. (Mazis, Tr. 2741).

2717. Professor Mazis has no evidence that "any substantial number of the people in the non-POM drinking group actually were former users of POM who quit." (Mazis, Tr. 2718).

2718. Professor Mazis declined to rule out the Reibstein Survey "as probative evidence." (Mazis, Tr. 2709).

6. Professor David Stewart Offered No Opinion on the Materiality of the Asserted Implied Claims

2719. It was not within the scope of Professor Stewart's assignment, and he did not opine in his export report, deposition or trial testimony, on the materiality of the asserted implied claims, including how consumers perceive them. (Stewart, Tr. 3226; CX1295; PX0357 (Stewart, Dep. at 1-194)).

2720. Professor Stewart does not know of any evidence in the record on how consumers perceive POM's challenged advertisements. (Stewart, Tr. 3226-27).

C. Complaint Counsel's Attempt to Identify An "Intent" Sufficient to Obtain a Presumption or Rebuff Respondents' Survey Expert on Materiality Was Unsuccessful

1. The Consumer Research Relied Upon By Complaint Counsel Do Not Show the Challenged Claims Were Material to Consumers

(a) The A&U Study is Methodologically Flawed and Unreliable

2721. In June 2009, a study was conducted by OTX Corporation of 200 current POM Juice users, 200 other pomegranate juice users, and 200 non-pomegranate juice users who were asked closed-ended questions regarding the reasons they buy pomegranate juice ("A&U Study"). (PX0224-0002, 0004; Reibstein, Tr. at 2517).

2722. The A&U Survey does not address whether POM is advertisements were material to the purchase decision of the respondents. (Mazis, Tr. 2743).

2723. The A&U Study used closed-ended questions in that it provided respondents with a list of 5 choices as to why they drink pomegranate juice. (PX0227-0006; Reibstein, Tr. at 2518-2520).

2724. By providing respondents with a list of choices respondents were cued to select from attributes that they may not otherwise have thought of. (Reibstein, Tr. at 2518).

2725. Utilizing closed-end questions also results in the exclusion of potential answers that were not included on the list of choices because survey respondents often feel compelled to select one of the answers provided on the list of choices. (Reibstein, Tr. at 2519).

2726. Utilizing closed-end questions results in the exclusion of potential answers that were not included on the list of choices because respondents often feel compelled

to select one of the answers provided on the list of choices. (Reibstein, Tr. at 2519).

2727. Question B1 asked respondents why they drink pomegranate juice and provided a limited number of choices, none of which were "don't know or "no opinion." (PX0227-006).

2728. Respondents who selected "health" from the list of choices as a reason why they drink pomegranate juice were asked in Question B2 "Which specific health reasons below describe why you personally drink pomegranate juice?" Respondents were provided a list of only 11 reasons. (PX0227-0006).

2729. The results from Questions B1 and B2 as well as any closed-ended questions are unreliable and inflated because the questions to those set of choices to the exclusion of others are leading in that the respondents are given a limited number of choices and/or cued to select from attributes that they might otherwise have thought of. (Reibstein, Tr. at 2518-2520).

2730. When questions are open-ended as in the Reibstein Survey, other reasons for purchase are given that are not listed in the A&U Study. (PX0223-0006; PX0227-0006).

2731. In the A&U Survey, 88-91% of the respondents answered that they bought pomegranate juice because it had antioxidants (PX0224-0012), which contrasts significantly with the Reibstein Survey, which showed that less than 10% of respondents purchase for that reason, and which were based on open-ended questions. (Reibstein, Tr. at 2519; PX0223-0006).

2732. By using the phrase "antioxidant-rich fruit juices" in two of the screening questions and the phrase "antioxidant-rich fruit" in the Intro, the A&U Study cued respondents on the issue of antioxidants even before asking them why they buy pomegranate juice. (PX0227-0003-0004; Reibstein, Tr. at 2519).

2733. The A&U Study was methodologically flawed and unreliable because the sample size of 200 POM Juice users was too small to reach statistical significance. (Reibstein, Tr. at 2520).

2734. The A&U Study was conducted in two markets, one in which POM advertised and another in which POM ran no advertising. More respondents in the non-POM advertising markets (15%) thought POM's pomegranate juice was healthier than other brands than in the POM advertising markets (10%). (PX0224-0024; Reibstein, Tr. at 2521).

2735. To eliminate the effect of yea-saying, inattention, the halo effect, or other noise, and to get the true impact of advertisements on the test group, the responses to the

control group are subtracted from the responses to the test group. (Stewart, Tr. 3238; Mazis, Tr. 2735-2736).

2736. When the responses of the control group of people non-POM Juice drinker is subtracted from the responses of the test group of POM Juice drinkers, the percentage of POM Juice drinkers who mentioned "promotes heart health" is only 8%. (PX0224-0012).

2737. When the responses of the control group of people non-POM Juice drinker is subtracted from the responses of the test group of POM Juice drinkers, the percentage of POM Juice drinkers who mentioned "helping prevent prostate cancer" is only 7%. (PX0224-0012).

2738. Professor Mazis testified that the A&U Study does not state whether "POM ads were material to [consumers'] purchase decision[s]." (Mazis, Tr. 2743).

2739. Professor Mazis testified that he understood that many of the figures in the A&U Study did not reach a 90% confidence level, but that he did not have a full understanding of what was done and he did not think it was done properly. (Mazis, Tr. 2751-2752).

2740. Professor Mazis agreed that the A&U Study asked only closed-ended questions. (Mazis, Tr. 2681).

2741. Professor Mazis agreed that closed-end questions have the potential to direct participants to certain aspects of an advertisement, so that participants may respond to such questions based upon yea-saying, inattention, preconceptions or other noise. (Mazis, Tr. 2733).

2742. Professor Mazis testified that "open-ended questions make it significantly less likely that the participant will be led into giving a particular answer." (Mazis, Tr. 2732).

2743. Professor Mazis testified that the A&U Study was flawed because it "primed" the survey participants by asking numerous screening questions about "antioxidant juices" and the word "antioxidant" was repeated a few times throughout the screening questions so that in considering the main survey questions, the participants may have been focused on health and health issues. (Mazis, Tr. 2686-2687, 2739-2740).

2744. Professor Mazis criticized the A&U Study as lacking a "true control" (Mazis, Tr. 2740-2741) but also testified that a control was not necessary in the A&U Study because it was not what he called a "causal study." (Mazis, Tr. 2734-2736, 2741).

2745. Professor Mazis agreed with a quote from *Telebrands* that responses to control questions "measure the number of participants who answered based upon yea-saying, inattention, the halo effect, or other 'noise'" and "[t]o eliminate the effect of such external factors, the responses to the control or masking questions are subtracted from the responses to the test questions." (Mazis, Tr. 2735-2736).

2746. Professor Mazis conceded that, with respect to the results in the A&U Study, he did not subtract the results to the control questions from the results to the test questions (Mazis, Tr. 2735-2738) because the A&U Study was not what he calls a "causal" survey, and only "causal" surveys require the subtraction outlined in *Telebrands*. (Mazis, Tr. 2733-2737).

2747. Professor Mazis testified that asking participants the "cause" of their purchase was not a "causal study." (Mazis, Tr. 2734-2735).

2748. Professor Mazis testified that on page 12 of the A&U Study that there is no statistically significant difference among the three groups of respondents regarding the "helps protect against prostate cancer" response. (Mazis, Tr. 2742). He further testified that "[t]hose numbers are quite similar. And I'm sure other information out in the marketplace, on the Internet and other places certainly influenced all of those people, but it doesn't really say anything about what the influence of specific POM claims would be on consumers exposed to those claims." (Mazis, Tr. 2743).

2749. Professor Mazis agreed that, even though the A&U Study found that a very substantial number of the three groups of respondents said that they thought that POM Juice and other juices help protect against urinary tract infections, neither of the three groups could have gotten that information from a POM advertisement if POM never advertised such information. (Mazis, Tr. 2747-48).

2750. Professor Mazis agreed that, even though the A&U Study found that approximately 49% of respondents said that POM and the other juices provided immunity from colds and flu, none of those respondents could have gotten that information from a POM advertisement if POM never advertised such information. (Mazis, Tr. 2748).

2751. Despite his criticisms of the A&U Study, Professor Mazis testified that he finds the A&U Study more reliable than the Reibstein Survey on the likely importance of the challenged claims on consumers' purchase or use decisions. (Mazis, Tr. 2689).

(b) The Bovitz Survey Is Methodological Flawed, Unreliable and Does Not Address Consumers' Purchasing Decisions

2752. Professor Mazis did not consider and offered no expert opinion in his expert report on the survey conducted by the Bovitz Research Group comparing consumers' perception of ten (10) billboard advertisements from POM's *Super Hero* and *Dressed Bottle* advertising campaigns (the "Bovitz Survey"). (PX0296-0003).

2753. In the Bovitz Survey, a total of 150 target consumers and 100 POM users were recruited and exposed to each campaign (PX0225-0002-0003).

2754. Respondents to the Bovitz Survey were not asked why they purchase POM Juice. (PX0236-0001-0015; Reibstein, Tr. at 2509).

2755. The Bovitz Survey is unreliable for measuring consumers' motivations for purchasing POM Juice because respondents were not asked why they purchase POM Juice. (Reibstein, Tr. at 2509, 2513).

2756. The Bovitz Survey is methodologically flawed and unreliable because respondents were shown specific advertisements in a tightly controlled environment, which is not how consumers normally view advertisements. (Reibstein, Tr. at 2509-2510).

2757. The Bovitz Survey is methodologically flawed and unreliable because it had no control and, thus respondents might have had preconceived perceptions about pomegranate juice before being exposed to POM's billboard advertisements. (Reibstein, Tr. at 2510-2511).

2758. As measured by survey Question E, the Bovitz Survey imposed strict qualification requirements, including the fact that individuals had to engage in a health-conscious lifestyle and/or hold attitudes toward improving their overall health. (PX0225-0003; PX0236-0002).

2759. The Bovitz Survey is methodologically flawed and unreliable because Question E creates a bias towards extremely health-focused people, which is not representative of the overall consumer population. (Reibstein, Tr. at 2511-2512).

2760. The Bovitz Survey is methodologically flawed and unreliable because the sample size of only 100 POM users and 150 target consumers was too small to reach statistical significance at the 95% confidence level. (Reibstein, Tr. at 2512-2513).

2761. The Bovitz Survey is unreliable for determining consumers' perceptions of POM's billboard advertising because of the sample size was too small. (Reibstein, Tr. at 2513).

2762. The Bovitz Survey is unreliable for determining consumers' perceptions of POM's billboard advertising because of the tightly controlled environment in which the respondents were exposed to the billboard advertisements. (Reibstein, Tr. at 2513-2514).

2763. The Bovitz Survey is unreliable for determining whether what was observed within the survey applies to a normal advertising viewing context. (Reibstein, Tr. at 2513-2514).

2764. Question 9 of the Bovitz Survey states: "Other than trying to get you to buy the product, what do you think is the main idea these ads are trying to get across to you?" (PX0236-0009). When asked this general question, 5% of the respondents answered that the billboard advertisements conveyed a message about helping/lowering blood pressure. (PX0235-0011).

2765. Question 10 of the Bovitz Survey states: "Based on the ads you just saw, what are the specific benefits, if any, of drinking POM Wonderful?" (PX0236-0009). When asked this leading question, 21% of the health-conscious respondents answered that the billboard advertisements conveyed a message about helping/lowering blood pressure. (PX0235-0011).

2766. In regard to the 5% of respondents who answered in response to Question 9 that the billboard advertisements conveyed a message about helping/lowering blood pressure, the Bovitz Survey is unreliable because the sample size is too small and the tightly controlled environment is not the normal advertising viewing context. (Reibstein, Tr. at 2516).

2767. In regard to the 21% of respondents who answered in response to Question 10 that the billboard advertisements conveyed a message about helping/lowering blood pressure, the Bovitz Survey are unreliable because the sample size is too small and the question is leading and biasing in that it directs respondents to select a "specific benefit" which pressures them to identify a particular benefit from the list of choices even if they had not perceived one of those benefits being conveyed to them. (Reibstein, Tr. at 2515-2516).

2768. With respect to consumers' perception of the "Decompress" billboard advertisement, the Bovitz Survey is unreliable because the sample size is small and the question is leading and biasing in that it directs respondents to select a "specific benefit" which pressures them to identify a particular benefit from the list of choices even if they had not perceived one of those benefits being conveyed to them. (Reibstein, Tr. at 2515-2516).

2769. Over 90% of respondents answered that the billboard advertisements were about general health versus a specific disease. (Reibstein, Tr. at 2516-2517; PX0225-0012-0013).

2770. The Complaint Counsel is not challenging POM's billboard advertisements in this case. (Stewart, Tr. 3208; Reibstein, Tr. at 2574).

2771. The Bovitz Survey exposed respondents only to POM's billboard advertising. (Reibstein, Tr. at 2573,2575; Stewart, Tr. 3207, 3209; PX0225-0005-0006).

(c) The AccentHealth Study Is Methodological Flawed and Unreliable

2772. Professor Mazis did not consider the AccentHealth Study in preparing his expert report and proffered no opinion on it in his expert report. (PX0296-0003).

2773. In December 2008, Roper Public Affairs and Media, a division of Gfk Custom Research, was commissioned by AccentHealth to conduct a survey of POM's advertising in select AccentHealth offices (the "AccentHealth Study"). (PX0235-0006).

2774. The AccentHealth Study surveyed patients as they left their urologists' offices, asking them about a wall mounted poster in the waiting area of the doctor's office that featured a POM advertisement. (PX0234-0001; PX0235-0006).

2775. The AccentHealth Study was methodologically flawed and unreliable because the patient was intercepted immediately after leaving his urologist's office, heightening whatever issues the patient had about helping his prostate. (Reibstein, Tr. at 2522; PX0223-0021).

2776. The AccentHealth Study was methodologically flawed and unreliable because it had no control and, thus survey respondents might have believed that POM Juice was good for their prostate before seeing the wall-mounted poster advertisement in their urologist's office. (Reibstein, Tr. at 2522; PX0223-0021).

2777. Because of the methodological flaws of the AccentHealth Study, the results of the AccentHealth Study are biased. (Reibstein, Tr. at 2522).

2778. The AccentHealth Study was conducted by AccentHealth who has a vested interest in convincing businesses to place advertisements in doctors' offices. Thus, AccentHealth had the motivation to skew the results of the AccentHealth Study by designing the study such that the results would show that the advertisement it selected to be surveyed had a positive impact on patient's perceptions of helping their prostates. (Reibstein, Tr. at 2522).

2. POM's Consumer Comment Logs Do Not Show that the Challenged Claims Were Material to Consumers' Purchasing Decisions

2779. POM maintains a consumer comment log. Once a consumer comment is received by POM, it is given a unique "ID" number. The consumer comment is then listed in sequential order by ID number on the consumer comment log. POM has

received at least 24,470 consumer comments over the years and its consumer comment log is at least 2,297 pages. (CX0454; CX0455; CX0456).

2780. From the nearly 25,000 consumer comments, POM provided Complaint Counsel the 53 consumer comment log entries that referenced a specific disease, health study or POM advertisement. An only a few of those53 log entries referenced any health-related advertising claim made by POM. (CX0454; CX0455; CX0456).

D. Professor Reibstein Was Extremely Well Qualified To Provide the Opinions He Offered In This Case

2781. Dr. Reibstein is a tenured Professor of Marketing at the University of Pennsylvania in The Wharton School. Dr. Reibstein has taught courses in marketing management, marketing strategy and marketing metrics to MBA Program and Executive MBA Program students; marketing research courses to MBA Program students; and other marketing courses to undergraduate students. Many of these courses involve the use and design of surveys. (Reibstein, Tr. at 2482; PX0356a01-0002-0003).

2782. Dr. Reibstein has been a visiting professor at Stanford Business School, Harvard Business School and Purdue University where he taught marketing courses. Dr. Reibstein has taught courses in marketing strategy and advanced industrial marketing strategy at INSEAD, a top business school in Europe. (Reibstein, Tr. at 2483; PX0356a01-0002, 0003).

2783. Dr. Reibstein received Doctor of Industrial Administration from the Herman C. Krannert Graduate School of Industrial Administration at Purdue University with major in marketing and a minor in behavioral science. (Reibstein, Tr. at 2481). Dr. Reibstein's doctoral dissertation was titled "An Empirical Study of Brand Choice and Switching Behavior." (PX0356a01-0001). Dr. Reibstein attended the Master of Business Administration Program at the Graduate Business School at Tulane University. (Reibstein, Tr. at 2480-81; PX0356a01-0001). Dr. David Reibstein received a B.S. in Business Administration and a B.Z. in Statistics and Political Science from the University of Kansas. (Reibstein, Tr. at 2480; PX0356a01-0001).

2784. Dr. Reibstein has been awarded an Honorary Master of Science by The Wharton School at the University of Pennsylvania. (PX0356a01-0001).

2785. From 1985 to 1989, Dr. Reibstein was the Director of the Wharton/PIMS Strategy Research Center at the University of Pennsylvania. (PX0356a01-0002). From 1987 to 1992, Dr. Reibstein was the Vice Dean and Director of The Wharton Graduate Division at the University of Pennsylvania. (Reibstein, Tr. at 2482; PX0356a01-0002).

2786. Dr. Reibstein was the Executive Director for the Marketing Science Institute, an organization of 72 company-members. The Marketing Science Institute works closely with its members to identify the major marketing issues confronting them. The Marketing Science Institute prepares reports on various marketing issues which are disseminated to its members and the general business community. The Marketing Science Institute sets the research agenda for marketing academia globally. (Reibstein, Tr. at 2483-84; PX0356a01-0002).

2787. Throughout his teaching career, Dr. Reibstein has received numerous awards recognizing him for excellence in teaching. (PX0356a01-0003).

2788. Dr. Reibstein has published extensively in prestigious peer-reviewed marketing journals, including many articles on marketing and marketing research. Those journals include, among others, the Journal of Consumer Research, Journal of Marketing Research, Marketing Science and the Harvard Business Review. (Reibstein, Tr. at 2484; PX0356a01-0004-0007).

2789. Dr. Reibstein has written over 7 books and numerous chapters in books on marketing and marketing research. (Reibstein, Tr. at 2484; PX0356 (Reibstein, Dep. at 14; (PX0356a01-0007,0008).

2790. Dr. Reibstein authored the book "Marketing Metrics: 50+ Metrics Every Executive Should Master (2006)" which was named as the "Best Business Book: Marketing" by Strategy & Business in 2007. (PX0356a01-0004).

2791. Dr. Reibstein has spoken or presented at over 100 conferences on marketing and marketing research. (PX0356 (Reibstein, Dep. at 14; (PX0356a01-0008-0013).

2792. Dr. Reibstein is the Chairman elect of the American Marketing Association. (Reibstein, Tr. at 2484; Reibstein, Dep. at 14).

2793. Dr. Reibstein has designed, executed and supervised market research studies for over 30 years, including studies concerning consumer behavior. (Reibstein, Tr. at 2485-86).

2794. Dr. Reibstein has designed, executed or supervised hundreds of surveys during his career. (Reibstein, Tr. at 2485-86).

2795. Dr. Reibstein has performed consulting research for a variety of companies where is work focuses on understanding why it is that customers buy, what motivates customers to buy, and the interface with customer behavior and a company's marketing activities, price, product, place, and promotion. (Reibstein, Tr. at 2484-2485; PX0356 (Reibstein, Dep. at 14-15)).

2796. Dr. Reibstein's consulting work for companies involves collecting and processing information to better inform the company about what has or might influence customers to make the purchase decisions they do, and in the manner they do to reduce uncertainty in the decisions they make. Dr. Reibstein's consulting work also involves determining the messages consumers take from certain advertising. (PX0356 (Reibstein, Dep. at 16)).

2797. Dr. Reibstein has also provided extensive management education in the field of marketing to more than 300 companies over his career. (Reibstein, Tr. at 2485).

2798. Dr. Reibstein serves on the board of the Marketing Accountability Standards Board. This board sets the standards on what are the most important marketing metrics and how to measure them both in the United States and globally. (Reibstein, Tr. at 2485).

2799. Pomegranates are naturally safe, Pomegranate, Punica granatum, is a fruit-bearing plant native to high-altitude regions of Central Asia. Humans have consumed pomegranates for thousands of years as a safe and nutritious food. The FDA identifies pomegranate as being "generally recognized as safe" for human consumption. See generally 32 U.S.C. § 231(s); 21 C.F.R. § 182.20.

RESPONDENTS' PROPOSED CONCLUSIONS OF LAW

I. OVERVIEW OF APPLICABLE LAW

1. The FTC's authority to regulate health benefit claims for food derives from the FTC Act. Section 5 of the Federal Trade Commission Act ("FTC Act") prohibits "unfair or deceptive acts or practices in or affecting commerce." 15 U.S.C. § 45, *et seq*. Section 12 of the FTC Act declares dissemination of false advertisements regarding "food" or "drugs" to constitute an unfair or deceptive act or practice under Section 5. 15 U.S.C. § 52.

A. The FTC And FDA's Respective Roles in Regulating Health Benefit Claims.

2. In addition to the FTC, another federal agency, namely the Food & Drug Administration, may also regulate health benefit claims for food under the authority provided in the Federal Food Drug & Cosmetic Act ("FDCA"). While both the FDCA and FTC Act give the FDA and FTC overlapping jurisdiction over food labeling and advertising, the FDA and FTC proceed under a longstanding liaison agreement under which the FDA regulates food labeling (i.e., the actual package label and any written, printed, or graphic matter that accompanies the sale of the food) and the FTC regulates food advertising, including non-labeling marketing communications, such as television and print advertising. *See* Working Agreement Between FTC and Food and Drug Administration, 4 Trade Reg. Rep. (CCH) ¶ 9,850.01 (1971).

3. The FTC's and FDA's respective regulation of health benefit claims differ in several important respects. For example, in addition to its authority to determine whether labeling renders a food misbranded, the FDA may also look to claims made in advertising as evidence of a company's intended use for its product, because, under the FDCA, articles may be defined by their intended use, as evidenced by marketing claims. Thus, the FDA's approach to health benefit claims for food is driven in large measure by the definition of a "drug" under the FDCA, which includes "articles intended for use in the . . . cure, mitigation, treatment or prevention of disease in man or other animals." 21 U.S.C. § 321(g)(1). Under the FDA's approach, claims that state or imply that a food is intended for such a use may be deemed by the FDA to be drug claims not permitted for food, even if they are true and substantiated by evidence. *See* Wallach v. Crawford, No. 04-CV-216 BTM (WMC), 2005 WL 6054963, at *5-6 (S.D. Cal. Mar. 29, 2005).

4. The Commission, however, does not enforce the FDCA. See generally Buckman Co. v. Plaintiff's Legal Comm'n, 531 U.S. 341 (2001). Whether a product meets the definition of "food" or "drug" in either the FDCA or the FTC Act is not in itself an indication of a violation of the FTC Act. Instead, the FTC evaluates whether claims concerning products are truthful, non-misleading, and substantiated. This approach is required by the FTC Act, which grants the FTC the statutory authority to regulate only those claims that are false or misleading. *See* FTC Act Sections 5 and 12, 15 U.S.C. §§ 45, 52. Thus, if a claim is truthful, non-misleading, and substantiated by evidence, the FTC cannot prohibit the claim (even if the FDA determines that such claims should be prohibited under its separate regulatory scheme).

5. Moreover, unlike the FDA, which pre-approves health claims for foods and drugs, the FTC does not pre-approve advertising claims, but instead takes post-market enforcement action against false, misleading, or unsubstantiated claims. The rationale behind the FTC's post-market review of advertising claims and narrow tailoring of remedies is to "curb deception without overly restricting truthful commercial speech, thus promoting the goals embodied in the First Amendment." *See* In the Matter of Request for Comment on First Amendment Issues, Docket No. 02N-0209: Comments of the Staff of the Bureau of Economics, the Bureau of Consumer Protection, and the Office of Policy Planning of the Federal Trade Commission. Indeed, in the past, the FTC's Bureau of Consumer Protection has urged the FDA to adopt an approach to health claim regulation that would allow for dissemination of information to consumers and has noted that the pre-market approval approach of the FDA may wrongly prohibit claims even if substantiated by evidence, and had the potential to discourage the dissemination of useful information to consumers. Id.

B. The FTC's Traditional Approach in Evaluating Health Benefit Claims

6. The FTC's decision in In re Pfizer, Inc., 81 F.T.C. 23 (1972), established the basic requirements for advertising substantiation. In that decision, the FTC identified various factors used to determine the amount of substantiation necessary to determine whether an advertiser has a reasonable basis for a particular claim, including (1) the type and specificity of the claim made—*e.g.*, safety, efficacy, dietary, health, or medical; (2) the type of product— *e.g.* food, drug, potentially hazardous consumer product; (3) the possible consequences of a false claim—*e.g.*, personal injury, property damage; (4) the ease and cost of developing

substantiation for the claim; (5) the degree of reliance by consumers on the claims; and (6) the level of substantiation experts would agree is reasonable. Id. at 30.

7. The FTC's approach to evaluating advertising claims was later memorialized in the FTC's Deception Policy Statement and Substantiation Policy Statement. *See* FTC Policy Statement on Deception ("FTC Deception Policy Statement"), appended to In the Matter of Cliffdale Associates, Inc., et al., 103 F.T.C. 110, 174 (1984); FTC Policy Statement Regarding Advertising Substantiation ("FTC Substantiation Policy Statement"), appended to In the Matter of Thompson Medical Co., Inc., 104 F.T.C. 648, 839 (1984), *aff'd*, 791 F.2d 189 (D.C. Cir. 1986), *cert. denied*, 479 U.S. 1086 (1987).

8. The standard for determining whether a particular advertising claim is substantiated is, accordingly, a flexible one.[1] The Commission has previously explicitly rejected proposals to adopt a more "rigid standard that, in some instances, could be higher than necessary to ensure adequate scientific support for certain specific claims."[2]

9. For claims relating to health and safety, as well as some claims of product efficacy, the FTC has defined the reasonable basis requirement more specifically to require "competent and reliable scientific evidence," which the FTC defines as "tests, analyses, research, studies, or other evidence based on the expertise of professionals in the relevant area, that have been conducted and evaluated in an objective manner by persons qualified to do so, using procedures generally accepted in the profession to yield accurate and reliable results." In the Matter of Schering Corp., 118 FTC 1030, 1120-1121. Again, this standard is a flexible one that does not require a fixed number or type of studies. However, it does allow experts to determine the nature and quantity of evidence that an expert in the relevant field would believe is needed to substantiate the claim being made. *See, e.g.*, FTC v. QT, Inc., 512 F.3d 858, 861 (7th Cir. 2008) ("Nothing in the Federal Trade Commission Act…requires placebo-controlled, double-blind studies. The

---

[1] *See* Dietary Supplements: An Advertising Guide for Industry at 8 ("[T]he FTC's standard for evaluating substantiation is sufficiently flexible to ensure that consumers have access to information about emerging areas of science."), available at http://business.ftc.gov/sites/default/files/pdf/bus09-dietary-supplements-advertising-guide-industry.pdf.

[2] Letter from Donald S. Clark to Jonathan Emord Denying Petition for Rulemaking, (FTC. Nov. 30, 2000), available at http://www.ftc.gov/os/2000/12/dietletter.htm.

Act forbids false and misleading statements, and a statement that is plausible but has not been tested in the most reliable way cannot be condemned out of hand. The burden is on the Commission to prove that the statements are false. (This is one way in which the Federal Trade Commission Act differs from the Food and Drug Act.)").

C. The New, Higher Standard the FTC Seeks to Establish in this Case

10. In recent years, following the district court's decision in FTC v. Lane Labs,[3] the FTC has attempted to impose a new standard for advertising substantiation that would require, among other things, randomized placebo-controlled clinical trials, with statistically significant results (hereinafter "RCT's"), for health benefit claims and prior FDA approval of certain health benefit claims.

11. The FTC's new approach to evaluating health benefit claims is evidenced in consent orders which it has obtained from Iovate Health Sciences, Nestlé HealthCare Nutrition, Inc., and The Dannon Company, Inc., among others.[4] This matter, however, is the first litigated case in which the FTC is advocating this standard, both as to the assessment of the Respondents' existing substantiation and as a matter of proposed remedy.

12. This new standard is inappropriate as a matter of law and is unsupported by the record in this case. *See* Matrixx Initiatives, Inc. v. Siracusano, — U.S. —,131 S.Ct. 1309, 1320 (2011) ("medical professionals and researchers [and the FDA] do not limit the data they consider to the results of randomized clinical trials or to statistically significant evidence") (internal quotations omitted). Every expert offered by Complaint Counsel, while initially repeating the FTC's purported new standard on direct examination, was forced to back down and repudiate that standard by the end of cross-examination. *See* RFF 1215-1248.

---

[3] 2009 WL 2496532 (D.N.J. Aug. 11, 2009), *aff'd and rev'd in part*, by FTC v. Lane Labs-USA, Inc., 624 F.3d 575 (3d Cir. 2010).

[4] *See* In the Matter of Nestlé HealthCare Nutrition, Inc., Consent Agreement, FTC File No. 092 3087 (July 14, 2010), available at: http://www.ftc.gov/os/caselist/0923087/110118nestledo.pdf.; FTC v. Iovate Health Sciences, Inc., Stipulated Final Judgment and Order for Permanent Injunction and Other Equitable Relief, Case No. 10-CV-587 (July 29, 2010), available at: http://www.ftc.gov/os/caselist/0723187/100729iovatestip.pdf.; In the Matter of The Dannon Company, Inc., Decision and Order, Case No. C-4313 (Jan. 31, 2011), available at: http:// http://www.ftc.gov/os/caselist/0823158/110204dannondo.pdf.

II. COMPLAINT COUNSEL HAVE FAILED TO SATISFY THEIR BURDEN OF PROVING THAT RESPONDENTS VIOLATED THE FTCA

A. The Burden of Proof

13. The parties' burdens of proof are governed by Federal Trade Commission Rule 3.43(a), Section 556(d) of the Administrative Procedure Act ("APA"), and case law. Pursuant to Commission Rule 3.43(a), "[c]ounsel representing the Commission . . . shall have the burden of proof, but the proponent of any factual proposition shall be required to sustain the burden of proof with respect thereto." Under the APA, "[e]xcept as otherwise provided by statute, the proponent of a rule or order has the burden of proof." 5 U.S.C. § 556(d). *See also* In re Rambus, 2006 FTC LEXIS 101, at *45.

14. "The burden of showing something by a 'preponderance of the evidence' ...requires the trier of fact to believe that the existence of a fact is more probable than its nonexistence before he may find in favor of the party who has the burden to persuade the judge of the fact's existence." Concrete Pipe & Prods., Inc. v. Construction Laborers Pension Trust, 508 U.S. 602, 622 (1993) (internal quotations and citations omitted); Smith v. United States, 726 F.2d 428,430 (8th Cir. 1984) ("If, upon any issue in the case, the evidence appears to be equally balanced, or if it cannot be said upon which side it weighs heavier, then plaintiff has not met his or her burden of proof.").

15. Complaint Counsel has the burden of proving by a preponderance of credible evidence that Respondents made the alleged claims in the challenged advertising and did not have a reasonable basis for such claims. In the Matter of Bristol-Myers Co., 102 F.T.C. 21, 1983 FTC LEXIS 64, at *143 (requiring proof by "preponderance of credible evidence"); FTC v. QT, Inc., 448 F. Supp. 2d 908, 959 (N.D. Ill. 2006) (holding that to prevail on a reasonable basis theory, the FTC must prove that the advertiser lacked a reasonable basis for asserting the challenged claim, that the advertiser has the burden of establishing the substantiation it relied on for its claim, and that the FTC has the burden of proving that the advertiser's substantiation is inadequate), aff'd, 512 F.3d 858 (7th Cir. 2008).

16. Further, Complaint Counsel must demonstrate that the alleged claims are "material," or likely to affect a consumer's purchasing decision. In the Matter of Telebrands Corp., et al., 140 F.T.C. 278 ; Kraft, Inc. v. F.T.C., 970 F.2d 311, 314 (7th Cir. 1992); Joint Stipulations of Law and Facts, dated May 24, 2011,

Stipulations of Law ¶ 1. Although Complaint Counsel is entitled to a presumption of materiality as to claims involving health, that presumption may be rebutted, and if so the burden remains on Complaint Counsel to prove materiality by a preponderance of the evidence. In the Matter of Novartis Corp., et al., 127 F.T.C. 580 at 686 - 87.

B. Complaint Counsel Have Failed to Meet Their Burden to Prove that the Challenged Advertisements Convey the Alleged Claims

1. The Legal Standard for Proving What Claims Are Conveyed in an Advertisement

17. For analytical purposes, the Commission distinguishes between express claims and implied claims in evaluating what messages an advertisement can reasonably be interpreted as containing. In the Matter of Kraft, Inc., 114 F.T.C. 40 at 120; Joint Stipulations of Law and Facts, dated May 24, 2011, Stipulations of Law ¶ 2 ("Advertisements may convey two kinds of claims, express and implied.").

18. Express claims unequivocally state the representation at issue. No further proof about the meaning of an express claim is necessary because the express claim itself (rather than a paraphrase about what it "implies") is explicitly stated. *See* FTC Deception Policy Statement, appended to Cliffdale Assocs., Inc., 103 F.T.C. at 176; Thompson Medical Co., 104 F.T.C. at 788.

19. Implied claims are any claims that are not express. *See* Kraft, Inc., 114 F.T.C. 40, 120 (1991), *aff'd*, 970 F.2d 311 (7th Cir. 1992), *cert. denied*, 507 U.S. 909 (1993); Thompson Medical Co., 104 F.T.C. at 789. Because implied claims are not stated explicitly, the FTC must prove that they are likely conveyed to a significant portion of reasonable consumers. Id.

20. In determining if reasonable consumers are likely to take an implied claim, the FTC looks at the net impression created by the ad as a whole. *See* FTC Deception Policy Statement, appended to Cliffdale Assocs., Inc.,103 F.T.C. at 179, n.32; In the Matter of Stouffer Foods Corp., 118 F.T.C. 746, 799 (1994); Joint Stipulations of Law and Facts, dated May 24, 2011, Stipulations of Law ¶ 3 ("The Commission considers the overall net impression created by the advertisement as a whole, by evaluating the interaction of such elements as language and visual images. The entire mosaic should be viewed rather than each tile separately.").

21. Implied claims may only be found where it may be determined with confidence, after examining all of the constituent elements of the advertising, that the challenged implied claims are conspicuous, self-evident, or reasonably clear on the face of the ad. Stouffer, 118 F.T.C. at 777 (citing Kraft, 970 F.2d at 318); Thompson Medical Co., Inc., 104 F.T.C. at 320. When an implied claim is not clear enough to permit the FTC to determine its existence by examining the advertisement alone, extrinsic evidence may be required. *See* Stouffer Foods Corp., 118 F.T.C. at 798 - 99.

2. POM's Advertising Does Not Make the Alleged Express or Implied Claims

22. The threshold question in this matter is what claims may reasonably be ascribed to the advertising for the Challenged Products. Novartis Corp., 127 F.T.C. 580, 679 (1999), *aff'd*, 223 F.3d 783 (D.C. Cir. 2000).

23. A related threshold question is the identification of the particular advertising at issue. Complaint Counsel have greatly complicated this matter by failing to identify with specificity particular ads that allegedly convey the claims at issue.

24. The Court agrees with the conclusions of Respondents' linguistic expert, Dr. Ronald Butters, that Respondents' advertisements do not "expressly" or "by implication" convey that (1) that the Challenged Products treat, prevent, and/or reduce the risk of cardiovascular health, prostate cancer, or erectile function or (2) that Respondents' scientific research proves the same. Professor Reibstein's study also showed that consumers did not take the alleged claims from the advertisements.

25. To the extent Complaint Counsel has attempted to identify particular advertisements at issue, this Court finds that in none of this material has Respondent expressly claimed that (1) the Challenged Products treat and/or prevent or reduce the risk of heart disease, prostate cancer, and erectile dysfunction or (2) that Respondents' scientific research proves the same.

26. Complaint Counsel has also failed to demonstrate that the Commission, notwithstanding its ability to do a facial analysis of advertisements, could conclude with confidence that the advertisements convey by implication, clearly and conspicuously, that (1) the Challenged Products treat and/or prevent or reduce the risk of heart disease, prostate cancer, and erectile dysfunction or (2) that

Respondents' scientific research proves the same. Although proof of actual deception is not required, Complaint Counsel must establish that consumers, acting reasonably under the circumstances, would interpret the message of the advertisement to have made the alleged claims. Id.; Kraft, 114 F.T.C. 40, 120 (1991), *aff'd*, 970 F.2d 311 (7th Cir. 1992), *cert. denied*, 113 S. Ct. 1254 (1993). A facial review of the advertising in question is insufficient to meet this burden.

27. It was therefore incumbent on Complaint Counsel to provide extrinsic evidence of the alleged implied claims. In evaluating implied claims, the Commission will carefully consider any extrinsic evidence that is introduced, taking into account the quality and reliability of the evidence. Kraft, 114 F.T.C. at 122 (*citing* FTC Deception Policy Statement, appended to Cliffdale Assocs., Inc., 103 F.T.C. at 176). The Commission can consider evidence respecting the common usage of terms, as well as generally accepted principles drawn from market research showing that consumers generally respond in a certain manner to advertisements that are presented in a particular way. *See* Thompson Medical Co., Inc., 104 F.T.C. at 790. The Commission will also consider the opinion of expert witnesses in the proceeding as to how an advertisement might reasonably be interpreted. Id. However, where the opinions voiced by experts are not adequately supported, the Commission will ordinarily give those opinions little weight. Id. The Commission considers "to be adequately supported [those] opinions that describe empirical research or analyses based on generally recognized marketing principles or other objective manifestations of professional expertise. Opinions not so supported may easily be contradicted by the contrary opinions of opposing experts and thus may be of little value in resolving the issue." Id. n. 11.

28. Complaint Counsel did not present any expert opinion to rebut the conclusions of Dr. Butters or Professor Reibstein or any competent affirmative evidence that consumers understand and/or interpret Respondents' advertisements to imply that drinking eight ounces of POM Wonderful 100% Pomegranate Juice or taking one POMx Pill or one teaspoon of POMx Liquid will treat and/or prevent or reduce the risk of heart disease, prostate cancer, and erectile dysfunction, or that Respondents' scientific research proves the same.

29. Accordingly, Complaint Counsel has failed to demonstrate the existence of the alleged implied claims in Respondents' advertisements.

3. Complaint Counsel Attacks Material that is Not Actionable "Advertising"

30. "'Advertisement' is not defined in the FTC Act." In re Daniel Chapter One, FTC Docket 9329 (2009), Initial Decision at p. 79.

31. "[U]nless [an] advertisement can be classified as commercial speech, it is not subject to the Commission's jurisdiction." In the Matter of R.J. Reynolds Co., Inc., FTC Docket No. 9206 (Mar. 4, 1988), 1988 WL 490114 at *2.

32. The FTC stated that it "understand[s an advertisement] to mean a notice or announcement that is publicly published or broadcast and is paid-for." Id. at *6

(a) Respondents' Advertising Consists Largely of "Puffery"

33. The FTC has long recognized that highly subjective claims that consumers are not likely to take seriously are non-actionable "puffery." *See, e.g.,* Bristol-Meyers Co., 102 F.T.C. 21, 321 (1983), *aff'd.* 738 F.2d 554 (2d. Cir. 1984).

34. A manufacturer's statement that "is not specific and measurable," or that does not provide "a benchmark by which the veracity of the statement be ascertained," constitutes puffery. *Am. Italian Pasta Co. v. New World Pasta Co.,* 371 F.3d 387, 391 (8th Cir. 2004).

35. The following statements are just a few examples in Respondents' advertisements related to the Challenged Products of non-actionable puffery: (a) "Drink it daily. Feel it forever."; (b) "Cheat death"; (c) "Floss your arteries"; (d) "Amaze your cardiologist"; and "Decompress."

(b) Interviews and Publications Are Not "Advertising"

36. Books and public addresses "set[ting] forth primarily matter[s] of opinion" do not constitute "advertisement[s] covered by Sections 5, 12, or 15(a)" of the FTC Act. Koch et al. v. FTC, 206 F.2d 311, 317-18 (6th Cir. 1953). Consequently, "prohibiting dissemination of such [communications] . . . would violate the First Amendment. . . ." Id.

37. While no court appears to have considered whether media interviews constitute commercial speech for purposes of determining whether a statement is an advertisement under the FTC Act, courts have done so in construing Section 43(a) of the Lanham Act, which has a similarly undefined "commercial advertising or

promotion" jurisdictional prerequisite. See Oxycal Labs., Inc. v. Jeffers, 909 F. Supp. 719, 722, 723 (S.D. Cal. 1995) ("to even fall within the category of commercial advertising and promotion, the communications must first be found to be commercial speech."). In doing so, courts routinely find that media interviews do not constitute actionable commercial speech. *See*, *e.g.*, Galerie Gmurzynska v. Hutton, 355 F.3d 206, 210-11 (2d Cir. 2004) ("[t]he journalist's article is not commercial advertising, commercial promotion, or commercial speech. Rather, it is speech that is traditionally granted full protection under the First Amendment."); Boule v. Hutton, 70 F. Supp. 2d 378, 390 (S.D.N.Y. 1999) (the Lanham Act "does not cover a response to an unsolicited inquiry by a magazine reporter seeking comment on a topic of public concern.").

38. Wholly apart from that distinction, the Second Circuit affirmed because the defendant's statements were "inextricably intertwined with the reporter's coverage of their topic," and "related to the reporter's discussion of an issue of public importance and occur[ed] in a forum that has traditionally been granted full protection under the First Amendment." Boule Hutton, 328 F.3d 84, 91 (2d Cir. 2003).

39. Even when non-commercial speech is tinged with commercial speech, the entirety is nonetheless treated as non-commercial speech, provided the latter is the "main purpose" and is "not merely a mask for the essentially commercial nature. . . ." Oxycal, 909 F. Supp. at 725-26. See also Edwards v. District of Columbia, 765 F. Supp. 2d 3, 13 (D.D.C. 2011) (addressing the distinction between "speech-for-profit" and commercial speech, the latter subjected to lesser protection under the First Amendment); City of Lakewood v. Plain Dealer Publ'g Co., 486 U.S. 750, 756, n.5 (1988) ("the degree of First Amendment protection is not diminished merely because the newspaper or speech is sold rather than given away").

40. Mrs. Resnick's and Mr. Tupper's media interviews on matters of public concern and to which they offered "reactive" statements are not actionable advertisements under the FTC Act.

(c) Distribution of Scientific Research Papers Is Not Advertising

41. Respondents' posting or citation to peer-reviewed, scientific articles, written by prominent experts in the field, on the health benefits of pomegranate juice does not constitute the making of false or misleading drug claims.

42. The Respondents' posting and/or citation to full scientific articles is constitutionally protected speech against government suppression and subject to strict scrutiny. See Edwards 765 F. Supp. 2d at 13.

43. Respondents' scientific speech, including the publication of full scientific journal articles for the edification of the public, does not cause the speech in question to lose its heightened First Amendment protection. See Wallach, 2005 WL 6054963 at *8-9; see also Edwards 765 F. Supp. 2d at 13; Enten v. District of Columbia, 675 F. Supp. 2d 42, 50 (D.D.C. 2009) ("the degree of First Amendment is not diminished merely because…speech is sold rather than given away"); City of Lakewood v. Plain Dealer Publ'g Co., 486 U.S. 750, 756 n.5 (1988).

4. Complaint Counsel's Attempt to Rely on "Intent" to Prove the Existence or Materiality of the Alleged Claims Fails

44. Complaint Counsel relies heavily on internal documents such as "creative briefs" in an attempt to establish the existence and materiality of the alleged claims. Evidence at trial, however, failed to establish that any specific ads reflected any of the factors discussed in these documents.

45. The Court agrees with Professor Butters that in these circumstances the only proper source of evidence of what the advertisements claim is the advertisements themselves, not the intent of individuals involved in various preliminary stages of the development of the advertisements.

46. Similarly Complaint Counsel relies on the issuance of a "warning letter" by the FDA as evidence of the existence of unsubstantiated claims and the Respondents' supposed awareness of such claims. It is well-established, however, that such letters do not constitute final agency action, and are not formal opinions or findings of the FDA,[5] represent only the preliminary and informal views of the

[5] *E.g.*, Holistic Candlers and Consumers Assoc. v. FDA, No. 11-5118 (D.C. Cir. Jan. 3, 2012); Dietary Supplemental Coalition, Inc. v. Sullivan, 978 F.2d 560, 563 (9th Cir. 1992), *cert. denied*, 508 U.S. 906 (1993) (citing Biotics Research Corp. v. Heckler, 710 F.2d 1375 (9th Cir. 1983)); Genendo Pharmaceutical N.V. v. Thompson, 308 F. Supp. 2d 881, 885 (N.D. Ill. 2003); Estee Lauder, Inc. v. FDA, 727 F. Supp. 1 (D.D.C. 1989); IMS Ltd. v. Califano, 453 F. Supp. 157 (C.D. Cal. 1977).

individual who signed the letter, and that the letter does not bind or otherwise obligate or commit FDA to the views expressed.[6]

C. The Health Claims Actually Made in POM's Ads Are Neither False Nor Lacking in a Reasonable Basis

1. Complaint Counsel Did Not Meet Its Burden of Showing that POM's Ads Are False or Lack a Reasonable Basis

(a) This Court Should Not Accept Complaint Counsel' Invitation to Modify the Conventional Standards of Substantiation

47. The FTC's decision in In the Matter of Pfizer Inc., 81 F.T.C. 23 (1972), established the basic requirements for advertising substantiation. In that decision, the FTC identified various factors used to determine the amount of substantiation necessary to determine whether an advertiser has a reasonable basis for a particular claim, including (1) the type and specificity of the claim made—*e.g.*, safety, efficacy, dietary, health, or medical; (2) the type of product— *e.g.* food, drug, potentially hazardous consumer product; (3) the possible consequences of a false claim—*e.g.*, personal injury, property damage; (4) the case and cost of developing substantiation for the claim; (5) the degree of reliance by consumers on the claims; and (6) the level of substantiation experts would agree is reasonable. Id. at 30. The FTC's approach to evaluating advertising claims was later memorialized in the FTC's Deception Policy Statement and Substantiation Policy Statement. *See* FTC Deception Policy Statement, appended to Cliffdale Assocs., Inc., 103 F.T.C. at 174; FTC Substantiation Policy Statement, appended to Thompson Medical Co., 104 F.T.C. at 839 (1984), *aff'd*, 791 F.2d 189 (D.C. Cir. 1986), *cert. denied*, 479 U.S. 1086 (1987).

48. For health or safety claims, the Commission has typically required a relatively high level of substantiation, usually "competent and reliable scientific evidence," typically defined as "tests, analyses, research, studies, or other evidence based

---

[6] *See* 21 C.F.R. § 10.85(k) ("A statement or advice given by an FDA employee orally, or given in writing but not under this section [governing advisory opinions] or § 10.90 [governing regulations, formal recommendations, and formal agreements], is an informal communication that represents the best judgment of that employee at that time but does not constitute an advisory opinion, does not necessarily represent the formal position of FDA, and does not bind or otherwise obligate or commit the agency to the views expressed.").

upon the expertise of professionals in the relevant area, that has been conducted and evaluated in an objective manner by persons qualified to do so, using procedures generally accepted in the profession to yield accurate and reliable results." See, e.g., In the Matter of Brake Guard Products, Inc., 125 F.T.C. 138, 217 (1998); In the Matter of Automatic Breakthrough Sciences, Inc., 126 F.T.C. 229 (1998); see also Dietary Supplements: An Advertising Guide for Industry (Nov. 1998).

49. Since 1972, the FTC has flexibly applied the Pfizer factors when evaluating health-related advertising claims. See Pfizer, 81 F.T.C. 23 (1972); FTC Deception Policy Statement, appended to Cliffdale Assocs., Inc., 103 F.T.C. 110 (1984); Thompson Medical Co., 104 F.T.C. 648, 839 (1984), aff'd, 791 F.2d 189 (D.C. Cir. 1986), cert. denied, 479 U.S. 1086 (1987)).

50. In performing a cost-benefit analysis of health claims, the agency should prefer "disclosure over outright suppression." Pearson v. Shalala, 164 F.3d 650, 657 (D.D.C. 1999) ("Pearson I"). Where there is doubt as to the completeness or accuracy of an ad, the courts should favor providing the information to the public over suppressing it. Id. This policy has also been endorsed by federal courts following the command in *Pearson I* stating "that under the First Amendment commercial speech doctrine, there is a 'preference for disclosure over outright suppression.'" Alliance for Natural Health U.S. v. Sebelius, 714 F. Supp. 2d at 48, 52-53 (D.D.C. 2010); s*ee also* Whitaker v. Thompson, 248 F. Supp. 2d at 1, 9 (D.D.C. 2002) ("Whitaker I") ("in finding that speech is misleading, the government must consider that 'people will perceive their own best interests if only they are well enough informed, and . . . the best means to that end is to open the channels of communication, rather than to close them.").

51. As summarized in Pearson I, 164 F.3d at 656 and n.6, the courts should distinguish between products (*e.g*., dietary supplements) that do not "in any fashion threaten consumer's health and safety" and "drugs," which "appear to be in an entirely different category," *e.g*., "wherein the potential harm presumably is much greater."

52. As the Court in Whitaker I, reasoned: "It is especially important to recognize that, in the present case, the potential harm to consumers from deception is severely limited . . . . At worst any deception resulting from plaintiff's health claim will result in consumers spending money on a product that they might not otherwise have purchased. This type of injury, while obviously not insignificant, cannot

compare to the harm resulting from the unlawful suppression of speech." 248 F. Supp. 2d at 16.

53. Under Pfizer, Respondents' basic science, *in vivo* and *in vitro* laboratory tests and clinical studies, even if not costly RCT studies, are sufficient to substantiate the advertisements for the Challenged Products, including the alleged claims which Complaint Counsel contends are being made in its Complaint.

54. By adopting an approach that equates a natural food, such as the pomegranate, to a drug, and by requiring RCT's and prior FDA-approval, Complaint Counsel in effect would suppress truthful information regarding pomegranates contrary to Pearson I, Whitaker I, and Alliance for Natural Health.

55. Under Pfizer and Pearson I and its progeny, given the exorbitant cost of conducting drug studies, the proven safety of pomegranate juice and its extracts, and lack of patent protection for a food, and the inferiority of conducting a RCT on a nutrient, disclosure of Respondents' alleged claims is favored over suppression.

56. In substantiating health or safety claims, the Commission has required "competent and reliable scientific evidence," typically defined as "tests, analyses, research, studies, or other evidence based upon the expertise of professionals in the relevant area, that has been conducted and evaluated in an objective manner by persons qualified to do so, using procedures generally accepted in the profession to yield accurate and reliable results." S*ee, e.g.*, Brake Guard Products, Inc., 125 F.T.C. 138, 256 (1998); ABS, Inc., 126 F.T.C. 229, 314 (1998); *see also* Dietary Supplements: An Advertising Guide for Industry (Nov. 1998).

57. In evaluating nutritional science, Respondents' experts have defined "competent and reliable science" to mean the totality of available, scientific evidence, including basic science, animal studies, and human clinical trials, and it is well-accepted that RCTs are not the best source of valid and reliable information on nutrition.

58. Although the FTC has accepted use of RCT's in limited circumstances for establishment claims regarding disease (especially in the context of over-the-counter prescription medications and ointments), *see e.g.,* Thompson Medical Co., Inc., 104 F.T.C. 648, 842-43 (1984), *aff'd*, 791 F.2d 189 (D.C. Cir. 1986), *cert. denied*, 479 U.S. 1086 (1987), the FTC and courts have never required such tests

for all nutrient disease relationship claims in advertising—and have certainly not required them for claims regarding nutritious foods, such as the Challenged Products in this case. *See, e.g.*, FTC v. QT, Inc., *supra*, 512 F.3d at 861. Instead, the standard should be a flexible one that considers the nature of the claims made, the totality of the science conducted, and the product at issue. *See, e.g.*, Pfizer, *supra*, 81 F.T.C. at 30.

59. As the United States Supreme Court recently recognized: "A lack of statistically significant data does not mean that medical experts have no reliable basis for inferring a causal link between a drug and adverse events." Matrixx Initiatives, Inc. v. Siracusano, — U.S. —,131 S.Ct. 1309, 1319 (2011). "[C]ourts frequently permit expert testimony on causation based on evidence other than statistical significance." Id. "[M]edical professionals and researchers do not limit the data they consider to the results of randomized clinical trials or to statistically significant evidence." Id. at 1320 (internal quotations omitted).

60. "The FDA similarly does not limit the evidence it considers for purposes of assessing causation and taking regulatory action to statistically significant data." Id. "Not only does the FDA rely on a wide range of evidence of causation, it sometimes acts on the basis of evidence that suggests, but does not prove, causation." Id.

61. Under Matrixx Initiatives, findings and results in Respondents' studies that do not meet an arbitrary p-value of 0.05 or are not randomized and placebo-controlled should nevertheless be considered as substantiation for claims.

62. Complaint Counsel attempts to rely on various decisions to support its novel conclusions that Respondents' have to have conducted two double-blind RCTs. None of them stand for the proposition that RCTs are the only evidence that is required. For example, the district court decision in FTC v. Direct Mktg. Concepts, Inc., 569 F. Supp. 2d. 285 (D. Mass 2008) does not stand for the proposition that double-blind, placebo controlled studies are required for health claims. The First Circuit, when reviewing the district court's opinion, expressly noted that, although the FTC had argued and produced expert testimony that the claims at issue should be substantiated by double-blind, placebo-controlled studies, "*there may be other scientific evidence that could be sufficient, and we may assume for these purposes that a double-blind study is not necessarily required*." 624 F.3d 1, 9 (1st Cir. 2010) (emphasis added). The First Circuit's decision is consistent with the Supreme Court's statement in Matrixx Initiatives.

63. Similarly, FTC v. National Urological Group, Inc., 645 F. Supp. 2d 1167 (N.D. Ga. 2008) does not hold that claims for erectile dysfunction "require" double-blind placebo-controlled studies. Rather, the court noted that the defendants in that case had not countered the FTC's expert evidence that such studies were required and granted summary judgment on that basis. Id. at 1202. Had defendants in that case relied on other competent and reliable evidence, as Respondents do here, the court may well have rejected Complaint Counsel's insistence on well-controlled human studies.

64. The Court's Initial Decision in Daniel Chapter One does not stand for the proposition that controlled clinical testing is required for all health benefit claims. In that case, the Court specifically noted that Respondents "did not possess or rely upon **any** adequate substantiation for their claims that the Challenged Products prevent, treat, or cure cancer." See Initial Decision (PX0531 at 109). Indeed, the Court noted that "Respondents had no studies whatsoever of the effects of the Challenged Products themselves." Id. The facts of Daniel Chapter One are in stark contrast to the situation here, where Respondents have a vast body of scientific research and literature supporting their advertising claims, including published peer-reviewed clinical studies.

65. Complaint Counsel does not (and cannot) cite to any prior legal authority defining "competent and reliable" science to require RCT's for whole food health claims, *e.g*. broccoli, spinach.

66. Nor can they rely on the FTC's 1994 Enforcement Policy Statement on Food Advertising. Indeed, the FTC's 1994 Enforcement Policy Statement on Food Advertising does not disturb the FTC's well-settled, flexible approach to evaluating advertising substantiation outlined in Pfizer. Although the Statement indicates that the FTC will consider the "scientific agreement" standard adopted by the FDA in determining whether a claim is substantiated, it expressly states that the FTC "does not require food advertisers to establish that there is scientific consensus in support of their claims." The Statement also provides that there will be some instances in which it is possible for an advertiser to craft a qualified, truthful, and non-misleading claim even if the claim does not meet the FDA's standards for regulation. *See also* "Advertising: Interpretation and Enforcement Policy," Remarks by Commissioner Mary Azcuenaga before the American

Advertising Federation (1994) (suggesting FTC should not ban claims even if supporting evidence has not reached the level required for FDA approval).[7]

67. To the extent that the Statement on Food Advertising mentions that it is "likely that the Commission will reach the same conclusion as FDA as to whether an unqualified claim about the relationship between a nutrient or substance in a food and a disease or health-related condition is adequately supported by the scientific evidence," this pronouncement cannot be taken to mean that the FTCA requires an advertiser to rely on RCT's, as opposed to other competent and reliable science. Indeed, the Statement merely notes that, to the extent that the FDA concludes that an advertiser can make a health claim on its label, the FTC will likely agree with the FDA's conclusion. Obviously, if the FDA expressly permits a health claim after its lengthy regulatory review, the FTC would hardly be in a position to criticize advertisers who market the claim. The Statement, however, does not suggest that the FTC should categorically apply the FDA's methodology when determining whether a claim is false or misleading. This categorical reliance is inconsistent with the FTC's authority under the FTCA, as well as the governing scientific standards with which Complaint Counsel purport to comply.

(b) The Standard Advocated by Complaint Counsel Raises Significant Constitutional Issues

68. The government may not suppress commercial speech by requiring excessively high levels of supporting scientific evidence and that a claim may not be barred "simply because the scientific literature is inconclusive." Pearson v. Thompson, 141 F. Supp. 2d 105, 110 (D.D.C. 2001) ("Pearson III"). In addition, even if some studies show a likely benefit, the fact that other studies may produce no such result does not justify suppression of the information. *See* Whitaker I, 248 F. Supp. at 13 (where only one-third of studies show claimed benefit and were criticized as procedurally flawed, the court held that suppression of information was improper.) The Whitaker I court further stated that because there was "some" evidence, "a complete ban of the [c]laim cannot be justified." 248 F. Supp. at 13.

69. The NLEA amended the FDCA to create a "'safe harbor' from the 'drug' designation for foods . . . labeled with health claims." Alliance for Natural Health,

[7] Available at http://www.ftc/gov/speeches/azcuenaga/aaf94.shtm.

714 F. Supp. 2d at 51. For labeling to bear such health claims under the NLEA, the FDA required "that 'significant scientific agreement,' based on the 'totality of publicly available scientific evidence' supports the claim." Id. Because the NLEA did not provide for approval of health claims that are based on less than significant scientific agreement, the FDA previously declined to approve health claims that were supported by credible, but inconclusive scientific evidence: "The problem with these claims, according to the FDA, was not a dearth of supporting evidence; rather, the agency concluded that the evidence was inconclusive for one reason or another and thus failed to give rise to 'significant scientific agreement.'" Pearson I, 164 F.3d at 653.

70. In the landmark Pearson I case, however, the D.C. Circuit applied the commercial speech test in Central Hudson Gas & Elec. Corp. v. Public Service Commission of New York, 447 U.S. at 557 (1980), to invalidate the FDA's position: "first, that health claims lacking 'significant scientific agreement' are *inherently* misleading and thus entirely outside the protection of the First Amendment; and second, that even if the claims are only *potentially* misleading, . . . the government is not obliged to consider requiring disclaimers in lieu of an outright ban on all claims that lack significant scientific agreement." Pearson I, 164 F.3d at 655. Pearson I held that the claim qualification requirement was the government's burden. It was not incumbent upon a claim proponent to establish a suitable qualification as a condition precedent to speech. Rather, it was incumbent on the government to prove that no qualification would suffice as a less speech-restrictive alternative to outright claim suppression. 164 F.3d at 659.

71. Furthermore, in Pearson III, in the context of the FTC's enforcement action, the district court identified the relevant burden on the administrative agencies: "[T]he FDA [may] impos[e] an outright ban on a claim where evidence in support of the claim is *qualitatively* weaker than evidence against the claim-for example, where the claim rests on only one or two old studies or where the evidence in support of a claim is outweighed by evidence against the claim. *Pearson II* fleshes out the term 'against': The mere absence of significant affirmative evidence in support of a particular claim ... does not translate into negative evidence 'against' it." Id. at 112 (*citing* Pearson I, 164 F.3d at 660 & n.10; Pearson v. Shalala, 130 F. Supp. 2d 105 (DC 2001) ("Pearson II") (internal citations omitted; emphasis added). Accordingly, the "question which must be answered under Pearson [I] is whether there is any 'credible evidence.'" Pearson II, 130 F. Supp. 2d at 118 (emphasis added).

72. In Alliance for Natural Health, the district court overturned the FDA's rejection of various health claims regarding the role of the nutrient mineral, selenium, in the prevention of various cancers, based on evidence of selenium's antioxidant effects (among others) that was credible but not conclusive. 714 F. Supp. 2d at 70-71.

73. Under Pearson III, Complaint Counsel may not suppress Respondents' commercial speech by requiring excessively high levels of supporting evidence or bar the alleged claims regarding the Challenged Products because the scientific literature supporting the claims is deemed inconclusive.

74. Under Pearson III, because some of Respondents' studies show a likely benefit, the fact that other studies may produce no such result does not justify suppression of the information.

75. Under Pearson I, Complaint Counsel has not met its burden to prove that no qualification would suffice as a less speech restrictive alternative to outright claim suppression.

76. Because Respondents have "credible evidence" consistent with Pearson I and its progeny, the suppression of any alleged health claims regarding the Challenged Products is unconstitutional.

77. To the extent that Complaint Counsel is advocating a standard of substantiation that requires a consensus among scientists, this standard also violates the First Amendment and the line of cases led by Pearson I, because it requires the advertiser to "prove" its claim, which is more than what is required to show that the claim was non-deceptive. See Pearson I, 164 F.3d at 655.

2. POM's Advertisements Are Extensively Substantiated by Rigorous, Competent and Reliable Science.

78. Respondents' extensive, scientific research on the potential benefits of pomegranate juice and its extracts is valid, taken seriously by other scientists, and meets the minimal criteria of good science given that they have published their results in peer-reviewed articles in leading academic journals. *See* RFF Sections XI, XII, XIV, and XV.

79. Publication in a peer-reviewed journal is a "relevant, though not dispositive, consideration in assessing the scientific validity of a particular technique or methodology." *See* Daubert v. Merell Dow Pharmaceuticals, 509 U.S. 579, 594

(1993). The fact that a peer reviewed article was approved for publication is some evidence that the study is reliable. Riddell v. Schutt, 724 F. Supp. 2d 963, 974 (W.D. Wisc. 2010) (*citing* Daubert, 509 U.S. at 593). "That the research is accepted for publication in a reputable scientific journal after being subjected to the usual rigors of peer review is a significant indication that it is taken seriously by other scientists, i.e., that it meets at least the minimal criteria of good science." Daubert v. Merrell Dow Pharms, 43 F.3d 1311, 1318 (9th Cir. 1995). Furthermore, peer review and publication increase the "likelihood that substantive flaws in methodology will be detected." Daubert, 509 U.S. at 593 - 594 (*citing* J. Ziman, Reliable Knowledge: An Exploration of the Grounds for Belief in Science, 130–133 (1978); Relman & Angell, How Good Is Peer Review?, 321 New Eng. J. Med. 827 (1989)). There is a general correlation between a journal's prestige and the quality of the editorial peer review. Black v. Rhone-Poulenc, Inc., 19 F. Supp. 2d 592, 591, 600, n.18, 600 (S.D. W.V. 1998) (*citing* The "Brave New World" of Daubert: True Peer Review, Editorial Peer Review, and Scientific Validity, 70 N.Y.U. L. Rev. 100, 113 (1995)).

80. Prostate Health: Competent and reliable scientific evidence supports the conclusion that the consumption of pomegranate juice and pomegranate extract supports prostate health. (PX0161; PX0353 (Heber, Dep. at 84-85)).

81. Competent and reliable scientific evidence supports the conclusion that the same mechanism shown in the in vitro and animal studies and in the Pantuck and Carducci human studies also showed with a high degree of probability that the Challenged Products *inhibit the clinical development of prostate cancer cells* in men who have not been diagnosed. (deKernion, Tr. 3126; PX0351 (deKernion, Dep. at 76-77); CX1352 (Heber, Dep. at 329); PX0206 at 12; Heber, Tr. 2156).

82. Respondents have demonstrated through credible and reliable evidence that drinking eight ounces of POM Juice, or taking one POMx Pill or one teaspoon of POMx Liquid, daily, may help prevent or reduces the risk of prostate cancer, including by prolonging prostate-specific antigen doubling time ("PSADT").

83. Erectile Dysfunction: Competent and reliable basic scientific evidence and clinical evidence shows that pomegranate juice provides a definite benefit to erectile health/function. (Goldstein, Tr. 2605; PX0189 at ¶ 34; PX0149 at ¶ 17; Burnett, Tr. 2255 – 2256; PX0349 (Burnett, Dep. at 103, 116 – 118, 137); Heber, Tr. 2012).

84. Pomegranate juice would be recommended as a management to promote erectile health in men who are aware that their erectile function is declining but who do not yet meet the clinical definition of ED under the IIEF and therefore do not qualify for pharmacologic treatment. (PX0189 at ¶¶ 35 – 36; PX0352 (Goldstein, Dep. at 42 – 45); Goldstein, Tr. 2609; CX1352 (PX0341, Heber, Dep. at 85)).

85. Improving ones erectile function may also help improving ones erectile dysfunction. (Burnett, Tr. 2303).

86. The suggestion to utilize the Mediterranean diet, which the pomegranate fruit is part of, to improve endothelial function and erectile health is logical and rational in men who have been diagnosed with clinical ED but who have an insufficient response to PDE5 inhibitors (like Viagra) and who are unwilling to consider invasive or mechanical therapies (such as injecting needles into the penis, inserting urethral suppositories, using vacuum pumps, or having surgically implanted prostheses), (PX0189 at ¶¶ 14, 36; PX0352 (Goldstein, Dep. at 37 – 42); Goldstein, Tr. 2605, 2641; PX0190-0006, 0007).

87. Reasonable and competent science shows that pomegranate juice reduces the risk of, or ameliorates erectile dysfunction in men caused by endothelial dysfunction or blood flow impairment or oxidative stress. (Goldstein, Tr. 2605).

88. Respondents have demonstrated through credible and reliable evidence that drinking eight ounces of POM Juice, or taking one POMx Pill or one teaspoon of POMx Liquid, daily, prevents or reduces erectile dysfunction.

89. Respondents have demonstrated through credible and reliable evidence that drinking eight ounces of POM Juice, or taking one POMx Pill or one teaspoon of POMx Liquid, daily, treats erectile dysfunction.

90. Cardiovascular Health: Pomegranate juice is likely to decrease arterial plaque, may help lower blood pressure, and is likely to improve blood flow. (Ornish, Tr. 2374 - 75; PX0192 at 40-41; Heber, Tr. 2089).

91. Respondents' have demonstrated through credible and reliable evidence that their clinical studies, research, and/or trials prove that:

(a) drinking eight ounces of POM Juice, or taking one POMx Pill or one teaspoon of POMx Liquid, daily, prevents or reduces the risk of heart disease, including by (1)

decreasing arterial plaque, (2) lowering blood pressure, and/or (3) improving blood flow to the heart;

(b) drinking eight ounces of POM Juice, or taking one POMx Pill or one teaspoon of POMx Liquid, daily, treats heart disease, including by (1) decreasing arterial plaque, (2) lowering blood pressure, and/or (3) improving blood flow to the heart.

D. In Any Event, Consumers Do Not Buy POM Products Because They Believe that the Products Will Prevent, Treat, Or Reduce The Risk Of Disease.

92. "A 'material' misrepresentation or practice is one which is likely to affect a consumer's choice of or conduct regarding a product." FTC Deception Policy Statement, appended to Cliffdale Assocs., Inc., 103 F.T.C. 110, 182 (1984); Joint Stipulations of Law and Facts, dated May 24, 2011, Stipulations of Law ¶ 4. "In other words, it is information that is important to consumers." FTC Deception Policy Statement at 182 (1984).

93. "[A]n advertisement is deceptive under the Act if it is likely to mislead consumers, acting reasonably under the circumstances, in a material respect." Kraft, Inc., 970 F.2d at 314 (7th Cir. 1992) (citations omitted).

94. Although the FTC is entitled to apply, within reason, a presumption of materiality to express claims, deliberately made implied claims and claims that involve significant health concerns, the "[FTC] will always consider relevant and competent evidence offered to rebut presumptions of materiality." Cliffdale Assocs., Inc., at 182, n.47.

1. The Presumption of Materiality Does Not Apply.

95. The Commission's inference of materiality must be "within the bounds of reason." Thompson Medical Co., Inc., 104 F.T.C. at n.45. This presumption does not stand as an inflexible rule that eliminates the need for a court to look at materiality on a case-by-case basis. Id. Instead, the presumption simply reflects the "general judgment that substantive claims in advertisements (in other words, claims other than "puffery" or window-dressing) would not have been made except to affect a consumer's choice or conduct regarding a product." Id.

96. Such a presumption makes less sense in the context of nutritious foods such as fruit juices, when the pre-existing general understanding in the population of the

health properties of the product are nearly universal. In such circumstances, Complaint Counsel should in every case be made to demonstrate that the particular claims made are distinct from this widespread pre-existing belief, and that those claims specifically motivated a purchase.

2. If the Presumption Did Apply, It Was Successfully Rebutted by Respondents

97. Respondents are always free to counter a presumption of materiality either with arguments pertaining to the content of the ad itself or with extrinsic evidence. Id. In addition, the presumption does not preclude the court from exercising its own judgment and concluding from evidence in the advertisement (or extrinsic evidence) that a claim is not material even if the respondent does not dispute materiality. Id.

98. "Respondent can present evidence . . . directly contradicting the initial presumption of materiality. This is not a high hurdle . . . the fact finder next proceeds to weigh all the evidence presented by the parties on the issue . . . after the presumption drops out, 'the inquiry turns from the few generalized factors that establish [the presumption] to the specific proofs and rebuttals . . . the parties have introduced.'" Novartis Corp., 127 F.T.C. at 686 (1999) (citations omitted).

99. It is uncontested that the buyers of POM products are predominately affluent, well-educated consumers who are generally health conscious and seek a healthy lifestyle. RFF 530

100. It is similarly uncontested that it is Respondent's policy, in dealings with consumers, to make very clear that if consumers raise any issue relating to an actual disease or other adverse health condition, they should take up such matters with their physicians.

101. In addition, Respondents have adduced evidence to rebut the presumption of materiality by presenting the expert testimony of Dr. David Reibstein, who found in his survey, that less than 1% of POM buyers buy POM to prevent, cure or treat any disease and less than 1% even mentioned any disease in stating why they buy POM.

102. Complaint Counsel, based on the testimony of their own expert, Dr. Michael Mazis, have not presented any evidence that Respondents' advertisements were material to the purchase decisions of consumers.

103. Complaint Counsel have accordingly failed to substantiate their accusation that Respondents are marketing their products as "a silver bullet against disease," and have failed to show that any of the actual claims in Respondents' advertising regarding the health effects of their products were in fact material to purchasing decisions by consumers.

III. THE REMEDY COMPLAINT COUNSEL SEEK EXCEEDS THE FTC'S AUTHORITY, IS OVERBROAD, AND VIOLATES THE CONSTITUTION.

104. Complaint Counsel fails to justify the relief that they seek.

A. The FDA Pre-Approval Requirement Sought by Part I of the Notice Order Exceeds the FTC's Authority and Violates the First Amendment of the Constitution.

1. Part I of the Notice Order Exceeds the FTC's Authority

105. In Part I of the proposed Order, Complaint Counsel seeks for the first time in this Court relief requiring that Respondents obtain FDA approval before making certain advertising claims concerning POM's products.

106. The Commission's authority to prohibit false, misleading, deceptive and unfair advertising practices derives from the FTC Act.

107. The FTC Act permits the Commission to outlaw misleading and deceptive advertising. A claim is not misleading merely because it satisfies the definition of "drug" under the FTC Act.

108. Because the FTC's authority is limited to prohibiting misleading, deceptive, and false claims, the FTC Act does not allow the Commission to prohibit advertising practices that may not meet FDA approval standards, but which are nevertheless truthful or substantiated. In asking the Commission to enjoin the making of claims merely because the claims have not been approved by the FDA, Complaint Counsel is, in effect, asking that the Commission enforce FDA's standards under the Food, Drug, and Cosmetic Act ("FDCA"). But, nothing in the FTC Act gives the Commission the authority for such enforcement and, in any event, the plain language of the FDCA mandates that only the "United States," and not other agencies (such as the FTC), may bring actions to enforce provisions of the FDCA. Buckman Co. v. Plaintiff's Legal Comm'n, 531 U.S. 341 (2001).

109. Were the Commission to issue relief requiring pre-approval by the FDA of certain claims, such relief may well prevent dissemination of truthful claims that for whatever reason have not been reviewed by FDA or even would not meet FDA drug approval standards. This Commission has no authority under the FTC Act to prohibit truthful claims, even if such claims do not meet the approval standards of another agency.

110. Complaint Counsel relies on Thompson Medical Co., Inc. and other cases for the proposition that Respondents should be required to seek FDA approval in order to make certain health claims. Thompson Medical, however, merely determined based on the record in that case that the proper level of substation for the advertising in that case consistent of two well-controlled clinical trials, which happened to be consistent with FDA's standards. In that case, which, notably, involved an over-the-counter medicinal cream and not a 100% fruit product, the FTC stated that requiring two well-controlled studies for the health benefit claims at issue there was appropriate. Nowhere in Thompson Medical or in any other litigated case has the Commission, or courts for that matter, required a marketer to receive pre-approval from the FDA to make truthful and non-misleading health claims under the FTCA. And, to do so would vastly exceed this Commission's authority.

2. Part I of the Notice Order Does Not Pass First Amendment Scrutiny

111. The Commission may not prospectively enjoin Respondents from engaging in speech on the basis that the FDA's pre-approval has not been satisfied without first showing that no qualification is capable of rendering the future nutrient-disease advertising claims non-deceptive on a claim-by-claim basis. *See* F.T.C. v. Brown & Williamson Tobacco Corp., 778 F.2d 35, 45 (D.C. Cir. 1985) (explaining that FTC injunction violated First Amendment because it prevented B&W from advertising using information "in sufficient quantity to allow consumers to make informed decisions" and "[s]ince [that] would eliminate consumer confusion ... the FTC must bear the affirmative burden of demonstrating any inadequacy, and thus deceptiveness ..."); Peel v. Attorney Registration and Disciplinary Comm'n of Illinois, 496 U.S. 91, 109-11 (1990) (holding that burden is on the government, not the advertiser, to come up with a less restrictive regulation); F.T.C. v. Kraft, 970 F.2d at 325 (collecting cases).

112. The government is prohibited from keeping the public in the dark simply because there is a lack of scientific agreement on a particular health issue. The freedom of speech protected by the First Amendment includes the freedom to communicate potential health benefits, appropriately qualified.

113. Under Pearson I and its progeny, unless the Commission can meet its burden of showing that consumers will not understand the limits of scientific evidence bearing qualifications, it may not impose such a prior restraint instead. *See* 164 F.3d at 658 ("[a]lthough the government may have more leeway in choosing suppression over disclosure as a response to the problem of consumer confusion where the product affects health, it must still meet its burden of justifying a restriction on speech"); Ibanez v. Florida Department of Bus. and Prof. Reg., 512 U.S. 136, 146 (1994) ("[i]f the protections afforded commercial speech are to retain their force, we cannot allow rote invocation of the words 'potentially misleading' to supplant the [government's] burden to demonstrate that the harms it recites are real and that its restriction will in fact alleviate them to a material degree") (internal quotations and citations omitted); Edenfield v. Fane, 507 U.S. 761, 771 (1993) (concerning ban on solicitation by accountants and stating that the government "present[ed] no studies that suggest personal solicitation of prospective business clients by CPA's creates the dangers. . . .").

114. The Pearson III court explained that the "mere absence of significant affirmative evidence in support of a particular claim ... [is not] negative evidence 'against' it." 141 F. Supp. 2d at 112 (*citing* Pearson II, 130 F.2d at 115). Complaint Counsel presented no evidence in this case that there is no scientific evidence in support of the claims or that the evidence is for the claims made is qualitatively weaker than that against it.

115. Without satisfying its burden, the Commission is constitutionally barred from imposing the prior restraint set forth in Part I of the Notice Order on Respondents' future advertising.

B. Parts II and III of the Order Seek Over-Broad Fencing Relief that Is Not Warranted by the Record.

116. In Parts II and III of the Order, the Commission seeks broad, multi-product "fencing-in" relief that is not justified by the record in this case.

117. "Fencing-in" relief refers to provisions in an FTC order that are broader than the conduct that is declared unlawful and may extend to multiple products. Telebrands Corp. v. F.T.C., 457 F.3d 354, 357 n.5 (4th Cir. 2006) (*citing* In re Telebrands Corp., 140 F.T.C. at 281 n.3); Kraft v. F.T.C., 970 F.2d at 326 (*citing* FTC v. Colgate-Palmolive, 380 U.S. at 395)).

118. Notwithstanding the Commission's broad discretion in fashioning remedies, there must "be some relation between the violations found and the breadth of the order." *See* Country Tweeds, Inc. v. F.T.C., 326 F.2d 144, 148 -149 (2d Cir. 1964) (citing F.T.C. v. Mandel Bros., Inc., 359 U.S. 385 (1959); F.T.C. v. National Lead Co., 352 U.S. 419 (1957); N.L.R.B. v. Cromption-Highland Mills, Inc., 337 U.S. 217 (1949); N.L.R.B. v. Express Publishing Co., 312 U.S. 426 (1941)).

119. "Multi-products orders should be used with caution because they alter the scheme of penalties and enforcement procedures defined by the Act." Litton Indus., Inc. v. F.T.C., 676 F.2d 364, 371 (9th Cir. 1982) (citing Standard Oil Co. v. F.T.C., 577 F.2d at 661) (internal quotations omitted).

120. Here, the proposed Notice Order includes fencing-in provisions directed to a range of the Respondents' business activities that have nothing to do with the pomegranate products at issue in this case. In particular, in addition to seeking injunctive relief against Respondent POM Wonderful LLC, Complaint Counsel seeks an Order against Respondents' unrelated businesses, including FIJI Water (bottled artesian water), Paramount Citrus (citrus fruits), Paramount Farms (nuts and nut processing), and Justin Vineyards (winery), and unrelated products.

121. To determine whether the fencing-in relief bears reasonable relation to the violations in this case, the Commission considers whether there is a reasonable relationship between the conduct complained of and the requested relief. Traditionally, this Court has used three factors to evaluate reasonable relation: (1) the seriousness and deliberateness of the violation; (2) the ease with which the violative claim may be transferred to other products; and (3) whether the respondent has a history of prior violations. *See* Stouffer Foods Corp., 118 F.T.C. 746, 811 (1994); Sterling Drug, Inc. v. F.T.C., 741 F.2d 1146, 1155 (9th Cir. 1984); Sears Roebuck & Co. v. FTC, 676 F.2d 385, 391-392 (9th Cir. 1982); Standard Oil Co. v. F.T.C., 577 F.2d 653, 662 (1978). Balancing these factors, the Court finds that the broad fencing-in relief is not justified in this case.

122. The violations alleged in this case occurred years ago, and have been modified. *See generally* RFF 2254-2295. Thus, the conduct complained of is not sufficiently serious or deliberate to justify a broad sweeping order. Cf. Litton Indus., Inc., 676 F.2d at 371 (upholding multiproduct order when respondents continued practices after FTC had questioned the advertising practices).

123. In addition, Complaint Counsel has presented no evidence in this case that any of these businesses, which are wholly separate from POM Wonderful and its products, have improperly advertised their products. Without such evidence, the Commission rejects the broad fencing in provisions proposed by Complaint Counsel. In this case, the fencing-in relief also defies common sense, as the other companies and products that would be subject to Complaint Counsel's proposed Order have nothing to do with pomegranate products. There is, thus, no reasonable relation between the conduct at issue in this case and the products that Complaint Counsel seeks to subject to the proposed Order. *See, e.g.*, American Home Products Corp. v. F.T.C., 402 F.2d 232 (6th Cir. 1968) (finding multi-product order too broad when the only evidence presented in the proceeding concerned Preparation H cream (not the other products subject to the order); Grove Laboratories v. F.T.C., 418 F.2d 489 (5th Cir. 1969); cf. Kraft, Inc. v. F.T.C., 970 F.2d 311 (7th Cir. 1992) (upholding multiproduct order relating to cheese related products); Western Radio Corp. v. F.T.C., 339 F.2d 937 (7th Cir. 1964) (upholding order relating to similar products).

124. Finally, the Commission has declined to issue broad fencing-in relief in instances, as here, where a party does not have a history of prior violations. Respondents in this case have never been party to an FTC proceeding or subject to an FTC order. There is, thus, no basis for issuance of a multi-product order.

125. In the unlikely event that the Court finds that the record supports any order in this case (and, for the reasons described in the Proposed Findings it does not), the order should be narrowly tailored to the products and claims that the Court contends were made by the ads. The Commission cannot justify broad-sweeping, disproportional relief on the record presented in this case.

C. Complaint Counsel Have Not Justified Relief as to ROLL Global or to Matthew Tupper

1. Complaint Counsel Has Not Shown that ROLL Global and POM Wonderful LLC Are a Common Enterprise

126. "In considering allegations of misrepresentations, courts engage in a fact-specific inquiry in which the pattern and frame-work of the whole enterprise must be taken into consideration. The factors to be considered include, *inter alia*: common control, the sharing of office space and officers, whether business is transacted through a maze of interrelated companies, the commingling of corporate funds and failure to maintain separation of companies, unified advertising, and evidence which reveals that no real distinction existed between the Corporate Defendants." F.T.C. v. AmeriDebt, Inc., 343 F. Supp. 2d 451, 462 (D. Md. 2004) (internal quotations and citations omitted).

127. Here, the record is clear that Respondents ROLL Global and POM Wonderful LLC are not a common enterprise. They maintain separate records and do not comingle their funds. *See, e.g.*, RFF 64-71.

2. Complaint Counsel Failed to Present Sufficient Evidence to Justify Imposition of Relief on Respondent Matthew Tupper

128. "When both a corporation and an individual are named in the complaint, to obtain a cease and desist order against the individual, Complaint Counsel must prove violations of the FTC Act by the corporation and that the individual either directly participated in the acts at issue or had authority to control them." Joint Stipulations of Law and Facts, dated May 24, 2011, Stipulations of Law at ¶ 6.

129. Individual liability is secondary and derivative of corporate liability and can only be imposed if the corporation is first found to have disseminated unfair, deceptive or otherwise misleading advertisements. F.T.C. v. Bay Area Business Council, Inc., 423 F. 3d 627 (7th Cir. 2005).

130. Assuming this threshold is met, individual liability then requires that the individual (1) directly participated in the challenged advertising or (2) had the ability to control it. *See* In the matter of Rentacolor, Inc., 103 F.T.C. 400, 438 (1984); Thiret v. F.T.C., 512 F.2d 176 (10th Cir. 1975).

131. Although the first prong of the test uses 'participate" language, liability focuses almost exclusively on the ability to control or limit the offending advertising and

not whether the individual actually did review or edit or approve the advertising at issue. *See* F.T.C. v. Direct Marketing Concepts, Inc., et al., 624 F.3d 1 (1st Cir. 2010) (finding 50% owner and officer liable because he had the ability to stop the challenged ads); F.T.C. v. Freecom Comm., Inc., 401 F.3d 1192, 1205 (10th Cir. 2005) (finding principal shareholder and decision maker at closely held corporation liable because he had the authority to control the deceptive acts or practices); In the Matter of Auslander Decorator Furniture, Inc., Trading As A.D.F., Etc., et al., 83 F.T.C. 1542 (1974) (finding individual respondents lacked sufficient control or responsibility for liability).

132. Individual liability cannot be imposed on an officer of a company for participation alone; instead the ability to control the offending conduct or advertising (*i.e.*, being the ultimate decision maker) is always the key inquiry. *See* In the Matter of Universal Electronics Corp., et al., 78 F.T.C. 265 (1971); F.T.C. v. Swish Marketing et al., 2010 WL 653486 (N.D. Cal. Feb. 22, 2010); F.T.C. v. Neovi, Inc. et al., 598 F. Supp. 2d 1104 (S.D. Cal. 2008); F.T.C. v. Transnet Wireless Corp., 506 F. Supp. 2d 1247, 1261-1265 (S.D. Fla. 2007); F.T.C. v. Verity Int'l, Ltd., 335 F. Supp. 2d 479, 499 (S.D.N.Y. 2004); F.T.C. v. Publishing Clearing House, 104 F. 3d 1168, 1171 (9th Cir. 1997); F.T.C. v. Amy Travel Service, Inc., 875 F. 2d 564, 574-575 (7th Cir. 1989); F.T.C. v. Think Achievement Corp., 144 F. Supp. 2d 993, 998-1002 (N.D. Ind. 2000); F.T.C. v. J.K. Publications, 99 F. Supp. 2d 1176, 1181-1185, (C.D. Cal. 2000); F.T.C. v. Direct Marketing Concepts, Inc. et al., 624 F.3d 1 (1st Cir. 2010).

133. Corporate officers may now be held individually liable for violations of the FTC Act, but only if the officer "owned, dominated and managed" the company and if naming the officer individually is necessary for the order to be fully effective in preventing the deceptive practices which the Commission had found to exist. F.T.C. v. Standard Education Society, 302 U.S. 112, 120 (1937) (officers/managers and sole shareholders of closely held corporation that was dominated and managed by these individuals were held personally liable and included in cease and desist order because it was anticipated from past conduct that these persons would simply try to evade the FTC's order by setting up another company).

134. Traditionally, the Commission has imposed individual liability as a method to preclude owners of closely held corporations from dissolving the offending corporation and beginning a new one to avoid a cease and desist order of the FTC.

Standard Education Society, 302 U.S. at 119. This later evolved into allowing non-owner officers to be found liable if they met the above described "ability to control" tests or otherwise "formulat[ed], direct[ed] or controll[ed] any of the acts and practices" at issue. In the Matter of Griffin Systems, Inc. et al., 117 F.T.C. 515, 563-564 (1994) (finding individual who was vice president, treasurer and director liable for distributing solicitation in violation of the FTC Act because he was in charge of the company and was considered the control person by the employees).

135. Complaint Counsel named POM Wonderful President Matthew Tupper as an individual respondent in the Complaint. Mr. Tupper neither owns, dominates, nor ultimately controls POM. *See generally* RFF 84-107. During the relevant period, Mr. Tupper was not involved in final advertising decisions and he worked directly for the owners of the company. He, therefore, is not subject to liability under the FTC Act. Auslander Decorator Furniture, 83 F.T.C. 1542 (finding individual respondents lacked sufficient control or responsibility for liability); F.T.C. v. Standard Education Society, 302 U.S. 112, 119 (1937) (officers/managers and sole shareholders of closely held corporation that dominated and managed the company were included in cease and desist order to ensure compliance with the order as these persons were ultimately in control).

136. Unlike the typical President of a private company, Mr. Tupper's authority was derivative of and subject to private owner individuals above him (the Resnicks) and cannot be seen as a typical ultimate decision maker officer subject to liability in FTC cases. *See e.g.* Publ'g Clearing House, 104 F. 3d at 1171; Neovi, Inc. et al., 598 F.Supp.2d 1104.

137. Mr. Tupper's inclusion in any injunctive or related order, is not necessary to effectuate the cessation of the alleged offending conduct (the primary purpose of such orders), as he does not and never did ultimately control it. Standard Education Society, 302 U.S. at 119 (officers/managers and sole shareholders of closely held corporation that dominated and managed the company were included in cease and desist order to ensure compliance with the order as these persons were ultimately in control).

138. Moreover, Mr. Tupper has resigned from POM and has no plans to return to the corporation. Because Mr. Tupper never had control over the alleged offending conduct and that Mr. Tupper is retired from POM and not planning to return, no liability will be imposed.

UNITED STATES OF AMERICA
FEDERAL TRADE COMMISSION

In the Matter of	)	
	)	
POM WONDERFUL LLC and	)	
ROLL GLOBAL LLC,	)	
as successor in interest to Roll	)	
International Corporation,	)	
	)	
companies, and	)	Docket No. 9344
	)	PUBLIC
STEWART A. RESNICK,	)	
LYNDA RAE RESNICK, and	)	
MATTHEW TUPPER, individually and	)	
as officers of the companies.	)	

CERTIFICATE OF SERVICE

I hereby certify that this is a true and correct copy of Respondents' **FINDINGS OF FACT AND CONCLUSIONS OF LAW**, and that on this 11th day of January, 2012, I caused the foregoing to be served by FTC E-File, hand delivery and e-mail on the following:

Donald S. Clark
The Office of the Secretary
Federal Trade Commission
600 Pennsylvania Avenue, NW
H-159
Washington, DC 20580

The Honorable D. Michael Chappell
Administrative Law Judge
Federal Trade Commission
600 Pennsylvania Avenue, NW
Rm. H-110
Washington, DC 20580

I hereby certify that this is a true and correct copy of Respondents' **FINDINGS OF FACT AND CONCLUSIONS OF LAW**, and that on this 11th day of January, 2012, I caused the foregoing to be served by e-mail on the following:

Mary Engle
Associate Director for Advertising Practices
Bureau of Consumer Protection
Federal Trade Commission
601 New Jersey Avenue, NW
Washington, DC 20580

Mary Johnson, Senior Counsel
Heather Hippsley
Tawana Davis
Federal Trade Commission
Bureau of Consumer Protection
601 New Jersey Avenue, NW
Washington, DC 20580

Counsel for Complainant

/s Skye Perryman

John D. Graubert
Skye L. Perryman
COVINGTON & BURLING LLP
1201 Pennsylvania Ave. NW
Washington, DC 20004-2401
Telephone: 202.662.5938
Facsimile: 202.778.5938
E-mail: JGraubert@cov.com
SPerryman@cov.com

Kristina M. Diaz
Roll Law Group P.C.
11444 West Olympic Boulevard, 10th Floor
Los Angeles, CA 90064
Telephone: 310.966.8775
E-mail: kdiaz@roll.com

Bertram Fields
Greenberg Glusker
1900 Avenue of the Stars
21st Floor
Los Angeles, California 90067
Telephone: 310.201.7454

Counsel for Respondents

Dated: January 11, 2012

1988 WL 490114 (F.T.C.)

FEDERAL TRADE COMMISSION (F.T.C.)

***1** In the Matter of
R.J. REYNOLDS TOBACCO COMPANY, INC., a corporation.

Docket No. 9206

ISSUED: March 4, 1988

COMMISSIONERS:

Daniel Oliver, Chairman

Patricia P. Bailey

Terry Calvani

Mary L. Azcuenaga

Andrew J. Strenio, Jr.

ORDER

This matter has been heard by the Commission upon the appeal of counsel supporting the complaint from the initial decision, and upon briefs and oral argument in support of and in opposition to the appeal. For the reasons stated in the accompanying opinion, the Commission has determined to reverse the initial decision and remand the matter for further proceedings. Therefore,

IT IS ORDERED that the initial decision of the Administrative Law Judge is reversed and the matter remanded for further proceedings in accordance with this order and accompanying opinion.

By the Commission, Chairman Oliver dissenting.

Benjamin I. Berman

Acting Secretary

OPINION OF THE COMMISSION

By Strenio, Commissioner.

The issue presented here is whether the Administrative Law Judge ("ALJ") erred when he granted respondent R.J. Reynolds Tobacco Company, Inc.'s ("Reynolds") motion to dismiss on the ground that "Of Cigarettes and Science" was not commercial speech and, thus, not subject to the Commission's jurisdiction. We find that the

ALJ erred when he granted the motion to dismiss. We also find that the ALJ erred when he ruled that further opportunity to discover and present facts relating to jurisdiction was not permitted. His order is reversed and the matter remanded for further proceedings consistent with this opinion.

I. Procedural History.

This case involves an advertisement, entitled "Of Cigarettes and Science," allegedly disseminated by Reynolds in the course of its business of manufacturing, advertising and selling cigarettes. Complaint, ¶ ¶ 2–4. The advertisement discusses, among other things, the procedures that scientists use to test scientific hypotheses and sets forth information about a scientific study known as the Multiple Risk Factor Intervention Trial ("MR FIT"). Complaint, Attachment A.

On June 16, 1986, the Federal Trade Commission ("Commission" or "FTC") issued a complaint alleging that the Reynolds advertisement falsely and misleadingly represents: that the purpose of the MR FIT study was to determine whether heart disease is caused by cigarette smoking; that the MR FIT study provides credible scientific evidence that smoking is not as hazardous as the public or the reader has been led to believe; and that the MR FIT study tends to refute the theory that smoking causes coronary heart disease. Complaint, ¶ ¶ 5–6. In addition, the complaint alleges that the advertisement fails to disclose certain material facts about the MR FIT study. Complaint, ¶ 7.

Respondent filed a motion to dismiss the complaint on June 26, 1986. The motion sought dismissal on the ground that the Commission had no subject matter jurisdiction over the "Of Cigarettes and Science" advertisement because "the acts and practices complained of are expressions of opinion on issues of social and political importance which cannot be regulated by the Federal Trade Commission consistent with the First Amendment." FN;B1[FN1] Motion to Dismiss, ¶ 1. According to Reynolds, the ALJ was required to determine the jurisdictional issue on the basis of the pleadings alone; consideration of extrinsic evidence was both irrelevant and itself violative of the First Amendment. FN;B2[FN2]

***2** Complaint counsel opposed the motion to dismiss, arguing alternatively that the motion should be denied because the challenged advertisement was properly classified as commercial speech and, thus, properly subject to the Commission's jurisdiction or because the motion raised issues that required further factual development. FN;B3[FN3]

After hearing argument on the motion, the ALJ concluded that the advertisement was not commercial speech but rather speech fully protected by the First Amendment. The ALJ thus ruled that the advertisement was outside the jurisdiction of the Commission. Order, dated August 4, 1986. In his decision, the ALJ rejected the argument that complaint counsel should be granted further opportunity to discover and present facts relating to jurisdiction. Id. at 14–15. He concluded that further discovery was "contrary to law and unacceptable" because categorization of speech as either commercial or noncommercial has been "customarily resolved by the courts on the basis of what is contained in the ads" and, in any event, he had already granted complaint counsel "ample time" for discovery. Id.

Counsel supporting the complaint appealed the ALJ's initial decision to the Commission.

II. FTC Jurisdiction.

We agree with the parties and the ALJ that unless the Reynolds advertisement can be classified as commercial

speech, it is not subject to the Commission's jurisdiction. Thus, consideration of whether the ALJ erred when he concluded, at this stage of the proceeding, that the complaint should be dismissed necessarily begins with an analysis of the legal standards applicable to classification of speech as commercial or noncommercial.

Following that analysis, the facts of this case will be applied to the legal framework. When making this analysis, the procedural standards applicable to motions to dismiss apply. Under those standards, the complaint must allege facts sufficient to confer jurisdiction. For purposes of this analysis, all of the factual allegations of the complaint concerning jurisdiction are presumed true. See, e.g., Scheuer v. Rhodes, 416 U.S. 232, 236 (1974). See also 2A J. Moore, J. Lucas & G. Grotheer, Moore's Federal Practice, ¶ 12.07 [2.–1] at 12–46 to 12–47 (2d ed. 1987). If the complaint does not allege sufficient facts to confer jurisdiction, it must be dismissed.

If, on the other hand, the complaint does allege facts which—if true—would be sufficient to establish jurisdiction, then another inquiry is required. Specifically, the question then becomes whether the facts alleged are supported by the evidence. In making this determination, there is no presumption that the allegations are true, and the burden is on complaint counsel to prove jurisdiction by a preponderance of the evidence. See, e.g., Menchaca v. Chrysler Credit Corp., 613 F.2d 507, 511 (5th Cir.), cert. denied, 449 U.S. 953 (1980); Mortensen v. First Federal Savings & Loan Ass'n, 549 F.2d 884 (3d Cir.1977).

***3** Finally, we also address whether, and to what extent, consideration of extrinsic evidence is permitted to resolve the jurisdictional issue.

A. The First Amendment Guarantee of Freedom of Speech.

The protections afforded by the First Amendment guarantee against laws “abridging the freedom of speech” are of fundamental importance to a democratic society. Justice Cardozo once characterized the First Amendment as “the matrix, the indispensible condition of nearly every other form of freedom.” FN;B4[FN4] The reach of the First Amendment extends to individuals as well as to corporations and other entities. First National Bank of Boston v. Bellotti, 435 U.S. 765 (1978).

The Constitution, however, accords different degrees of protection based upon the type of speech at issue. The core examples of speech entitled to the highest level of protection are political discourse and expressions about philosophical, religious, artistic, literary or ethical matters. In light of its high societal value, regulation of such “fully protected” speech generally is limited to reasonable time, place and manner restrictions.

Commercial speech, by contrast, is accorded less constitutional protection, but protection that is “nonetheless substantial.” Bolger v. Youngs Drug Products Corp., 463 U.S. 60, 68 (1983).FN;B5[FN5] Unlike fully protected speech, commercial speech can be regulated on the basis of its content.

The more limited protection accorded commercial speech permits the FTC to act when necessary to challenge false or deceptive advertising. FN;B6[FN6] See, e.g., Thompson Medical Co. v. FTC, 791 F.2d 189 (D.C.Cir.1986), cert. denied, 107 S.Ct. 1289 (1987); Sears, Roebuck & Co. v. FTC, 676 F.2d 385 (9th Cir.1982); Warner–Lambert Co. v. FTC, 562 F.2d 749 (D.C.Cir.1977), cert. denied, 435 U.S. 950 (1978); Beneficial Corp. v. FTC, 542 F.2d 611 (3d Cir.1976), cert. denied, 430 U.S. 983 (1977). Commission action to prevent false or deceptive advertising, in turn, serves the important public interest in informed commercial decision-making.

B. Commercial Speech.

The Supreme Court has referred to the "core notion" of commercial speech as speech proposing a commercial transaction. Bolger v. Youngs Drug Products, 463 U.S. at 66 (citing Virginia State Board of Pharmacy v. Virginia Citizens Consumer Council, Inc., 425 U.S. 748, 762 (1976) and Pittsburgh Press Co. v. Pittsburgh Comm'n on Human Relations, 413 U.S. 376, 385 (1973)). See also Central Hudson Gas & Electric Corp. v. Public Service Comm'n, 447 U.S. 557, 562 (1980); Linmark Associates, Inc. v. Township of Willingboro, 431 U.S. 85 (1977). In Central Hudson, the Court also discussed commercial speech as speech solely related to the economic interests of both the speaker and the speaker's audience. 447 U.S. at 561.

The Court also has made it clear that commercial speech may include speech that links a product to important public issues or matters subject to current public debate. Central Hudson, 447 U.S. at 562 n. 5; Bolger v. Youngs Drug Products Corp., 463 U.S. at 67–68; Zauderer v. Office of Disciplinary Counsel of the Supreme Court of Ohio, 471 U.S. 626, 637 n. 7 (1985). Indeed, in Central Hudson, the Court majority found that the New York State Public Service Commission order banning all advertising intended to promote the sale of utility services or electricity involved "only commercial speech." 447 U.S. at 561. The majority expressly rejected Justice Stevens' suggestion that the category "promotional advertising" would also include fully protected speech if, for example, the speech touted the environmental benefits of electricity, noting:

> ***4** [Justice Stevens' approach] would grant broad constitutional protection to any advertising that links a product to a current public debate. But many, if not most, products may be tied to public concerns with the environment, energy, economic policy, or individual health and safety.

Id. at 562 n. 5. The Court observed that companies have full constitutional protection for their direct comments on public issues and thus, there did not appear to be a need for similar protection "when such statements are made only in the context of commercial transactions. In that context, the State retains the power to 'ensur[e] that the stream of commercial information flow[s] cleanly as well as freely.' " Id. (citing Virginia State Board of Pharmacy, 425 U.S. at 772).

The Supreme Court has not established a bright line test for ascertaining the boundary between commercial speech that may also include information about matters of important public interest and speech that constitutes direct comments on public issues. Indeed, the Court has noted the complexities of delineating the boundary. See Zauderer v. Office of Disciplinary Counsel, 471 U.S. at 637 (the "precise bounds" of commercial speech are "subject to doubt"); In re Primus, 436 U.S. 412, 438 n. 32 (1978) (line between commercial and noncommercial speech "will not always be easy to draw"). Moreover, the Court has recognized that "the diverse motives, means, and messages of advertising may make speech 'commercial' in widely varying degrees." Bigelow v. Virginia, 421 U.S. 809, 826 (1975).

The Court, however, has offered guidance for determining what constitutes commercial speech by mentioning a number of characteristics of commercial speech. The Commission considers it premature, particularly in the absence of a full record, to say which characteristics will be determinative in deciding whether the Reynolds advertisement constitutes commercial speech. It is appropriate, however, to start with those characteristics that the Court has considered in its relatively few commercial speech decisions. FN;B7[FN7]

We begin with the content of the speech in question. See Bates v. State Bar of Arizona, 433 U.S. 350, 363 (1977). The Court in Central Hudson identified speech containing a message promoting the demand for a product or service as speech that can be classified as commercial. See 447 U.S. at 559–62.

In addition, commercial speech typically refers to a specific product or service. Bolger v. Youngs Drug Products, 463 U.S. at 66. In many cases, the product reference includes the brand name of a product offered for

sale. However, the Bolger Court stated that a generic reference to a product would not necessarily remove it from the category of commercial speech: "For example, a company with sufficient control of the market for a product may be able to promote the product without reference to its own brand name. Or, a trade association may make statements about a product, without reference to specific brand names." 463 U.S. at 66–67 n. 13 (citing with approval National Commission on Egg Nutrition v. FTC, 570 F.2d 157 (7th Cir.1977), cert. denied, 439 U.S. 821 (1978)).FN;B8[FN8]

***5** In Friedman v. Rogers, 440 U.S. 1, 11 (1979), the Court noted that information about attributes of a product or service offered for sale, such as type, price, or quality, is also indicative of commercial speech. FN;B9[FN9] Likewise, the Court has indicated that information about health effects associated with the use of a product can properly be classified as commercial speech. FN;B10[FN10] See Bolger v. Youngs Drug Products, 463 U.S. at 66–67 (claims discussing the benefits of condoms for the prevention of venereal disease). See also National Commission on Egg Nutrition, 570 F.2d at 163 (deceptive claims to the effect that no scientific evidence supported the claim that eating eggs increases the risk of heart disease).

In addition to content, the Court has found that the means used to publish speech is relevant to the classification issue. For example, the Court has recognized that commercial speech frequently takes the form of paid-for advertising. See Bolger v. Youngs Drug Products, 463 U.S. at 66 (citing New York Times Co. v. Sullivan, 376 U.S. 254, 265–66 (1964)). See also Bates v. State Bar of Arizona, 433 U.S. at 363–64; Virginia State Board of Pharmacy, 425 U.S. at 761.

The Court also has indicated that the speaker's economic or commercial motivation is germane to the issue of whether speech is commercial. In re Primus, 436 U.S. at 438 n. 32 (line between commercial and noncommercial speech is "based in part on the motive of the speaker"); Bolger v. Youngs Drug Products, 463 U.S. at 67. See also National Commission on Egg Nutrition, where the Seventh Circuit held that commercial speech should not "be narrowly limited to the mere proposal of a particular commercial transaction but [should] extend to false claims as to the harmlessness of the advertiser's product asserted for the purpose of persuading members of the reading public to buy the product." 570 F.2d at 163.

It would appear for purposes of this analysis that an important consideration will be whether the speech is promotional in nature. Does the speech benefit or seek to benefit the economic interests of the speaker by promoting sales of its products? And, does the speech affect or seek to affect purchasing decisions by the receivers of the information?

This type of speech can be contrasted with speech that does not benefit the economic interests of the speaker by influencing the reader or listener in the role of consumer, but instead provides, for example, information relevant to individual political decisions, or to artistic or cultural choices. Such speech may not further the informational function of commercial decision-making. See, e.g., Consolidated Edison Co. of N.Y., Inc. v. Public Service Comm'n, 447 U.S. 530 (1980) (billing insert was not addressed to informed decision-making about the purchase of a specific product, i.e., nuclear-generated electricity, but concerned the human and environmental risks that could result from a malfunction or accident at a nuclear power plant); First National Bank of Boston v. Bellotti, 435 U.S. 765 (1978) (speech in question was limited to expression directed to the reader or listener as a voter).FN;B11[FN11]

***6** Although it may be difficult in some cases, the Commission thinks that it is possible to determine whether a specific advertisement that includes information connected to public issues nonetheless addresses the concerns

of a purchaser of the advertiser's product or service. To conclude otherwise would allow sellers of certain products to avoid the proscription against false and misleading advertising merely by linking their product to a public issue. Indeed, in National Commission on Egg Nutrition, the product—eggs—was inextricably linked to the cholesterol-and-heart-disease issue. Despite the connection, the Seventh Circuit ruled that the advertisements, including "Cholesterol and the Egg: A Mystery," were commercial speech.

C. The ALJ's Decision to Grant Respondent's Motion.

The question remains, of course, whether the ALJ erred when he granted respondent's motion to dismiss. In reaching his decision, the ALJ was required to consider the various "messages, means, and motives" of the advertisement (see Bigelow, 421 U.S. at 826), including the presence or absence of the characteristics identified by the case law as relevant to whether speech is commercial.

Accepting the allegations of the complaint concerning jurisdiction as true for purposes of this appeal, FN;B12 [FN12] the content of the Reynolds advertisement includes words and messages that are characteristic of commercial speech. The advertisement refers to a specific product, cigarettes. Complaint, ¶ ¶ 2, 4; Bolger v. Youngs Drug Products, 463 U.S. at 66. Moreover, the advertisement discusses an important product attribute—the alleged connection between smoking and heart disease. Complaint, ¶ ¶ 4, 5; Friedman v. Rogers, 444 U.S. at 11; National Commission on Egg Nutrition, 570 F.2d at 163. A message that addresses health concerns that may be faced by purchasers or potential purchasers of the speaker's product may constitute commercial speech. See Bolger v. Youngs Drug Products, 463 U.S. at 66–67; National Commission on Egg Nutrition, 570 F.2d at 163.

Similarly, the complaint alleges that "Of Cigarettes and Science" is an advertisement (Complaint, ¶ 2), which we understand to mean a notice or announcement that is publicly published or broadcast and is paid-for. Thus, viewed in light of the allegations of the complaint, the "means" used to disseminate the Reynolds advertisement—paid-for advertising—is typical of commercial speech. Bolger v. Youngs Drug Products, 463 U.S. at 66; Virginia State Board of Pharmacy, 425 U.S. at 761.

Finally, the complaint alleges that respondent is in the business of selling cigarettes. Complaint, ¶ 4. It is reasonable to infer that Reynolds, as a seller of cigarettes, had a direct, sales-related motive for disseminating the "Of Cigarettes and Science" advertisement. As discussed above, economic motivation also may be indicative of commercial speech. In re Primus, 436 U.S. at 438 n. 32; Bolger v. Youngs Drug Products, 463 U.S. at 67; National Commission on Egg Nutrition, 570 F.2d at 163.

***7** Thus, viewed in light of the allegations contained in the complaint, we conclude that the ALJ erred when he granted respondent's motion to dismiss at this stage of the proceeding.

It should be clear, however, that the Commission makes no final determination of jurisdiction. As we noted above, supra at 4–5, any such conclusion requires proof that the complaint allegations concerning jurisdiction are true. Inasmuch as respondent has not answered the complaint, the record does not indicate what factual allegations concerning jurisdiction, if any, are controverted. Thus, final findings of fact with respect to jurisdiction at this stage of the proceeding would be premature.

Instead, we think it is appropriate to remand the matter to the ALJ for the purpose of determining whether application of the facts to the appropriate legal standards supports a finding of jurisdiction. Upon remand, the ALJ may weigh the evidence and resolve any factual disputes. If the ALJ determines that additional evidence is needed to make a final determination on jurisdiction, FN;B13[FN13] he shall permit further opportunity to de-

velop and present evidence on the issue. See Part II.D, infra at 17–22. We emphasize, however, that we have not concluded that presentation of extrinsic evidence is necessarily required for determining whether the Reynolds advertisement is commercial speech. The decision of what evidence to present in order to attempt to meet their burden of proving jurisdiction is a decision to be made properly by counsel supporting the complaint.

D. Consideration of Extrinsic Evidence.

Another issue that arose below is whether, and to what extent, consideration of extrinsic evidence is permitted to resolve the jurisdictional issue. As a general matter, a party may establish the existence of subject matter jurisdiction through the use of extrinsic evidence. FN;B14[FN14] Respondent, however, contends that reliance upon extrinsic evidence is irrelevant and itself violative of the First Amendment.

We agree that consideration of extrinsic evidence is permitted only if the evidence is relevant to the issues presented and is not barred by any evidentiary privilege. FN;B15[FN15] Nonetheless, we disagree with respondent's sweeping assertion that this standard prohibits any and all consideration of extrinsic evidence in determining whether the Reynolds advertisement is subject to the Commission's jurisdiction. We are aware of no decision holding that consideration of extrinsic evidence is impermissible in determining whether an advertisement constitutes commercial speech.

Indeed, the Supreme Court in In re Primus, 436 U.S. 412 (1978), clearly relied upon extrinsic evidence for its finding that application by the Supreme Court of South Carolina of its Disciplinary Rules to appellant's solicitation by letter on the American Civil Liberties Union's (“ACLU”) behalf violated the First Amendment. In addition to considering the solicitation letter, the Court looked to evidence relating to the circumstances that led to appellant's letter and the events that took place after the letter was sent, the aims and practices of the ACLU, and the appellant's lack of any economic motivation—a characteristic which the Court noted distinguished the appellant's solicitation from the purely commercial solicitation present in Ohralik v. Ohio State Bar Ass'n, 436 U.S. 447 (1978), decided the same day.

***8** Moreover, in Herbert v. Lando, 441 U.S. 153, 175 (1979), the Supreme Court held that the First Amendment did not bar a plaintiff in a defamation action from inquiring into the editorial processes of the respondent members of the press because the information sought to be discovered was directly relevant to proof of a critical element of the plaintiff's cause of action. FN;B16[FN16] Instead, the Court found that the relevancy requirement of Rule 26(b)(1) was sufficient protection against improper forays into the respondents' thought processes. We find the reasoning in Herbert v. Lando applicable here.FN;B17[FN17] Thus, we find no basis for concluding that discovery and presentation of relevant and non-privileged evidence concerning jurisdiction must be categorically barred.

Evidence that may be relevant to deciding whether the Reynolds advertisement is commercial speech includes facts concerning the publication or dissemination of the advertisement, such as whether it was paid-for, where and in which publications it was disseminated, whether it was placed in editorial space (such as an opened page) or advertising space in the publication, whether it was prepared as a letter to the editor, whether it was sent to representatives of the media for selection on merit by editorial boards, and to whom it was disseminated outside the media.

Evidence about the promotional nature of the advertisement also may be relevant. Therefore, it might be useful to consider the circumstances surrounding the development of the advertisement, such as whether it was targeted to consumers or legislators; whether it was intended to affect demand for Reynolds' cigarettes or brands or to af-

fect particular legislative or regulatory proposals; whether the advertisement was subjected to copy testing or to review by focus groups and, if so, the nature of the questions used in the copy tests or focus group sessions; and the results of those procedures both in terms of what they showed and what changes, if any, Reynolds made in response to those showings. Evidence relating to the message(s) Reynolds itself intended to convey through the advertisement also may be relevant. In addition, Reynolds' share of the cigarette market may be relevant to deciding whether including a brand name reference is a prerequisite to a determination that the advertisement constitutes commercial speech. FN;B18[FN18]

Of course, to the extent that any specific facts are protected by an evidentiary privilege, their use would not be permitted even if relevant. Determination of whether or not evidence is privileged, however, should be made on an individual basis. In this connection, we disagree with respondent's contention that use of all evidence other than the "Of Cigarettes and Science" advertisement would violate the First Amendment. See Herbert v. Lando, 441 U.S. at 175.

In sum, other than the relevancy and privilege requirements, we find no categorical evidentiary bar against discovery or presentation of extrinsic evidence that might assist in determining on the record whether the Reynolds advertisement constitutes commercial speech, and consequently, would be subject to the Commission's jurisdiction.

***9** III. Conclusion.

For the reasons discussed above, we reverse the Administrative Law Judge's order granting respondent's motion to dismiss for lack of subject matter jurisdiction, and remand for further proceedings consistent with this opin- ion.

> But if the claimed inhibition flows from the fear of damages liability for publishing knowing or reckless falsehoods, those effects are precisely what New York Times and other cases have held to be consistent with the First Amendment. Spreading false information in and of itself carries no First Amendment credentials.

441 U.S. at 171.

***10** SEPARATE STATEMENT OF CHAIRMAN OLIVER, DISSENTING

I. INTRODUCTION

The First Amendment prohibits the federal government from acting as umpire in the contest of ideas. The government cannot select which issues are worth debating nor selectively exclude certain participants from that debate. Under the First Amendment, individuals and corporations alike have a fully protected right to engage in direct comment on public issues free from governmental regulation or censorship.

First Amendment protection of public debate generally coexists very peacefully with the Federal Trade Commission's exercise of its authority to ban deceptive commercial speech. While the First Amendment protects unfair and false statements in the public marketplace of ideas, it does not protect such statements in the commercial marketplace for goods and services. The Commission's jurisdictional authority extends to the hawking of wares, not the hawking of ideas.

The American marketplace for ideas is decentralized and occurs in numerous arenas: in Congress, in academia, in books and pamphlets, in newspapers, over the airways, over backyard fences, at the workplace, door-to-door.

Seldom does the government step in to crown a victor or promulgate an official version of the truth. In the debate over public policies regarding smoking, however, the government has not only based its policies on an official version of the truth, it has compelled private citizens to propagandize in favor of that version of the truth. FN;B1XXa[FN1] In this case, the Federal Trade Commission is attempting to go one step further and regulate a challenge to the official orthodoxy.

At issue in this case is whether R.J. Reynolds Tobacco Co. (RJR) has a fully protected right under the First Amendment to question the officially accepted view regarding the link between cigarette smoking and heart disease. In March 1985, RJR paid various newspapers and magazines to publish a communication captioned "Of Cigarettes and Science," in which RJR questioned the objectivity of the scientists who examine the issue of smoking and health. FN;B2XXa[FN2] Relying on data from a governmentally funded study, RJR argued that there is still a scientific question about the link between cigarettes and heart disease.

The Federal Trade Commission responded by issuing a complaint that alleges that the RJR communication is deceptive. RJR has in turn challenged the subject matter jurisdiction of the FTC, arguing that the publication at issue is fully protected under the First Amendment. The Administrative Law Judge ruled that RJR is correct, that the publication is an editorial rather than commercial speech, and dismissed the complaint for lack of subject matter jurisdiction.

In my opinion, RJR and the Administrative Law Judge are clearly correct. The RJR publication is, without doubt, a direct comment on a matter of public concern—the link between cigarette smoking and heart disease. Any commercial effect of the RJR communication is inextricably intertwined with RJR's participation in the contest of ideas. Accordingly, the RJR publication is fully protected by the First Amendment, even if one of the consequences of the publication is to affect cigarette consumption. R.J. Reynolds cannot be disqualified from questioning scientific certitude merely because its potential success in persuading the general public that the question remains open could also have an effect on sales of its product.

***11** The Commission majority attempts to finesse the issue of whether the RJR communication is commercial speech (which the Commission has subject matter jurisdiction over) or fully protected speech (thus requiring dismissal). The Administrative Law Judge is reversed, and the case remanded, but the reasons for doing so are not immediately apparent. Although finding that the words and message of the RJR communication are characteristic of commercial speech, the Commission majority purportedly declines to decide whether the communication is commercial speech. Further, without ruling that additional extrinsic evidence is needed to decide the key jurisdictional issue, FN;B3XXa[FN3] the majority nonetheless sets forth the facts it believes may be relevant. On closer examination, it becomes apparent that the majority makes determinations that logically compel it to conclude that the piece is commercial speech, but seeks to duck the issue, sending the matter back to the ALJ for further discovery that might bolster a finding that the Commission has subject matter jurisdiction.

In my considered opinion there is no reason why the Commission cannot make an explicit determination today. The text and the context of RJR's communication are before the Commission. From the face of the document itself we can determine that the communication is a direct comment on a matter of public debate. The piece is not a solicitation for a commercial transaction with a gratuitous reference to a public debate thrown in to evade laws relevant to commercial advertising. RJR's direct comment on a matter of public debate is inextricably intertwined with any commercial effect that may result from RJR's participation in that debate. As Supreme Court precedent establishes, direct comment on a matter of public debate is fully protected under the First Amendment, even if it has a commercial effect, unless the comment on the public issue is merely gratuitously linked with a

commercial message. No discovery is needed or justified prior to a ruling on the Commission's subject matter jurisdiction. The factual inquiry that the majority proposes would either produce unnecessary background information or engage the Commission in an irrelevant quest to establish RJR's "intent" in running this piece. The facts before the Administrative Law Judge and the Commission establish that we lack subject matter jurisdiction. Consistent with the First Amendment, we have no choice but to dismiss the complaint.

II. RELEVANT BACKGROUND FACTS

The RJR piece, FN;B4XXa[FN4] "Of Cigarettes and Science," was published in March 1985 in a number of newspapers and magazines. (Abrams Aff. ¶ 2) In that communication, RJR argues that one set of scientific principles is being used to judge most scientific matters but that a different set is being used for experiments involving cigarettes. In support of this thesis, RJR cites its version of the scientific treatment of a study called the Multiple Risk Factor Intervention Trial (MR FIT). The study, funded by the federal government, cost $115,000,000 and took ten years. RJR's communication describes the study as follows:

> ***12** The subjects were over 12,000 men who were thought to have a high risk of heart disease because of three risk factors that are statistically associated with this disease: smoking, high blood pressure and high cholesterol levels.
>
> Half of the men received no special medical intervention. The other half received medical treatment that consistently reduced all three risk factors, compared with the first group.
>
> It was assumed that the group with lower risk factors would, over time, suffer significantly fewer deaths from heart disease than the higher risk factor group.
>
> But that is not the way it turned out.
>
> After 10 years, there was no statistically significant difference between the two groups in the number of hear disease deaths.

The Commission does not allege that this description of the study is inaccurate. FN;B5XXa[FN5] Nor is it disputed that the results of the MR FIT were not as expected. FN;B6XXa[FN6]

After describing the study, RJR provides its view of the scientific reaction to that study:

> We at R.J. Reynolds do not claim this study proves that smoking doesn't cause heart disease. But we do wish to make a point.
>
> Despite the results of MR FIT and other experiments like it, many scientists have not abandoned or modified their original theory, or re-examined its assumptions.
>
> They continue to believe these factors cause heart disease. But it is important to label their belief accurately. It is an opinion. A judgment. But not scientific fact.
>
> We believe in science. That is why we continue to provide funding for independent research into smoking and health.
>
> But we do not believe there should be one set of scientific principles for the whole world, and a different set for experiments involving cigarettes. Science is science. Proof is proof. That is why the controversy over smoking and health remains an open one. FN;B7XXa[FN7]

The Administrative Law Judge determined that the characterization of "Of Cigarettes and Science" as commercial speech or fully protected speech can be made from the face of the publication. FN;B8XXa[FN8] In summary, his conclusion was: "From a common sense approach, Reynolds' 'Of cigarettes and science' is clearly an editorial; it is not commercial speech by any stretch of the imagination." FN;B9XXa[FN9]

III. CONTROLLING SUPREME COURT PRECEDENT

The Supreme Court has recognized that corporations are free to engage in public debate and have a fully protected right to do so, noting that: "[t]he inherent worth of the speech in terms of its capacity for informing the public does not depend upon the identity of its source, whether corporation, association, union, or individual." First National Bank of Boston v. Belotti, 435 U.S. 765, 777 (1978), rehearing denied, 438 U.S. 907 (1978). Corporations, like others, do not lose the protection of the First Amendment by virtue of the fact that they pay to make their views known. In rejecting a claim that libelous statements received no protection because they had been paid for in an advertisement attempting to raise funds, the Supreme Court stated:

> ***13** That the Times was paid for publishing the advertisement is as immaterial in this connection as is the fact that newspapers and books are sold. Any other conclusion would discourage newspapers from carrying "editorial advertisements" of this type, and so might shut off an important outlet for the promulgation of information and ideas by persons who do not themselves have access to publishing facilities—who wish to exercise their freedom of speech even though they are not members of the press. The effect would be to shackle the First Amendment in its attempt to secure the "widest possible dissemination of information from diverse and antagonistic sources."

New York Times v. Sullivan, 376 U.S. 254, 266 (1964) (citations omitted).FN;B10XXa[FN10]

Public debate is protected because, "above all else, the First Amendment means that government has no power to restrict expression because of its message, its ideas, its subject matter, or its content." FN;B11XXa[FN11] The government may not "select which issues are worth discussing or debating" and "must afford all points of view an equal opportunity to be heard." FN;B12XXa[FN12] "Selective exclusions from a public forum may not be based on content alone, and may not be justified by reference to content alone." FN;B13XXa[FN13]

The First Amendment evidences a deliberate policy choice to limit the government's ability to control speech and to rely instead on the abilities of the citizenry to judge the facts and opinions offered by themselves. That choice is made with a clear view of the consequences, that "erroneous statement of fact is ... inevitable in free debate.... The First Amendment requires that we protect some falsehood in order to protect speech that matters." Gertz v. Robert Welch, Inc., 418 U.S. 323, 340–41 (1974). Such an accommodation is necessary to give freedom of speech the "breathing space" which is necessary for its "fruitful exercise" (Id. at 342) and "survival." NAACP v. Button, 371 U.S. 415, 433 (1963). Indeed, "[u]nder the First Amendment there is no such thing as a false idea." Gertz, supra, 418 U.S. at 339. This does not imply that the truth is not preferred, but that the arbiters should be the public rather than the government. "If there be time to expose through discussion the falsehood and fallacies, to avert the evil by the processes of education, the remedy to be applied is more speech, not enforced silence." FN;B14XXa[FN14]

Commercial speech, like debate over ideas, is protected under the First Amendment, but it receives a lower level of protection. FN;B15XXa[FN15] The distinction is drawn to avoid "dilution, simply by a leveling process, of the force of the Amendment's guarantee with respect to [noncommercial speech]." FN;B16XXa[FN16]

Unlike noncommercial speech, commercial speech can be regulated to prohibit false and deceptive advertising. The Supreme Court has cited two aspects of commercial speech that justify regulation based on the content of the message:

> First, commercial speakers have extensive knowledge of both the market and their products. Thus, they are well situated to evaluate the accuracy of their messages and the lawfulness of the underlying activity. Bates

> v. State Bar of Arizona, 433 U.S. 350, 381 (1977). In addition, commercial speech, the offspring of economic self-interest, is a hardy breed of expression that is not "particularly susceptible to being crushed by overbroad regulation."

***14** Central Hudson Gas & Electric Corp. v. Public Service Comm'n of New York, 447 U.S. at 564 n. 6.

The first basis for affording less protection to commercial speech, the relative costs of avoiding injury from untruthful speech, is discussed more fully in Bates:

> the advertiser seeks to disseminate information about a product or service that he provides, and presumably he can determine more readily than others whether his speech is truthful and protected.

Bates v. State Bar of Arizona, 433 U.S. 350, 381 (1977).

The second basis for affording less protection to commercial speech, its hardiness because it is the offspring of economic self-interest, was discussed in Virginia State Board of Pharmacy v. Virginia Citizens Consumer Council, Inc., 425 U.S. 748, n. 24 at 771–72 (1976):

> Also, commercial speech may be more durable than other kinds. Since advertising is the sine qua non of commercial profits, there is little likelihood of its being chilled by proper regulation and foregone entirely.

Since commercial speech is used to sell goods and services and is "related solely to the economic interests of the speaker and its audience," Central Hudson, supra, at 561, an advertiser expects to be able to capture a large percent of the value of his commercial speech. By contrast, speech dealing with matters of public concern is potentially of value to a much broader audience, i.e., to the public at large. Self-censorship is more likely to occur when speech relates to matters of public concern. To provide the necessary breathing space for vigorous public debate involving matters of public controversy, potentially false statements in communications relating to such matters receive a greater degree of protection under the First Amendment.FN;B17XXa[FN17]

To aid in the process of distinguishing commercial speech from more traditional First Amendment expression, the Supreme Court has provided two definitions of commercial speech. First, there is a " 'common-sense' distinction between speech proposing a commercial transaction, which occurs in an area traditionally subject to government regulation, and other varieties of speech," FN;B18XXa[FN18] or, as restated, the "core notion of commercial speech" is "speech which does 'no more than propose a commercial transaction'." Bolger v. Youngs Drug Products Corp., 463 U.S. 60, 66 (1983). The other definition of commercial speech is "expression related solely to the economic interest of the speaker and its audience." Central Hudson Gas & Electric Corp. v. Public Service Commission, 447 U.S. 557, 561 (1980).

These two definitions of commercial speech may not comprehend all commercial speech, as evidenced by Bolger v. Youngs Drug Products Corp., supra. Bolger involved a challenge to the application of a federal statute that prohibited the mailing of unsolicited advertisements for contraceptives. After the Postal Service had advised Youngs that certain proposed mailings would violate the statute, Youngs sought a ruling that the statute was unconstitutional as applied to the mailings in question. The district court held that the three types of mailings in question were all commercial solicitations but that the statutory prohibition was more extensive than necessary to protect the interests asserted by the Government. FN;B19[FN19] Accordingly, the district court held that the statute was unconstitutional as applied.

***15** The Supreme Court affirmed the district court's ruling, but in the process addressed the question whether the mailings were commercial speech. The Supreme Court concluded that the mailings were commercial speech. Most of the mailings, it held, fell "within the core notion of commercial speech" since they did 'no more than

propose a commercial transaction.' Id. at 66. But the informational pamphlets could not "be characterized merely as proposals to engage in commercial transactions." FN;B20[FN20]

The Court concluded that the pamphlets could not be classified as commercial speech merely because they were "conceded to be advertisements" (id. at 66), merely because of a "reference to a specific product" (id. at 66), or merely because "Youngs has an economic motivation for mailing the pamphlets" (id. at 67). These three facts taken together, in this particular case, were, however, enough to satisfy the Court that the pamphlets were commercial speech: "The combination of all these characteristics, however, provides strong support for the District Court's conclusion that the informational pamphlets are properly characterized as commercial speech." (id. at 67).

The Bolger Court noted that the pamphlets at issue "contain[ed] discussions of important public issues," Id. at 67–68, but held that the informational pamphlets were commercial speech notwithstanding the discussion of important public issues:

> The mailings constitute commercial speech notwithstanding the fact that they contain discussions of important public issues such as venereal disease and family planning. We have made clear that advertising which "links a product to a current public debate" is not thereby entitled to the constitutional protection afforded noncommercial speech. A company has the full panoply of protections available to its direct comments on public issues, so there is no reason for providing similar constitutional protection when such statements are made in the context of commercial transactions. Advertisers should not be permitted to immunize false or misleading product information from government regulation simply by including references to public issues.

Id. at 67–68 (emphasis provided) (quoting Central Hudson Gas & Electric Corp. v. Public Service Commission of New York, 447 U.S. 563, n. 5).

The Bolger Court's distinction between "direct comments on public issues" and "advertising which 'links a product to a current public debate' " is best understood by reference to two Supreme Court decisions cited in Bolger: Consolidated Edison Co. v. Public Service Commission, supra, and Central Hudson Gas & Electric Corp. v. Public Service Commission of New York, supra.

In Consolidated Edison, Con Ed challenged a rule forbidding it from mailing, along with its billing statements, leaflets discussing controversial issues of public policy. The rule had been promulgated in response to a Con Ed leaflet proclaiming the benefits of nuclear power. The Supreme Court held that the rule conflicted with the First Amendment, emphasizing that "[t]he First Amendment's hostility to content-based regulation extends not only to restrictions on particular viewpoints, but also to prohibition of public discussion of an entire topic." Consolidated Edison Co. v. Public Service Commission, 447 U.S. at 537. The Court discussed its Consolidated Edison holding in the companion Central Hudson case, stating: "[w]e rule today in Consolidated Edison Co. v. Public Service Commission ... that utilities enjoy the full panoply of First Amendment protections for their direct comments on public issues." Central Hudson Gas & Electric Corp. v. Public Service Commission of New York, 477 U.S. at 563 n. 5.

***16** In the Central Hudson case, the plaintiff utility company challenged a rule that banned an electric utility from advertising to promote the use of electricity. The rule was enacted in response to the perceived energy shortage. The Supreme Court struck down the rule, holding that the public utility commissions' rule was more extensive than necessary to further the state's interest in energy conservation.

In a concurring opinion, Justice Stevens criticized the regulation as banning all promotional advertising and thus

being overly broad:

> This ban encompasses a great deal more than mere proposals to engage in certain kinds of commercial transactions. It prohibits all advocacy of the immediate or future use of electricity. It curtails expression by an informed and interested group of persons of their point of view on questions relating to the production and consumption of electrical energy—questions frequently discussed and debated by our political leaders.

Id. at 580–81 (Stevens, J., concurring in judgment).

In a footnote, the majority in Central Hudson discussed Justice Stevens' concerns. The majority concluded that the advertising ban "was restricted to all advertising 'clearly intended to promote sales'." Id. at 562 n. 5. Further, while the complaint and the lower court opinions viewed the litigation as involving only commercial speech, the majority addressed the issue whether full First Amendment protection should be afforded to "all promotional advertising that includes claims 'relating to ... questions frequently discussed and debated by our political leaders' ":

> Although this approach responds to the serious issues surrounding our national energy policy as raised in this case, we think it would blur further the line the Court has sought to draw in commercial speech cases. It would grant broad constitutional protection to any advertising that links a product to a current public debate. But many, if not most, products may be tied to public concerns with the environment, energy, economic policy, or individual health and safety. We rule today in Consolidated Edison Co. v. Public Service Comm'n, ante, 530, that utilities enjoy the full panoply of First Amendment protection for their direct comments on public issues. There is no reason for providing similar constitutional protection when such statements are made only in the context of commercial transactions.

Id. at 563 n. 5.

A simple message flows from these cases. In Consolidated Edison the Court held that the First Amendment did not allow the government to foreclose discussion of an entire topic—the benefits of nuclear power. In dealing with broad categories of messages, the Court has gone no further than deciding that those 'clearly intended to promote sales' could be treated as commercial speech. Central Hudson, supra, at 565 n. 5. Moreover, if companies attempt to evade regulation of commercial speech by including gratuitous references to public issues the court will not countenance it. Bolger, supra, at 68. There is no need to allow that sort of subterfuge because companies have full First Amendment rights to make their views known in other ways. Id.

***17** The dividing line is thus clear—if, by a common sense view, the advertisement is clearly intended to promote sales it is commercial speech. If, in addition, there is a public message incorporated, the advertisement can be regulated if inclusion of that public message is simply a gratuitous linkage. If, however, the message is direct comment on a public issue, the full protection of the First Amendment applies. If direct comment on public issues cannot be severed from speech that otherwise might be characterized as commercial speech because it may affect sales, i.e., if the two parts are inextricably intertwined, the full protection of the First Amendment must be afforded to direct comment on public issues. Otherwise, the speaker would be selectively excluded from participating in a public discussion of an entire topic, an outcome precluded by the First Amendment.

I point out, however, that my reading of the controlling Supreme Court precedent is not shared by the Commission majority. The Commission majority (pp. 13–14) reasons as follows:

> Although it may be difficult in some cases, the Commission thinks that it is possible to determine whether a specific advertisement that includes information connected to public issues nonetheless addresses the concerns of a purchaser of the advertiser's product or service. To conclude otherwise would allow sellers of certain products to avoid the proscription against false and misleading advertising merely by linking their

product to a public issue.

Note that the Commission majority uses the words “whether” and “nonetheless.” In the view of the Commission majority, a communication that “addresses the concerns of a purchaser of the advertiser's product or service” can never be fully protected speech, no matter how close the link between the public issue addressed and the potential commercial effect that may arise because the communication deals in part with a characteristic of the speaker's product or service of interest to consumers. Under the Commission majority's analysis, a product manufacturer loses its fully protected right to engage in debate over a matter of public concern whenever the public issue is the manufacturer's product.

On this critical issue, the Commission majority and I part company. On my reading of the controlling Supreme Court precedent, a product manufacturer cannot be selectively excluded from participating in a public discussion of an entire topic. I conclude that product manufacturers, like everyone else, “enjoy the full panoply of First Amendment protection for their direct comments on public issues,” Central Hudson, supra, at 563 n. 5; that they cannot be singled out for “[s]elective exclusions from a public forum ... based on content alone ... [or] justified by reference to content alone,” Police Department of Chicago v. Mosely, supra, at 96; that they cannot be barred from “public discussion of an entire topic,” Consolidated Edison Co. v. Public Service Commission, supra, at 537; and that this full First Amendment protection is not lost unless the consequence would be to allow a product manufacturer “to immunize false or misleading product information from government regulation simply by including references to public issues.” Bolger, supra, at 68 (emphasis supplied).

III. CHARACTERIZATION OF THE RJR COMMUNICATION

***18** RJR's “Of Cigarettes and Science” does not come within either of the two Supreme Court definitions of commercial advertising. It does more—far more—than propose a commercial transaction. It does not relate solely to the economic interest of the speaker and its audience.

Nor would regulation of the RJR piece come within the rationales provided for the commercial speech distinction. The verifiability rationale does not apply because the claims made in “Of Cigarettes and Science” do not address an aspect of cigarettes uniquely within the knowledge of RJR. Since the MR FIT study was not conducted by RJR, others can determine as readily as RJR whether the statements in “Of Cigarettes and Science” are truthful. FN;B21[FN21] Nor does the hardiness rationale apply. Since the subject matter discussed by RJR is a matter of public concern, this type of speech by RJR is particularly susceptible to being crushed by regulation. Noncommercial speech by a firm such as RJR about public issues related to its products may well be chilled by discriminatory governmental regulation or by the threat of expensive investigations or litigation. Indeed, RJR terminated its entire series of editorial-like communications once the FTC began this proceeding.

In addition to not fitting within the definitions or the rationales of commercial speech, the RJR communication does not fit within the three Bolger criteria. Although RJR undoubtedly had an economic motivation in paying for its publication, “Of Cigarettes and Science” is hardly an advertisement in the ordinary sense of that word; FN;B22[FN22] indeed, it refers only to a generic rather than a particular product. FN;B23[FN23]

Even if “Of Cigarettes and Science” affects the sales of cigarettes, there is no question that it is also a direct comment on a matter of public concern.FN;B24[FN24] The question thus arises whether “Of Cigarettes and Science” gratuitously invokes a matter of public concern. The answer is clear. There is no gratuitous link. The effect of cigarettes on health is itself the issue of public concern. RJR cannot possibly make its argument about the correct conclusions to be drawn from MR FIT without at the same time discussing an attribute of cigarette

smoking of concern to purchasers of its product.

If RJR is not permitted to publish a piece such as "Of Cigarettes and Science" without the fear of government censorship, then there is simply no way for RJR to engage effectively in the debate over cigarette smoking and health free from governmental oversight determining the truth or falsity of RJR's arguments.FN;B25[FN25] RJR cannot argue about the lack of conclusiveness of scientific evidence without at the same time potentially influencing consumers' purchase decisions.

Virtually every other person and corporation in America is free to participate in the debate about cigarette smoking and health, without government evaluation whether their claims are true or false. Whether or not RJR's participation in the debate is "unfair or deceptive," its speech challenged by this proceeding is undoubtedly a part of the contest of ideas. Under the First Amendment, RJR cannot be selectively excluded from participating in that debate merely because it produces cigarettes.

***19** Since "Of Cigarettes and Science" is a direct comment on a public issue, RJR cannot, consistent with the First Amendment, be precluded from publishing that comment. Can anyone doubt that a Congressional ban on all cigarette advertising FN;B26[FN26] could not constitutionally be applied to the type of statement at issue in this case? And if Congress cannot ban such a communication, how can the Federal Trade Commission regulate its content?

Consider the ironic result if "Of Cigarettes and Science" were held to be commercial speech. In that event, the RJR communication would be deemed to be a cigarette advertisement. As such, it would have to carry one of the four Surgeon General rotational health warnings. FN;B27[FN27] Thus, an RJR editorial arguing that there is lack of definitive evidence on smoking and heart disease would have to be accompanied by a governmentally mandated warning that "Smoking Causes ... Heart Disease ..."

Quite simply, this case involves attempted federal regulation of the content of a communication that engages in a debate over ideas. RJR is forced to undergo this proceeding in part because it has the temerity to argue, in the words of the Commission's complaint, that "[a] major government study about smoking and coronary heart disease (the MR FIT study) provides credible scientific evidence that smoking is not as hazardous as the public or the reader has been led to believe ..." FN;B28[FN28] RJR is in a distinct minority. It has challenged the official position taken by the Surgeon General and the United States Congress. RJR may be wrong. But on my reading of the Constitution, that determination is to be made by each individual, not by the government.

IV. THE MAJORITY'S BASES FOR NOT DISMISSING THE COMPLAINT

A. Propriety of Postponing a Ruling on Jurisdiction

Although this case in on appeal from an Administrative Law Judge's determination that the Commission lacks subject matter jurisdiction because the communication is fully protected speech, the majority has declined to determine whether the RJR communication is commercial speech or noncommercial speech. Postponing a ruling on the determinative First Amendment question might be understandable (even if wrong) if the majority had determined that further discovery were necessary before the Commission could make such a ruling. The Commission majority has not, however, made any such determination. Absent a holding that the Commission needs more evidence to decide whether the communication is commercial speech, the majority has no justifiable basis for not ruling on that issue.

The apparent explanation for the majority's action (or inaction) is their assertion: "Accepting the allegations of

the complaint concerning jurisdiction as true for purposes of this appeal, the content of the Reynolds advertisement includes words and messages that are characteristic of commercial speech." (p. 15, citation omitted) This explanation, however, provides no basis for not ruling on the commercial speech question. The complaint's allegations referred to by the majority discuss facts that are apparent from the face of the RJR communication itself. Since the RJR communication is itself attached to and incorporated within the complaint, the complaint by itself, under the majority's own reasoning, provides a full basis for ruling on the question of commercial versus noncommercial speech.

***20** Consider the complaint allegations cited by the majority. First, the majority cites the complaint for the proposition that RJR's communication "refers to a specific product, cigarettes" and "discusses an important product attribute—the alleged connection between smoking and heart disease." (p. 15) These facts are apparent from the face of the communication. Second, the majority states: "the Complaint alleges that 'Of Cigarettes and Science' is an advertisement (Complaint ¶ 2), which we understand to mean a notice or announcement that is publicly published or broadcast and is paid-for." (pp. 15–16) The communication evidences on its face that it was publicly published. RJR's name at the bottom of the communication indicates that the communication was paid for by RJR. Finally, the majority states: "the Complaint alleges that Respondent is in the business of selling cigarettes." The communication itself reveals that it was presented by R.J. Reynolds Tobacco Company; the name and the content of the communication indicate that RJR is in the business of selling cigarettes.

On the basis of the complaint allegations cited above, the majority asserts, "the content of the Reynolds advertisement includes words and messages that are characteristic of commercial speech." Having made this determination, the Commission majority must logically conclude that the communication is commercial speech unless (1) there is some step between having the characteristics of commercial speech and being commercial speech or (2) there is a possible characteristic of a communication that will cause it be fully protected even though it also has the characteristics of commercial speech. Since the Commission majority has already excluded the second possibility, FN;B29[FN29] only the first possibility could possibly remain. As to that possibility, I can only ask: what step could there be between having the characteristics of commercial speech and being commercial speech? As I read the complaint and the majority opinion, the Commission majority has, whether it realizes it or not, already concluded that the communication is commercial speech.

B. Propriety of Further Discovery

As a means of possibly garnering additional support for a finding that the Commission has subject matter jurisdiction, the majority has instructed the Administrative Law Judge to permit further discovery. The further discovery suggested by the majority is irrelevant. Accordingly, such discovery itself would be an unjustifiable burden on RJR's exercise of the First Amendment rights.

The Commission majority suggests two lines of discovery. The first line relates to the publication itself (p. 20):

> Evidence that may be relevant to deciding whether the Reynolds advertisement is commercial speech includes facts concerning the publication or dissemination of the advertisement, such as whether it was paid-for, where and in which publications it was disseminated, whether it was placed in editorial space (such as an op-ed page) or advertising space in the publication, whether it was prepared as a letter to the editor, whether it was sent to representatives of the media for selection on merit by editorial boards, and to whom it was disseminated outside the media.

***21** No discovery is necessary or relevant regarding background information of this type. FN;B30[FN30] From the face of the publication, it is self-evident where it was published. The communication was not on an opened

page nor a “letter to the editor.” Since RJR's name appears at the bottom of the communication, the indication is that RJR paid for the publication. Whether the communication “was disseminated outside the media” is irrelevant. If the communication as published is commercial speech, it does not become any less so by virtue of having been disseminated outside the media. If the communication as published is not commercial speech, dissemination outside the media would not provide a basis for Commission action because such dissemination is not alleged in the complaint.

The second line of discovery suggested by the majority relates to RJR's intent in publishing the communication. (p. 20–21):

> Evidence about the promotional nature of the advertisement also may be relevant. Therefore, it might be useful to consider the circumstances surrounding the development of the advertisement, such as whether it was targeted to consumers or legislators; whether it was intended to affect demand for Reynolds' cigarettes or brands or to affect particular legislative or regulatory proposals; whether the advertisement was subjected to copy testing or to review by focus groups and, if so, the nature of the questions used in the copy tests or focus group sessions; and the results of those procedures both in terms of what they showed and what changes, if any, Reynolds made in response to those showings. Evidence relating to the message(s) Reynolds itself intended to convey through the advertisement also may be relevant. In addition, Reynolds' share of the cigarette market may be relevant to deciding whether including a brand name reference is a prerequisite to a determination that the advertisement constitutes commercial speech.

In deciding whether a publication is commercial speech, the Supreme Court has never looked to the subjective intent of the speaker. FN;B31[FN31] Objective standards are essential. Otherwise, there will be a chilling of fully protected speech. If the Commission cannot determine from the face of a publication that it is commercial speech, it has no basis for challenging such a publication. A fishing expedition to determine the subjective intent of particular RJR employees would impose an unjustifiable burden on RJR and chill its right to engage in free speech.

V. CONCLUSION

R.J. Reynolds has full First Amendment rights for its direct comments on public issues. “Of Cigarettes and Science” is patently direct comment on a public issue. In this case, it is precisely the product that is the public issue. Discussion of the health consequences of smoking can hardly be labeled a mere gratuitous linking of a product with a current public debate.FN;B32[FN32] If corporations have full First Amendment rights they must be allowed to participate in the public debate about issues involving their products, at least in an editorial format. Effectively removing a company from a debate by contending that its message about its product is deceptive would infringe on its basic constitutional rights. In such a public debate the decision regarding truth and falsity must be made by the public, not the government. This is particularly true when the government itself has taken a public position and established its own orthodoxy. Having done so, it cannot then prohibit challenges to the governmentally approved version of the truth.

***22** Publication of RJR's communication may or may not have an effect on cigarettes sales and such an effect may or may not have been intended. In my view, that is irrelevant. Extrinsic evidence of RJR's intentions is not needed to decide whether this communication is fully protected. It is, on its face, direct comment on a public issue and not commercial speech. To conclude otherwise would turn a common-sense distinction into an intrusive inquiry into facts about the motives of the speaker. If the editorial is deceptive, or not believable, or runs counter to other information on the health question that the public is aware of, consumers are free to reject the message

in the editorial. But it is critical for First Amendment purposes that the public, and not the government, decide the answer to this question. To conclude otherwise would erode First Amendment protection by extending the commercial speech doctrine into areas traditionally thought to be fully protected. Governmental inquiry into the motives of the speaker to determine if his views are to be constitutionally protected seems to me completely antithetical to the goals the First Amendment as intended to further. I would affirm the Administrative Law Judge and dismiss the complaint.

SURGEON GENERAL'S WARNING: Smoking Causes Lung Cancer, Heart Disease, Emphysema, And May Complicate Pregnancy.

SURGEON GENERAL'S WARNING: Quitting Smoking Now Greatly Reduces Serious Risks to Your Health.

SURGEON GENERAL'S WARNING: Smoking by Pregnant Women May Result in Fetal Injury, Premature Birth, And Low Birth Weight.

SURGEON GENERAL'S WARNING: Cigarette Smoke Contains Carbon Monoxide.

EXHIBIT 1

***23** Of cigarettes and science.

This is the way science is supposed to work.

A scientist observes a certain set of facts. To explain these facts, the scientist comes up with a theory.

Then, to check the validity of the theory, the scientist performs an experiment. If the experiment yields positive results, and is duplicated by other scientists, then the theory is supported. If the experiment produces negative results, the theory is re-examined, modified or discarded.

But, to a scientist, both positive and negative results should be important. Because both produce valuable learn- ing.

Now let's talk about cigarettes.

You probably know about research that links smoking to certain diseases. Coronary heart disease is one of them.

Much of this evidence consists of studies that show a statistical association between smoking and the disease.

But statistics themselves cannot explain why smoking and heart disease are associated. Thus, scientists have developed a theory: that heart disease is caused by smoking. Then they performed various experiments to check this theory.

We would like to tell you about one of the most important of these experiments.

A little-known study

It was called the Multiple Risk Factor Intervention Trial (MRFIT).

In the words of the Wall Street Journal, it was “one of the largest medical experiments ever attempted.” Funded

by the Federal government, it cost $115,000,000 and took 10 years, ending in 1982.

The subjects were over 12,000 men who were thought to have a high risk of heart disease because of three risk factors that are statistically associated with this disease: smoking, high blood pressure and high cholesterol levels.

Half of the men received no special medical intervention. The other half received medical treatment that consistently reduced all three risk factors, compared with the first group.

It was assumed that the group with lower risk factors would, over time, suffer significantly fewer deaths from heart disease than the higher risk factor group.

But that is not the way it turned out.

After 10 years, there was no statistically significant difference between the two groups in the number of heart disease deaths.

The theory persists

We at R.J. Reynolds do not claim this study proves that smoking doesn't cause heart disease. But we do wish to make a point.

Despite the results of MR FIT and other experiments like it, many scientists have not abandoned or modified their original theory, or re-examined its assumptions.

They continue to believe these factors cause heart disease. But it is important to label their belief accurately. It is an opinion. A judgment. But not scientific fact.

We believe in science. That is why we continue to provide funding for independent research into smoking and health.

But we do not believe there should be one set of scientific principles for the whole world, and a different set for experiments involving cigarettes. Science is science. Proof is proof. That is why the controversy over smoking and health remains an open one.

***24** R.J. Reynolds Tobacco Company

EXHIBIT 2–A

Can we have an open debate about smoking?

The issues that surround smoking are so complex, and so emotional, it's hard to debate them objectively.

In fact, many of you probably believe there is nothing to debate.

Over the years, you've heard so many negative reports about smoking and health—and so little to challenge these reports—that you may assume the case against smoking is closed.

But this is far from the truth.

Studies which conclude that smoking causes disease have regularly ignored significant evidence to the contrary. These scientific findings come from research completely independent of the tobacco industry.

We at R.J. Reynolds think you will find such evidence very interesting. Because we think reasonable people who analyze it may come to see this issue not as a closed case, but as an open controversy.

We know some of you may be suspicious of what we'll say, simply because we're a cigarette company.

We know some of you may question our motives.

But we also know that by keeping silent, we've contributed to this climate of doubt and distrust. We may also have created the mistaken impression that we have nothing to say on these issues.

That is why we've decided to speak out now, and why we intend to continue speaking out in the future.

During the coming months we will discuss a number of key questions relating to smoking and health. We will also explore other important issues including relations between smokers and non-smokers, smoking among our youth, and “passive smoking.”

Some of the things we say may surprise you. Even the fact that we say them may prove controversial.

But we won't shy away from the controversy because, quite frankly, that's our whole point.

We don't say there are no questions about smoking. Just the opposite. We say there are lots of questions—but, as yet, no simple answers.

Like any controversy, this one has more than one side. We hope the debate will be an open one.

R.J. Reynolds Tobacco Company

EXHIBIT–2B

What not to do in bed.

You can read.
You can rest.
You can sleep.
You can make phone calls.
You can eat breakfast.
You can watch television.
You can listen to music.
You can exercise.
You can snore.
You can even eat crackers—provided you're alone.
And yes, you can snuggle.
But don't ever light up a cigarette when you're in bed.
Because if you doze off just once, all your dreams can go up in smoke.

R.J. Reynolds Tobacco Company

EXHIBIT 2–C

A message from those who don't to those who do.

We're uncomfortable.

To us, the smoke from your cigarettes can be anything from a minor nuisance to a real annoyance.

We're frustrated.

Even though we've chosen not to smoke, we're exposed to second-hand smoke anyway.

We feel a little powerless.

Because you can invade our privacy without even trying. Often without noticing.

***25** And sometimes when we speak up and let you know how we feel, you react as though we were the bad guys.

We're not fanatics. We're not out to deprive you of something you enjoy. We don't want to be your enemies.

We just wish you'd be more considerate and responsible about how, when, and where you smoke.

We know you've got rights and feelings. We just want you to respect our rights and feelings, as well.

A message from those who do to those who don't.

We're on the spot.

Smoking is something we consider to be a very personal choice, yet it's become a very public issue.

We're confused.

Smoking is something that gives us enjoyment, but it gives you offense.

We feel singled out.

We're doing something perfectly legal, yet we're often segregated, discriminated against, even legislated against.

Total strangers feel free to abuse us verbally in public without warning.

We're not criminals. We don't mean to bother or offend you. And we don't like confrontations with you.

We're just doing something we enjoy, and trying to understand your concerns.

We know you've got rights and feelings. We just want you to respect our rights and feelings, as well.

Brought to you in the interest of common courtesy by

R.J. Reynolds Tobacco Company

EXHIBIT 2–D

Smoking in public:

Let's separate fact

from friction.

There has always been some friction between smokers and non-smokers. But lately this friction has grown more heated.

The controversy has been fueled by questionable reports which claim that “second-hand smoke” is a cause of serious diseases among non-smokers.

But, in fact, there is little evidence—and certainly nothing which proves scientifically—that cigarette smoke causes disease in non-smokers.

Skeptics might call this the wishful thinking of a tobacco company. But consider the scientific judgment of some of the leading authorities in the field—including outspoken critics of smoking.

For example, in 1983 the organizer of an international conference on environmental tobacco smoke (ETS) summarized the evidence on lung cancer as follows: “An overall evaluation based upon available scientific data leads to the conclusion that an increased risk for non-smokers from ETS exposure has not been established.”

Even the chief statistician of the American Cancer Society, Lawrence Garfinkel, has gone on record as saying, “passive smoking may be a political matter, but it is not a main issue in terms of health policy.”

Which brings us back to our original point: cigarette smoke can be very annoying to non-smokers.

But how shall we as a society deal with this problem?

Confrontation? Segregation? Legislation?

No. We think annoyance is neither a governmental problem nor a medical problem. It's a people problem.

Smokers and non-smokers have to talk to one another. Not yell, preach, threaten, badger or bully. Talk.

Smokers can help by being more considerate and responsible. Non-smokers can help by being more tolerant. And both groups can help by showing more respect for each other's rights and feelings.

***26** But eliminating rumor and rhetoric will help most of all.

Because when you stick to the facts, it's a lot easier to deal with the friction.

R.J. Reynolds Tobacco Company

EXHIBIT 2–E

We don't advertise to children.

Who are you kidding?

The newspapers and magazines and billboards are filled with cigarette ads. Kids can't help but see them.

How can you expect us to believe you're not trying to reach and influence our children?

We're not surprised if many people feel this way—especially when years of negative publicity have made them totally cynical about our industry.

Nevertheless, we'd like to set the record straight.

First of all, we don't want young people to smoke. And we're running ads aimed specifically at young people advising them that we think smoking is strictly for adults.

Second, research shows that among all the factors that can influence a young person to start smoking, advertising is insignificant. Kids just don't pay attention to cigarette ads, and that's exactly as it should be.

Finally—and this is sometimes hard for people outside the marketing field to understand—all of our cigarette ads are what we call “brand advertising.” Its purpose is to get smokers of competitive products to switch to one of our brands, and to build the loyalty of those who already smoke one of our brands.

At the present there are some 200 different cigarette brands for sale in the U.S. Many of them have only a very small fraction of the total cigarette market. Getting smokers to switch is virtually the only way a cigarette brand can meaningfully increase its business.

That's why we don't advertise to young people.

Of course, if you'd like to share this ad with your children, that would be just fine with us.

R.J. Reynolds Tobacco Company

EXHIBIT 2–F

Second–Hand Smoke:

The Myth

and The Reality.

Many non-smokers are annoyed by cigarette smoke. This is a reality that's been with us for a long time.

Lately, however, many non-smokers have come to believe that cigarette smoke in the air can actually cause disease.

But, in fact, there is little evidence—and certainly nothing which proves scientifically—that cigarette smoke causes disease in non-smokers.

We know this statement may seem biased. But it is supported by findings and views of independent scientists—including some of the tobacco industry's biggest critics.

Lawrence Garfinkel of the American Cancer Society, for example. Mr. Garfinkel, who is the Society's chief statistician, published a study in 1981 covering over 175,000 people, and reported that “passive smoking” had “very little, if any” effect on lung cancer rates among non-smokers.

You may have seen reports stating that in the course of an evening, a non-smoker could breathe in an amount of smoke equivalent to several cigarettes or more.

But a scientific study by the Harvard School of Public Health, conducted in various public places, found that non-smokers might inhale anywhere from 1/1000th to 1/100th of one filter cigarette per hour. At that rate, it would take you at least 4 days to inhale the equivalent of a single cigarette.

***27** Often our own concerns about our health can take an unproven claim and magnify it out of all proportion; so, what begins as a misconception turns into a frightening myth.

Is “second-hand smoke” one of these myths? We hope the information we've offered will help you sort out some of the realities.

R.J. Reynolds Tobacco Company

EXHIBIT 2–G

Second-hand smoke:

Let's clear the air.

Can cigarette smoke in the air cause disease in non-smokers?

That's an emotional question for smokers and non-smokers alike. So we'll try to set the record straight in the most direct way we know.

There is little evidence—and certainly nothing which proves scientifically—that cigarette smoke causes disease among non-smokers.

You don't have to take our word for it.

U.S. Surgeon General Julius B. Richmond—who was no friend of smoking—said in his 1979 Report: “Healthy non-smokers exposed to cigarette smoke have little or no physiologic response to the smoke, and what response does occur may be due to psychological factors.”

And in the 1982 Report, Surgeon General C. Everett Koop could not conclude that passive smoking is a cause of cancer in non-smokers.

The director of the National Heart, Lung and Blood Institute, Dr. Claude Lenfant, has been one of the tobacco industry's sharpest critics. Yet Dr. Lenfant stated in 1980 (and we believe it remains true today) that “the evidence that passive smoking in a general environment has health effects remains sparse, incomplete and sometimes unconvincing.”

We've decided to speak out on passive smoking because there is so much rumor and rhetoric on this subject today. And we intend to continue, from time to time, to speak out on other topics of concern to you and to us.

Our critics may try to discredit these messages as self-serving. In a sense, they will be right. We will challenge allegations that are unproven and attacks we think are unfounded. If that is self-serving, so be it.

The questions that surround smoking raise many important issues. We believe that you're entitled to hear all sides of these controversies.

R.J. Reynolds Tobacco Company

EXHIBIT 2–H

How to handle

peer pressure.

If some of your friends smoke, and they make you feel like you should smoke, too, that's “peer pressure.”

But even though we're a cigarette company, we think young people shouldn't smoke. Even the decision to smoke or not to smoke should wait until you're an adult.

So we put together these ideas to help you recognize peer pressure—and resist it.

Tactic # 1: Go ahead and take a puff—what's the matter, are you chicken?

Answer: You must think I'm pretty dumb to fall for that one. It takes a lot more guts to do your own thing than to just go along with the crowd.

Tactic # 2: Come on, all the cool kids smoke.

Answer: Maybe the kids who smoke are trying to look cool. But if they really were cool, maybe they wouldn't have to try so hard.

***28** Tactic # 3: Hey, I'm your friend—would I steer you wrong?

Answer: Friends are people who like you for who you are, not for what they want you to be. If you're really my friend, back off.

Tactic # 4: Do you want everybody to think you're a nerd?

Answer: Sure I care what other kids think of me. But if they base their opinions on stuff like smoking, their opinions aren't worth much.

Tactic # 5: I bet you're just scared your parents will find out.

Answer: I wouldn't blame my parents for getting teed off. How can I expect them to treat me like an adult if I sneak around and act like a kid?

It's natural for you to want to be just like your friends.

But if you don't smoke, maybe your friends will want to be just like you.

R.J. Reynolds Tobacco Company

EXHIBIT 2–I

Some surprising advice to young people from R.J. Reynolds Tobacco.

Don't smoke.

For one thing, smoking has always been an adult custom. And even for adults, smoking has become very contro-

versial.

So even though we're a tobacco company, we don't think it's a good idea for young people to smoke.

Now, we know that giving this kind of advice to young people can sometimes backfire.

But if you take up smoking just to prove you're an adult, you're really proving just the opposite.

Because deciding to smoke or not to smoke is something you should do when you don't have anything to prove.

Think it over.

After all, you may not be old enough to smoke. But you're old enough to think.

R.J. Reynolds Tobacco Company

EXHIBIT 2–J

Passive smoking:

An active controversy.

Periodically the public hears about an individual scientific study which claims to show that “environmental tobacco smoke” (ETS) may be harmful to non-smokers. These reports usually receive sensational media coverage.

Yet, three times within two years, groups of distinguished experts have gathered to review not just one study but the whole body of evidence on this subject. In all three cases, the scientists came to similar—and far less sensational—conclusions.

Yet the media have remained almost silent.

In March 1983 there was the “Second Workshop on Environmental Tobacco Smoke” in Geneva, Switzerland. In May 1983 there was the “Workshop on Respiratory Effects of Involuntary Smoke Exposure” in Bethesda, Maryland.

And, most recently, in April 1984, leading experts from around the world gathered in Vienna for a symposium, “Passive Smoking from a Medical Point of View.”

After this symposium was over, the presidents of the two organizing groups issued a press release summarizing their findings.

The summary said, “the connection between [ETS] and lung cancer has not been scientifically established to date.” It also said “there is a high probability that cardiovascular damage due to [ETS] can be ruled out in healthy people.”

And it went on to say, “Should law-makers wish to take legislative measures with regard to [ETS], they will, for the present, not be able to base their efforts on a demonstrated health hazard from [ETS].”

***29** Perhaps the media would say they cannot be blamed for devoting little attention to what some would consider “non-news.” But we at R.J. Reynolds are concerned about the effects such one-sided coverage may be hav-

ing on the public.

For today, many non-smokers who once saw cigarette smoke merely as an annoyance now view it as a threat to their health. Their growing alarm is being translated into heightened social strife and unfair anti-smoker legisla- tion.

We believe these actions are unwarranted by the scientific facts—and that it is rhetoric, more than research, which makes passive smoking an active controversy.

R.J. Reynolds Tobacco Company

EXHIBIT 2–K

Of cigarettes and science.

This is the way science is supposed to work.

A scientist observes a certain set of facts. To explain these facts, the scientist comes up with a theory.

Then, to check the validity of the theory, the scientist performs an experiment. If the experiment yields positive results, and is duplicated by other scientists, then the theory is supported. If the experiment produces negative results, the theory is re-examined, modified or discarded.

But, to a scientist, both positive and negative results should be important. Because both produce valuable learn- ing.

Now let's talk about cigarettes.

You probably know about research that links smoking to certain diseases. Coronary heart disease is one of them.

Much of this evidence consists of studies that show a statistical association between smoking and the disease.

But statistics themselves cannot explain why smoking and heart disease are associated. Thus, scientists have developed a theory: that heart disease is caused by smoking. Then they performed various experiments to check this theory.

We would like to tell you about one of the most important of these experiments.

A little-known study

It was called the Multiple Risk Factor Intervention Trial (MRFIT).

In the words of the Wall Street Journal, it was “one of the largest medical experiments ever attempted.” Funded by the Federal government, it cost $115,000,000 and took 10 years, ending in 1982.

The subjects were over 12,000 men who were thought to have a high risk of heart disease because of three risk factors that are statistically associated with this disease: smoking, high blood pressure and high cholesterol levels.

Half of the men received no special medical intervention. The other half received medical treatment that consist-

ently reduced all three risk factors, compared with the first group.

It was assumed that the group with lower risk factors would, over time, suffer significantly fewer deaths from heart disease than the higher risk factor group.

But that is not the way it turned out.

After 10 years, there was no statistically significant difference between the two groups in the number of heart disease deaths.

The theory persists
We at R.J. Reynolds do not claim this study proves that smoking doesn't cause heart disease. But we do wish to make a point.

***30** Despite the results of MRFIT and other experiments like it, many scientists have not abandoned or modified their original theory, or re-examined its assumptions.

They continue to believe these factors cause heart disease. But it is important to label their belief accurately. It is an opinion. A judgment. But not scientific fact.

We believe in science. That is why we continue to provide funding for independent research into smoking and health.

But we do not believe there should be one set of scientific principles for the whole world, and a different set for experiments involving cigarettes. Science is science. Proof is proof. That is why the controversy over smoking and health remains an open one.

R.J. Reynolds Tobacco Company

EXHIBIT 2–L

Smoking in public:

A radical proposal.

These days the level of social discourse between smokers and non-smokers is approaching that of a tag-team wrestling match.

While some people try to solve this problem through segregation or confrontation, we at R.J. Reynolds have been proposing a more daring solution: greater courtesy.

For these outlandish views we might be called dreamers and cockeyed optimists. But we continue to believe in the power of politeness to change the world.

We can almost imagine how it might begin.

A smoker is about to light a cigarette in public. He pauses in mid-match, suddenly conscious of the non-smoker next to him. Bracing himself for a hostile response, he asks, “Excuse me, do you mind if I smoke?”

The non-smoker is momentarily stunned by this unexpected act of courtesy. She stifles several witty replies that leap to mind; she cannot let his politeness go unchallenged. “I don't mind,” she answers, “as long as you don't let your smoke blow in my face.”

Her flagrant tolerance puts the smoker on the defensive. But he tries to regain the upper hand. “I'll do my best,” he responds. “Let me know if the smoke bothers you.”

A deft comeback. But the non-smoker presses her attack: “I will—and thanks for asking.” Not to be outdone, the smoker brazenly replies, “Thanks for being so understanding.”

An unlikely dialogue? Perhaps. But, who knows? If this sort of thing ever caught on, it might lead to a sudden outbreak of civil decency. Or even escalate into full-scale friendliness.

Common courtesy. It's just crazy enough, it might work.

Brought to you in the interest of common courtesy by

R.J. Reynolds Tobacco Company

EXHIBIT 2–M

The most inflammatory question of our time.

“Hey, would you put out that cigarette?”

Just seven little words. But in today's over-heated climate of opinion, they can make sparks fly.

For with all the rhetoric about “second-hand smoke,” many non-smokers are beginning to feel not just bothered but threatened by cigarettes.

And with all the talk about anti-smoking legislation, many smokers are beginning to feel threatened by non-smokers.

***31** This is not exactly a recipe for social harmony. In fact, it's practically a guarantee of further discord.

Since we have discussed scientific aspects of the “passive smoking” controversy in previous messages, we'd like to focus here on the social questions.

Will more confrontation or more segregation produce less abrasion? Do we solve anything by creating yet another way to divide our society? Shouldn't all of us be wary of inviting government to involve itself further in our private lives?

At R.J. Reynolds, we see an alternative.

We think we should start not by raising barriers, but by lowering our voices. We think smokers and non-smokers can work out their differences together, in a spirit of tolerance and fairness and respect for each other's rights and feelings. We think common courtesy can succeed where coercion is bound to fail.

And maybe, after we have learned peaceful coexistence by talking to each other civilly and sensibly, we can ap-

ply the same approach to our many other problems.

Because, after all, this is hardly the most inflammatory question of our time.

Brought to you in the interest of common courtesy by

R.J. Reynolds Tobacco Company

EXHIBIT 2–N

Does smoking really make you look more grown up?

It's a crazy world.

Most adults we know would love to look younger than they really are. While most young people are busy trying to look more adult.

This is one reason why many young people take up smoking.

Well, we wish they wouldn't.

For one thing, it doesn't work. A fifteen-year-old smoking a cigarette looks like nothing more or less than a fifteen-year-old smoking a cigarette.

Even though we're a tobacco company, we don't think young people should smoke. There is plenty of time later on to think about whether or not smoking is right for you.

Besides, when you think about it, being grown up is highly overrated. You have to go to work, pay taxes, wear normal clothes and raise kids who grow up to be teenagers.

Why be in such a hurry?

R.J. Reynolds Tobacco Company

EXHIBIT 2–O

The second-hand smokescreen.
For decades, public and private organizations have waged a massive campaign to discourage cigarette smoking. For most of that time, the target of this effort has been the smoker.

Recently, however, the emphasis has undergone a major shift. Today there are scientists who claim that cigarette smoke in the air can actually cause disease in non-smokers. We hear a great deal about “second-hand smoke” and “passive smoking.”

But is this new approach wholly motivated by concern for the non-smoker, or is it the same old war on smoking in a new guise?

These doubts are raised when we recall statements like the following, by a spokesperson for the American Lung Association:

Probably the only way we can win a substantial reduction [in smoking] is if we can somehow make it non-

> acceptable socially.... We thought the scare of medical statistics and opinions would produce a major reduction. It really didn't.

***32** Obviously, one way to make smoking “nonacceptable socially” would be to suggest that second-hand smoke could cause disease. So it is not surprising that we are now seeing a flurry of research seeking scientific support for these suggestions.

Many independent experts believe the scientific evidence on passive smoking is questionable. But a zealous group of anti-smokers are using this issue in their campaign against tobacco as if the claims were established scientific fact.

We deplore the actions of those who try to manipulate public opinion through scare tactics. As the late, respected pathologist, Dr. H. Russell Fisher, stated in testimony submitted to a Congressional hearing on passive smoking:

> ... [I]n the absence of any scientific proof of harm from atmospheric tobacco smoke, we are dealing with a social question and not a medical one. In this regard it should be noted that, since fears and phobias can lead to ill health, those who urge policies based on fear and not scientific facts could be making a medical problem out of a social one. This is indeed a strange prospect to see coming from the efforts of members of the medical profession.

We are not ignoring the fact that cigarette smoke can be bothersome to many non-smokers. But we believe this problem is best solved not by governments but by individuals, and not with more rhetoric but more common sense and courtesy.

Of course, if anti-smoking advocates want to work for the abolition of smoking, that is their right. We only wish they would come out from behind their second-hand smokescreen.

R.J. Reynolds Tobacco Company

EXHIBIT 2–P

Some straight talk about smoking for young people.

We're R.J. Reynolds Tobacco, and we're urging you not to smoke.

We're saying this because, throughout the world, smoking has always been an adult custom. And because today, even among adults, smoking is controversial.

Your first reaction might be to ignore this advice. Maybe you feel we're talking to you as if you were a child. And you probably don't think of yourself that way.

But just because you're no longer a child doesn't mean you're already an adult. And if you take up smoking just to prove you're not a kid, you're kidding yourself.

So please don't smoke. You'll have plenty of time as an adult to decide whether smoking is right for you.

That's about as straight as we can put it.

R.J. Reynolds Tobacco Company

EXHIBIT 2–Q

Workplace smoking restrictions:

A trend that never was.

Reports in the news media may have given you the impression that restrictive corporate smoking policies are the wave of the future.

But, when the facts are analyzed, the wave shrinks to just a ripple.

Today, most of corporate America continues to rely on the common sense and common courtesy of employees—not on formal policy—to resolve differences arising out of smoking in the workplace.

This is the key finding of a major new survey of America's leading companies. The survey, commissioned by the Tobacco Institute and completed early in 1985, was conducted by the Human Resources Policy Corporation of Los Angeles among the Fortune 1000 service and industrial companies and Inc. magazine's 100 fastest-growing companies.

***33** Only about one-third of the responding companies said they had any official smoking guidelines in effect. Furthermore, the reasons most frequently given centered around common-sense situations where workers dealt with hazardous substances, sensitive equipment or food. And almost half of these policies had been in effect for over five years.

Two-thirds of the companies reported they prefer to encourage individual workers to settle smoking issues with mutual respect for each other's legitimate rights and feelings.

We at R.J. Reynolds think this is not just common sense, but good business. Because it also gives managers the flexibility they need to make decisions in the best interest of the company as a whole.

That's the way it's worked in the past. And we think it's the best blueprint for the future.

R.J. Reynolds Tobacco Company

EXHIBIT 2–R

Workplace smoking restrictions:

A trend that never was.

Reports in the news media may have given you the impression that restrictive corporate smoking policies are the wave of the future.

But, when the facts are analyzed, the wave shrinks to just a ripple.

Today, most of corporate America continues to rely on the common sense and common courtesy of employees—not on formal policy—to resolve differences arising out of smoking in the workplace.

This is the key finding of a major new survey of America's leading companies. The survey, commissioned by the

Tobacco Institute and completed early in 1985, was conducted by the Human Resources Policy Corporation of Los Angeles among the top 1000 service and industrial companies ranked by Fortune magazine and Inc. magazine's 100 fastest-growing companies.

Only about one-third of the responding companies said they had any official smoking guidelines in effect. Furthermore, the reasons most frequently given centered around common-sense situations where workers dealt with hazardous substances, sensitive equipment or food. And almost half of these policies had been in effect for over five years.

Two-thirds of the companies reported they prefer to encourage individual workers to settle smoking issues with mutual respect for each other's legitimate rights and feelings.

We at R.J. Reynolds think this is not just common sense, but good business. Because it also gives managers the flexibility they need to make decisions in the best interest of the company as a whole.

That's the way it's worked in the past. And we think it's the best blueprint for the future.

R.J. Reynolds Tobacco Company

FTC

1988 WL 490114 (F.T.C.)

END OF DOCUMENT

Not Reported in F.Supp.2d, 2005 WL 6054963 (S.D.Cal.)
(Cite as: 2005 WL 6054963 (S.D.Cal.))

Only the Westlaw citation is currently available.

United States District Court,
S.D. California.
Joel D. WALLACH, D.V.M., N.D., an individual, and American Longevity, Inc., a California Corporation, Plaintiffs,
v.
Lester M. CRAWFORD, D.V.M., in his official capacity as Acting Commissioner of the United States Food and Drug Administration; the Food and Drug Administration; Tommy G. Thompson, in his official capacity as Secretary of the Department of Health and Human Services; the Department of Health and Human Services; and the United States of America, Defendants.

No. 04CV216 BTM (WMC).
March 29, 2005.

Jonathan W. Emord, Andrea G. Ferrenz, Kathryn E. Balmford, Emord and Associates, Reston, VA, Steven W. Haskins, Haskins and Associates, Bonita, CA, for Plaintiffs.

U.S. Attorney CV, U.S. Attorneys Office Southern, San Diego, CA, for Defendants.

ORDER DENYING PLAINTIFFS' MOTION FOR SUMMARY JUDGMENT; GRANTING IN PART AND DENYING IN PART DEFENDANTS' MOTION TO DISMISS AND DEFENDANTS' MOTION FOR SUMMARY JUDGMENT

BARRY TED MOSKOWITZ, District Judge.

***1** On February 3, 2004, Plaintiff Dr. Wallach and American Longevity, Inc. (collectively "Plaintiffs") filed a complaint against the Food and Drug Administration ("FDA"), Commissioner Lester Crawford, the Department of Health and Human Services, Secretary Tommy Thompson and the United States (collectively "Defendants"). On April 23, 2004, Plaintiffs amended their Complaint alleging two primary causes of action: (1) that 21 U.S.C. § 343-2(a)(2-5) on its face violates the First Amendment to the United States Constitution; and (2) that the FDA's enforcement policy, which construes all scientific literature distributed by a supplement manufacturer as evidence of the manufacturer's intent to sell an unapproved new drug *even if* the distribution squarely falls under the § 343-2(a) labeling exemption, also violates the First Amendment.

On May, 13, 2004, Plaintiffs filed a motion for summary judgment moving the Court to find that 21 U.S.C. § 343-2(a)(2-5) and the FDA's enforcement policy regarding scientific literature violate the First Amendment as a matter of law. On August 9, 2004, Defendants conjunctively opposed Plaintiffs' summary judgement motion and filed a motion to dismiss and an alternative cross-motion for summary judgment. Defendants contend that Plaintiffs lack standing to sue and that in any case, both § 343-2(a) and the FDA's enforcement policy do not violate the First Amendment as a matter of law.

I. *FACTUAL BACKGROUND*

Plaintiffs American Longevity and its president, Dr. Wallach, distribute dietary supplements and food products to a network of United States distributors who, in turn, sell Plaintiffs' products to customers. Plaintiffs sell more than 50 different dietary supplements and food products including 14 different supplements containing magnesium.

Plaintiffs seek to send a "Magnesium Package" to their distributors which includes the following materials: (1) a cover letter inviting the distributors to purchase Plaintiffs' magnesium dietary supplements; (2) a reprint of the Physicians Desk Reference describing magnesium's effect on health and disease, as well as magnesium's use for treating certain medical conditions; (3) a listing of Plaintiffs' supplements containing magnesium, prices, and ordering information; and (4) stickers which are af-

fixed to every page of the package bearing the American Longevity name and logo and the statement "To Order Call American Longevity 1-800-982-3197." (*See* Pls.' First. Am. Compl., Ex. 1.)

The Physicians Desk Reference ("PDR") chapter on magnesium is a peer-reviewed, scientific reference text published by Medical Economics Company, Inc. The chapter contains basic nutrient information about magnesium and also includes information on how magnesium is currently used to treat to certain diseases. (*See* Pls.' Statement of Material Facts, Ex. 5.)

Plaintiffs have refrained from distributing the Magnesium Package to its distributors and sales force fearing that the Package fails to qualify for a 21 U.S.C. § 343-2(a) labeling exemption and will therefore invoke an adverse FDA enforcement action against American Longevity. Plaintiffs also fear that the FDA will invoke its intended use enforcement policy regardless of whether their distribution of the Magnesium Package meets the criteria of 21 U.S.C. § 343-2(a) and construe Plaintiffs' magnesium supplements as unapproved new drugs. To date, the FDA has taken no affirmative enforcement action against Plaintiffs.[FN1] Plaintiffs move this Court to declare 21 U.S.C. § 343-2(a)(2-5) and the FDA's enforcement policy unconstitutional, and to enjoin the FDA from restricting Plaintiffs' planned distribution of the Magnesium Package.

> FN1. Plaintiff states that they sent the FDA a letter regarding the legality of their planned Magnesium package distribution, but received no reply. (*See* Pls.' Surreply at 1.)

II. *STATUTORY BACKGROUND*

***2** The Food and Drug Administration is established within the Department of Health and Human Services. 21 U.S.C. § 393(a). The FDA's statutory mission, in part, is to promote and protect the public health by promptly reviewing clinical research and ensuring that foods and drugs are safe and properly labeled, and there is reasonable assurance of the safety and effectiveness of devices intended for human use. 21 U.S.C. § 393(b).

The Food, Drug and Cosmetics Act ("FDCA") regulates and defines dietary supplements, drugs, and their labeling. *See generally* 21 U.S.C. § 301-97. In 1990, Congress passed the Nutrition Labeling and Education Act ("NLEA") which amended the FDCA to specifically authorize certain types of claims in dietary supplement labeling without triggering formal drug regulations. *See* 21 U.S.C. §§ 343(r)(1)(B), (r)(5)(D); 21 C.F.R. §§ 101.14, 101.70. In 1994, Congress enacted the Dietary Supplement Heath and Education Act ("DSHEA"), PUB.L. NO. 103-417, 108 Stat. 4325, which established a new regulatory category for "dietary supplements" defining them as a product (other than tobacco) intended to supplement the diet that contains vitamins, minerals, herbs or other botanical, amino acid, or dietary substances for use by humans to supplement their diet. 21 U.S.C. § 321(ff)(1).

In drafting the DSHEA, Congress for the first time defined a "dietary supplement" so as to differentiate it from a "drug." S.Rep. No. 103-410 at 34-35. Moreover, the DSHEA established "dietary supplements as a separate category of product under the Federal Food, Drug and Cosmetic Act." *Id.* at 35. Congress understood that "if a product meets the new definition of a dietary supplement, it is not a drug under ... the Act (unless its labeling makes disease claims prohibited by the Act)." *Id.* (parenthetical in original). The Senate Report noted that "under current law [pre-DSHEA and § 343-2(a)], any literature used in connection with the sale or distribution of a product becomes 'labeling' for that product, meaning that any claims contained in that literature are considered as if they were printed on the label of the product." S.Rep. No. 103-410 at 36.

Congress amended the law to exclude truthful scientific literature from the definition of labeling such that "any claims found in scientific reports, for

example, would not be attributed to the person who sold or distributed a supplement described in that report." *id.* Specifically, the DSHEA amended the FDCA to include 21 U.S.C. § 343-2(a) which creates a dietary supplement labeling exception for certain qualified publications. The DSHEA also added § 343(r)(6) to the FDCA which lists requirements and allowable statements for disease/health related claims in labeling that fall under § 343(r)(1)(B).

III. *DISCUSSION*

Plaintiffs essentially argue that both 21 U.S.C. § 343-2(a)(2-5) and the FDA's enforcement policy regarding distribution of scientific literature violate the First Amendment. Defendants contend that Plaintiffs lack standing and that neither 21 U.S.C. § 343-2(a)(2-5) nor the FDA's enforcement policy violate the First Amendment.

A. *STANDING*

***3** Article III of the United States Constitution requires that a party have standing to bring an action in federal court. *Luian v. Defenders of Wildlife,* 504 U.S. 555, 560, 112 S.Ct. 2130, 119 L.Ed.2d 351 (1992) ("[T]he core component of standing is an essential and unchanging part of the case-or-controversy requirement of Article III."). The doctrine of standing contains three elements: (1) plaintiff must have suffered an injury in fact; (2) the injury must be fairly traceable to the challenged action of the defendant; and (3) it must be likely that the injury will be redressed by a favorable court decision. *Id.* at 560-61 (citations omitted). The party invoking federal jurisdiction bears the burden of establishing these elements. *Id.* at 561 (citations omitted). "Since they are not mere pleading requirements but rather an indispensable part of the plaintiff's case, each element must be supported in the same way as any other matter on which the plaintiff bears the burden of proof ...." *Lujan,* 504 U.S. at 561.

1. *PLAINTIFFS' FIRST CAUSE OF ACTION*

Plaintiffs first claim that 21 U.S.C. § 343-2(a)(2-5) violates the First Amendment as an undue burden on speech. Defendants contend that Plaintiffs lack standing to challenge 21 U.S.C. § 343-2(a)(2-5) as unconstitutional because § 343-2(a) on its face is not a prohibitive statute. Defendants point to the fact that failing to meet the criteria of § 343-2(a) does not create any violation under the FDCA or authorize the FDA to prohibit or sanction any speech. Moreover, Defendants contend that § 343-2(a) is merely a "safe harbor" provision that exempts certain scientific literature from the FDCA "labeling" definition, and therefore, § 343-2(a) in and of itself cannot serve as an injury in fact that is fairly traceable to Defendants. Plaintiffs maintain that they have standing to raise a First Amendment pre-enforcement challenge of § 343-2(a)(2-5) because these subsection requirements have a clear speech suppressive impact when read in context with the FDCA enforcement scheme as a whole. The Court agrees.

On its face, § 343-2(a) does not prohibit or sanction any speech or conduct. Nor does it create an express violation for non-qualifying scientific literature. 21 U.S.C. § 343-2(a) reads:

> A publication, including an article, a chapter in a book, or an official abstract of a peer-reviewed scientific publication that appears in an article and was prepared by the author or the editors of the publication, which is reprinted in its entirety, shall not be defined as labeling when used in connection with the sale of a dietary supplement to consumers when it-
>
> (1) is not false or misleading;
>
> (2) does not promote a particular manufacturer or brand of a dietary supplement;
>
> (3) is displayed or presented, or is displayed or presented with other such items on the same subject matter, so as to present a balanced view of the available scientific information on a dietary supplement;
>
> ***4** (4) if displayed in an establishment, is physic-

ally separate from the dietary supplements; and

(5) does not have appended to it any information by sticker or any other method.

21 U.S.C. § 343-2(a)(1)-(5).

Clearly, this section exempts qualified publications from being construed as labeling. *Id.* However, § 343-2(a) is not immune from constitutional attack merely because the statute, read in vacuum, does not create an express violation for failure to meet its criteria or independently authorize the FDA to restrict speech. To fully understand § 343-2(a)'s speech implications, the Court must necessarily look to its interplay with the other FDA statutes and regulations regarding labeling. As Plaintiffs point out, § 343-2(a) should be read together with the FDA's definitions of labeling, drugs, and the prohibition against the sale of unapproved and/or misbranded drugs. In this light, Section 343-2(a) clearly has speech restrictive implications when viewed in conjunction with the overall FDA enforcement scheme. Simply put, if Plaintiffs' promotional Magnesium Package fails to qualify for a § 343-2(a) labeling exemption, it will be construed as labeling thereby exposing Plaintiffs to heightened regulations and a clear threat of enforcement. Indeed, the Magnesium Package, construed as labeling, could transform Plaintiffs' magnesium supplements themselves into unapproved new drugs in terms of FDA enforcement. This constitutes a patent chilling effect on Plaintiffs' speech which effects their day to day operations.[FN2]

FN2. *Cf., e.g., National Park Hospitality Ass'n v. Department of Interior,* 538 U.S. 803, 810, 123 S.Ct. 2026, 155 L.Ed.2d 1017 (2003) ("conclud[ing that] the case was not ripe for judicial review because the impact of the regulation could not 'be said to be felt immediately by those subject to it in conducting their day-to-day affairs' ") (quoting *Toilet Goods Ass'n. Inc. v. Gardner,* 387 U.S. 158, 164, 87 S.Ct. 1520, 18 L.Ed.2d 697 (1967)); *Municipality of Anchorage v. United States,* 980 F.2d 1320, 1326 (9th Cir.1992) ("[P]laintiffs have failed to show that they will suffer any immediate, direct, or significant hardship ... [where the policy] imposes no present, affirmative duties on plaintiffs, requires no immediate changes in plaintiffs' conduct, and does not impact, in any way, plaintiffs' day-to-day affairs.").

"Labeling" is defined as "all labels and other written, printed, or graphic matter (1) upon any article or any of its containers or wrappers, or (2) accompanying such article." 21 U.S.C. § 321(m). The Supreme Court, in *Kordel v. United States,* expanded the definition of labeling by holding that "the phrase 'accompanying such article' is not restricted to labels that are on or in the article o[r] package that is transported." 335 U.S. 345, 349, 69 S.Ct. 106, 93 L.Ed. 52 (1948). The Court in *Kordel* held that promotional pamphlets and circulars distributed by the drug manufacturerto its vendors, though *separate* from the drug product, nevertheless constituted "labeling" thereby rendering the product misbranded.[FN3] *Id.* at 346-49.

FN3. *Kordel* reasoned that the "products and the literature were interdependent" because "the drugs and the literature had a common origin and a common destination ... [t]he literature was used in the sale of the drugs ... it explained their uses ... [n]owhere else was the purchaser advised how to use them [and] ... it constituted an essential supplement to the label attached to the package." *Kordel.* 335 U.S. at 348.

A "drug" is defined as:

(A) articles recognized in the official United States Pharmacopoeia, official Homoeopathic Pharmacopoeia of the United States, or official National Formulary, or any supplement to any of them; and (B) articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or other animals; and (C) art-

> icles (other than food) intended to affect the structure or any function of the body of man or other animals; and (D) articles intended for use as a component of any article specified in clause (A), (B), or (C).

21 U.S.C. § 321(g)(1). Section 321(g)(1) goes on to specifically provide that a dietary supplement's label containing a claim that links a nutrient to a disease or health related condition will not render the supplement a "drug" if the claim otherwise complies with 21 U.S.C. § 343(r). *See id.* Importantly, 21 U.S.C. § 343(r)(5)(D) provides that a dietary supplement with such a disease/health claim in its labeling is not subject to § 343(r) (1)(B)'s pre-publication FDA approval process.[FN4]

> FN4. *See also* 21 U.S.C. § 343(r)(6) (delineating the FDA pre-approval requirements to make such a claim under § 343(r)(1) (B)); 21 C.F.R. 101.14(a)(1) (defining a "health claim" made in the labeling of a dietary supplement).

***5** However, under § 343(r)(5)(D), the dietary supplement with a disease/health claim in its labeling remains "subject to a procedure and standard, respecting the validity of such claim, established by regulation of the Secretary." 21 U.S.C. § 343(r) (5)(D).[FN5] Here, the FDA still requires a pre-authorization process. *See* 21 C.F.R. §§ 101.14, 101.70. Moreover, a disease/health claim in a dietary supplement's labeling will not render the underlying supplement a drug only if the FDA, after reviewing appropriate scientific evidence, promulgates a specific regulation authorizing such a claim. 21 C.F.R. § 101.14(c).[FN6]

> FN5. *See also* 21 U.S.C. § 321(d) ("The term 'Secretary' means the Secretary of Health and Human Services.").

> FN6. Specifically, 21 C.F.R. § 101.14(c) provides that the FDA "will promulgate regulations authorizing a health claim *only when* it determines, based on the totality of publicly available scientific evidence ... that there is significant scientific agreement, among experts qualified by scientific training and experience to evaluate such claims, that the claim is supported by such evidence." *Id.* (emphasis added). *See also id.* § 101.14(a), (d).
>
> Oddly, § 101.14(c) is identical to the § 343(r)(3)(B)(i) pre-authorization requirement that § 343(r)(5)(D) expressly exempts dietary supplements from in the first place. *Compare* 21 U.S.C. § 343(r)(3)(B)(i) *with id.* § (5)(D) *and* 21 C.F.R. § 101.14(c). Thus, it appears that the FDA has avoided § 343(r)(5) (D) s express exemption for dietary supplements (from § 343(r)(3)'s pre-approval regulation) by placing the same subparagraph (3) pre-approval regulation as a backdoor requirement pursuant to § 343(r)(5)(D). In any case, the point remains the same-heightened regulation exists if a dietary supplement publication is deemed labeling.

Thus, if Plaintiffs' Magnesium Package publication is considered labeling, the health/disease claims in the PDR section will subject Plaintiffs to pre-approval regulations and restrictions established by the FDA. *See* 21 U.S.C. § 343(r)(5)(D); 21 C.F.R. §§ 101.14, 101.70. Indeed, Defendants themselves state that the FDA imposes these requirements on dietary supplement labeling via "the pre-authorization requirement for health claims and the postmarket notification requirement for structure/function and classic nutrient deficiency disease claims." (Def.'s Reply at 5; *see also* Def. Mem. in Support of Motions at 6-7.) Defendants further agree that these two restrictions require prior submission to the FDA. (*Id.*)

The FDCA itself also provides that a dietary supplement will be deemed misbranded if its *labeling* fails to contain certain minimum requirements. *See* 21 U.S.C. § 321(s)(2)(A)(E). Thus, if

the Magnesium Package is considered labeling, Plaintiffs will then be subject to heightened regulations and restrictions established under 21 U.S.C. § 321(s) to ensure that the magnesium supplements are not misbranded or sold as an unapproved new drug.

Under the FDCA, a dietary supplement's labeling can readily transform the supplement into a "drug" pursuant to the "intended use" drug definition. *See* 21 U.S.C. 321(g)(1) (defining a drug, in part, as "articles *intended for use* in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or other animals ... and articles (other than food) *intended* to affect the structure or any function of the body of man or other animals") (emphasis added). If a manufacturer's publication is considered labeling, then the claims in the publication/label may be construed as evidence of the manufacturer's "intended use" of its supplement as an unapproved new drug. *See id. Accord Kordel,* 335 U.S. at 350; *National Nutritional Foods Ass'n v. Mathews,* 557 F.2d 325, 334 (2nd Cir.1977); *U.S. v. Article Consisting of 36 Boxes, More or Less, Labeled "Line Away Temporary Wrinkle Smoother, Coty",* 415 F.2d 369, 371 (3d Cir.1969); 21 U.S.C. § 321(g)(1). Moreover, any promotional publication that fails to qualify for a § 343-2(a) labeling exemption, will expose the manufacturer to heightened regulation over the claims in the publication/label as well as the underlying supplement the manufacturer distributes, which could then be defined as a drug. Thus, if the Magnesium Package is construed as labeling because it fails to qualify for a § 343-2(a) exemption, then the claims within the PDR chapter could transform Plaintiffs' magnesium supplements into unapproved new drugs. *See* 21 U.S.C. § 321(g)(1). At oral argument, Defendants admitted that FDA enforcement would no doubt follow such a scenario.

***6** As such, failing to meet the criteria of § 343-2(a)-which exempts qualified publications from the definition of labeling-serves to restrict Plaintiffs' speech by imposing heightened regulation via coexisting statues within the interdependent enforcement scheme. Plaintiffs submit that their planned distribution of the Magnesium Package does not comply with § 343-2(a) and therefore is ineligible for a labeling exemption. Thus, Plaintiffs' planned distribution of the Magnesium Package will be construed as labeling under *Kordel* and therefore subject Plaintiffs to heightened FDA regulation and a imminent threat of enforcement action. *See Abbott Laboratories v. Gardner,* 387 U.S. 136, 152-56, 87 S.Ct. 1507, 18 L.Ed.2d 681 (1967) (holding that a pre-enforcement challenge to drug labeling regulations was ripe for review where the impact of the regulations upon the petitioners was sufficiently direct and immediate). Indeed, distributing the promotional publication as labeling would inevitably be evidence of Plaintiffs' intended use of their product as a drug, which could potentially render their underlying magnesium supplements "drugs" under 21 U.S.C. § 321(g) (1). The chilling effect on Plaintiffs' speech here is obvious.

Taken together, the role that § 343-2(a) plays within the overall FDA enforcement scheme constitutes a "concrete and particularized" injury in fact that is "not conjectural or hypothetical." *Lujan,* 504 U.S. at 560. Furthermore, Plaintiffs face a direct threat of enforcement that affects their day to day business as well as their vendor and customer relationships. *See Abbott Labs.,* 387 U.S. at 152-53. This injury is fairly traceable to Defendants. *See Luian,* 504 U.S. at 560. Indeed, the Court could remedy Plaintiffs' alleged injury by striking certain provisions of § 343-2(a) thereby permitting Plaintiffs' Magnesium Package to qualify for the labeling exemption. *See Gonzales v. Gorsuch,* 688 F.2d 1263, 1267 (9th Cir.1982) ("It is a prerequisite of justiciability that judicial relief will prevent or redress the claimed injury, or that there is a significant likelihood of such redress."). Accordingly, the Court finds that Plaintiffs have standing to challenge § 343-2(a)(2-5) as violating the First Amendment.

2. *PLAINTIFFS' SECOND CAUSE OF ACTION*

Plaintiffs next claim that the FDA's enforcement policy of using promotional scientific literature exempted from labeling under § 343-2(a) as evidence of a manufacturer's intent to distribute an unapproved new *drug* rather than just a dietary supplement violates the First Amendment. Plaintiffs contend that if a manufacturer's publication qualifies for a § 343-2(a) labeling exemption, the FDA can no longer construe it as evidence of the manufacturer's intended use to market an unapproved new drug instead of a dietary supplement under 21 U.S.C. 321(g)(1).

Plaintiffs, however, concede that their Magnesium Package does not satisfy § 343-2(a)'s criteria and therefore does not qualify for a labeling exemption. (*See* Pls.' Mot. for Summ. J. at 6; Pls.' Statement of Material Facts at 4.) Furthermore, Plaintiffs do not contest the FDA's intended use enforcement policy regarding manufacturer publications that do *not* qualify for a § 343-2(a) labeling exception.[FN7]

> FN7. lndeed, in arguing that Plaintiffs have standing to challenge § 343-2(a), Plaintiffs contend that the FDA may properly look to third party literature distributed by the manufacturer, which fails to qualify for a labeling exemption, as evidence of that manufacturer's intended use for its product. *Cf. United States v. Lane Labs-USA, Inc.*, 328 F.Supp.2d 547, 568-69 (D.N.J.2004) (holding that promotional third party literature distributed by the defendant manufacturer did not qualify for a § 343-2(a) labeling exemption and thus construing the publications as the manufacturer's intended use for its product).

***7** The Magnesium Package, as presented to this Court, patently fails to meet § 343-2(a)(2), (3), and (5).[FN8] Plaintiffs admit that their planned distribution of the Magnesium Package does not qualify for a § 343-2(a) labeling exception and have thus refrained from sending it out. While Plaintiffs submit that they will include a disclaimer on the Package if necessary, Plaintiffs do not contend that they will or can change the Package itself to comply with § 343-2(a)(2-5). Thus, the FDA's enforcement policy of construing publications that meet § 343-2(a) as evidence of intended use, cannot be invoked against Plaintiffs because their Package does not and cannot meet § 343-2(a) as it currently stands. *See Citizens for Honesty and Integrity in Regional Planning v. County of San Diego*, 399 F.3d 1067, 2005 WL 433598, *1 (9th Cir. Feb 25, 2005) (finding no basis for federal jurisdiction, in part, where "there [was] no threat of prosecution, imminent or otherwise, or evidence that the County intend[ed] to employ the local definition against [the plaintiffs]"); *Black Faculty Ass'n of Mesa College v. San Diego Community College Dist.*, 664 F.2d 1153, 1155 (9th Cir.1981) (the plaintiff must "show a direct, individualized injury") (citation omitted). Moreover, the FDA's contested enforcement policy at issue here does not even apply to Plaintiffs' Magnesium Package in this case. *See Warth v. Seldin*, 422 U.S. 490, 501, 95 S.Ct. 2197, 45 L.Ed.2d 343 (1975) (Article III requires that "the plaintiff ... must allege a distinct and palpable injury to himself"). At best, Plaintiffs' allegations here are generalized, conjectural and hypothetical. *Lujan*, 504 U.S. at 560. This does not amount to a concrete injury in fact sufficient to confer Article III standing. *See id. See also City of Los Angeles v. Lyons*, 461 U.S. 95, 101, 103 S.Ct. 1660, 75 L.Ed.2d 675 (1983) ("Plaintiffs must demonstrate a 'personal stake in the outcome' in order to 'assure that concrete adverseness which sharpens the presentation of issues' necessary for the proper resolution of constitutional questions.") (quoting *Baker v. Carr*, 369 U.S. 186, 204, 82 S.Ct. 691, 7 L.Ed.2d 663 (1962)); *Whitmore v. Arkansas*, 495 U.S. 149, 155-156, 110 S.Ct. 1717, 109 L.Ed.2d 135 (1990) (the injury in fact "must be concrete in both a qualitative and temporal sense"). As such, Plaintiffs lack standing to bring their second claim and the Court dismisses it on that ground.[FN9]

> FN8. Plaintiffs submit that the Magnesium Package also fails to meet § 343-2(a)(4)

Because the Package has not been distributed, the Court cannot determine its compliance with § 343-2(a)(4) at this time. As to § 343-2(a)(1), Plaintiffs do not contest its validity and contend that the Magnesium Package meets this requirement.

FN9. *See Whitmore* 495 U.S. at 155-156 ("A federal court is powerless to create its own jurisdiction by embellishing otherwise deficient allegations of standing."). If the Court were to alter § 343-2(a) by striking sub-sections (2) through (5) as unconstitutional (as Plaintiff requests), then, and only then, would Plaintiffs' Magnesium Package potentially comply with § 343-2(a) (as severed) thereby triggering the FDA's "intended use" enforcement policy as to them. However, this protracted scenario, dependent on future action by this Court, does not constitute a concrete injury in fact. *See Lyons,* 461 U.S. at 102 ("Abstract injury is not enough. The plaintiff must show that he has sustained or is immediately in danger of sustaining some direct injury as the result of the challenged official conduct ...."') (internal quotation marks omitted).

B. *WHETHER 21 U.S.C. § 343-2(A)(2-5) VIOLATES THE FIRST AMENDMENT*

Plaintiffs contend that 21 U.S.C. § 343-2(a) (2-5) violates the First Amendment as an undue burden on speech. Specifically, Plaintiffs purport to argue that subsections (2) through (5) do not comply with the legislative intent behind § 343-2(a). Further, they argue that those subsections fail the " *Central Hudson* " test because they are irrational requirements that do not directly advance the government's substantial interest in protecting the public health and ensuring the accuracy of information in the marketplace. *See Central Hudson Gas and Elec. Corp., v. Pub. Serv. Comm'n,* 447 U.S. 557, 100 S.Ct. 2343, 65 L.Ed.2d 341 (1980). Thus, Plaintiffs argue that because the subsection provisions (2) through (5) are severable, they should therefore be stricken leaving only § 343-2(a)(1).[FN10]

FN10. Basically, Plaintiffs would have § 343-2(a) read as follows:

> A publication, including an article, a chapter in a book, or an official abstract of a peer-reviewed scientific publication that appears in an article and was prepared by the author or the editors of the publication, which is reprinted in its entirety, shall not be defined as labeling when used in connection with the sale of a dietary supplement to consumers when it-
>
> (1) is not false or misleading.

(*See* Pl.'s Mot. for Summ. J. at 23.) *Cf.* 21 U.S.C. § 343-2(a)(1)-(5).

***8** The Court does not find § 343-2(a) unconstitutional on its face. Moreover, the Court concludes that subsections (2) through (5) clearly effectuate the legislative intent and constitute rational requirements that directly advance the government's interest under the established *Central Hudson* test.

1. *THE CENTRAL HUDSON TEST: REGULATING COMMERCIAL SPEECH*

Scientific literature distributed by a manufacturer in connection with the sale of dietary supplements is commercial speech. *Cf. Bolger v. Youngs Drug Prods. Corp.,* 463 U.S. 60, 67-68, 103 S.Ct. 2875, 77 L.Ed.2d 469 (1983); *Pearson v. Shalala,* 164 F.3d 650, 655 (D.C.Cir.1999). "Although commercial speech is protected by the First Amendment, not all regulation of such speech is unconstitutional." *Thompson v. Western States Medical Center,* 535 U.S. 357, 367, 122 S.Ct. 1497, 152 L.Ed.2d 563 (2002) (citing *Virginia Bd. of Pharmacy v. Virginia Citizens Consumer Council, Inc.,* 425 U.S. 748, 770, 96 S.Ct. 1817, 48 L.Ed.2d 346 (1976)). *See also Central Hudson,* 447 U.S. at 561 ("The First Amendment ... protects commercial

speech from unwarranted governmental regulation.") (citation omitted). The Supreme Court in *Central Hudson* established a four prong test to determine whether a particular commercial speech regulation is constitutionally permissible. 447 U.S. at 562-563. *See also Thompson,* 535 U.S. at 367. The first prong involves a threshold inquiry into whether the communication is misleading or related to an unlawful activity. *Central Hudson,* 447 U.S. at 563-64. If so, the government may ban the speech without "constitutional objection." *id.* at 563. If the commercial speech is neither misleading nor related to an unlawful activity, then the "government's power is more circumscribed." *Id.* at 564. In this event, the government may only restrict the speech if: (1) the government interest is substantial; (2) the regulation directly advances the government interest involved; and (3) the regulation is no more extensive than necessary to serve the interest. *Id.* The government, as "[t]he party seeking to uphold a restriction on commercial speech carries the burden of justifying it." *Bolger,* 463 U.S. at 71, n. 20. *See also Edenfield v. Fane,* 507 U.S. 761, 770, 113 S.Ct. 1792, 123 L.Ed.2d 543 (1993).

a. *THRESHOLD INQUIRY: MISLEADING OR RELATED TO UNLAWFUL ACTIVITY*

Plaintiffs claim that the Magnesium Package pertains to the lawful activity of selling their magnesium supplements. Plaintiffs contend that the Magnesium Package consists primarily of the PDR chapter on magnesium and therefore is commercial speech of a very high order.[FN11] Defendants, on the other hand, argue that the Magnesium Package is misleading because the PDR chapter contains drug related claims. Furthermore, Defendants argue thatthe drug use claims turn Plaintiffs' planned distribution of the Package into an effort to market unapproved new drugs rather than magnesium supplements. As such, Defendants submit that the Magnesium Package relates to unlawful activity and warrants no constitutional protection.

FN11. The First Amendment protects scientific speech and expression. *See Miller v. California,* 413 U.S. 15, 34, 93 S.Ct. 2607, 37 L.Ed.2d 419 (1973); *Kevishian v. Board of Regents,* 385 U.S. 589, 603, 87 S.Ct. 675, 17 L.Ed.2d 629 (1967); *Board of Trustees of Leland Stanford Jr. Univ. v. Sullivan,* 773 F.Supp. 472 (D.D.C.1991).

***9** The government may ban *inherently* misleading speech outright. *See In re R.M. J.,* 455 U.S. 191, 203, 102 S.Ct. 929, 71 L.Ed.2d 64 (1982). However, the government "may not place an absolute prohibition on certain types of *potentially* misleading information ... if the information also may be presented in a way that is not deceptive." *Id.* (emphasis added). The Magnesium Package is not inherently misleading. The cover page states that the Package includes a reprinted chapter on magnesium from the PDR. While the Package is distributed in connection with the sale of a dietary supplement (not a drug), the PDR chapter does make repeated drug related claims. Specifically, the PDR chapter states that magnesium is used to treat certain diseases and makes other disease/health claims. However, the PDR chapter has its own disclaimer page on the cover. Furthermore, Plaintiffs attest to their willingness to put any disclaimer on the package necessary to cure any perceived ambiguity regarding their intent to distribute non-treating supplements. At worst, the Magnesium Package is only potentially misleading. Plaintiffs have demonstrated that the Package can be presented in a non-deceptive fashion by utilizing disclaimers.

As to being related to unlawful activity, Defendants' circular argument-that distributing the Magnesium Package is unlawful and therefore Plaintiffs cannot challenge the statutes that make it unlawful-should not bar a full-blown constitutional analysis under *Central Hudson.* Plaintiffs lawfully manufacture and distribute magnesium supplements. The fact that Plaintiffs seek to distribute the Magnesium Package to their distributors and sales force does not make their otherwise lawful activities unlawful. Plaintiffs have not distributed the

Magnesium Package nor has the FDA, in reply to Plaintiffs' letter, stated that they hold the Package as violating the law. While Defendants argue that the Package will render Plaintiffs' magnesium products "drugs" underthe intended use definition, the FDA has not formally taken any action. Plaintiffs' plan to distribute the Package does not relate to unlawful activity.

Accordingly, the Magnesium Package is not inherently misleading nor does it pertain to unlawful activity per se. Thus, the government may not place a absolute ban on Plaintiffs' proposed distribution of the Package.[FN12] The Court must move to the second prong of the *Central Hudson* test. *In re R.M.J.*, 455 U.S. at 203 ("Even when a communication is not misleading, the State retains some authority to regulate.").

> FN12. In any case, § 343-2(a)(2-5) does not place an absolute ban on Plaintiffs' proposed speech. *See In re R.M. J.*, 455 U.S. at 203. If the Magnesium Package failed to qualify for a § 343-2(a) labeling exemption, then Plaintiffs would be exposed to heightened regulation and pre-approval restrictions under the FDCA. At worst, the Magnesium Package's drug claims could render Plaintiffs' underlying products drugs under the intended use definition thereby subjecting Plaintiffs to the formal FDA drug approval process. Even so, § 343-2(a)(2-5) is not an absolute ban on Plaintiffs' speech.

b. *THE GOVERNMENT INTEREST*

The FDA's mission is to promote and protect the public health. 21 U.S.C. § 393(b). Plaintiffs concede that the government has a substantial interest in protecting the public health and safety. (*See* Pl.s Mot. for Summ. J. at 9.) Furthermore, they admit that the government has a substantial interest in protecting the public from harm. (*Id.*)

The Supreme Court has said "there is no question that [the government's] interest in ensuring the accuracy of commercial information in the marketplace is substantial," *Edenfield*, 507 U.S. at 769, and that government has a substantial interest in "promoting the health, safety, and welfare of its citizens," *Rubin v. Coors Brewing Co.*, 514 U.S. 476, 485, 115 S.Ct. 1585, 131 L.Ed.2d 532 (1995). "At this level of generality, therefore, a substantial governmental interest is undeniable." *Pearson v. Shalala*, 164 F.3d 650, 656 (D.C.Cir.1999).

c. *DIRECT ADVANCEMENT OF THE GOVERNMENT INTEREST*

***10** The Supreme Court has "declined to uphold regulations that only *indirectly* advance the state interest involved." *Central Hudson*, 447 U.S. at 564-565 (emphasis added). In *Bates v. State Bar of California*, the Court overturned an advertising prohibition that was designed to protect the "quality" of a lawyer's work because the "restraints on advertising ... [were] an ineffective way of deterring shoddy work." 433 U.S. 350, 378, 97 S.Ct. 2691, 53 L.Ed.2d 810 (1977). The regulation must *directly* advance the government interest. *Central Hudson*, 447 U.S. at 566; *Pearson*, 164 F.3d at 656.

Here, both Plaintiffs' and Defendants' arguments miss the mark. Plaintiffs purport to argue that § 343-2(a)(2-5) fails to comply with the underlying congressional intent and therefore does not directly advance the government's substantial interest. Defendants argue that the FDCA *drug approval requirement* directly advances the government interest instead of addressing the subsection regulations found in § 343-2(a) itself.

i. *CONGRESSIONAL INTENT*

As a threshold issue, Defendants argue that the Court should not even resort to an analysis of congressional intent because Plaintiffs have failed to meet their initial burden to demonstrate any ambiguity in § 343-2(a). (Def.'s Reply at 4.) *See Church of Scientology v. Dep't of Justice*, 612 F.2d 417, 421 (9th Cir.1979) ("If the language of a statute is clear and there is no ambiguity, then there is no need to interpret the language by resorting to the legislative history or other extrinsic aids."); *Califor-*

nia v. Montrose Chemical Corp., 104 F.3d 1507, 1514-15 (9th Cir.1997) (party claiming that statutory language is ambiguous bears the burden to show it). Insofar as Plaintiffs contest the constitutionality of § 343-2(a)(2-5), Plaintiffs have not demonstrated any ambiguity in the language of the statute or its individual subsection requirements. Section 343-2(a) is clear on its face in what it requires for a labeling exemption. *See* § 343-2(a)(1)-(5). Thus, the Court need not belabor an inquiry into the congressional intent as it applies to Plaintiffs' first cause of action.[FN13] *Rubin v. U.S.*, 449 U.S. 424, 430, 101 S.Ct. 698, 66 L.Ed.2d 633 (1981) ("When we find the terms of a statute unambiguous, judicial inquiry is complete, except in rare and exceptional circumstances [and] ... [n]o such circumstances are present here, for our reading of the statute is wholly consistent with the history and the purposes of the Securities Act of 1933.") (internal quotation marks and citations omitted).

> FN13. The Court notes that some ambiguity exists as to whether a § 343-2(a) labeling exemption also provides a shelter from the intended use definition of a drug. *See* 21 U.S.C. § 321(g)(1). However, this ambiguity only applies to Plaintiffs' second cause of action regarding the validity of the FDA's intended use enforcement policy, for which they lack standing. This ambiguity does not reach Plaintiffs' first cause of action challenging § 343-2(a) it- self.

However, even assuming that § 343-2(a) is ambiguous at some level, the Court finds that the legislative intent behind § 343-2(a) overwhelmingly supports the statute as it currently stands. In interpreting the meaning of a statute, a court must first look to the language of the statute itself. *See U.S. v. Ron Pair Enterprises, Inc.*, 489 U.S. 235, 241, 109 S.Ct. 1026, 103 L.Ed.2d 290 (1989) ("The task of resolving the dispute over the meaning of [a statute] ... begins where all such inquiries must begin: with the language of the statute itself."). Under this first, cardinal canon of construction, the Supreme Court has "stated time and again that courts must presume that a legislature says in a statute what it means and means in a statute what it says there." *Connecticut Nat. Bank v. Germain*, 503 U.S. 249, 253-54, 112 S.Ct. 1146, 117 L.Ed.2d 391 (1992) (citations omitted).

***11** Here, § 343-2(a) is sufficiently clear on it-face. The subsection provisions (1)through (5) are likewise clear in what they expressly mandate as prerequisites for exemption. *See* 21 U.S.C. § 343-2(a)(1)-(5). Plaintiffs have not demonstrated that the statute *does not mean what it says* in 4 out of its 5 subsection requirements. Moreover, "when the words of a statute are unambiguous, then, this first canon is also the last: 'judicial inquiry is complete.' " *Germain*, 503 U.S. at 253-54 (quoting *Rubin*, 449 U.S. at 430). *See also Ron Pair Enterprises*, 489 U.S. at 241 (although the party claimed that legislative history pointed to a different result, the court held that "judicial inquiry" into the applicability of the statute "begins and ends with what [the statute] does say").

A deeper examination into the legislative history as well makes clear that § 343-2(a)(2-5) directly advances the government's interest and Congress' intent in passing the statute to begin with. Congress essentially intended § 343-2(a) to provide a labeling exemption for "the use of certain types of third party literature in direct connection with the sale of dietary supplement products." S.Rep. No. 103-410 at 25.[FN14] However, Congress expressly cautioned that:

> FN14. *See also* S.Rep. No. 103-410 at 36 (Congress intended to create a labeling exception for "truthful scientific literature [used] in connection with the sale or distribution of dietary supplements."). This overall intent is clearly reflected in the plain words of the statute itself. *See* 21 U.S.C. § 343-2(a).

The literature would need to meet certain criteria

> that would generally establish the independence and reliability of the material, i.e. the bill would require (a) that any such item would need to be "not false or misleading," (b) that it "not promote a particular brand of dietary supplement," (c) that it be displayed or presented so as to present a "balanced view" of the available information, and (d) that if displayed in a location in an establishment, it be displayed "physically separate" from the dietary supplements.
> *Id. See also id.* at 36, 47. No doubt, Congress intended these requirements to advance the substantial government interest in promoting and protecting the public health and safety. Importantly, this summary report of the legislative intent behind the § 343-2(a) labeling exemption is nearly identical to the final version of the statute. *See* 21 U.S.C. § 343-2(a). As Plaintiffs themselves point out, "[t]he only difference between the summary appearing in the Senate Report and the statute is that the summary does not have the requirement of § 343-2(a)(5) (restricting the appended information by sticker or other method)." (Pls.' Surreply at 5.) Moreover, Plaintiffs concede that "[o]therwise the summary and the final law are identical." (*id.*) Thus, there in no evidence that § 343-2(a)(2-5) defies the true congressional intent behind the statute's inception. To the contrary, there is every indication that the statute and each of its subsection provisions patently meet Congress' expressed intent. *Compare* 21 U.S.C. § 343-2(a) *with* S. Rep. No 103-410 at 25, 36, 47.

While § 343-2(a)(5) is not specifically mentioned in the Senate Report summary, its relevance and importance to the other subsections as well as the overriding purpose of the statute cannot be doubted. Section 343-2(a)(5) requires that the qualified publication cannot have any additional information appended to it by sticker or any other method. 21 U.S.C. § 343-2(a)(5). Thus, a manufacturer cannot backdoor the other subsection requirements by adding new information via sticker or attachment to the otherwise content-neutral scientific literature. For instance, without § 343-2(a)(5), a manufacturer could simply place a sticker on the publication stating the manufacturer's name, address, ordering information, or product listings in an effort to get around § 343-2(a)(2)'s requirement that the literature itself not promote a particular brand of dietary supplement. Furthermore, adding a sticker or other attachment to the publication may render it misleading in that, in many circumstances, the reader would not know whether the third party author, the manufacturer, or the distributor added the additional information by sticker. *See* 21 U.S.C. § 343-2(a)(1). In this way, § 343-2(a)(5) ensures compliance with the other subsection requirements and serves the overall legislative purpose of exempting only truthful, non-misleading, and non-promotional publications. Thus, it materially advances the government's interest here.

***12** Overall, § 343-2(a), in its entirety, directly advances the government's interest in promoting public safety and protecting the public from fraud. *See Pearson*, 164 F.3d at 656 ("We also recognize that the government's interest in preventing consumer fraud/confusion may well take on added importance in the context of a product, such as dietary supplements, that can affect the public's health.") On its face, § 343-2(a)(2-5) ensures that the labeling exemption only applies to publications that are non-promotional and not misleading. This directly advances the government interest because § 343-2(a) exempted publications may contain health/disease claims or even drug claims regarding the underlying supplement.

Importantly, if § 343-2(a)'s labeling exemption does in fact provide a shelter from the FDA's intended use enforcement policy and drug definition, the government has an even greater interest in proscribing and regulating the qualifications necessary for the labeling exemption. Moreover, § 343-2(a) would then allow manufacturers to distribute scientific publications with drug claims regarding their underlying supplements without fear that those publications could render their supplements drugs under the intended use definition. In this light, §

343-2(a) must positively ensure that a publication is non-promotional in order to provide the intended use exception in the first place. Thus, § 343-2(a) (2-5) directly advances the government's special interest as well as the statute's intended purpose.

d. *REASONABLE FIT BETWEEN GOVERNMENT'S INTEREST AND CHOSEN MEANS*

The First Amendment mandates that speech restrictions be "narrowly drawn." *In re Primus,* 436 U.S. 412, 438, 98 S.Ct. 1893, 56 L.Ed.2d 417 (1978). "The regulatory technique may extend only as far as the interest it serves. The State cannot regulate speech that poses no danger to the asserted state interest ...." *Central Hudson,* 447 U.S. at 565 (citation omitted). Furthermore, the government cannot "completely suppress information when narrower restrictions on expression would serve its interest as well." *Id.* For example, in *Bates* the Supreme Court did not "foreclose the possibility that some limited supplementation, by way of warning or disclaimer or the like, might be required" in promotional materials. 433 U.S. at 384.

However, the regulation need not be the least restrictive measure that could effectively protect the government interest. *Board of Trustees of the State University of New York v. Fox,* 492 U.S. 469, 480, 109 S.Ct. 3028, 106 L.Ed.2d 388 (1989). In *Fox,* the Supreme Court explained that *Central Hudson* does not impose a least restrictive means requirement. *Id.* (the Court does not require that the "manner of restriction is absolutely the least severe that will achieve the desired end"). Rather, *Fox* made clear that the Supreme Court only requires a " 'fit between the legislature's ends and the means chosen to accomplish those ends,' ... that is *not necessarily perfect, but reasonable* ...." *Id.* (quoting *Posadas de Puerto Rico Associates v. Tourism Company of Puerto Rico,* 478 U.S. 328, 341, 106 S.Ct. 2968, 92 L.Ed.2d 266 (1986)) (emphasis added).

***13** Plaintiffs argue that § 343-2(a)(2-5) fails this requirement because the subsection provisions suppress far more speech than necessary to serve the government's substantial interest. Moreover, Plaintiffs contend that because a disclaimer regime would be a far less restrictive and more precise means of serving the government interest, § 343-2(a)'s subsection requirements (2) through (5) are necessarily overbroad and unconstitutional. Again, Defendants' counter-argument incorrectly centers on the FDA's drug approval requirement and not on § 343-2(a). However, Defendants do stress that a disclaimer regime is simply inadequate to protect the government interest.

It is important to note that § 343-2(a)(2-5) does not ban truthful commercial speech outright. These provisions only act as requirements to qualify for the labeling exemption. If the publication does not meet all the subsection criteria, the manufacturer's speech is not foreclosed; rather, the speech simply does not qualify for a labeling exemption and will consequently trigger other FDCA statutes that may expose the manufacturer to heightened FDA regulation.

Section 343-2(a)(2-5) does not restrict more speech than necessary and constitutes a "reasonable fit" between the means and end. Significantly, subsection requirements (2) through (5) do not prevent, let alone restrict, the dissemination of truthful, non-misleading scientific publications as Plaintiffs suggest. Section 343-2(a)(2-5) is designed to restrict additional advertising and promotional statements attached to or woven into the truthful scientific literature itself. As explained earlier, the subsection requirements ensure that a § 343-2(a) labeling exemption only applies to truthful publications that are non-promotional, not misleading and manufacturer-neutral. The subsection requirements-(2) that the publication not promote a particular manufacturer or brand, (3) present a "balanced view" of the available scientific data, (4) is "physically separate" form the dietary supplements displayed in a store, and (5) not have any additional information appended to it by sticker or other means-are all "narrowly tailored" to achieve this end. Moreover, they comply with Congress' intent behind § 343-2(a).

Furthermore, Plaintiffs do not contest the validity of § 343-2(a) (1) that the publication not be "false or misleading." Indeed, Plaintiffs suggest that this is the overall thrust of the § 343-2(a) exemption. Assuming this is correct, Plaintiffs' argument nevertheless fails because § 343-2(a)(2-5) still constitutes a *reasonable fit* to ensure that the publication is not false or misleading. From any angle, § 343-2(a)(2-5) does not restrict more speech than necessary. The fact that Plaintiffs are now willing to place a disclaimer on the Magnesium Package does not change this. A disclaimer regime simply cannot provide the same protection that Congress envisioned and provided for in § 343-2(a)(2-5). Moreover, a disclaimer regime will not ensure that a § 343-2(a) labeling exemption only covers non-promotional publications.

***14** Accordingly, § 343-2(a)(2)-(5) are constitutional restrictions on commercial speech that comply with the legislative intent driving the labeling exemption. As such, the Court will not alter § 343-2(a) in its present form by striking four out of its five subsection requirements.[FN15] Plaintiffs' motion for summary judgment is **DENIED** and Defendants' cross motion for summary judgement is **GRANTED.**

FN15. Because the Court does not find § 343-2(a)(2-5) unconstitutional, it need not reach the issue of severability.

IV. *CONCLUSION AND ORDER*

The Court hereby **GRANTS** Defendants' motion to dismiss Plaintiffs' second claim pursuant to Fed.R.Civ.P. 12(b)(1) for lack of standing. The Court **GRANTS** Defendants' cross motion for summary judgment on Plaintiffs' first claim. Accordingly, the Court **DENIES** Plaintiffs' summary judgement motion in its entirety. The Clerk shall enter a final judgment in accordance with this Order.

IT IS SO ORDERED.

S.D.Cal.,2005.

Wallach v. Crawford
Not Reported in F.Supp.2d, 2005 WL 6054963 (S.D.Cal.)

END OF DOCUMENT

Respondents' PX Exhibit Index

JX2 - Attachment A

PX	Description	Where Admitted	Tr. Pages Where Discussed	In Camera
RX5007	Stampfer, et al., Evidence-based criteria in the nutritional context, Nut. Rev. Vol. 68 (8); 478 - 484	Tr. 885	Tr. 796 - 885	
PX0002	Khateeb J, Gantman A, Kreitenberg A, Aviram M, Fuhrman B, Paroxonase 1 (PON1) expression in hepatocytes in upregulated by pomegranate polyphenols: a role for PPAR-ã pathway (unpublished manuscript, 2009)	JX2, dated May 24, 2011; Tr. 7		
PX0003	Averill M, Effects of Pomegranate Juice on Atherosclerosis: Studies in Early and Advanced Stages of Disease (unpublished dissertation, 2005).	JX2, dated May 24, 2011; Tr. 7		
PX0004	Aviram M, Dornfeld L, Rosenblat M, Volkova N, Kaplan M, Coleman R, Hayek T, Presser D, and Fuhrman B, Pomegranate juice consumption reduces oxidative stress, atherogenic modifications to LDL, and platelet aggregation: studies in humans and in atherosclero	JX2, dated May 24, 2011; Tr. 7		
PX0005	Aviram M and Dornfled L, Pomegranate juice consumption inhibits serum angiotensin converting	JX2, dated May 24, 2011; Tr. 7		

PX	Description	Where Admitted	Tr. Pages Where Discussed	In Camera
	enzyme activity and reduces systolic blood pressure, Atherosclerosis 158 (2001) 195-198.			
PX0007	Shiner M, Fuhrman B, and Aviram M, Macrophage paraoxonase 2 (PON2) expression is up-regulated by pomegranate juice phenolic antioxidants via PPARã and AP-1 pathway activation, Atherosclerosis 195 (2007) 313-321.	JX2, dated May 24, 2011; Tr. 7		
PX0008	Aviram M, Volkova N, Coleman R, Dreher M, Reddy MK, Ferreira D, Rosenblat M, Pomegranate Phenolics from the Peels, Arils, and Flowers Are Antiatherogenic: Studies in Vivo and in Atherosclerotic Apolipoprotein Edeficient (E) Mice and in Vitro in Cultured	JX2, dated May 24, 2011; Tr. 7	Tr. 689 - 884	
PX0009	Fuhrman B, Volkova N, Aviram M, Pomegranate juice polyphenols increase recombinant paroxonase 1 binding to HDL: studies in-vitro and in diabetic patients (unpublished manuscript draft, 2009).	JX2, dated May 24, 2011; Tr. 7		
PX0010	Rosenblat M and Aviram M, Pomegranate Juice Protects Macrophages from Triglyceride Accumulation: Inhibitory Effect on DGAT1 Activity and on Triglyceride Biosynthesis, Ann. Nutr. Metab. (2011), 58:1-9.	JX2, dated May 24, 2011; Tr. 7		

PX	Description	Where Admitted	Tr. Pages Where Discussed	In Camera
PX0011	Broughton Pipkin F and Loughna P, Confirmatory Pilot Studies of the Effect of Pomegranate Juice on Blood Pressure and Some Hormonal Parameters in Apparently Healthy Young Volunteers (Abstract, 2008).	JX2, dated May 24, 2011; Tr. 7		
PX0012	Conway C, Carpenter L, Broughton Pipkin F, and Heptinstall S, Report on the effect of two weeks' dietary supplementation with Pom Wonderful on P-selectin in young, healthy volunteers (unpublished, 2009).	JX2, dated May 24, 2011; Tr. 7		
PX0013	Corder R, Investigation of Pomegranate Polyphenol Interactions with Fructose (proposal, 2008).	JX2, dated May 24, 2011; Tr. 7		
PX0014	Davidson MH, Maki KC, Dicklin MR, Feinstein SB, Witchger MS, Bell M, McGuire DK, Provost JC, Liker H, and Aviram M, Effects of Consumption of Pomegranate Juice on Carotid Intima-Media Thickness in Men and Women at Moderate Risk for Coronary Heart Disease,	JX2, dated May 24, 2011; Tr. 7		
PX0015	Aviram, et al., Uptake and cholesterol biosynthesis in macrophages, Journal of Nutritional Biochemistry 16 (2005) 570-576	JX2, dated May 24, 2011; Tr. 7		
PX0017	Mattiello T, Trifiro E, Jotti GS, Pulcinelli FM, Effects of Pomegranate Juice and Extract Polyphenols on Platelet Function, J. Medicinal Foods	JX2, dated May 24, 2011; Tr. 7		

PX	Description	Where Admitted	Tr. Pages Where Discussed	In Camera
	12 (2) (2009).			
PX0018	Ornish D, Bev 2 Summary, (unpublished, 2004)	JX2, dated May 24, 2011; Tr. 7		
PX0019	Brief Summary of Results re: Protocol #202528;BART-The Effects of Pomegrate Juice of Flow-Mediated Vasodilation	JX2, dated May 24, 2011; Tr. 7		
PX0020	Rosenblat M, Hayek T, Aviram M, Anti-oxidative effects of pomegranate juice (PJ) consumption by diabetic patients on serum and on macrophages, Atherosclerosis 187 (2006) 363-371.	JX2, dated May 24, 2011; Tr. 7		
PX0021	Rosenblat M, Volkova N, Attias J, Mahamid R, and Aviram M, Consumption of polyphenolic-rich beverages (mostly pomegranate and black currant juices) by healthy subjects for a short term increased serum antioxidant status, and the serum's ability to attenua	JX2, dated May 24, 2011; Tr. 7		
PX0022	Rozenberg O, Howell A, Aviram M, Pomegranate juice sugar fraction reduces macrophage oxidative state, whereas white grape juice sugar fraction increases it, Atherosclerosis 188 (2006) 68-76.	JX2, dated May 24, 2011; Tr. 7		
PX0023	Sumner M, Elliott-Eller M, Weidner G, Daubenmier JJ, Chew MH, Marlin R, Raisin CJ, and Ornish D, Effects of	JX2, dated May 24, 2011; Tr. 7		

PX	Description	Where Admitted	Tr. Pages Where Discussed	In Camera
	Pomegranate Juice Consumption on Myocardial Perfusion in Patients with Coronary Heart Disease, 96 Am. J. Cardiology 810 (2005).			
PX0024	Wilund K, Pomegranate Hemodialysis Study Proposal (unpublished proposal, 2009).	JX2, dated May 24, 2011; Tr. 7		JX2, dated May 24, 2011; Tr. 7
PX0025	Expert Report and attached Exhibits or Appendices of Dean Ornish, M.D., re In the Matter of Pom Wonderful LLC and Roll International Corp and Stewart A. Resnick, Lynda Rae Resnick, and Matthew Tupper, Docket No. 9344	JX2, dated May 24, 2011; Tr. 7	Tr. 1675 - 1794	
PX0026	Sacks FM, Ornish DM, Rosner B, McLanahan S, Castelli WP, and Kass EH. Dietary predictors of blood pressure and plasma lipoproteins in lactovegetarians. JAMA. 1985;254:1337-1341.	JX2, dated May 24, 2011; Tr. 7		
PX0027	Block KI, Cohen AJ, Dobs AS, Ornish D, Tripathy D. The challenges of randomized trials in integrative cancer care. Integr Cancer Ther. 2004 Jun;3(2):112-27.	JX2, dated May 24, 2011; Tr. 7		
PX0028	Chong MF, Macdonald R, Lovegrove JA. Fruit polyphenols and CVD risk: a review of human intervention studies. Br J Nutr. 2010 Oct;104 Suppl 3:S28 - 39.	JX2, dated May 24, 2011; Tr. 7		
PX0029	Hashemi M et al. Acute and long-term	JX2, dated May 24, 2011;		

PX	Description	Where Admitted	Tr. Pages Where Discussed	In Camera
	effects of grape and pomegranate juice consumption on vascular reactivity in paediatric metabolic syndrome. Cardiol Young. 2010 Feb; 20(1):73-7. Epub 2010 Feb 22.	Tr. 7		
PX0030	Glagov S et al. Compensatory enlargement of human atherosclerotic coronary arteries. N Engl J Med. 1987 May 28; 316(22):1371-5.	JX2, dated May 24, 2011; Tr. 7		
PX0031	Gibson RS, Watson DD, Craddock GB, et al. Prediction of cardiac events after uncomplicated myocardial infarction: a prospective study comparing predischarge exercise thallium-201 scintigraphy and coronary angiography. Circulation. 1983;68(2):321-336.	JX2, dated May 24, 2011; Tr. 7		
PX0032	Gimelli A, Rossi G, Landi P, et al. Abnormalities by Gated SPECT: Still the Best Predictor of Cardiac Events in Stable Ischemic Heart Disease. J Nucl Med 2009; 50:546–553	JX2, dated May 24, 2011; Tr. 7		
PX0033	Hollis S, Campbell F. What is meant by intention to treat analysis? Survey of published randomised controlled trials. BMJ 1999; 319 : 670.	JX2, dated May 24, 2011; Tr. 7		
PX0034	Julious SA, Mullee MA. Issues with using baseline in last observation carried forward analysis. Pharmaceut. Statist. 2008; 7: 142–146.	JX2, dated May 24, 2011; Tr. 7		
PX0035	Trichopoulou A, Costacou T, Bamia	JX2, dated May 24, 2011;		

PX	Description	Where Admitted	Tr. Pages Where Discussed	In Camera
	C, Trichopoulos D. Adherence to a Mediterranean diet and survival in a Greek population. N Engl J Med. 2003; 348:2595-2596,2599-2608.	Tr. 7		
PX0036	Smith SR. A look at the lowcarbohydrate diet. N Engl J Med. 2009;361:23.	JX2, dated May 24, 2011; Tr. 7		
PX0037	Walter, M. F., Jacob, R. F., Jeffers, B., Ghadanfar, M. M., Preston, G. M., Buch, J., Mason, P. Serum levels of thiobarbituric acid reactive substances predict cardiovascular events in patients with stable coronary artery disease. J. Am. College Cardiol.	JX2, dated May 24, 2011; Tr. 7		
PX0038	Esmaillzadeh A, Tahbaz F, Gaieni I, Alavi-Majd H, and Azadbakht, Concentrated Pomegranate Juice Improves Lipid Profiles in Diabetic Patients with Hyperlipidemia, J. Med. Food 7(3) 2004, 305-308	JX2, dated May 24, 2011; Tr. 7		
PX0040	Email from R. deGroof to G. Thames re UCLA & Accelovance Study	JX2, dated May 24, 2011; Tr. 7		
PX0041	Protocol 07-0878, Antioxidant Effects of Pomegranate Juice (PJ) vs. Placebo in Adults with Type II Diabetes Mellitus following a Glucose Load, Principal Investigator: James O. Hill, Ph.D., Co-Investigator: Holly R. Wyatt, M.D.	JX2, dated May 24, 2011; Tr. 7		JX2, dated May 24, 2011; Tr. 7
PX0045	Expert Report On Scientific Studies in Support of Health Benefits of	JX2, dated May 24, 2011; Tr. 7		

PX	Description	Where Admitted	Tr. Pages Where Discussed	In Camera
	Pomegranate Juice by David Heber, MD, PhD, FACP, FACN, CNS In re: Pom Wonderful LLC v. Tropicana Products, Inc. Case No. CV-09-00566 DSM dated July 12, 2010			
PX0046	Expert Report On Scientific Studies in Support of Health Benefits of Pomegranate Juice by David Heber, MD, PhD, FACP, FACN, CNS In re: Pom Wonderful LLC v. Welch Foods, Inc. Case No. CV-09-00567 AHM (AGRx) dated July 12, 2010	JX2, dated May 24, 2011; Tr. 7	Tr. 2067 - 2188	
PX0047	Expert Report On Scientific Studies in Support of Health Benefits of Pomegranate Juice by David Heber, MD, PhD, FACP, FACN, CNS In re: Pom Wonderful LLC v. Ocean Spray Cranberries, Inc. Case No. CV09-00565DDP (RZx) dated September 10, 2010	JX2, dated May 24, 2011; Tr. 7		
PX0048	Expert Report On Scientific Studies in Support of Health Benefits of Pomegranate Juice by David Heber, MD, PhD, FACP, FACN, CNS In re: Pom Wonderful LLC v. Ocean Spray Cranberries, Inc. Case No. CV09-00565DDP (RZx) dated November 10, 2010	JX2, dated May 24, 2011; Tr. 7		
PX0049	Azadzoi KM, Prevention of Prostate Smooth Muscle Dysfunction by Standardized Pomegranate Extract	JX2, dated May 24, 2011; Tr. 7		

PX	Description	Where Admitted	Tr. Pages Where Discussed	In Camera
	(unpublished, 2008)			
PX0051	Azadzoi kM, Schulman RN, Aviram M, and Stroky MB, Oxidative Stress in Arteriogenic Erectile Dysfunction: Prophylactic Role of Antioxidants, J. Urology 174: 386-393 (2005)	JX2, dated May 24, 2011; Tr. 7		
PX0052	Zhang Q, Radisavljevic ZM, Siroky MB, Azadzoi KM, Dietary antioxidants improve arteriogenic erectile dysfunction, International Journal of Andrology 33, 1-11 (2010)	JX2, dated May 24, 2011; Tr. 7		
PX0053	A Randomized, Placebo-Controlled, Double-Blind, Parallel Design Trial to Evaluate the Safety and Efficacy of POM Wonderful Pomegranate Extract Capsules in Male Subjects with Moderate to Severe Erectile Dysfunction (Unpublished protocol, 2010)	JX2, dated May 24, 2011; Tr. 7		JX2, dated May 24, 2011; Tr. 7
PX0055	De Nigris F, Williams-Ignarro S, Botti C, Sica V, Ignarro LJ, Napoli C, Pomegranate juice reduces oxidized low-density lipoprotein downregulation of endothelial nitric oxide synthase in human coronary endothelial cells, Nitric Oxide 15 (2006) 259-362.	JX2, dated May 24, 2011; Tr. 7		
PX0056	De Nigris F, Williams-Ignarro S, Sica V, Lerman LO, D'Armiento FP, Byrns RE, Casamassimi A, Carpentiero D,	JX2, dated May 24, 2011; Tr. 7		

PX	Description	Where Admitted	Tr. Pages Where Discussed	In Camera
	Schiano C, Sumi D, Fiorito C, Ignarro LJ, and Napoli C, Effects of Pomegranate Fruit Extract rich in punicalagin on oxidation-sensitive genes and eN			
PX0057	De Nigris F, Balestrieri ML, Williams-Ignarro S, D'Armiento P, Fiorito C, Ignarro LJ, Napoli C, The influence of pomegranate fruit extract in comparison to regular pomegranate juice and seed oil on nitric oxide and arterial function in obese Zucker rats	JX2, dated May 24, 2011; Tr. 7		
PX0058	Ignarro LJ, Byrns RE, Sumi D, de Nigris F, and Napoli C, Pomegranate juice protects nitric oxide against oxidative destruction and enhances the biological actions of nitric oxide, Nitric Oxide 15 (2006) 93-102.	JX2, dated May 24, 2011; Tr. 7		
PX0059	De Nigris F, Williams-Ignarro S, Lerman LO, Crimi E, Botti C, Mansueto G, D'Armiento FP, De Rosa G, Sica V, Ignarro LJ, Napoli C, Beneficial effects of pomegranate juice on oxidation-sensitive genes and endothelial nitric oxide synthase activity at sites	JX2, dated May 24, 2011; Tr. 7	Tr. 689 - 884	
PX0060	Pantuck AJ, Leppert JT, Zomorodian N, Aronson W, Hong J, Bardnard RJ, Seeram N, Liker H, Wang J, Elashoff R, Heber D, Aviram M, Ignarro L, Belldegrun A, Phase II Study of	JX2, dated May 24, 2011; Tr. 7	Tr. 1204 - 1351	

PX	Description	Where Admitted	Tr. Pages Where Discussed	In Camera
	Pomegranate Juice for Men with Rising Prostate-Specific Antigen following Surgery or			
PX0061	Pantuck AJ, Zomorodian N, Rettig M, Aronson WJ, Heber D, Belldegrun AS, Long Term Follow Up of Phase 2 Study of Pomegranate Juice for Men with Prostate Cancer Shows Durable Prolongation of PSA Doubling Time, J. of Urology Vol. 181 No. 4, Supplement (2009)	JX2, dated May 24, 2011; Tr. 7		
PX0063	Carducci MA, Safety and Efficacy of POMx in Men with Prostate Cancer: An 18-Month, Randomized, Double-Blind, Dose-Finding Study of the Effects of Two (2) Doses of Pomegranate Juice Extract Capsules (1 or 3 capsules/day) on Rising Prostate Specific Antigen	JX2, dated May 24, 2011; Tr. 7		
PX0064	Carducci M, Heber D, Belldegrun A, Pantuck A, A Randomized, Placebo-Controlled, Pre-Surgical Study of the Effects of Pomegranate Pills in Men with Prostate Cancer (unpublished protocol, 2007)	JX2, dated May 24, 2011; Tr. 7		JX2, dated May 24, 2011; Tr. 7
PX0065	Agensys, Investigation of the Effect of Pomegranate Juice (PJC) on Human Prostate Cancer (Unpublished Study Results, 2001)	JX2, dated May 24, 2011; Tr. 7		
PX0066	Agensys, Investigation of the Effect of	JX2, dated May 24, 2011;		

PX	Description	Where Admitted	Tr. Pages Where Discussed	In Camera
	Pomegranate Juice (PJC) on Human Prostate Cancer, Final Power Point Presentation (2003)	Tr. 7		
PX0068	Hong MY, Seeram NP, and Heber D, Pomegranate polyphenols downregulate expression of androgensynthesizing genes in human prostate cancer cells overexpressing the androgen receptor, Journal of Nutritional Biochemistry 19 (2008) 848-855.	JX2, dated May 24, 2011; Tr. 7	Tr. 689 - 884	
PX0069	Seeram NP, Aronson WJ, Zhang Y, Henning SM, Moro A, Lee R, Sartippour M, Harris DM, Rettig M, Suchard MA, Pantuck AJ, Belldegrun A, and Heber D, Pomegranate Ellagitannin-Derived Metabolites Inhibit Prostate Cancer Growth and Localize to the Mouse Prostate	JX2, dated May 24, 2011; Tr. 7	Tr. 689 - 884	
PX0070	Rettig MB, Heber D, An J, Seeram NP, Rao JY, Liu H, Klatt T, Belldegrun A, Moro A, Henning SM, Mo D, Aronson WJ, and Pantuck A, Pomegranate extract inhibits androgen-independent prostate cancer growth through a nuclear factor-êB-dependent echanism, Molec	JX2, dated May 24, 2011; Tr. 7		
PX0071	Sartippour MR, Seeram NP, Rao JY, Moro A, Harris DM, Henning SM,	JX2, dated May 24, 2011; Tr. 7	Tr. 689 - 884	

PX	Description	Where Admitted	Tr. Pages Where Discussed	In Camera
	Firouzi A, Rettig MB, Aronson WJ, Pantuck AJ, and Heber D, Ellagitannin-rich pomegranate extract inhibits angiogenesis in prostate cancer in vitro and in vivo, International Journal of Oncol			
PX0072	Kasimetty SG, et al., Effects of Pomegranate Chemical Constituents/Intestinal Microbial Metabolites on CYP1B1 in 22Rv1 Prostate Cancer Cells, J. Agric. Food Chem. 2009, 57, 10636-10644.	JX2, dated May 24, 2011; Tr. 7		
PX0073	Heber, et al, Pomegranate Juice and Extracts Provide Similar Levels of Plasma and Urinary Ellagitannin Metabolites in Human Subject	JX2, dated May 24, 2011; Tr. 7		
PX0074	Heber, et al, Pomegranate Juice Ellagitannin Metabolites Are Present in Human Plasma and Some Persist in Urine for Up to 48 Hours, J. Nutrition 136:2481-2485 (2006).	JX2, dated May 24, 2011; Tr. 7		
PX0075	Heber, et al., Bioavailability of ellagic acid in human plasma after consumption of ellagitannins from pomegranate (Punica granatum L.) juice, Clinica Chimica Acta 348 (2004) 63-68.	JX2, dated May 24, 2011; Tr. 7		
PX0076	Martinez AE, A Randomized, Placebo-Controlled, Double-Blind,	JX2, dated May 24, 2011; Tr. 7		JX2, dated May 24, 2011; Tr. 7

PX	Description	Where Admitted	Tr. Pages Where Discussed	In Camera
	Parallel Design Trial to Evaluate the Safety and Efficacy of Pomegranate Extract Capsules in Post-Menopausal Subjects with Decreased Bone Mineral Density (Unpublished Research Protocol, 2010).			
PX0077	Adams LS, Zhang Y, Seeram NP, Heber D, Chen S, Pomegranate Ellagitannin-Derived Compounds Exhibit Antiproliferative and Antiaromatase Activity in Breast cancer Cells In vitro, Cancer Prev Res; 3(1); 108-13 (2010).	JX2, dated May 24, 2011; Tr. 7		
PX0079	Finn RS, Preclinical Studies with POM Extract in Human Breast Cancer Cell Lines (Unpublished Power Point Presentation, 2007)	JX2, dated May 24, 2011; Tr. 7		
PX0081	Adams LS, Seeram NP, Aggarwal BB, Takada Y, Sand D, and Heber D, Pomegranate Juice, Total Pomegranate Ellagitannins, and Punicalagin Suppress Inflammatory Cell Signaling in Colon Cancer Cells, J. Agric. Food Chem. 2006, 54, 980-985.	JX2, dated May 24, 2011; Tr. 7		
PX0083	Heber, et al, In vitro antiproliferative, apoptotic and antioxidant activities of punicalagin, ellagic acid and a total pomegranate tannin extract are enhanced in combination with other polyphenols as	JX2, dated May 24, 2011; Tr. 7		

PX	Description	Where Admitted	Tr. Pages Where Discussed	In Camera
	found in pomegranate juice, Journal of Nutritional Biochemistry 16 (2005) 360-367.			
PX0085	Joseph JA, The Effects of 100% POM juice (PJ) and purified polyphenol powder (PyP) (2%) on Cognitive and Motor Deficits in Aging (unpublished research proposal, 2005)	JX2, dated May 24, 2011; Tr. 7		
PX0086	Joseph JA and Skukitt-Hale B, The Effects of POMX Powder on Cognitive and Motor Deficits in Aging (unpublished Power Point, 2006)	JX2, dated May 24, 2011; Tr. 7		
PX0087	Hartman RE, Shah A, Fagan A, Schwetye KE, Parsadanian M, Schulman RN, Finn MB, and Holtzman DM, Pomegranate juice decreases amyloid load and improves behavior in a mouse model of Alzheimer's disease, Neurobiology of Disease 24 (2006) 506-515.	JX2, dated May 24, 2011; Tr. 7		
PX0088	Inder, Impact of maternal pomegranate juice intake on brain injury in infants with Intrauterine Growth Restriction (Unpublished Research Proposal, 2009)	JX2, dated May 24, 2011; Tr. 7		JX2, dated May 24, 2011; Tr. 7
PX0089	Loren DJ, Seeram NP, Schulman RN, and Holtzman DM, Maternal Dietary Supplementation with Pomegranate Juice is Neuroprotective in an Animal Model of Neonatal Hypoxic-Ischemic	JX2, dated May 24, 2011; Tr. 7		

PX	Description	Where Admitted	Tr. Pages Where Discussed	In Camera
	Brain Injury, Pediatric Research 57(6): 858-864 (2005).			
PX0090	Ropacki S, Hartman R, Sabate J, Razzouk A, The Effects of Pomegranate Supplementation on Cognitive Functioning Following Coronary Artery Bypass Grafting Surgery (Unpublished Research Proposal, 2010)	JX2, dated May 24, 2011; Tr. 7		JX2, dated May 24, 2011; Tr. 7
PX0091	DeGroof R, A Placebo Controlled, Randomized, Double Blind Study to Compare Antioxidant Levels in Normal Subjects with Elevated Waist Circumference When Administered 1 or 2 Pomegranate Dietary Supplement Capsules for 4 Weeks (Unpublished Clinical Study Rep	JX2, dated May 24, 2011; Tr. 7		
PX0092	Aviram M, Antioxidant Effect of Pomegranate juice consumption by healthy males: A dose response study (Unpublished report, 2003)	JX2, dated May 24, 2011; Tr. 7		
PX0094	Bolling B, Blumberg J, Chen O, Total antioxidant capacity and phenolics of pomegranate and grape juices: contribution of polyphenols, interaction with vitamin C, and assay differences (Unpublished report, 2009)	JX2, dated May 24, 2011; Tr. 7		
PX0095	From Dr. Heber to Dr. Zhang , Rupo Lee, and David Wang, Pomegranate Juice Specification:	JX2, dated May 24, 2011; Tr. 7		JX2, dated May 24, 2011; Tr. 7

PX	Description	Where Admitted	Tr. Pages Where Discussed	In Camera
	Anthocyanins and Color Analysis Part 10: POM Juice Anthocyanin Profile and Contents of Other Commercial Available Pomegranate Juice Blend (Unpublished)			
PX0096	Bialonska D, Kasimetty SG, Schrader KK, and Ferreira D, The Effect of Pomegranate (punica granatum L.) Byproducts and Ellagitannins on the Growth of Human Gut Bacteria, J. Agric. Food Chem. 2009, 57, 8344-8349	JX2, dated May 24, 2011; Tr. 7		
PX0097	Gil MI, Tomas-Barberan FA, Hess-Pierce B, Holcroft DM, and Kader AA, Antioxidant Activity of Pomegranate Juice and Its Relationship with Phenolic Composition and Processing, J. Agric. Food Chem.2000, 48, 4581-4589	JX2, dated May 24, 2011; Tr. 7		
PX0098	Seeram NP, Aviram M, Zhang Y, Henning SM, Feng L, Dreher M, and Heber D, Comparison of Antioxidant Potency of Commonly Consumed Polyphenol-Rich Beverages in the United States, J. Agric. Food Chem. 2008,56, 1415-1422	JX2, dated May 24, 2011; Tr. 7		
PX0099	Heber et al., Absence of Pomegranate Ellagitannins in the Majority of Commercial Pomegranate	JX2, dated May 24, 2011; Tr. 7		

PX	Description	Where Admitted	Tr. Pages Where Discussed	In Camera
	Extracts: Implications for Standardization and Quality Control, J. Agric Food Chem. 2009, 57, 7395-7400			
PX0100	Szpylka, Proposed AOAC Collaborative Study (Unpublished Proposal and Summary of Results, 2009)	JX2, dated May 24, 2011; Tr. 7		JX2, dated May 24, 2011; Tr. 7
PX0101	Aviram M, Anti-atherogenic Effects of Pomegranate Flower Fractions (Unpublished report, 2008)	JX2, dated May 24, 2011; Tr. 7		
PX0103	Zhang Y and Heber D, Total Phenolic Contents of Pomegranate Concentrates and Juices (Unpublished Report 2009)	JX2, dated May 24, 2011; Tr. 7		
PX0104	Heber et al, International Multidimensional Authenticity Specification (IMAS) Algorithm for Detection of Commercial Pomegranate Juice Adulteration, J. Agric Food Chem., 2009, 57(6), 2550-2557.	JX2, dated May 24, 2011; Tr. 7		
PX0106	Martin KR, Krueger CG, Rodriguez G, Dreher M, and Reed JD, Development of a novel pomegranate standard and new method for the quantitative measurement of pomegranate polyphenols, J. Sci. Food Agric, 89: 157-12 (2009)	JX2, dated May 24, 2011; Tr. 7		
PX0107	Madrigal-Carballo S, Rodriguez G, Krueger CG, Dreher M, Reed JD,	JX2, dated May 24, 2011; Tr. 7		

PX	Description	Where Admitted	Tr. Pages Where Discussed	In Camera
	Pomegranate (Punica granatum) supplements: Authenticity, antioxidant and polyphenol composition, J. of Functional Foods I (2009) 324-329			
PX0110	Reh S, Smith W, and Cullor J, Brief Overview of Bovine Mastitis (Unpublished report, 2007)	JX2, dated May 24, 2011; Tr. 7		
PX0111	Reddy MK, Gupta Sk, Jacob MR,Khan SI, Ferreira, D, Antioxidant, Antimalarial and Antimicrobial Activities of Tannin-Rich Fractions, Ellagitannins and Phenolic Acids from Punica granatum L., Planta Medica73:461-467 (2007)	JX2, dated May 24, 2011; Tr. 7		
PX0112	Madjid M, Alfred A, Ali M, Haidari M, Dreher M, and Casscells W, Pomegranate Polyphenols Reduce Common Cold and Influenza-Like Symptoms: A Double-Blind, Placebo-Controlled Randomized Clinical Trial (Unpublished Manuscript)	JX2, dated May 24, 2011; Tr. 7		
PX0114	Turner RB, A Placebo Controlled, Randomized, Double Blind Pilot Study to Evaluate the Use of Pomegranate Concentrate (POMx) for thePrevention of Experimental Rhinovirus Infection in Human Subjects (Unpublished Report 2008)	JX2, dated May 24, 2011; Tr. 7		
PX0115	Sundararajan A, Ganapathy R, Huan L, Dunlap JR, Webby RJ, Kotwal GJ, and Sanster MY, Influenza Virus	JX2, dated May 24, 2011; Tr. 7		

PX	Description	Where Admitted	Tr. Pages Where Discussed	In Camera
	variation in susceptibility to inactivation by pomegranate polyphenols is determined by envelope glycoproteins, Antiviral Research 88 (2010) 1-9			
PX0116	Brown SJ, A Phase I, Proof of Concept, Randomized, Placebo-Controlled, Double-Blind Study to Evaluate the Effects of Punica Granatum (Pomegranate) Juice on the Indices of Quality of Life in HIV Positive Patients (Unpublished Protocol)	JX2, dated May 24, 2011; Tr. 7		JX2, dated May 24, 2011; Tr. 7
PX0117	Oliveira RA, Narciso CD, BisinottoRS, Perdomo MC, Ballou MA, DreherM, and Santos JEP, Effects of feeding polyphenols from pomegranate extract on health growth, nutrient digestion, and immunocompetence of calves, J. Dairy Sci. 93:4280-4291 (2010)	JX2, dated May 24, 2011; Tr. 7		
PX0119	Bialonska D, Ramnani P, Kasimetty SG, Muntha KR,Gibson GR, Ferreira D, The influence of pomegranate by-product and punicalagins on selected groups of human intestinalmicrobiota, International Journal ofFood Microbiology 140 (2010) 175-182	JX2, dated May 24, 2011; Tr. 7		
PX0120	Howell A, Bacterial Anti-adhesionActivity of Human Urine Following27% POM Juice vs. 27%	JX2, dated May 24, 2011; Tr. 7		

PX	Description	Where Admitted	Tr. Pages Where Discussed	In Camera
	Cranberry Juice vs. POMx Capsule Consumption (Unpublished results2009)			
PX0121	Howell A, Pomegranates vs. Bacteria: The Battle Rages On (Unpublished Power Point Presentation 2004)	JX2, dated May 24, 2011; Tr. 7		
PX0122	Funk J, Pilot Study to Examine Anti-Inflammatory Effects and Tolerability of Pomegranate Extract in Rheumatoid Arthritis (Unpublished Proposal, 2008)	JX2, dated May 24, 2011; Tr. 7		
PX0123	Aviram M, Consumption of pomegranate decreases serum oxidative stress and reduces disease activity in patients with active rheumatoid arthritis: a preliminary study (Unpublished 2010)	JX2, dated May 24, 2011; Tr. 7		
PX0124	Shukla M, Gupta K, Rasheed Z, KhanK, Haqqi TM, Consumption of hydrolysable tannins-rich pomegranate extract suppresses inflammation and joint damage in rheumatoid arthritis, Nutrition 24 (2008) 733-743	JX2, dated May 24, 2011; Tr. 7		
PX0125	Rasheed Z, Akhtar N, AnbazhaganAN, Ramamurthy S, ShuklaM, and Haqqi T, Polyphenol-rich pomegranate fruit extract(POMx) suppresses PMACI-induced expression of proinflammatory cytokines by inhibiting the activation	JX2, dated May 24, 2011; Tr. 7		

PX	Description	Where Admitted	Tr. Pages Where Discussed	In Camera
	of MAPKinases and NF-κB in human KU812			
PX0126	Mortensen OH, Broholm C, andPedersen BK, Pomegranate inhibits TLR4 signaling in myotubes and adipocytes and increases glucose uptake (Unpublished manuscript2007)	JX2, dated May 24, 2011; Tr. 7		
PX0127	Rock W, Rosenblat M, Miller-Lotan R, Levy AP, Elias M, and Aviram M, Consumption of Wonderful Variety Pomegranate Juice and Extract by Diabetic Patients Increases Paraoxonase 1 Association with High-Density Lipoprotein and Stimulates Its Catalytic Activit	JX2, dated May 24, 2011; Tr. 7	Tr. 1410 - 1627	
PX0128	McFarlin BK, Strohacker KA, andKueht ML, Pomegranate seed oil consumption during a period of high-fat feeding reduces weight gain and reduces type 2 diabetes risk in CD-1 mice, British Journal of Nutrition (2009), 102, 54-59	JX2, dated May 24, 2011; Tr. 7		
PX0129	Wolever, Pom Wonderful FINAL REPORT, Determination of Glycaemic Index of: Pomegranate Juice, Blueberry Juice, Welch's Grape Juice (Unpublished Report,2003)	JX2, dated May 24, 2011; Tr. 7		
PX0130	Atkinson, Glycaemic Index Research Report, For POM Wonderful LLC., March, 2009 (Unpublished Report2009)	JX2, dated May 24, 2011; Tr. 7		

PX	Description	Where Admitted	Tr. Pages Where Discussed	In Camera
PX0132	Aviram M. Dornfeld L, Kaplan M,Coleman R, Gaitini D, Nitecki S, Hofman A, Rosenblat M. Volkova N, Presser D, Attias J, Hayek T, Fuhrman B, Pomegranate juice flavonoids inhibit low-density lipoprotein oxidation and cardiovascular diseases: Studies in the	JX2, dated May 24, 2011; Tr. 7		
PX0133	American Botanical Council, Proprietary Botanical Food Product, Scientific and Clinical Monograph for Pom Wonderful Pomegranate Juice (2008)	JX2, dated May 24, 2011; Tr. 7		
PX0134	PCRI Insights, New Developments inProstate Cancer Research, August2008, Vol 11: NO 3	JX2, dated May 24, 2011; Tr. 7		
PX0136	Farkas D, Oleson LE, Zhao Y, Harmatz JS, Zinny MA, Court MH, and Greenblat DJ, Pomegranate Juice Does Not Impair Clearance of Oral or Intravenous Midazolam, a Probe for Cytochrome P450-3A Activity: Comparison with Grapefruit Juice, J. Clin. Pharmacology 4	JX2, dated May 24, 2011; Tr. 7		
PX0138	Merkel DJ, POM Oil: Subtronic Toxicity Study (90 Day Dietary Study in Rats) (Unpublished 2007)	JX2, dated May 24, 2011; Tr. 7		
PX0139	Heber D, Seeram NP, Wyatt H, Henning SM, Zhang Y, Ogden LG, Dreher M, and Hill JO, Safety and Antioxidant Activity of a Pomegranate	JX2, dated May 24, 2011; Tr. 7		

PX	Description	Where Admitted	Tr. Pages Where Discussed	In Camera
	Ellagitannin-Enriched Polyphenol Dietary Supplement in Overweight Individuals with Increased Waist Size, J. Agric. Food Che			
PX0140	Warren MP, Ng E, Ramos RH, andHalpert S, Absence of Significant Estrogenic Effects in the Postmenopausal Population, Pomegranates Ancient Roots to Modern Med. Taylor and Francis, pp.157-166 (2006)	JX2, dated May 24, 2011; Tr. 7		
PX0141	Clinical Research Laboratories, Inc., Final Report, An Evaluation to Determine the Efficacy and Tolerance of an Anti-Aging Regime(Unpublished Report 2009)	JX2, dated May 24, 2011; Tr. 7		
PX0142	Clinical Research Laboratories, Inc., Final Report, Evaluation and Comparison of the Efficacy and Tolerability of Skin Clarifying Regimes (Unpublished 2007)	JX2, dated May 24, 2011; Tr. 7		
PX0143	Clinical Research Laboratories, FinalReport, An In vivo Evaluation, by a Non-Invasive Technique, for the Measurement of the Reservoir Effect of five Cosmetic Products Containing Free Radical Scavengers (Unpublished 2007)	JX2, dated May 24, 2011; Tr. 7		
PX0144	Zaid MA, Afaq F, Syed DN, Dreher M, and Mukhtar H, Inhibition of UVB- mediated Oxidative Stress and	JX2, dated May 24, 2011; Tr. 7		

PX	Description	Where Admitted	Tr. Pages Where Discussed	In Camera
	Markers of Photoaging inImmortalized HaCaT Keratinocytes by Pomegranate Extract POMx, Photochemistry and Photobiology,2007, 83: 882-888			
PX0146	Trombold JR, Barnes JN, Critchley L,and Coyle EF, Ellagitannin Consumption Improves Strength Recovery 2-3 d after Eccentric Exercise, Med. Sci. Sports Exerc., Vol. 42, No. 3, pp. 493-498, 2010	JX2, dated May 24, 2011; Tr. 7		
PX0148	Cooper CB, Investigation of the Effect of Pomegranate Juice on Aerobic Exercise Performance (Unpublished Power Point Presentation 2005)	JX2, dated May 24, 2011; Tr. 7		
PX0149	Expert Report and Attached Exhibitsor Appendices of Arthur Burnett, M.D. re In the Matter of Pom Wonderful LLC and Roll International Corp and Stewart A. Resnick, Lynda Rae Resnick, and Matthew Tupper,Docket No. 9344	JX2, dated May 24, 2011; Tr. 7		
PX0150	Burnett AL, Lowenstein CJ, Bredt DS, Chang TSK, Snyder SH, Nitric Oxide: A Physiological Mediator of Penile Erection, Science, 257 (1992), 401-3	JX2, dated May 24, 2011; Tr. 7		
PX0151	Burnett AL, Nitric Oxide Regulation of Penile Erection: Biology and Therapeutic Implications, Journal of Andrology, Vol. 23, No. 5,	JX2, dated May 24, 2011; Tr. 7		

PX	Description	Where Admitted	Tr. Pages Where Discussed	In Camera
	September/October 2002			
PX0152	Burnett AL, Novel pharmacological approaches in the treatment of erectile dysfunction, World J. Urol. (2001) 19: 57-66	JX2, dated May 24, 2011; Tr. 7		
PX0153	Burnett AL and Musicki B, The Nitric Oxide Signaling Pathway in the Penis, Current Pharmaceutical Design, 2005, 11, 3987-3994	JX2, dated May 24, 2011; Tr. 7		
PX0154	Hurt KJ, Musicki B, Palese MA,Crone JK, Becker RE, Moriarty JL, Snyder SH, Burnett AL, Akt- dependent phosphorylation of endothelial nitric-oxide synthase mediates penile erection, Proc. Natl. Acad. Sci. USA, 2002 Mar 19; 99(6):4061-4066	JX2, dated May 24, 2011; Tr. 7		
PX0155	Burnett AL, Musicki B, Jin L, andBivalacqua TJ, Nitric oxide/redox-based signaling as a therapeutic target for penile disorders, ExpertOpin. Ther. Targets (2006) 10(3): 455-457	JX2, dated May 24, 2011; Tr. 7		
PX0156	Burnett AL, Novel nitric oxide signaling mechanisms regulate the erectile response, International Journal of Impotence Research (2004) 16, S15-S19	JX2, dated May 24, 2011; Tr. 7		
PX0157	Burnett AL, Phosphodiesterase 5Mechanisms and Therapeutic Applications, Am. J. Cardiol. 96 (2005), 29-31	JX2, dated May 24, 2011; Tr. 7		
PX0158	Expert Report and Attached	JX2, dated May 24, 2011;	Tr. 2811 - 2965	

PX	Description	Where Admitted	Tr. Pages Where Discussed	In Camera
	Exhibitsor Appendices of Ronald R. Butters, PH.D., re In the Matter of Pom Wonderful LLC and Roll International Corp and Stewart A. Resnick, Lynda Rae Resnick, and Matthew Tupper, Docket No. 9344	Tr. 7		
PX0159	Curriculum Vitae of Ronald R. Butters, PH.D.	JX2, dated May 24, 2011; Tr. 7		
PX0160	Exhibit 2 Attached to the Expert Report of Ronald R. Butters, PH.D. containing all References Cited in Report	JX2, dated May 24, 2011; Tr. 7		
PX0161	Expert Report and Attached Exhibitsor Appendices of Jean deKernion, M.D., re In the Matter of Pom Wonderful LLC and Roll International Corp and Stewart A. Resnick, Lynda Rae Resnick, and Matthew Tupper, Docket No. 9344	JX2, dated May 24, 2011; Tr. 7		
PX0162	Patel, et al., Recurrence Patterns After Radical Retropubic Prostatectomy: Clinical Usefulness of Prostate Specific Antigen Doubling Times and Log Slope Prostate Specific Antigen, Journal of Urology, Vol. 158, 1441-1445, October 1997.	JX2, dated May 24, 2011; Tr. 7		
PX0163	Pound, et al., Natural History of Progression After PSA Elevation Following Radical Prostatectomy (Abstract), JAMA 1999; 281(17):1591-1597	JX2, dated May 24, 2011; Tr. 7		

PX	Description	Where Admitted	Tr. Pages Where Discussed	In Camera
PX0164	Giovacchini, et al., PSA Doubling Time for Prediction of [(11)C]choline PET/CT Findings in Prostate Cancer Patients with Biochemical Failure after Radical Rrostatectomy (Abstract), Eur. J. Nucl. Med. Mol. Imaging, 2010 June; 37(6): 1106-16	JX2, dated May 24, 2011; Tr. 7		
PX0165	Freedland, et al., Risk of Prostate Cancer-Specific Mortality Following Biochemical Recurrence After Radical Prostatectomy (Abstract), JAMA,2005; 294(4): 433-439	JX2, dated May 24, 2011; Tr. 7		
PX0166	Tollefson, et al., Stratification ofPatient Risk Based on Prostate-Specific Antigen Doubling Time after Tadical Retropubic Prostatectomy (Abstract), Mayo Clin. Proc. 2007Apr; 82(4): 422-7	JX2, dated May 24, 2011; Tr. 7		
PX0167	Teeter, et al., Does PSADT after Prostatectomy Correlate with Overall Survival?—A Report from the SEARCH Database Group, Urology.2011 January; 77(1): 149-53	JX2, dated May 24, 2011; Tr. 7		
PX0168	Carmody, et al., A dietary Intervention for Recurrent Prostate Cancer after Definitive Primary Treatment: Results of a Randomized Pilot Trial, Urology2008 December; 72(6): 1324-8	JX2, dated May 24, 2011; Tr. 7		
PX0169	Schroder, et al., Randomized, Double-Blind, Placebo-Controlled Crossover	JX2, dated May 24, 2011; Tr. 7		

PX	Description	Where Admitted	Tr. Pages Where Discussed	In Camera
	Study in Men with Prostate Cancerand Rising PSA: Effectiveness of aDietary Supplement, Eur. Urol. 2005December; 48(6): 922-30			
PX0170	Zhang, et al., Effect of Lycopene on Androgen Receptor and Prostate-Specific Antigen Velocity, Chin. Med(Engl) 2010 August; 123(16): 2231-6	JX2, dated May 24, 2011; Tr. 7		
PX0171	Trapasso, et al, The Incidence and Significance of Detectable Levles of Serum Prostate Specific Antigen After Radical Prostatectomy, Journal of Urology, Vol. 152, 1821-1825, November 1994	JX2, dated May 24, 2011; Tr. 7		
PX0172	Smith MR, et al., Rosiglitazoneversus Placebo for Men with Prostate Cancer and a Rising Serum Prostate Specific Antigen after Radical Rrostatectomy and/or Radiation Therapy, Cancer, 2004 October 1;101(7): 1569-74	JX2, dated May 24, 2011; Tr. 7	Tr. 3039 - 3127	
PX0173	Malik, et al., Pomegranate Fruit Juice for Chemoprevention and Chemotherapy of Prostate Cancer, Proc. Natl. Acad. Sci. USA, 2005 Oct11; 102(41): 14813-8	JX2, dated May 24, 2011; Tr. 7		
PX0174	deNigris et al., Beneficial Effects of Antioxidants and L-arginine on Oxidation-Sensitive Gene Expression and Endothelial NO Synthase Activity at Sites of Disturbed Shear Stress,	JX2, dated May 24, 2011; Tr. 7		

PX	Description	Where Admitted	Tr. Pages Where Discussed	In Camera
	PNAS 2003 100: 1420-1425			
PX0175	Carducci, et al., A Phase II Study of Pomegranate Extract for Men with Rising Prostate-Specific Antigen Following Primary Therapy, J. Clin. Oncol. 29: 2011 (suppl 7; abstr 11)	JX2, dated May 24, 2011; Tr. 7	Tr. 1204 - 1351	
PX0176	Leung, et al., Exercise Alters the IGF Axis In Vivo and Increases P54Protein in Prostate Tumor Cells InVitro, J. Appl. Physiol. 96: 450-454,2004; 10.1152/japplphysiol.00871.203	JX2, dated May 24, 2011; Tr. 7		
PX0177	Andriole, et al., Treatment With Finasteride Following Radical Prostatectomy for Prostate Cancer, Urology, March 1995, Volume 45, Number 3	JX2, dated May 24, 2011; Tr. 7		
PX0178	Eastham, Prostate Specific Antigen Doubling Time as a Prognostic Marker in Prostate Cancer, Nat. Clin. Pract. Urol. 2005 Oct: 2(10): 482-91.	JX2, dated May 24, 2011; Tr. 7		
PX0179	Finley, et al., The Natural History of Ultrasensitive PSA Following Radical Prostatectomy, Unpublished.	JX2, dated May 24, 2011; Tr. 7		
PX0180	Danella, et al., Detectable Prostate Specific Antigen Levels Following Radical Prostatectomy: Relationshipof Doubling Time to Clinical Outcome, Presented at the American Urological Association 88th Annual Meeting,San Antonio, Texas, May 1993.	JX2, dated May 24, 2011; Tr. 7		

PX	Description	Where Admitted	Tr. Pages Where Discussed	In Camera
PX0181	Oudard, et al., Prostate Specific Antigen Doubling Time before Onset of Chemotherapy as a Predictor of Survival for Hormone-refractory Prostate Cancer Patients, Ann Oncol.2007 Nov; 18(11): 1828-33.	JX2, dated May 24, 2011; Tr. 7		
PX0182	Trock, et al., Prostate Cancer- Specific Survival Following Salvage Radiotherapy vs Observation in Men with Biochemical Recurrence after Radical Prostatectomy, JAMA 2008; Jun 18; 299(23): 2760-9.	JX2, dated May 24, 2011; Tr. 7		
PX0183	Koyama, et al., Pomegranate Extract Induces Apoptosis in Human Prostate Cancer Cells by Modulation of theIGF-IGFBP Axis, Growth Horm IGF Res. 2010 Feb; 20(1): 55-62.	JX2, dated May 24, 2011; Tr. 7		
PX0184	Rettig, et al., Pomegranate ExtractInhibits Androgen-Independent Prostate Cancer Growth Through a Nuclear Factor-kappaB-dependent Mechanism, Mol. Cancer Ther 2008;7(9): 2662-71.	JX2, dated May 24, 2011; Tr. 7		
PX0185	Petrylak, et al., Evaluation of Prostate-Specific Antigen Declines for Surrogacy in Patients Treated on SWOG 99-16, J. Natl Cancer Inst. Volume 98 Issue 8: pp. 516-521	JX2, dated May 24, 2011; Tr. 7		
PX0186	Beer, et al., Double-Blinded Randomized Study of High-Dose Calcitriol Plus Docetaxel in	JX2, dated May 24, 2011; Tr. 7		

PX	Description	Where Admitted	Tr. Pages Where Discussed	In Camera
	Androgen- Independent Prostate Cancer: A Report From the ASCENT Investigators, J. Clin. Oncol. 2007Feb 20; 25(6): 669-74			
PX0187	Benchikh El Fegoun, et al., PSA and Follow-up after Treatment of Prostate Cancer, Prog. Urol. 2008 Mar; 18(3):137-44	JX2, dated May 24, 2011; Tr. 7		
PX0188	Roberts, et al., PSA Doubling Time as a Predictor of Clinical Progression after Biochemical Failure Following Radical Prostatectomy for Prostate Cancer, Mayo Clin. Proc. 2001 Jun;76(6): 576-81	JX2, dated May 24, 2011; Tr. 7		
PX0189	Expert Report and Attached Exhibitsor Appendices of Irwin Goldstein, M.D., re In the Matter of Pom Wonderful LLC and Roll International Corp and Stewart A. Resnick, Lynda Rae Resnick, and Matthew Tupper, Docket No. 9344	JX2, dated May 24, 2011; Tr. 7		
PX0190	Esposito K, Giugliano F, Maiorino MI, and Giugliano D, Dietary Factors, Mediterranean Diet and Erectile Dysfunction, J. Sex Med 2010; 7:2338-2345	JX2, dated May 24, 2011; Tr. 7		
PX0191	Bechara A, Casabe A, De Bonis W,Helien A, and Bertolino MV, Recreational Use of Phsphodiesterase Type 5 Inhibitors by Healthy Young Men, J. Sex Med.2010; 7: 3736-3742	JX2, dated May 24, 2011; Tr. 7		

PX	Description	Where Admitted	Tr. Pages Where Discussed	In Camera
PX0192	Expert Report and Attached Exhibits or Appendices of David Heber, MD, PhD, FACP, FACN, CNS, re In the Matter of Pom Wonderful LLC andRoll International Corp and Stewart A. Resnick, Lynda Rae Resnick, and Matthew Tupper, Docket No. 9344	JX2, dated May 24, 2011; Tr. 7	Tr. 2067 - 2188 Tr. 2256 - 2313	
PX0192a01	David Heber CV	JX2, dated May 24, 2011; Tr. 7		
PX0193	Michels KB, Willett WC, The Women's Health Initiative Randomized Controlled Dietary Modification Trial: a post mortem, Breast Cancer Res Treat. 2009;114:1-6	JX2, dated May 24, 2011; Tr. 7		
PX0194	Wallace K, Baron JA, Cole BF, Sandler RS, Karagas MR, Beach MA, Haile RW, Burke CA, Pearson LH, Mandel JS, Rothstein R, Snover DC, Effect of calcium supplementation on the risk of large bowel polyps, J. Natl. Cancer Inst. 2004; 96:921-5	JX2, dated May 24, 2011; Tr. 7		
PX0195	Perez-Vicente A, Gil-Izquierdo A,Garcia-Viguera C, In vitro gastrointestinal digestion study of pomegranate juice phenolic compounds, anthocyanins, and vitamin C, J. Agric. Food Chem.2002;50:2308-12	JX2, dated May 24, 2011; Tr. 7		
PX0196	Mullen W, Edwards CA, Serafini	JX2, dated May 24, 2011;		

PX	Description	Where Admitted	Tr. Pages Where Discussed	In Camera
	M,Crozier A, Bioavailability of pelargonidin-3-O-glucoside and its metabolites in humans following the ingestion of strawberries with and without cream, J. Agric. Food Chem.2008;56:713-9	Tr. 7		
PX0197	Heber D, Unpublished Data Presented to the California Strawberry Commission	JX2, dated May 24, 2011; Tr. 7		
PX0198	"What Color is Your Diet" by DavidHeber, M.D., Ph.D.	JX2, dated May 24, 2011; Tr. 7		
PX0199	Borges G, Mullen W, Crozier A, Comparison of the polyphenolic composition and antioxidant activity of European commercial fruit juices, Food Funct., 2010, 1, 73-83	JX2, dated May 24, 2011; Tr. 7		
PX0200	Pollard HB, Levine MA, Eidelman O, Pollard M, Pharmacological ascorbic acid suppresses syngeneic tumor growth and metastases in hormone refractory prostate cancer, In Vivo.2010 May-June 24(3):249-55	JX2, dated May 24, 2011; Tr. 7		
PX0201	Li Z, Seeram NP, Lee R, Thames G, Minutti C, Wang HJ, Heber D,Plasma clearance of lovastatin versus Chinese red yeast rice in healthy volunteers, J. Altern. Complement. Med., 2005; 11:1031-8	JX2, dated May 24, 2011; Tr. 7		
PX0202	Ridker PM, Statin therapy for elevated hsCRP: what are the public health implications?, Am. J. Manag. Care,	JX2, dated May 24, 2011; Tr. 7		

PX	Description	Where Admitted	Tr. Pages Where Discussed	In Camera
	2010; 16:561-2			
PX0203	Van Helden YG, Keijer J, Heil SG,Pico C, Palou A, Oliver P, Munnia A, Briede JJ, Peluso M. Franssen-van Hal NL, van Schooten FJ, Goldschalk RW, Beta-carotene affects oxidative stress-related DNA damage in lung epithelial cells and in ferret lung, Carcino	JX2, dated May 24, 2011; Tr. 7		
PX0204	Blumberg JB, Frei B, Why Clinical Trials of vitamin E and cardiovascular diseases may be fatally flawed, Free Radical Biol. Med, 2007; 43:1388-93	JX2, dated May 24, 2011; Tr. 7		
PX0205	Wolff T, Miller T, Ko S, Aspirin for the primary prevention of cardiovascular events: an update of the evidence for the U.S. Preventive services Task Force, Ann Intern Med., 2009;150:405-10	JX2, dated May 24, 2011; Tr. 7		
PX0206	Expert Report and Attached Exhibitsor Appendices of Denis R. Miller, MD, re In the Matter of Pom Wonderful LLC and Roll International Corp and Stewart A. Resnick, Lynda Rae Resnick, and Matthew Tupper,Docket No. 9344	JX2, dated May 24, 2011; Tr. 7	Tr. 2067 - 2188	
PX0207	Albrecht M, Jiang W, Kumi-Diaka J, et al. (2004). Pomegranate extracts potently suppress proliferation, xenograft growth, and invasion of human prostate cancer cells. J Med	JX2, dated May 24, 2011; Tr. 7		

PX	Description	Where Admitted	Tr. Pages Where Discussed	In Camera
	Food 7: 274-283, 2004			
PX0208	Armstrong AJ, Garrett-Mayer ES, Yang YC, et al (2007). A contemporary prognostic nomogram for men with hormone-refractory metastatic prostate cancer: a TAX327study analysis. Clin Cancer Res 2007;13: 6396-6403	JX2, dated May 24, 2011; Tr. 7		
PX0209	Beals JH, Muris TJ, Pitofsky R, InDefense of the Pfizer Factors, August2010	JX2, dated May 24, 2011; Tr. 7		
PX0210	Freedland SJ, Humphreys EB, Mangold LA, et al. Death in patients with recurrent prostate cancer after radical prostatectomy: prostate-specific antigen doubling time subgroups and their associated contribution to all-cause mortality. J Clin Oncol 2007; 25:	JX2, dated May 24, 2011; Tr. 7		
PX0211	Hafeez BB, Siddiqui IA, Asim M, et al. A dietary anthocyanidin delphinidin induces apoptosis of human prostate cancer PC3 cells: in vitro and in vivo involvement of nuclear factor-.B, Cancer Research 2008; 68: 8564-72	JX2, dated May 24, 2011; Tr. 7		
PX0212	Kahn N, Hadi N, Afaq F, et al. Pomegranate fruit extract inhibits prosurvival pathways in human A549 lung carcinoma cells and tumor growth in athymic nude mice.	JX2, dated May 24, 2011; Tr. 7		

PX	Description	Where Admitted	Tr. Pages Where Discussed	In Camera
	Carcinogenesis 2007; 28: 163-173			
PX0213	Kahn N, Afaq F, Kweon M-H. Oral consumption of pomegranate fruit extract inhibits growth and progression of primary lung tumors in mice. Cancer Res 2007; 67: 3475-82	JX2, dated May 24, 2011; Tr. 7		
PX0214	Lansky EP, Jiang W, Mo H, et al. Possible synergistic CaP suppression by anatomically discrete pomegranate fractions. Invest New Drugs 2005; 23:11-20	JX2, dated May 24, 2011; Tr. 7		
PX0215	Loeb S, Catalona WJ.What to do with an abnormal PSA test? Oncologist2008;13:299-05	JX2, dated May 24, 2011; Tr. 7		
PX0216	Miller DR, Anderson GT, Stark JJ, et al. Phase I/II trial of shark cartilage in the treatment of advanced cancer, J Clin Oncol 1998; 16: 3649-3655	JX2, dated May 24, 2011; Tr. 7		
PX0217	Roberts SG, Blute ML, Bergstrath EJ et al PSA doubling time as a predictor of clinical progression after biochemical failure following radical prostatectomy for prostate cancer. Mayo Clin Proc 2001; 76: 571-72	JX2, dated May 24, 2011; Tr. 7		
PX0218	Scher HI, Halabi S, Tannock I, et al. Prostate cancer clinical trial endpoints: ”RECIST”ing a step backwards. Clin Cancer Res 2005;11: 5223-32	JX2, dated May 24, 2011; Tr. 7		
PX0219	Scher HI, Halabi S, Tannock I, et al.Design and endpoints of clinical trials for patients with progressive	JX2, dated May 24, 2011; Tr. 7		

PX	Description	Where Admitted	Tr. Pages Where Discussed	In Camera
	prostate cancer and castrate levels of testosterone: recommendations of the Prostate Cancer Clinical Trials Working Group. J Clin Oncol 2008;26: 1			
PX0220	Senn HJ, Morant R. Chemoprevention of breast and prostate cancers: where do we stand? Ann Oncol 2006; 19: 4234-4247	JX2, dated May 24, 2011; Tr. 7		
PX0221	Singh RP, Agarwal R. Mechanism of action of novel agents for prostate cancer chemoprevention. Endocrine Related Cancer 2006; 13: 751-778	JX2, dated May 24, 2011; Tr. 7		
PX0222	Walczak JR, Carducci MA. Prostate cancer: a practical approach in current management of recurrent disease. Mayo Clin Proc 2007; 82:243-249	JX2, dated May 24, 2011; Tr. 7		
PX0223	Expert Report and Attached Exhibits or Appendices of David J. Reibstein, Survey of POM wonderful 100% Pomegranate Users, Survey Analysis, re In the Matter of Pom WonderfulLLC and Roll International Corp and Stewart A. Resnick, Lynda Rae Resnick, and Matt	JX2, dated May 24, 2011; Tr. 7	Tr. 2480 - 2586 Tr. 2651 - 2761	
PX0224	Pom Wonderful A&U study FullReport, June 2009	JX2, dated May 24, 2011; Tr. 7	Tr. 2480 - 2586 Tr. 2651 - 2761	
PX0225	POM Wonderful Ad Campaign evaluation-Presentation by Bovitz Research Group	JX2, dated May 24, 2011; Tr. 7	Tr. 2480 - 2586	
PX0226	Esomar 26 Sample	JX2, dated May 24, 2011;		

PX	Description	Where Admitted	Tr. Pages Where Discussed	In Camera
		Tr. 7		
PX0227	POM A&U Study Questionnaire	JX2, dated May 24, 2011; Tr. 7	Tr. 2480 - 2586 Tr. 2651 - 2761	
PX0228	Reibstein Table E with Text and IDfor Responses	JX2, dated May 24, 2011; Tr. 7		
PX0229	Reibstein Table F2I2 with Text and IDfor Responses	JX2, dated May 24, 2011; Tr. 7		
PX0230	Reibstein Table G2J2 with Text andID for Responses	JX2, dated May 24, 2011; Tr. 7		
PX0231	Reibstein Table K1 with Text and IDfor Responses	JX2, dated May 24, 2011; Tr. 7		
PX0232	Reibstein Verbatim Responses	JX2, dated May 24, 2011; Tr. 7		
PX0233	Reibstein Data Tables	JX2, dated May 24, 2011; Tr. 7	Tr. 2480 - 2586	
PX0234	December 2008 AccentHealth PanelAd Effectiveness	JX2, dated May 24, 2011; Tr. 7		
PX0235	Accent Health POM Wonderful AdImpact & Effectiveness Study March2009	JX2, dated May 24, 2011; Tr. 7		
PX0236	Bovitz FINAL POM CampaignEvaluation	JX2, dated May 24, 2011; Tr. 7		
PX0237	Reibstein Survey Questionnaire	JX2, dated May 24, 2011; Tr. 7	Tr. 2651 - 2761	
PX0238	Reibstein Table F1I1	JX2, dated May 24, 2011; Tr. 7		
PX0239	Reibstein Table G1J1	JX2, dated May 24, 2011; Tr. 7		
PX0240	Reibstein Table H	JX2, dated May 24, 2011; Tr. 7		
PX0241	Reibstein Table L1	JX2, dated May 24, 2011;		

PX	Description	Where Admitted	Tr. Pages Where Discussed	In Camera
		Tr. 7		
PX0242	Reibstein CV	JX2, dated May 24, 2011; Tr. 7		
PX0243	Objections of Respondent Roll Global LLC to Notice of Deposition Pursuant to Rule of Practice §3.33(c)(1)	JX2, dated May 24, 2011; Tr. 7		
PX0244	Objections of Respondent POM Wonderful LLC to Notice of Deposition Pursuant to Rule of Practice §3.33(c)(1)	JX2, dated May 24, 2011; Tr. 7		
PX0245	POM Wonderful's Deposition Notice of Frank M. Sacks, M.D.	JX2, dated May 24, 2011; Tr. 7		
PX0246	POM Wonderful's Deposition Notice of Jonathan Stampfer, M.D.	JX2, dated May 24, 2011; Tr. 7		
PX0247	POM Wonderful's Deposition Notice of James A. Eastham, M.D.	JX2, dated May 24, 2011; Tr. 7		
PX0248	POM Wonderful's Deposition Notice of Arnold Melman, M.D.	JX2, dated May 24, 2011; Tr. 7		
PX0249	Lynda Rae Resnick's Responses and Objections to FTC's First Request for Production of Documents and Not Objected to by Respondents	JX2, dated May 24, 2011; Tr. 7		
PX0250	Lynda Rae Resnick's Response to First Set of Interrogatories and Documents Referenced Therein and Not Objected to by Respondents	JX2, dated May 24, 2011; Tr. 7		
PX0252	Matthew Tupper's Responses and Objections to FTC's First Request for Production of Documents and Documents Referenced Therein and Not Objected to by Respondents	JX2, dated May 24, 2011; Tr. 7		

PX	Description	Where Admitted	Tr. Pages Where Discussed	In Camera
PX0253	Roll International Corp.'s Response to First set of Interrogatories and Documents Referenced Therein and Not Objected to by Respondents	JX2, dated May 24, 2011; Tr. 7		
PX0255	POM Wonderful LLC's Response to First set of Interrogatories and Documents Referenced Therein and Not Objected to by Respondents	JX2, dated May 24, 2011; Tr. 7		
PX0258	POM Wonderful LLC's Responses toand Objections to FTC's First Request For Production of Documents and Documents Referenced Therein and Not Objected to by Respondents	JX2, dated May 24, 2011; Tr. 7		
PX0260	Stewart A. Resnick's Response to First Set of Interrogatories and Documents Referenced Therein and Not Objected to by Respondents	JX2, dated May 24, 2011; Tr. 7		
PX0261	Stewart A. Resnick's Supplemental Responses to First Set of Interrogatories and Documents Referenced Therein and Not Objected to by Respondents	JX2, dated May 24, 2011; Tr. 7		
PX0262	Stewart A. Resnick's Responses and Objections to FTC's First Request for Production of Documents and Documents Referenced Therein and Not Objected to by Respondents	JX2, dated May 24, 2011; Tr. 7		
PX0263	Complaint Counsel's Response to Respondent POM Wonderful LLC's First Set of Interrogatories and Documents Referenced Therein and	JX2, dated May 24, 2011; Tr. 7		

PX	Description	Where Admitted	Tr. Pages Where Discussed	In Camera
	Not Objected to by Respondents			
PX0264	Complaint Counsel's Response to Respondent POM Wonderful LLC's First Set of Requests for Production of Documents and Things and Documents and Documents Referenced Therein and Not Objected to by Respondents	JX2, dated May 24, 2011; Tr. 7		
PX0265	Complaint Counsel's Response to Respondent POM Wonderful LLC's Second Set of Interrogatories and Documents Referenced Therein and Not Objected to by Respondents	JX2, dated May 24, 2011; Tr. 7		
PX0266	Complaint Counsel's Response to Respondent POM Wonderful LLC's Second Set of Requests for Production of Documents and Things and Documents Referenced Therein and Not Objected to by Respondents	JX2, dated May 24, 2011; Tr. 7		
PX0267	Complaint Counsel's Second Supplemental Response to Respondent POM Wonderful LLC's First Set of Interrogatories and Documents Referenced Therein and Not Objected to by Respondents	JX2, dated May 24, 2011; Tr. 7		
PX0268	Complaint Counsel's Response to Respondent POM Wonderful LLC's Requests for Admissions and Documents Referenced Therein and Not Objected to by Respondents	JX2, dated May 24, 2011; Tr. 7		
PX0269	Complaint Counsel's Response to	JX2, dated May 24, 2011;		

PX	Description	Where Admitted	Tr. Pages Where Discussed	In Camera
	Respondent Roll International Corporation's Requests for Admission and Documents Referenced Therein and Not Objected to by Respondents	Tr. 7		
PX0270	Complaint Counsel's Response to Respondent Matthew Tupper's Requests for Admission and Documents Referenced Therein and Not Objected to by Respondents	JX2, dated May 24, 2011; Tr. 7		
PX0271	Non-Party Bovitz Research Group Inc.'s Responses to Complaint Counsel's Subpoena Duces Tecum and Documents Referenced Therein and Not Objected to by Respondents	JX2, dated May 24, 2011; Tr. 7		
PX0276	Initial Disclosures of Respondents and Documents Referenced Therein and Not Objected to by Respondents	JX2, dated May 24, 2011; Tr. 7		
PX0277	Respondent's First Supplemental Disclosures and Documents Referenced Therein and Not Objected to by Respondents	JX2, dated May 24, 2011; Tr. 7		
PX0278	Third Supplemental Initial Disclosures of Respondents and Documents Referenced Therein and NotObjected to by Respondents	JX2, dated May 24, 2011; Tr. 7		
PX0279	Complaint Counsel's Initial Disclosures and Documents Referenced Therein and Not Objected to by Respondents	JX2, dated May 24, 2011; Tr. 7		
PX0280	Complaint Counsel's First Supplement to Initial Disclosures and	JX2, dated May 24, 2011; Tr. 7		

PX	Description	Where Admitted	Tr. Pages Where Discussed	In Camera
	Documents Referenced Therein and Not Objected to by Respondents			
PX0281	Protective Order Governing DiscoveryMaterial	JX2, dated May 24, 2011; Tr. 7		
PX0294	Picture of Elixir Sulfanilamide (Available at http://www.asmalldoseof.org/historyof tox/1900-1930s/sulfanilamide.gif)	JX2, dated May 24, 2011; Tr. 7		
PX0296	Rebuttal Report and SupportingMaterials Submitted by Michael B. Mazis, Ph.D re In the Matter of Pom Wonderful LLC and Roll International Corp and Stewart A. Resnick, Lynda Rae Resnick, and Matthew Tupper, Docket No. 9344			JX2, dated May 24, 2011; Tr. 7
PX0325	Exhibits to Deposition of Fiona Posell In the Matter of Pom Wonderful dated January 19, 2011 and accompanying exhibits not objected to by Respondents	JX2, dated May 24, 2011; Tr. 7		
PX0326	Transcripts and Exhibits to Deposition of Bradley Gillespie In the Matter of Pom Wonderful dated January 20, 2011 and accompanying exhibits not objected to by Respondents	JX2, dated May 24, 2011; Tr. 7		JX2, dated May 24, 2011; Tr. 7
PX0327	Exhibits to Deposition of Staci Glovsky In the Matter of Pom Wonderful dated January 12, 2011 and accompanying exhibits not objected to by Respondents	JX2, dated May 24, 2011; Tr. 7		JX2, dated May 24, 2011; Tr. 7
PX0328	Exhibits to Deposition of Jeffrey A.	JX2, dated May 24, 2011;		

PX	Description	Where Admitted	Tr. Pages Where Discussed	In Camera
	Rushton In the Matter of Pom Wonderful dated December 21, 2010 and accompanying exhibits not objected to by Respondents	Tr. 7		
PX0329	Exhibits to Deposition of Diane Kuyoomjian In the Matter of Pom Wonderful dated February 10, 2011 and accompanying exhibits not objected to by Respondents	JX2, dated May 24, 2011; Tr. 7		JX2, dated May 24, 2011; Tr. 7
PX0330	Exhibits to Deposition of Elizabeth Leow In the Matter of Pom Wonderful dated February 4, 2011 and accompanying exhibits not objected to by Respondents	JX2, dated May 24, 2011; Tr. 7	Tr. 2972 - 3038	JX2, dated May 24, 2011; Tr. 7
PX0331	Exhibits to Deposition of Matthew Tupper In the Matter of Pom Wonderful dated February 2, 2011 and accompanying exhibits not objected to by Respondents	JX2, dated May 24, 2011; Tr. 7		JX2, dated May 24, 2011; Tr. 7
PX0332	Exhibits to Deposition of Monique McLaws In the Matter of Pom Wonderful dated January 21, 2011 and accompanying exhibits not objected to by Respondents	JX2, dated May 24, 2011; Tr. 7		
PX0333	Exhibits to Deposition of Michael Perdigao In the Matter of Pom Wonderful dated January 14, 2011 and accompanying exhibits not objected to by Respondents	JX2, dated May 24, 2011; Tr. 7		JX2, dated May 24, 2011; Tr. 7
PX0334	Exhibits to Deposition of Robert Bryant In the Matter of Pom	JX2, dated May 24, 2011; Tr. 7		JX2, dated May 24, 2011; Tr. 7

PX	Description	Where Admitted	Tr. Pages Where Discussed	In Camera
	Wonderful dated February 3, 2011 and accompanying exhibits not objected to by Respondents			
PX0335	Exhibits to Deposition of Sarah Hemmati In the Matter of Pom Wonderful dated February 3, 2011 and accompanying exhibits not objected to by Respondents	JX2, dated May 24, 2011; Tr. 7		JX2, dated May 24, 2011; Tr. 7
PX0336	Exhibits to Deposition of Michael Aviram In the Matter of Pom Wonderful dated March 7, 2011 and accompanying exhibits not objected to by Respondents	JX2, dated May 24, 2011; Tr. 7		JX2, dated May 24, 2011; Tr. 7
PX0337	Exhibits to Deposition of Michael Anthony Carducci, M.D. In the Matter of Pom Wonderful dated December 13, 2010 and accompanying exhibits not objected to by Respondents	JX2, dated May 24, 2011; Tr. 7		JX2, dated May 24, 2011; Tr. 7
PX0338	Exhibits to Deposition of Michael H. Davidson In the Matter of Pom Wonderful dated December 3,2010 and accompanying exhibits not objected to by Respondents	JX2, dated May 24, 2011; Tr. 7		
PX0339	Exhibits to Deposition of Robert Clifford deGroof In the Matter of Pom Wonderful dated December21, 2010 and accompanying exhibits not objected to by Respondents	JX2, dated May 24, 2011; Tr. 7		JX2, dated May 24, 2011; Tr. 7
PX0340	Exhibits to Deposition of Christopher Forest In the Matter of Pom Wonderful dated December 6, 2010	JX2, dated May 24, 2011; Tr. 7		

PX	Description	Where Admitted	Tr. Pages Where Discussed	In Camera
	and accompanying exhibits not objected to by Respondents]			
PX0341	Exhibits to Deposition of David Heber, M.D., Ph.D. In the Matter of Pom Wonderful dated January 28,2011 and accompanying exhibits not objected to by Respondents	JX2, dated May 24, 2011; Tr. 7		JX2, dated May 24, 2011; Tr. 7
PX0342	Exhibits to Deposition of James O. Hill, Ph.D. In the Matter of Pom Wonderful dated December 15,2010 and accompanying exhibits not objectedto by Respondents	JX2, dated May 24, 2011; Tr. 7		
PX0343	Exhibits to Deposition of Kristen Hirsch In the Matter of Pom Wonderful dated December 15, 2010 and accompanying exhibits not objectedto by Respondents	JX2, dated May 24, 2011; Tr. 7		
PX0344	Exhibits to Deposition of Harley R. Liker, M.D. In the Matter of Pom Wonderful dated January 21, 2011 and accompanying exhibits not objected to by Respondents	JX2, dated May 24, 2011; Tr. 7		
PX0345	Exhibits to Deposition of Dr. Dean Ornish In the Matter of Pom Wonderful dated December 10,2010 and accompanying exhibits not objected to by Respondents	JX2, dated May 24, 2011; Tr. 7		JX2, dated May 24, 2011; Tr. 7
PX0346	Exhibits to Deposition of Harin Padma-Nathan, M.D. In the Matter of Pom Wonderful dated December7, 2010 and accompanying exhibits not	JX2, dated May 24, 2011; Tr. 7		JX2, dated May 24, 2011; Tr. 7

PX	Description	Where Admitted	Tr. Pages Where Discussed	In Camera
	objected to by Respondents			
PX0347	Exhibits to Deposition of Allan Pantuck, M.D. In the Matter of Pom Wonderful dated December 15, 2010 and accompanying exhibits not objected to by Respondents	JX2, dated May 24, 2011; Tr. 7		
PX0348	Transcript and Exhibits to Deposition of Dr. Michael Sumner In the Matter of Pom Wonderful dated December17, 2010 and accompanying exhibits not objected to by Respondents	JX2, dated May 24, 2011; Tr. 7		JX2, dated May 24, 2011; Tr. 7
PX0349	Transcript and Exhibits to Deposition of Arthur Burnett In the Matter of Pom Wonderful and accompanying exhibits not objectedto by Respondents	JX2, dated May 24, 2011; Tr. 7		
PX0350	Transcript and Exhibits to Deposition of Ronald Butters In the Matter of Pom Wonderful and accompanying exhibits not objected to by Respondents	JX2, dated May 24, 2011; Tr. 7	Tr. 2811 - 2965	
PX0351	Transcript and Exhibits to Deposition of Jean deKernion In the Matter of Pom Wonderful and accompanying exhibits not objected to by Respondents	JX2, dated May 24, 2011; Tr. 7	Tr. 3039 - 3127	
PX0352	Transcript and Exhibits to Deposition of Irwin Goldstein In the Matter of Pom Wonderful and accompanying exhibits not objected to by Respondents	JX2, dated May 24, 2011; Tr. 7	Tr. 2587 - 2644	

PX	Description	Where Admitted	Tr. Pages Where Discussed	In Camera
PX0353	Transcript and Exhibits to Deposition of David Heber In the Matter of Pom Wonderful and accompanying exhibits not objected to by Respondents	JX2, dated May 24, 2011; Tr. 7	Tr. 2067 - 2188	
PX0354	Transcript and Exhibits to Deposition of Denis Miller In the Matter of Pom Wonderful and accompanying exhibits not objectedto by Respondents	JX2, dated May 24, 2011; Tr. 7		
PX0355	Transcript and Exhibits to Deposition of Dean Ornish In the Matter of Pom Wonderful and accompanying exhibits not objected to by Respondents	JX2, dated May 24, 2011; Tr. 7		
PX0356	Transcript and Exhibits to Deposition of David Reibstein In the Matter of Pom Wonderful and accompanying exhibits not objected to by Respondents	JX2, dated May 24, 2011; Tr. 7	Tr. 2480 - 2586	
PX0357	Deposition transcript and accompanying exhibits of David Stewart In the Matter of Pom Wonderful	JX2, dated May 24, 2011; Tr. 7		
PX0358	Deposition transcript and accompanying exhibits of James Eastham In the Matter of Pom Wonderful	JX2, dated May 24, 2011; Tr. 7		
PX0359	Deposition transcript and accompanying exhibits of Michael Mazis In the Matter of Pom Wonderful	JX2, dated May 24, 2011; Tr. 7		
PX0360	Deposition transcript and accompanying exhibits of Arnold	JX2, dated May 24, 2011; Tr. 7		JX2, dated May 24, 2011; Tr. 7

PX	Description	Where Admitted	Tr. Pages Where Discussed	In Camera
	Melman In the Matter of Pom Wonderful			
PX0361	Deposition transcript and accompanying exhibits of Frank Sacks In the Matter of Pom Wonderful	JX2, dated May 24, 2011; Tr. 7		
PX0362	Deposition transcript and accompanying exhibits of Jonathan Stampfer In the Matter of Pom Wonderful	JX2, dated May 24, 2011; Tr. 7		
PX0364	Answer and Defenses ofRespondents and Attached Exhibits re In the Matter of Pom Wonderful LLC and Roll International Corp and Stewart A. Resnick, Lynda Rae Resnick, and Matthew Tupper, Docket No. 9344	JX2, dated May 24, 2011; Tr. 7		
PX0365	Michels KB, Nutritional epidemiology—past, present, future, International Journal of Epidemiology2003; 32: 486-488	JX2, dated May 24, 2011; Tr. 7		
PX0368-0001_001	POM Wonderful Medical Research Expenses Spreadsheet	JX2, dated May 24, 2011; Tr. 7		JX2, dated May 24, 2011; Tr. 7
PX0370	"Rubies in the Orchard" by LyndaResnick	JX2, dated May 24, 2011; Tr. 7		
PX0371	POM 100% Pomegranate 16 oz. Bottle (product and photos)	JX2, dated May 24, 2011; Tr. 7		
PX0372	POM 100% Pomegranate 8 oz. Bottle(product and photos)	JX2, dated May 24, 2011; Tr. 7		
PX0373	POMx Pills (product and photos)	JX2, dated May 24, 2011; Tr. 7		
PX0374	POMx Liquid (product and photos)	JX2, dated May 24, 2011; Tr. 7		

PX	Description	Where Admitted	Tr. Pages Where Discussed	In Camera
PX0382	Published Research on Pomegranate(CD)	JX2, dated May 24, 2011; Tr. 7		
PX0383	POM Wonderful Research Summit2003	JX2, dated May 24, 2011; Tr. 7		
PX0384	POM Wonderful Research Summit2004	JX2, dated May 24, 2011; Tr. 7		
PX0385	POM Wonderful Research Summit2005	JX2, dated May 24, 2011; Tr. 7		
PX0386-0001_001	POM Wonderful Research Summit2007	JX2, dated May 24, 2011; Tr. 7		
PX0387	POM Wonderful Research Summit2008	JX2, dated May 24, 2011; Tr. 7		
PX0429	Spec Sheets for POMx Pills, POMxLiquid, and 100% POM	JX2, dated May 24, 2011; Tr. 7		JX2, dated May 24, 2011; Tr. 7
PX0430	"Studies Show that 10 out of 10 People Don't Want to Die" Advertisement	JX2, dated May 24, 2011; Tr. 7		
PX0431	"The Power of POM in one little Pill" POMx Advertisement	JX2, dated May 24, 2011; Tr. 7		
PX0432	"The antioxidant superpill" POMxAdvertisement	JX2, dated May 24, 2011; Tr. 7		
PX0433	"Science, not Fiction" POMX Advertisement	JX2, dated May 24, 2011; Tr. 7		
PX0434	"Live Long Enough to Watch Your401(k) Recover" POMxAdvertisement	JX2, dated May 24, 2011; Tr. 7		
PX0435	"Healthy, Wealthy, Wise" POMxAdvertisement	JX2, dated May 24, 2011; Tr. 7		
PX0436	"Healthy, Wealthy, Wise" POMxAdvertisement	JX2, dated May 24, 2011; Tr. 7		
PX0437	"Your New Health Care Plan (No	JX2, dated May 24, 2011;		

PX	Description	Where Admitted	Tr. Pages Where Discussed	In Camera
	Town Hall Meeting Required.)" POMx Advertisement	Tr. 7		
PX0438	"The First Bottle You Should Open in 2010" POMx Advertisement	JX2, dated May 24, 2011; Tr. 7		
PX0439	"Take Out a Life InsuranceSupplement" POMx Advertisement	JX2, dated May 24, 2011; Tr. 7		
PX0440	"The Only Antioxidant SupplementRated X" POMx Advertisement	JX2, dated May 24, 2011; Tr. 7		
PX0441	"The Official Antioxidant ofCentenarians" POMx Advertisement	JX2, dated May 24, 2011; Tr. 7		
PX0442	"24 Scientific Studies Now in One Easy-to-Swallow Pill." POMx Advertisement	JX2, dated May 24, 2011; Tr. 7		
PX0443	"Make Them Wait Longer for TheirInheritance" POMx Advertisement	JX2, dated May 24, 2011; Tr. 7		
PX0444	"Our Philosophy on Aging: De-Fense! De-Fense!" POMx Advertisement	JX2, dated May 24, 2011; Tr. 7		
PX0445	"The power of POM in one little pill" POMx Advertisement	JX2, dated May 24, 2011; Tr. 7		
PX0446	Remarks by David C. Vladeck Director, FTC Bureau of Consumer Protection at the Promotion Marketing Association 32nd Annual Marketing Law Conference in Chicago, Illinois	JX2, dated May 24, 2011; Tr. 7		
PX0447	Remarks by David C. Vladeck,Director FTC Bureau of Consumer Protection at the Council for Responsible Nutrition Annual	JX2, dated May 24, 2011; Tr. 7		

PX	Description	Where Admitted	Tr. Pages Where Discussed	In Camera
	Symposium for the Dietary Supplement Industry in Rancho Palos Verdes, CA			
PX0448	Remarks by David C. Vladeck Director, FTC Bureau of Consumer Protection at the National Advertising Division Annual Conference in New York, NY	JX2, dated May 24, 2011; Tr. 7		
PX0449	Ben Rooney, POM Wonderful Charged with Selling Snake Oil, CNNMoney.com, quoting David C. Vladeck	JX2, dated May 24, 2011; Tr. 7		
PX0460	Ltr from D. Heber to M. Johnson re: Civil Investigative Demand	JX2, dated May 24, 2011; Tr. 7		
PX0461	Email string from J. Boubelik to M. Johnson re UCLA- Responses to Quereis	JX2, dated May 24, 2011; Tr. 7		
PX0462	Email string from E. Nach to C. Forest re CID Submmission	JX2, dated May 24, 2011; Tr. 7		
PX0463	Email string from E. Nach to J. Goldman re CID to Dean Ornish	JX2, dated May 24, 2011; Tr. 7		
PX0464	Email string from E. Whang to P. Harin re Civil Investigative Demand	JX2, dated May 24, 2011; Tr. 7		
PX0466	Iovate Health Science USA, Inc. Stipulated Final Judgment and Order for Permanent Injunction and Other Equitable Relief with the FTC	JX2, dated May 24, 2011; Tr. 7		
PX0467	Nestle Healthcare Nutrition Inc. Agreement Containing Consent Order with the FTC	JX2, dated May 24, 2011; Tr. 7		
PX0468	Nestle Healthcare Nutrition Inc.	JX2, dated May 24, 2011;		

PX	Description	Where Admitted	Tr. Pages Where Discussed	In Camera
	Decision and Order with FTC	Tr. 7		
PX0469	The Dannon Company, Inc. Agreement Containing Consent Order with FTC	JX2, dated May 24, 2011; Tr. 7		
PX0470	The Dannon Company, Inc. Decision and Order with FTC	JX2, dated May 24, 2011; Tr. 7		
PX0471	Mark Dreher Agreement ContainingConsent Order with FTC	JX2, dated May 24, 2011; Tr. 7		
PX0472	Memo from Risa Schulman to Stewart Resnick, et al., re: Summary of tests used to measure antioxidant power	JX2, dated May 24, 2011; Tr. 7		
PX0473	Memo from Risa Schulman to Matt Tupper re: Published articles on antioxidant activity of Poms – follow up to Norwegian article	JX2, dated May 24, 2011; Tr. 7		
PX0474	Memo from Risa Schulman to Matt Tupper, et al., re: Published articles on antioxidant activity of Poms – follow up to Norwegian article	JX2, dated May 24, 2011; Tr. 7		
PX0475	Aviram, DPPH assay v. other markers (ORAC, FRAP, TEAC) for antioxidant activity (with handwritten notations)	JX2, dated May 24, 2011; Tr. 7		
PX0476	Email from M. Aviram to L. Resnick, et al. re: POM (with attachment)	JX2, dated May 24, 2011; Tr. 7		
PX0477	Email from M. Dreher to L. Resnick, et al., re: Our Paper on the health benefits of the various parts of the pomegranate fruit was accepted	JX2, dated May 24, 2011; Tr. 7		
PX0478	Email from M. Aviram to L. Resnick, et al. re: The phrase for POM cardio	JX2, dated May 24, 2011; Tr. 7		

PX	Description	Where Admitted	Tr. Pages Where Discussed	In Camera
	protection			
PX0479	Email from M. Aviram to L. Resnick, et al. re: Our paper on the health benefits of the various parts of the pomegranate fruit was accepted	JX2, dated May 24, 2011; Tr. 7		
PX0480	Email from M. Dreher to L. Resnick re POM Wonderful Publications – Expert Reports	JX2, dated May 24, 2011; Tr. 7		
PX0481	Email from M. Aviram to M. Dreher w/attachment	JX2, dated May 24, 2011; Tr. 7		
PX0482-0001_001	Aviram PowerPoint titled The LipidResearch Laboratory	JX2, dated May 24, 2011; Tr. 7		
PX0484	Email string from L. Resnick to S. Resnick re Quote	JX2, dated May 24, 2011; Tr. 7	Tr. 2256 - 2313	
PX0485	Email string from R. Schulman to M. Tupper re: good news	JX2, dated May 24, 2011; Tr. 7		
PX0486	Email string from M. Dreher to M. Tupper re: Antioxidant article	JX2, dated May 24, 2011; Tr. 7		
PX0487	Email string from L. Resnick to D. Ornish	JX2, dated May 24, 2011; Tr. 7		
PX0488	Email string from M. Aviram to L. Resnick re: POM	JX2, dated May 24, 2011; Tr. 7		
PX0489	Email from M. Aviram to L. Resnick re: our research analyses plan for the beverage comparison to POM	JX2, dated May 24, 2011; Tr. 7		
PX0490	Email from M. Dreher to M. Tupperre: Scientists question benefits/risk of polyphenols	JX2, dated May 24, 2011; Tr. 7		
PX0494	Email from D. Heber to M. Dreher re: Letter for Marketing	JX2, dated May 24, 2011; Tr. 7		
PX0495	Email from M. Aviram to B. Gillespie	JX2, dated May 24, 2011;		

PX	Description	Where Admitted	Tr. Pages Where Discussed	In Camera
	re: study in RA patients	Tr. 7		
PX0496	Email from M. Aviram to B. Gillespie re: POM chapter	JX2, dated May 24, 2011; Tr. 7		
PX0497	Email from M. Aviram to B. Gillespie re: selective effect of PJ in patients with Haptoglobin 1 vs HP2	JX2, dated May 24, 2011; Tr. 7		
PX0498	Email from M. Aviram to M. Dreher re: our next report in our serious of POM cardio	JX2, dated May 24, 2011; Tr. 7		
PX0500	Email string from M. Aviram to M. Dreher re: Cardiovascular Health	JX2, dated May 24, 2011; Tr. 7		
PX0501	Email string from M. Aviram to M. Dreher re: who said that ACAI is even close to potency to PJ	JX2, dated May 24, 2011; Tr. 7		
PX0502	Email from M. Aviram to M. Dreher re: Cherries are goo but PJ is better	JX2, dated May 24, 2011; Tr. 7		
PX0503	Email string from M. Aviram to L. Resnick re: Our paper on the health benefits of the various parts of the pomegranate fruit was accepted	JX2, dated May 24, 2011; Tr. 7		
PX0504	Email string from M. Tupper to R. Pfeffer re: New Study – Pomegranate Juice Reduces Arterial Plaque	JX2, dated May 24, 2011; Tr. 7		
PX0505	Email from M. Aviram to L. Resnick re: The phrase for POM cardio protection	JX2, dated May 24, 2011; Tr. 7		
PX0506	Email string from M. Dreher to M. Tupper re Lou Ignarro Research Summary	JX2, dated May 24, 2011; Tr. 7		
PX0507	Ltr from D. Ornish to H. Liker	JX2, dated May 24, 2011; Tr. 7		

PX	Description	Where Admitted	Tr. Pages Where Discussed	In Camera
PX0508	Email string from M. Tupper to D. Ornish re: Good News	JX2, dated May 24, 2011; Tr. 7		
PX0510	Email from D. Ornish to S. Resnick re: good news	JX2, dated May 24, 2011; Tr. 7		
PX0511	Email from D. Ornish to M. Ohara re: Monday Interview	JX2, dated May 24, 2011; Tr. 7		
PX0512	Martin PowerPoint titled Top Ten Findings 4th Annual 2007 POM Wonderful Research Summit	JX2, dated May 24, 2011; Tr. 7		
PX0513	Email from D. Ornish to S. Resnick re: research manuscript	JX2, dated May 24, 2011; Tr. 7		
PX0514	Email sting from M. Aviram to L. Resnick re: New York Times article on heart disease	JX2, dated May 24, 2011; Tr. 7		
PX0515	POMx Your Partner in Promoting Lifelong Health, Volume 1, Issue 2: Prostate Health	JX2, dated May 24, 2011; Tr. 7		
PX0516	Creative Brief: POMx FSI	JX2, dated May 24, 2011; Tr. 7		
PX0517	Email from C. Nelson to B. Fisher re: Creative Brief – pomtruth web advertising	JX2, dated May 24, 2011; Tr. 7		
PX0518	Creative Brief: POMx WebsitePotency	JX2, dated May 24, 2011; Tr. 7		
PX0519	Email string from C. Nelson to C. Nelson re: Pomegranatetruth.com	JX2, dated May 24, 2011; Tr. 7		
PX0520	Email from M. Cregar to M. Perdigao re: Creative Briefs_2008 POM Juice	JX2, dated May 24, 2011; Tr. 7		
PX0521	Creative Brief: 2008 POM Juice – Real Age Dedicated Email Blast	JX2, dated May 24, 2011; Tr. 7		
PX0522	Email from C. Nelson to M. Perdigao	JX2, dated May 24, 2011;		

PX	Description	Where Admitted	Tr. Pages Where Discussed	In Camera
	re: TV Creative brief	Tr. 7		
PX0523	Email string from M. Shreeves to D. Kuyoomjian re: Creative Brief Event Booth	JX2, dated May 24, 2011; Tr. 7		
PX0524	Exhibits to Deposition of Stewart A. Resnick In the Matter of Pom Wonderful and accompanying exhibits not objected to by Respondents	JX2, dated May 24, 2011; Tr. 7		
PX0525	Deposition transcript of Lynda Resnick In the Matter of Pom Wonderful and accompanying exhibits not objected to by Respondents	JX2, dated May 24, 2011; Tr. 7		
PX0531	In the Matter of Daniel Chapter One, Initial Decision, Docket No. 9329	JX2, dated May 24, 2011; Tr. 7		

JX2 - Attachment B

PX	Description	Where Admitted	Tr. Pages Where Discussed	In Camera
PX0109	Schiffenbauer, The Anti-Bacterial and Anti-Viral Effects of 34 Natural Beverages (Unpublished report, 2006)	JX2, dated May 24, 2011; Tr. 7		
PX0137	Merkel DJ, Subtronic Toxicity Study (28 days) (Unpublished data 2006)	JX2, dated May 24, 2011; Tr. 7		
PX0301	Dietary Guidelines for Americans 2010	JX2, dated May 24, 2011; Tr. 7		
PX0302	2010 Dietary Guidelines for Americans, Backgrounder: History and	JX2, dated May 24, 2011; Tr. 7		

PX	Description	Where Admitted	Tr. Pages Where Discussed	In Camera
	Process			
PX0303	"MyPyramid.gov-Why is it important to eat fruit?" (http://www.mypyramid.gov/pyramid/fruits_why_print.htm l)	JX2, dated May 24, 2011; Tr. 7		
PX0304	Dietary Guidelines for Americans 2005	JX2, dated May 24, 2011; Tr. 7		
PX0305	2005 Dietary Guidelines Advisory Committee Report, Part D: Science Base, section 6: Selected Food Groups (Fruits and Vegetables, Whole Grains, and Milk Products)	JX2, dated May 24, 2011; Tr. 7		
PX0306	"Pomegranate: A Backyard Favorite", Agricultural Research/September 2001 by Marcia Wood	JX2, dated May 24, 2011; Tr. 7		
PX0307	"Food Compounds that Kill Test-Tube Cancer Cells Analyzed" by Marcia Wood (http://www.ars.usda.gov/is/pr/2008/080304)	JX2, dated May 24, 2011; Tr. 7		
PX0308	"Eating is Stressful, but Antioxidants Can Help" by Marcia Wood (http://www.ars.usda.gov/is/pr/2008/080313.htm)	JX2, dated May 24, 2011; Tr. 7		
PX0309	"More Strawberries, More Antioxidant Absorption" by Rosalie Marion Bliss (http://www.ars.usda.gov/is/pr/2008/080821.htm)	JX2, dated May 24, 2011; Tr. 7		
PX0310	Food and Nutrition Research Briefs January 2007 (http://www.ars.usda.gov/is/np/fnrb/fnrb01017.htm)	JX2, dated May 24, 2011; Tr. 7		

PX	Description	Where Admitted	Tr. Pages Where Discussed	In Camera
PX0311	Food and Nutrition Research Briefs April 2007 (http://www.ars.usda.gov/is/np/fnrb/fnrb0407.htm)	JX2, dated May 24, 2011; Tr. 7		
PX0312	Food and Nutrition Research Briefs July 2006 (http://www.ars.usda.gov/is/np/fnrb/fnrb0706.htm)	JX2, dated May 24, 2011; Tr. 7		
PX0313	Food and Nutrition Research Briefs October 2006 (http://www.ars.usda.gov/is/np/fnrb/fnrb1006.htm)	JX2, dated May 24, 2011; Tr. 7		
PX0314	"With Inflammation, It's Better to Have a Cool Head" by Rosalie Marion Bliss (http://www.ars.usda.gov/is/pr/2007/070821.htm)	JX2, dated May 24, 2011; Tr. 7		
PX0315	Food and Nutrition Research Briefs October 2005 (http://www.ars.usda.gov/is/np/fnrb1005.htm)	JX2, dated May 24, 2011; Tr. 7		
PX0316	Food and Nutrition Research Briefs July 2004 (http://www.ars.usda.gov/is/np/fnrb/fnrb0704.htm)	JX2, dated May 24, 2011; Tr. 7		
PX0317	Food and Nutrition Research Briefs January 2002 (http://www.ars.usda.gov/is/np/fnrb/fnrb102.htm)	JX2, dated May 24, 2011; Tr. 7		
PX0318	"Antioxidant effects from Eating Almonds" by Rosalie Marion Bliss (http://www.ars.usda.gov/is/pr/2	JX2, dated May 24, 2011; Tr. 7		

PX	Description	Where Admitted	Tr. Pages Where Discussed	In Camera
	008/081017.htm)			
PX0319	"Eat for a Healthy Heart," FDA Consumer Health Information/U.S. Food and Drug Administration January 2010	JX2, dated May 24, 2011; Tr. 7		
PX0320	Fruit and Vegetable of the Month: Pomegranate (http://www.fruitsandveggiesmatter.gov/month/pomegranate.html)	JX2, dated May 24, 2011; Tr. 7		
PX0321	NCI Cancer Bulletin: Featured Clinical Trial: Pomegranate Juice for PSA-Only Prostate Cancer Recurrence (http://www.cancer.gov/ncicancerbulletin/NCI_Cancer_Bulletin_092507/page9)	JX2, dated May 24, 2011; Tr. 7		
PX0322	Influences on Nutritional Practices and Wellness Across the Lifespan: Psychological, Cultural and Social Influences on Food Choices Lesson Grade Levels: 7-12 (http://healthymeals.nal.usda.gov/hsmrs/Nutrition%20Expeditions/Unit%20I%20Lesson%201%20%20Psycho	JX2, dated May 24, 2011; Tr. 7		
PX0323	"Common Prostate Cancer Questions Answered" by the American Cancer Society (http://www.cancer.org/Cancer/news/Features/commonprostate-cancer-questionsanswered?)	JX2, dated May 24, 2011; Tr. 7		

PX	Description	Where Admitted	Tr. Pages Where Discussed	In Camera
PX0324	"Pomegranate: MedlinePlus Supplements" by the U.S. National Library of Medicine, NIH National Institutes of Health (http://www.nlm.nih.gov/medlineplus/druginfo/natural/392.html?debugMode=false)	JX2, dated May 24, 2011; Tr. 7		
PX0377	Hodi FS et al, Improved Survival with Ipilimumab in Patients with Metastatic Melanoma, N. Engl. J. Med. 2010;363:711-23	JX2, dated May 24, 2011; Tr. 7		
PX0378	NY Times Article "Approval for Drug that Treats Melanoma" by Andrew Pollack	JX2, dated May 24, 2011; Tr. 7		
PX0379	FDA News Release "FDA approves new treatment for a type of late-stage skin cancer"	JX2, dated May 24, 2011; Tr. 7		
PX0380	LA Times Article "FDA approves melanoma drug" by Andrew Zajac	JX2, dated May 24, 2011; Tr. 7		
PX0381	Press Release "FDA Approves Yervoy (ipilimumab) for the Treatment of Patients with Newly Diagnosed or Previously-Treated Unresectable or Metastatic Melanoma, the Deadliest Form of Skin Cancer"	JX2, dated May 24, 2011; Tr. 7		
PX0389	Prostate Cancer Research Institute "Pomegranates and Prostate Health: A Research Report" (http://www.prostatecancer.org/education/selfempower/Pomegranates_Prostate	JX2, dated May 24, 2011; Tr. 7		

PX	Description	Where Admitted	Tr. Pages Where Discussed	In Camera
	_Health_Dr)			
PX0390	"Pomegranate juice helps keep PSA levels stable in men with prostate cancer" (http://www.fonteine.com/nieuws/prostate1.html)	JX2, dated May 24, 2011; Tr. 7		
PX0391	Research Studies on Blueberries (CD)	JX2, dated May 24, 2011; Tr. 7		
PX0392	Afaq, Farrukh, Cancer Chemoprevention by Pomegranate Fruit Extract, Project No. 5R1AT002429-02 (NIH Website)	JX2, dated May 24, 2011; Tr. 7		
PX0393	Afaq, Farrukh, Cancer Chemoprevention by Pomegranate Fruit Extract, Project No. 1R21AT002429-01A2 (NIH Website)	JX2, dated May 24, 2011; Tr. 7		
PX0394	Farkas D, Interactions Between Pomegranate Juice and CYP3A, ,Project No. 5F32AT003540-02 (NIH Website)	JX2, dated May 24, 2011; Tr. 7		
PX0395	Farkas D, Interactions Between Pomgranate and CYP3A, Project No. 1F32AT003540-01 (NIH Website)	JX2, dated May 24, 2011; Tr. 7		
PX0396	Ferriero DM, Mechanisms of Ischemic Neonatal Brain Injury, Project No. 5P50NS035902-13 (NIH Website)	JX2, dated May 24, 2011; Tr. 7		
PX0397	Ferriero DM, Mechanisms of Ischemic Neonatal Brain Injury, Project No. 5P50NS035902-12 (NIH Website)	JX2, dated May 24, 2011; Tr. 7		

PX	Description	Where Admitted	Tr. Pages Where Discussed	In Camera
PX0398	Ferriero DM, Mechanisms of Ischemic Neonatal Brain Injury, Project No. 2P5ONS035902-11A1 (NIH Website)	JX2, dated May 24, 2011; Tr. 7		
PX0399	Haqqi TM, Mechanisms of Chondroprotection by Pomegranate Fruit Extract, Project No. 5R01AT003627-05 (NIH Website)	JX2, dated May 24, 2011; Tr. 7		
PX0400	Haqqi TM, Suppression of MMP-13 Expression in Arthritis by Pomegranate, Project No. 1R01AT005520-01A1 (NIH Website)	JX2, dated May 24, 2011; Tr. 7		
PX0401	Haqqi TM, Chondroprotective Activity of Pomegranate Extract, Project No. 5R21AT004026-03 (NIH Website)	JX2, dated May 24, 2011; Tr. 7		
PX0402	Haqqi TM, Mechanisms of Chondroprotection by Pomegranate Fruit Extract, Project No. 7R01AT003627-04 (NIH Website)	JX2, dated May 24, 2011; Tr. 7		
PX0403	Haqqi TM, Chondroprotective Activity of Pomegranate Extract, Project No. 1R21AT004026-01A2 (NIH Website)	JX2, dated May 24, 2011; Tr. 7		
PX0404	Haqqi TM, Chondroprotective Activity of Pomegranate Extract, Project No. 7R21AT004026-02 (NIH Website)	JX2, dated May 24, 2011; Tr. 7		
PX0405	Haqqi TM, Mechanisms of Chondroprotection by Pomegranate	JX2, dated May 24, 2011; Tr. 7		

PX	Description	Where Admitted	Tr. Pages Where Discussed	In Camera
	Fruit Extract, Project No. 7R01AT003627-02 (NIH Website)			
PX0406	Haqqi TM, Mechanisms of Chondroprotection by Pomegranate Fruit Extract, Project No. 1R01AT003627-01A1 (NIH Website)	JX2, dated May 24, 2011; Tr. 7		
PX0407	Holtzman DM, Effects of Polyphenols on Neonatal HI Brain Injury, Project No. 2P50NS035902-11A1 (NIH Website)	JX2, dated May 24, 2011; Tr. 7		
PX0408	Mukhtar H, Pomegranate for Chemoprevention and Chemotherapy of Prostate Cancer, Project No. 5R01CA120451-04 (NIH Website)	JX2, dated May 24, 2011; Tr. 7		
PX0409	Mukhtar H, Pomegranate for Chemoprevention and Chemotherapy of Prostate Cancer, Project No. 5R01CA120451-03 (NIH Website)	JX2, dated May 24, 2011; Tr. 7		
PX0410	Mukhtar H, Pomegranate for Chemoprevention and Chemotherapy of Prostate Cancer, Project No. 5R01CA120451-02 (NIH Website)	JX2, dated May 24, 2011; Tr. 7		
PX0411	Mukhtar H, Pomegranate for Chemoprevention and Chemotherapy of Prostate Cancer, Project No. 1R01CA120451-01A1 (NIH Website)	JX2, dated May 24, 2011; Tr. 7		
PX0412	Ramanujam RP, Innovative Cell-Based Urinalysis for Patient Adherence, Project No. 3R44AT004118-03S1	JX2, dated May 24, 2011; Tr. 7		

PX	Description	Where Admitted	Tr. Pages Where Discussed	In Camera
	(NIH Website)			
PX0413	Ramanujam RP, Innovative Cell-Based Urinalysis for Patient Adherence, Project No. 2R44AT004118-02 (NIH Website)	JX2, dated May 24, 2011; Tr. 7		
PX0414	Reliene R, Prevention of Genetic Instability by Pomegranate in OGG1/MYH Deficient Mice, Project No. 5R03CA133928-02 (NIH Website)	JX2, dated May 24, 2011; Tr. 7		
PX0415	Reliene R, Prevention of Genetic Instability by Pomegranate in OGG1/MYH Deficient Mice, Project No. 7R03CA133928-03 (NIH Website)	JX2, dated May 24, 2011; Tr. 7		
PX0416	Reliene R, Prevention of Genetic Instability by Pomegranate in OGG1/MYH Deficient Mice, Project No. 1R03CA133928-01 (NIH Website)	JX2, dated May 24, 2011; Tr. 7		
PX0417	Ronningen L, Pomegranate Tablets vs Placebo: Effects on Symptoms of Benign Prostatic Hypera, Project No. 5M01RR000827-33 (NIH Website)	JX2, dated May 24, 2011; Tr. 7		
PX0418	Vadhanam MV, Identification and Synergism of Bioactive Components of Pomegranate Juice in Pros, Project No. 1R21CA143676-01A1 (NIH Website)	JX2, dated May 24, 2011; Tr. 7		
PX0419	"Pomegranate: For Cancer and Heart Disease" (http://www.healthfreedom.info/ pomegranates_for_cancer _and_heart%20disease.htm)	JX2, dated May 24, 2011; Tr. 7		
PX0420	"Pomegranate Juice Could Benefit	JX2, dated May 24, 2011;		

PX	Description	Where Admitted	Tr. Pages Where Discussed	In Camera
	Diabetics (press release)" Natural News (http://www.naturalnews.com/020754.html)	Tr. 7		
PX0421	"Pomegranate-More than just a Juice" Your Diet, April 2011 Issue (http://umanitoba.fitdv.com/new/articles/article.php?artid= 715)	JX2, dated May 24, 2011; Tr. 7		
PX0422	"Pomegranates and PSA Scores" WebUrology (http://weburology.org/2011/03/03/pomegranates-and-psascores/)	JX2, dated May 24, 2011; Tr. 7		
PX0423	"Pomegranate packs a punch" Chicago Tribune (http://articles.chicagotribune.com/2004-03-09/news/0403090044_1_pomegranate-juice-pomegranatecouncil-polyphenols)	JX2, dated May 24, 2011; Tr. 7		
PX0424	"Moderate Drinking May Reduce Men's Risk of Heart Disease" Modern Medicine (http://www.modernmedicine.com/modernmedicine/Family+Medicine/Moderate-Drinking-May-Reduce-Mens-Risk-of-Heart-Di/ArticleNewsFeed/Article/detail/629588)	JX2, dated May 24, 2011; Tr. 7		
PX0425	"Pomegranate Juice May Affect the Progression of Coronary Heart Disease" All Business (http://www.allbusiness.com/m	JX2, dated May 24, 2011; Tr. 7		

PX	Description	Where Admitted	Tr. Pages Where Discussed	In Camera
	edicine-health/medical-sciencemedical-research/5066647-1.html)			
PX0426	"Pomegranate Juice May Slow Prostate Cancer" Daily News Central (http://health.dailynewscentral.com/index2.php?option=content&do_pdf=1&id=0001702)	JX2, dated May 24, 2011; Tr. 7		
PX0427	"Pomegranate Juice may ease erectile dysfunction" by Stephen Daniells (http://www.nutraingredientsusa.com/Research/Pomegranate-juice-may-ease-erectiledysfunction)	JX2, dated May 24, 2011; Tr. 7		
PX0428	"Pomegranate Juice Helps Keep PSA Levels Stable in Men with Prostate Cancer, UCLA study Finds" by Kim Irwin (http://newsroom.ucla.edu/portal/ucla/Pomegranate-Juice-Helps-Keep-PSA-7165.aspx)	JX2, dated May 24, 2011; Tr. 7		
PX0526	Sexual Medicine Alvarado Hospital Brochure	JX2, dated May 24, 2011; Tr. 7		
PX0527	Sexual Medicine Program at Alvarado Hospital	JX2, dated May 24, 2011; Tr. 7		
PX0528	Food Pyramid	JX2, dated May 24, 2011; Tr. 7		

UNITED STATES OF AMERICA
FEDERAL TRADE COMMISSION

In the Matter of	)	
	)	
POM WONDERFUL LLC and	)	
ROLL GLOBAL, as successor in interest	)	
to Roll International companies, and	)	**Docket No. 9344**
	)	**CONFIDENTIAL**
	)	
STEWART A. RESNICK,	)	
LYNDA RAE RESNICK, and	)	
MATTHEW TUPPER, individually and	)	
as officers of the companies.	)	
_____	)	

RESPONDENTS' POST-TRIAL BRIEF

Kristina M. Diaz, Esq.
Alicia Mew, Esq.
Johnny Traboulsi, Esq.
Brooke Hammond, Esq.
Roll Law Group P.C.
11444 West Olympic Blvd., 10th Floor
Los Angeles, CA, 90064
Tel: 310.966.8400
Fax: 310.966.8810
Email: kdiaz@roll.com

John Graubert, Esq.
Skye Perryman, Esq.
Covington & Burling LLP
1201 Pennsylvania Avenue, NW
Washington, DC 20004
Tel: 202.662.6000
Fax: 202.662.6291
Email: jgraubert@cov.com

Bertram Fields, Esq.
Greenberg Glusker Fields
Claman & Machtinger, LLP
1900 Avenue of the Stars, Suite 2100
Los Angeles, CA 90067
Tel: 310.553.3610
Fax: 310.553.0687
Email: bfields@greenbergglusker.com

TABLE OF CONTENTS

TABLE OF AUTHORITIES

Cases

Statutes

Other Authorities

Regulations

I. SUMMARY OF THE CASE

While trial of this matter was complex, it confirmed that Complaint Counsels' central argument is straightforward scientific and legal error. Complaint Counsel asserts that Respondent POM Wonderful LLC's ("POM") extraordinary science is insufficient to substantiate its health benefit claims because, in Complaint Counsels' view, such claims may only be substantiated by large clinical randomized placebo controlled trials ("RCTs"). That assertion is false, however, as the evidence and expert testimony at trial established. Nutritional science cannot be reduced, by regulatory fiat, into a pharmaceutical testing regime for any health claim about wholesome foods. If Complaint Counsel succeeds in imposing its rigid new RCT requirement to POM's whole food products, Complaint Counsel would, in effect, prohibit the dissemination of all emerging science on the benefits of any food product, even those benefits relating to obviously safe and healthy whole food products derived from fruits or vegetables. POM would be just one victim of that crusade to impose a strict regulatory regime on food under the false guise of scientific propriety. When the best-possible scientific information on human nutrition is suppressed by unscientific paternalism, the American public also suffers.

The United States Supreme Court has already decided this precise point against Complaint Counsel. In *Matrixx Initiatives, Inc. v. Siracusano*, 131 S.Ct. 1309 (2011), the Supreme Court recognized that RCTs are not required to show a causal relationship between a health benefit and a product. The Supreme Court explained that medical researchers "do not limit the data they consider to the results of randomized clinical trials or to statistically significant evidence." *Id.* at 1320. The Supreme Court further recognized that even the FDA "sometimes acts on the basis of evidence that suggests, but does not prove causation." *Id*. Other courts have likewise recognized that Complaint Counsels' attempt to substitute a "one size fits all" approach is both scientifically and legally indefensible. *See In re Pfizer*, 81 F.T.C. 23 (1972) (requiring six part cost-benefit analysis that includes considering claim and type of product); *Pearson v. Shalala*, 164 F.3d 650, 656-58 (D.C. Cir. 1999) (advocating cost-benefit analysis and preferring "disclosure over outright suppression").

If that were not enough -- and it is -- in sometimes dramatic fashion at trial, Complaint Counsels' own science experts repeatedly betrayed the fallacy of Complaint Counsels' extreme and unscientific position on RCTs. As one of the more spectacular examples, Complaint Counsels' star expert witness, Professor Meir Stampfer, had explained in a recently published article that RCTs are not necessarily a superior or even an appropriate method for testing the health benefits of nutrients, as distinguished from drugs. [Cite] In his paper, Professor Stampfer opined specifically that (1) RCTs may not be appropriate for nutrient recommendations to prevent disease, as distinguished from testing drugs used to treat disease; and (2) because RCT study designs may not be "available" (economically or scientifically) for nutrients, "nutrient related decisions could be made at a level of certainty somewhat below that required for drugs." [Cite] That is the scientific truth, and Complaint Counsels' legalistic arguments against it are incorrect and unavailing.

Complaint Counsels' other experts fared no better, admitting at trial that (1) they had personally made significant public health recommendations based on evidence falling far short of RCTs; (2) they had previously performed hundreds of therapies and surgical procedures on patients without the benefit of RCTs (and based only on animal studies), despite the fact that, unlike drinking pomegranate juice, the risks imposed by those procedures included serious bodily injury, and even death; and (3) RCTs may not be scientifically or economically appropriate for testing fruit products. [Cite.] Professor Stampfer and other experts of Complaint Counsel conceded further the central point of this case--that when the risk of harm is slight, an advertiser should err on giving the public information about the potential benefits of the product – without more firmly establishing causality. [Cite Professor Stampfer and Sacks.]

Complaint Counsel have also argued that a singular scientific RCT standard should apply to all "dietary supplements," focusing on POM's pill and liquid extract products, as was required in *Daniel Chapter One*. However, Complaint Counsels' assumptions were countered by their own former expert witness in that case, Dr. Dennis Miller. Significantly, Dr. Miller testified that

the health benefits of POM's 100% juice product, as well as POM's extract products, can certainly be shown without RCTs. [Cite]

According to Dr. Miller, the primary issues that determine the level of science required to support a health benefit claim are (a) the type of product at issue and (b) whether it is advertised as a replacement for conventional medical care. [Cite] As Dr. Miller testified, because POM's products are obviously safe and are not being advertised as a replacement for conventional medical care, RCTs are not required to substantiate claims of a health benefit. Dr. Miller reasoned further that, at least with respect to the areas of within his clinical expertise, POM's claims regarding its products were supported by competent and reliable scientific evidence. He added that under circumstances such as these, where the product is so obviously safe, even sound basic science could be enough to support a health benefit claim. [Cite]

The standard described by Dr. Miller, consistent with the *Matrixx* and *Pfizer*, is the governing scientific standard for this action. And under that standard, or indeed any credible scientific standard, Respondents have an unprecedented level of science to support their health benefit claims, science which includes RCTs, but is also much broader.

In stark contrast to the science made available to the Commission in *Daniel Chapter One*, Respondents have more than sufficient reliable and credible scientific evidence to form a "reasonable basis" for their claims, including under the FTC's "competent and reliable" standard. The trial covered an unparalleled range of scientific studies supporting the benefits of pomegranate juice for human health. Moreover, while POM has not conducted colossal pharmaceutical-style RCTs at a cost of hundreds of millions of dollars, it has nonetheless conducted significant studies, including RCTs that show health benefits from consuming the challenged products. [Cite]

Complaint Counsels' case also fails because it is premised on an extremely aggressive and unrealistic view of what POM's advertising actually conveys. Specifically, Complaint Counsel construe all POM's advertising regarding health benefits as conveying the message that the products are "clinically proven" to "reduce the risk of, prevent or treat disease" or that its

consumption is a "silver bullet" against disease. [Cite] But Complaint Counsels' proffered interpretations are inconsistent with a reasonable facial reading of the advertisements in question. Rational consumers understand puffery. They do not believe, for example, that the slogan "Live Forever" means "you will be immortal if you drink this product."

There are clear and important distinctions between saying that (1) a product is good for you, or may assist in improving your odds against disease (just like the Mediterranean diet and regular exercise reduce the risk of disease) and (2) saying it is a "silver bullet" against disease, or is a powerful drug. The public understands that exercise may improve your odds against certain diseases, but they do not thereby consider exercise to be a "silver bullet" against all manner of illness. They must be credited with significantly more intelligence and reason than Complaint Counsel grants them. Additionally, Complaint Counsel attempts to mimic the FDA's regulatory scheme by refusing to distinguish between the alleged "disease claims" types ('treat" or "reduce the risk"), treating them as identical in order to impose a pharmaceutical paradigm upon nutritional advertising. Yet their own medical experts distinguish between "prevent" and "treat" claims in examining the level of scientific support that each claim may require. (CITE).

In another example of Complaint Counsels' unwillingness to engage the facts that underlie their allegations, Complaint Counsel ignore that consumers know POM's pomegranate juice is a fruit juice. Reasonable consumers do not interpret POM's advertising as conveying claims that the product can treat their diseases, such that they should disregard conventional medical treatments. Instead, reasonable consumers want to be more educated about their diet and nutrition, without thereby abandoning their doctor or conventional medical therapies. As POM's expert, Professor David Reibstein, testified at trial, only 1.9% of POM's juice consumers in the real world reference any specific disease when asked why they purchase the product. Complaint Counsel ask the Commission to ignore the real evidence of how reasonable consumers view the benefits of POM's products, without presenting any of their own extrinsic evidence to support their implausible assertions about what POM'S advertising supposedly conveys.

Indeed, Complaint Counsel have exercised a complete turnabout in this case. Complaint Counsel conspicuously failed to ask their marketing expert, Professor Michael Mazis, to provide any expert opinion to support their claims on subjects they have previously relied on him for. Specifically, (1) Professor Mazis did not conduct any facial analysis of POM's ads or offer expert opinion on them, the messages they conveyed, or their materiality to the purchasing decisions of consumers; (2) Professor Mazis failed to conduct any independent surveys of the ads to counter the survey presented by Professor Reibstein; and (3) Professor Mazis did not provide any expert opinion on the number of exposures to the ads received by consumers, despite testifying that repeated exposures were critical to having any effect at all on consumers. (Mazis, Tr. 2752; Stewart, Tr. 3228-3229). He testified, in fact, that there was no evidence that Respondents' advertisements caused anyone to buy the Challenged Products. (Mazis, Tr. 90, 95, 96, 2700). Accordingly, on the required element of materiality, and assuming that the presumption in favor of Complaint Counsel applied, Respondents successfully rebutted the presumption and Complaint Counsel has failed to meet their burden of proof.

Consistent with their preference for legal argument over empirical evidence, Complaint Counsel also did not present other evidence significant to their claims.

1. On the issue of falsity, Complaint Counsel failed to present any expert opinion or extrinsic evidence that POM's health benefits were, in fact, false, i.e., that the Challenged Products did not, in fact, provide the health benefits that Complaint Counsel claims POM promised.

2. Although Complaint Counsel challenged the benefits of antioxidants in their pretrial briefing, they essentially forfeited the argument at trial, and presented absolutely no expert testimony on the subject. Professor Stampfer, their sole nutritionist, expressed no opinion on the subject. By contrast, POM's expert witness, Dr. David Heber, opined that there is strong support for the benefits of antioxidants, the safety of POM's products, the bioavailability of POM's products, the equivalency of POM Juice and POMx, the several mechanisms of action at play in the human body from the pomegranate's antioxidant and anti-inflammatory properties, as

well as the general benefits of the Challenged Products in several areas of human health, including the heart, prostate, and erectile health.

3. Complaint Counsel presented no expert opinion challenging the Challenged Products' safety, despite its importance to the case under *Pfizer* [Cite]. That omission reflects the fact that Complaint Counsels' own witness, Professor Stampfer, had previously taken a public position on this issue that contradicts Complaint Counsels' position.

4. Complaint Counsel presented no expert opinion or argument on the constituents or contents of the Challenged Products, never denying that they are wholly derived from the pomegranate fruit.

5. Complaint Counsel do not allege and have not presented any expert opinion suggesting that the advertising for the Challenged Products convey the explicit or implied message that the product can be or should be used as a substitute for conventional medical therapies.

As Respondents' pretrial briefing explained, this action is particularly significant because it involves an attempted sea change in American regulatory jurisdiction. In essence, Complaint Counsel wants to seize ground from the FDA, anointing themselves as the primary regulator of claims that manufacturers make about the health benefits of food products. In doing so, Complaint Counsel implicitly derogates the FDA's authority, and improperly subjects all American advertising and promotion to Complaint Counsels' misinterpretation of the FDA's pharmaceutical regulation regime. That short cut is not permitted by law.

Instead, Complaint Counsel is bound by the flexible standards reflected in *Matrixx* and *Pfizer*, and consistent with Dr. Millers' assessment of the relevant cost-benefit considerations to determine the type of science necessary to support a claim. And under that standard, Complaint Counsel have entirely failed to prove their case against POM's advertising.

II. THE PARTIES' PRESENTATION OF EVIDENCE AT TRIAL

An exceptional amount of evidence was presented at trial and is part of this record. During nineteen days of trial, twenty-four live witnesses testified, including all fourteen experts,

and over fifteen hundred exhibits were admitted into the record. Moreover, the amount of scientific evidence presented in support of Respondents' position is unprecedented for a food company, such as POM. Complaint Counsel, in essence, agreed with this very proposition at the outset of the trial. Indeed, Complaint Counsel conceded during the course of Ms. Hippsley's opening statement that this case is different from previous cases brought before the Commission. (Tr. 69). Specifically, more than ninety scientific studies and reports are part of the record in support of Respondents' case. (PX Exhibit Nos. 2-12, 14-23, 38-41, 49-51, 53-66, 68-71, 73-77, 81-130, 136-148, 174-175). Thus, as is reflected by Respondents' extensive body of scientific evidence and Complaint Counsels' admission, Respondents are indeed not selling "snake oil." (Tr. 69).

A. Respondents' Experts

Respondents offered the testimony of eight expert witnesses during the course of the trial. Respondents' experts testified regarding the extraordinary body of credible scientific evidence demonstrating that the Challenged Products have significant health benefits supporting any reasonable construction of POM's advertisements. With respect to the science, Respondents offered the testimony of Drs. Denis Miller, David Heber, Dean Ornish, Arthur Burnett, Irwin Goldstein and Jean deKernion. Respondents also presented expert testimony of Professor Ronald Butters that none of POM's advertisements stated or implied that the Challenged Products actually prevented or treated any disease. Respondents also presented expert testimony of Professor David Reibstein who rebutted any presumption of materiality.

1. Dr. Denis Miller

Dr. Denis Miller, who is an esteemed pediatric oncologist with over forty years of clinical and research experience, confirmed that the consensus of the scientific community would be that Respondents do not need RCTs to substantiate POM's claims because the Challenged Products are absolutely safe, pure fruit products. He also opined that Respondents have never suggested that the Challenged Products be used as substitutes for conventional medical treatment. Above all else, Dr. Miller recognized that the nature of the product and its safety are the linchpins in

determining the level of substantiation required to support one's claim. (PX0206 at 1-2; PX0354 (Miller, Dep. at 16); Miller, Tr. 2194).

Moreover, Dr. Miller has previously testified as an expert for Complaint Counsel in several other matters, such as the *Daniel Chapter One* case. (PX0206 at 5, 18). Dr. Miller made it clear that the case against Respondents is absolutely different from the case against the respondents in *Daniel Chapter One*. Unlike the facts here, the respondents in *Daniel Chapter One* produced no reliable science, their product was recommended in place of conventional medical treatment and had potentially toxic side effects. (Miller, Tr. 2193).

2. Dr. David Heber

Respondents offered Dr. David Heber, a practicing physician, Professor of Medicine and Public Health at UCLA and the Director of the UCLA Center for Human Nutrition which he founded in 1996 within the UCLA School of Medicine. (Heber, Tr. 1937; CX1407 (Heber, Tropicana Tr. 76)). Dr. Heber conclusively established that the Challenged Products are safe, bioavailable and bioequivalent in providing health benefits to humans. (Heber, Tr. 2009; Heber, Tr. 2186-87).

Dr. Heber also reviewed Respondents' substantive bodies of science in the areas of cardiovascular, prostate and erectile health. He concluded that Respondents' science showed that the Challenged Products were likely to cause a significant improvement in cardiovascular health and help to reduce the risk of cardiovascular disease. (Heber, Tr. 2012). Dr. Heber also concluded that it is likely that the Challenged Products lengthen PSA doubling time for men who have prostate cancer and that those men may experience a deferred recurrence of the disease or death from prostate cancer. (Heber, Tr. 2012). Moreover, Dr. Heber opined that the Challenged Products are likely to reduce the risk of prostate problems for men who have not yet been diagnosed with prostate cancer. (Heber, Tr. 2012-13).

Furthermore, Dr. Heber opined that animal studies showed that pomegranate juice markedly improved proper erectile function and would probably do so in humans due to the effect of pomegranate juice prolongation on the lifespan of nitric oxide in the body. (Heber, Tr.

1968-69; CX1407 (Heber, Tropicana Tr. 242)). Additionally, Dr. Heber opined that the *Forest/Padma-Nathan RCT Study* (as defined herein) showed that consumption of POM Juice significantly improved erectile function among men with erectile dysfunction. Dr. Heber opined that that the study had major clinical significance in showing a benefit from POM Juice despite barely missing statistical significance. (Heber, Tr. 1830-31, 1979).

Dr. Heber testified as to the proper substantiation standard applicable to the Challenged Products. Dr. Heber, like Dr. Miller, agreed that POM's health claims with respect to the Challenged Products can be properly substantiated without RCTS, which he opined are both expensive and often unreliable in dealing with foods, as opposed to drugs. (Heber, Tr. 1949-50, 2166, 2179, 2182). Dr. Heber opined that experts in nutrition evaluate whether competent and reliable science support health claims for safe, pure fruit products such as pomegranate juice based on the totality of evidence, which does not necessarily include RCTs, (Heber, Tr. 2182).

3. Dr. Dean Ornish

Respondents offered Dr. Dean Ornish as an expert in the area of cardiovascular health, a world renowned medical doctor and clinical professor of medicine at the University of California at San Francisco. (Ornish, Tr. 2314). Dr. Ornish validated POM's use of basic science to support POM's cardiovascular health claims and affirmed pomegranate juice's beneficial impact on reducing the risk of cardiovascular disease.

Dr. Ornish testified that, in a nutritional context, *in vitro* and animal studies may be more effective in testing the efficacy of a nutrient. (Ornish, Tr. 2327-30, 2331-55). Dr. Ornish opined that the totality of Respondents' scientific evidence must be considered when making cardiovascular health claims, which need not be substantiated by expensive RCTs. (Ornish, Tr. 2320-31). Moreover, Dr. Ornish opined that Complaint Counsels' rigid position that only RCTs are good science is overly simplistic and runs the danger of depriving the public of important nutritional information by discouraging research on natural products. (Ornish, Tr. 2325-28). Dr. Ornish testified that the totality of Respondents' scientific studies conducted on the

cardiovascular system convinces him that pomegranate juice is effective in reducing the risk of cardiovascular problems. (Ornish, Tr. 2354-55).

4. Dr. Arthur Burnett

Respondents offered Dr. Arthur Burnett as an expert in the area erectile health, a Professor of Urology at the Johns Hopkins University School of Medicine/Johns Hopkins Hospital who is world-renowned for his groundbreaking work on nitric oxide. (PX0149-0001, 0003; Burnett, Tr. 2241). Dr. Burnett has treated between 10,000 and 15,000 patients for erectile dysfunction. (Burnett, Tr. 2244). Dr. Burnett validated POM's science that establishes that pomegranate juice is beneficial to erectile health.

Dr. Burnett opined that Respondents' basic scientific and clinical evidence supports the conclusion that pomegranate juice's high antioxidant content improves erectile health and function by increasing the level and preservation of nitric oxide. (PX0149-0004-07; PX0349 (Burnett, Dep. at 87-90, 103, 118, 137); Burnett, Tr. 2250-56, 2303). Dr. Burnett also concluded that a safe pure fruit juice, like pomegranate juice, which is not used as a substitute for proper medical treatment, does not require RCTs to substantiate health claims. (Burnett, Tr. 2272-74).

5. Dr. Irwin Goldstein

Respondents offered Dr. Irwin Goldstein as an expert in sexual medicine and on the impact of pomegranate juice, antioxidants, and nitric oxide on erectile function and dysfunction. (Goldstein, Tr. 2592). Dr. Goldstein is a board certified urologist and sexual medicine physician who has been involved in sexual medicine clinical practice, clinical research, and basic research since 1980. (PX0189-0001-0002; PX0352 (Goldstein, Dep. at 14)). Dr. Goldstein affirmed that competent and reliable scientific evidence fully supports that pomegranate juice produces a benefit to proper and effective erectile function. (Goldstein, Tr. 2605).

Dr. Goldstein opined that RCT studies are not required to substantiate claims that pomegranate juice can aid in erectile health and that *in vitro* and animal studies demonstrated a likelihood that pomegranate juice improves erectile health. (Goldstein, Tr. 2601-02, 2605; PX0352 (Goldstein, Dep. at 37-42)). Dr. Goldstein also opined that the consumption of

pomegranate juice is a logical option for men who are not responsive to conventional drugs or who are unwilling to consider invasive or mechanical therapies for treatment of their erectile dysfunction. (PX0189-0005; PX0352 (Goldstein, Dep. at 37-42); Goldstein, Tr. 2605, 2641).

6. Dr. Jean deKernion

Respondents offered Dr. Jean deKernion as an expert in the area of prostate health. (deKernion, Tr. 3044) Dr. deKernion is the Chairman of the Department of Urology and Senior Associate Dean for Clinical Affairs at the UCLA School of Medicine and served as the Dean of Urology at the UCLA School of Medicine for twenty-six years. (PX0160-0001; deKernion, Tr. 3039). Dr. deKernion is also a practicing urologist certified by both the American Board of Surgery and the America Board of Urology. (deKernion, Tr. 3039-40). Dr. deKernion confirmed that the Challenged Products are beneficial to prostate health.

Dr. deKernion opined there is a high degree of probability that the Challenged Products inhibit the clinical development of prostate cancer cells even in men that have not diagnosed with prostate cancer. (deKernion, Tr. 3061, 3119, 3126). Dr. deKernion also concluded there was a high degree of probability that the Challenged Products provide a special benefit to men with PSA after radical prostatectomy and that POM products lengthened PSA doubling time and, thus, may defer death from prostate cancer. (deKernion, Tr. 3126). Dr. deKernion confirmed the findings of the PSA doubling-time studies of Drs. Pantuck and Carducci which both showed a dramatic lengthening of PSA doubling time. Dr. deKernion further opined that that PSA doubling-time is a valid and effective endpoint for recurrence and death from prostate cancer after a radical prostatectomy. (deKernion, Tr. 3061).

7. Professor Ronald Butters

Moreover, Respondents offered Professor Ronald Butters as an expert in the field of linguistics, and he testified to the meaning of Respondents' advertisements. (Butters, Tr. 281, 2816). Professor Butters viewed all of Respondents' advertisements listed in Complaint Counsels' complaint and all the advertisements admitted into evidence. He considered all of Respondents advertisements in their totality. (Butters, Tr. 2817). He also took into account the

nature of the Challenged Products and based his opinion on the actual language in the advertisements and the implied messages as would be interpreted by a reasonable person. (Butters, Tr. 2817-18).

In summary, Professor Butters concluded that none of Respondents advertisements stated explicitly or implied that the Challenged Products actually prevented or cured any disease. (Butters, Tr. 2818-19). He also testified that none of Respondents' advertisements stated explicitly or implied that the Challenged products "treated" disease in the sense that the Challenged products were a form of medical treatment or a substitute for conventional medical treatment. (Butters, Tr. 2819).

8. Professor David Reibstein

Respondents offered Professor Reibstein as an expert on materiality. Professor Reibstein is a professor of marketing at The Wharton School at The University of Pennsylvania, has designed and executed hundreds of surveys and market research studies, including studies concerning consumer behavior. RFF . Professor Reibstein's survey demonstrated that fewer than 1.5% of buyers (i) bought (ii) would buy again or (iii) would recommend to a friend POM Juice because they believe it cures or prevents a specific disease. RFF .

III. COMPLAINT COUNSELS' EXPERTS

Unlike Respondents' experts, all of Complaint Counsels' proffered experts were significantly impeached and failed to offer opinions on many of the critical subjects at issue in this case. First, although they initially espoused a drug standard requiring RCTs to substantiate the health benefits of a natural food product, Complaint Counsels' experts subsequently contradicted themselves and conceded a lesser standard of evidence is in fact appropriate. Second, Complaint Counsels' experts did not provide any testimony denying the bioavailability, absorbency, or safety of the Challenged Products or challenging the equivalency of POM Juice and POMx. In addition, Complaint Counsel failed to provide any expert testimony on what message Respondents' advertisements convey or on materiality, including a factual analysis of the ads or a competing survey.

A. Professor Meir Stampfer

Complaint Counsel offered the expert opinion of Professor Meir Stampfer on the subject of nutrition and its relationship to the prevention and treatment of cardiovascular disease, and prostate cancer. (Stampfer, Tr. 704). Professor Stampfer, however, is not a practicing physician, cardiologist, or urologist. (Stampfer, Tr. 868). At trial, contrary to opinions expressed in his expert report, Professor Stampfer conceded that are RCTs are not required (or even better) for nutritional-based research and admitted that he has made public statements or recommendations that food and beverage products lower the risk of certain diseases, in the absence of RCTs and even when the product is not completely safe. (Stampfer, Tr. 801-02, 805, 810; 813-14).

Moreover, Professor Stampfer provided no opinion on the specific chemical structure of pomegranate antioxidants and no opinion about how pomegranate antioxidants are metabolized in the human body (i.e. mechanisms of action). (PX0362 (Stampfer, Dep. at 199-200)).

B. Dr. Arnold Melman

Dr. Arnold Melman testified as Complaint Counsels' expert in the field of urology and erectile health. (Melman, Tr. 1081). Dr. Melman, like Professor Stampfer, also contradicted himself when he confessed to have marketed a gene transfer therapy for erectile dysfunction (described as "modifying the aging process" and "fountain of youth") based solely on animal research. Dr. Melman admitted he made such recommendations knowing that people have died and become very sick from gene transfer therapy and without the support of elaborate clinical studies he previously required. (Melman, Tr. 1155, 1158; PX0360 (Melman, Dep. at 59, 130-31)).

C. Dr. James Eastham

Dr. James Eastham testified as Complaint Counsels' expert in the field of urology, specializing in prostate cancer. (Eastham, Tr. 1234). At trial, Dr. Eastham testified that RCTs are necessarily required for health claims and that disease prevention studies should involve ten to thirty thousand men, which are "incredibly expensive" and in the range of $600 million. (Eastham, Tr. 1322-28). Despite his insistence that RCTs are needed to support claims made

about a harmless product, such as fruit juice, Dr. Eastham nonetheless has performed hundreds of prostatectomies, which carry the risk of very serious side effects, even without the support of RCTs. (Eastham, Tr. 1329-32). Dr. Eastham also insisted that no one accepts PSA doubling time as a surrogate for progression or death from prostate cancer. (CITE) However, Dr. Eastham was impeached by his own article which characterizes PSA doubling time "as an important factor in the evaluation of men with newly diagnosed prostate cancer or prostate cancer that recurs after treatment", and that it "can be used as a surrogate marker for prostate cancer specific death." (Eastham, Tr. 1339-40; PX0178-0001, 0006, 0009).

D. Dr. Frank Sacks

Dr. Frank Sacks testified as Complaint Counsels' expert in nutrition and cardiovascular disease. (Sacks, Tr. 1429). Dr. Sacks insisted that RCTs, which can cost hundreds of millions of dollars, are required to substantiate health claims even where a product is safe and provides a benefit to the public. (Sacks, Tr. 1535-37). However, he conceded that his requirement of two RCTs is the FDA standard for drugs, and he admitted that in evaluating a natural food, RCTs are simply not necessary in all cases. (Sacks, Tr. 1541-46). For example, when discussing the DASH Diet recommendation, Dr. Sacks stated that fruits as a category, including pomegranates, should be held to a lower standard of evidence than that of a drug and RCTs are not necessary. (Sacks, Tr. at 1545-46, 1554; PX0361 (Sacks, Dep. at 142-43)).

E. Professor David Stewart

Complaint Counsel offered Professor David Stewart as a rebuttal witness to Professor Ronald Butters. (Stewart, Tr. 3168-69). Professor Stewart conceded that he was not offering any opinion on how consumers would interpret Respondents' advertisements, but was only criticizing Professor Butters' methodology. (CITE). Indeed, he stated that he did not even know if Complaint Counsel had any evidence on the meaning of the advertisements. (PX0357 (Stewart, Dep. at 52)). Additionally, Professor Stewart conceded that he was not opining on Respondents' intent and did not know the intent of POM's advertising. (Stewart, Tr. 3233-34; PX0357 (Stewart, Dep. at 120, 130)).

F. Professor Michael Mazis

Complaint Counsel offered Professor Michael Mazis as a rebuttal expert to Professor Reibstein. (CX1297_0002). Professor Mazis testified that a statement is material only if it affects consumers' purchasing decision. RFF . However, Professor Mazis conceded that, to his knowledge, there was no evidence that Respondents' advertisements caused anyone to buy the Challenged Products because they prevented, cured or treated any disease or even that "POM ads were material to the purchase decision." (Mazis, Tr. 2700-01).

IV. THE MANUFACTURE, SALE AND SAFETY OF THE CHALLENGED PRODUCTS

A. The Challenged Products Are Wholly Derived From The Pomegranate

The Challenged Products are either a safe food product or dietary supplement wholly derived from the pomegranate fruit. RFF . The products are produced using the same building blocks and produced via similar methods. RFF . The POM Juice is produced by pressing the whole fruit containing both arils (pomegranate berries) and the peel (aka husk) and internal membrane. POMx is an extract from the pomegranate, made through a process by which POMx Liquid is first derived from the whole fruit, and then POMx is extracted from the POMx Liquid. (CX1363 (S. Resnick, Dep. at 46-47).

B. The Challenged Products Are Not Advertised Or Marketed As Drug Products

POM has never advertised the Challenged Products as drugs. (Tupper Tr. at 3008). Nor has POM ever intended to advertise POM Juice as a drug. (Tupper Tr. at 3008). Neither of the Challenged Products are labeled to say they are drugs or that they "treat" or "prevent" any condition. For example, the drug aisles of a grocery store may contain products such as "'Tough Actin' Tinactin," that state on the product that it "prevents" or "cures" most athlete's foot, or ads for Bengay that state the product "stops pain" and provides "fast relief from minor arthritis, backache, muscle & joint pain." The Challenged Products, however, are not advertised or marketed in this way. RFF .

POM Juice is sold in the refrigerated produce section of the grocery store, not in the "drug" counter or section of any establishment, or advertised or marketed in conjunction with or in comparison to any drug product. RFF . Consumers must go to the fresh produce aisle of a store to purchase any POM Juice product. RFF . (CX0967_0014). Further, the marketing for POMx includes the whole food nutritional story that it is "The Power of Pom, now in a Pill." There is no advertising for POMx comparing it to over-the-counter medications. RFF .

C. The Challenged Products Are Safe for Human Consumption

The pomegranate in its various forms (including POM Juice, POMx Pills and POMx Liquid) is safe for human consumption. The safety of these products has been clearly established by FDA regulations regarding pomegranates, scientific studies conducted by premier scientists and the expert opinion of Dr. David Heber. Complaint Counsel have failed to rebut these facts.

First and foremost, Complaint Counsel presented no evidence that the Challenged Products are not safe for human consumption. RFF ¶. Indeed, Complaint Counsel presented no affirmative evidence such as expert opinion, scientific studies or literature, lay testimony or any other evidence relevant to whether the Challenged Products are safe for human consumption. RFF ¶. In fact, it was not within the scope of any of Complaint Counsels' experts' assignments, and none opined in their expert report, on the safety of the Challenged Products. RFF ¶. Complaint Counsels' expert, Dr. Sacks and Professor Stampfer, admitted that both have nno opinion about whether the Challenged Products are safe or not. RFF ¶.

Moreover, Complaint Counsels' experts, Drs. Sacks and Melman, both conceded that there are no adverse side effects associated with consuming pomegranate juice. RFF ¶¶. And Professor Stampfer conceded that there is no safety concern with consuming pomegranate juice apart from it being a sugary beverage, "but that is not specific to pomegranate juice." RFF ¶.

Second, the FDA identifies pomegranate as being "generally recognized as safe" ("GRAS") for human consumption. See 32 U.S.C. § 231(s); 21 C.F.R. § 182.20; RFF ¶¶. To establish such recognition, it must be shown that there is a consensus of expert opinion regarding the safety of the use of the substance. 21 C.F.R. § 170.30(a).

Third, the body of modern science also confirms that POM Juice and POMx are safe for human consumption. *See, e.g.,* 21 CFR §§ 170.30, 182.20. Researchers at Accelovanc Inc. in San Diego also validated the safety of POMx Pills in a clinical study where no adverse events or changes in blood count, serum chemistry or urinalysis was observed in the human subjects after consuming the extract for four weeks. RFF ¶. Researchers at Tufts University School of Medicine also confirmed in a clinical study that the consumption of pomegranate juice had no drug interaction in the human volunteers. RFF ¶. The results of another study examining the toxicity of POMx oil in rats continuously exposed to the product over a 90-day test period also revealed no adverse events that were considered to be of toxicological significance. RFF ¶.

Finally, Respondents' expert, Dr. Heber, opined that pomegranate juice and its extract have a "high degree" of safety and are safe for human consumption if consumed within the nutritional range. RFF ¶¶. Dr. Heber testified that humans have consumed pomegranate juice for centuries as a safe and nutritious food and confirmed that unlike some drugs, pomegranate juice has no adverse side effects. RFF ¶. Complaint Counsel presented no contradictory evidence. RFF ¶. Similarly, Dr. Heber is not personally aware of any reported cases of toxicity where consumers were injured by drinking pomegranate juice. RFF ¶.

V. THE DEVELOPMENT OF POM'S SCIENCE PROGRAM

A. Initiation Of The Program

Years before selling POM Juice, the Resnicks set out to better understand the health benefits of the pomegranate, both because of Mr. Resnick's own personal battle with cancer and the folklore surrounding the fruit's medicinal properties. RFF . In 1998, the Resnicks collaborated with Dr. Michael Aviram, world-renowned for his groundbreaking work exploring the antioxidant properties of red wine, to assist them in learning about the antioxidant power and potential health benefits of pomegranate juice. (CX1374 (Tupper, Ocean Spray Dep. at 87); CX1358 (Aviram Dep. at 4); CX1363 (S. Resnick, Coke Dep. at 61-63, 65-66); CX1367 (S. Resnick, Welch Dep. at 15); CX0001_0010-0011; L. Resnick, Tr.150; PX0004). What Dr. Aviram saw in his initial research was remarkable and he told Mr. Resnick that the antioxidant

properties in the pomegranate were the most powerful he had ever researched. (CX1358 (Aviram, Dep. at 7); PX0004; CX1363 (S. Resnick, Coke Dep. at 66)).

Dr. Aviram's initial research spawned a massive scientific undertaking by the Resnicks, who invested more than $35 million in scientific research. (S. Resnick, Tr. 1864; CX1363 (S. Resnick, Coke Dep. at 74; Tupper, Tr. 1015). The Resnicks have recruited renowned scientists to conduct research at some of the most prestigious academic and research institutions in the world. (Liker, Tr. 1878-80, 1887-89; CX1350 (Liker, Dep. at 32-33); S. Resnick, Tr. 1857, 1860-61). Indeed, POM has sponsored more than a hundred studies on the pomegranate, including seventeen published human studies, at forty-four respected institutions. (Liker, Tr. 1887-88; PX0014; PX0050; PX0060; PX0061; PX0004; PX0006; PX0020; PX0021; PX0023; PX0073; PX0074; PX0075; PX0005; PX0127; PX0136; PX0139; PX0146; Trombold JR, Barnes JN, Critchley L, and Coyle EF, Ellagitannin Consumption Improves Strength Recovery 2-3 d after Eccentric Exercise, Med. Sci. Sports Exerc., Vol. 42, No. 3, pp. 493-498, 2010).

B. Respondents' Methodology In Sponsoring Studies

Respondents established that they engage in a diligent effort to ascertain the truth about the existence of the health benefits from consuming pomegranates. In doing so, they consulted with many of the most esteemed scientists and scientific advisors in the country to help guide them in designing the studies, in interpreting results and in setting the direction of Respondents' future research. (Liker, Tr. 1889-91). The goal in substantial part was to conduct well-designed research that would yield credible and reliable results. (Liker, Tr. 1878-80, 1887-89; CX1350 (Liker, Dep. at 32-33); S. Resnick, Tr. 1857, 1860-61).

Multiple groups of distinguished scientists and advisors help guide Mr. Resnick in his selection of the science. (Liker, Tr. 1889-91). Mr. Resnick has regular meetings with POM's Medical Director, Dr. Harley Liker, and POM's Chief Science Officer. (Liker, Tr. 1889-91; PX0524 (S. Resnick Dep. at 32); PX0326 (Gillespie Dep. at 32-34, 36-37). Mr. Resnick also attends POM's research summits wherein the scientists conducting the research discuss the

ongoing findings of their research. (Liker, Tr. 1890-92; Tupper, Tr. 1026-27; S. Resnick, Tr. 1858-59, 1872; CX1360 (S. Resnick, Dep. at 157-58)).

Mr. Resnick is also advised by experts in their respective fields who participate in POM's advisory board meetings. (S. Resnick, Tr. 1859; Liker, Tr. 1892-93). Generally speaking, members of POM's scientific advisory boards are individuals who do not conduct the research for Respondents but who are experts in certain disease or health areas. (Liker, Tr. 1889-93). Members of POM's advisory boards discuss the studies that are ongoing as well as those that have been completed and make recommendations about the direction of POM's future research. (S. Resnick, Tr. 1859; Liker, Tr. 1892-93). POM's scientific advisory boards are divided by health areas but each is made up of highly regarded individuals in the scientific and regulatory world. (Liker, Tr. 1892-93). Members of POM's scientific advisory boards have included Dr. Phillip Kantoff, who is employed at the Dana-Farber Cancer Institute at Harvard Medical School and runs the genitourinary oncology program. (Liker, Tr. 1892; Kantoff, Tr. 3257). Dr. David Kessler, the former head of the FDA, has also participated in POM's research advisory meetings. (S. Resnick, Tr. 1859, 1872). Impressively, Dr. P.K. Shah of Cedars-Sinai Medical Center, who is a world-renowned cardiologist, has also been involved with POM's advisory group. (Liker, Tr. 1893).

C. The High Cost Of Conducting RCTs

Respondents have chosen to sponsor basic research, animal studies and some RCTs. Mr. Resnick, however, has not sponsored any large RCTs that would typically be required for drug approval because economics necessarily play a role in defining the parameters of Respondents' research. (Liker, Tr.1886-87; S. Resnick, Tr. 1716). For example, Mr. Resnick has sometimes declined to add more participants to a study when asked. (S. Resnick, Tr. 1716; Liker, Tr. 1886-87; PX0050; PX0344 (Liker, Dep. at 37-38, 188-89)).

Respondents believe that, despite not conducting large and lengthy RCTs, their science is both competent and reliable. Moreover, Respondents deny that they have ever sacrificed the

studies' scientific integrity, soundness, or reliability. Instead, Respondents characterize their decisions as normal economic-based decisions necessary to moderate costs. (S. Resnick, Tr.1716-18; CX1360 (S. Resnick, Dep. at 228-29)).

D. Respondents' Reliance Upon The Peer-Review Process

Respondents also relied, in part, on the peer-review process, including the publication in prestigious, peer-reviewed journals as an indication that the sponsored science was both credible and reliable. (Liker, Tr. 1899-1900). *See, e.g., Daubert v. Merrell Dow Pharms,* 43 F.3d 1311, 1318 (9th Cir. 1995) ("[A]ccept[ance] for publication in a reputable scientific journal after being subjected to the usual rigors of peer review is a significant indication that [the research] is taken seriously by other scientists, *i.e.*, that it meets at least the minimal criteria of good science.").

In this case, more than seventy of Respondents' studies have been published in prestigious peer-reviewed journals. (Liker, Tr. 1888). At a minimum, the publication of Respondents' research is evidence that the scientists at those prestigious journals had vetted the research Respondents conducted and considered the studies important enough to publish them.

E. Respondents Relied Upon The Statements Of Scientists To Understand The Benefits Shown From The Research

Respondents also reasonably relied, in part, upon statements by well-regarded scientists regarding the results of the studies. (CX1363 (S. Resnick, Coke Dep. at 57-58, 66, 77-78); S. Resnick, Tr. 1662, 1734, 1736; CX1372 (S. Resnick, Tropicana Dep. at 44); PX0484; CX0004_0012; (CX1376 (S. Resnick, Ocean Spray Dep. at 31-32, 289)).

1. Statements Regarding Respondents' Promising Cardiovascular Research

Many of Respondents' scientists made promising statements regarding the results of Respondents' cardiovascular research conducted on pomegranate products. Respondents reasonably relied on those statements to evaluate the results of the research.

For example, after reviewing the findings of his initial antioxidant research:

- Dr. Michael Aviram represented to Stewart Resnick that the antioxidant properties found in the pomegranate were the most powerful he had ever

researched. (CX1363 (S. Resnick, Coke Dep. at 57, 66)).Dep. at 57-58, 66, 77-78); S. Resnick, Tr. 1662, 1734, 1736; CX1372 (S. Resnick, Tropicana Dep. at 44); PX0484; CX0004_0012; (CX1376 (S. Resnick, Ocean Spray Dep. at 31-32, 289))

- Similarly, in an August 2008 email, sent to Stewart and Lynda Resnick and Matt Tupper, Dr. Aviram stated "[t]he use of Anti-oxidants, and Anti-inflammatory agents (POM WONDERFUL), could be of major importance in the protection against the other 70% cardiovascular events." (PX0476)

- Dr. Aviram stated in a January 2008 email that pomegranate juice and POMx were "very potent protectors against cardiovascular diseases." (PX0479-0001). Dr. Aviram provided Respondents with a written statement that his research was the first to show that POMx polyphenols had similar cardio protective effects to those of pomegranate juice polyphenols in the reduction of atherosclerotic risks and promoting cardiovascular health. (PX0500-0003). Dr. Aviram provided his opinion to Respondents that POMx "indeed promotes cardiovascular health." (PX0500-0003)

- Dr. Davidson told Mr. Resnick and Dr. Liker that he believed the data from his CIMT study shows a signal of a benefit in the subgroup and should be presented. (CX1336 (Davidson, Dep. at 182-83). POM's cardiovascular advisory panel, who advise Mr. Resnick, also believed that cardiovascular benefits have been shown by the research. (CX1336 (Davidson, Dep. at 224)). For example, Dr. Davidson recalled that members of POM's cardiovascular advisory panel believed that the findings in his CIMT trial were a real, true signal of a benefit in the subgroup. (CX1336 (Davidson, Dep. at 224))

- Dr. Ornish, in an email to Respondent Stewart Resnick and cc'ing Respondent Matt Tupper, announced the acceptance of his myocardial perfusion study and stated, "As you know, this study showed, for the first time, that the progression of coronary heart disease may be reversed by drinking pomegranate juice as evidenced by improved blood flow to the heart measured by thallium scans." (PX0485-0001). Additionally, in an email cc'ing both Stewart and Lynda Resnick, Dr. Dean Ornish characterized the health benefits of pomegranate juice as "extraordinary." (PX0511).

Additionally, other doctors and cardiovascular researchers who were deposed in this case further corroborated that Respondents research showed a benefit from consuming pomegranate juice. (CX1350 (Liker, Dep. at 222); CX1358 (Aviram, Dep. at 6):

- For example, Dr. Aviram stated at his deposition that he is a great believer in pomegranate juice as an anti-atherosclerotic, and he believes that doctors and the public should be informed about those benefits. CX1358 (Aviram, Dep. 48-49). He also testified that after a year of studying the consumption of pomegranate juice, he concluded that pomegranate juice had greater antioxidant potencies than red wine. (CX1358 (Aviram, Dep. at 6)).

- Based upon Dr. Aviram's research, Dr. Liker stated in his deposition that he believes that drinking POM Wonderful juice lowers other risk factors for heart disease. (CX1350 (Liker, Dep. at 221-22)). Indeed, he testified that "[o]ne glass

a day has been shown to drastically reduce heart artery plaque" is an accurate statement. (CX1350 (Liker, Dep. at 221-22)).

Most notable is the fact that the cardiovascular researchers have also made statements to the public and recommendations to their patients regarding the benefits of pomegranates. (PX0423-0001; CX1336 (Davidson, Dep. at 225-26)):

- For example, Dr. Michael Davidson was quoted in a 2004 article in the Chicago Tribune stating, "It is the concentration of polyphenols that appear to make [pomegranate juice] the most potent antioxidant in nature." (PX0423-0001). Indeed, Dr. Davidson testified in deposition that he has recommended pomegranate juice or POMx to some of his patients and the data from his research on pomegranates supports a likely cardiovascular health benefit. (CX1336 (Davidson, Dep. at 225-26)).

2. Statements Regarding Respondents' Promising Prostate Health Research

There were also many statements concerning the promising results of prostate research on pomegranate products that Respondents reasonably relied on to evaluate the reliability and significance of the research. At trial, Mr. Resnick testified that scientists reviewing the results of basic and animal studies done on prostate health told him that the results were the best they had ever seen. (S. Resnick, Tr. 1734, 1736):

- For example, with respect to the Pantuck Phase II study, Dr. Harley Liker told Respondents that the study proves that pomegranate juice slows down the progression PSA. (CX1350 (Liker, Dep. at 174-75))

- Similarly, in a January 2007 email, Dr. Heber stated to Mark Dreher, "The prolongation of PSA doubling time is considered clinically significant by urologists and is being confirmed in large multicenter trials." (PX0494).

- Dr. Liker recalled that Dr. David Heber has shared his view that POM products could contribute to the prevention of prostate cancer. (CX1350 (Liker, Dep. at 174)).

Additionally, like the cardiovascular researchers, the prostate health researchers also testified that consumption of the Challenged Products results in some benefit to prostate health. (CX1341 (Pantuck Dep. at 108, 254-55, 264)):

- For example, Dr. Pantuck, in deposition, stood behind the results of his research and selection of endpoints. (CX1341 (Pantuck Dep. at 108, 254-55). In his deposition, Dr. Pantuck supported the findings of his study that PSA doubling time was prolonged for men with prostate cancer when they were given pomegranate juice and affirmed that PSA doubling time is clinically important for prostate cancer treatment and one of the most

important variables that you can discuss to characterize a prostate cancer patient. (CX1341 (Pantuck Dep. at 108, 254-55)). Dr. Pantuck confirmed at his deposition that from a patient care standpoint PSA doubling time is extremely important. (CX1341 (Pantuck Dep. at 255)).

Dr. Pantuck also made public statements regarding the promising research on the benefits of pomegranates on prostate health. (PX0428-0001); (PX0347 (Pantuck, Dep. at 270-71)). For example, Dr. Pantuck has publicly made positive remarks about the findings in his research done for Respondents. (PX0428-0001):

- In connection with his follow-up research to his 2006 study, Dr. Pantuck publicly remarked that the increase in doubling time from 15 to 54 months was a "big increase." He said that he was "surprised to see such an improvement in PSA numbers" and that "[i]n older men 65 to 70, who have been treated for prostate cancer, we can give them pomegranate juice and it may be possible for them to outlive their risk of dying from their cancer." He also commented, "The juice seems to be working." (PX0428-0001; PX0347 (Pantuck, Dep. at 270-71)).

- Dr. Pantuck also discusses the benefits of pomegranate juice with his patients. (PX0347 (Pantuck, Dep. at 270-71)).

3. Statements Regarding Respondents' Promising Erectile Health Research

Respondents similarly reasonably relied upon the statements of Nobel Laureate Dr. Louis Ignarro concerning the promising results of erectile health research:

- Dr. Ignarro represented to Mr. Resnick that he strongly believes pomegranate juice is 40% as effective as Viagra in helping with erectile dysfunction. (CX1363 (S. Resnick, Coke Dep. at 77-78); CX1372 (S. Resnick, Tropicana Dep. at 44)).

- Dr. Ignarro also told Respondents, "Based on studies conducted in my laboratory, pomegranate juice was 20 times better than any other fruit juice at increasing nitric oxide. It's astonishing – I've been working in this field for 20 years and I have never seen anything like it. I drink it 3 times a day without fail." (PX0484).

F. Respondents' Insistence on Scientific Rigor and Integrity

Notwithstanding the enthusiasm Respondents' received from the scientists themselves, Respondents double-check both positive and negative results and independently verify the results to ensure the information is accurate before it is published or made publicly available. (CX1360 (S. Resnick, Dep. at 200-01, 1693); (Liker, Tr. 1903-04); PX0023).

For example, Respondents delayed the publication of Dr. Aviram's 2011 study that showed an amazing 30% reduction of arterial plaque so the data could be verified. (Liker, Tr. 1903). Similarly, Respondents delayed the publication of Dr. Ornish's Bev I study on myocardial perfusion, which showed a statistically significant benefit, so that an independent third-party could double-check the results. (S. Resnick, Tr. 1693; Liker, Tr. 1904; PX0023).

G. POM's Policy Regarding Publication Of The Research

Mr. Resnick has never improperly interfered with the publication of any report or dictated the contents of any report. (CX1372 (S. Resnick, Tropicana Dep. at 33)). Nor has he ever asked any scientist not to publish a manuscript or report. (CX1360 (S. Resnick, Dep. at 75); CX1358 (Aviram, Dep. at 76); CX1339 (Ornish, Dep. at 85)).

Complaint counsel, however, have insinuated that the delay in the publication of the Davidson CIMT study was nefarious or motivated by a desire to hide the results. There is absolutely no support for this assertion. In fact, the evidence shows the exact opposite. (Liker, Tr. 1903); CX1372 (S. Resnick, Tropicana Dep. at 33); CX1360 (S. Resnick, Dep. at 75); CX1358 (Aviram Dep. at 76); CX1336 (Davidson, Dep. at 230)).

The delay of the publication of Dr. Davidson's CIMT study was solely caused by confusion within POM's internal scientific team, which necessitated that the results of the study be re-read by a blinded independent group. (Liker, Tr. 1895-96; CX1350 (Liker, Dep. at 146, 149-50, 163-64)). Individuals at POM, including Mr. Tupper and Mr. Resnick, collectively made the decision to go forward with the publication of Dr. Davidson's CIMT study and let the peer-review process decide whether or not the study was worthy of publication. (CX1350 (Liker, Dep. at 165-66)). Indeed, any suggestion that Respondents attempted to hide the 18-month results of the Davidson CIMT study is belied by the fact that both the 18-month and 12-month results were ultimately published in the American Journal of Cardiology, one of the leading journals in cardiovascular medicine. (Liker, Tr. 1902; PX0014).

Accordingly, the breadth of evidence and testimony establishes that Respondents relied upon both the peer-review process and the information conveyed to them by the scientists to inform them regarding credibility and reliability of the research.

H. POM's Continued Investment In Research

The Resnicks' investment in POM's research program has and continues to be motivated by a desire to better understand the health benefits of the Challenged Products. (S. Resnick, Tr.1859; Liker, Tr. 1881-84; CX1336 (Davidson, Dep. at 142)). As set forth in detail below, (1) POM does not artificially "power-up" the research to reach statistical significance; (2) POM continues to invest in basic and animal research; (3) POM is motivated to expand the scope of its research; (4) POM has conducted a review of its science portfolio; and (5) POM is seeking FDA botanical drug approval for POMx pills. (CX1363 (S. Resnick, Coke Dep. at 59); S. Resnick, Tr. 1752-1753, 1859; CX1336 (Davidson Dep. at 142); CX1374 (Tupper, Ocean Spray Dep. at 87); Tupper, Tr. 3001; CX1360 (S. Resnick, Dep. at 145-146); Tupper, Tr. 3006-08; CX1353 (Tupper, Dep. at 47-49); Tupper, Tr. 2979-81); Liker, Tr. 188101884, 1887-88). In sum, the evidence overwhelming shows that the Resnicks were and are motivated to do a social good by investing in POM's research and sharing it with the public rather than, as Complaint Counsel suggests, attempting to exploit the research to make unsupported health claims and gain market share.

1. POM Does Not Artificially Power-Up the Research to Reach Statistical Significance

In developing POM's research program, the Resnicks' approach has been to listen to the advice of their scientific advisors and fund those studies that were more likely to show the real effects, whether positive or negative, from the consumption of pomegranate juice. (S. Resnick, Tr. 1662, 1859; Liker, Tr. 1881; CX1336 (Davidson Dep. at 142)). Neither the REsnicks nor POM ever attempted to "game the system" by pre-selecting studies they knew would show a positive result by "powering up" the study so that statistical significance could be reached, even though negligible benefits to study participants occurred. (S. Resnick, Tr. 1859). Instead, the

Resnicks have always aspired to better understand how the Challenged Products work and whether a real benefit can be shown. Whether the findings reached statistical significance was not their focus. (S. Resnick, Tr.1859; Liker, Tr. 1881-84; CX1336 (Davidson, Dep. at 142)).

As recently noted by the Supreme Court in *Mattrix*, clinically significant research can come in many different forms; not just RCTs or research that reaches an FDA-approved level of science or statistical significance. That fact that a study is small or just shy of statistical significance does not mean the research is not useful or truthful. 131 S.Ct. at 1320.

2. POM Continues to Invest in Basic and Animal Research Even When Human Studies Have Demonstrated Positive Results

POM's continued investment in basic and *in vitro* research in areas where it has seen positive human studies is further evidence of the Resnicks' commitment to the truth and desire to expand the boundaries of scientific knowledge regarding the benefits of pomegranates. CX1363 (S. Resnick, Coke Dep. at 59); S. Resnick, Tr. 1752-1753; CX1336 (Davidson Dep. at 142); CX1374 (Tupper, Ocean Spray Dep. at 87); Tupper, Tr. 984-85, 3001; CX1360 (S. Resnick, Dep. at 145-146); (PX0009, PX0002, PX0125, PX0017, PX0010).). Indeed, POM currently has ongoing basic research in the areas of cardiovascular health and prostate health despite having previously sponsored human clinical research yielding positive results. (Tupper, Tr. 984-985, 994; PX0023; PX0014; PX0060; PX0061).

3. POM Continues to Expand the Scope of Its Research

Additionally, POM continues to invest in many different areas of science to expand the breadth of POM's research to include many different health conditions that are connected to inflammation and oxidation. (Tupper, Tr. 2999-3002; deKernion, Tr.3046; Heber Tr.1957, 2112-13, 2185). Because additional beneficial characteristics of the Challenged Products and its derivatives have come to light over time, POM's research efforts have branched out in several directions to examine the role that oxidation and inflammation play in many seemingly unrelated diseases and conditions. (CX1353 (Tupper, Dep. at 47-49); Tupper, Tr. 2979-81; Heber Tr.1957, 2112-13, 2185).

Moreover, the Resnicks continue to invest in research examining regarding a variety of different health conditions because of their belief that all of POM's research builds upon itself and is interrelated, whether or not the results show positive or negative results. (Tupper, Tr. 2999). Indeed, POM finds value in all of its studies even if they are not ultimately published. (Tupper, Tr. 3000-02).

4. POM Has Undertaken a Review of Its Entire Science Portfolio to Evaluate the Rigor of Its Research

As part of their internal preparation to potentially submit an application to the FDA for botanical drug approval, Respondents conducted candid reviews of POM's entire science portfolio to examine whether and to what extent their research would meet the FDA requirements, with its current limited recognition of the surrogate markers used in Respondents' research. (Tupper, Tr. 3011). In connection with this review, several summaries of POM's science program were examined, including a summary entitled "Medical Portfolio Review." The Medical Portfolio Review was prepared by Respondent Matt Tupper for an internal meeting with POM's advisors, including Mr. Tupper, Mark Dreher, Dr. Harley Liker, Dr. David Kessler and Dr. David Heber, and Mr. Resnick. (Tupper, Tr. 942, 939, 3008-09; CX1353 (Tupper, Dep. at 248-49)). In this summary, POM ranked its portfolio of cardiovascular research as a three on a scale of ten. (Tupper, Tr. 3010-11; CX1029_0003). This ranking referred to an assessment given by doctors who were oriented to drug approval. (Tupper, Tr. 3001). That score was also due to the fact that POM previously considered using different endpoints than those used by the FDA to approve a drug for heart disease. (Tupper, Tr. 3011).

Nevertheless, putting aside the strict FDA requirements and FDA lens, Mr. Tupper testified that he personally ranks POM's portfolio of erectile, prostate and cardiovascular science each as an eight on a scale of ten. (Tupper, Tr. 3012).

5. POM is Seeking FDA Botanical Drug Approval of POMx

As a corollary to the Resnicks' continued investment and expansion of POM's research program, POM is currently seeking botanical drug approval for POMx from the FDA under two

different health indications. (Tupper, Tr. 3006-08). The desire to do so is not motivated by the belief that POM advertised its products as drugs, but instead to distinguish their products from their competitors in the marketplace. (Tupper, Tr. 3006-08).

6. Like POM, Leading Government and Medical Research Centers Focus On The Relationship Between Nutrients, Foods And Disease

POM is not alone in its focus on the relationship between nutrients and diseases. Instead, it stands with the most prestigious government and medical research institutions, which have recognized the importance of such research, including research on pomegranates and POM-sponsored studies and the need to disseminate it to the public. (PX0301-PX0324). Indeed, both the USDA and the National Institutes of Health fund research exploring the connection between foods and improving health and reducing illness. (PX0301-PX0318; PX0392-PX0418; http://www.nih.gov/about/ and http://www.nih.gov/about/mission.htm (last visited, Jan. 8, 2012).

Similarly, prestigious medical institutions regularly publicize the relationship between the pomegranate fruit and its role in alleviating disease on their websites or publications:

- University of Texas MD Anderson Cancer Center (pomegranate juice may decrease PSA levels and is being studied for its ability to delay or prevent recurrent prostate cancer);
- MD Anderson Cancer Center (pomegranate inhibits "aromatase, which plays a key role in breast cancer growth," pomegranates are high in antioxidants "known to reduce the inflammation that plays a part in heart disease, cancer, high blood pressure and other diseases," and pomegranate may be beneficial for erectile dysfunction and high cholesterol);
- Memorial Sloan-Kettering Cancer Center (pomegranate juice shown to "suppress inflammatory cell signaling, inhibit prostate tumor grown, and lower serum PSA levels," and "benefit patients with carotid artery stenosis, in those with hypertension, hyperlipdemia, mild to moderate erectile dysfunction," citing POM sponsored Pantuck, Aviram, and Forest studies);
- Johns Hopkins Hospital ("among men with prostate cancer, daily glasses of pomegranate juice have slowed the increase in PSA levels after treatment," pomegranate juice can reduce the progression of atherosclerosis in the coronary arteries by inhibiting the oxidation of LDL cholesterol, pomegranate juice also "appears to stimulate the production of nitric oxide, a chemical that helps blood vessels relax.");

- Mayo Clinic ("it's thought that pomegranate juice could block or slow the buildup of cholesterol in your arteries", citing to POM-sponsored Davidson study, and "drinking pomegranate juice may slow the progression of prostate cancer".)

VI. POM'S CARE IN ADVERTISING AND CHANGES IN ADVERTISING OVER TIME

Respondents have proceeded conservatively to fully understand the physiological effects of pomegranates before using such research results in their advertising. (Tupper, Tr. 2981). Even when initial research findings are positive, POM will delay sharing the results from the public until the science is sufficiently developed. (Tupper, Tr. 2979). In fact, POM has independent institutions double-check even very positive results to verify their accuracy. (S. Resnick, Tr. 1693; Heber, Tr. 1964; S. Resnick, dep. at 200-201). Moreover, even though very encouraging research has been completed and published on many areas of science, such as immunity, cold and flu, cognitive function, skin and dental health, POM has exercised restraint and has chosen not to discuss those results in its advertising. (Tupper, Tr. 2979-81) The purpose of POM's conservative approach is to ensure that what is portrayed in the advertisements is consistent and accurate with the results of the scientific studies themselves. (Tupper, Tr. 2979; S. Resnick, dep. at 200-201).

As a result of two NAD decisions in 2005 and 2006, POM's advertisements changed significantly. (L. Resnick, Tr. 162, 168). Prior to these decisions, from 2003 through 2006, the language and graphics in POM's advertisements regarding the health benefits of POM Juice appeared to be more aggressive. After the decisions, however, POM qualified its messages and began to describe the scientific studies in its advertisements. (Tupper, Tr. 2985-87; 3029).

Largely as a result of the 2005 and 2006 NAD decisions, POM stopped making generalized statements in advertisements about its science. (Tupper, Tr. 2986-87). Since 2006, when discussing the health benefits of the Challenged Products, POM's policy has been to discuss and describe what research was done, where it was done and to summarize the results of the specific scientific studies described in its advertisements. (Tupper, Tr. 2986-87). In some cases, POM would direct consumers back to its website to read the full scientific study. (Tupper,

Tr. 2985). In addition, as a result of the NAD decisions, POM has implemented a more formalized process for vetting advertisements and describing the health benefits of its products. (Tupper, Tr. 2977-78). All of these changes are designed to better ensure that accurate information is presented to the public through POM's advertising. (Tupper, Tr. 2985-86).

VII. HOW TO EVALUATE THE SCIENCE BEHIND THE CHALLENGED PRODUCTS

Complaint Counsel and Respondents seem to agree that the totality of scientific evidence can and should be considered in determining what constitutes competent and reliable scientific evidence to prove the health benefits of the Challenged Products at issue, but disagree on what that means, *e.g.* whether only RCTs can be considered in demonstrating effects in humans, whether both positive and so-called "negative" studies should be considered in that analysis and whether any scientific value can be derived from small or "pilot" studies.

A. In Evaluating the Potential Health Benefits Of A Natural and Safe Foods Such As The Challenged Products, The Totality Of The Scientific Evidence Should Be Considered, Including Basic Science, Animal Research And "Pilot" Studies

In evaluating the health benefits of a natural and safe food, the totality and preponderance of the evidence should be examined, given that: (1) pomegranate juice and its extracts are safe; and (2) no one suggests that pomegranate juice or extracts should be offered in lieu of conventional medical treatment. (Heber, Tr. 1948-40, 2166, 2182; Miller, Tr. 2194; PX0206-0007, 15; Ornish, Tr. 2327-31). In examining the totality of the evidence, basic science, animal research and "pilot" studies, not just RCT can be relied upon as competent and reliable evidence to substantiate a health benefit claim. In some cases, basic science alone can be sufficient substantiation. (PX0206-0010-0011, 0013; Miller, Tr. 2194). While there may be limitations to extrapolating results from *in vitro* and animal studies to predict an effect in humans, it is false to suggest, as Complaint Counsel do, that such research has no value in determining the therapeutic efficacy of a food product. (PX0025-0007).

In fact, Complaint Counsels' own cardiovascular expert, Dr. Sacks, testified that *in vitro* studies can be competent and reliable evidence of an agent's effect on a particular mechanism.

(Sacks, Tr. 1578; PX0361 (Sacks, Dep. at 123-124)). Dr. Sacks admits there is value in conducting *in vitro* studies and animal studies because you can isolate mechanisms of action and accomplish toxicity or safety testing. (PX0361 (Sacks, Dep. at 89 -91)). Therefore, it is no surprise that Dr. Sacks considers all levels of science in issuing national guidelines for the prevention or treatment of cardiovascular disease. (PX0361 (Sacks Dep. at 71)).

In addition, small studies or "pilot" studies are also instructive and generally considered by other scientists and clinicians in the scientific community to be perfectly valid, accurate and reliable studies. (CX1336 (Davidson, Dep. at 232-233); CX1342 (Hill, Dep. at 48, 49, 53); CX1339 (Ornish, Dep. at 23)). In fact, "sometimes small studies can be more informative than large studies." (Heber, Tr. 1963). Although a study with a small number of participants may make it more difficult to achieve overall statistical significance, any positive finding just means the treatment has to be that much more powerful and consistent. (Ornish, Tr. 2362-2363; CX1338 (Padma-Nathan, Dep. at 108-109); PX0349 (Burnett, Dep. at 138-141); Ornish, Tr. 2352-53; Liker, Tr. 1884-86). For these reasons, Complaint Counsel err by insisting that RCTs can be the only evidence capable of substantiating a health benefit claim.

B. The Lack Of A Statistically Significant Result Does Not Undermine The Value Of The Study And Does Not Mean That Experts Cannot Rely Upon The Study To Infer A Causal Link

Complaint Counsel and their experts have repeatedly argued that the results of Respondents' scientific research should be disregarded in their entirety if the findings do not achieve statistical significance or if the studies are "underpowered." (CX1287_0012, 0014; CX1289_0004, 0008, 0010, 0012, 0015; CX1291_0012-0013, 0035, 0038; CX1293_0020-0021; Stampfer, Tr. at 710-11; Melman, Tr. at 1092; Eastham, Tr. at 1273; Sacks, Tr. at 1440). This is inconsistent with the holding in *Mattrix*, where the Supreme Court held "[a] lack of statistically significant data does not mean that medical experts have no reliable basis for inferring a causal link between a drug and adverse events." 131 S.Ct. at 1319. Indeed, "courts frequently permit expert testimony on causation based on evidence other than statistical significance." *Id.*

"[M]edical professionals and researchers do not limit the data they consider to the results of randomized clinical trials or to statistically significant evidence." *Id.* at 1320.

In this case, evidentiary support for Respondents' advertising claims should not be so narrowly limited as to include only research whose end result reaches statistical significance. Instead, Respondents have presented significant, contrary testimony and evidence demonstrating that a study may show clinically significant results even where statistical significance is not reached. PX0352 (Goldstein, Dep. at 108-109); Goldstein, Tr. at 2599; PX0189-0013; PX0361 (Sacks, Dep. at 109); PX0349 (Burnett, Dep. at 138-139)). Indeed, strict reliance on statistical significance in determining whether or not pomegranate juice offers a beneficial health benefit is an arbitrary and unnecessary convention. (Ornish, Tr. at 2340).

C. The Absence Of A Statistically Significant Or Positive Results Do Not Prove The Opposite Conclusion

Complaint Counsel and their experts dispute the health benefits of the Challenged Products because Respondents' scientific research allegedly did not produce statistically significant changes in certain and/or all of their studies and, as a result, Complaint Counsel contend that no benefit can be derived from the Challenged Products. (Melman, Tr. 1130-31; Sacks, Tr. 1488-89, 1507, 1512-13, 1516-19). The mere absence of significant, affirmative evidence in support of a particular claim, however, does not translate into negative evidence against the claim. *Pearson v. Shalala*, 130 F.Supp.2d 105, 115 (D.D.C 2001) ("Pearson II").

It is well-established in the scientific community that the absence of a statistically significant positive result in a study does not prove the negative, or in the other words, the absence of evidence is not evidence of absence. (Heber, Tr. 1981). In science, it is possible for a "type II" error to occur, which means there could be a statistically significant difference, but the sample size was not sufficiently large to detect a change. (PX0025-0019; CX1339 (Ornish, Dep. at 70-71)). Indeed, even Complaint Counsels' own expert, Dr. Sacks, concedes that the lack of statistical significance for a positive result is not proof of a negative and does not suggest that pomegranate juice did not cause the intended result. (Sacks, Tr. 1608).

Importantly, Complaint Counsel allege that Respondents deliberately violated the FTCA by continuing to make false and misleading representations after studies by Drs. Davidson and Ornish and others purportedly "showed no significant difference[s]" following the consumption of pomegranate juice. (CX1426_0017-0018). Respondents, however, did not (and cannot have) deliberately violated the FTCA when their scientific research on pomegranate juice and/or its extracts never proved the opposite hypothesis: that pomegranate juice and/or their extracts do not have a positive benefit. (Heber, Tr. 1981; PX0025-0019; Sacks, Tr. 1608-09; CX1352 (Heber, Dep. at 218); PX0361 (Sacks, Dep. at 223-224, 230, 238, 243); Goldstein, Tr. 2598-99)).

D. Rcts Are Not Required To Substantiate The Health Benefits Of Natural And Safe Foods Such As The Challenged Products

Complaint Counsel claim, contrary to mainstream nutritional science, that RCTs are required in all cases to demonstrate the efficacy of a natural and safe food product. Complaint Counsel are mistaken legally and scientifically. First, as a matter of law, "[n]othing in the Federal Trade Commission Act…. requires placebo-controlled, double-blind studies. The Act forbids false and misleading statements, and a statement that is plausible but has not been tested in the most reliable way cannot be condemned out of hand." *F.T.C. v. QT, Inc.*, 512 F.3d 858, 861 (7th Cir. 2008); *see also F.T.C. v. Direct Mktg. Concepts, Inc.*, 624 F.3d 1, 9 (1st Cir. 2010) ("a double-blind study is not necessarily required" to satisfy a reasonable basis claim).

1. RCTs Are Sometimes Not Possible or Even Better in Evaluating The Health Benefits Of A Food Or Nutrient

There is widespread scientific agreement that RCTs are not possible or even better for evaluating the health benefits of a food or nutrient. (RFF at ¶__[[cite section F]]; Miller, Tr. 2194; Heber, Tr. 1948-50, 2056, 2166, 2182; Ornish, Tr. 2327-31; RX5007; Stampfer, Tr. 831, 834; PX0362 (Stampfer, Dep. at 73-79)). In fact, in the field of nutritional epidemiology, which analyzes the connections between nutrition and disease, it is well-accepted that RCTs are not the best source of valid and reliable information on nutrition. (RFF at ¶__[[cite section Stampfer FF]]).

There are multiple reasons for this consensus. First, ethical principles do not permit randomizing individuals to diets that may have negative health effects. (RX5007; PX0362 (Stampfer, Dep. at 78)). It is very difficult to ensure that large numbers of participants adhere to an altered diet over long-term periods. (RX5007; PX0362 (Stampfer, Dep. at 75-76)). Second, the cost of such studies creates an almost insurmountable barrier, given that no exclusive intellectual property rights (like a pharmaceutical patent) will result from a nutritional trial. (RX5007; PX0362 (Stampfer, Dep. at 75-76)). Third, in a nutritional context, a hypothesis about disease causation can, rarely, if ever, be directly tested in humans using the RCT design. (Stampfer, Tr. 832-833; PX0362 (Stampfer, Dep. at 73, 98); RX5007). If RCTs were required before it could be said that scientific evidence supports a particular claim about the health benefits of food, the field of nutrition science would be almost eliminated.

Notably, Complaint Counsels' own expert witness in this area, Professor Stampfer, openly concedes that evidence-based medicine/nutrition is not restricted to RCTs. (Stampfer, Tr. 831, 837; RX5007). Professor Stampfer indicated that scientific evidentiary support for nutritional claims will necessarily be based on observational studies, and RCT trials, due to the various feasibility issues pertaining to RCTs. (Stampfer, Tr. 830, 834; PX0362 (Stampfer, Dep. at 73-79); RX5007). Professor Stampfer even goes so far as to concede that "there are situations where you would determine causality in the absence of a randomized trial," and that an RCT is not required to conclude a causal link regarding a nutrient and disease. (PX0362 (Stampfer, Dep. at 73, 99).

Indeed, in an article entitled "*Evidence-based criteria in the nutritional context*," Professor Stampfer opined that the general principles of evidence-based nutrition "can provide a sufficient foundation for establishing nutrient requirements and dietary guidelines in the absence of RCTs for every nutrient and food group." (Stampfer, Tr. 831; RX5007). Professor Stampfer further stated that "it seems clear that requiring RCT-level evidence to answer questions for which the RCT may not be an available study design will surely impede the application of nutrition research to public health issues." (RX5007).

2. Many Factors Favor Disclosure of Potential Health Benefits to the Public in the Absence of RCTs

Respondents' expert, Dr. Miller, confirms that when a food product is absolutely safe and where there is no suggestion that the product be used as a substitute for conventional medical treatment, then it is appropriate to rely on the totality of the science (and in some cases, only basic science), and not require only RCTs, to substantiate health claims. (Miller, Tr. 2194, 2201; PX0206-0010-0015; Heber, Tr. at 1948-50, 2056, 2166; PX0149-0006-0007; Burnett, Tr. 2272-74, 2303; PX0189-0003; Goldstein, Tr. 2600-02, 2611, 2620); deKernion, Tr. 3060; PX0025-0007).

Complaint Counsels' own expert, Professor Stampfer, conceded that he "believe[s] that it may be appropriate to use evidence short of an RCT for crafting public health recommendations regarding nutrient guidelines even when causality cannot be established, because everyone eats and the public should be given advice based on the best evidence available." (CX1293_0029-0030). As such, it is no surprise that Professor Stampfer testified that when there is little risk and little cost involved we should "definitely" make that potential benefit available to the public rather than withhold it. (Stampfer, Tr. 838).

This view is evidenced by the number of public health recommendations and clinical practices followed in the absence of RCTs. Federal agencies and internationally recognized academic institutions have publicized their research on some of the same health benefits at issue in this case using *in vitro*, animal and small-scale human models as the bases for their scientific inquiries. (RFF at ¶__[[cite section F]]). For example, the Agricultural Research Service, which is the U.S. Department of Agriculture's chief scientific research agency, has investigated and funded research on fruits, vegetables and nuts and publicized studies examining various foods and their potential impact on various human ailments based on *in vitro*, animal and small-scale human models. (PX0301-PX0318). Even the FDA has approved pharmaceutical products without requiring the type of rigorous clinical trials Complaint Counsel argues are applicable here. From 1973 through 2006, the FDA approved 31 oncology drugs without an RCT using the Accelerated Approval and Priority Review Program ("Fast Track Program").

Finally, much of what physicians provide patients in their clinical practices have not been proven to be beneficial in RCTs. (PX0025-0007; Sacks, Tr. 1559; PX0361 (Sacks Dep. at 111); CX1341 (Pantuck, Dep. at 276-277)). For example, Complaint Counsels' own expert, Dr. Eastham, admitted he has performed over 200 radical prostatectomies per year for a number of years before there were any RCTs showing that it actually worked. (Eastham Tr. 1331-32; PX0358 (Eastham, Dep. at 154-155)). Also, Dr. Pantuck stated that clinicians remove kidneys without a RCT showing the benefits of nephrectomy. (CX1341 (Pantuck, Dep. at 276-277)). Further, Complaint Counsels' experts, Professor Stampfer and Dr. Sacks, admitted that they have made public health recommendations that were not supported by RCTs. (Stampfer, Tr. at 810, 813-814; PX0300 (Stampfer, Dep. at 173); PX0361 (Sacks, Dep. at 35-38, 130-131)).

VIII. THE SCIENCE BEHIND THE ANTIOXIDANT AND ANTI-INFLAMMATORY PROPERTIES OF THE CHALLENGED PRODUCTS

A. The Challenged Products Contain Power Antioxidants Which Stabilize Free Radicals And Reduce The Cellular Damage Caused By Oxidation

Respondents have shown that the Challenged Products have beneficial nutritional effects on cardiovascular, prostate and erectile health. The human body suffers harmful effects from the biological processes know as oxidative stress and inflammation. Through numerous peer-reviewed scientific studies confirmed (at the *in vitro*, animal and human level) and expert opinions, Respondents have presented competent and reliable evidence supporting the anti-oxidative and anti-inflammatory properties of the Challenged Products. Additionally, Respondents offered into evidence scientific studies and expert opinions showing that the compounds found in the Challenged Products are bioavailable in humans, that POMx is bioequivalent to POM Juice and the Challenged Products are safe for human consumption.

1. Respondents Presented Substantial Evidence on the Potency of the Polyphenol Antioxidants in the Challenged Products

Humans are constantly exposed to oxidative stress. RFF . Normal cellular metabolism produces as its by-products various highly reactive molecules, collectively termed "oxidants." RFF . These oxidants, known as "free radicals," include a variety of different chemicals which,

like oxygen, are capable of inflicting oxidation damage. Free radicals and oxidative stress have been implicated in a wide variety of degenerative processes and diseases, including aging and age-related diseases like cancer and cardiovascular disease. RFF . Although the body has mechanisms to curtail free radical damage, over the long term, the human body cannot eliminate oxidative damage by relying on its own antioxidant defenses. RFF . Net oxidative damage accrues, contributing to cardiovascular disease, cancer and other ailments. RFF .

However, antioxidants neutralize free radicals by inhibiting oxidation at a molecular, cellular and organ level or helping to repair the damage caused by oxidation. RFF . These mechanisms of action of antioxidants thereby prevent some of the damaging health effects of oxidation. RFF . Thus, consuming foods with increased antioxidant potency promotes overall health in a number of organ systems by different mechanisms, which is well accepted with the scientific community. RFF . In fact, research agencies of the United States Government recognize the health benefits of antioxidants, including their ability to fight the cellular damage caused by free radicals. RFF .

Here, Respondents have presented substantial evidence that antioxidants play a critical role in protecting cells against the harmful effects of free radicals. RFF . Respondents have also shown that the Challenged Products have exceptionally powerful antioxidant effects and contain among the most potent naturally-occurring polyphenol antioxidants found in foods or dietary supplements. RFF . The exceptional potency of the Challenged Products have been scientifically demonstrated in numerous *in vitro*, animal and in human clinical studies showing that the consumption of the products can, among other health benefits, reduce the oxidation of LDL and early and late stage plaque development and have positive effects on, among other things, cardiovascular, prostate and erectile health.

2. Complaint Counsel Have Failed To Rebut Respondents' Evidence on the Nutritional Benefits of Antioxidants' in Fighting Free Radicals

Complaint Counsel failed to rebut Respondents' evidence on the exceptional antioxidant effects of the Challenged Products on the maintenance of human health. First, Complaint

Counsels' experts, Professor Stampfer and Dr. Eastham, never opined in this case that the Challenged Products actually do not provide the health benefits advertised by Respondents. RFF . Rather, they avoid making this bold, unsustainable assertion by merely opining that, based on the limited materials they reviewed, there is no competent or reliable scientific evidence to support Respondents' health benefit claims. RFF . This qualified opinion is a far cry from affirmatively claiming that the Challenged Products do not provide health benefits. In this regard, Complaint Counsel did not conduct their own testing of the Challenged Products to prove or disprove any of Respondents' health-benefit claims.

Moreover, Complaint Counsel presented no expert opinion or affirmative evidence rebutting Respondents' evidence concerning either the antioxidant potency of the Challenged Products or that they contain more antioxidants than comparative fruit juices or supplements. RFF . Indeed, Complaint Counsels' expert, Professor Stampfer, concedes that he has no opinion about the particular classes of antioxidant compounds within pomegranates or the extent to which the antioxidant effect of pomegranate juice on human health is attributable to anthocyanins as opposed to other antioxidants such as punicalagins. RFF . Conversely, Respondents presented the expert opinion of Dr. David Heber, a world-renowned expert in nutrition, who has opined that antioxidants are beneficial to one's health, including cardiovascular, erectile and prostate health.

Complaint Counsel presented no evidence refuting the fact that antioxidants, including the hydrolysable tannins and ellagic acid found in the Challenged Products, neutralize free radicals or that free radicals play an role in cardiovascular disease and cancer. RFF . Nor could Complaint Counsel advance such a frivolous argument given the great weight of scientific research and literature clearly establishes the facts as advanced by Respondents. RFF .

B. Antioxidants Impact The Level And Preservation Of Nitric Oxide In The Body Which Is Beneficial To Cardiovascular Health And Erectile Function

Respondents have also shown that the antioxidants in the Challenged Products are beneficial to health through the mechanism of impacting nitric oxide ("NO") in the body. NO

plays a key role in inflammation, blood flow regulation, cell growth and smooth muscle relaxation, all of which offer protection against atherosclerosis. RFF . For example, NO helps maintain healthy blood vessels, which improves blood flow to almost every organ in the body. RFF . Maintaining healthy blood vessels and the flow of blood to the heart and penis are important to cardiovascular health and erectile function. RFF . Antioxidants are well known to increase and prolong cellular concentrations of NO by protecting it from oxidation. RFF .

Here, Respondents presented competent and reliable scientific evidence as well as expert opinion that consumption of the Challenged Products also affects NO in that they increase and prolong cellular concentrations of NO by protecting it from oxidation. RFF . As for erectile health, because NO plays a crucial role in the erectile process (RFF), the Challenged Products demonstrated an ability to increase the level and prolong the concentration of NO, and support the conclusion that consumption of the products supports erectile health. RFF .

Complaint Counsel provided no credible evidence contradicting Respondents' evidence of the beneficial effects of the Challenged Products on NO. For example, Complaint Counsel provided no expert opinion that NO does not help maintain healthy blood vessels and blood flow or that antioxidants do not protect NO against oxidative destruction. RFF . Nor did Complaint Counsel dispute NO's role in cardiovascular and erectile health. RFF . Complaint Counsel also presented no expert opinion sufficient to prove that Respondents' heart, prostate and erectile health claims are not substantiated by competent and reliance evidence.

C. Antioxidants Lessen Inflammation Which Provides Health Benefits In Regard To Cardiovascular Health, Cancer And Erectile Function

Respondents provided competent and reliable scientific evidence and expert opinion that the antioxidants in the Challenged Properties have anti-inflammatory properties, which are beneficial to human health. Complaint Counsel have failed to contradict this evidence.

It is well established in the scientific community that inflammation plays a critical role in mediating atherosclerosis, the narrowing of arteries caused by buildup of cholesterol-based fatty plaques. RFF . Atherosclerosis is the primary cause of heart disease, and because it leads to

restricted blood flow, is a causative factor in erectile dysfunction. RFF . Inflammation is also a characteristic prostate cancer. RFF . Each of these facts is undisputed. RFF .

Although inflammation can be caused by many factors, activation of nuclear factor-kB ("NF-kB"), the oxidative stress responsive transcription factor, has been linked with a variety of inflammatory diseases and ailments, including prostate cancer, cardiovascular disease and erectile dysfunction. RFF . However, the pathway that activates NF-kB can be inhibited by phytochemicals, thus limiting the development of these inflammatory diseases and ailments. RFF . Each of these facts is undisputed. RFF . In regard to the role of NF-kB in anti-inflammatory disease, Respondents have presented competent and reliable evidence in the form of scientific studies and expert opinion demonstrating that the antioxidants in the Challenged Products inhibit the pathway that activates NF-kB, thereby reducing inflammation and improving blood flow in the arteries. RFF . This fact is not disputed. RFF.

Moreover, Respondents also demonstrated that the Challenged Products are impactful on human health by lessening inflammation in another way. High-density lipoprotein ("HDL") contains an antioxidant enzyme called PON1 that protects against oxidation. RFF . Respondents presented scientific studies and expert opinion showing that the antioxidants in the Challenged Products increase PON1 association with HDL, thereby reducing inflammation in coronary arteries which is beneficial to cardiovascular health and other inflammatory diseases. RFF .

In sum, the anti-inflammatory properties of the Challenged Products have been established through competent and reliable scientific studies and expert opinion and offer yet another pathway through which the Challenged Products may contribute to health.

D. The Antioxidants In The Challenged Products Are Bioavailable In Humans

Studies on the human metabolism of the Challenged Products conclusively demonstrate that the polyphenol antioxidants found in the products are bioavailable in humans, meaning the body is able to absorb and use them. No evidence in the record contradicts this fact.

The only evidence on the bioavailabilty of the Challenged Products was presented by Respondents in the form of scientific studies examining the bioavailability of pomegranate-based

products in humans and the expert opinion of Dr. David Heber. RFF . When confronted with the overwhelming evidence supporting the bioavailability of the Challenged Products in humans, Complaint Counsel did not present any contradictory evidence. RFF . For example, it was not within the scope of Complaint Counsels' experts' assignment, and none opined in their expert report that credible and reliable scientific evidence shows that the Challenged Products are not bioavailable in humans. RFF . Despite Complaint Counsels' failure to present any evidence on bioavailability, the record is replete with credible scientific evidence and expert opinion presented by Respondents supporting the bioavailability of the Challenged Products in humans. RFF .

As stated by Dr. Heber in his expert report, scientific studies conclusively "demonstrate the bioavailability of the antioxidants found in pomegranate juice." RFF . Complaint Counsel presented no scientific evidence refuting either Dr. Heber's expert opinion or the scientific studies presented by Respondents. RFF .

E. POMx Pills And POMx Liquid Are Bioequivalent To POM Juice

Studies consistently and persuasively establish the equivalency of the POMx to POM Juice. These studies show, not only that the POMx products contain similar amounts of active pomegranate polyphenol antioxidants as POM Juice, but also that these antioxidants are similarly bioavailable, thereby providing similar health benefits. RFF . The scientific equivalence of the active antioxidants in the POMx products and POM Juice is confirmed by the expert opinion of Dr. Heber. RFF . Complaint Counsel presented no evidence to the contrary. RFF .

In sum, the evidence in the record fully supports the conclusion that POMx Pills and POMx Liquid have equivalent antioxidant power as POM Juice.

IX. RESPONDENTS' HEART, PROSTATE AND ERECTILE CLAIMS ARE SUBSTANTIATED BY COMPETENT AND RELIABLE SCIENTIFIC EVIDENCE

A. POM's Heart Health Claims Are Substantiated

Complaint Counsel allege that Respondents have falsely represented in their advertisements, either expressly or by implication, that: (1) drinking eight ounces of POM Juice,

or taking one POMx Pill or one teaspoon of POMx Liquid, daily, prevents or reduces the risk of, or treats, heart disease by: (a) decreasing arterial plaque; (b) lowering blood pressure; and/or (c) improving blood flow to the heart; and (2) studies prove the same. (Compl, §§ 12, 19).

Although Respondents deny that they make these purported claims, the totality of Respondents' scientific evidence from in vitro studies, animal research, and human clinical trials nevertheless demonstrates that the Challenged Products are likely to be beneficial in maintaining cardiovascular health and help reduce the risk of cardiovascular disease by reducing arterial plaque, lowering blood pressure, and improving blood flow.

B. Overview of Cardiovascular Heart Disease

Heart disease, including heart attacks or angina, occurs as the result of decades long damage to blood vessels. The process begins with the oxidation of the protein known as low density lipoprotein ("LDL" or bad cholesterol) which circulates in the blood. Once LDL becomes oxidized, the chemical nature of the protein changes, causing it to reside and accumulate in the blood vessel. Macrophages, white blood cells that respond to inflammation by digesting cellular debris, begin to engulf and devour the oxidized cholesterol. These macrophages continue to accumulate until they develop into "foam cells." These foam cells become full of cholesterol and actually burst, bringing in more macrophages and more inflammation. As this process progresses, plaque begins to form as yellow steaks in the coronary arteries.

In addition, blood flow becomes disturbed when blood passes through plaque or atherosclerotic lesions. This disturbance leads to an increase in shear stress that damages endothelial cells, the thin layer of cells that lines the interior of blood vessels, further contributes to oxidative stress, and initiates the development of atherosclerosis. Ultimately, the build-up of plaque or the rupture of an inflamed plaque can interrupt blood flow to the heart either temporarily (resulting in chest pain or angina) or longer (resulting in scarring or death to the heart muscle, commonly referred to as a heart attack).

Antioxidants play an important role in mitigating heart disease by, among other things, inhibiting oxidative stress, including reducing LDL oxidation (and its uptake) and inflammation. In addition, the presence of nitric oxide in the body also helps offer protection against atherosclerosis by regulating blood flow and contributing to smooth muscle relaxation.

C. Respondents' Basic Science Demonstrates the Beneficial Effects of Pomegranate Juice and Its Derivatives on Cardiovascular Health.

Respondents have sponsored at least 15 published studies evaluating the effects of pomegranate juice and/or its derivatives on cardiovascular health in vitro and animals. Beginning around 2000 and continuing to the present, Dr. Michael Aviram began the earliest studies investigating pomegranate juice's potential benefits to the cardiovascular system. Dr. Aviram and his colleagues observed several beneficial effects of pomegranate juice and its extracts at the cellular and animal stage, including but not limited to: (1) reduction in oxidation of LDL cholesterol; (2) lessening the "uptake" of oxidized LDL by macrophage foam cells; (3) decrease in size of atherosclerotic lesions and foam cells; and (4) diminishing of platelet aggregation.

Respondents also funded considerable in vitro and animal studies to examine the impact of pomegranate juice on nitric oxide and its effects cardiovascular health. Dr. Louis Ignarro, recipient of the Nobel Prize, Dr. deNegris, and Dr. Napoli conducted a number of studies in which they found that pomegranate juice and/or POMx; among other things: (1) increased and preserved levels of nitric oxide in cell cultures; (2) decreased LDL oxidation, the size of atherosclerotic plaques, and foam cell formation; and (3) reversed effects of shear stress.

D. Respondents' Clinical Research Confirms Results Found in Earlier Cellular and Animal Studies and Shows Positive Effects on Arterial Plaque, Blood Pressure and Blood Flow.

In addition to 15 published studies at the cellular and animal level, Respondents have sponsored approximately 10 published studies analyzing the effects of pomegranate juice and/or its extracts on cardiovascular health in human subjects. Among these studies, Dr. Dean Ornish, Respondents' own expert in cardiovascular health, examined the effects of POM Juice on a

patient's myocardial perfusion (blood flow). After three months, patients drinking POM Juice experienced a 35 percent comparative benefit in blood flow. In another study by Dr. Michael Davidson, a subgroup of patients at high risk for cardiovascular disease experienced a statistically significant reduction in carotid intima-media thickness ("CIMT") after 18 months. Given the subgroup at risk, Dr. Davidson's finding alone could benefit tens of millions of people in the United States.

Respondents' body of human research is consistent with, and confirms, the findings made in Respondents' basic science. Together, the totality of Respondents' scientific of evidence at the cellular, animal, and human level constitutes competent and reliable evidence that the Challenged Products are beneficial to cardiovascular health by decreasing arterial plaque, lowering blood pressure, and improving blood flow to the heart.

E. Complaint Counsels' Expert on Cardiovascular Disease/Health, Dr. Frank Sacks, Fails to Rebut the Conclusions of Respondents' Experts, Dr. Dean Ornish and Dr. David Heber, that Competent and Reliable Scientific Evidence Exists to Show that the Challenged Products Are Beneficial in Reducing Arterial Plaque, Lowering Blood Pressure, and Improving Blood Flow.

Complaint Counsels' expert on cardiovascular disease, Dr. Frank Sacks, fails to (and cannot) diminish the validity of Respondents' extensive body of research on pomegranate juice and its effects on cardiovascular health. Here, Dr. Sacks attempts to discredit Respondent's heart health studies by adopting an indefensible "drug" standard for evaluating cardiovascular research and by trying to isolate and pick apart Respondents' studies, one by one, rather than considering the entire body of science as a whole. Dr. Sacks' expert opinions should be dismissed on both counts.

1. RCTs Are Not Necessary (or Even a Better Method) to Prove the Health Benefits of a Natural Food or Juice, Such as Pomegranate Juice and Its Various Forms.

Dr. Sacks' rigid requirement that only RCTs should be considered in evaluating the therapeutic value of a food is not only contradicted by the scientific community (including Complaint Counsels' own expert, Dr. Meir Stampfer), but also by Dr. Sacks' own concessions at

trial and deposition. Although he claims RCTs (some costing $6, $60, or $600 million) are absolutely needed to substantiate health claims even if a product is completely safe and provides a potential benefit to the public, Dr. Sacks nevertheless concedes that we should weigh the risk that the product will do harm against the potential of keeping information from the public. (Sacks, Tr. 1530-1540; 1558-1559; RX 5007).

Indeed, in his testimony, Dr. Sacks admits that in evaluating a natural food, RCTs are simply not necessary in all cases. For instance, Dr. Sacks served as the Chair of the Design and Analysis Committee for the DASH ("Dietary Approaches to Stop Hypertension") diet sponsored by the National Heart, Lung and Blood Institute, part of the National Institute of Health. (PX0361a03). In researching and developing the DASH diet, Dr. Sacks concedes that it is not necessary to test the efficacy of all individual fruits that a person may decide to choose to consume by conducting a RCT because the "category of fruit," including pomegranates, has already been studied. (Sacks, Tr. 1541-1546). Moreover, in designing the DASH diet, Dr. Sacks admits that fruits and fruit juices are treated same. (Sacks, Tr. 1549-55).

In addition, Dr. Sacks also acknowledges that RCTs are not feasible because of logistical, financial, and ethical considerations. For example, in some cases, studies cannot be blinded, i.e., the subjects would know whether they are being subjected to a high or low sodium diet or, in other cases, the studies would be too expensive. (Sacks, Tr. 1435, 1561-62). Finally, Dr. Sacks actually proves the point that RCTs are not necessary to substantiate the health benefit claim of a food or nutrient when he confessed that he has recommended (or would recommend) fish oil (Omega-3) or a reduction in sodium to patients with coronary heart disease even though no RCTs have been conducted on them. (Sacks, Dep. at 35-38; 55-56)

In short, as validated by Respondents' experts, Dr. Ornish, Dr. Heber, and Dr. Miller, and even Complaint Counsels' own expert, Dr. Meir Stampfer, the appropriate standard for evaluating whether a food is beneficial in maintaining cardiovascular health and lessening the risk of cardiovascular disease is that the totality of the evidence should be examined given that: (1) pomegranate juice and its extracts are safe; (2) no one suggests that pomegranate juice or its

extracts should be offered in lieu of conventional medical treatment or surgery; (3) the expense associated for conducting a FDA drug study for a non-patentable, natural food is exorbitant and prohibitive; and (4) the potential benefit or information to be gained by the public outweighs any plausible harm.

2. Dr. Sacks' Individual Criticisms of Respondents' Cardiovascular Science Lack Merit and Should Be Disregarded.

Dr. Sacks also tries to depict Respondents' cardiovascular research on humans to be inconsistent and therefore unreliable. In particular, Dr. Sacks claims that Dr. Aviram's finding of a 30 percent reduction in arterial plaque and 21 percent reduction in systolic blood pressure to be contradicted by subsequent studies, published and unpublished, conducted by Dr. Ornish, Dr. Davidson, and others. Dr. Sacks, however, is wrong. First, Dr. Aviram's finding of a 30 percent reduction in arterial plaque in his 2004 study (PX ____) remains valid following Dr. Ornish's unpublished 2005 IMT study ("Bev II") and Dr. Davidson's published 2009 IMT study because: (1) Dr. Ornish's Bev II study was underpowered, never reached statistical significance, and accordingly, as Dr. Sacks confesses, the absence of a positive result does not prove a negative benefit (i.e. that pomegranate juice did not improve IMT); (2) Dr. Davidson's study examined a healthier patient group, those at moderate risk of coronary heart disease (carotid artery plaque of less than 2.0 mm), while Dr. Aviram's study investigated those with carotid artery stenosis (a narrowing of the carotid artery due to plaque). Furthermore, Dr. Aviram's and Dr. Davidson's studies are entirely consistent because Dr. Aviram examined a group of patients with high oxidative stress which is similar to the high-risk subgroup in Dr. Davidson's study. Thus, neither Dr. Ornish's nor Dr. Davidson's studies could (or should) be interpreted to contradict, in any way, Dr. Aviram's published finding on arterial plaque.

F. Respondents' Prostate Health Claims Are Substantiated by Competent and Reliable Scientific Evidence

In its Complaint and during the proceedings, Complaint Counsel accused POM, through its advertisements, of making unsubstantiated claims that drinking POM Juice and/or taking POMx (pill and/or liquid) daily (1) prevents or reduces the risk of prostate cancer and (2) treats

prostate cancer. (CX1426, ¶¶14-15, 19). POM denies ever making such claims and a review of the Challenged Advertisements, as demonstrated through the proceedings, show that POM never made such claims. (RFF ¶ CITE AD FINDINGS). POM's "prostate" ads instead used cheeky puffery phrases concerning prostate health like "Drink to prostate health" or "I'm off to save PROSTATES!" combined with qualifying text stating, "improve prostate health" or "*hopeful results for prostate health*" or "hopeful results for men with prostate cancer." *Id.* Not once has POM claimed that the Challenged Products "prevents" or "treats" prostate cancer. Even when the advertisements cited some of POM's underlying research, those statements were qualified with language like, "an initial UCLA medical study" or the study showed "statistically significant prolongation of PSA doubling times." *Id.*

Even assuming that POM did make "prevents" or "treats" prostate cancer claims, a multitude of basic and clinical studies underlying POM's prostate advertising demonstrates there is competent and reliable science to support such claims. Further, the testimony and cross-examination of the parties' experts has only served to highlight and confirm that POM's prostate health claims are substantiated and the peer-reviewed science behind them is well-founded.

1. PSA Doubling Time Is A Valid Surrogate For Recurrence And/Or Death From Prostate Cancer

PSA doubling time ("PSADT"), a measure of the time it takes the levels of prostate specific antigen ("PSA")—a protein made by prostate cells—to double in a man's blood, is currently the best marker for recurrence of prostate cancer following radical prostatectomy or radiation therapy. (deKernion, Tr. 3055). Generally, the shorter the doubling time the greater the risk of recurrence of cancer. (deKernion, Tr. 3084, 3124). As studied and demonstrated in multiple peer reviewed articles in very reputable journals, PSADT accurately reflects prostate cancer cell behavior and there is now widespread acceptance of PSADT as a valid surrogate and predictor of recurrence of prostate cancer and death. For example, in a study by *Pound, et al.* (JAMA 1999), the investigators found a strong correlation between the length of the PSADT after radical prostatectomy and biochemical recurrence and the expected clinical recurrence

(PX0163). Similarly, in a study by *Patel, et al.* (Journal of Urology 1997), the authors found that PSADT was correlated with the risk of clinical recurrence—the longer the doubling time the lower of the risk of clinical recurrence (PX0162).

In yet another study by *Tollefson, et al.* (Mayo. Clin. Proc. 2007) (PX0166), the authors found that PSADT was a "highly significant and reliable test" to determine the likelihood of disease recurrence and death: "an excellent indicator of clinical disease recurrence" and the "the only significant factor that predicts clinical progression." (PX0166-0001, 6 (emphasis added)). And a recent study by *Teeter, et al.* (Urology 2011) (PX0167) similarly correlated length of PSADT with risk of mortality noting the "widespread acceptance" that PSADT after radical prostatectomy predicts prostate cancer mortality and that this has been "well established" and that PSADT is "a powerful predictor of overall survival." (PX0167-0001, 3, 5). The multitude of additional peer-reviewed articles cited by Respondents' prostate expert, Dr. deKernion, only serve to confirm this fact. *See* Dr. deKernion Expert Report and Reference Articles appended to thereto. (PX0161-PX0188).

2. Complaint Counsels' Expert's Challenge of PSADT as a Marker Is Not Well-Taken

Complaint Counsels' prostate expert, Dr. James Eastham, challenged the appropriateness of PSADT as a surrogate marker for prostate cancer clinical recurrence or survival. (PX0298-0010-0011; Eastham, Tr. 1340-44). His logic and conclusion is suspect for a number of reasons.

First, as noted above, it is anathema to literally dozens of published articles over the last 20 years that have found PSADT to be the best marker for prostate cancer clinical recurrence and eventual mortality. (PX0161-PX0188).

Second, even Dr. Eastham himself explicitly admitted in a 2005 article he authored that: "PSA doubling time has emerged as an important factor in the evaluation of men with newly diagnosed prostate cancer or prostate cancer that recurs after treatment. PSA doubling time can be used as a surrogate marker for prostate cancer specific death." (PX0178-0001). He further admits in the article that "PSADT is an important marker in men with biochemical failure after

local therapy for prostate cancer, and it predicts the probable response to salvage radiotherapy, progression to metastatic disease and prostate cancer specific death." (PX0178-0009). Dr. Eastham failed to explain his apparent change of heart (during these proceedings) as to the usefulness of PSADT.

Third, most, if not all of treating urologists, including Dr. Eastham and Dr. deKernion, utilize PSADT as a prognostic marker for recurrence of prostate cancer and mortality following radical prostatectomy. (deKernion Tr., 3051; Eastham, Tr. 1343-44; PX0161-0004, 0007). Why it is useful and prognostic in his practice but not otherwise was again not explained, by Dr. Eastham.

Tellingly, and only after being challenged about the obvious contradiction in his testimony and his article cited above, did Dr. Eastham concede that PSADT following radical prostatectomy was a prognostic marker for clinical progression and death from prostate cancer following radical local treatment. (Eastham Tr. 1342-44). He attempted to qualify this admission by stating that PSADT is only accepted as a prognostic marker for clinical progression and recurrence of prostate cancer and death at baseline, meaning immediately after radical prostate treatment, but stops being predictive after baseline. (Eastham, Tr. 1342-44). He was unable to articulate why PSADT is predictive and useful immediately following treatment but no longer useful after that. He was similarly unable to state when in time following treatment, PSADT stops being predictive. (Eastham Tr., 1340-44).

His apparent explanation only further convolutes his analysis: changes or modulation of PSADT have not been accepted as a surrogate for clinical recurrence of prostate cancer or death even though the marker itself may be useful as such at baseline. (Eastham, Tr. 1342-44; Tr. 1340-41). Again, Dr. Eastham had no explanation for this novel theory. *Id.* If a marker is prognostic of one's chances of recurrence of disease, why would something that is able to modulate the readings from that marker not be indicative of changes to the underlying disease? Dr. Eastham even suggested that no physician or researcher would ever propose that changes in PSADT are prognostic of prostate cancer behavior following radical prostate treatment, and yet

Drs. deKernion and Heber both do. (Heber, Tr. 2151; deKernion, Tr. 3055; PX0161-0007, 0011-0012). Complaint Counsels' expert, Dr. Meir Stampfer similarly opined that PSADT was "a predictor of disease of mortality" and that, if the extension of PSADT time is true, it would substantially prolong lives. (Stampfer, Tr. 869, 873). This view is the dominant one and consistent with several peer reviewed articles that specifically studied changes or modulation of PSADT and correlated them with chances of clinical recurrence of prostate cancer. (PX0168-PX0170).

In sum, PSADT is a widely accepted surrogate for prostate cancer clinical recurrence and death following radical prostatectomy and Complaint Counsels' challenge to it fails. (PX0161-PX0188).

3. The Evidence is "Very Convincing" That Pomegranate Juice Affects, Promotes And Supports Prostate Health

In a 2006 study, entitled "(*Phase II Study of Pomegranate Juice for Men with Rising Prostate-Specific Antigen Following Surgery or Radiation for Prostate Cancer)*," published in the prestigious Clinical Cancer Research Journal, *Pantuck, et al.* (UCLA Medical School) (PX0060), studying men that had undergone radical prostatectomy or radiotherapy, found that drinking 8 ounces of POM juice daily materially lengthened PSADT in nearly 50% of men after 18 months - in fact, PSADT almost tripled. The study also found that when POM Juice was tested *in vitro* on prostate cell assays, it was found to both decrease prostate cancer cell proliferation by 12% (i.e., slow its growth) and stimulate prostate cancer cell apoptosis (cell death) by 17%. Additionally, serum nitric oxide increased by 23% in men that consumed POM. *Id.* As testified to during the proceedings, nitric oxide is a molecule that has been found to inhibit inflammation, which is correlated with higher risk of cancer. (PX0060; CX1407_0228-0231).

In 2008, Dr. Pantuck presented a follow-up report to his 2006 study to the American Society of Clinical Oncology. (PX0061). His follow-up work demonstrated that for those subjects that continued with the pomegranate juice regimen, they maintained the lengthening of

their PSADT as compared to those who did not continue the pomegranate juice. (CX1341 (Pantuck, Dep. at 136); Eastham, Tr. 1305). This study was subsequently published in the prestigious Journal of Urology in 2009. (PX0061).

A randomized Phase II trial by *Carducci, et al.* (Johns Hopkins School of Medicine) in 2011 (PX0175) entitled "(*A Phase II Study of Pomegranate Extract for Men with Rising Prostate-Specific Antigen Following Primary Therapy*)," published in the highly respected Journal of Clinical Oncology, confirmed the initial clinical findings demonstrated by the first *Pantuck, et al.* study. In the *Carducci* study, 104 men who had previously been treated for prostate cancer, were randomized into a double-blind clinical trial and were given either 1 or 3 doses of POMx Pills (equivalent to 8 ounces of pomegranate juice) for 18 months. Their PSADT was measured over that time and it was again found that there was a significant effect of POMx Pills on PSADT independent of dose—it lengthened it significantly—nearly doubling it.

4. The Clinical Research On POM Is Consistent With The Pre-Clinical Basic Science Which Shows A Robust Effect Of POM On Prostate Cancer Cells

The *Pantuck* and *Carducci* clinical studies were consistent with earlier (and later) pre-clinical laboratory and animal studies that showed a robust effect of POM Juice on prostate cancer in *in vitro* and in *in vivo* mouse models. (PX0065-PX0071). In this pre-clinical research, which studied human prostate cancer in the lab and inside of mouse models, POM Juice was found to inhibit cancer cell growth, promote prostate cell death, and inhibit the inflammatory process which is correlated with the growth of cancer. *Id.*

For example, in a study by *Seeram, Heber et al.*, "(*Pomegranate Ellagitannin-Derived Metabolites Inhibit Prostate Cancer Growth and Localize to the Mouse Prostate Gland*)," J. of Agric. Food Chem. 2007 (PX0069), the researchers evaluated the effects of pomegranate extract on prostate cancer growth in severe combined immunedeficient mice injected with human prostate cancer cells and on prostate cancer cells *in vitro* (in a Petri dish). (PX0069-0001). The study showed that the pomegranate extract significantly inhibited the growth of the human prostate cancer in the mouse as compared to the control. (*Id.*) Similarly, it was found that the

hydrolyzed derivatives of ellagitannins—the most abundant polyphenol anti-oxidant present in pomegranate juice, significantly inhibited the growth of human prostate cancer cells *in vitro.* (*Id.*) Finally, it was found that the bioactive derivatives of ellagitannins discussed above, was found to localize in the mouse prostate tissue. (*Id.*) All of these findings strongly suggest that POM has a significant anti-tumor effect on prostate cancer.

In another study, by *Rettig MB*, *Heber et al.*, "(*Pomegranate Extract Inhibits Androgen-Independent Prostate Cancer Growth Through a Nuclear Factor-κB-Dependent Mechanism*)," Molecular Cancer Therapy 2008 (PX0070), the researchers evaluated POMx Pills and POM Juice and found that their consumption in immunedeficient mouse with human prostate cancer grafts led to cancer cell growth reduction and decreased PSA levels. As explained by Dr. deKernion during his testimony, one of the most well-established signaling pathways mediating inflammatory responses relevant to cancer is the NF-kB pathway, which serves as a predictor for recurrence of prostate cancer after radical prostatectomy. (deKernion, Tr. 3044-47). In this study, POMx was found to inhibit NF-kB and cancer cell viability in a dose response fashion *in vitro* and in the human prostate cancer graft mice model—this was similar to the juice. (PX0070). Based on these results, the researchers concluded that pomegranate juice could have potential as a dietary agent to prevent the emergence of androgen-independence, thus potentially prolonging life expectancy of prostate cancer patients, and suggested that this may be a high priority area for future clinical investigation. (RFF____)

Similarly, in another study by *Sartippour MR et al.,* "*Ellagitannin-rich Pomegranate Extract Inhibits Angiogenesis in Prostate Cancer in vitro and in vivo*," International Journal of Oncology 2008 (PX0071), it was found that POMx significantly inhibited angiogenesis (blood vessel growth) both *in vitro* on human prostate cancer tissue and in immunedeficient mice grafted with human prostate cancer tissue. Angiogenesis is a critical element of cancer growth as sufficient blood flow is necessary to support the fast growing cancer cells. (PX0071-0001). Prostate cancer cell growth in turn is directly linked to PSADT. (PX0161-PX0188). Given this, the researchers concluded, "[t]hese findings strongly suggest the potential of pomegranate

ellagitannins for prevention of the multi-focal development of prostate cancer as well as to prolong survival in the growing population of prostate cancer survivors of primary therapy. (PX0071).

5. RCTs Are Not Necessary In The Context Of A Food Like Pomegranate Juice

Despite a significant body of published research showing a profound effect of POM Juice on prostate cancer (both basic and clinical), Complaint Counsel still challenged the science supporting the likely beneficial effects of pomegranate juice on prostate heath and prostate cancer. In doing so, Complaint Counsel ignore, as it must, the significant pre-clinical science performed on antioxidants and pomegranate juice, and attempts to apply a scientific standard used only with drugs in order to downplay the clinical research showing a significant benefit.

Complaint Counsels' criticism, through Dr. Eastham, was that the research performed on pomegranate juice with regard to prostate cancer was not done to the standard of the FDA and that of a drug—in other words RCT. Dr. Eastham insisted that RCT studies are <u>always</u> required for health claims no matter the risk (or lack thereof). (Eastham, Tr. 1329-1331). But such a standard is simply misplaced in the context of a food. Particularly in the context of prostate cancer, which can take decades to clinically affect or ultimately kill the patient, Complaint Counsels' position would almost certainly discourage or eliminate altogether the dissemination to the public of any information regarding food that may potentially positively affect prostate health or prostate cancer progression. Given the limited treatment options available to men for prostate cancer pre and post radical local treatment, and the significant potential side-effects, this makes little sense. (Eastham, Tr. 1331-32) Nevertheless, Dr. Eastham insisted an RCT is always required, despite the fact that such a study would involve between 10,000 to 30,000 participants, cost in the range of $600 million, and likely take decades to complete. (Eastham, Tr. 1322-28).

Tellingly, Dr. Eastham does not practice what he preaches. During cross-examination, he reluctantly admitted that although he allegedly believes no health claims can be made and no treatment untaken without RCTs "proving" the efficacy of the substance or treatment being

studied, Dr. Eastham himself performed about 200 radical prostatectomies per year for a number of years, even though no RCT showed that the operation provided any benefit to the patient. (Eastham, Tr. 1323-32). And unlike drinking pomegranate juice, the potential side-effects of Dr. Eastham's many prostatectomies include impotence, bleeding, embolisms, infection plus the risks of general anesthesia. *Id.* Dr. Eastham's admission is fatal to his extreme position and demonstrates that his alleged purity as to required level of substantiation of RCT is simply not true.

6. Competent And Reliable Evidence Supports POM's Prostate Health Claims

The basic science showing a direct effect of The Challenged Products on prostate cancer cell apoptosis, proliferation and serum nitric oxide levels, and the clinical research showing POM Juice materially lengthened PSADT, support the "very convincing" science that POM Juice has a significant inhibitory effect on prostate cancer. (PX0351 (deKernion, Dep. at 53-56); Heber, Tr. 1993-96). Similarly, and based on the above science, Dr. deKernion testified that there is a "high degree of probability" that POM Juice can inhibit the clinical development of prostate cancer in men who have not been diagnosed with that disease and "compelling" evidence that it may prevent or reduce the risk of ever contracting prostate cancer. (PX00161; deKernion, Tr. 3119-20). And at the very least, POM Juice can delay very invasive and more radical treatments and their concomitant severe side-effects and can be used as a reasonable adjunct (meaning in addition to but not as a substitute) to traditional medical care. (PX00161; deKernion, Tr. 3104). Dr. Heber shares this opinion, as he testified, "there's a significant body of scientific evidence to indicate that both pomegranate fruit juice and pomegranate extract can help to prevent or reduce the risk or help to treat prostate cancer." (Heber, Tr. 2156).

In sum: (1) basic pre-clinical science supports the clinical findings of a robust effect of the Challenged Products on prostate cancer tumor behavior; (2) PSADT is the best marker for risk of clinical recurrence of prostate cancer and mortality following radical local treatment; (3) consumption of the Challenged Products has been shown to materially lengthen PSADT

following radical prostatectomy; (4) the Challenged Products are not drugs and therefore should not be governed by an FDA drug standard; and (5) given the above, there is competent and reliable scientific evidence that the Challenged Products support prostate health and with a hight degree of probability inhibit the clinical development of prostate cancer and the public has a right to have this information. (RFF __).

G. POM's Erectile Health Claims Are Substantiated By Competent And Reliable Evidence

It is "[w]ithout a question" that competent and reliable scientific evidence demonstrates that pomegranate juice in its various forms (including POM Juice, POMx, and POM Pills) provides a positive benefit to erectile health and erectile function. (RFF ¶¶ 1893-72, 2047-84). (Goldstein, Tr. 2605; PX0189-0014; PX0149-0006-0007; Burnett, Tr. 2255-56; PX0349 (Burnett, Dep. at 103, 116-118, 137; Heber, Tr. 2012). The mechanism by which this fruit promotes erectile health and function is via its potent antioxidant components and its impact on nitric oxide ("NO"), which is of "paramount importance" to good erectile health and function and is the key molecule that governs penile erections. (RFF ¶¶ 2032-78). (PX0149-0004; Burnett, Tr. 2249-50, 2276; PX0190-0006; Melman, Tr. 1169; PX0149-0005-0006; Burnett, Tr. 2250-51; PX0189-0011).

1. The Totality Of POM's *In Vitro* And *In Vivo* Studies Demonstrate The Beneficial Effects Of Pomegranate Juice On Erectile Health And Function

Nobel-prize laureate, Dr. Louis Ignarro, for his discoveries concerning nitric oxide, conducted an *in vitro* study to evaluate pomegranate juice's capacity to protect nitric oxide against oxidative destruction. (RFF ¶ 1931; PX0189-0011; PX0058; Goldstein, Tr. 2593-94; Heber, Tr. 1995-96). Based on his findings, Dr. Ignarro concluded that pomegranate juice possesses potent antioxidant activity that results in marked protection of nitric oxide against oxidative destruction, thereby resulting in augmentation of the biological actions of NO. (RFF ¶¶ 1932-34). (PX0189-0011; PX0058). Dr. Ignarro later proclaimed "pomegranate juice was 20

times better than any other fruit juice at increasing nitric oxide." (RFF ¶¶ 2058-59). (PX484; Burnett, Tr. 2254-55; PX0484).

Using an animal model, for example, Dr. Azadzoi and colleagues found that, due to its high antioxidant capacity, long-term pomegranate juice intake increased intracavernosal blood flow in the penis, improved erectile responses, improved smooth muscle relaxation, and decreased erectile tissue fibrosis. (RFF ¶¶ 1911-30). (PX0189-0011-0012; PX0051; Goldstein, Tr. 2595-96, 2597).

In addition to these *in vitro* and *in vivo* studies, multiple other significant scientific studies exist that demonstrate, not only the antioxidative powers of pomegranates in enhancing and preserving nitric oxide, but also support the general proposition that antioxidants positively influence erectile health. (RFF ¶¶ 1902-10; 1920-30; 1956-57). (PX0189-0010-0012; PX0056; PX0059; PX0004; Goldstein, Tr. 2604-05; PX0352 (Goldstein, Dep. at 100-104)).

2. POM's Clinical Study Supports The Conclusion That The Positive Erectile Health Results In The Basic Science Are Borne Out In Human Function

Building on this strong basic scientific foundation, Dr. Padma-Nathan performed a RCT of pomegranate juice versus placebo in men with erectile dysfunction, which is the first and only clinical trial of its kind in the field. (RFF ¶¶ 1940-44). (PX0189-0012-0013; CX0908; Goldstein, Tr. 2598). The study, which had all the same scientific rigors of any drug study, was published in the very reputable International Journal of Impotence Research in 2007. (Hereinafter referred to as the "*Forest/Padma-Nathan RCT Study*"). (RFF ¶¶1941, 1943). (PX0189-0012-0013; CX0908; CX1337 (Forest, Dep. at 220-221, 225); CX1338 (Padma-Nathan, Dep. at 195-197)). The study engaged 53 completed subjects with mild-to-moderate erectile dysfunction who underwent two four-week treatment periods separated by a two-week washout. (RFF ¶ 1942). (PX0189-0012-0013; CX0908). Using a global assessment questionaire ("GAQ"), Dr. Padma-Nathan found that participants rated pomegranate juice 50% more effective than placebo at improving erections. (RFF ¶ 1951). (CX0908-0003; PX0352 (Goldstein, Dep. at 109, 144); CX1338 (Padma-Nathan, Dep. at 191-192)). The GAQ results

achieved a probability value ("p-value") of 0.058, meaning that the positive results of the study were 94.2% likely to be the result of something other than "chance." (RFF ¶¶ 1948-49). (Heber, Tr. 1978; Goldstein, Tr. 2599; Burnett, Tr. 2305). Although the p-value was a few thousandths of a percentage point shy of an arbitrary 95% threshold, the study has major clinical significance in showing a benefit from pomegranate juice on erectile tissue physiology and health. (RFF ¶¶ 1952). (PX0189-0013; PX0149-0006; CX0908; Heber, Tr. 1979, 2001; Goldstein, Tr. 2598 -99; Burnett, Tr. 2256; PX0349 (Burnett, Dep. at 138-139)).

POM's basic science, animal studies and clinical study are significant as testified to by Respondents' experts, Dr. Burnett and Dr. Goldstein.

3. Respondents' Expert, Dr. Burnett, Has Testified That POM's Studies Are Sufficient To Support The Conclusion That It Is Likely That Pomegranate Juice Has Beneficial Effects On Erectile Health And Function

Dr. Arthur Burnett of Johns Hopkins University Medical School, Respondents' expert regarding nitric oxide, explained the basic scientific mechanisms by which pomegranate juice, through its high antioxidant content, aids and enhances the critical function of nitric oxide in improving vascular blood flow to the penis and promoting the vascular biological health of the penis. (PX0149-0004-0007; PX0349 (Burnett, Dep. at 87-90, 103, 118, 137); Burnett, Tr. 2250-56, 2303). Dr. Burnett testified that the basic scientific studies alone "provide a powerful support for pomegranate juice . . . as antioxidants; that they work with very potent effects on the nitric oxide regulatory mechanism" and that "there's good basic science support that pomegranate juice is a very effective agent factor . . . in vascular function." (PX0349 (Burnett, Dep. at 116-117)). Dr. Burnett also testified that the *Forest/Padma-Nathan RCT Study* demonstrates pomegranate juice is "a potential treatment for ED." (PX0349 (Burnett, Dep. at 116-117, 142)). Dr. Burnett concluded that the basic scientific and clinical evidence is sufficient to support the conclusion that it is likely that pomegranate juice has a beneficial effect on erectile function. (PX0149-0006-0007 PX0349 (Burnett, Dep. at 103, 118, 137); Burnett, Tr. 2255-56).

Dr. Burnett indicated that because pomegranate juice creates no material risk of harm and assuming that drinking pomegranate juice is not advocated as an alternative to following medical advice, information of pomegranate juice's likely benefit may be communicated to consumers. (PX0149-0006-0007). Dr. Burnett also opined that RCTs should not be required to substantiate such claims for harmless pure fruit products like pomegranates, before permitting this information to be given to the public. (PX149-0006-0007; Burnett, Tr. 2272-74, 2303; PX0349 (Burnett, Dep. at 118, 137)).

4. Respondents' Expert, Dr. Goldstein, Testified That "Without a Question" Pomegranate Juice Promotes Erectile Health And Function

Not surprisingly, against this scientific backdrop, Dr. Irwin Goldstein, Respondents' expert in the clinical aspects of erectile health, concluded that "without a question," "competent and reliable scientific evidence exists upon which clinicians who treat men with erectile health concerns would rely in concluding that pomegranate juice promotes erectile health." (PX0189-0010, 0014; Goldstein, Tr. 2605). Dr. Goldstein also concluded that reasonable and competent scientific evidence shows that pomegranate juice reduces the risk of or ameliorates erectile dysfunction caused by endothelial dysfunction, blood flow impairment or oxidative stress. (Goldstein, Tr. 2605).

Dr. Goldstein testified that the existing *in vitro* and animal studies definitely show the likelihood that pomegranate juice improves erectile function. (Goldstein, Tr. 2601-02, 2605; PX0352 (Goldstein, Dep. at 37-42)). Dr. Goldstein noted that the "Ignarro study is another part of the sequence of evidence that supports that a nutraceutical, specifically pomegranate juice, has incredible vascular-sparing properties that ultimately . . . leads to the improvement of erectile function in men with erectile health issues." (PX0352 (Goldstein, Dep. at 133); PX0189-0011; Goldstein, Tr. 2594-95).

Dr. Goldstein also testified that the *Forest/Padma-Nathan RCT Study* showed that, in fact, pomegranate juice did improve erectile function for men who had suffered from erectile dysfunction, and that this "absolutely" had important clinical significance, even though it fell

slightly short of statistical significance, generating a 94.2%, rather than 95% confidence level. (PX0189-0013; PX0352 (Goldstein, Dep. at 108-109); Goldstein, Tr. 2598-99). Dr. Goldstein indicated that the study is "clinically significant because it supports the conclusion that the positive results in the basic science are borne out in human function." (PX0189-0013).

Further, Dr. Goldstein concluded that since pomegranate juice is not a pharmaceutical drug, physicians who treat patients concerned with erectile health would not hold pomegranate juice to the standards traditionally required by the FDA for approval of a pharmaceutical drug (including performance of an RCT) before recommending pomegranate juice to their patients. (PX0189-0003; Goldstein, Tr. 2600, 2601-02, 2611, 2620).

Finally, Dr. Goldstein opined that he would recommend pomegranate juice as a management to promote erectile health in men who are aware that their erectile function is declining but who do not yet meet the clinical definition of ED under the IIEF and therefore do not qualify for pharmacologic treatment. (PX0189-0014-0015; PX0352 (Goldstein, Dep. at 42-45); Goldstein, Tr. 2609). Moreover, Dr. Goldstein opined that men who have been diagnosed with clinical ED but who have an insufficient response to PDE5 inhibitors (like Viagra) and who are unwilling to consider invasive or mechanical therapies (such as injecting needles into the penis, inserting urethral suppositories, using vacuum pumps, or having surgically implanted prostheses), the suggestion to utilize the Mediterranean diet, which the pomegranate fruit is part of, to improve endothelial function and erectile health is logical and rational given the risk-benefit ratio. (PX0189-0005, 0014-0015; PX0352 (Goldstein, Dep. at 37-42); Goldstein, Tr. 2605, 2641).

5. Complaint Counsels' Erectile Expert, Dr. Melman, Demonstrated That His Opinions Were Extreme, Uninformed and Motivated By Bias

Although Complaint Counsels' expert, Dr. Arnold Melman, testified that he did not know the meaning of a "RCT" (Melman, Tr. 1134-35), Dr. Melman asserted, contrary to widespread scientific agreement, that erectile health and function claims can only be substantiated by two large, randomized, double-blind, placebo controlled studies, conducted by two different

institutions, with the answers of the participants confirmed by their sexual partners. (Melman, Tr. 1137-43). In addition, for a study to claim any improvement in the participants, the men must have reached orgasm, and that, to be considered at all, each of the two large randomized studies had to reach statistical significance. (Melman, Tr. 1137-43).

Dr. Melman testified that, in requiring such randomized controlled tests, he was applying the FDA standard for drugs because he insisted that pomegranate juice "is a drug," and that, frankly, by his definition "everything is a drug", including water, because it is composed of hydrogen and oxygen molecules. (PX0360 (Melman, Dep. at 17-19); Melman, Tr. 1140, 1141, 1165).

Further, when Dr. Melman was asked whether he would acknowledge that an "improvement" had occurred if a man who had been impotent for five years could finally get an erection and penetrate his sexual partner after trying the product, Dr. Melman responded that he would not recognize an improvement unless the man also reached an orgasm. (Melman, Tr. 1141-47). According to Dr. Melman, short of an orgasm, a mere sustained erection, even if it hadn't occurred in a long while, would not warrant the recognition of a benefit. (Melman, Tr. 1141-47). In that regard, Dr. Goldstein testified that he "couldn't disagree more" with Dr. Melman's statement requiring orgasm as a test of erectile improvement. (Goldstein, Tr. 2604). Dr. Goldstein also testified that Dr. Melman's statement was flatly contrary to all medical thinking in the field as it is contrary to the IIEF. (Goldstein, Tr. 2604).

On cross-examination, Dr. Melman conceded that he had patented a gene transfer therapy for erectile dysfunction called "hMaxi-K," which he hoped to market and make money from doing so, and that he announced to the public, in an interview with the New York Observer, that his "hMaxi-K" product produced spontaneous normal erections in men suffering from erectile dysfunction, that the men who tried it became like they were young again, that his "hMaxi-K" was "modifying the aging process" and that it was the "the fountain of youth." (Melman, Tr. 1148, 1153-55). Ironically, Dr. Melman's public claims about the wonders of his "fountain of youth" were not supported by the kind of elaborate clinical studies he testified were essential to

making such claims or by RCTs of any kind. On the contrary, they were based on an animal study. (Melman, Tr. 1155).

Dr. Melman was given to exaggerated pronouncements such as that pomegranate juice is "a product that doesn't work," and that, before he would suggest pomegranate juice to his patients, he'd tell them to "stop having intercourse". (Melman, Tr. 1171, 1192-94; PX0360 (Melman, Dep. at 31)). The basis of Dr. Melman's claim that pomegranate juice "doesn't work" was, first, that the *Forest/Padma-Nathan RCT Study* used the GAQ questionnaire, which Dr. Melman called a "lousy test" and, second, that the study didn't reach statistical significance. (Melman, Tr. 1171-78). Dr. Melman insisted that if a difference over placebo doesn't reach statistical significance, it's not a difference (Melman, Tr. 1176-78). Surprisingly, Dr. Melman had no experience with the GAQ questionnaire prior to this case, knew nothing about it and made no effort to acquire such knowledge. (Melman, Tr. 1180-82). The GAQ questionnaire, however, is widely used. (Goldstein, Tr. 2602, 2603; Burnett, Tr. 2304; PX0349 (Burnett, Dep. at 127)), and commonly accepted as a standardized instrument among those conducting erectile dysfunction research. (CX1337 (Forest, Dep. at 79)). Dr. Goldstein testified that for Dr. Melman to not know the GAQ is widely used "is a little embarrassing." (Goldstein, Tr. 2602).

Finally, most telling, on cross-examination, Dr. Melman was read the Supreme Court's recent opinion in *Mattrixx*, 131 S.Ct. at 1320 that "medical professionals and researchers do not limit the data they consider to statistically significant evidence." (Melman, Tr. 1178-80). Not realizing that the quote was from the opinion of the United States Supreme Court, Dr. Melman said he completely disagreed with it. (Melman, Tr. 1178-80).

6. Health Claims Respondents Can Support

In summary, competent and reliable scientific evidence and clinical evidence supports the conclusion that pomegranate juice provides a benefit to erectile health and function. (Goldstein, Tr. 2605; PX0189-0014; PX0149-0006-0007; Burnett, Tr. 2255-56; PX0349 (Burnett, Dep. at 103, 116-118, 137); Heber, Tr. 2012). Also, since improving one's erectile function may also help improve one's erectile dysfunction, urologists would recommend pomegranate juice as an

option to promote erectile health in men who are aware that their erectile function is declining but who do not yet meet the clinical definition of ED and therefore do not qualify for pharmacologic treatment. (Burnett, Tr. 2303; PX0189-0014-0015; PX0352 (Goldstein, Dep. at 42-45); Goldstein, Tr. 2609; CX2007 (Heber, Dep. at 85)).

Moreover, reasonable and competent science shows that pomegranate juice reduces the risk of, or ameliorates erectile dysfunction in men caused by endothelial dysfunction or blood flow impairment or oxidative stress. (Goldstein, Tr. 2605). Therefore, men who have been diagnosed with clinical ED but who have an insufficient response to PDE5 inhibitors (like Viagra) and who are unwilling to consider invasive or mechanical therapies, the suggestion to utilize the Mediterranean diet, which the pomegranate fruit is part of, to improve endothelial function and erectile health, is logical and rational. (PX0189-0005, 0014-0015; PX0352 (Goldstein, Dep. at 37-42); Goldstein, Tr. 2605, 2641; PX0190-0006-0007).

X. COMPLAINT COUNSEL FAIL TO SATISFY THEIR BURDEN OF PROVING THAT RESPONDENTS VIOLATED THE FTCA

To find that an advertisement is deceptive, Complaint Counsel bear the burden of proving that claims (1) are conveyed in the advertisement; (2) [are] "false or misleading;" and (3) "material to prospective consumers." *Kraft, Inc v. F.T.C.*., 970 F.2d 311, 314 (7th Cir. 1992).

A. The Legal Standard For Determining What Claims the Challenged Advertisements Convey

In general, advertisements may convey two kinds of claims, express and implied. Express claims "unequivocally" and "directly state the representation at issue," and as a result, that representation necessarily constitutes the meaning of the claim. *In the Matter of Thompson Med. Co.*, 104 F.T.C. 648, 788 (1984), *aff'd*, 791F.2d 189 (D.C. Cir. 1985), *cert. denied*, 479 U.S. 1086 (1987). No further proof of the meaning of an express claim is required because the express claim itself (rather than a paraphrase about what it "implies") is explicitly stated. *See* Deception Policy Statement, 103 F.T.C. at 176; *Thompson Med.*, 104 F.T.C. at 788.

By contrast, implied claims are claims that the advertisement communicates to reasonable consumers but that are not expressly stated. *See In re Kraft, Inc.* 114 F.T.C. 40, 120 (1991),

aff'd, 950 F.2d 311 (7th Cir. 1992), *cert. denied*, 507 U.S. 909 (1993); *Thompson Med.*, 104 F.T.C. at 789. Because such claims are not stated explicitly, the Commission must find that they are likely conveyed to a significant portion of reasonable consumers. In determining whether reasonable consumers are likely to take away an implied claim, the Commission looks at the net impression created by the ad as a whole. *See* Deception Policy Statement, 103 F.T.C. at 179 & n.32; *In re Stouffer Foods Corp.*, 118 F.T.C. 746, 799 (1994).

Complaint Counsel have the burden to prove, by a preponderance of the credible evidence, that a significant portion of reasonable consumers, acting reasonably under the circumstances, would interpret the message of an advertisement to have conveyed the allegedly implied claim. *See In the Matter of Bristol-Myers Co.*, 1983 F.T.C. LEXIS 63, *373 (1983) (Initial Decision; Conclusions of Law) (requiring proof by "preponderance of credible evidence."); *Stouffer*, 118 F.T.C. at 776 (citing *Kraft,* 970 F.2d at 318) (noting that the "standard by which advertising is judged is whether it is likely to mislead reasonable consumers."); *Thompson Med.*, 104 F.T.C. at 320; Deception Policy Statement, 103 F.T.C. at 179.

Solely in the limited circumstances in which an implied claim is "conspicuous, self-evident, or reasonably clear on the fact of the ad," Complaint Counsel are permitted, in meeting their burden of proof, to exclusively rely on their own reasoned analysis to determine what "reasonably clear" implied claims are conveyed by the challenged advertisement. *Stouffer*, 118 F.T.C. at 777 (citing *Kraft*, 970 F.2d at 314, 319). Complaint Counsel must look at the "net impression" created by the ads as a whole, examining "the entire mosaic, rather than each tile separately." *See* Deception Policy Statement, 103 F.T.C. at 179 & n.32; *Stouffer*, 118 F.T.C. at 799; *FTC v. Sterling Drug*, 317 F.2d 669, 674 (2d Cir. 1964).

Complaint Counsel, however, "do] not have a license to go on a fishing expedition to pin liability on advertisers. . . ." *Stouffer*, 118 F.T.C. at 777. Thus, if "the implied claims may not be determined with confidence from the face of the ad, extrinsic evidence must be examined, including consumer surveys and expert testimony." *Id.* (citing *Kraft*, 970 F.2d at 318) (emphasis added). If extrinsic evidence is available, the Commission will consider it, taking into account

its relative quality and reliability. *See Kraft*, 114 F.T.C. at 121. Indeed, "[t]he most convincing extrinsic evidence is a survey 'of what consumers thought upon reading the advertisement in question….'" *Kraft*, 970 F.2d at 318 (citing *Thompson Med.*, 104 F.T.C. at 788-89) (noting that other permissible extrinsic evidence includes consumer testimony, expert opinion and copy tests of ads)

B. Complaint Counsel Fail To Meet Their Burden To Prove That The Challenged Advertisements Convey The Alleged Disease Claims

Here, Complaint Counsel claim that in certain of Respondents' advertising and promotional materials for the Challenged Products, Respondents have represented, expressly or by implication, that clinical studies, research, and/or trials prove to consumers that the Challenged Products will prevent, treat or reduce the risk of heart disease, prostate cancer and erectile dysfunction. (CX1426 at 0017-0020). Complaint Counsel, however, failed to meet their burden to establish that any of the Challenged Advertisements make either (a) an unequivocal and directly stated express claim or (b) an implied claim that can be "determined with confidence from the face of the advertisement" that is "conspicuous, self-evident, or reasonably clear on the fact of the ad."

As a result, Complaint Counsel are required to present extrinsic evidence (which they failed to do) to establish that any of the alleged claims in the Challenged Advertisements were conveyed to a significant portion of reasonable consumers. *See Stouffer*, 118 F.T.C. at 777 (citing *Kraft*, 970 F.2d at 318).

Moreover, paramount to any analysis of whether the Challenged Advertisements make either express or implied "clinically proven" disease claims is the nature of the product itself. (Butters, Tr. 2817-18). What consumers might take away from an advertisement of a healthy whole food product – like a pomegranate or pomegranate juice – should be the focal point of the analysis. This is quite different than the lens consumers would use to view advertising for a topical ointment or drug. Complaint Counsel completely ignore this very significant distinction. *See infra* Part __.

1. Respondents' Eight "Outlier" Advertisements, Which Used More Aggressive Imagery and Language and Were Disseminated Only in the Very Early Years, Make Up a Miniscule Percentage of the Total Advertisements Disseminated by Respondents and Are Ancillary to the Remedy Analysis

As a threshold matter, many of the advertisements that Complaint Counsel attack ran in the 2003-2006 time frame and ceased running thereafter. RFF ¶ __. Such advertisements include what Respondents term "outlier" ads – ads where the images in the ads and the language in the body copy regarding the health benefits of POM Juice were more aggressive than was typical of Respondents.

The "outliers" include these eight ads: (a) Cheat death (CX CX0036_0001); (b) Drink and be healthy (CX0016_0001); (c) Decompress (CX0103_0001; CX0459_0001); (d) Floss your arteries. Daily.; (CX0031-0001); (e) Amaze your cardiologist (CX0034_0001;CX0471_0012); (f) Imitation may be sincere. But is it pure? (PX0330a47; CX0251_001); (g) Ingredients: pomegranates, $25 million in medical research (CX314_010); and (h) pomwonderful.com "Real Studies" web.

To the extent Complaint Counsel seek relief based on these "outliers," which were discontinued anywhere from three to eight years prior to the Commission bringing this action or even instituting an investigation, the relief is not appropriate here. RFF __. *See, e.g., FTC v. Evans Products Co.,* 775 F.2d 1084, 1087 (9th Cir. 1985) ("'Past wrongs are not enough for the grant of an injunction,' an injunction will issue only if the wrongs are ongoing or likely to recur."). The "outliers" are thus ancillary to the remedy analysis.

With the exception of an inadvertent blood pressure reference on the "Real Studies" web page, the "outliers" were disseminated during the very early years (2003-2006) and ceased running thereafter. RFF __. In fact, a few of these outlier ads were issued as the result of staff mistakes, which were immediately stopped when the mistake was discovered. For example, the reference to the number of "published studies" in the "Imitation May Be Sincere. But Is It Pure?" ad, which according to Complaint Counsel ran one time on November 1, 2008, was simply an inadvertent mistake because some of the studies had not been "published." The ad

should have said "$25 million in medical research." RFF __. When the mistake was discovered, the word "published" was quickly eliminated, and Respondents never ran the version with the mistake again. RFF __.

Such inadvertent mistakes, however, are not likely to occur in the future because Respondents' current advertising review policy is a formalized process, which culminates in legal review. RFF __. Moreover, Complaint Counsel ave presented no evidence that it is probable that Respondents would run these types of ads again. RFF __.

Accordingly, because Respondents stopped running the "outlier" ads long ago, corrective measures have been implemented to ensure that the conduct is not repeated, and there is little probability that the conduct in question will occur in the future, the "outlier" ads are ancillary to the analysis of whether a broad order, such as the one proposed by Complaint Counsel, is appropriate here. *See, e.g., Country Tweeds, Inc. v. FTC*, 326 F.2d 144 (2d Cir. 1964):

> We think it advisable again to note that petitioners in this case have ceased to engage in the advertising practice which prompted the order, and voluntarily did so well before the Commission filed its complaint. Cessation of the offending activity, with the likelihood that the petitioner will not again resume it or a related activity, has been one factor which courts have considered in limiting broad Commission orders.

Country Tweeds, 326 F.2d at 148-49 (citing *Grand Union Co. v. FTC*, 300 F.2d 92, 100 (2d Cir. 1962); *Swanee Paper Corp. v. FTC*, 291 F.2d 833, 838 (2d Cir. 1961).

2. The Challenged Advertisements Do Not Convey the Express Claims Complaint Counsel Attribute to the Challenged Advertisements

Complaint Counsel take an aggressive position regarding what Respondents' advertisements convey and apparently contend that, on the face of many of the Challenged Ads, Respondents expressly convey "clinically proven" disease claims that the Challenged Products "prevent," "treat" or "reduce the risk" of heart disease, prostate cancer and erectile dysfunction. RFF __. Such contentions are erroneous.

The Challenged Advertisements do not expressly convey the disease messages that Complaint Counsel assert are made in them. RFF __. Indeed, nowhere do Respondents

expressly (*i.e.*, unequivocally and directly) state that the Challenged Products are "clinically proven" to "prevent," "treat," or "reduce the risk" of heart disease, prostate cancer and erectile dysfunction. RFF __. Similarly, nowhere do Respondents expressly (*i.e.*, unequivocally and directly) state that the Challenged Products "prevent," "treat," or "reduce the risk" of heart disease, prostate cancer and erectile dysfunction. RFF __. Indeed, by definition, because such advertisements instead use qualified language, such as "promising," "encouraging" or "hopeful," Complaint Counsel cannot maintain that any of the Challenged Advertisements expressly convey claims of being "clinically proven" to prevent, treat or reduce the risk heart disease, prostate cancer or erectile dysfunction. RFF __; Appendix of Advertisements.

For example, even the most aggressive "outlier" ads, such as the 2005 "Amaze your cardiologist" ad, which Complaint Counsel contend makes an express claim, *see* PX0267-0006, did not unequivocally and directly state that POM Juice is "clinically proven" to prevent heart disease. The ad read as follows:

> **Amaze your cardiologist**.
>
> Ace your EKG: just drink 8 ounces of delicious POM Wonderful Pomegranate juice a day. It has more naturally occurring antioxidants than any other drink. Antioxidants fight free radicals . . . nasty little molecules that can cause sticky, artery clogging plaque. A glass a day can reduce plaque by up to 30%! Trust us, your cardiologist will be amazed.
>
> **POM Wonderful Pomegranate Juice. The Antioxidant Superpower**.

(CX0034_0001;CX0471_0012) (emphasis in original). Indeed, in 2005, the NAD agreed with Respondents on this point and found that the statement "A glass a day can reduce plaque by up to 30%" was not an establishment claim (*i.e.*, a "clinically proven" claim). RFF ¶ __.

3. The Challenged Advertisements Do Not Convey the Implied Claims Complaint Counsel Attribute to the Challenged Advertisements

Complaint Counsel further contend that, in many of the Challenged Ads, Respondents impliedly convey "clinically proven" disease claims that the Challenged Products "prevent,"

"treat" or "reduce the risk" of heart disease, prostate cancer and erectile dysfunction. RFF ¶ __. Such contentions are erroneous.

Complaint Counsel completely ignore the important distinction that when consumers view Respondents' advertising it is through a different lens than consumers would use if viewing an advertisement for a drug or an over-the-counter medication. Because POM consumers understand that the Challenged Products are wholly derived from the pomegranate fruit (which is a fact heavily emphasized in POM's advertising), no reasonable consumer would reasonably take away the message from Respondents' advertising that the Challenged Products can treat their diseases or that they should disregard conventional medical treatment if they were to consume the Challenged Products. Instead, POM consumers view the Challenged Products the way they perceive any other whole food, like broccoli, or blueberries which may help prevent or improve your odds against disease, but which would not "stop" anything and did not involve a single target of action against a particular disease or condition.

a. The Challenged Advertisements, Viewed as a Whole, Do Not Clearly and Conspicuously Convey "Clinically Proven" Disease Claims to a Reasonable Consumer

Complaint Counsel cannot maintain with confidence that such claims are impliedly made based on the face of the advertisements. Indeed, it is wholly impossible for Complaint Counsel to "conclude with confidence" that the Challenged Advertisements convey the "clinically proven" claims, as alleged, on the face of the ads. RFF __. S*ee Thompson Med.*, 104 F.T.C. at 789. Respondents' advertising, viewed as a whole, do not clearly and conspicuously convey to a reasonable consumer that the Challenged Products prevent, treat or reduce the risk of heart disease, prostate cancer and erectile dysfunction, or that such Challenged Products are "clinically proven" to do so, under Complaint Counsels' "net impression" analysis or any analysis for implied claims. RFF __.

Indeed, to the extent a "treat" claim can conceivably be implied from any of the Challenged Advertisements (which it cannot), the overall net impression of any ad is not (and certainly cannot be determined with confidence from the face of the advertisement) that the

Challenged Products are a substitute for conventional medical treatment. RFF __. Instead, the overall net impression of any ad is not that the Challenged Products "reduce the risk" of heart disease, prostate cancer or erectile dysfunction, like a drug with a single target of action, but "reduce the risk" like a healthy diet and exercise "reduce the risk" of disease. (Butters Tr. 2817-18).

Additionally, to the extent a "reduce the risk" claim can be implied from any of the Challenged Advertisements, the overall net impression of any ad is not (and certainly cannot be determined with confidence from the face of the advertisement) that the Challenged Products "reduce the risk" of heart disease, prostate cancer or erectile dysfunction, like a drug with a single target of action, but "reduce the risk" like broccoli, a healthy diet, or exercise "reduce the risk" of disease. (Butters Tr. 2817-18).

Thus, because Complaint's Counsels' assertions that the Challenged Advertisements impliedly convey that the Challenged Products are "clinically proven" to prevent, treat or reduce the risk of disease cannot be determined with confidence from the face of such advertisements, Complaint Counsel is required to rely on extrinsic evidence. *Stouffer*, 118 F.T.C. at 777 (citing *Kraft*, 970 F.2d at 318); s*ee supra* Part I.A.

b. Complaint Counsel Failed to Present Any Reliable Extrinsic Evidence To Establish The Claims They Attribute To The Challenged Advertisements

Kraft states that "[t]he most convincing extrinsic evidence is a survey 'of what consumers thought upon reading the advertisement in question…'" *Kraft*, 970 F.2d at 318. Here, in contrast to Respondents, Complaint Counsel presented no evidence on the meaning of the ads or what a reasonable person would take away from them. Instead, they erroneously rely on "creative briefs" and "consumer logs" to supposedly show what Respondents intended their ads to say. *See infra/supra* Part ___.

Even, Complaint Counsels' survey expert, Professor Mazis, in stark contrast to work he had previously done for Complaint Counsel, did not conduct any facial analysis of Respondents' ads or offer any expert opinion on them. RFF __. Nor did he conduct any survey or copy test of

Respondents' ads. *See, e.g., Thompson Med*, 104 F.T.C. at 788-89 (other permissible extrinsic evidence includes expert opinion and copy tests of ads). Likewise, Complaint Counsels' linguist expert, Professor Stewart, conceded that he was not offering any opinion on how consumers would interpret Respondents' ads, but was only criticizing Professor Butters' methodology in doing so. RFF __. Indeed, Professor Stewart testified that he did not even know if Complaint Counsel had any evidence on the meaning of the ads. RFF __. Certainly, Complaint Counsel has produced no such evidence. RFF __.

Moreover, Complaint Counsel also failed to present any reliable extrinsic evidence or expert opinion rebutting the fact that many of the ads were meant to be hyperbolic, puffery and humorous. RFF __. *See, e.g.*, *Sterling Drug, Inc. v. F.T.C.*, 741 F.2d 1146, 1150 (9th Cir. 1984). Indeed, most of the statements in the majority of the ads were not meant to be taken literally and cannot be objectively verified, and thus constitute puffery. RFF__. *In re Thompson Med.*, 104 F.T.C. at 788-89 n.6.

The only evidence on the meaning of the Challenged Advertisements was presented by Respondents through the testimony of Professor Butters. Professor Butters viewed all of Respondents' ads in the complaint and all of the additional ads in Complaint Counsels' supplementary responses to interrogatories. RFF __.

Professor Butters based his opinion not only on what the ads said, but also on what they implied, in the sense, as he put it, of what message a reasonable person would "take away" from the ads. RFF __. Professor Butters testified that none of Respondents' ads stated or implied that their products actually prevented or treated any disease. RFF __. He further testified that the term "treat" would ordinarily mean that the product was a form of "medical treatment" or was a "substitute" for a medical treatment. RFF __. In that sense of the term, he testified that none of Respondents' ads stated or implied that their products "treated" any disease. RFF __. If, on the other hand, "treat" means only that the product "can help" with a disease, Respondents' science strongly supports a claim that the Challenged Products can help with heart disease, prostate cancer and proper erectile function. RFF ¶ __.

Dr. Butters acknowledged that his corrected deposition answers to triple compound questions indicated that some people could understand Respondents' ads to mean that their products "reduced the risk" of particular diseases, although he doubted that they would, in fact, reach that understanding. RFF __. Assuming *arguendo* that such "reduce the risk" claims can be implied in any of the Challenged Advertisements, Respondents' science strongly supports a claim that the Challenged Products do "reduce the risk" of heart disease, erectile dysfunction and even prostate cancer. RFF __.

Accordingly, because Complaint Counsel failed to present any extrinsic evidence on the meaning of the ads or what a reasonable person would take away from them, they have failed to meet their burden that a preponderance of the credible evidence shows that such implied "clinically proven" disease claims were actually conveyed to a substantial segment of the reasonable consumer. RFF __.

c. The Vast Majority of the Challenged Advertisements Fall Into Three Categories, Which Do Not Convey The Implied Claims Complaint Counsel Attribute To The Challenged Advertisements

The vast majority of Respondents' Challenged Advertisements from 2006 through 2010 fall into one or more of three general categories: (a) specific study; (b) "backed by" and (c) antioxidant. RFF __. None of the ads in the three categories convey the implied claims Complaint Counsel attribute to the Challenged Advertisements. RFF __. No matter how such ads are categorized, the overarching commonality among all the ads is that they used qualified language to describe the health-related benefits of the Challenged Products. RFF __.

Respondents' ads generally conveyed the restrained and qualified message that scientific studies show results that are merely "promising," "encouraging" or "hopeful" for prostate, cardiovascular and erectile health or stated that POM "may" help with a particular condition or that POM is "fighting" for better health in a particular area.

i. Specific Study Ads Truthfully Describe Scientific Studies

The first category of ads, "specific study" ads, summarized some of Respondents' scientific studies on the Challenged Products in the areas of cardiovascular, prostate and erectile health. Each of these ads were substantiated by competent and reliable scientific evidence. RFF __. In fact, while Respondents have sponsored at least one hundred scientific studies on the Challenged Products, Respondents only specifically described six of these studies in the areas of prostate, cardiovascular and erectile health in their ads. RFF __.

For example, the "Drink to prostate health" ad described the results of the Pantuck Study (2006), stating:

> A recently published preliminary medical study followed 46 men previously treated for prostate cancer, either with surgery or radiation. After drinking 8 ounces of POM Wonderful 100% Pomegranate Juice daily for at least two years, these men experienced significantly longer PSA doubling times.

CX_0260 and CX1426, Exh. B.

Similarly, the "Antioxidant Superpill" ad summarized the results of the Bev I Coronary Perfusion Study:

> An additional study at the University of California, San Francisco included 45 patients with impaired blood flow to the heart. Patients who consumed 8 oz of POM Wonderful 100% Pomegranate Juice daily for three months experienced a 17% improvement in blood flow. Initial studies on POMx share similar promise for heart health, and our research continues.

CX1426, Exh. I and CX1426_0038-0042. In looking at these ads through the lens that POM Juice and POMx are wholly derived from pomegranates, neither of these ads implies that the Challenged Products prevent, treat or reduce the risk of heart disease or prostate cancer. Moreover, Complaint Counsel presented no evidence that consumers took away the message presumed by Complaint Counsel just because Respondents referred to "prostate cancer," "PSA doubling times," "impaired blood flow," and "improved blood flow" in the Challenged Advertisements. Nor could such a finding be consistent with First Amendment precedent

holding that the government may not aggressively suppress the publication of nutrition science on the theory that the science itself may mislead consumers, or when a qualification of some form is sufficient. *See Wallach v. Crawford*, 2005 WL 6054963, at *8-9 (S.D. Cal. Mar. 29, 2005); *see also Edwards v. District of Columbia*, 2011 WL 667950, at *6 (765 F.Supp. 2d 3 (2011); *Enten v. District of Columbia*, 675 F. Supp. 2d 42, 50 (D.D.C. 2009) ("the degree of First Amendment is not diminished merely because…speech is sold rather than given away"); *City of Lakewood v. Plain Dealer Publ'g Co*., 486 U.S. 750, 756 n.5 (1988).

ii. "Backed By" Ads Truthfully Represent the Respondents' Scientific Expenditures

The second category, "backed by" ads, stated that Respondents spent a particular amount of money on their scientific studies on the Challenged Products to back-up Respondents' healthy claims. RFF ¶ __. Examples of the body copy used in the "backed by" ads include:

> POM Wonderful Pomegranate Juice is supported by $20 million of initial scientific research from leading universities, which has uncovered encouraging results in prostate and cardiovascular health, CX0109 (Heart therapy); and
>
> POM Wonderful 100% Pomegranate Juice is supported by $23 million of initial scientific research from leading universities, which has uncovered encouraging results in prostate and cardiovascular health. CX0188 (Cheat death); CX0192 (What gets your heart pumping?).

Complaint Counsel presented no evidence that consumers took away the message presumed by Complaint Counsel because Respondents' spent a certain amount of money on science and research. RFF ¶ __. Moreover, Complaint Counsels' assertion that the "backed by" were overinflated because a number of Respondents' scientific studies had a null or even negative result is without merit. Mr. Tupper testified that Respondents learned a great deal even from the unsuccessful studies, and all of Respondents' studies were important sources of knowledge that allowed them to make informed decisions. RFF ¶ __. For example, studies on the effect of antioxidants and nitric oxide on blood flow applied to the heart as well as erectile function and probably also to prostate health. RFF __. In fact, Respondents substantially understated the dollars spent on research in their advertising because they excluded all overhead

items, such as rent and salaries, which were very significant added costs. RFF __. These "backed by" ads accurately and truthfully represented the dollars spent by Respondents on the totality of the science on the Challenged Products. RFF __.

iii. "Antioxidant" Ads

The third category, "antioxidant" ads, includes general antioxidant ads, comparative antioxidant ads, antioxidant benefits ads and multi-step ads. Generally, these antioxidant ads discussed the potential benefits of antioxidants and stated that the Challenged Products contained antioxidants and that antioxidants are good for your health . RFF __. Examples of the body copy used in the four "antioxidant" categories include:

> General Antioxidant:
> The Antioxidant Superpower. CX1426, Exh. A (Super HEALTH Powers);
>
> Comparative Antioxidant:
> Sip for sip, POM Wonderful 100% Pomegranate Juice has more polyphenol antioxidants than red wine, green tea and other juices. CX0314_0005 (The proof is in the POM);
>
> Antioxidant Benefits
> Emerging science suggests that antioxidants are critically important to maintaining good health because they protect you from free radicals, which can damage your body. Taking one POMx pill a day will help protect you against free radicals and keep you at your healthy best. CX0328 (Your New Health Care Plan); and
>
> Multi-Step Antioxidant
> What's it like to have a personal superhero? Find out by drinking delicious and refreshing POM Wonderful 100% Pomegranate Juice. It has more naturally occurring antioxidants than other drinks. Antioxidants fight free radicals, villainous little molecules that may cause premature aging, heart disease, stroke, Alzheimer's, even cancer. CX0314_0006 (The Antioxidant Superpower).

As exemplified in the body copy quoted above, the overall net impression of the "antioxidant" ads, especially when viewing them through a "food lens," is not that the Challenged Products are "clinically proven" to prevent, treat or reduce the risk of heart disease, prostate cancer or erectile dysfunction. RFF __. Indeed, many of these ads were meant to be

hyperbolic, humorous and use puffery. For example, Dr. Butters testified, that the "superpower" ad were intended to be "a work of fiction" in that they are personifying the pomegranate bottle by comparing the bottle to a superhero. RFF __. Similarly, some of the "multi-step" ads are also accompanied by humorous, comical and frivolous images. For example, the "Life support" ad has an intravenous line ("IV") with a pomegranate bottle in place of IV solution. RFF __. Dr. Butters testified that this image is a "frivolous exaggeration" and that it is not possible that the IV imagery was conveying drugs and medicine. RFF __. Moreover, Complaint Counsel failed to present any evidence to the contrary regarding consumer take away of the antioxidant ads or any expert opinion negating the extensive support for the benefits of antioxidants. RFF __.

d. Complaint Counsel Conflate the Terms "Prevent," "Treat" and "Reduce the Risk" and Refuse to Distinguish Among the Terms in Assigning Disease Messages to the Challenged Advertisements, Even Though Their Own Experts Do

Complaint Counsel would have us believe that there are no distinctions between the terms "prevent," "treat" or "reduce the risk" and repeatedly address them as identical and interchangeable terms, even though their own medical experts distinguish between "prevent" and "treat" claims in examining the level of scientific support that might be required for each. (RX5007). Indeed, Complaint Counsels' own expert, Professor Stampfer, opined in an article he authored that that (1) RCTs may not be appropriate for nutrient recommendations to prevent disease, as distinguished from drugs used to treat disease; and (2) recognized that, because RCT study designs may not be "available" (economically or scientifically) for nutrients, "nutrient related decisions could be made at a level of certainty somewhat below that required for drugs." RX5007.

i. Prevent

Without any expert opinion or extrinsic evidence to support their claims, Complaint Counsel allege that the Challenged Advertisements convey to reasonable consumers that the Challenged Products prevent, in an absolute and targeted sense, certain diseases, including heart disease, prostate cancer, and erectile dysfunction. RFF __. Respondents deny that any such

message was conveyed at all to any reasonable consumer through any of the Challenged Advertisements. Appendix of Advertisements. Indeed, to the extent any "prevent" message was conveyed, it was not conveyed to consumers in an absolute or targeted sense, like a drug with a single target of action or a medical treatment such as a coronary bypass surgery. Instead, the evidence shows that the Challenged Advertisements conveyed that the Challenged Products help prevent disease, in the same way that broccoli, or blueberries or a healthy diet, exercise and lifestyle are preventative in the sense that they improve your odds of fending off disease and illness. RFF __. Indeed, Professor Butters confirmed in his trial testimony that the message conveyed to a reasonable consumer in a food-product advertisement is "different from what they would imply about an advertisement for a five-syllable drug." (Butters Tr. 2817-1818).

There is no question that the Challenged Products are wholly derived from pomegranates, and as such, are entirely harmless food products. RFF __. POM Juice is a 100% juice product wholly derived from the pomegranate fruit, and POMx has the same content as the pomegranate fruit itself and nothing beyond which provides the same, powerful benefits of drinking POM Juice because it is derived from the exact same fruit. RFF __. Indeed, Respondents have never advertised their products as a drug, nor intended to advertise their products as a drug. (Tupper Tr. at 3008). Rather, the Challenged Products have always been marketed for what they intrinsically are: whole-food products. Appendix of Advertisements.

POM Juice is sold in the refrigerated produce section of the grocery store. (CX0967_0014). It is not sold in the "drug" or "over the counter" section, or advertised or marketed in conjunction with or in comparison to any drug product, nor is it sold anywhere near such drug products or any products stating that they prevent some specific medical disease. *Id.* Indeed, the drug aisles of a grocery store may contain products such as "Tough Actin' Tinactin," that state on the product that it "prevents" the specific disease of athlete's foot; or Prilosec, which advertises that "it prevents heartburn before it even starts." Or take Prilosec, "That way, you don't get heartburn in the first place."

By contrast, none of the Challenged Advertisements make any claims that they prevent any specific diseases. Rather, the reasonable consumer would view the Challenged Advertising in the context of a whole-food (*i.e.* broccoli or blueberries) and understand that the Challenged Advertisements convey, not that the Challenged Products prevent a disease, but instead that they promote a healthy lifestyle that improves your odds of staving off illness. (Butters Tr. 2817-1818)

Finally, even if the Challenged Advertisements convey that they prevent a specific disease in the same sense that a drug or over-the-counter medication prevents disease (which they do not), the Challenged Advertisement contain carefully qualified statements that convey accurate messages about the actual health benefits of the Challenged Products, the results of the scientific studies and related information. RFF ___.

ii. Reduce the Risk

Complaint Counsel contend that the Challenged Advertisements convey the message to reasonable consumers that drinking eight ounces of POM Juice or taking one POMx Pill daily reduces the risk of certain diseases, such as heart disease, prostate cancer or erectile dysfunction, or that they are "clinically proven" to reduce the risk of certain diseases. RFF ___. Contrary to Complaint Counsels' allegations, where Respondents use the phrase "reduce the risk" in the Challenged Advertising, the message conveyed is that the Challenged Products improve your odds of staving off illness. Indeed, the overall net impression to reasonable consumers of ads that use the phrase "reduce the risk" is that the Challenged Products "reduce the risk" of heart disease, prostate cancer or erectile dysfunction in the same manner that a whole-food like broccoli, blueberries or a healthy diet and exercise reduce the risk of disease. Appendix of Advertisements. As explained above, this is a different standard than reduce the risk in the context of a drug or over-the-counter medication, such as "Tough Actin' Tinactin" or Prilosec. (Butters Tr. 2817-1818). In any event, even if a consumer were to take away such a message, all the Challenged Advertisements use qualifiers and convey accurate messages about the actual health benefits of the Challenged Products. RFF ___.

iii. Treat

Complaint Counsel also allege without support that the Challenged Advertisements convey to reasonable consumers that the Challenged Products "treat" certain diseases, including heart disease, prostate cancer, and erectile dysfunction. Yet, the clear evidence establishes that no such "treat" claims were conveyed. RFF __. Indeed, none of the Challenged Advertisements use the word "treat" in the manner in which Complaint Counsel contend. *See* Appendix of Advertisements. Nor do any of the Challenged Advertisements imply that any of the Challenged Products are used to "treat" any disease in any context, even in Respondents' earlier "outlier" ads. *See* Appendix of Advertisements.

To the extent a "treat" claim can be implied from any of Respondents' advertising (which it cannot), the overall net impression of any ad is not that the Challenged Products are a substitute for conventional medical treatment. (Butters, Tr. 2821-22; Appendix of Advertisements). Indeed, this is common-sense, as a reasonable consumer would not view information regarding whole-food product, like broccoli or pomegranates, as a substitute or replacement for doctor's advice. (Butters Tr. 2817-1818).

Respondents have competent and reliable scientific evidence in the areas of cardiovascular, prostate and erectile health to support claims that patients could benefit from consuming the Challenged Products. As such, had Respondents made "treat" claims, these would be supportable and not a basis for liability under the FDCA.

C. In Any Event, Consumers Do Not Buy POM Products Because They Believe That the Products Will Prevent, Treat Or Reduce the Risk Of Disease

In addition to proving a misrepresentation, Complaint Counsel must show that the misrepresentation was "material" to consumers' purchase decision. *In re Cliffdale Assocs.*, 103 F.T.C. 110, 165 (1984); 1983 FTC Policy Statement on Deception ("FTC Policy Statement"), *appended to Cliffdale Assocs.*, 103 F.T.C. at 182 ("A 'material' misrepresentation or practice is one which is likely to affect a consumer's choice of or conduct regarding a product"). "In other words, it is information that is important to consumers." FTC Policy Statement , 103 F.T.C. at 182. Although the Commission is entitled to apply, within reason, a presumption of materiality

to express claims, deliberately made implied claims and claims that involve significant health concerns, *id.* at 182, the "Commission will always consider relevant and competent evidence offered to rebut presumptions of materiality." *Id.* at 182 n.47; *accord Kraft*, 970 F.2d at 323 (recognizing that if the presumption does not apply, "the Commission examines the record and makes a finding of materiality or immateriality.").

Where, however, respondent adduces evidence to rebut the presumption, it disappears, and the ALJ weighs the evidence on materiality presented by each side, as with any other factual issue, to decide if Complaint Counsel have met their burden of providing a preponderance of evidence on the issue. *In the Matter of Novartis Corp.*, 127 F.T.C. 580, 686 (1999), citing *St. Mary's Honor Ctr. v. Hicks*, 509 U.S. 502, 506 (1993). As held in *Novartis*, "Respondents can present evidence … directly contradicting the initial presumption of materiality. This is not a high hurdle … the fact finder next proceeds to weigh all the evidence presented by the parties on the issue … after the presumption drops out, 'the inquiry turns from the few generalized factors that establish [the presumption] to the specific proofs and rebuttals … the parties have introduced.'" *Novartis*, 127 F.T.C. at 686, quoting *St. Mary's Honor Ct.,* 509 U.S. at 516.

Here, Respondents adduced evidence to rebut any presumption of materiality by presenting the expert testimony of Professor David Reibstein, who found in his Survey of POM Wonderful 100% Pomegranate Juice Users ("Reibstein Survey"), that fewer than 1.5% of buyers (i) bought (ii) would buy again or (iii) would recommend to a friend POM Juice because they believe it cures or prevents a specific disease. RFF . Professor Reibstein further found that less than 1% of pomegranate juice buyers who saw a POM advertisement and who (i) bought (ii) would buy again or (iii) would recommend to a friend pomegranate juice to others because they believe it cures or prevents a specific disease. RFF . Complaint Counsel presented no expert opinion that the asserted implied claims ("Challenged Claims") were material to consumers' purchase decision nor have they submitted their own survey to discredit the Reibstein Survey results. RFF . Complaint Counsel have accordingly failed to show that the Challenged Claims

were material. Both *St. Mary's* and *Novartis* hold that rebutting the initial presumption "is not a high hurdle," and Professor Reibstein's testimony and survey certainly surmount it.

1. The Reibstein Survey Proves that Consumers Purchase POM Juice For Reasons Other Than Disease-Related Advertising Claims

a. The Reibstein Survey Used Proper Survey Methodology

The Reibstein Survey was conducted in accordance with generally accepted survey principles. Professor Reibstein surveyed two groups, 406 respondents who purchased POM Juice in the past 6 months and 344 people who purchased brands of pomegranate juice other than POM. RFF . The Reibstein Survey was designed to reveal: (1) buyers' motivations for purchasing pomegranate juice; and (2) whether having previously seen POM advertisements in the normal sequence of viewing ads, and not in an artificial setting, the ads affected the buyers' motivations for buying pomegranate juice. RFF . To find out what motivated the respondents purchasing decision, the groups were asked three primary questions: (1) why they bought the product; (2) would they buy the product again and, if so why; and (3) would they recommend the juice to others and, if so why. RFF . The participants were also directed to "include as many specific details" in each answer as to why they did or would act as they indicated. RFF . Because "close-end questions ... suggest the desired answer … [and] also tend to elicit bias" (*Stouffer*, 118 F.T.C. at 781; *accord CKE Rest. v. Jack In The Box, Inc.*, 494 F.Supp.2d 1139, 1144-45 (C.D. Cal. 2007)), all three primary questions were asked in an open-ended format to reduce the likelihood of biased results. RFF . Moreover, Question K of the Reibstein Survey asked all 750 participants (both POM and non-POM pomegranate juice buyers) whether they had ever seen a POM Juice advertisement and, if they had, what they remembered about the advertisement. RFF . Participants were directed to provide "as many specific details" as they could remember about the POM advertisement. RFF .

2. The Results of the Reibstein Survey Prove The Challenged Claims Are Not Material To Consumers' Purchase Decision

The data from the Reibstein's Survey shows that less than 1.5% of participants bought, would buy again or would recommend to a friend POM Juice because they believe that it cures or prevents a specific disease. RFF . Moreover, there is also no significant difference in the perception of how pomegranate juice can cure or prevent disease between POM Juice buyers (1.48%) and the control group of non-POM Juice buyers (1.74%). RFF ¶. Likewise, the results from each of the three primary questions that were asked seeking to understand customer motivation for buying, repeat purchasing, or recommending to friends, shows that there was very little reference (1% or less) to pomegranate juice's impact on any disease. RFF . This was true for POM Juice buyers and non-POM buyers. RFF . The statistically signficiant results of the Reibstein Survey overwhelmingly prove the unimportance in consumers' purchasing decision of the belief that pomegranate juice cures or prevents specific diseases.

Rather, the data from the Reibstein Survey confirms that POM Juice buyers' purchasing decisions are significantly motivated by other factors such as, among others, taste (43.6%), a general belief that the juice is healthy (35.2%), curiosity (14%), bottle design (8.4%), recommendation from others (7.4%) and price (5.9%). RFF . The Reibstein Survey also confirms that taste (74%), a belief that the drink is healthy (35.2%), price (6.1%) and quality (3.3%) would drive POM Juice buyers' repurchasing decision. RFF . Professor Reibstein found comparable results for participants who answered that they would recommend POM Juice to others. RFF .

Additionally, the study of the impact of POM's advertisements on buyers' purchasing or recommendation decisions establishes that POM's ads had no impact on buyers' beliefs that pomegranate juice can or will cure or prevent disease. RFF . As set forth in the Reibstein Survey, a total of 12 unique respondents out of 750, including non-POM Juice buyers, mentioned a specific disease as a reason they bought, would buy, or would recommend pomegranate juice. RFF . Among these respondents, only 4 of them have seen a POM advertisement at some point and 8 never have. RFF . The data, therefore, show that the portion of buyers believing in the curative or preventive attributes of pomegranate juice is very similar between the two groups of

buyers: the ones who have seen a POM advertisement and the ones who have not. RFF . The data in the Reibstein Survey also demonstrates that the amount of money POM spent on its research was not a factor in why respondents purchased POM Juice. RFF .

Professor Reibstein's testimony and survey not only rebutted the presumption of materiality, they provided powerful evidence that, to the extent any of POM's advertisements may have made claims concerning diseases, those claims were not "material" to consumers' purchase decision. Respondents having rebutted the presumption of materiality, the burden of proving materiality by a preponderance of evidence remains on Complaint Counsel (*see Novartis*, 127 F.T.C. at 686-87), and they have failed to provide evidence to meet that burden.

3. Complaint Counsel Failed to Rebut Respondents' Substantial Evidence Establishing the Immateriality of the Challenged Claims

a. Professor Mazis Offered No Opinion on the Materiality of the Challenged Claims But Conceded that an Advertising Claim is Material Only if It Affects Consumers' Purchasing Decision

Complaint Counsel presented no evidence showing that the Challenged Claims were material to consumers' decision to buy. Complaint Counsels' sole witness on materiality, Professor Michael Mazis, offered no opinion on the materiality of the Challenged Claims in his expert report, deposition, or at trial. RFF . Complaint Counsels' failure to present evidence on materiality is not surprising because it was not even within the scope of their expert's assignment to examine this critical issue. RFF . Rather, Professor Mazis merely evaluated the narrow issue of the "scientific adequacy" of the Reibstein Survey. RFF . Thus, unlike Professor Reibstein, Professor Mazis did not conduct a consumer survey in this case. RFF . Professor Mazis also provided no expert opinion based on a facial analysis of POM's ads. RFF . Nor contrary to his work as a marketing witness for Complaint Counsel in previous cases, did he analyze the impact or "indirect effects" of POM's advertisements on consumers (RFF), or examine POM's ads based on the psychological and consumer behavior theory of "categorization." RFF .

According to Professor Mazis, "the appropriate measure of materiality" is "the potential impact of the challenged claim on purchase or usage behavior." RFF . Moreover, he concedes

that "an advertising claim may involve information important to consumers, but to be material is has to be important to their decision to buy." RFF . Consequently, Complaint Counsels' failure to have Professor Mazis conduct a consumer survey or opine on the materiality of the Challenged Claims is baffling given "materiality" is a critical issue in this case and Professor Mazis's concession that a statement is material only if it is likely to affect a consumer's choice to purchase a product. RFF . Of course, given the results of the Reibstein Survey, which decisively demonstrated the lack of materiality of the Challenged Claims, it is not totally surprising that Complaint Counsel failed to seriously address the materiality of the Challenged Claims.

Of course, for an advertising claim to be material requires the advertisement to actually affect consumer behavior. However, Complaint Counsels' expert, Professor Stewart, conceded that it takes "three good exposures" to an advertisement before the ad can have an effect on the consumer (RFF) and that it takes "many exposures" to constitute three good exposures. RFF . Professor Mazis concurred testifying that a "couple of exposures to an ad" are "probably . . . not going to affect people's belief about a product." RFF . There is no evidence that any POM advertisement making a disease claim of any nature had more than a single run, much less brining about "many" exposures of the advertisement to any consumer. RFF . Therefore, based on the opinions of Complaint Counsels' own experts, Complaint Counsel is unable to credibly argue that the Challenged Claims effected consumer behavior. As to this point, Professor Mazis agrees: "I don't think there's any evidence in the record on that," meaning whether "any POM Juice or POMx advertisement was likely to affect anyone's belief about POM." RFF .

In sum, given that the Reibstein Survey rebutted the initial presumption of materiality, and Professor Mazis' concession about the lack of evidence in the record on materiality, Complaint Counsels' failure to present any evidence that consumers place any importance on the Challenged Claims is fatal to their ability to prove deception under the FTC Act.

b. Professor Mazis Declined to Rule Out the Reibstein Survey as Probative Evidence of Materiality

Professor Mazis declined to rule out the Reibstein Survey "as probative evidence." RFF . Indeed, on cross-examination, Professor Mazis admitted that he wrote an article entitled *Use of Consumer Surveys in FTC Advertising Cases* in which he suggested, as one way of proving that an advertisement was immaterial to consumers, a survey asking why the participants buy the advertised product. RFF . The open-ended questions Professor Mazis used as examples of how to prove the claim was not material were: (1) "what are the reasons you buy cheese?"; (2) "what are the reasons for your buying individually wrapped cheese food slices?"; and (3) what are "'all the reasons you can think of as to why you buy Kraft singles?'' RFF . These were almost identical to the open-ended questions asked in the Reibstein Survey. According to Professor Mazis, these open-ended questions have "probative value" in showing an advertisement is immaterial. RFF .

4. Complaint Counsels' Attempt to Identify An "Intent" Sufficient To Obtain A Presumption Or Rebut Respondents' Survey Expert On Materiality Was Unsuccessful

In an attempt to obtain the initial presumption of materiality and rebut the expert opinions of Professor Reibstein, Complaint Counsel relies on some irrelevant consumer research and POM's consumer comment logs. However, these documents shed no light on the materiality of the Challenged Claims.

a. The Consumer Research Relied Cited By Complaint Counsel Does Not Address the Materiality of the Challenged Claims

i. The A&U Study is Methodologically Flawed and Unreliable and Should Be Disregarded

Complaint Counsels' reliance on OTX Corporation's Attitude and Usage Study ("A&U Study") is misplaced because it is seriously flawed and unreliable.

First and foremost, Complaint Counsels' expert, Professor Mazis, conceded that the A&U Study does not address whether POM ads were material to the participants' purchase decision. RFF . That concession is dispositive on the question of whether the A&U Study is relevant to the issues at hand.

Nevertheless, Professor Reibstein testified that the results of the A&U Study are unreliable and inflated because the closed-ended questions are leading in that the participants are given a limited number of choices and/or cued to select from attributes that they may not otherwise have thought of. RFF . Utilizing closed-end questions also results in the exclusion of potential answers that were not included on the list of choices because survey participants often feel compelled to select one of the answers provided on the list of choices. RFF . *See, e.,g., Procter & Gamble Pharms., Inc. v. Hoffman-La Roche Inc.*, 2006 WL 2588002, *23 (S.D.N.Y. Sept. 6, 2006) (finding survey flawed where, among other reasons, questions did not offer "don't know" or "no opinion" option). That was the case with the A&U Study, as respondents were forced to select one of the six choices. RFF .

Professor Mazis conceded at trial that the A&U Study was seriously flawed because it "primed" the survey participants by asking numerous screening questions about "antioxidant juices" and the word "antioxidant" was repeated a few times throughout the screening questions so that in considering the main survey questions, the participants may have been focused on health and health issues. RFF . Professor Reibstein concurred that the use of the word "antioxidant" in the screening questions was a serious design flaw. RFF .

b. The Bovitz Survey Is Flawed, Unreliable and Does Not Address Consumers' Purchasing Decisions

For countless reasons, Complaint Counsel cannot rely on the survey conducted by the Bovitz Research Group comparing consumers' perception of ten billboard advertisements from POM's *Super Hero* and *Dressed Bottle* advertising campaigns ("Bovitz Survey") to establish the materiality in this case of the Challenged Claims. Initially, the Bovitz Survey exposed participants only to POM's billboard advertising; however, Complaint Counsel is not challenging billboard advertisements in this case. RFF . Thus, the Bovitz Survey is irrelevant to this case.

Respondents presented substantial evidence that the Bovitz Survey is seriously flawed and does not address materiality. Moreover Professor Mazis did not consider the Bovitz Survey in preparing his expert report and offered no opinion on it in his expert report. RFF .

Professor Reibstein testified that the Bovitz Survey is unreliable for measuring consumers' motivations for purchasing POM products because the survey participants were not asked why they purchase POM Juice and because the sample size of only 100 POM users and 150 target consumers was too small to reach statistical significance at the 95% confidence level. RFF .

The Bovitz Survey is also methodologically flawed because participants were shown specific advertisements in a tightly controlled environment, which is not how consumers normally view advertisements. RFF . Thus, the results of the Bovitz Survey cannot be used to determine whether what was observed in the survey applies to a normal advertising viewing context. RFF . The Bovitz Survey is also had no control and, thus participants might have had preconceived perceptions about pomegranate juice before being exposed to POM's billboard advertisements which could skew their perception of POM's billboard advertisements. RFF .

Finally, as measured by Question E of the Bovitz Survey, the survey imposed strict qualification requirements, including the fact that individuals had to engage in a health-conscious lifestyle and/or hold attitudes toward improving their overall health. RFF . Thus, the Bovitz Survey is methodologically flawed and unreliable because Question E creates a bias towards extremely health-focused people, which is not representative of the overall consumer population. RFF .

c. The AccentHealth Study Is Methodological Flawed and Unreliable

The AccentHealth Study of POM's advertising is seriously flawed and unreliable. Complaint Counsel presented no contradictory expert opinion. Indeed, Complaint Counsels' expert, Professor Mazis, did not consider the Accent Health Study in preparing his expert report and offered no opinion on it in his expert report. RFF .

Professor Reibstein testified that the AccentHealth Study was methodologically flawed and unreliable because the patient was intercepted and interviewed immediately after leaving his urologist's office, heightening whatever issues the patient had about helping his prostate. RFF .

The AccentHealth Study was also flawed and unreliable because it had no control. RFF . Accordingly, the results of the AccentHealth Study are biased. RFF .

5. POM's Consumer Comment Logs Do Not Show that the Challenged Claims Were Material to Consumers' Purchasing Decisions

Complaint Counsel have failed to prove that the Challenged Claims were material to consumers' purchasing decision based on POM's consumer comment log. POM has received at least 24,470 consumer comments over the years. RFF . From the nearly 25,000 consumer comments, Respondents provided Complaint Counsel the 53 consumer comment log entries that referenced a specific disease, health study or POM advertisement. RFF . Only a handful of these 53 consumer comment log entries actually referenced any health-related advertising claim made by POM, which is entirely consistent with the Reibstein Survey results. RFF . Moreover, Complaint Counsel presented no affirmative evidence that anyone listed on the consumer comment logs purchased the Challenged Products as a result of the claims made in the Challenged Advertisements.

D. Some Of The "Advertisements" Complaint Counsel Allege Are Not Actually Advertisements and/or Actionable Under the FTCA.

In their November 9, 2011 Proposed Ad Stipulation, Complaint Counsel contend that four media interviews (three by Mrs. Resnick and one by Mr. Tupper) and one university lecture by Mrs. Resnick allegedly constitute "advertising" in violation of Sections 5 and 12 of the FTCA. The four media interview and one discussion include the following:

(a) Mrs. Resnick's November 2008 television appearance on *The Martha Stewart Show* ("*Martha Stewart*") in which she shared personal recipes for a POMtini cocktail and Thanksgiving stuffing, (CX1426, E-6);

(b) Mrs. Resnick's February 2009 television appearance on *The Early Show* in which she shared some marketing ideas for POM and FIJI Water, (CX472_0003);

(c) an interview of Mrs. Resnick in *Newsweek* magazine, dated March 20, 2009, discussing the economy, her business acumen, and promoting the sale of her book, *Rubies in the Orchard*, (CX1426, Exh. F);

(d) an April 2009 discussion with Mrs. Resnick at USC's Annenberg School of Communication with Dean Ernest J. Wilson III on "How to Uncover the Hidden Gems in Your Business," (CX472_0002); and

(e) a June 2008 television interview of Mr. Tupper on FOX Business discussing the newest "hot" wave in foods - the pomegranate - and the pomegranate juice industry, (CX1426, Exh E-7).

These four interviews and single university presentation, however, are not actionable under the FTCA because they: (1) do not constitute "advertising"; (2) represent constitutionally protected speech; and (3) in any event, cannot be considered as material to the purchasing decision of any consumers.

1. The Interviews and Presentation Cannot Be Considered Advertisements Under the FTCA.

Although "advertisement" is not defined in the FTCA itself, the FTC "understand [an advertisement] to mean a notice or announcement that is publicly published or broadcast and is paid-for." *In re R.J. Reynolds Tobacco Co.*, FTC Docket No. 9206, 1988 WL 490114, *6 (Mar. 4, 1988) (emphasis added); *Daniel Chapter One I,* FTC Docket No. 9329 (2009), Initial Decision at p. 79 (finding a daily, two-hour radio program to be "advertising" when respondents counseled listeners, who identified themselves as cancer patients, to use respondents' products as cancer treatments and broadcasted a toll-free phone number for listeners to order their products). There is no evidence that the Respondents, including Matt Tupper, paid to anyone for their participation in the interviews or to allow them to speak about pomegranate juice. (RFF). Thus, using the FTC's own "understanding," the individual Respondents' unpaid media appearances do not constitute actionable advertising. That alone should end the inquiry. But Complaint Counsels' overreaching also fails under a more rigorous commercial speech inquiry.

In deciding whether a statement included in a book, article, or public address is an advertisement or commercial speech, courts have looked to the "main purpose" of the publication or address and to the "primary" motivation of the speaker or writer in making the speech or writing the book. *E.g.*, *Oxycal Labs., Inc. v. Jeffers*, 909 F.Supp. 719, 723 (S.D. Cal. 1995). In *Oxycal*, the Court held that having a commercial motivation to sell books does not

make statements in a book about a food product's curative powers an advertisement or commercial speech, even though the author also had an interest in a store that sold such products. *Id.* at 725. Complaint Counsel have not presented any evidence that the individual respondents' "main purpose" or "primary motivation" for participating in the media appearances was to sell Mrs. Resnick's book, *Rubies in the Orchard*, or the Challenged Products. Indeed, the "main purpose" of Ms. Resnick's participation in the Newsweek interview was not to sell "Pom." Her motivation for even agreeing to the interview was that allowing the public to get to know her might help sell her book. The "main purpose" of the interview itself was to provide the viewer or reader with a wide-ranging discussion of Ms. Resnick herself, her views, interests and accomplishments, not to sell Pom or even to propose that people buy her book . (CX1426, Exh. F)

The court in *Oxycal* also considered the length of the targeted statements in comparison to the entire segment. *E.g.*, *Oxycal*, 909 F.Supp. at 725. Each of the references to pomegranate juice were very short and only a miniscule portion of the lengthy appearances which covered a variety of other subjects. For example, Mrs. Resnick's reference to the health benefits of pomegranate juice was only about 35 sections out of the two segment interview, which lasted 12 minutes and 30 seconds. (CX1426, Exh. E-6; Lynda Resnick Interview on *Martha Stewart* (November 20, 2008), available on You Tube at http://www.youtube.com/watch?v=IBejxwUTGAQ.

Another factor to be considered is whether the speaker's statement was "proactive or reactive." *E.g.*, *Boulé v. Hutton*, 70 F.Supp.2d 378, 389-390 (S.D.N.Y. 1999). Mrs. Resnick's and Mr. Tupper's references to pomegranate juice in the course of their interviews were strictly "reactive." In other words, they were responses to questions posed by the interviewers. For example, Mrs. Resnick's reference to the "medical benefits" of pomegranate juice during the course of her interview with Martha Stewart was strictly "reactive" and was directly in response to a question posed by Martha Stewart. (CX1426, Exh. E-6). In *Boulé*, the court noted that the

statements that were found to be not advertisements were "a response to an unsolicited inquiry by a magazine reporter seeking comment on a topic of public concern." *Id.*

Lastly, to be classified as commercial speech and thus as "advertising," speech must, in addition to the requirements listed above, "propose a commercial transaction" and must be "solely related to the economic interests of the speaker and its audience." *Oxycal*, 909 F.Supp. at 724. (emphasis added). Statements that can be classified as commercial speech and thus subject to FTC jurisdiction must be "speech proposing a commercial transaction." *In re R. J. Reynolds,* FTC Docket No. 9206 at 3.

Neither Mrs. Resnick's interviews nor even her specific opinions on the benefits of pomegranate juice "proposed a commercial transaction." Certainly, her Newsweek interview was not "solely related to the economic interests of the speaker and [her] audience." The readers were interested in learning about the life, views and accomplishments of a successful female entrepreneur, not in furthering their own "economic interests." RFF . Similarly, Mr. Tupper's interview discussing the newest superfood was not proposing a commercial transaction. RFF .

2. The Interviews and Presentation Represent Constitutionally Protected Speech

The statements made by Mrs. Resnick and Mr. Tupper at their media appearances are also not actionable under the FTCA because they are statements of opinion and therefore constitutionally protected speech. In *Koch v. F.T.C.*, 206 F.2d 311, 314 (6th Cir. 1953), the Sixth Circuit held that respondent's statements, which were published in a book and made during a public address, promoting the sale of medicinal preparations for cancer, were not "advertisement[s] covered by Sections 5, 12, or 15(a)" of the FTCA because the book "sets forth primarily matter of opinion," and "prohibiting dissemination of such a book . . . would violate the First Amendment. . . ." *Id*. at 317-18. Here, Mrs. Resnick's and Mr. Tupper's responses to questions concerning pomegranate juice are mere expressions of opinion. RFF . Thus, these statements call for First Amendment protection and preclude a finding that these statements are advertising in violation of federal statutes.

3. The Media Appearances Cannot Be Considered Material To The Purchasing Decision Of Any Consumer

Additionally, assuming *arguendo*, that Mrs. Resnick's speech and the interviews were considered "advertising," they were not material to the purchasing decision of POM's consumers. Dr. Reibstein's survey demonstrated that, even if the ads conveyed the messages that Complaint Counsel assign to them, any alleged disease claims made by Respondents were not material to the purchasing decisions of POM consumers. RFF . And, as discussed above, Complaint Counsel adduced no evidence that showed any causal relationship between any of Respondents' advertising and the consumers' purchase decision. RFF .

Rather than confine themselves to POM's conventional advertisements, Complaint Counsel also allege as violations of the FTCA a handful of media interviews given by Mrs. Resnick and Mr. Tupper. In doing so, however, Complaint Counsel have overstepped their jurisdiction. For "unless [an] advertisement can be classified as commercial speech it is not subject to the Commission's jurisdiction." *In re RJ Reynolds*, FTC Docket No. 9206 (Mar. 4, 1988), Order at 3.

E. POM's Health Claims Are Neither False Nor Lacking in a Reasonable Basis

Complaint Counsel have not produced any evidence or testimony suggesting that POM's claims of health benefits are affirmatively false, *i.e.* that the claimed benefits do not exist, nor can Complaint Counsel carry the heavy burden of proving that all of the alleged claims are expressly conveyed in the ads. ere.

Complaint Counsel completely ignore the considerations and cost benefit analysis required by *Pfizer Inc*., *supra*, 81 F.T.C. 23, including the type of product at issue, the possible consequences of a false claim, and the cost of developing substantiation for the claim. A careful weighing of the relevant factors is not at all what Complaint Counsel advocate. Nor is it the position taken by their experts. Indeed, Complaint Counsel would disseminate or publicize no health information to the public that is not backed by RCT, no matter how great the cost of those studies, or how slight the risk of harm, or what other forms of science support the information, no matter the type of product at issue and regardless if it is entirely safe. Complaint Counsel

ignores the required cost benefit analysis under *Pfizer*—precisely because their claims should be rejected under this analysis.

Moreover, this Court should prefer "disclosure over outright suppression." *Pearson I*, 164 F.3d at 657. Where there is doubt as to the completeness or accuracy of an ad, the courts favor providing the information to the public over suppressing it. *Id*. This policy has also been endorsed by federal courts following the command in *Pearson I* stating "that, under the First Amendment commercial speech doctrine, there is a 'preference for disclosure over outright suppression.'" *Alliance for Natural Health*, 714 F.Supp.2d at 52-53; *see also Whitaker v. Thompson*, 248 F.Supp.2d 1, 9 (D.D.C. 2002) (*Whitacker I*) ("in finding that speech is misleading, the government must consider that 'people will perceive their own best interests if only they are well enough informed, and . . . the best means to this end is to open the channels of communication, rather than to close them").

An approach that equates food to drugs makes communicating truthful information regarding the potential health benefits of a whole food product economically impossible to "substantiate." Unlike a drug, wherein the manufacturer receives patent protection and market exclusivity in return for cost intensive research, producers of natural food products receive no comparable compensation for their investment. Requiring RCTs here will necessarily suppress truthful information. In stark contrast, where the product at issue is a potentially harmful drug, and its expected patent rights and likely high price justifies the massive expense of RCTs, requiring two such studies before informing the public of the drug's potential benefit may be appropriate. For example, Bristol Myers' new melanoma drug Yervoy creates a serious danger of death. Its patent gives the company a monopoly, and the treatment costs $120,000. Under such circumstances, the FDA may have good reasons for requiring RCTs.

On the other hand, where we are dealing with a pure food or juice that creates no risk of harm, has no patent protection, and sells for a few dollars, requiring two enormously costly RCTs, as the only way the public can be given information about the product's health benefits, is contrary to the Commission's previously announced positions and is manifestly bad public

policy. As summarized in *Pearson I,* 164 F.3d at 656 n.6, the courts should distinguish between products (*e.g.,* dietary supplements) that do not "in any fashion threaten consumer's health and safety" and "drugs," which "appear to be in an entirely different category," *e.g.*, "wherein the potential harm presumably is much greater." As the Court in *Whitaker I,* reasoned:

> It is especially important to recognize that, in the present case, the potential harm to consumers from deception is severely limited . . . . At worst any deception resulting from Plaintiffs' health claim will result in consumers spending money on a product that they might not otherwise have purchased. This type of injury, while obviously not insignificant, cannot compare to the harm resulting from the unlawful suppression of speech.

Whitacker I, 248 F. Supp.2d at 16.

Respondents' experts in each field support the distinction drawn by the Court of Appeal in *Pearson I* and by the district court in the subsequent *Pearson II* case and in *Whitaker I.* For example, Dr. Miller, an esteemed pediatric oncologist, has testified that where the product is absolutely safe, like the Challenged Products, and where the claim or advertisement does not suggest that the product be used as a substitute for conventional medical care or treatment, then it is appropriate to favor disclosure; and credible evidence is enough. RCT are not required or even necessarily superior.

Notably, Dr. Miller, who previously testified as an expert for Complaint Counsel in *In re Daniel Chapter One*, FTC Docket No. 9329, Initial Decision (Aug. 5, 2009) recognized that in this case—involving a 100% pure fruit juice or wholly-derived pomegranate products, and threatening no material risk of harm—costly RCTs should not be required as a barrier to providing information as to the likely health benefits of pomegranate products to the public. RFF .

Considering all of the relevant factors, RCTs should not be arbitrarily required from Respondents as the only way to justify future advertising about potential nutrient disease effects of pomegranate products. Basic science, *in vivo* and *in vitro* laboratory tests and clinical studies, even if not costly RCT studies, are sufficient. That view is supported by the expert testimony of distinguished scientists in each medical field at issue. RFF .

XI. THE REMEDY COMPLAINT COUNSEL SEEK EXCEEDS THE COMMISSION'S AUTHORITY, IS OVERBROAD, AND VIOLATES THE CONSTITUTION

Complaint Counsel fails to justify the relief that they seek.

A. The FDA Pre-Approval Requirement Sought By Part I Of The Notice Order Exceeds The Commission's Authority And Violates the First Amendment of the Constitution.

In Part I of the proposed Order, Complaint Counsel seek for the first time in this Court relief requiring that Respondents obtain FDA approval before making certain advertising claims concerning the Challenged Products. Complaint Counsels' proposed Order exceeds the Commission's authority and violates the First Amendment of the U.S. Constitution.

The Commission's authority to prohibit false, misleading, deceptive and unfair advertising practices derives from the FTCA. The FTCA permits the Commission to outlaw misleading and deceptive advertising. A claim is not misleading merely because it satisfies the definition of "drug" under the FTCA; rather, the Commission has to demonstrate that the claim made about the product is false, misleading, or deceptive.

Because the Commission's authority is limited to prohibiting misleading, deceptive and false claims, the FTCA also does not allow the Commission to prohibit advertising practices that may not meet FDA approval standards, but which are nevertheless truthful or substantiated. In asking the Commission to enjoin the making of claims merely because the claims have not been approved by the FDA, Complaint Counsel are, in effect, asking that the Commission enforce FDA's standards under the Food, Drug, and Cosmetic Act ("FDCA"). But, nothing in the FTCA gives the Commission the authority for such enforcement and, in any event, the plain language of the FDCA mandates that only the "United States," and not other agencies (such as the Commission), may bring actions to enforce provisions of the FDCA. *Buckman Co. v. Plaintiff's Legal Comm'n*, 531 U.S. 341 (2001).

Were the Commission to issue relief requiring pre-approval by the FDA of certain claims, such relief may well prevent dissemination of truthful claims that for whatever reason have not been reviewed by FDA or even would not meet FDA drug approval standards. The Commission

has no authority under the FTCA to prohibit truthful claims, even if such claims do not meet the approval standards of another agency.

Complaint Counsel relies on *Thompson Med.*, *supra*, 104 F.T.C. 648 and other cases for the proposition that Respondents should be required to seek FDA approval in order to make certain health claims. *Thompson Medical*, however, merely determined, based on the record in that case that the proper level of substation for the advertising in that case consistent of two well-controlled clinical trials, which happened to be consistent with the FDA's standards. In that case, which, notably, involved an over-the-counter medicinal cream and not a 100% fruit product, the Commission stated that requiring two well-controlled studies for the health benefit claims at issue there was appropriate. Nowhere in *Thompson Medical* or in any other litigated case has the Commission, or courts for that matter, required a marketer to receive pre-approval from the FDA to make truthful and non-misleading health claims under the FTCA. And, to do so would vastly exceed this Commission's authority.

Part I of the Order also violates the First Amendment of the Constitution. The law is clear that the Commission may not prospectively enjoin Respondents from engaging in speech on the basis that the FDA's pre-approval has not been satisfied without first showing that no qualification is capable of rendering the future nutrient-disease advertising claims non-deceptive on a claim-by-claim basis. *See FTC v. Brown & Williamson Tobacco Corp*., 778 F.2d 35, 45 (D.C. Cir. 1985) (explaining that the Commission's injunction violated the First Amendment because it prevented Brown & Williamson from advertising information "in sufficient quantity to allow consumers to make informed decisions" and "[s]ince [that] would eliminate consumer confusion ... the FTC must bear the affirmative burden of demonstrating any inadequacy, and thus deceptiveness ..."); *Peel v. Attorney Registration and Disciplinary Com'n of Illinois*, 496 U.S. 91 ___, 109-11 (_____) (holding that burden is on the government, not the advertiser, to come up with a less restrictive regulation); *Kraft, supra*, 970 F.2d at 325 (collecting cases). Indeed, the government is prohibited from keeping the public in the dark simply because there is a lack of scientific agreement on a particular health issue. The freedom of speech protected by

the First Amendment includes the freedom to communicate potential health benefits, appropriately qualified.

Under *Pearson I* and its progeny, unless the Commission can meet its burden of showing that consumers will not understand the limits of scientific evidence bearing qualifications, it may not impose such a prior restraint instead. *See Pearson I*, 164 F.3d at 658 ("[a]lthough the government may have more leeway in choosing suppression over disclosure as a response to the problem of consumer confusion where the product affects health, it must still meet its burden of justifying a restriction on speech"); *Ibanez v. Florida Department of Bus. and Prof. Reg.*, 512 U.S. 136, 146 (1994) ("[i]f the protections afforded commercial speech are to retain their force, we cannot allow rote invocation of the words 'potentially misleading' to supplant the [government's] burden to demonstrate that the harms it recites are real and that its restriction will in fact alleviate them to a material degree"); *Edenfield v. Fane*, 407 U.S. 761, 771 (1993) (concerning ban on solicitation by accountants and stating that the government "present[ed] no studies that suggest personal solicitation of prospective business clients by CPA's creates the dangers. . . ."). The *Pearson III* court explained that the "mere absence of significant affirmative evidence in support of a particular claim ... [is not] negative evidence 'against' it." 141 F. Supp. 2d 105 (citing *Pearson I*, 164 F.3d at 660). Complaint Counsel presented no evidence in this case that there is no scientific evidence in support of the claims or that the evidence is for the claims made is qualitatively weaker than that against it. Without satisfying their burden, the Commission is constitutionally barred from imposing the prior restraint set forth in Part I of the Notice Order on Respondents' future advertising.

B. Parts II and III of the Order Seek Over-Broad Fencing In Relief That Is Not Warranted By The Record

In Parts II and III of the Order, the Commission seeks broad, multi-product "fencing-in" relief that is not justified by the record in this case. Notwithstanding the Commission's broad discretion in fashioning remedies, there must "be some relation between the violations found and the breadth of the order." *See Country Tweeds, Inc. v. F.T.C.*, 326 F.2d 144, 148-149 (2d Cir.

1964) (citing *F.T.C. v. Mandel Bros., Inc.*, 359 U.S. 385 (1959); *F.T.C. v. National Lead Co.*, 352 U.S. 419 (1957); N.*L.R.B. v. Cromption-Highland Mills, Inc.*, 337 U.S. 217 (1949); N.*L.R.B. v. Express Publishing Co.*, 312 U.S. 426 (1941)).

"Multi-products orders should be used with caution because they alter the scheme of penalties and enforcement procedures defined by the Act." *Litton Indus., Inc. v. F.T.C.*, 676 F.2d 364, 371 (9th Cir. 1982) (citing *Standard Oil Co. v. F.T.C.*, 577 F.2d at 661). Here, the proposed Notice Order includes fencing-in provisions directed to a range of the Respondents' business activities that have nothing to do with the Challenged Products. In addition to seeking injunctive relief against POM, Complaint Counsel seek an Order against Respondents' unrelated businesses, including FIJI Water (bottled artesian water), Paramount Citrus (citrus fruits), Paramount Farms (nuts and nut processing), Justin Vineyards (winery) and unrelated products. The record in this case does not justify such broad relief.

To determine whether the fencing-in relief bears reasonable relation to the violations in this case, the Commission considers whether there is a reasonable relationship between the conduct complained of and the requested relief. Traditionally, this ALJ has used three factors to evaluate reasonable relation: (1) the seriousness and deliberateness of the violation; (2) the ease with which the violative claim may be transferred to other products; and (3) whether the respondent has a history of prior violations. *See Stouffer Foods Corp.*, 118 F.T.C. 746, 811 (1994); *Sterling Drug, Inc. v. F.T.C.*, 741 F.2d 1146, 1155 (9th Cir. 1984); *Sears Roebuck & Co. v. F.T.C.*, 676 F.2d 385, 391-392 (9th Cir. 1982); *Standard Oil Co. v. F.T.C.*, 577 F.2d 653, 662 (1978). Balancing these factors, the broad fencing-in relief is impermissibly braod and wholly unwarranted in this case.

As an initial matter, the violations alleged in this case occurred years ago have been corrected. RFF . Thus, the conduct complained of is not sufficiently serious or deliberate to justify a broad sweeping order. *Cf. Litton Indus., Inc. v. .FT.C.*, 676 F.2d 364, 371 (9th Cir. 1982) (upholding multiproduct order when respondents continued practices after Commission had questioned the advertising practices). In addition, Complaint Counsel presented no evidence

that any of these businesses, which are wholly separate from POM and the Challenged Products, have improperly advertised their products. Without such evidence, the Commission should reject the broad fencing in provisions proposed by Complaint Counsel.

Moreover, the fencing-in relief also defies common sense, as the other POM-related companies and products that would be subject to Complaint Counsels' proposed Order have nothing to do with the Challenged Products. There is, thus, no reasonable relation between the conduct at issue in this case and the products that Complaint Counsel seek to subject to the proposed Order. *See, e.g., American Home Products Corp. v. F.T.C.*, 402 F.2d 232 (6th Cir. 1968) (finding multi-product order too broad when the only evidence presented in the proceeding concerned Preparation H cream (not the other products subject to the order); *Grove Labs. v. F.T.C.*, 418 F.2d 489 (5th Cir. 1969); *cf. Kraft*, 970 F.2d 311 (upholding multiproduct order relating to cheese related products); *Western Radio Corp. v. F.T.C.*, 339 F.2d 937 (7th Cir. 1964) (upholding order relating to similar products).

Finally, the Commission has declined to issue broad fencing-in relief in instances, as here, where a party does not have a history of prior violations. [Citations] Respondents in this case have never been party to an FTC proceeding or subject to an FTC order. There is, thus, no basis for issuance of a multi-product order.

XII. LIABILITY SHOULD NTO ATTACH TO ROLL GLOBA LLLC OR RESPONDENT MATTHEW TUPPER

A. Complaint Counsel Have Not Shown That Roll Global LLC and POM Are A Common Enterprise

"In considering allegations of misrepresentations, courts engage in a fact-specific inquiry in which the 'pattern and frame-work of the whole enterprise must be taken into consideration. The factors to be considered include, inter alia: common control, the sharing of office space and officers, whether business is transacted through 'a maze of interrelated companies,' the commingling of corporate funds and failure to maintain separation of companies, unified advertising, and evidence which reveals that no real distinction existed between the Corporate Defendants." *F.T.C. v. Ameridebt*, 343 F. Supp. 2d 451, 462 (D. Md. 2004) (internal quotations

and citations omitted). Here, the record is clear that Respondents ROLL Global LLC ("Roll") and POM are not a common enterprise. They maintain separate records and do not comingle their funds. RFF . Because ROLL was not involved in the underlying conduct complained of, and because they are a separate enterprise from POM, there is no basis to impose liability on them.

B. Complaint Counsel Failed to Present Sufficient Evidence To Justify Imposition of Relief on Respondent Matthew Tupper

Individual liability is secondary and derivative of corporate liability and can only be imposed if the corporation is first found to have disseminated unfair, deceptive or otherwise misleading advertisements. F.T.C. v. Bay Area Business Council, Inc., 423 F. 3d 627 (7th Cir. 2005). Individual liability cannot be imposed on an officer of a company for participation alone; instead the ability to control the offending conduct or advertising (i.e., being the ultimate decision maker) is always the key inquiry. S*ee In the Matter of Universal Electronics Corp., et al*., 1971 WL 128754 (F.T.C.) (1971); F*.T.C. v. Swish Marketing et al*., 2010 WL 653486 (N.D. Cal. Feb. 22, 2010); *F.T.C. v. Neovi, Inc. et al*., 598 F.Supp.2d 1104 (S.D. Cal. 2008); *F.T.C. v. Transnet Wireless Corp.*, 506 F. Supp. 2d 1247, 1261-1265 (S.D. Fla. 2007); *F.T.C. v. Verity Int'l, Ltd*., 335 F. Supp. 2d 479, 499 (S.D.N.Y. 2004); *F.T.C. v. Publishing Clearing House*, 104 F. 3d 1168, 1171 (9th Cir. 1997); F*.T.C. v. Amy Travel Service, Inc*., 875 F. 2d 564, 574-575 (7th Cir. 1997); *F.T.C. v. Think Achievement Corp*., 144 F. Supp. 2d 993, 998-1002 (N.D. Ind. 2000); F*.T.C. v. J.K. Publications*, 99 F. Supp. 2d 1176, 1181-1185, (C.D. Cal. 2000); *F.T.C. v. Direct Marketing Concepts, Inc. et al.*, 624 F.3d 1 (1st Cir. 2010). Here, Mr. Tupper did not control the conduct at issue in this case. RFF .

Corporate officers may be held individually liable for violations of the FTCA, but only if the officer "owned, dominated and managed" the company and if naming the officer individually is necessary for the order to be fully effective in preventing the deceptive practices which the Commission had found to exist. *F.T.C. v. Standard Educ. Society*, 302 U.S. 112 (1937) (officers/managers and sole shareholders of closely held corporation that was dominated and

managed by these individuals were held personally liable and included in cease and desist order because it was anticipated from past conduct that these persons would simply try to evade the FTC's order by setting up another company). Complaint Counsel named POM's President Matthew Tupper as an individual respondent in the Complaint. Mr. Tupper neither owns, dominates, nor ultimately controls POM. RFF . During the relevant period, Mr. Tupper was not involved in final advertising decisions and he worked directly for the owners of the company. RFF . He, therefore, is not subject to liability under the FTCA. *In the Matter of Auslander Decorator Furniture, Inc., Trading As A.D.F., Etc. et al.*, 1974 WL 175916 (F.T.C.) (1974) (finding individual respondents lacked sufficient control or responsibility for liability); *Standard Educ. Society*, 302 U.S. at 119 (officers/managers and sole shareholders of closely held corporation that dominated and managed the company were included in cease and desist order to ensure compliance with the order as these persons were ultimately in control).

Traditionally, the Commission has imposed individual liability as a method to preclude owners of closely held corporations from dissolving the offending corporation and beginning a new one to avoid a cease and desist order of the FTC. *Standard Educ. Society*, 302 U.S. at 119. This later evolved into allowing non-owner officers to be found liable if they met the above described "ability to control" tests or otherwise "formulated, directed or controlled any of the acts and practices" at issue. *In re Griffin Systems, Inc. et al.*, 117 F.T.C. 515, 563-564 (1994) (finding individual who was vice president, treasurer and director liable for distributing solicitation in violation of the FTCA because he was in charge of the company and was considered the control person by the employees).

Unlike the typical president of a private company, Mr. Tupper's authority was derivative of and subject to private owner individuals above him (the Resnicks) and cannot be seen as a typical ultimate decision maker officer subject to liability in FTC cases. *See e.g. F.T.C. v. Publishing Clearing House*, 104 F. 3d 1168, 1171 (9th Cir. 1997); *F.T.C. v. Neovi, Inc. et al.*, 598 F.Supp.2d 1104 (S.D. Cal. 2008). Mr. Tupper's inclusion in any injunctive or related order, is not necessary to effectuate the cessation of the alleged offending conduct (the primary purpose

of such orders), as he does not and never did ultimately control it. RFF ; *Standard Educ. Society*, 302 U.S. at 119 (officers/managers and sole shareholders of closely held corporation that dominated and managed the company were included in cease and desist order to ensure compliance with the order as these persons were ultimately in control).

Moreover, Mr. Tupper has resigned from POM and has no plans to return to POM or Roll. Because Mr. Tupper never had control over the alleged offending conduct and he retired from POM and is not planning to return, no liability should be imposed.

XIII. CONCLUSION

Setting aside for the moment the constitutional issues, it is clear that Respondents have abundant competent and reliable preclinical and clinical evidence to support their claims—even if this Court were to adopt Complaint Counsels' argument that claims beyond supportive health have been made. As summarized in *Whitaker* and *Pearson*, and their progeny, while a complete ban would be reasonable where there was no evidence to support a claim or if there were only "qualitatively weak support" in "one or two old studies," where, as here, there exists ample, significant and credible evidence to support the claim, more disclosure rather than less is the preferred approach. POM's studies are rigorous, scientifically executed studies, published in peer-reviewed scientific journals, which certainly show health benefits from the consumption of POM's pomegranate products. The claims are supported under *Pfizer* and the FTC's "competent and reliable" standard—even those claims which Respondents dispute were conveyed by the advertisements. The advertisements, however, do not convey that the products are "silver bullets" against disease as alleged by the FTC. Consequently, the proposed order against Respondents, including its definition of "Covered Products" is not supportable.

In addition, the mechanism in the order requiring FDA prior approval is not appropriate or warranted by the facts of this case, and is constitutionally flawed. This requirement should be barred outright.

Respectfully submitted,

/s/ Kristina M. Diaz

Kristina M. Diaz, Esq.
Alicia Mew, Esq.
Johnny Traboulsi, Esq.
Brooke Hammond, Esq.
Roll Law Group P.C.
11444 West Olympic Blvd., 10th Floor
Los Angeles, CA, 90064
Tel: 310.966.8400
Fax: 310.966.8810
Email: kdiaz@roll.com

John D. Graubert
Skye L. Perryman
COVINGTON & BURLING LLP
1201 Pennsylvania Ave. NW
Washington, DC 20004-2401
Telephone: 202.662.5938
Facsimile: 202.778.5938
E-mail: JGraubert@cov.com
SPerryman@cov.com

Bertram Fields
Greenberg Glusker
1900 Avenue of the Stars
21st Floor
Los Angeles, CA 90067
Telephone: 310.201.7454
Counsel for Respondents Stewart Resnick and Lynda Rae Resnick

RESPONDENTS' WEBSITE APPENDIX

Exhibit	Document Description
1	FTC, "FTC Complaint Charges Deceptive Advertising by POM Wonderful" (dtd 9/27/10); http://www.ftc.gov/opa/2010/09/pom.shtm, Accessed 1/10/12
2	FDA For Consumers "Fast Track, Accelerated Approval and Priority Review" (undated); http://www.fda.gov/,Accessed 1/10/12
3 A.	NIH, "NIH at a Glance" (dtd 12/5/11); http://www.nih.gov/about/, Accessed 1/10/12
B.	NIH, "Mission" (dtd 3/3/11); http://www.nih.gov/about/mission.htm, Accessed 1/10/12
4	CDC, "Highlights: How Smoking Harms People of All Ages" (dtd 5/27/04); http://www.cdc.gov/tobacco/data_statistics/sgr/2004/highlights/harm/, Accessed 1/10/12
5	U.S. Department of Health and Human Services, Office on Smoking and Health "The Health Consequences of Smoking: What it Means to You" (2004)
6	CDC, "Health Across Lifespan" (dtd 9/28/09); http://www.cdc.gov/visionhealth/basic_information/lifespan.htm, Accessed 1/10/12
7	CDC, "Alice Hamilton Award Winners and Honorable Mentions: Descriptions, 2003" (dtd 4/28/11); www.cdc.gov/niosh/awards/hailton/aliceabs03.html, Accessed 1/10/12
8	US National Library of Medicine, NIH "Antioxidants: MedlinePlus" (dtd 1/9/12); http:l'-... m.nlh.gOiimedllneplu./antloxldant8.html, Accessed 1/10/12
9	National Center for Complementary and Alternative Medicine, "Antioxidant Supplements for Health: An Introduction" (dtd 10/2011); nccam.nih.gov/health/antioxidants/Introduction.htm, Accessed 1/10/12
10	NIH, "Search of: Open Studies | antioxidants"; clinicaltrials.gov/search/open/intervention=antioxidants, Accessed 1/10/12
11	National Cancer Institute, "Antioxidants and Cancer Prevention: Fact Sheet" (undated); www.cancer.gov/cancertopics/factsheet/prevention/antioxidants, Accessed 1/10/12
12	USDA, "Ressearch Project: Dietary Factors early in Human Development: Health Consequences of Phytochemical Intake" (dtd 1/10/12); www.ars.usda.gov/research/publications/publications.htm…, Accessed 1/10/12
13	FDA, "Guidance for Industry: Food Labeling; Nutrient Content Claims; Definition for 'High Potency' and Definition for 'Antioxidant'" (dtd 7/18/08); fda.gov/Food/GuidanceComplianceRegulatoryInformation/…/ucm063064.htm, Accessed 1/10/12
14 A.	Nutrition.gov, "What's In Food: Antioxidants & Phytonutrients" (dtd 10/20/11); riley.nal.usda.gov/nal_display/index.php?info_center=11&tax_level=2&tax_s…, Accessed 1/10/12
B.	USDA, "Consumer Corner: Antioxidants, Phytochemicals and Functional Foods" (dtd 1/5/12); fnic.nal.usda.gov/nal_display/index.php…, Accessed 1/10/12
15	U.S. News, "Best Hospitals: Cancer" (2012); http://health.usnews.com/health-news/best-hospitals/articles/2011/07/1…, Accessed 1/10/12
16	University of Texas MD Anderson Cancer Center, "Glossary of Cancer Terms" (2011); http:www.mdanderson.org/patient-and-cancer-information…/glossary-of-

	cancer-terms…, Accessed 1/10/12
17	University of Texas MD Anderson Cancer Center, "Inside Integrative Medicine: A Newsletter for Staff, Participants, and Friends…" (February/March 2010), Accessed 1/10/12
18	U.S. News, "Best Hospitals 2011-12: the Honor Roll" (2012)
19	Memorial Sloan-Kettering Cancer Center, "Integrative Medicine: Disclaimer" http://www.mskcc.org/cancer-care/integrative-medicine/disclaimer…, Accessed 1/10/12
20	Johns Hopkins Sidney Kimmel Comprehensive Cancer Center "New Treatments and Research" http://www.hopkinsmedicine.org/kimmel_cancer_center/types_cancer/prostate_cancer/ne..., Accessed 1/10/12
21	Johns Hopkins Medicine, "Prostate Disorders Special Report: Simple Steps to Protect Yourself Against Prostate Cancer" (dtd 5/29/08); http://www.johnshopkinshealthalerts.com/reports/prostate_disorders/2016-1.html, Accessed 1/10/12
22	Mayo Clinic, "Prostrate caner: Question - Pomegranate juice: A cure for prostate cancer?" (dtd 11/30/10), http://www.mayoclinic.com/health/pomegranate-juice/AN01477, Accessed 1/10/12
23	University of Chicago Medical Center, "Biography of Michael H. Davidson, MD" (2012); http://www.uchospitals.edu/physicians/michael-davidson.html, Accessed 1/10/12

Federal Trade Commission
Protecting America's Consumers

For Release: 09/27/2010

FTC Complaint Charges Deceptive Advertising by POM Wonderful

Agency Proceedings Will Determine Whether Health Claims for Pomegranate Products Are False and Not Supported by Scientific Evidence

As part of its ongoing efforts to uncover over-hyped health claims in food advertising, the Federal Trade Commission has issued an administrative complaint charging the makers of POM Wonderful 100% Pomegranate Juice and POMx supplements with making false and unsubstantiated claims that their products will prevent or treat heart disease, prostate cancer, and erectile dysfunction.

The FTC complaint charges that POM Wonderful LLC, sister corporation Roll International Corp., and principals Stewart Resnick, Lynda Resnick, and Matthew Tupper violated federal law by making deceptive disease prevention and treatment claims. The ads in question appeared in national publications such as *Parade*, *Fitness*, *The New York Times*, and *Prevention* magazines; on Internet sites such as pomtruth.com, pomwonderful.com, and pompills.com; on bus stops and billboards; in newsletters to customers; and on tags attached to the product. POM Wonderful Pomegranate Juice is widely available at grocery stores nationwide, and a 16 oz. bottle retails for approximately $3.99. POMx pills and liquid extract are sold via direct mail, with a one-month supply costing approximately $30.

"Any consumer who sees POM Wonderful products as a silver bullet against disease has been misled," said David Vladeck, Director of the FTC's Bureau of Consumer Protection. "When a company touts scientific research in its advertising, the research must squarely support the claims made. Contrary to POM Wonderful's advertising, the available scientific information does not prove that POM Juice or POMx effectively treats or prevents these illnesses."
The advertisements touted POM Juice and POMx supplements with statements such as:

- "SUPER HEALTH POWERS! … 100% PURE POMEGRANATE JUICE. … Backed by $25 million in medical research. Proven to fight for cardiovascular, prostate and erectile health."
- "NEW RESEARCH OFFERS FURTHER PROOF OF THE HEART-HEALTHY BENEFITS OF POM WONDERFUL JUICE. 30% DECREASE IN ARTERIAL PLAQUE … 17% IMPROVED BLOOD FLOW … PROMOTES HEALTHY BLOOD VESSELS … "
- "**Prostate health.** Prostate cancer is the most commonly diagnosed cancer among men in the United States and the second-leading cause of cancer death in men after lung cancer.
  Time pill. Stable levels of prostate-specific antigens (or PSA levels) are critical for men with prostate cancer. Patients with quick PSA doubling times are more likely to die from their cancer. According to a UCLA study of 46 men age 65 to 70 with advanced prostate cancer, drinking an 8 oz glass of POM Wonderful 100% Pomegranate Juice every day slowed their PSA doubling time by nearly 350%. … 83% of those who participated in the study showed a significant decrease in their cancer regrowth rate."
- "You have to be on pomegranate juice. You have a 50 percent chance of getting [prostate cancer]. Listen to me. It is the one thing that will keep your PSA normal. You have to drink pomegranate juice. There is nothing else we know of that will keep your PSA in check. … It's also 40 percent as effective as Viagra." The FTC's administrative complaint against POM Wonderful alleges that these claims are false and unsubstantiated:
- Clinical studies prove that POM Juice and POMx prevent, reduce the risk of, and treat heart disease, including by decreasing arterial plaque, lowering blood pressure, and improving blood flow to the heart;
- Clinical studies prove that POM Juice and POMx prevent, reduce the risk of, and treat prostate cancer, including by prolonging prostate-specific antigen doubling time;
- Clinical studies prove that POM Juice prevents, reduces the risk of, and treats, erectile dysfunction.

The FTC complaint alleges that POM Wonderful's heart disease claims are false and unsubstantiated because many of the scientific studies conducted by POM Wonderful did not show heart disease benefit from use of its products. It alleges that the prostate cancer claims are false and unsubstantiated because, among other reasons, the study POM Wonderful relied on was neither "blinded" nor controlled. Finally, it alleges that the erectile dysfunction claims are false and unsubstantiated because

the study on which the company relied did not show that POM Juice was any more effective than a placebo.

The complaint sets forth a proposed order that would prevent future law violations by POM Wonderful. In part, the proposed order would require that future claims that any pomegranate-based product cures, prevents, treats, or reduces the risk of any disease not be misleading and comply with Food and Drug Administration regulations for the claim. Although FDA approval of health claims generally is not required for compliance with the FTC Act, the proposed order would require FDA pre-approval before POM Wonderful makes future claims that certain products prevent or treat serious diseases, in order to provide clearer guidance for the company, facilitate POM Wonderful's compliance with the proposed order, and make it easier to enforce. The complaint also proposes to prohibit the respondents from making any other health claim about any food, drug, or dietary supplement without competent and reliable scientific evidence.

In a related case, Mark Dreher, POM Wonderful's former head of scientific and regulatory affairs and expert endorser, has agreed to a settlement that bars him from making any disease treatment or prevention claims in advertising for a POM Wonderful product unless the claim is not misleading and comports with FDA requirements for the claim. The settlement also prohibits Dreher from making other health claims for a food, drug, or dietary supplement for human use without competent and reliable scientific evidence to support the claim. The settlement contains a cooperation clause and reporting provisions to assist the FTC in monitoring compliance with the order.

The FTC votes to approve the two administrative complaints, the notice order against the proposed respondents, and the proposed consent agreement with Dreher were 5-0.

Copies of the POM Wonderful complaint and notice order, and of the Dreher complaint and consent agreement, are available from the FTC's website at http://www.ftc.gov and the FTC's Consumer Response Center, Room 130, 600 Pennsylvania Avenue, N.W., Washington, DC 20580. The Dreher consent agreement will be subject to public comment for 30 days, until October 27, 2010, after which the Commission will decide whether to make it final. Written comment should be sent to: FTC, Office of the Secretary, 600 Pennsylvania Ave., N.W., Washington, DC 20580. To file a public comment electronically, please click on the following hyperlink: https://ftcpublic.commentworks.com/ftc/markdreher.

NOTE: The Commission issues an administrative complaint when it has reason to believe that the law has been or is being violated, and it appears to the Commission that a proceeding is in the public interest. The complaint is not a finding or ruling that the respondents have actually violated the law. A hearing will be held before the administrative law judge in eight months. The consent agreement is for settlement purposes only and does not constitute an admission by respondents of a law violation. When the Commission issues a consent order on a final basis, it carries the force of law with respect to future actions. Each violation of such an order may result in a civil penalty of up to $16,000.

The Federal Trade Commission works for consumers to prevent fraudulent, deceptive, and unfair business practices and to provide information to help spot, stop, and avoid them. To file a complaint in English or Spanish, visit the FTC's online Complaint Assistant or call 1-877-FTC-HELP (1-877-382-4357). The FTC enters complaints into Consumer Sentinel, a secure, online database available to more than 1,800 civil and criminal law enforcement agencies in the U.S. and abroad. The FTC's website provides free information on a variety of consumer topics.

MEDIA CONTACT:

Betsy Lordan
Office of Public Affairs
202-326-3707

STAFF CONTACT:

Mary Johnson
Bureau of Consumer Protection
202-326-3115

Heather Hippsley
Bureau of Consumer Protection
202-326-3285

(FTC File No. 0823122)
(POM NR)

E-mail this News Release

If you send this link to someone else, the FTC will not collect any personal information about you or the recipient.

Related Items:

***In the Matter of* POM Wonderful LLC and Roll International Corp., companies, and Stewart A. Resnick, Lynda Rae Resnick, and Matthew Tupper, individually and as officers of the companies**
FTC File No. 082-3122
Docket No. 9344

***In the Matter of* Mark Dreher, Ph.D.**
FTC File No. 082-3122

Business Information:

- Advertising FAQ's: A Guide for Small Business

POM Ads:

- Washington Post Advertisement
- Banner Advertisement
- Fitness magazine Advertisement

Last Modified: Friday, June 24, 2011

backgrounder

Antioxidant Supplements for Health: An Introduction

Introduction

Antioxidants are substances that may prevent potentially disease-producing cell damage that can result from natural bodily processes and from exposure to certain chemicals. There are a number of different antioxidants found in foods and available as dietary supplements. This fact sheet provides a general overview of antioxidants—with a focus on dietary supplements—and suggests sources for additional information.

Key Points

- People take antioxidant supplements in an effort to improve their health and to prevent various diseases. Examples of commonly used antioxidant supplements include vitamins C and E, selenium, and beta-carotene.
- Although observational studies suggest that eating a diet high in antioxidant-rich vegetables and fruits is associated with a lower risk for many chronic diseases, there is limited evidence to support the use of antioxidant supplements to prevent disease. Additional research, including studies supported by the National Center for Complementary and Alternative Medicine (NCCAM) and other components of the National Institutes of Health (NIH), is under way.
- Tell all of your health care providers about any complementary and alternative practices you use, including antioxidant supplements. Give them a full picture of what you do to manage your health. This will help ensure coordinated and safe care.

About Antioxidants

Oxidation—one of the body's natural chemical processes—can produce "free radicals," which are highly unstable molecules that can damage cells. For example, free radicals are produced when the body breaks down foods for use or storage. They are also

produced when the body is exposed to tobacco smoke, radiation, and environmental contaminants. Free radicals can cause damage, known as "oxidative stress," which is thought to play a role in the development of many diseases, including Alzheimer's disease, cancer, eye disease, heart disease, Parkinson's disease, and rheumatoid arthritis. In laboratory experiments, antioxidant molecules counter oxidative stress and its associated damage.

The body can produce its own antioxidants and also obtain them from food. Antioxidants are abundant in vegetables and fruits and are also found in grain cereals, teas, legumes, and nuts. Examples of antioxidants include anthocyanins, beta-carotene, catechins, coenzyme Q10, flavonoids, lipoic acid, lutein, lycopene, selenium, and vitamins C and E. Many antioxidants are also available as dietary supplements.

Although antioxidant molecules counter oxidative stress in laboratory experiments, there is some debate as to whether consuming antioxidants—in food or supplement form—actually benefits health. Antioxidant supplements are often synthetic (man-made), but some of these synthetic forms may not have the same effects on the body as antioxidants that occur naturally in foods. In addition, some beneficial properties may be lost when antioxidants are extracted from foods to manufacture supplements. There is also some concern that consuming antioxidants in excessive doses may have negative effects.

Use of Antioxidant Supplements in the United States

In the National Health and Nutrition Examination Survey (NHANES, 1999–2000), over 5,000 of the approximately 10,000 respondents (52 percent), reported taking a dietary supplement in the previous month. Of the 1,900 dietary supplements included in the survey, more than 900 (47 percent) contained an antioxidant: vitamin C, vitamin E, beta-carotene, selenium, flavonoids, or isoflavones. More than 3,000 of the respondents (37 percent) reported taking dietary supplements that contained one of the antioxidants mentioned.

A 2009 study looked at data from NHANES (1999–2000 and 2001–2002) and the U.S. Department of Agriculture Flavonoid Database to estimate the total antioxidant intake (from diet and supplements) of adults in the United States. The researchers calculated the daily intake of vitamin C, vitamin E, carotenes, selenium, and flavonoids. They found that supplements accounted for 54 percent of vitamin C; 64 percent of vitamin E (alpha-tocopherol); 14 percent of carotenes; 11 percent of selenium; and 2 percent of flavonoid intake.

Status of Research on Antioxidant Supplements

There is limited scientific evidence to support the use of antioxidant supplements to prevent disease. Observational studies (which track a group of people without changing their activities or providing special treatments) have shown that a higher intake of antioxidant-rich vegetables and fruits is associated with a reduced risk of certain chronic diseases. It is not clear, however, that the benefits are due to the antioxidants. Although observational studies, as well as laboratory research on the biochemistry of antioxidants, suggest that antioxidant supplements may have beneficial effects, clinical trials (controlled studies in people) have generally found no benefit.

Systematic reviews of the research literature have analyzed the use of antioxidant supplements for preventing cancer, cardiovascular disease, and eye disease, and reducing overall mortality in healthy people and people with various diseases. In general, these reviews have concluded that there is not enough evidence to support the use of antioxidant supplements for these purposes.

Many antioxidants are sold as dietary supplements
© Bob Stockfield

Large, long-term studies (randomized, controlled trials) funded primarily by NIH have generally found that antioxidant supplements have no beneficial effects. For example:

- The Physicians Health Study II, which included more than 14,000 healthy male physicians aged 50 or older, found that neither vitamin E nor vitamin C supplements reduced the risk of major cardiovascular events (e.g., heart attack, stroke, or death) or cancer.
- The Selenium and Vitamin E Cancer Prevention Trial (SELECT)—a study of more than 35,000 healthy men aged 50 or older—found that selenium and vitamin E taken alone or together did not prevent prostate cancer. (Two earlier reviews suggested that preliminary evidence for selenium appeared promising). A 2011 updated analysis from this trial concluded that vitamin E supplements significantly increased the incidence of prostate cancer in healthy men. At a median followup of 7 years, the researchers observed that the incidence of prostate cancer was increased by 17 percent in men who received the vitamin E supplement alone compared with those who received placebo. There was no increased incidence of prostate cancer when vitamin E and selenium were taken together.
- The Women's Health Study, which included almost 40,000 healthy women at least 45 years of age, found that overall, vitamin E did not reduce the risk of death, major cardiovascular events (e.g., heart attack, stroke, or death), or

cancer. However, it was associated with reduced deaths from cardiovascular causes and also reduced major cardiovascular events in a subgroup of women aged 65 or older.

- The Women's Antioxidant Cardiovascular Study found no beneficial effects of vitamin C, vitamin E, or beta-carotene on cardiovascular events (e.g., heart attack, stroke, or death) in more than 8,000 female health professionals, aged 40 years or older, who were at high risk for cardiovascular disease.

An important exception to this trend is a National Eye Institute study of age-related eye disease, which found that the combination of antioxidants and zinc reduced the risk of developing advanced stages of age-related macular degeneration (AMD) by 25 percent in people who had intermediate AMD or advanced AMD in only one eye. Antioxidant supplements used alone reduced the risk by about 17 percent.

Thus, despite widespread scientific interest and clear plausibility of benefit, the body of evidence for antioxidant supplements has not, to date, demonstrated substantial health benefits. Additional research, some of it aimed at understanding the "disconnect" between findings of laboratory and observational studies and results of clinical trials, is under way.

Safety

Antioxidants in foods are generally considered safe, and studies of antioxident supplements generally have not reported adverse effects. However, the research does point to some potential concerns; for example, beta-carotene supplements may increase the risk of lung cancer in smokers, and vitamin E supplements may increase the risk of bleeding in certain individuals. More research is needed to better understand the safety aspects of dietary supplementation. For more information about dietary supplements, see the NCCAM fact sheets *Using Dietary Supplements Wisely* and *Are You Considering CAM?*

If You Are Thinking About Using Antioxidant Supplements

- Do not use antioxidant supplements as a replacement for a healthful diet or conventional medical care, or as a reason to postpone seeing a doctor about a medical problem.
- Consult your health care provider before deciding to use antioxidant supplements.
- Look for published research studies on antioxidant supplements for the health condition that interests you.
- Tell all of your health care providers about any complementary and alternative

practices you use. Give them a full picture of what you do to manage your health. This will help ensure coordinated and safe care. For tips about talking with your health care providers about complementary and alternative medicine (CAM), see NCCAM's Time to Talk campaign.

NCCAM-Funded Research

Because antioxidants are widely used, and because there is laboratory and observational evidence of potential health benefits, antioxidants are the subject of extensive research across NIH, including recent NCCAM-sponsored studies that have been investigating:

- Three antioxidant regimens—***Ginkgo biloba*, alpha-lipoic acid/essential fatty acids,** and **vitamin E/selenium**—as potential treatments for multiple sclerosis
- **Lipoic acid,** an antioxidant used in the treatment of diabetic neuropathy, to improve blood vessel reactivity and decrease oxidative stress in people with high cholesterol
- The safety of the vitamin E supplement **gamma-tocopherol** in healthy people and those with asthma and allergies
- The combination of **vitamins** E and C to enhance airway antioxidant levels in people with allergic asthma and reduce the incidence of preeclampsia among pregnant women with chronic hypertension or a history of preeclampsia/eclampsia
- **Alpha-lipoic acid** and fish oil to slow the progression of Alzheimer's disease
- Whether **alpha-tocopherol** (vitamin E) supplementation affects the progression of carotid atherosclerosis (narrowing or hardening of the carotid artery) in patients with coronary artery disease
- The safety and efficacy of **vitamin E** in slowing the rate of cognitive and functional decline in older persons with Down syndrome.

NCCAM also funds research centers that are studying the effects of antioxidants on aging; amyotrophic lateral sclerosis (ALS, commonly known as Lou Gehrig's disease); cardiovascular, infectious, and pancreatic diseases; nerve function; and prostate cancer.

Other NIH Studies on Antioxidants Have Been Investigating:

- The effects of **vitamin C** on the lung development and function of babies born to women who smoke during pregnancy
- Whether an antioxidant drug (**n-acetylcysteine**) taken orally will improve glucose tolerance and insulin secretion in type 2 diabetic subjects

- The safety and effectiveness of **coenzyme Q10** (combined with **vitamin E**) to slow the progression of Parkinson's disease
- The side effects and best dose of **high-selenium *Brassica juncea*** (mustard plant) and capecitabine (a cancer drug) given together with irinotecan (a cancer drug) as a treatment for patients with advanced cancer
- Whether antioxidants (**beta-carotene, vitamin C,** and **vitamin E**) combined with magnesium can prevent noise-induced hearing loss.

Selected References

- Agency for Healthcare Research and Quality. *Effect of the Supplemental Use of Antioxidants Vitamin C, Vitamin E, and Coenzyme Q10 for the Prevention and Treatment of Cancer*. Evidence Report/Technology Assessment no. 75. Rockville, MD: Agency for Healthcare Research and Quality; 2003. AHRQ publication no. 04-E002.
- Agency for Healthcare Research and Quality. *Effect of the Supplemental Use of Antioxidants Vitamin C, Vitamin E, and Coenzyme Q10 for the Prevention and Treatment of Cardiovascular Disease*. Evidence Report/Technology Assessment no. 83. Rockville, MD: Agency for Healthcare Research and Quality; 2003. AHRQ publication no. 03-E043.
- Antioxidants. Natural Standard Database Web site. Accessed on March 22, 2010.
- Antioxidants and cancer prevention: fact sheet. National Cancer Institute Web site. Accessed at www.cancer.gov/cancertopics/factsheet/prevention/antioxidants/ on March 22, 2010.
- Bjelakovic G, Nikolova D, Gluud LL, et al. Antioxidant supplements for prevention of mortality in healthy participants and patients with various diseases. *Cochrane Database of Systematic Reviews*. 2008;(2):CD007176.
- Cook NR, Albert CM, Gaziano JM, et al. A randomized factorial trial of vitamins C and E and beta carotene in the secondary prevention of cardiovascular events in women: results from the Women's Antioxidant Cardiovascular Study. *Archives of Internal Medicine*. 2007;167(15):1610–1618.
- Evans JR, Henshaw K. Antioxidant vitamin and mineral supplements for preventing age-related macular degeneration. *Cochrane Database of Systematic Reviews*. 2008;(1):CD000253.
- Gaziano JM, Glynn RJ, Christen WG, et al. Vitamins E and C in the prevention of prostate and total cancer in men: the Physicians' Health Study II randomized controlled trial. *Journal of the American Medical Association*. 2009;301(1):52–62.

- Klein EA, Thompson IM Jr, Tangen CM, et al. Vitamin E and the risk of prostate cancer: the Selenium and Vitamin E Cancer Prevention Trial (SELECT). *Journal of the American Medical Association*. 2011;306(14):1549–1556.
- Lee IM, Cook NR, Gaziano JM, et al. Vitamin E in the primary prevention of cardiovascular disease and cancer: the Women's Health Study: a randomized controlled trial. *Journal of the American Medical Association*. 2005;294(1):56–65.
- Lippman SM, Klein EA, Goodman PJ, et al. Effect of selenium and vitamin E on risk of prostate cancer and other cancers. *Journal of the American Medical Association*. 2009;301(1):39–51.
- Sesso HD, Buring JE, Christen WG, et al. Vitamins E and C in the prevention of cardiovascular disease in men: the Physicians' Health Study II randomized controlled trial. *Journal of the American Medical Association*. 2008;300(18):2123–2133.
- Steinhubl SR. Why have antioxidants failed in clinical trials? *American Journal of Cardiology*. 2008;101[suppl]:14D–19D.
- U.S. Preventive Services Task Force. Routine vitamin supplementation to prevent cancer and cardiovascular disease: recommendations and rationale. *Annals of Internal Medicine*. 2003;139(1):51–55.

For More Information

NCCAM Clearinghouse

The NCCAM Clearinghouse provides information on CAM and NCCAM, including publications and searches of Federal databases of scientific and medical literature. The Clearinghouse does not provide medical advice, treatment recommendations, or referrals to practitioners.

Toll-free in the U.S.: 1-888-644-6226
TTY (for deaf and hard-of-hearing callers): 1-866-464-3615
Web site: nccam.nih.gov
E-mail: info@nccam.nih.gov

PubMed®

A service of the National Library of Medicine (NLM), PubMed® contains publication information and (in most cases) brief summaries of articles from scientific and medical journals.

Web site: www.ncbi.nlm.nih.gov/sites/entrez

ClinicalTrials.gov

ClinicalTrials.gov is a database of information on federally and privately supported clinical trials (research studies in people) for a wide range of diseases and conditions. It is sponsored by the National Institutes of Health and the U.S. Food and Drug Administration.

Web site: www.clinicaltrials.gov

Research Portfolio Online Reporting Tools Expenditures & Results (RePORTER)

RePORTER is a database of information on federally funded scientific and medical research projects being conducted at research institutions.

Web site: projectreporter.nih.gov

NIH National Library of Medicine's MedlinePlus

To provide resources that help answer health questions, MedlinePlus brings together authoritative information from the National Institutes of Health as well as other Government agencies and health-related organizations.

Web site: www.medlineplus.gov

Acknowledgements

NCCAM thanks the following people for their technical expertise and review of this publication: Balz Frei, Ph.D., The Linus Pauling Institute, Oregon State University; Christopher Gardner, Ph.D., Stanford University School of Medicine; Carol Ponzter, Ph.D., and John (Jack) Killen, Jr., M.D., NCCAM.

NCCAM Publication No. D450
Created May 2010
Updated October 2011

* Note: PDF files require a viewer such as the free Adobe Reader.

NCCAM, National Institutes of Health, 9000 Rockville Pike, Bethesda, Maryland 20892 USA, E-mail: info@nccam.nih.gov

NIH...Turning Discovery Into Health

- 
- 
- 

This site complies with the HONcode standard for trustworthy health information:
verify here. (Health on the Net Foundation)

ClinicalTrials.gov
A service of the U.S. National Institutes of Health

Found 549 studies with search of: Open Studies | antioxidants

Include studies that are not seeking new volunteers.
Hide studies with unknown recruitment status.

Display Options

Rank	Status	Study
1	Recruiting	Antioxidant Supplements in the Reversal of Schistosomal Peri-portal Fibrosis Conditions: Schistosomiasis; Liver Fibrosis; Periportal Fibrosis; Oxidative Stress Interventions: Dietary Supplement: Praziquantel+antioxidant suppl; Other: Praziquantel + placebo 2mths then antioxidant for 10 mths; Dietary Supplement: Praziquantel therapy and placebo as supplement; Dietary Supplement: Praziquantel+antioxidant
2	Recruiting	Trial of Glutamine and Antioxidant Supplementation in Critically Ill Patients Conditions: Critical Illness; Sepsis; Multiple Organ Failure Interventions: Other: Glutamine; Other: Antioxidants; Other: Glutamine + Antioxidants; Other: Placebo
3	Recruiting	Micronutrients and Antioxidants in HIV Infection Condition: HIV Infection Interventions: Dietary Supplement: Micronutrients and antioxidants; Dietary Supplement: Multivitamins and minerals
4	Unknown †	Antioxidant Supplementation in Patients With Kashin-Beck Disease Condition: Kashin-Beck Disease Intervention: Dietary Supplement: Biological Antioxidant Supplementation
5	Recruiting	Antioxidant Therapy to Reduce Inflammation in Sickle Cell Disease Condition: Anemia, Sickle Cell Intervention: Drug: alpha-lipoic acid and acetyl-L-carnitine
6	Unknown †	Study of Antioxidants on MRI Detectable Early Stage Prostate Cancer Among Men on Active Surveillance Conditions: Cancer of the Prostate; Prostate Cancer; Prostatic Neoplasms Interventions: Dietary Supplement: Lycopene, Vitamin D3, Selenium, Green Tea Extract, Vitamin E; Drug: Placebo
7	Recruiting	Inflammatory Mediators in Obstructive Sleep Apnoea Syndrome: Mechanisms of Production and the Effect of Long Term Antioxidants Administration Condition: Obstructive Sleep Apnea Syndrome Interventions: Device: n-CPAP; Device: Oxygen supplementation; Drug: Vitamin A, Vitamin C, Vitamin E, Allopurinol, N-Acetylcysteine
8	Recruiting	Dietary Antioxidants, Redox Tone and Health Promotion: an Orthomolecular Study of Interactions Condition: Type 2 Diabetes Mellitus Intervention: Dietary Supplement: Green tea
9	Recruiting	A 4-month Intervention of Antioxidant Supplementation in Overweight Children Condition: Metabolic Syndrome Intervention: Dietary Supplement: Vitamin C Vitamin E Selenital all from Burgerstein Vitamine
10	Unknown †	Effects of Polyphenol Containing Antioxidants on Oxidative Stress in Diabetic Patients Condition: Type 2 Diabetes Intervention: Dietary Supplement: PomGT (500 mg pomegranate extracts, 300 mg green tea

and 60mg vitamin C)

11 **Recruiting** [Study of Antioxidants on Prostate Tumors in Men Undergoing Radical Prostatectomy for Prostate Cancer]
Conditions: Cancer of the Prostate; Prostate Cancer; Prostatic Neoplasms
Interventions: Dietary Supplement: Lycopene, Vitamin D3, Selenium, Green Tea Extract, Vitamin E; Drug: Placebo

12 **Unknown †** [The DIEP Flap as a Model of Ischemia-Reperfusion: an Intervention Study]
Condition: Ischemia-Reperfusion
Interventions: Drug: Antioxidant; Other: Placebo; Drug: Anti-inflammatory drug

13 **Recruiting** [Physiological Effects of Grape Seed Extract in Diastolic Heart Failure]
Conditions: Diastolic Heart Failure; Hypertensive Heart Disease; Heart Failure With Preserved Ejection Fraction; Hypertension; Oxidative Stress
Intervention: Drug: grape seed extract (MegaNatural BP, Polyphenolics, Inc.)

14 **Recruiting** [Respiratory and Autonomic Plasticity Following Intermittent Hypoxia]
Condition: Sleep Apnea Syndromes
Intervention: Dietary Supplement: Antioxidant cocktail

15 **Recruiting** [Nitric Oxide Bioavailability in Chronic Obstructive Pulmonary Disease (COPD)]
Condition: Pulmonary Disease, Chronic Obstructive
Interventions: Drug: Tetrahydrobiopterin (BH4); Drug: non-acetylated salicylate; Dietary Supplement: High Fat Meal; Drug: L-NMMA; Dietary Supplement: Antioxidant Cocktail

16 **Not yet recruiting** [Docosahexaenoic Acid (DHA) Nutritional Supplementation to Prevent Age-related Macular Degeneration (AMD)]
Condition: Age-related Macular Degeneration
Intervention: Dietary Supplement: Ocean Nutrition MEG3 4020EE product

17 **Unknown †** [Glutamine and Intestinal Protein Metabolism]
Condition: Healthy Volunteers
Interventions: Drug: Glutamine; Drug: Glucose; Drug: glutamine-antioxidants containing solution

18 **Unknown †** [Dose Response Bioavailability of Coffee and Green Tea Antioxidants In Humans]
Condition: Healthy
Interventions: Other: Green tea; Other: Coffee

19 **Recruiting** [Effect of Antioxidants on Oxygen Induced Vasoconstriction in Lipopolysaccharide (LPS) Induced Inflammatory Model in Humans]
Condition: Healthy
Interventions: Drug: Vitamin and mineral supplement; Drug: Placebo; Drug: 100% Oxygen; Drug: Escherichia coli Endotoxin

20 **Recruiting** [A Clinical Trial for AMN: Validation of Biomarkers of Oxidative Stress, Efficacy and Safety of a Mixture of Antioxidants]
Condition: Adrenomyeloneuropathy
Interventions: Drug: N-acetylcysteine; Drug: lipoic acid; Drug: vitamin E

Previous Page **Studies Shown (1-20)** Next Page (21-40)

† Indicates status has not been verified in more than two years

Save this search by bookmarking this page.
When you use your bookmark, the search will be performed again on the most recent collection of studies.

RSS Feeds for studies found by your search that were:

First received in the last 14 days, Last updated (includes received) in the last 30 days

Download Options

Antioxidants and Cancer Prevention: Fact Sheet

Key Points

Antioxidants protect cells from damage caused by unstable molecules known as free radicals (see Questions 1 and 3).

Laboratory and animal research have shown that antioxidants help prevent the free radical damage tha is associated with cancer. However, results from recent studies in people (clinical trials) are not consistent (see Question 2).

Antioxidants are provided by a healthy diet that includes a variety of fruits and vegetables (see Question 4).

1. What are antioxidants?

Antioxidants are substances that may protect cells from the damage caused by unstable molecules known as free radicals. Free radical damage may lead to cancer. Antioxidants interact with and stabili free radicals and may prevent some of the damage free radicals might otherwise cause. Examples of antioxidants include beta-carotene, lycopene, vitamins C, E, and A, and other substances.

2. Can antioxidants prevent cancer?

Considerable laboratory evidence from chemical, cell culture, and animal studies indicates that antioxidants may slow or possibly prevent the development of cancer. However, information from recen clinical trials is less clear. In recent years, large-scale, randomized clinical trials reached inconsistent conclusions.

3. What was shown in previously published large-scale clinical trials?

Five large-scale clinical trials published in the 1990s reached differing conclusions about the effect of antioxidants on cancer. The studies examined the effect of beta-carotene and other antioxidants on cancer in different patient groups. However, beta-carotene appeared to have different effects depending upon the patient population. The conclusions of each study are summarized below.

The first large randomized trial on antioxidants and cancer risk was the Chinese Cancer Preventi Study, published in 1993. This trial investigated the effect of a combination of beta-carotene, vitar E, and selenium on cancer in healthy Chinese men and women at high risk for gastric cancer. Th study showed a combination of beta-carotene, vitamin E, and selenium significantly reduced incidence of both gastric cancer and cancer overall (1).

A 1994 cancer prevention study entitled the Alpha-Tocopherol (Vitamin E)/ Beta-Carotene Cancer Prevention Study (ATBC) demonstrated that lung cancer rates of Finnish male smokers increase significantly with beta-carotene and were not affected by vitamin E (2).

Another 1994 study, the Beta-Carotene and Retinol (Vitamin A) Efficacy Trial (CARET), also demonstrated a possible increase in lung cancer associated with antioxidants (3).

The 1996 Physicians' Health Study I (PHS) found no change in cancer rates associated with beta carotene and aspirin taken by U.S. male physicians (4).

The 1999 Women's Health Study (WHS) tested effects of vitamin E and beta-carotene in the prevention of cancer and cardiovascular disease among women age 45 years or older. Among apparently healthy women, there was no benefit or harm from beta-carotene supplementation. Investigation of the effect of vitamin E is ongoing (5).

4. Are antioxidants under investigation in current large-scale clinical trials?

Three large-scale clinical trials continue to investigate the effect of antioxidants on cancer. The objecti of each of these studies is described below. More information about clinical trials can be obtained usin http://www.cancer.gov/clinicaltrials, http://www.clinicaltrials.gov, or the RePORT Expenditures and

Results (RePORTER) query tool at http://projectreporter.nih.gov/reporter.cfm on the Internet.

The Women's Health Study (WHS) is currently evaluating the effect of vitamin E in the primary prevention of cancer among U.S. female health professionals age 45 and older. The WHS is expected to conclude in August 2004.

The Selenium and Vitamin E Cancer Prevention Trial (SELECT) is taking place in the United States, Puerto Rico, and Canada. SELECT is trying to find out if taking selenium and/or vitamin E supplements can prevent prostate cancer in men age 50 or older. The SELECT trial is expected t stop recruiting patients in May 2006.

The Physicians' Health Study II (PHS II) is a follow up to the earlier clinical trial by the same nam The study is investigating the effects of vitamin E, C, and multivitamins on prostate cancer and tc cancer incidence. The PHS II is expected to conclude in August 2007.

5. **Will the National Cancer Institute (NCI) continue to investigate the effect of beta-carotene on cancer?**

Given the unexpected results of ATBC and CARET, and the finding of no effect of beta-carotene in the PHS and WHS, NCI will follow the people who participated in these studies and will examine the long-term health effects of beta-carotene supplements. Post-trial follow-up has already been funded by NCI CARET, ATBC, the Chinese Cancer Prevention Study, and the two smaller trials of skin cancer and cc polyps. Post-trial follow-up results have been published for ATBC, and as of July 2004 are in press for CARET and are in progress for the Chinese Cancer Prevention Study.

6. **How might antioxidants prevent cancer?**

Antioxidants neutralize free radicals as the natural by-product of normal cell processes. Free radicals a molecules with incomplete electron shells which make them more chemically reactive than those with complete electron shells. Exposure to various environmental factors, including tobacco smoke and radiation, can also lead to free radical formation. In humans, the most common form of free radicals is oxygen. When an oxygen molecule (O_2) becomes electrically charged or "radicalized" it tries to steal electrons from other molecules, causing damage to the DNA and other molecules. Over time, such damage may become irreversible and lead to disease including cancer. Antioxidants are often describe as "mopping up" free radicals, meaning they neutralize the electrical charge and prevent the free radica from taking electrons from other molecules.

7. **Which foods are rich in antioxidants?**

Antioxidants are abundant in fruits and vegetables, as well as in other foods including nuts, grains, anc some meats, poultry, and fish. The list below describes food sources of common antioxidants.

Beta-carotene is found in many foods that are orange in color, including sweet potatoes, carrots, cantaloupe, squash, apricots, pumpkin, and mangos. Some green, leafy vegetables, including collard greens, spinach, and kale, are also rich in beta-carotene.

Lutein, best known for its association with healthy eyes, is abundant in green, leafy vegetables such as collard greens, spinach, and kale.

Lycopene is a potent antioxidant found in tomatoes, watermelon, guava, papaya, apricots, pink grapefruit, blood oranges, and other foods. Estimates suggest 85 percent of American dietary intake of lycopene comes from tomatoes and tomato products.

Selenium is a mineral, not an antioxidant nutrient. However, it is a component of antioxidant enzymes. Plant foods like rice and wheat are the major dietary sources of selenium in most countries. The amount of selenium in soil, which varies by region, determines the amount of selenium in the foods grown in that soil. Animals that eat grains or plants grown in selenium-rich soil have higher levels of selenium in their muscle. In the United States, meats and bread are common sources of dietary selenium. Brazil nuts also contain large quantities of selenium.

Vitamin A is found in three main forms: retinol (Vitamin A1), 3,4-didehydroretinol (Vitamin A2), ar 3-hydroxy-retinol (Vitamin A3). Foods rich in vitamin A include liver, sweet potatoes, carrots, milk egg yolks, and mozzarella cheese.

Vitamin C is also called ascorbic acid, and can be found in high abundance in many fruits and vegetables and is also found in cereals, beef, poultry, and fish.

Vitamin E, also known as alpha-tocopherol, is found in almonds, in many oils including wheat germ, safflower, corn, and soybean oils, and is also found in mangos, nuts, broccoli, and other foods.

Selected References

1. Blot WJ, Li JY, Taylor PR, et al. Nutrition intervention trials in Linxian, China: supplementation with specific vitamin/mineral combinations, cancer incidence, and disease-specific mortality in the general population. J Natl Cancer Inst 1993;85:1483–91.

2. The Alpha-Tocopherol, Beta Carotene Cancer Prevention Study Group. The effects of vitamin E and be carotene on the incidence of lung cancer and other cancers in male smokers. N Engl J Med 1994;330:1029–35.

3. Omenn GS, Goodman G, Thornquist M, et al. The beta-carotene and retinol efficacy trial (CARET) for chemoprevention of lung cancer in high risk populations: smokers and asbestos-exposed workers. Ca Res 1994;54(7 Suppl):2038s–43s.

4. Hennekens CH, Buring JE, Manson JE, Stampfer M, Rosner B, Cook NR, et al. Lack of effect of long-term supplementation with beta carotene on the incidence of malignant neoplasms and cardiovascular disease. N Engl J Med 1996;334:1145–9.

5. Lee IM, Cook NR, Manson JE. Beta-carotene supplementation and incidence of cancer and cardiovascular disease: Women's Health Study. J Natl Cancer Inst 1999;91:2102–6.

###

Related NCI materials and Web pages:

Cancer Causes and Risk Factors Home Page
(http://www.cancer.gov/cancertopics/prevention-genetics-causes/causes)

Cancer Prevention Home Page
(http://www.cancer.gov/cancertopics/prevention-genetics-causes/prevention)

How can we help?

We offer comprehensive research-based information for patients and their families, health professionals, canc researchers, advocates, and the public.

Call NCI's Cancer Information Service at 1–800–4–CANCER (1–800–422–6237)

Visit us at http://www.cancer.gov or http://www.cancer.gov/espanol

Chat using LiveHelp, NCI's instant messaging service, at http://www.cancer.gov/livehelp

E-mail us at cancergovstaff@mail.nih.gov

Order publications at http://www.cancer.gov/publications or by calling 1–800–4–CANCER

Get help with quitting smoking at 1–877–44U–QUIT (1–877–448–7848)

Research

Research Project: DIETARY FACTORS EARLY IN HUMAN DEVELOPMENT: HEALTH CONSEQUENCES OF PHYTOCHEMICAL INTAKE

Location: Arkansas Children Nutrition Center

Title: Fate of Anthocyanins and Antioxidant Capacity in Contents of the Gastrointestinal Tract of Weanling Pigs Following Black Raspberry Consumption

Authors

- Wu, Xianli - ACNC/UAMS
- Pittman, Hoy - ACNC
- Prior, Ronald

Submitted to: Journal of Agricultural and Food Chemistry
Publication Type: Peer Reviewed Journal
Publication Acceptance Date: November 16, 2005
Publication Date: January 15, 2006
Citation: Wu, X., Pittman, H.E., Prior, R.L. 2006. Fate of anthocyanins and antioxidant capacity in contents of the gastrointestinal tract of weanling pigs following black raspberry consumption. Journal of Agricultural and Food Chemistry. 54(1):583-589.

Interpretive Summary: Many fruits/berries are rich in anthocyanins, which are the pigments that give the dark blue/red colors to berries. Anthocyanins have high antioxidant capacity, but due to their apparent low absorption, their possible roles in health promotion in vivo are still in question. The objectives of these studies were to determine the fate of anthocyanins within the gastrointestinal tract and the effect on the absorption and subsequent metabolism of anthocyanins. Weanling pigs were used as an animal model in this study since the pig seems to handle these components similarly to the human. Recovery of anthocyanins within the gastrointestinal tract was positively and linearly associated with urinary anthocyanin recovery. The environment of different segments of the gastrointestinal tract clearly determines the stability of individual anthocyanins. Anthocyanins with complex chemical structures were observed to be more stable in the gastrointestinal tract than simple anthocyanins.

Anthocyanins were shown to provide significant antioxidant protection in the environment of the gastrointestinal tract. This effect may have significant implications in the protection against the development of colon cancer.

Technical Abstract: Many fruits are rich in anthocyanins

Technical Abstract: Many fruits are rich in anthocyanins (ACNs). ACNs have high antioxidant capacity, but due to their apparent low bioavailability, their possible roles in health promotion in vivo are still in question. The objectives of these studies were to determine the fate of ACNs within the gastrointestinal GI tract and the effect on the bioavailability and subsequent metabolism of ACNs. Five weanling pigs (16.3 +/- 5.9 kg) were fed freeze-dried black raspberry powder by oral administration which provided 1146.1 +/- 44.6 umol TE total ORACFL per kg and 50.5 +/- 3.7 mg per kg total ACNs. After 4 h, the pigs were sacrificed and the contents of five GI segments [duodenum, jejunum, ileum, cecum and colon] were collected and analyzed for their total antioxidant capacity (TAC, measured as ORACFL) and ACNs. The recoveries of TAC and total ACNs were 46.5 +/- 3.5% and 41.7 +/- 4.9%, respectively. Both total ACNs and TAC were recovered primarily in the ileum, cecum, and colon at 4 h after a meal. Cyanidin aglycone with different sugar moieties showed significant differences in their recovery within the GI tract with sambubiose > -sambubiose-rhamnose = rutinose >> glucose. Recovery of ACNs within the GI tract was positively and linearly associated with urinary ACN recovery. The environment of different segments of the GI tract clearly determines the stability of individual ACNs. Complex ACNs containing di- or tri-glycosides were observed to be more stable in the GI tract than simple ACNs as a monoglucoside. TAC and total ACNs remained high after 4 h after feeding, which indicates that ACNs provide significant antioxidant protection in the environment of the gut epithelium.

Last Modified: 01/10/2012

U.S. Food and Drug Administration
Protecting and Promoting Your Health
U.S. Food & Drug Administration

Food

Guidance for Industry: Food Labeling; Nutrient Content Claims; Definition for "High Potency" and Definition for "Antioxidant" for Use in Nutrient Content Claims for Dietary Supplements and Conventional Foods; Small Entity Compliance Guide

Contains Nonbinding Recommendations

July 18, 2008

You may submit written or electronic comments regarding this guidance at any time. Submit written comments on the guidance to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. Submit electronic comments to http://www.regulations.gov[1].

Additional copies are available from:
Office of Nutrition, Labeling, and Dietary Supplements
Division of Dietary Supplement Programs HFS-810
Center for Food Safety and Applied Nutrition
Food and Drug Administration
5100 Paint Branch Parkway
College Park, MD 20740
(Tel) 301-436-2375 (Updated phone: 240-402-2375)
http://www.cfsan.fda.gov/guidance.html

U.S. Department of Health and Human Service
Food and Drug Administratio
Center for Food Safety and Applied Nutritio
July 200

Contains Nonbinding Recommendations

Table of Contents

Guidance for Industry [1]
Food Labeling; Nutrient Content Claims: Definition for "High Potency" and Definition of "Antioxidant" for Use in Nutrient Content Claims for Dietary Supplements and Conventional Foods
Small Entity Compliance Guide

This guidance represents the Food and Drug Administration's (FDA's) current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. You can use an alternative approach if the approach satisfies the requirements of the applicable statutes and regulations. If you want to discuss an alternative approach, contact the FDA staff

responsible for implementing this guidance. If you cannot identify the appropriate FDA staff, call the appropriate telephone number listed on the title page of this guidance.

I. Introduction

On September 23, 1997, FDA published in the Federal Register a final rule amended regulations concerning certain nutrient content claims. The amended regulations defined the term "High potency" as a nutrient content claim; defined nutrient content claims using the term "antioxidant" (e.g., "good source of antioxidants," "high in antioxidants," "more antioxidants"); and corrected an omission pertaining to the use of "sugar free" claims on dietary supplements (62 FR 49868). FDA took these actions to provide for the use of additional nutrient content claims on labels or in labeling in accordance with provisions of the Nutrition Labelin and Education Act of 1990. The final rule is effective on March 23, 1999. FDA has prepared this Small Entity Compliance Guide in accordance with section 212 of the Small Business Regulatory Enforcement Fairness Act (Public Law 104-121). This guidance document restates in plain language the legal requirements set forth in 21 CFR 101.54(f) and (g) and 21 CFR 101.60(c)(1)(iii)(A) concerning dietary supplement use of certain nutrient content claims. This regulation is binding and has the full force and effect of law.

FDA's guidance documents, including this guidance, do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* i Agency guidances means that something is suggested or recommended, but not required.

II. Questions and Answers

1. **High Potency Claims**
    1. What is the definition of "high potency?"

       The regulation states that the term "high potency" may be used in a claim on the label or in labelin to describe individual vitamins or minerals that are present at 100 percent or more of the Reference Daily Intakes (RDI) per reference amount customarily consumed (21 CFR 101.54(f)(1)(i)). This mean a supplement may be labeled as "high potency" for each nutrient(s) that is present at 100% of the RDI per serving.
    2. How should the label or labeling describe the nutrients that are the subject of the high potency claim?
       When the term "high potency" is used to describe individual vitamins or minerals in a product that contains other nutrients, then the label or labeling must clearly identify which specific vitamins or minerals are being described as "high potency." For example, "Botanical X with high potency vitami E." (21 CFR 101.54(f)(1)(ii))
    3. Can I name an entire product "high potency" when not all ingredients are present at 100% or greater?

       The term "high potency" may be used on the label or in labeling of a multi-ingredient product to describe the product (as opposed to describing the level of individual ingredients) if the product contains 100 percent or more of the RDI for at least two-thirds of the vitamins and minerals that ar listed in 21 CFR 101.9(c)(8)(iv) and that are present in the product at 2 percent or more of the RDI. For example, "High potency multivitamin, multimineral dietary supplement tablets." (21 CFR 101.54(f)(2))
    4. Do any other requirements apply to the use of the term "High potency" in foods?

       Yes. If the nutrient that is the subject of a high potency claims is added to a food that is not a dietary supplement, then that fortification must be in accordance with the policy on food fortificatior in 21 CFR 104.20 (21 CFR 101.54(f)(3)).
2. **Antioxidant nutrient content claims**

    1. Is an antioxidant claim a nutrient content claim?

       Yes. A claim that describes the level of antioxidant nutrients present in a food is a nutrient content claim and may be used on the label or in the labeling of a food when the conditions of use in the regulation are met (21 CFR 101.54(g)).
    2. Can I make an antioxidant nutrient content claim for any ingredient in a food?
       No. An antioxidant nutrient content claim can only be made for nutrients for which there is an RDI established in 21 CFR 101.9 (21 CFR 101.54(g)(1)).
    3. Does the claim apply to all nutrients listed in 21 CFR 101.9?

No. The nutrient that is the subject of the claim must have recognized antioxidant activity. That is, there must be scientific evidence that after it is eaten and absorbed from the gastrointestinal tract, the substance participates in physiological, biochemical, or cellular processes that inactivate free radicals or prevent free radical-initiated chemical reactions (21 CFR 101.54(g)(2)).

4. How much of the nutrient must be present in each serving in order to use the antioxidant nutrient content claim?

   The antioxidant nutrient must meet the requirements for nutrient content claims in 21 CFR 101.54(b), (c), or (e) for "High" claims, "Good source" claims, and "More" claims, respectively. For example, to use a "high" claim, the food would have to contain 20% or more of the Daily Reference Value (DRV) or RDI per serving. For a "good source" claim, the food would have to contain between 10-19% of the DRV or RDI per serving (21 CFR 101.54(g)(3)).

5. What special requirements apply to an antioxidant nutrient content claim for beta-carotene?

   Beta-carotene may be the subject of an antioxidant claim when the level of vitamin A present as beta-carotene in the food using the claim is sufficient to qualify for the claim. For example, if the claim is "good source of antioxidant beta-carotene," then at least 10% of the RDI for vitamin A must be present as beta-carotene per serving (21 CFR 101.54(g)(3)).

6. Does the label claim have to include the name of the nutrient that is an antioxidant, or can the claim simply say "antioxidants?"

   The names of the nutrients that are the antioxidants must appear in the claim. For example, "high in antioxidant vitamins C and E."

   Alternatively, when used as part of a nutrient content claim, the term "antioxidant" or "antioxidants" (such as "high in antioxidants"), may be linked by a symbol (such as an asterisk) that refers to the same symbol that appears elsewhere on the same panel of a product label followed by the name or names of the nutrients with the recognized antioxidant activity. If this is done, the list of nutrients must appear in letters of a type size height no smaller than the larger of one half of the type size of the largest nutrient content claim or 1/16 inch (21 CFR 101.54(g)(4)).

3. Sugar-free claims

   1. Can dietary supplements include claims on their label such as "sugar free," "free of sugar," "no sugar," "zero sugar," "without sugar," "sugarless," "trivial source of sugar," negligible source of sugar," or "dietarily insignificant source of sugar"?

      Yes. A dietary supplement may include claims in labeling such as "sugar free," "no sugar," or other claims described in 21 CFR 101.60(c) provided it meets all of the eligibility criteria set forth in the regulation (21 CFR 101.60(c)(1)(i)-(iii)). Among other requirements, a food must be labeled as "low calorie" or "reduced calorie" or bear a relative claim of special dietary usefulness. However, a dietary supplement that is prohibited from bearing a "low calorie" or "reduced calorie" claim by 21 CFR 101.13(b)(5) and 101.60(a)(4) can still use a sugar-free claim provided it meets the "low calorie" requirement in 21 CFR 101.60(b)(2) (21 CFR 101.60(c)(1)(iii)).

[1] This guidance has been prepared by the Division of Dietary Supplement Programs in the Center for Food Safety and Applied Nutrition at the U.S. Food and Drug Administration.

U.S. Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993
Ph. 1-888-INFO-FDA (1-888-463-6332)

Links on this page:

1. http://www.regulations.gov/

What's In Food

Antioxidants & Phytonutrients

MedlinePlus: Antioxidants
DHHS. NIH. National Library of Medicine.
Provides a gateway to the latest news and information on the topic of antioxidants. Also offers links to research and related issues. Also in **Spanish**.

USDA Nutrient Database Lists for Antioxidant Nutrients and Phytonutrients (Vitamin E, Vitamin C, Beta-carotene, Lycopene, Lutein+Zeaxanthin, Selenium)
USDA. ARS. Nutrient Data Laboratory.
Find out the antioxidant content of foods, sorted either alphabetically by food description (select **A**) or in descending order by nutrient content (select **C**) in common household measures. Note: lists are PDF files.
- **Vitamin E (alpha-tocopherol)** - **A** or **C**
- **Vitamin C** - **A** or **C**
- **Beta-carotene** - **A** or **C**
- **Lycopene** - **A** or **C**
- **Lutein+zeaxanthin** - **A** or **C**
- **Selenium** - **A** or **C**

USDA Database for the Flavonoid Content of Selected Foods - Release 3 (2011)
USDA. ARS. Nutrient Data Laboratory.
Provides a table of the flavonoid content of over 200 foods and includes values for five subclasses of flavonoids - Flavonols, Flavones, Flavanones, Flavan-3-ols, and Anthocyanidins.

USDA Database for the Isoflavone Content of Selected Foods - Release 2.0 (2008)
USDA. ARS. Nutrient Data Laboratory.
Tables list foods alphabetically with the values of the specific isoflavones (daidzein, genistein, glycitein and total isoflavones) in the edible portion of the food. Database includes infant formulas.

USDA Database for the Proanthocyanidin Content of Selected Foods - 2004
USDA. ARS. Nutrient Data Laboratory.
Contains proanthocyanidin content values for 205 food items.

Oxalic Acid Content of Selected Vegetables
USDA. ARS. Nutrient Data Laboratory.
Table of oxalic acid content of certain vegetables, originally published in Agriculture Handbook No. 8-11, Vegetables and Vegetable Products, 1984.

USDA ARS Phytochemical Database
USDA. ARS. Beltsville Agricultural Research Center.
Contains chemical structure, formula, molecular weight, synonyms, biological activities, and references on a large number of phytochemicals.

Dr. Duke's Phytochemical and Ethnobotanical Databases

To view PDF files you must have Adobe Acrobat Reader installed on your computer.

To view Flash files you must have Macromedia Flash Player installed on your computer.

USDA. Agricultural Research Service.
Allows plant, chemical, activity and ethnobotany database searches. Also includes an ethnobotanical dictionary, and links to nutritional databases, plants and cancer treatments and other plant related databases.

Antioxidants and Cancer Prevention: Fact Sheet
DHHS. NIH. National Cancer Institute.
Find out more about antioxidants and their role in cancer prevention, including research study summaries.

Last Modified: Oct 20, 2011

Consumer Corner

Antioxidants, Phytochemicals and Functional Foods

Functional Foods Fact Sheet: Antioxidants
International Food Information Council Foundation.
Find out what antioxidants are and why there is so much interest in them.

What is the Role of Antioxidants in Health?
Columbia University. Go Ask Alice!
What is an antioxidant? Learn about the role of these compounds and how to add more of them to your diet.

Functional Foods?
American Council on Science and Health.
Learn what the term functional foods means and how you can evaluate manufacture's claims for their products.

Phytochemicals
Dole Food Company.
Learn about phytochemicals, where you get them, and why they are important to your health. Includes interactive charts to find phytochemicals in fruits and vegetables.

Functional Foods: Their Role in Disease Prevention and Health Promotion
Institute of Food technologists; Nutriwatch.
Wondering about functional foods and where they are found? Read a review article and find research references.

Water-Soluble Vitamins (PDF|495 KB)
Colorado State University Extension.
Information on B-complex vitamins and vitamin C including common food sources, major functions, and deficiency symptoms.

Lycopene: an Antioxidant for Good Health
American Dietetic Association.
Find out more about this antioxidant that gives vegetables and fruits, such as tomatoes, pink grapefruit and watermelon, their red color.

Last Modified: Jan 5, 2012

I Want To...

- See Professional & Other Resources on Phytonutrients

Consumer Corner

- All About Food
  - Antioxidants, Phytochemicals and Functional Foods
  - Cooking
  - Food Biotechnology
  - Food Facts and History
  - Food Labels
  - Food Safety
  - Food Storage and Preservation
  - Green Nutrition
  - Nutrient Composition of Foods
  - Shopping and Meal Planning Tips
- Eating for Health
- Ages & Stages
- DIY - Do It Yourself
- Can't Find What You Want?

Media Help

To view PDF files you must have Adobe Acrobat Reader installed on your computer.

To view Flash files you must have Macromedia Flash Player installed on your computer.

U.S. News Best Hospitals: Cancer

Top-Ranked Hospitals for Cancer

Best Hospitals Rankings Methodology

Nearly 900 hospitals are listed in Cancer. All are experienced in treating difficult cases—a hospital is listed only if at least 254 inpatients in need of high level of expertise in this specialty were treated there in 2007, 2008, and 2009. The top 50 hospitals are ranked, based on score. The rest are listed alphabetically.

Search for Cancer hospitals

See all specialty rankings

TOP DOCTORS: CANCER

Gynecologic Oncologists

Hematologists

Medical Oncologists

Oncologists

Pediatric Hematologist-Oncologists

Radiation Oncologists

RANKINGS DATA

#1

University of Texas M.D. Anderson Cancer Center

Houston, TX

Hospital type: Cancer
Number of beds: 507
Parent system: University of Texas System

Ranked **#1** in Cancer

Ranked **#6** in Ear, Nose & Throat

Ranked **#6** in Gynecology

See more rankings

Reputation with specialists: **Very strong**

Nurse staffing — Highest

Survival — Much better than expected

#2

Memorial Sloan-Kettering Cancer Center

New York, NY

Hospital type: Cancer
Number of beds: 434

Ranked **#2** in Cancer

Ranked **#5** in Urology

Ranked **#7** in Pediatrics: Cancer

See more rankings

Reputation with specialists: **Very strong**

Nurse staffing — High

Survival — Much better than expected

#3

Johns Hopkins Hospital

Baltimore, MD

Hospital type: General medical and surgical
Number of beds: 918
Parent system: Johns Hopkins Health System

Ranked **#1** in Ear, Nose & Throat

Ranked **#1** in Neurology & Neurosurgery

Reputation with specialists: **Strong**

Nurse staffing — Highest

PRESS ROOM - SPONSORED NEWS

Mount Sinai Medical Center
Grape Seed Polyphenols — a natural antioxidant — May Prevent Alzheimer's

Children's Hospital of Philadelphia
CHOP's Genome Center Contributes to Large Gene Study of Adult Dimentia

Menninger Clinic
The Menninger Newsroom offers our contact information, news releases, selected news coverage, and links to the Menninger officers, facts and history.

PROMOTE YOUR HOSPITAL

Display your ranked hospital's **Best Hospitals badge** on your website.

Tell consumers what makes your hospital unique through our

Ranked **#1** in Psychiatry

See more rankings

Survival — Much better

#4

Mayo Clinic
Rochester, MN

Hospital type: General medical and surgical
Number of beds: 1302
Parent system: Mayo Clinic

Reputation with specialists — **Strong**

Ranked **#1** in Diabetes & Endocrinology

Ranked **#1** in Gastroenterology

Ranked **#1** in Gynecology

See more rankings

Nurse staffing — Highest

Survival — Much better than expected

FEATURED CANCER HOSPITALS

The Tisch Cancer Institute at Mount Sinai
Patient-centered cancer care, backed by outstanding physicians, exceptional researchers, and cutting-edge treatments.

#5

Dana-Farber/Brigham and Women's Cancer Center
Boston, MA

Hospital type: General medical and surgical
Number of beds: 773
Parent system: Partners HealthCare System, Inc.

Reputation with specialists — **Strong**

Ranked **#3** in Gynecology

Ranked **#5** in Cancer

Ranked **#5** in Rheumatology

See more rankings

Nurse staffing — Highest

Survival — Much better than expected

#6

University of Washington Medical Center
Seattle, WA

Hospital type: General medical and surgical
Number of beds: 396
Parent system: UW Medicine Health System

Reputation with specialists — **Strong**

Ranked **#3** in Rehabilitation

Ranked **#6** in Cancer

Ranked **#10** in Diabetes & Endocrinology

See more rankings

Nurse staffing — Highest

Survival — Much better than expected

#7

Massachusetts General Hospital
Boston, MA

Hospital type: General medical and surgical
Number of beds: 907
Parent system: Partners HealthCare System, Inc.

Reputation with specialists — **Strong**

Ranked **#1** in Psychiatry

Ranked **#2** in Diabetes & Endocrinology

Ranked **#2** in Ear, Nose & Throat

See more rankings

Nurse staffing — Highest

Survival — Much better than expected

#8

UCSF Medical Center

San Francisco, CA

Hospital type: General medical and surgical
Number of beds: 660
Parent system: University of California-Systemwide Administration

Ranked **#4** in Diabetes & Endocrinology

Ranked **#5** in Neurology & Neurosurgery

Ranked **#6** in Urology

See more rankings

Reputation with specialists: **Strong**

Nurse staffing: Highest

Survival: Much better than expected

#9

Cleveland Clinic

Cleveland, OH

Hospital type: General medical and surgical
Number of beds: 1214
Parent system: Cleveland Clinic Health System

Ranked **#1** in Cardiology & Heart Surgery

Ranked **#2** in Gastroenterology

Ranked **#2** in Nephrology

See more rankings

Reputation with specialists: **Significant**

Nurse staffing: Highest

Survival: Much better than expected

#10

Ronald Reagan UCLA Medical Center

Los Angeles, CA

Hospital type: General medical and surgical
Number of beds: 456
Parent system: University of California-Systemwide Administration

Ranked **#2** in Geriatrics

Ranked **#4** in Urology

Ranked **#5** in Ophthalmology

See more rankings

Reputation with specialists: **Significant**

Nurse staffing: Highest

Survival: Much better than expected

1 2 3 .. 87 >

HOSPITALS »
Hospitals by Specialty
Cancer Hospitals
Cardiology & Heart Surgery Hospitals
Diabetes & Endocrinology Hospitals
Orthopedics Hospitals

HOSPITALS »
Hospitals by City
Chicago Hospitals
Dallas-Fort Worth Hospitals
Los Angeles Hospitals
New York City Hospitals
Philadelphia Hospitals

DIETS »
Best Diets for You
Best Diets Overall
Best Weight-Loss Diets
Best Diabetes Diets
Best Heart-Healthy Diets
Best Commercial Diet Plans

SENIOR HOUSING »
Best Nursing Homes
California Nursing Homes
Florida Nursing Homes
Illinois Nursing Homes
New York Nursing Homes
Penn. Nursing Homes

HEALTH PLANS »
Top Health Insurance Companies
Calif. Health Insurance
Florida Health Insurance
Mass. Health Insurance
Texas Health Insurance
Virginia Health Insurance

THE UNIVERSITY OF TEXAS
MD Anderson Cancer Center
Making Cancer History®

Glossary of Cancer Terms

P

P-32 A radioactive form of phosphorus used in the treatment of cancer.

p-value A statistics term. A measure of probability that a difference between groups during an experiment happened by chance. For example, a p-value of .01 (p = .01) means there is a 1 in 100 chance the result occurred by chance. The lower the p-value, the more likely it is that the difference between groups was caused by treatment.

p53 gene A tumor suppressor gene that normally inhibits the growth of tumors. This gene is altered in many types of cancer.

pacemaker An electronic device that is implanted in the body to monitor heart rate and rhythm. It gives the heart electrical stimulation when it does not beat normally. An artificial pacemaker runs on batteries and has long, thin wires that connect it to the heart. Also called artificial pacemaker and cardiac pacemaker.

Pacific valerian Valeriana officinalis. A plant whose roots are used as a sedative and to treat certain medical conditions. It is being studied as a way to improve sleep in cancer patients undergoing treatment. Also called valerian, garden valerian, Indian valerian, Mexican valerian, garden heliotrope, Valeriana officinalis and Valerianae radix.

pack year A way to measure the amount a person has smoked over a long period of time. It is calculated by multiplying the number of packs of cigarettes smoked per day by the number of years the person has smoked. For example, 1 pack year is equal to smoking 1 pack per day for 1 year, or 2 packs per day for half a year, and so on.

paclitaxel A drug used to treat breast cancer, ovarian cancer, and AIDS-related Kaposi's sarcoma. It is also used together with another drug to treat non-small cell lung cancer. Paclitaxel is also being studied in the treatment of other types of cancer. It belongs to the family of drugs called mitotic inhibitors. Also called Taxol.

Paclitaxel (Albumin-Stabilized Nanoparticle Formulation) A drug used to treat breast cancer that has spread or that has come back within 6 months after chemotherapy. It is also being studied in the treatment of newly diagnosed breast cancer and other types of cancer. Paclitaxel (albumin-stabilized nanoparticle formulation) belongs to the family of drugs called mitotic inhibitors. Also called nanoparticle paclitaxel, protein-bound paclitaxel, Abraxane and ABI-007.

paclitaxel liposome A form of the anticancer drug paclitaxel that may have fewer side effects and work better than paclitaxel. It is being studied in the treatment of cancer. It belongs to the family of drugs called mitotic inhibitors. Also called LEP-ETU and PNU-93914.

paclitaxel poliglumex A form of the anticancer drug paclitaxel combined with a protein called poliglumex that may have fewer side effects and work better than paclitaxel. It is being studied in the treatment of breast cancer, ovarian cancer, lung cancer and other types of cancer. It belongs to the family of drugs called mitotic inhibitors. Also called paclitaxel polyglutamate, Xyotax and CT-2103.

paclitaxel polyglutamate A form of the anticancer drug paclitaxel combined with a protein called poliglumex that may have fewer side effects and work better than paclitaxel. It is being studied in the treatment of breast cancer, ovarian cancer, lung cancer and other types of cancer. It belongs to the family of drugs called mitotic inhibitors. Also called paclitaxel poliglumex, Xyotax and CT-2103.

Paget's disease of bone A chronic condition in which both the breakdown and regrowth of bone are increased. Paget's disease of bone occurs most frequently in the pelvic and leg bones, skull, and lower spine. It is most common in older individuals, and may lead to bone pain, deformities and fractures. Also called osteitis deformans.

Paget's disease of the nipple A form of breast cancer in which the tumor grows from ducts beneath the nipple onto the surface of the nipple. Symptoms commonly include itching and burning and an eczema-like condition around the nipple, sometimes accompanied by oozing or bleeding.

pain threshold The point at which a person becomes aware of pain.

PALA A substance that is being studied for its ability to increase the effectiveness of the anticancer drug fluorouracil.

palate The roof of the mouth. The front portion is bony (hard palate), and the back portion is muscular (soft palate).

palatine uvula The soft flap of tissue that hangs down at the back of the mouth (at the edge of the soft palate). Also called uvula.

palifermin A form of keratinocyte growth factor (KGF) that is made in the laboratory. KGF stimulates the growth of cells that line the surface of the mouth and intestinal tract. Palifermin is used to prevent and treat oral mucositis (mouth sores) caused by high-dose chemotherapy and radiation therapy in leukemia and lymphoma. It is also being studied in the prevention and treatment of oral mucositis and dysphagia (difficulty swallowing) in other types of cancer. Palifermin belongs to the family of drugs called recombinant human keratinocyte growth factors. Also called Kepivance.

palliation Relief of symptoms and suffering caused by cancer and other life-threatening diseases. Palliation helps a patient feel more comfortable and improves the quality of life, but does not cure the disease.

palliative care Care given to improve the quality of life of patients who have a serious or life-threatening disease. The goal of palliative care is to prevent or treat as early as possible the symptoms of the disease, side effects caused by treatment of the disease, and psychological, social and spiritual problems related to the disease or its treatment. Also called comfort care, supportive care and symptom management.

palliative therapy Treatment given to relieve the symptoms and reduce the suffering caused by cancer and other life-threatening diseases. Palliative cancer therapies are given together with other cancer treatments, from the time of diagnosis, through treatment, survivorship, recurrent or advanced disease and at the end of life.

palmar-plantar erythrodysesthesia A condition marked by pain, swelling, numbness, tingling or redness of the hands or feet. It sometimes occurs as a side effect of certain anticancer drugs. Also called hand-foot syndrome.

palpable disease A term used to describe cancer that can be felt by touch, usually present in lymph nodes, skin or other organs of the body such as the liver or colon.

palpation Examination by pressing on the surface of the body to feel the organs or tissues underneath.

pamidronate A drug that is used to treat hypercalcemia (too much calcium in the blood) and cancer that has spread to the bones. It belongs to the family of drugs called bisphosphonates.

panacea A cure-all.

Pancoast tumor A type of lung cancer that begins in the upper part of a lung and spreads to nearby tissues such as the ribs and vertebrae. Most Pancoast tumors are non-small cell cancers. Also called pulmonary sulcus tumor.

pancreas A glandular organ located in the abdomen. It makes pancreatic juices, which contain enzymes that aid in digestion, and it produces several hormones, including insulin. The pancreas is surrounded by the stomach, intestines and other organs.

pancreatectomy Surgery to remove all or part of the pancreas. In a total pancreatectomy, part of the stomach, part of the small intestine, the common bile duct, gallbladder, spleen and nearby lymph nodes also are removed.

pancreatic Having to do with the pancreas.

pancreatic cancer A disease in which malignant (cancer) cells are found in the tissues of the pancreas. Also called exocrine cancer.

pancreatic duct Part of a system of ducts in the pancreas. Pancreatic juices containing enzymes are released into these ducts and flow into the small intestine.

pancreatic endocrine cancer A rare cancer that forms in the islets of Langerhans cells (a type of cell found in the pancreas). Also called islet cell carcinoma.

pancreatic enzyme A protein secreted by the pancreas that aids in the digestion of food.

pancreatic juice Fluid made by the pancreas. Pancreatic juices contain proteins called enzymes that aid in digestion.

pancreatitis Inflammation of the pancreas. Chronic pancreatitis may cause diabetes and problems with digestion. Pain is the primary symptom.

panic Sudden extreme anxiety or fear that may cause irrational thoughts or actions. Panic may include rapid heart rate, flushing (a hot, red face), sweating and trouble breathing.

panitumumab A human monoclonal antibody that is being used to treat colorectal cancer that has spread to other parts of the body. It is used in patients whose disease has not gotten better during or after treatment with other anticancer drugs. It is also being studied in the treatment of other types of cancer. Monoclonal antibodies are made in the laboratory and can locate and bind to cancer cells. Panitumumab binds to the epidermal growth factor receptor (EGFR) and may block tumor cell growth. Also called ABX-EGF and Vectibix.

PAP Prostatic acid phosphatase. An enzyme produced by the prostate. It may be found in increased amounts in men who have prostate cancer. Also called prostatic acid phosphatase.

Pap smear A procedure in which cells are scraped from the cervix for examination under a microscope. It is used to detect cancer and changes that may lead to cancer. A Pap smear can also show noncancerous conditions, such as infection or inflammation. Also called a Pap test.

Pap test A procedure in which cells are scraped from the cervix for examination under a microscope. It is used to detect cancer and changes that may lead to cancer. A Pap test can also show noncancerous conditions, such as infection or inflammation. Also called a Pap smear.

papillary serous carcinoma An aggressive cancer that usually affects the uterus/endometrium, peritoneum or ovary.

papillary thyroid cancer Cancer that forms in cells in the thyroid and grows in small finger-like shapes. It grows slowly, is more common in women than in men, and often occurs before age 40. It is the most common type of thyroid cancer.

papillary tumor A tumor shaped like a small mushroom, with its stem attached to the epithelial layer (inner lining) of an organ.

papilledema Swelling around the optic disk, the area where the optic nerve (the nerve that carries messages from the eye to the brain) enters the eyeball. Papilledema occurs when increased brain pressure caused by tumors or other problems results in swelling of the optic nerve.

paracentesis A procedure in which a thin needle or tube is put into the abdomen to remove fluid from the peritoneal cavity (the space within the abdomen that contains the intestines, the stomach and the liver).

paraganglia A collection of cells that came from embryonic nervous tissue, and are found near the adrenal glands and some blood vessels and nerves. Most paraganglia secrete epinephrine and norepinephrine.

paraganglioma A rare, usually benign tumor that develops from cells of the paraganglia. Paraganglia are a collection of cells that came from embryonic nervous tissue, and are found near the adrenal glands and some blood vessels and nerves. Paragangliomas that develop in the adrenal gland are called pheochromocytomas. Those that develop outside of the adrenal glands near blood vessels or nerves are called glomus tumors or chemodectomas.

parageusia A bad taste in the mouth. Also called dysgeusia.

paralysis Loss of ability to move all or part of the body.

paramyxovirus A type of virus that has hemagglutinin-neuraminidase proteins in the outer coat and RNA as the genetic material. Measles (rubeola) virus, mumps virus and Newcastle disease virus are paramyxoviruses.

paranasal sinus One of many small hollow spaces in the bones around the nose. Paranasal sinuses are named after the bones that contain them: frontal (the lower forehead), maxillary (cheekbones), ethmoid (beside the upper nose), and sphenoid (behind the nose). The paranasal sinuses open into the nasal cavity (space inside the nose) and are lined with cells that make mucus to keep the nose from drying out during breathing.

paranasal sinus and nasal cavity cancer Cancer that forms in tissues of the paranasal sinuses (small hollow spaces in the bones around the nose) or nasal cavity (the inside of the nose). The most common type of paranasal sinus and nasal cavity cancer is squamous cell carcinoma (cancer that begins in flat cells lining these tissues and cavities).

paraneoplastic syndrome A group of symptoms that may develop when substances released by some cancer cells disrupt the normal function of surrounding cells and tissue.

paranoia A mental disorder in which a person has an extreme fear and distrust of others. A paranoid person may have delusions that people are trying to harm him or her.

parasite An animal or plant that gets nutrients by living on or in an organism of another species. A complete parasite gets all of its nutrients from the host organism, but a semi-parasite gets only some of its nutrients from the host.

parasitic Having to do with or being a parasite (an animal or plant that gets nutrients by living on or in an organism of another species).

parasomnia An abnormal disruption of sleep, such as sleep walking, sleep talking, nightmares, bedwetting, sleep apnea (problems with breathing that cause loud snoring) or nighttime seizures.

parasympathetic nervous system The part of the nervous system that slows the heart, dilates blood vessels, decreases pupil size, increases digestive juices and relaxes muscles in the gastrointestinal tract.

parathormone A substance made by the parathyroid gland that helps the body store and use calcium. A higher-than-normal amount of parathormone causes high levels of calcium in the blood and may be a sign of disease. Also called parathyroid hormone, parathyrin and PTH.

parathyrin A substance made by the parathyroid gland that helps the body store and use calcium. A higher-than-normal amount of parathyrin causes high levels of calcium in the blood and may be a sign of disease. Also called parathormone, parathyroid hormone and PTH.

parathyroid cancer A rare cancer that forms in tissues of one or more of the parathyroid glands (four pea-sized glands in the neck that make parathyroid hormone, which helps the body store and use calcium).

parathyroid gland One of four pea-sized glands found on the thyroid. The parathyroid hormone produced by these glands increases the calcium level in the blood.

parathyroid hormone A substance made by the parathyroid gland that helps the body store and use calcium. A higher-than-normal amount of parathyroid hormone causes high levels of calcium in the blood and may be a sign of disease. Also called parathormone, parathyrin and PTH.

parathyroidectomy Surgery to remove one or more parathyroid glands (four pea-sized organs found on the thyroid).

parenchyma The essential or functional elements of an organ.

parenteral nutrition A form of nutrition that is delivered into a vein. Parenteral nutrition does not use the digestive system. It may be given to people who are unable to absorb nutrients through the intestinal tract because of vomiting that won't stop, severe diarrhea, or intestinal disease. It may also be given to those undergoing high-dose chemotherapy or radiation and bone marrow transplantation. It is possible to give all of the protein, calories, vitamins and minerals a person needs using parenteral nutrition. Also called hyperalimentation, total parenteral nutrition and TPN.

paresthesia An abnormal touch sensation, such as burning or prickling, that occurs without an outside stimulus.

paricalcitol A substance that is being used to treat overactive parathyroid glands in patients with kidney failure. It is also being studied in the treatment of cancer. Paricalcitol belongs to the family of drugs called vitamin D analogs.

parietal pericardium The outer layer of the pericardium, which is a thin sac of tissue that surrounds the heart.

parietal peritoneum The layers of tissue that line the abdominal wall and the pelvic cavity.

Parkinson's disease A progressive disorder of the nervous system marked by muscle tremors, muscle rigidity, decreased mobility, stooped posture, slow voluntary movements and a mask-like facial expression.

parotid gland cancer Cancer that forms in a parotid gland, the largest of the salivary glands, which make saliva and release it into the mouth. There are 2 parotid glands, one in front of and just below each ear. Most salivary gland tumors begin in parotid glands.

parotidectomy Surgery to remove all or part of the parotid gland (a large salivary gland located in front of and just below the ear). In a radical parotidectomy, the entire gland is removed.

paroxetine hydrochloride A drug used to treat depression and anxiety disorders. It belongs to the family of drugs called selective serotonin reuptake inhibitors (SSRI). Also called Paxil.

paroxysmal nocturnal hemoglobinuria PNH. A rare disorder in which red blood cells are easily destroyed by certain immune system proteins. Symptoms include blood clots, and red or brownish urine in the morning. Aplastic anemia (decreased production of blood cells) may lead to PNH, and people with PNH are at increased risk of acute myelogenous leukemia. Also called PNH.

partial cystectomy The removal of the cancer as well as some of the bladder tissue around the tumor. Also called segmental cystectomy.

partial hysterectomy Surgery to remove the uterus only. When the uterus and part or all of the cervix are removed, it is called a total hysterectomy.

partial laryngectomy An operation to remove part of the larynx (voice box).

partial mastectomy The removal of cancer as well as some of the breast tissue around the tumor and the lining over the chest muscles below the tumor. Usually some of the lymph nodes under the arm are also taken out. Also called segmental mastectomy.

partial nephrectomy Surgery to remove part of one kidney or a kidney tumor, but not an entire kidney.

partial oophorectomy Surgery to remove part of one ovary or part of both ovaries.

partial remission A decrease in the size of a tumor, or in the extent of cancer in the body, in response to treatment. Also called partial response.

partial response A decrease in the size of a tumor, or in the extent of cancer in the body, in response to treatment. Also called partial remission.

partial vulvectomy Surgery to remove most, but not all, of the vulva (the external female genital organs, including the clitoris, vaginal lips and the opening to the vagina).

passive antibody therapy Treatment with injections of antibodies made in another animal or in the laboratory.

pastoral counselor A person who is trained to give spiritual and mental health advice.

patchouli A bushy herb that is a member of the mint family. A strong-smelling oil taken from the leaves is used in perfumes, incense, detergents and hair conditioners. It has been used in some cultures to prevent disease. The scientific name is Pogostemon cablin

Paterson-Kelly syndrome A disorder marked by anemia caused by iron deficiency, and a web-like growth of membranes in the throat that makes swallowing difficult. Having Paterson-Kelly syndrome may increase the risk of developing esophageal cancer. Also called Plummer-Vinson syndrome and sideropenic dysphagia.

pathognomonic Having to do with a sign or symptom that is specific to a certain disease.

pathologic fracture A broken bone caused by disease, often by the spread of cancer to the bone.

pathological staging A method used to determine the stage of cancer. Tissue samples are removed during surgery or a biopsy. The stage is determined based on how the cells in the samples look under a microscope.

pathologist A doctor who identifies diseases by studying cells and tissues under a microscope.

pathology report The description of cells and tissues made by a pathologist based on microscopic evidence, and sometimes used to make a diagnosis of a disease.

patient advocate A person who helps a patient work with others who have an effect on the patient's health, including doctors, insurance companies, employers, case managers and lawyers. A patient advocate helps resolve issues about health care, medical bills, and job discrimination related to a patient's medical condition. Cancer advocacy groups try to raise public awareness about important cancer issues, such as the need for cancer support services, education and research. Such groups work to bring about change that will help cancer patients and their families.

patient-controlled analgesia PCA. A method of pain relief in which the patient controls the amount of pain medicine that is used. When pain relief is needed, the person can receive a preset dose of pain medicine by pressing a button on a computerized pump that is connected to a small tube in the body. Also called PCA.

Paxil A drug used to treat depression and anxiety disorders. It belongs to the family of drugs called selective serotonin reuptake inhibitors (SSRI). Also called paroxetine hydrochloride.

pazopanib A substance being studied in the treatment of cancer. It is a type of protein tyrosine kinase inhibitor and angiogenesis inhibitor. Also called GW786034 and pazopanib hydrochloride.

pazopanib hydrochloride A substance being studied in the treatment of cancer. It is a type of protein tyrosine kinase inhibitor and angiogenesis inhibitor. Also called pazopanib and GW786034.

PCA Patient-controlled analgesia. A method of pain relief in which the patient controls the amount of pain medicine that is used. When pain relief is needed, the person can receive a preset dose of pain medicine by pressing a button on a computerized pump that is connected to a small tube in the body. Also called patient-controlled analgesia.

PCNSL Primary CNS lymphoma. Cancer that forms in the lymph tissue of the brain, spinal cord, meninges (outer covering of the brain), or eye (called ocular lymphoma). Also called primary CNS lymphoma and primary central nervous system lymphoma.

PCOS Polycystic ovary syndrome. A condition marked by infertility, enlarged ovaries, menstrual problems, high levels of male hormones, excess hair on the face and body, acne, and obesity. Women with PCOS have an increased risk of diabetes, high blood pressure, heart disease and endometrial cancer. Also called polycystic ovary syndrome.

PCR Polymerase chain reaction. A laboratory method used to make many copies of a specific DNA sequence. Also called polymerase chain reaction.

PDQ Physician Data Query. PDQ is an online database developed and maintained by the National Cancer Institute. Designed to make the most current, credible, and accurate cancer information available to health professionals and the public, PDQ contains peer-reviewed summaries on cancer treatment, screening, prevention, genetics, complementary and alternative medicine, and supportive care; a registry of cancer clinical trials from around the world; and directories of physicians, professionals who provide genetics services and organizations that provide cancer care. Most of this information, and more specific information about PDQ, can be found on the NCI's Web site at http://www.cancer.gov/cancertopics/pdq. Also called Physician Data Query.

peau d'orange A dimpled condition of the skin of the breast, resembling the skin of an orange, sometimes found in inflammatory breast cancer.

pediatric Having to do with children.

pediatric hematologist A doctor who specializes in treating blood disorders in children.

pediatric nurse specialist A registered nurse with an advanced degree in nursing who specializes in the care of children.

pediatric surgeon A surgeon who specializes in the treatment of children. A surgeon removes or repairs a part of the body by operating on the patient.

pedigree A record of one's ancestors, offspring, siblings and their offspring that may be used to determine the pattern of certain genes or disease inheritance within a family.

PEG-asparaginase A form of the drug asparaginase that is used together with other anticancer drugs to treat acute lymphoblastic leukemia (ALL). It belongs to the family of drugs called enzymes. Also called pegaspargase and Oncaspar.

PEG-interferon alfa-2a A drug used to treat hepatitis C infections. It is also being studied in the treatment and prevention of cancer. It is a cytokine that is modified in the laboratory. It belongs to the family of drugs called biological response modifiers. Also called Pegasys.

PEG-interferon alfa-2b A drug used to treat hepatitis C infections. It is also being studied in the treatment and prevention of cancer. It is a cytokine that is modified in the laboratory. It belongs to the family of drugs called biological response modifiers. Also called PEG-Intron and SCH 54031.

PEG-Intron A drug used to treat hepatitis C infections. It is also being studied in the treatment and prevention of cancer. It is a cytokine that is modified in the laboratory. It belongs to the family of drugs called biological response modifiers. Also called PEG-interferon alfa-2b and SCH 54031.

PEG-MGDF A form of megakaryocyte growth and development factor (MGDF) that is made in the laboratory. MGDF comes from the protein thrombopoietin, which is normally made in the body to help make platelets. PEG-MGDF is being studied as a way to increase the number of platelets in patients receiving chemotherapy. Also called polyethylene glycosylated recombinant human megakaryocyte growth and development factor and PEG-rhMGDF.

PEG-rhMGDF Polyethylene glycosylated recombinant human megakaryocyte growth and development factor. A form of megakaryocyte growth and development factor (MGDF) that is made in the laboratory. MGDF comes from the protein thrombopoietin, which is normally made in the body to help make platelets. PEG-rhMGDF is being studied as a way to increase the number of platelets in patients receiving chemotherapy. Also called PEG-MGDF and polyethylene glycosylated recombinant human megakaryocyte growth and develoment factor.

pegaspargase A form of the drug asparaginase that is used together with other anticancer drugs to treat acute lymphoblastic leukemia (ALL). It belongs to the family of drugs called enzymes. Also called PEG-asparaginase and Oncaspar.

Pegasys A drug used to treat hepatitis C infections. It is also being studied in the treatment and prevention of cancer. It is a cytokine that is modified in the laboratory. It belongs to the family of drugs called biological response modifiers. Also called PEG-interferon alfa-2a.

pegfilgrastim A drug used to increase numbers of white blood cells in patients who are receiving chemotherapy. It belongs to the family of drugs called colony-stimulating factors. Also called Neulasta and filgrastim-SD/01.

pegylated liposomal doxorubicin A form of the anticancer drug doxorubicin that may have fewer side effects and work better than doxorubicin. It is being studied in the treatment of ovarian cancer, breast cancer, Kaposi's sarcoma, and other types of cancer. It is a type of anthracycline antitumor antibiotic. Also called liposomal doxorubicin, doxorubicin hydrochloride pegylated liposomes, Caelyx and Doxil.

PEITC Phenethyl isothiocyanate. A substance being studied in the prevention of cancer. It is a naturally occurring compound found in some cruciferous vegetables. Also called phenethyl isothiocyanate.

peldesine A substance that is being studied for the treatment of cancer.

pelvic Having to do with the pelvis (the lower part of the abdomen located between the hip bones).

pelvic examination A physical examination in which the health care professional will feel for lumps or changes in the shape of the vagina, cervix, uterus, fallopian tubes, ovaries and rectum. The health care professional will also use a speculum to open the vagina to look at the cervix and take samples for a Pap test. Also called an internal examination.

pelvic exenteration Surgery to remove the lower colon, rectum, and bladder, and create stomata (openings) through which urine and stool are passed out of the body. In women, the cervix, vagina, ovaries and nearby lymph nodes are also removed.

pelvic lymphadenectomy Surgery to remove lymph nodes in the pelvis for examination under a microscope to see if they contain cancer.

pelvic wall The muscles and ligaments that line the part of the body between the hips.

pelvis The lower part of the abdomen, located between the hip bones.

pemetrexed disodium A drug that is used to treat malignant pleural mesothelioma and advanced non-small cell lung cancer and is being studied in the treatment of other types of cancer. It belongs to the family of drugs called enzyme inhibitors. Also called Alimta and LY231514

penclomedine A substance that is being studied in the treatment of cancer. It belongs to the family of drugs called alkylating agents.

penectomy Surgery to remove part or all of the penis.

penicillamine A drug that removes copper from the body and is used to treat diseases in which there is an excess of copper. It is also being studied as a possible angiogenesis inhibitor in the treatment of brain tumors.

penicillin A drug that is used to treat infection. It belongs to the family of drugs called antibiotics.

penile cancer A rare cancer that forms in the penis (the external male reproductive organ). Most penile cancers are squamous cell carcinomas (cancer that begins in flat cells lining the penis).

penile implant A firm rod or inflatable device that is placed in the penis during a surgical procedure. The implant makes it possible to have and keep an erection. Penile implants are used to treat erectile dysfunction or impotence.

penis An external male reproductive organ. It contains a tube called the urethra, which carries semen and urine to the outside of the body.

pentetic acid calcium A drug that protects healthy tissues from the toxic effects of anticancer drugs.

pentosan polysulfate A drug used to relieve pain or discomfort associated with chronic inflammation of the bladder. It is also being evaluated for its protective effects on the gastrointestinal tract in people undergoing radiation therapy.

pentostatin An anticancer drug that belongs to the family of drugs called antimetabolites.

pentoxifylline A drug used to prevent blood clotting and as a treatment that may help decrease weight loss in people with cancer.

peptide Any compound consisting of two or more amino acids, the building blocks of proteins.

peptide 946 A protein that causes white blood cells to recognize and destroy melanoma cells.

percutaneous Passing through the skin; as in an injection or a topical medicine.

percutaneous ethanol injection An injection of ethanol (alcohol) through the skin directly into the tumor to kill cancer cells.

percutaneous transhepatic biliary drainage A procedure to drain bile to relieve pressure in the bile ducts caused by a blockage. An X-ray of the liver and bile ducts locates the blockage of bile flow. Images made by ultrasound guide placement of a stent (tube), which remains in the liver. Bile drains through the stent into the small intestine or into a collection bag outside the body. This procedure may relieve jaundice before surgery. Also called percutaneous transhepatic cholangiodrainage and PTCD.

percutaneous transhepatic cholangiodrainage PTCD. A procedure to drain bile to relieve pressure in the bile ducts caused by a blockage. An X-ray of the liver and bile ducts locates the blockage of bile flow. Images made by ultrasound guide placement of a stent (tube), which remains in the liver. Bile drains through the stent into the small intestine or into a collection bag outside the body. This procedure may relieve jaundice before surgery. Also called percutaneous transhepatic biliary drainage and PTCD.

percutaneous transhepatic cholangiography PTC. A procedure to X-ray the hepatic and common bile ducts. A contrasting agent is injected into the liver or bile duct, and the ducts are then X-rayed to find the point of obstruction. Also called PTC.

performance status A measure of how well a patient is able to perform ordinary tasks and carry out daily activities.

perfusion Bathing an organ or tissue with fluid. In regional perfusion, a specific area of the body (usually an arm or a leg) receives high doses of anticancer drugs through a blood vessel. Such a procedure is performed to treat cancer that has not spread.

perfusion magnetic resonance imaging A special type of magnetic resonance imaging (MRI) that uses an injected dye in order to see blood flow through tissues. Also called magnetic resonance perfusion imaging.

pericardial effusion An abnormal collection of fluid inside the sac that covers the heart.

perifosine A substance that is being studied in the treatment of cancer. It belongs to the family of drugs called alkylphospholipids.

perillyl alcohol A substance that is being studied in the prevention of cancer. It belongs to the family of plant drugs called monoterpenes.

perimenopausal The time of a woman's life when menstrual periods become irregular. Refers to the time near menopause.

perineal colostomy An opening made surgically to allow the colon to exit the body through the perineum (the area of the body between the anus and the vulva in females, and between the anus and the scrotum in males). A colostomy provides a new path for waste material to leave the body after part of the colon has been removed.

perineal prostatectomy Surgery to remove the prostate through an incision made between the scrotum and the anus.

perineum The area of the body between the anus and the vulva in females, and between the anus and the scrotum in males.

perineural Around a nerve or group of nerves.

perioperative Around the time of surgery. This usually lasts from the time the patient goes into the hospital or doctor's office for surgery until the time the patient goes home.

peripheral blood Blood circulating throughout the body.

peripheral blood lymphocyte therapy A treatment for Epstein-Barr virus infection or overgrowth of white blood cells (lymphocytes) after an organ or bone marrow transplant. Specific lymphocytes from a sibling donor are infused into the patient to try and reverse these conditions.

peripheral blood smear A procedure in which a sample of blood is viewed under a microscope to count different circulating blood cells (red blood cells, white blood cells, platelets, etc.) and see whether the cells look normal.

peripheral neuropathy A condition of the nervous system that causes numbness, tingling, burning or weakness. It usually begins in the hands or feet, and can be caused by certain anticancer drugs.

peripheral primitive neuroectodermal tumor pPNET. A type of cancer that forms in bone or soft tissue. Also called pPNET and Ewing's sarcoma.

peripheral stem cell An immature cell found circulating in the bloodstream. New blood cells develop from peripheral stem cells.

peripheral stem cell support A method of replacing blood-forming cells destroyed by cancer treatment. Immature blood cells (stem cells) in the circulating blood that are similar to those in the bone marrow are given to the patient after treatment. This helps the bone marrow recover and continue producing healthy blood cells. Transplantation may be autologous (an individual's own blood cells saved earlier), allogeneic (blood cells donated by someone else), or syngeneic (blood cells donated by an identical twin). Also called peripheral stem cell transplantation.

peripheral stem cell transplantation A method of replacing blood-forming cells destroyed by cancer treatment. Immature blood cells (stem cells) in the circulating blood that are similar to those in the bone marrow are given to the patient after treatment. This helps the bone marrow recover and continue producing healthy blood cells. Transplantation may be autologous (an individual's own blood cells saved earlier), allogeneic (blood cells donated by someone else), or syngeneic (blood cells donated by an identical twin). Also called peripheral stem cell support.

peripheral T-cell lymphoma One of a group of aggressive (fast-growing) non-Hodgkin's lymphomas that begin in mature T lymphocytes (T cells that have matured in the thymus gland and gone to other lymphatic sites in the body, including lymph nodes, bone marrow and spleen.) Also called mature T-cell lymphoma.

peripheral venous catheter A small, flexible tube used to deliver fluids into the body. A needle is used to insert the catheter into a vein, usually in the back of the hand or in the forearm. The tubing is then taped to the skin to hold it in place.

peristalsis The rippling motion of muscles in the intestine or other tubular organs characterized by the alternate contraction and relaxation of the muscles that propel the contents onward.

peritoneal Having to do with the parietal peritoneum (the tissue that lines the abdominal wall and pelvic cavity) and visceral peritoneum (the tissue that covers most of the organs in the abdomen, including the intestines).

peritoneal cancer Cancer of the tissue that lines the abdominal wall and covers organs in the abdomen.

peritoneal cavity The space within the abdomen that contains the intestines, the stomach, and the liver. It is bound by thin membranes.

peritoneal fluid A liquid that is made in the abdominal cavity to lubricate the surface of the tissue that lines the abdominal wall and pelvic cavity and covers most of the organs in the abdomen.

peritoneal infusion A method of delivering fluids and drugs directly into the abdominal cavity through a thin tube. Also called intraperitoneal infusion.

peritoneal perfusion A method of delivering fluids and drugs directly to tumors in the peritoneal cavity.

peritoneum The tissue that lines the abdominal wall and covers most of the organs in the abdomen.

peritonitis Inflammation of the peritoneum (tissue that lines the abdominal wall and covers most of the organs in the abdomen). Peritonitis can result from infection, injury, or certain diseases. Symptoms may include swelling of the abdomen, severe pain, and weight loss.

pernicious anemia A type of anemia (low red blood cell count) caused by the body's inability to absorb vitamin B12.

perturbation A disruption or disturbance.

pertussis A serious bacterial infection of the lungs and breathing tubes that spreads easily. Pertussis begins like a cold, but develops into severe coughing and gasping for air. Long spells of coughing may cause vomiting, and broken blood vessels in the eyes and on the skin. Also called whooping cough.

pertuzumab A monoclonal antibody that is being studied in the treatment of cancer. Monoclonal antibodies are produced in the laboratory and can locate and bind to cancer cells.

pesticide A chemical that is used to kill insects and other pests.

PET scan Positron emission tomography scan. A procedure in which a small amount of radioactive glucose (sugar) is injected into a vein, and a scanner is used to make detailed, computerized pictures of areas inside the body where the glucose is used. Because cancer cells often use more glucose than normal cells, the pictures can be used to find cancer cells in the body. Also called positron emission tomography scan.

petechiae Pinpoint, unraised, round red spots under the skin caused by bleeding.

Peutz-Jeghers syndrome PJS. A genetic disorder in which polyps form in the intestine and dark spots appear on the mouth and fingers. Having PJS increases the risk of developing gastrointestinal and many other types of cancer. Also called PJS.

PF-00299804 A substance that is being studied in the treatment of cancer. It belongs to the family of drugs called protein tyrosine kinase inhibitors.

PF-3512676 A substance that is being studied in the treatment of some types of cancer. It belongs to the family of drugs called biological response modifiers. Also called CpG 7909 and ProMune.

PHA-739358 A substance being studied in the treatment of chronic myelogenous leukemia. PHA-739358 may stop tumor growth by blocking certain enzymes needed for cancer cells to divide and causing them to die. It is a type of kinase inhibitor.

phagocyte An immune system cell that can surround and kill microorganisms and remove dead cells. Phagocytes include macrophages.

phagocytosis The process by which a phagocyte (a type of white blood cell) surrounds and destroys foreign substances (such as bacteria) and removes dead cells.

phantom limb pain The sensation of pain or other unpleasant feelings in the place of a missing (phantom) limb.

pharmacokinetics The activity of drugs in the body over a period of time, including the processes by which drugs are absorbed, distributed in the body, localized in the tissues and excreted.

pharmacology The study of the origin, chemistry and uses of drugs and their effects on the body.

pharmacopoeia A book describing chemicals, drugs, and other substances and how they are used as medicines. It is prepared by a recognized authority.

pharyngeal cancer Cancer that forms in tissues of the pharynx (the hollow tube inside the neck that starts behind the nose and ends at the top of the windpipe and esophagus). Pharyngeal cancer includes cancer of the nasopharynx (the upper part of the throat behind the nose), the oropharynx (the middle part of the pharynx), and the hypopharynx (the bottom part of the pharynx). Cancer of the larynx (voice box) may also be included as a type of pharyngeal cancer. Most pharyngeal cancers are squamous cell carcinomas (cancer that begins in thin, flat cells that look like fish scales). Also called throat cancer.

pharynx The hollow tube inside the neck that starts behind the nose and ends at the top of the trachea (windpipe) and esophagus (the tube that goes to the stomach). The pharynx is about 5 inches long, depending on body size. Also called the throat.

phase I detoxification A process in which the liver uses one of two major enzyme pathways to change a toxic substance, such as an anticancer drug, into a less toxic substance that is easier for the body to excrete.

phase I trial The first step in testing a new treatment in humans. These studies test the best way to give a new treatment (for example, by mouth, intravenous infusion or injection) and the best dose. The dose is usually increased a little at a time in order to find the highest dose that does not cause harmful side effects. Because little is known about the possible risks and benefits of the treatments being tested, phase I trials usually include only a small number of patients who have not been helped by other treatments.

phase I/II trial A trial to study the safety, dosage levels and response to a new treatment.

phase II detoxification A process in which the liver uses one of two major enzyme pathways to change a toxic substance, such as an anticancer drug, into a less toxic substance that is easier for the body to excrete. In phase II detoxification, liver cells add a substance (such as cysteine, glycine, or a sulfur molecule) to a toxic chemical or drug, to make it less harmful.

phase II trial A study to test whether a new treatment has an anticancer effect (for example, whether it shrinks a tumor or improves blood test results) and whether it works against a certain type of cancer.

phase II/III trial A trial to study response to a new treatment and the effectiveness of the treatment compared with the standard treatment regimen.

phase III trial A study to compare the results of people taking a new treatment with the results of people taking the standard treatment (for example, which group has better survival rates or fewer side effects). In most cases, studies move into phase III only after a treatment seems to work in phases I and II. Phase III trials may include hundreds of people.

phase IV trial After a treatment has been approved and is being marketed, it is studied in a phase IV trial to evaluate side effects that were not apparent in the phase III trial. Thousands of people are involved in a phase IV trial.

phenethyl isothiocyanate PEITC. A substance being studied in the prevention of cancer. It is a naturally occurring compound found in some cruciferous vegetables. Also called PEITC.

phenobarbital A drug that is used to treat seizures and as a sedative. It is being studied in the treatment of diarrhea and for its ability to increase the antitumor effect of other therapies. It belongs to the family of drugs called barbiturates.

phenol A very poisonous chemical substance made from tar and also found in some plants and essential oils (scented liquid taken from plants). Phenol is used to make plastics, nylon, epoxy, medicines and to kill germs. Also called carbolic acid.

phenothiazine A type of drug that is used to treat severe mental and emotional disorders, severe nausea and vomiting, and certain other conditions. It belongs to the families of drugs called antipsychotics and antiemetics.

phenoxodiol A substance that is being studied in the treatment of cancer. It belongs to the family of drugs called signal transduction inhibitors.

phenylacetate A substance that is being studied in the treatment of cancer.

phenylbutyrate A substance that is being studied in the treatment of cancer. It belongs to the family of drugs called differentiating agents.

phenylketonuria PKU. An inherited disorder that causes a build-up of phenylalanine (an amino acid) in the blood. This can cause mental retardation, behavioral and movement problems, seizures, and delayed development. Using a blood test, PKU can easily be found in newborns, and treatment is a diet low in phenylalanine. Also called PKU.

pheochromocytoma Tumor that forms in the center of the adrenal gland (gland located above the kidney) that causes it to make too much adrenaline. Pheochromocytomas are usually benign (noncancerous) but can cause high blood pressure, pounding headaches, heart palpitations, flushing of the face, nausea and vomiting.

pheresis A procedure in which blood is collected, part of the blood such as platelets or white blood cells is taken out, and the rest of the blood is returned to the donor. Also called apheresis.

Philadelphia chromosome An abnormality of chromosome 22 in which part of chromosome 9 is transferred to it. Bone marrow cells that contain the Philadelphia chromosome are often found in chronic myelogenous leukemia.

philosophical Having to do with the deeper questions of life and with a person's basic beliefs, ideas and attitudes.

phlebotomy The puncture of a vein with a needle for the purpose of drawing blood. Also called venipuncture.

phlegm A more than normal amount of thick mucus made by the cells lining the upper airways and lungs. A buildup of phlegm may be caused by infection, irritation or chronic lung disease, and can cause discomfort in the chest and coughing.

phobia An extreme, irrational, fear of something that may cause a person to panic. Examples of common phobias include fear of spiders, flying in an airplane, elevators, heights, enclosed rooms, crowded public places and embarrassing oneself in front of other people.

phospholipid A lipid (fat) that contains phosphorus. Phospholipids are a major part of cell membranes.

phospholipid complex A chemical or drug that is attached to a lipid (fat) that contains phosphorus.

phosphoric Having to do with or containing the element phosphorus.

phosphorus A nonmetallic element that is found in the blood, muscles, nerves, bones, and teeth and is a component of adenosine triphosphate (ATP; the primary energy source for the body's cells).

phosphorus-32 A radioactive form of phosphorus used in the treatment of cancer. It is also used to help locate areas of DNA damage.

photoactivity The effect produced when certain substances are exposed to light. In cancer treatment, some drugs become active when exposed to light and are then able to kill tumor cells.

photodynamic therapy Treatment with drugs that become active when exposed to light. These drugs kill cancer cells.

Photofrin A drug used to treat some types of cancer. When absorbed by cancer cells and exposed to light, Photofrin becomes active and kills the cancer cells. It belongs to the family of drugs called photodynamic therapy agents. Also called porfimer sodium.

photon-beam radiation A type of radiation therapy that reaches deep tumors with high-energy X-rays made by a machine called a linear accelerator.

photopheresis A procedure in which blood is removed from the body and treated with ultraviolet light and drugs that become active when exposed to light. The blood is then returned to the body. It is being studied in the treatment of some blood and bone marrow diseases and graft-vs-host disease (GVHD). Also called extracorporeal photopheresis.

photophobia A condition in which the eyes are more sensitive than normal to light.

photosensitizer A drug used in photodynamic therapy. When absorbed by cancer cells and exposed to light, the drug becomes active and kills the cancer cells. Also called photosensitizing agent.

photosensitizing agent A drug used in photodynamic therapy. When absorbed by cancer cells and exposed to light, the drug becomes active and kills the cancer cells. Also called photosensitizer.

phototoxicity A condition in which the skin or eyes become very sensitive to sunlight or other forms of light. It can be caused by taking certain drugs, or rubbing certain essential oils (scented liquid taken from plants) or other topical agents into the skin. Phototoxicity causes sunburn, blisters and other skin problems.

phyllodes tumor A type of tumor found in breast tissue. It is often large and bulky and grows quickly. It is usually benign (not cancer), but may be malignant (cancer). Also called cystosarcoma phyllodes.

physical dependence A condition in which a person takes a drug over time, and unpleasant physical symptoms occur if the drug is suddenly stopped or taken in smaller doses.

physical examination An exam of the body to check for general signs of disease.

physical therapist A health professional who teaches exercises and physical activities that help condition muscles and restore strength and movement.

physical therapy The use of exercises and physical activities to help condition muscles and restore strength and movement. For example, physical therapy can be used to restore arm and shoulder movement and build back strength after breast cancer surgery.

physician Medical doctor.

Physician Data Query PDQ. The Physician Data Query is an online database developed and maintained by the National Cancer Institute. Designed to make the most current, credible, and accurate cancer information available to health professionals and the public, PDQ contains peer-reviewed summaries on cancer treatment, screening, prevention, genetics, complementary and alternative medicine, and supportive care; a registry of cancer clinical trials from around the world; and directories of physicians, professionals who provide genetics services and organizations that provide cancer care. Most of this information and more specific information about PDQ can be found on the NCI's Web site at http://www.cancer.gov/cancertopics/pdq. Also called PDQ.

physiologic Having to do with the functions of the body. When used in the phrase "physiologic age," it refers to an age assigned by general health, as opposed to calendar age.

phytic acid A substance found in many foods that come from plants, including corn, wheat, rice, and soybeans, and in large amounts in cereals and legumes. It is being studied in the prevention of cancer. Also called inositol hexaphosphate and IP6.

phytochemical A substance found in plants. Some phytochemicals may reduce the risk of cancer.

phytoestrogen An estrogen-like substance found in some plants and plant products. Phytoestrogens may have anticancer effects.

phytohemagglutinin A substance found in plants that causes red blood cells to clump together and certain white blood cells to divide.

phytol A chemical substance that comes from plants and is used to make vitamins E and K. Phytol is also found in soaps, beauty care products and household products.

phytosterol A plant-based compound that can compete with dietary cholesterol to be absorbed by the intestines, resulting in lower blood cholesterol levels. Phytosterols may have some effect in cancer prevention. Also called plant sterol.

PI-88 A substance that is being studied in the treatment of cancer. It belongs to the family of drugs called antiangiogenesis agents.

pigment A substance that gives color to tissue. Pigments are responsible for the color of skin, eyes and hair.

pilocarpine A drug used to increase salivation in people who have dry mouth caused by opioids or radiation therapy. Pilocarpine belongs to the family of drugs called alkaloids.

pilocytic Made up of cells that look like fibers when viewed under a microscope.

pilot study The initial study examining a new method or treatment.

PIN Prostatic intraepithelial neoplasia. Noncancerous growth of cells lining the internal and external surfaces of the prostate gland. Having high-grade PIN may increase the risk of developing prostate cancer. Also called prostatic intraepithelial neoplasia.

pineal body A tiny organ in the cerebrum that produces melatonin. Also called pineal gland or pineal organ.

pineal gland A tiny organ in the cerebrum that produces melatonin. Also called pineal body or pineal organ.

pineal organ A tiny organ in the cerebrum that produces melatonin. Also called pineal body or pineal gland.

pineal region tumor A type of brain tumor that occurs in or around the pineal gland, a tiny organ near the center of the brain.

pineoblastoma A fast-growing type of brain tumor that occurs in or around the pineal gland, a tiny organ near the center of the brain.

pineocytoma A slow-growing type of brain tumor that occurs in or around the pineal gland, a tiny organ near the center of the brain.

pinkeye A condition in which the conjunctiva (membranes lining the eyelids and covering the white part of the eye) become inflamed or infected. Also called conjunctivitis.

pioglitazone A drug that is used to treat type 2 diabetes and is being studied in the prevention of head and neck cancer. It may be able to stop leukoplakia (a precancerous condition affecting the mouth) from developing into cancer. It belongs to the family of drugs called thiazolidinediones. Also called Actos.

piperacillin-tazobactam A drug combination that is used to treat infection in people with cancer. Piperacillin is a synthetic penicillin; tazobactam enhances the effectiveness of piperacillin.

pirfenidone A substance that is being studied in the prevention and treatment of scar tissue caused by radiation therapy. It belongs to the family of drugs called anti-inflammatory agents.

Piritrexim A substance that is being studied in the treatment of cancer. It belongs to the family of drugs called folate antagonists.

pituitary gland The main endocrine gland. It produces hormones that control other glands and many body functions, especially growth.

pituitary tumor A tumor that forms in the pituitary gland. The pituitary is a pea-sized organ in the center of the brain above the back of the nose. It makes hormones that affect other glands and many body functions, especially growth. Most pituitary tumors are benign (not cancer).

pixantrone A substance that is being studied in the treatment of cancer. It belongs to the family of drugs called antitumor antibiotics. Also called BBR 2778.

PJS Peutz-Jeghers syndrome. A genetic disorder in which polyps form in the intestine and dark spots appear on the mouth and fingers. Having PJS increases the risk of developing gastrointestinal and many other types of cancer. Also called Peutz-Jeghers syndrome.

PKC Protein kinase C. An enzyme found throughout the body's tissues and organs. Several forms of PKC are involved in many cellular functions. PKC is being studied in the treatment of cancer. Also called protein kinase C.

PKC412 A substance that is being studied in the treatment of leukemia. It belongs to the family of drugs called protein kinase inhibitors. Also called N-benzoyl-staurosporine and midostaurin.

PKU Phenylketonuria. An inherited disorder that causes a build-up of phenylalanine (an amino acid) in the blood. This can cause mental retardation, behavioral and movement problems, seizures and delayed development. Using a blood test, PKU can easily be found in newborns, and treatment is a diet low in phenylalanine. Also called phenylketonuria.

placebo An inactive substance or treatment that looks the same as, and is given the same way as, an active drug or treatment being tested. The effects of the active drug or treatment are compared to the effects of the placebo.

placebo therapy An inactive treatment or procedure that is intended to mimic as closely as possible a therapy in a clinical trial. Also called sham therapy.

placebo-controlled Refers to a clinical study in which the control patients receive a placebo.

placenta The organ that nourishes the developing fetus in the uterus.

placental blood transplantation The transfer of blood from a placenta to an individual whose own blood production system is suppressed. Placental blood contains high levels of stem cells needed to produce new blood cells. It is being studied in the treatment of cancer and severe blood disorders such as aplastic anemia.

plant sterol A plant-based compound that can compete with dietary cholesterol to be absorbed by the intestines, resulting in lower blood cholesterol levels. Plant sterols may have some effect in cancer prevention. Also called phytosterol.

plaque In medicine, a small, abnormal patch of tissue on a body part or an organ. Plaques may also be a build-up of substances from a fluid, such as cholesterol in the blood vessels.

plasma The clear, yellowish, fluid part of the blood that carries the blood cells. The proteins that form blood clots are in plasma.

plasma cell A type of white blood cell that produces antibodies.

plasma cell myeloma A type of cancer that begins in plasma cells (white blood cells that produce antibodies). Also called multiple myeloma, Kahler’s disease or myelomatosis.

plasma cell tumor A tumor that begins in plasma cells (white blood cells that produce antibodies). Multiple myeloma, monoclonal gammopathy of undetermined significance (MGUS), and plasmacytoma are types of plasma cell tumors.

plasma membrane The outer membrane of a cell.

plasmacytic Having to do with plasma cells (a type of white blood cells).

plasmacytoma A type of cancer that begins in plasma cells (white blood cells that produce antibodies). A plasmacytoma may turn into multiple myeloma.

plasmapheresis The process of separating certain cells from the plasma in the blood by a machine; only the cells are returned to the person. Plasmapheresis can be used to remove excess antibodies from the blood.

plastic surgeon A surgeon who specializes in reducing scarring or disfigurement that may occur as a result of accidents, birth defects, or treatment for diseases.

plastic surgery An operation that restores or improves the appearance of body structures.

platelet A type of blood cell that helps prevent bleeding by causing blood clots to form. Also called a thrombocyte.

platinum A metal that is an important component of some anticancer drugs, such as cisplatin and carboplatin.

Plenaxis A drug used to reduce the amount of testosterone made in patients with advanced symptomatic prostate cancer for which no other treatment options are available. It belongs to the family of drugs called gonadotropin-releasing hormone (GnRH) antagonists. Also called abarelix.

pleomorphic Occurring in various distinct forms. In terms of cells, having variation in the size and shape of cells or their nuclei.

pleura A thin layer of tissue covering the lungs and lining the interior wall of the chest cavity. It protects and cushions the lungs. This tissue secretes a small amount of fluid that acts as a lubricant, allowing the lungs to move smoothly in the chest cavity while breathing.

pleural cavity The space enclosed by the pleura, which is a thin layer of tissue that covers the lungs and lines the interior wall of the chest cavity.

pleural effusion An abnormal collection of fluid between the thin layers of tissue (pleura) lining the lung and the wall of the chest cavity.

pleurodesis A medical procedure that uses chemicals or drugs to cause inflammation and adhesion between the layers of the pleura (the tissue that covers the lungs and lines the interior wall of the chest cavity). This prevents the buildup of fluid in the pleural cavity. It is used as a treatment for severe pleural effusion.

pleuropulmonary blastoma A rare and very aggressive (fast-growing) cancer that forms in tissues of the lung and pleura (a thin layer of tissue covering the lungs and the inside wall of the chest cavity). Pleuropulmonary blastoma is most common in children.

plexiform neurofibroma A nerve that has become thick and misshapen due to the abnormal growth of cells and tissues that cover the nerve.

plexopathy A disorder affecting a network of nerves, blood vessels or lymph vessels.

plicamycin A drug used to treat some types of testicular cancer, hypercalcemia (abnormally high levels of calcium in the blood), and hypercalciuria (abnormally high levels of calcium in the urine). It belongs to the families of drugs called antineoplastics and antibiotics. Also called Mithracin.

PLL Prolymphocytic leukemia. A type of chronic lymphocytic leukemia (CLL) in which too many immature white blood cells (prolymphocytes) are found in the blood and bone marrow. PLL usually progresses more rapidly than classic CLL. Also called prolymphocytic leukemia.

ploidy The number of sets of chromosomes in a cell or an organism. For example, haploid means one set and diploid means two sets.

Plummer-Vinson syndrome A disorder marked by anemia caused by iron deficiency, and a web-like growth of membranes in the throat that makes swallowing difficult. Having Plummer-Vinson syndrome may increase the risk of developing esophageal cancer. Also called Paterson-Kelly syndrome and sideropenic dysphagia.

pluripotent Able to mature or develop in any of several ways.

pluripotent stem cell A cell that is able to develop into several different types of cells or tissues in the body.

pM-81 A monoclonal antibody that is being studied in the detection and treatment of cancer. Monoclonal antibodies are produced in the laboratory and can locate and bind to cancer cells.

PN401 A substance that is being studied for its ability to protect against the gastrointestinal side effects caused by fluorouracil. It belongs to the family of drugs called cytoprotective agents. Also called triacetyluridine.

PNET Primitive neuroectodermal tumor. One of a group of cancers that develop from the same type of early cells, and share certain biochemical and genetic features. Some PNETs develop in the brain and central nervous system (CNS-PNET), and others develop in sites outside of the brain such as the limbs, pelvis and chest wall (peripheral PNET). Also called primitive neuroectodermal tumor.

pneumatic larynx A device that is used to help a person talk after a laryngectomy. It uses air to produce a humming sound, which is converted to speech by movement of the lips, tongue or glottis.

pneumonectomy An operation to remove an entire lung.

pneumonia An inflammatory infection that occurs in the lung.

PNH Paroxysmal nocturnal hemoglobinuria. A rare disorder in which red blood cells are easily destroyed by certain immune system proteins. Symptoms include blood clots, and red or brownish urine in the morning. Aplastic anemia (decreased production of blood cells) may lead to PNH, and people with PNH are at increased risk of acute myelogenous leukemia. Also called paroxysmal nocturnal hemoglobinuria.

PNU 166148 A substance that is being studied in the treatment of cancer. It belongs to the family of drugs called topoisomerase inhibitors.

PNU-93914 A form of the anticancer drug paclitaxel that may have fewer side effects and work better than paclitaxel. It is being studied in the treatment of cancer. It belongs to the family of drugs called mitotic inhibitors. Also called LEP-ETU and paclitaxel liposome.

polifeprosan 20 carmustine implant A biodegradable wafer that is used to deliver the anticancer drug carmustine directly into a brain tumor site after the tumor has been removed by surgery. Also called Gliadel Wafer.

poly-ICLC A substance that is being studied in the treatment of cancer and for its ability to stimulate the immune system. It is made in the laboratory by combining the nucleic acid RNA with the chemicals poly-L-lysine and carboxymethyl cellulose.

polycystic ovary syndrome PCOS. A condition marked by infertility, enlarged ovaries, menstrual problems, high levels of male hormones, excess hair on the face and body, acne and obesity. Women with PCOS have an increased risk of diabetes, high blood pressure, heart disease, and endometrial cancer. Also called PCOS.

polycythemia vera A disease in which there are too many red blood cells in the bone marrow and blood, causing the blood to thicken. The number of white blood cells and platelets may also increase. The extra blood cells may collect in the spleen and cause it to become enlarged. They may also cause bleeding problems and make clots form in blood vessels.

polyethylene glycosylated recombinant human megakaryocyte growth and development factor PEG-rhMGDF. A form of megakaryocyte growth and development factor (MGDF) that is made in the laboratory. MGDF comes from the protein thrombopoietin, which is normally made in the body to help make platelets. Polyethylene glycosylated recombinant human megakaryocyte growth and development factor is being studied as a way to increase the number of platelets in patients receiving chemotherapy. Also called PEG-

MGDF and PEG-rhMGDF.

polyglutamate camptothecin A form of the anticancer drug camptothecin that may have fewer side effects and work better than camptothecin. It is being studied in the treatment of cancer. It belongs to the family of drugs called DNA topoisomerase inhibitors. Also called CT-2106.

polymerase chain reaction PCR. A laboratory method used to make many copies of a specific DNA sequence. Also called PCR.

polymorphism A common variation or mutation in DNA.

polymyositis An inflammatory disease of the muscles closest to the center of the body. It causes weakness, inability to stand, climb stairs, lift or reach. It may also cause muscle pain and difficulty swallowing, and may affect the lungs and heart. Having polymyositis increases the risk of certain types of cancer.

polyneuritis Inflammation of several peripheral nerves at the same time.

polyp A growth that protrudes from a mucous membrane.

polypectomy Surgery to remove a polyp.

polyphenol A substance that is found in many plants and gives some flowers, fruits and vegetables their color. Polyphenols have antioxidant activity.

Polyphenon® E A substance that is being studied in the prevention of cancer. It is made from decaffeinated green tea, and contains chemicals called catechins, which are antioxidants. Also called green tea extract.

polyposis The development of numerous polyps (growths that protrude from a mucous membrane).

polysaccharide A type of carbohydrate. It contains sugar molecules that are linked together chemically.

polysomnogram A group of recordings taken during sleep that shows brain wave changes, eye movements, breathing rate, blood pressure, heart rate and the electrical activity of the heart and other muscles. A polysomnogram may be used to help diagnose sleep disorders.

polyvinylpyrrolidone-sodium hyaluronate gel A gel used to lessen pain from mouth sores caused by chemotherapy or radiation therapy, oral surgery, braces or disease. Polyvinylpyrrolidone-sodium hyaluronate gel is being studied in the treatment of pain caused by mouth sores in children receiving cancer treatment. It forms a thin layer over the surface of the mouth and throat to prevent irritation while eating, drinking and talking. Also called Gelclair.

pomegranate Punica granatum. A subtropical shrub or tree. Juice from the fruit may contain substances that decrease or slow the rise of prostate-specific antigen (PSA) levels. It is being studied for its ability to delay or prevent recurrent prostate cancer.

pons Part of the central nervous system, located at the base of the brain, between the medulla oblongata and the midbrain. It is part of the brainstem.

pontine Having to do with the pons (part of the central nervous system, located at the base of the brain, between the medulla oblongata and the midbrain).

porcine Having to do with or coming from pigs.

porfimer sodium A drug used to treat some types of cancer. When absorbed by cancer cells and exposed to light, porfimer sodium becomes active and kills the cancer cells. It belongs to the family of drugs called photodynamic therapy agents. Also called Photofrin.

porfiromycin A substance that is being studied in the treatment of cancer. It belongs to the family of drugs called anticancer antibiotics.

port An implanted device through which blood may be withdrawn and drugs may be infused without repeated needle sticks. Also called a port-a-cath.

port-a-cath An implanted device through which blood may be withdrawn and drugs may be infused without repeated needle sticks. Also called a port.

portal hypertension High blood pressure in the vein that carries blood to the liver from the stomach, small and large intestines, spleen, pancreas and gallbladder. It is usually caused by a block in the blood flow through the liver due to cirrhosis (scarring) of the liver.

portal vein A blood vessel that carries blood to the liver from the stomach, small and large intestines, spleen, pancreas and gallbladder. Also called hepatic portal vein.

positive axillary lymph node A lymph node in the area of the armpit (axilla) to which cancer has spread. This spread is determined by surgically removing some of the lymph nodes and examining them under a microscope to see whether cancer cells are present.

positive test result A test result that reveals the presence of a specific disease or condition for which the test is being done.

positron emission tomography scan PET scan. A procedure in which a small amount of radioactive glucose (sugar) is injected into a vein, and a scanner is used to make detailed, computerized pictures of areas inside the body where the glucose is used. Because cancer cells often use more glucose than normal cells, the pictures can be used to find cancer cells in the body. Also called PET scan.

post-transplant lymphoproliferative disorder PTLD. A condition in which a group of B-cells grow out of control after an organ transplant in patients with weakened immune systems. This usually happens if the patient has also been infected with Epstein-Barr virus. PTLD may progress to non-Hodgkin's lymphoma. Also called PTLD.

post-traumatic stress disorder PTSD. An anxiety disorder that develops in reaction to physical injury or severe mental or emotional distress, such as military combat, violent assault, natural disaster, or other life-threatening events. Having cancer may also lead to PTSD. Symptoms interfere with day-to-day living and include reliving the event in nightmares or flashbacks; avoiding people, places, and things connected to the event; feeling alone and losing interest in daily activities; and having trouble concentrating and sleeping. Also called PTSD.

posterior In human anatomy, has to do with the back of a structure or a structure found toward the back of the body.

posterior pelvic exenteration Surgery to remove the lower part of the bowel, rectum, uterus, cervix, ovaries, fallopian tubes and vagina. Pelvic lymph nodes may also be removed.

posterior urethral cancer A disease in which malignant (cancer) cells are found in the part of the urethra (the tube through which urine leaves the body) that connects to the bladder (the organ that stores urine).

postmenopausal Having to do with the time after menopause. Menopause ("change of life") is the time in a woman's life when menstrual periods stop permanently.

postmortem After death. Often used to describe an autopsy.

postoperative After surgery.

postprandial After a meal.

postremission therapy Anticancer drugs given to kill cancer cells that survive after remission induction therapy.

potassium A metallic element that is important in body functions such as regulation of blood pressure and of water content in cells, transmission of nerve impulses, digestion, muscle contraction and heartbeat.

potassium hydroxide A toxic and highly corrosive chemical used to make soap, in bleaching, and as a paint remover. It is used in small amounts as a food additive and in the preparation of some drugs.

potentiation In medicine, the effect of increasing the potency or effectiveness of a drug or other treatment.

power of attorney A document that gives a person (such as a relative, lawyer, or friend) the authority to make legal or financial decisions for another person. It may become active immediately, or when that person loses the ability to make decisions for himself or herself, depending on how it is written. Also called durable power of attorney and DPA.

pPNET Peripheral primitive neuroectodermal tumor. A type of cancer that forms in bone or soft tissue. Also called peripheral primitive neuroectodermal tumor and Ewing's sarcoma.

PR Progesterone receptor. A protein found inside the cells of the female reproductive tissue, some other types of tissue and some cancer cells. The hormone progesterone will bind to the receptors inside the cells and may cause the cells to grow. Also called progesterone receptor.

PR+ Progesterone receptor positive. Describes cells that have a protein to which the hormone progesterone will bind. Cancer cells that are PR+ need progesterone to grow and will usually stop growing when treated with hormones that block progesterone from binding. Also called progesterone receptor positive.

PR- Progesterone receptor negative. Describes cells that do not have a protein to which the hormone progesterone will bind. Cancer cells that are PR- do not need progesterone to grow, and usually do not stop growing when treated with hormones that block progesterone from binding. Also called progesterone receptor negative.

PR-104 A substance being studied in the treatment of cancer. PR-104 becomes active when cancer cells don't receive enough oxygen. It may kill cancer cells by damaging their DNA.

practitioner A person who works in a specific profession. For example, a doctor or nurse is a healthcare practitioner.

Pravachol A drug that lowers the amount of cholesterol in the blood. It may also make tumor cells more sensitive to anticancer drugs, and is being studied in the treatment of cancer. It belongs to the families of drugs called HMG-CoA reductase inhibitors (statins) and chemosensitizers. Also called pravastatin.

pravastatin A drug that lowers the amount of cholesterol in the blood. It may also make tumor cells more sensitive to anticancer drugs, and is being studied in the treatment of cancer. It belongs to the families of drugs called HMG-CoA reductase inhibitors (statins) and chemosensitizers. Also called Pravachol.

precancerous A term used to describe a condition that may (or is likely to) become cancer. Also called premalignant.

precancerous dermatitis A skin disease marked by scaly or thickened patches on the skin, and often caused by prolonged exposure to arsenic. The patches often occur on sunexposed areas of the skin and in older white men. These patches may become malignant (cancerous). Also called Bowen's disease or precancerous dermatosis.

precancerous dermatosis A skin disease marked by scaly or thickened patches on the skin, and often caused by prolonged exposure to arsenic. The patches often occur on sunexposed areas of the skin and in older white men. These patches may become malignant (cancerous). Also called Bowen's disease or precancerous dermatitis.

precancerous polyps Growths that protrude from a mucous membrane. Precancerous polyps may (or are likely to) become cancer.

preclinical study Research using animals to find out if a drug, procedure or treatment is likely to be useful. Preclinical studies take place before any testing in humans is done.

precursor T-lymphoblastic leukemia A type of leukemia (blood cancer) in which too many T-cell lymphoblasts (immature white blood cells) are found in the blood and bone marrow. Also called T-cell acute lymphoblastic leukemia and T-cell acute lymphocytic leukemia.

precursor T-lymphoblastic lymphoma A type of non-Hodgkin's lymphoma in which too many T-cell lymphoblasts (immature white blood cells) are found in the lymph nodes and spleen. It is most common in young men. Also called T-lymphoblastic lymphoma.

predictive factor A situation or condition that may increase a person's risk of developing a certain disease or disorder.

prednisolone A drug that is used to treat blood cell cancers (leukemias) and lymph system cancers (lymphomas). It belongs to the family of drugs called synthetic corticosteroids.

prednisone A drug that is used to treat several types of cancer and other disorders. Prednisone also inhibits the body's immune response. It belongs to the family of drugs called steroids.

preleukemia A group of diseases in which the bone marrow does not make enough healthy blood cells. Also called myelodysplastic syndromes and smoldering leukemia.

premalignant A term used to describe a condition that may (or is likely to) become cancer. Also called precancerous.

premature ovarian failure A condition in which the ovaries stop working before age 40. Symptoms include hot flashes, mood swings, night sweats, vaginal dryness and infertility. Some cancer treatments, such as chemotherapy, radiation therapy and surgery can cause premature ovarian failure. Ovarian failure caused by cancer treatment may be temporary or permanent and may be treated with hormone replacement therapy. Also called primary ovarian insufficiency or early menopause.

premenopausal Having to do with the time before menopause. Menopause ("change of life") is the time of life when a woman's menstrual periods stop permanently.

premycotic phase A phase of mycosis fungoides in which a patient has areas of red, scaly, itchy skin on areas of the body that are usually not exposed to sun. This is early-phase mycosis fungoides, but it is hard to diagnose the rash as mycosis fungoides during this phase. The premycotic phase may last from months to decades.

prescription A doctor's order for medicine or another intervention.

pretracheal space The area in front of the trachea (windpipe).

prevascular space The area in the front part of the chest between the lungs. Also called anterior mediastinum.

prevention In medicine, action taken to decrease the chance of getting a disease or condition. For example, cancer prevention includes avoiding risk factors (such as smoking, obesity, lack of exercise and radiation exposure) and increasing protective factors (such as getting regular physical activity, staying at a healthy weight and having a healthy diet).

preventive Used to prevent disease.

preventive mastectomy Surgery to reduce the risk of developing breast cancer by removing one or both breasts before disease develops. Also called prophylactic mastectomy.

primary care doctor A doctor who manages a person's health care over time. A primary care doctor is able to give a wide range of care, including prevention and treatment, can discuss cancer treatment choices, and can refer a patient to a specialist.

primary central nervous system lymphoma PCNSL. Cancer that forms in the lymph tissue of the brain, spinal cord, meninges (outer covering of the brain), or eye (called ocular lymphoma). Also called primary CNS lymphoma and PCNSL.

primary CNS lymphoma PCNSL. Cancer that forms in the lymph tissue of the brain, spinal cord, meninges (outer covering of the brain), or eye (called ocular lymphoma). Also called primary central nervous system lymphoma and PCNSL.

primary effusion lymphoma A rare, aggressive (fast-growing) type of B-cell non-Hodgkin’s lymphoma marked by an abnormal build-up of fluids in a body cavity. It usually occurs together with a human herpesvirus in people who have weakened immune systems, such as in AIDS.

primary endpoint The main result that is measured at the end of a study to see if a given treatment worked (e.g., the number of deaths or the difference in survival between the treatment group and the control group). What the primary endpoint will be is decided before the study begins.

primary myelofibrosis A progressive, chronic disease in which the bone marrow is replaced by fibrous tissue and blood is made in organs such as the liver and the spleen, instead of in the bone marrow. This disease is marked by an enlarged spleen and progressive anemia. Also called chronic idiopathic myelofibrosis, agnogenic myeloid metaplasia, myelosclerosis with myeloid metaplasia and idiopathic myelofibrosis.

primary ovarian insufficiency A condition in which the ovaries stop working before age 40. Symptoms include hot flashes, mood swings, night sweats, vaginal dryness and infertility. Some cancer treatments, such as chemotherapy, radiation therapy and surgery can cause primary ovarian insufficiency. Ovarian insufficiency caused by cancer treatment may be temporary or permanent and may be treated with hormone replacement therapy. Also called premature ovarian failure or early menopause.

primary tumor The original tumor.

primitive neuroectodermal tumor PNET. One of a group of cancers that develop from the same type of early cells, and share certain biochemical and genetic features. Some PNETs develop in the brain and central nervous system (CNS-PNET), and others develop in sites outside of the brain such as the limbs, pelvis and chest wall (peripheral PNET). Also called PNET.

prinomastat A substance that is being studied in the treatment of cancer. It is a matrix metalloproteinase inhibitor and belongs to the family of drugs called angiogenesis inhibitors. Also called AG3340.

pro-oxidant A substance that can produce oxygen byproducts of metabolism that can cause damage to cells.

probenecid A drug that is used to treat gout and is used together with some antibiotics to make them work better. It is being studied in the treatment of cancer. It belongs to the family of drugs called antibiotic therapy adjuncts.

procarbazine A drug that is used to treat cancer. It belongs to the family of drugs called alkylating agents.

prochlorperazine A drug used to prevent or reduce nausea and vomiting. It belongs to the family of drugs called antiemetics.

proctitis Inflammation of the mucous membrane that lines the rectum. Also called rectitis.

proctoscopy Examination of the rectum using a proctoscope, inserted into the rectum. A proctoscope is a thin, tube-like instrument with a light and a lens for viewing. It may also have a tool to remove tissue to be checked under a microscope for signs of disease.

proctosigmoidoscopy Examination of the lower colon using a sigmoidoscope, inserted into the rectum. A sigmoidoscope is a thin, tube-like instrument with a light and a lens for viewing. It may also have a tool to remove tissue to be checked under a microscope for signs of disease. Also called sigmoidoscopy.

progeny Offspring; the product of reproduction or replication.

progesterone A type of hormone made by the body that plays a role in the menstrual cycle and pregnancy. Progesterone can also be made in the laboratory. It may be used as a type of birth control and to treat menstrual disorders, infertility, symptoms of menopause and other conditions.

progesterone receptor PR. A protein found inside the cells of the female reproductive tissue, some other types of tissue, and some cancer cells. The hormone progesterone will bind to the receptors inside the cells and may cause the cells to grow. Also called PR.

progesterone receptor negative PR-. Describes cells that do not have a protein to which the hormone progesterone will bind. Cancer cells that are PR- do not need progesterone to grow, and usually do not stop growing when treated with hormones that block progesterone from binding. Also called PR-.

progesterone receptor positive PR+. Describes cells that have a protein to which the hormone progesterone will bind. Cancer cells that are PR+ need progesterone to grow and will usually stop growing when treated with hormones that block progesterone from binding. Also called PR+.

progesterone receptor test A lab test to find out if cancer cells have progesterone receptors (proteins to which the hormone progesterone will bind). If the cells have progesterone receptors, they may need progesterone to grow, and this can affect how the cancer is treated.

progestin Any natural or laboratory-made substance that has some or all of the biologic effects of progesterone, a female hormone.

prognosis The likely outcome or course of a disease; the chance of recovery or recurrence.

prognostic factor A situation or condition, or a characteristic of a patient, that can be used to estimate the chance of recovery from a disease or the chance of the disease recurring (coming back).

programmed cell death A type of cell death in which a series of molecular steps in a cell leads to its death. This is the body's normal way of getting rid of unneeded or abnormal cells. The process of programmed cell death may be blocked in cancer cells. Also called apoptosis.

progression Increase in the size of a tumor or spread of cancer in the body.

progression-free survival One type of measurement that can be used in a clinical study or trial to help determine whether a new treatment is effective. It refers to the probability that a patient will remain alive without the disease getting worse.

progressive disease Cancer that is growing, spreading or getting worse.

proliferating Multiplying or increasing in number. In biology, cell proliferation occurs by a process known as cell division.

proliferative index A measure of the number of cells in a tumor that are dividing (proliferating). May be used with the S-phase fraction to give a more complete understanding of how fast a tumor is growing.

prolymphocytic leukemia PLL. A type of chronic lymphocytic leukemia (CLL), in which too many immature white blood cells (prolymphocytes) are found in the blood and bone marrow. PLL usually progresses more rapidly than classic CLL. Also called PLL.

promegapoietin A drug given during chemotherapy to increase blood cell regeneration. Promegapoietin is a colony-stimulating factor that stimulates the production of blood cells, especially platelets. It is a cytokine and belongs to the family of drugs called hematopoietic (blood-forming) agents.

ProMune A substance that is being studied in the treatment of some types of cancer. It belongs to the family of drugs called biological response modifiers. Also called CpG 7909 and PF-3512676.

promyelocytic leukemia An aggressive (fast-growing) type of acute myeloid leukemia in which there are too many immature blood-forming cells in the blood and bone marrow. It is usually marked by an exchange of parts of chromosomes 15 and 17. Also called acute promyelocytic leukemia and APL.

prophylactic In medicine, something that prevents or protects.

prophylactic cranial irradiation Radiation therapy to the head to reduce the risk that cancer will spread to the brain.

prophylactic mastectomy Surgery to reduce the risk of developing breast cancer by removing one or both breasts before disease develops. Also called preventive mastectomy.

prophylactic oophorectomy Surgery intended to reduce the risk of ovarian cancer by removing the ovaries before disease develops.

prophylactic surgery Surgery to remove an organ or gland that shows no signs of cancer, in an attempt to prevent development of cancer of that organ or gland. Prophylactic surgery is sometimes chosen by people who know they are at high risk for developing cancer.

prophylaxis An attempt to prevent disease.

prospective In medicine, a study or clinical trial in which participants are identified and then followed forward in time.

prospective cohort study A research study that follows over time groups of individuals who are alike in many ways but differ by a certain characteristic (for example, female nurses who smoke and those who do not smoke) and compares them for a particular outcome (such as lung cancer).

Prost 30 A monoclonal antibody that is being studied in the detection and treatment of cancer. Monoclonal antibodies are produced in the laboratory and can locate and bind to cancer cells.

prostate A gland in the male reproductive system. The prostate surrounds the part of the urethra (the tube that empties the bladder) just below the bladder, and produces a fluid that forms part of the semen.

prostate cancer Cancer that forms in tissues of the prostate (a gland in the male reproductive system found below the bladder and in front of the rectum). Prostate cancer usually occurs in older men.

prostate-specific antigen PSA. A substance produced by the prostate that may be found in an increased amount in the blood of men who have prostate cancer, benign prostatic hyperplasia or infection or inflammation of the prostate. Also called PSA.

prostate-specific antigen test A blood test that measures the level of prostate-specific antigen (PSA), a substance produced by the prostate and some other tissues in the body. Increased levels of PSA may be a sign of prostate cancer.

prostatectomy An operation to remove part or all of the prostate. Radical (or total) prostatectomy is the removal of the entire prostate and some of the tissue around it.

prostatic acid phosphatase PAP. An enzyme produced by the prostate. It may be found in increased amounts in men who have prostate cancer. Also called PAP.

prostatic intraepithelial neoplasia PIN. Noncancerous growth of the cells lining the internal and external surfaces of the prostate gland. Having high-grade PIN may increase the risk of developing prostate cancer. Also called PIN.

prostatitis Inflammation of the prostate gland.

prostatocystectomy Surgery to remove the bladder (the organ that holds urine), the seminal vesicles, and the prostate. The seminal vesicles and prostate are glands in the male reproductive system that help make semen. Also called cystoprostatectomy.

prosthesis A device such as an artificial leg that replaces a part of the body.

prosthodontist A dentist who specializes in replacing missing teeth or other structures of the mouth to restore an individual's appearance, comfort or health.

prostration A condition in which a person is so tired or weak that he or she is unable to do anything.

protease inhibitor A compound that interferes with the ability of certain enzymes to break down proteins. Some protease inhibitors can keep a virus from making copies of itself (for example, AIDS virus protease inhibitors), and some can prevent cancer cells from spreading.

proteasome inhibitor A drug that blocks the action of proteasomes. A proteasome is a large protein complex that helps destroy other cellular proteins when they are no longer needed. Proteasome inhibitors are being studied in the treatment of cancer.

protective factor Something that may decrease the chance of getting a certain disease. Some examples of protective factors for cancer are getting regular physical activity, staying at a healthy weight and having a healthy diet.

protein A molecule made up of amino acids that are needed for the body to function properly. Proteins are the basis of body structures such as skin and hair and of substances such as enzymes, cytokines and antibodies.

protein kinase C PKC. An enzyme found throughout the body's tissues and organs. Several forms of PKC are involved in many cellular functions. PKC is being studied in the treatment of cancer. Also called PKC.

protein-bound paclitaxel A drug used to treat breast cancer that has spread or that has come back within 6 months after chemotherapy. It is also being studied in the treatment of newly diagnosed breast cancer and other types of cancer. Protein-bound paclitaxel belongs to the family of drugs called mitotic inhibitors. Also called nanoparticle paclitaxel, Paclitaxel (albumin-stabilized nanoparticle formulation), Abraxane and ABI-007.

proteoglycan A molecule that contains both protein and glycosaminoglycans, which are a type of polysaccharide. Proteoglycans are found in cartilage and other connective tissues.

proteomic profile An evaluation of proteins in a sample of blood. This may help detect early cancer or cancer recurrence, or help predict response to treatment.

proteomics The study of the structure and function of proteins, including the way they work and interact with each other inside cells.

protocol An action plan for a clinical trial. The plan states what the study will do, how, and why. It explains how many people will be in it, who is eligible to participate, what study agents or other interventions they will be given, what tests they will receive and how often and what information will be gathered.

proton A small, positively charged particle of matter found in the atoms of all elements. Streams of protons generated by special equipment can be used for radiation treatment.

proton beam radiation therapy A type of radiation therapy that uses protons generated by a special machine. A proton is a type of high-energy radiation that is different from an X-ray.

proton magnetic resonance spectroscopic imaging A noninvasive imaging method that provides information about cellular activity (metabolic information). It is used along with magnetic resonance imaging (MRI) which provides information about the shape and size of the tumor (spacial information). Also called magnetic resonance spectroscopic imaging and 1H-nuclear magnetic resonance spectroscopic imaging.

protozoal Having to do with the simplest organisms in the animal kingdom. Protozoa are single-cell organisms, such as amoeba, and are different from bacteria, which are not members of the animal kingdom. Some protozoa can be seen without a microscope.

proximal In medicine, refers to a part of the body that is closer to the center of the body than another part. For example, the knee is proximal to the toes. The opposite is distal.

Proxinium A substance being studied in the treatment of certain types of head and neck cancer. Proxinium is made by linking a monoclonal antibody fragment to a toxic protein that may kill cancer cells. It binds to EpCAM (a protein on the surface of epithelial cells and some types of cancer cells). Also called anti-EpCAM-Pseudomonas-exotoxin fusion protein and VB4-845.

pruritus Itching. Severe itching may be a side effect of some cancer treatments and a symptom of some types of cancers.

PS-341 A drug used to treat multiple myeloma that has gotten worse during treatment with other anticancer drugs. It is also used to treat mantle cell lymphoma in patients who have already received at least one other type of treatment. PS-341 is also being studied in the treatment of other types of cancer. It is a type of proteasome inhibitor and dipeptidyl boronic acid. Also called bortezomib and Velcade.

PSA Prostate-specific antigen. A substance produced by the prostate that may be found in an increased amount in the blood of men who have prostate cancer, benign prostatic hyperplasia or infection or inflammation of the prostate. Also called prostate-specific antigen.

psammoma body A structure found in some benign (noncancerous) or malignant (cancerous) tumor cells. Psammoma bodies look like hardened concentric rings when viewed under a microscope. They can be a sign of chronic inflammation.

PSC 833 A substance that is being studied for its ability to prevent or overcome the resistance of tumor cells to some anticancer drugs. It belongs to the family of drugs called cyclosporine analogs.

pseudomyxoma peritonei A build-up of mucus in the peritoneal cavity. The mucus may come from ruptured ovarian cysts, the appendix or from other abdominal tissues, and mucus-secreting cells may attach to the peritoneal lining and continue to secrete mucus.

psoralen A substance from plants that is sensitive to light (or can be activated by light). Psoralens are used together with UV light to treat psoriasis, vitiligo and skin nodules of cutaneous T-cell lymphoma. They are also being studied in the treatment of graft-versus-host disease. They belong to the family of drugs called furocoumarins. An example of a psoralen is methoxsalen.

psoralen and ultraviolet A therapy PUVA therapy. A type of photodynamic therapy used to treat skin conditions such as psoriasis, vitiligo, and skin nodules of cutaneous T-cell lymphoma. The patient receives psoralen (a drug that becomes active when it is exposed to light) by mouth or applied to the skin, followed by ultraviolet A radiation. PUVA therapy may increase the risk of getting skin cancer. Also called PUVA therapy.

psoriasis A chronic disease of the skin marked by red patches covered with white scales.

psychiatrist A medical doctor who specializes in the prevention, diagnosis and treatment of mental, emotional and behavioral disorders.

psychological Having to do with how the mind works and how thoughts and feelings affect behavior.

psychologist A specialist who can talk with patients and their families about emotional and personal matters, and can help them make decisions.

psychosis A severe mental disorder in which a person loses the ability to recognize reality or relate to others. The person is not able to cope with the demands of everyday life. Symptoms include being paranoid, having false ideas about what is taking place or who one is, and seeing, hearing or feeling things that are not there.

psychostimulant A drug that causes a sense of well-being, decreases fatigue and depression and increases the desire to eat. These drugs can also cause mood changes and trouble with sleeping.

psychotherapy Treatment of mental, emotional, personality and behavioral disorders using methods such as discussion, listening and counseling. Also called talk therapy.

PT-100 A substance being studied in the treatment of cancer, including certain types of lung, pancreas and brain cancer. PT-100 may help the immune system block the growth of cancer cells. It may also increase the growth of new blood cells. It is a type of enzyme inhibitor. Also called talabostat and talabostat mesylate.

PTC Percutaneous transhepatic cholangiography (per-kyoo-TAN-ee-us trans-heh-PAT-ik ko-LAN-jee-AH-gra-fee). A procedure to X-ray the hepatic and common bile ducts. A contrasting agent is injected into the liver or bile duct, and the ducts are then X-rayed to find the point of obstruction. Also called percutaneous transhepatic cholangiography.

PTCD Percutaneous transhepatic cholangiodrainage. A procedure to drain bile to relieve pressure in the bile ducts caused by a blockage. An X-ray of the liver and bile ducts locates the blockage of bile flow. Images made by ultrasound guide placement of a stent (tube), which remains in the liver. Bile drains through the stent into the small intestine or into a collection bag outside the body. This procedure may relieve jaundice before surgery. Also called percutaneous transhepatic biliary drainage and percutaneous transhepatic cholangiodrainage.

PTH A substance made by the parathyroid gland that helps the body store and use calcium. A higher-than-normal amount of PTH causes high levels of calcium in the blood and may be a sign of disease. Also called parathormone, parathyrin and parathyroid hormone.

PTK787/ZK 222584 A substance that is being studied in the treatment of cancer. It belongs to the families of drugs called protein tyrosine kinase inhibitors and VEGF receptor kinase inhibitors. Also called vatalanib.

PTLD Post-transplant lymphoproliferative disorder. A condition in which a group of B-cells grow out of control after an organ transplant in patients with weakened immune systems. This usually happens if the patient has also been infected with Epstein-Barr virus. PTLD may progress to non-Hodgkin's lymphoma. Also called post-transplant lymphoproliferative disorder.

ptosis Drooping of the upper eyelid.

PTSD Post-traumatic stress disorder. An anxiety disorder that develops in reaction to physical injury or severe mental or emotional distress, such as military combat, violent assault, natural disaster, or other life-threatening events. Having cancer may also lead to PTSD. Symptoms interfere with day-to-day living and include reliving the event in nightmares or flashbacks; avoiding people, places, and things connected to the event; feeling alone and losing interest in daily activities; and having trouble concentrating and sleeping. Also called post-traumatic stress disorder.

puberty The time of life when a child experiences physical and hormonal changes that mark a transition into adulthood. The child develops secondary sexual characteristics and becomes able to have children. Secondary sexual characteristics include growth of pubic, armpit, and leg hair; breast enlargement; and increased hip width in girls. In boys, they include growth of pubic, face, chest and armpit hair; voice changes; penis and testicle growth and increased shoulder width.

pulmonary Having to do with the lungs.

pulmonary rehabilitation education Education about behavior and lifestyle changes to help patients with chronic lung disease decrease breathing problems, return to daily activities, and improve quality of life. Education may include instruction about breathing exercises, nutrition, use of medicines and ways for the patient to reduce stress and save energy.

pulmonary sulcus tumor A type of lung cancer that begins in the upper part of a lung and spreads to nearby tissues such as the ribs and vertebrae. Most pulmonary sulcus tumors are non-small cell cancers. Also called Pancoast tumor.

pulmonologist A doctor who specializes in treating diseases of the lungs.

pump A device that is used to give a controlled amount of a liquid at a specific rate. For example, pumps are used to give drugs (such as chemotherapy or pain medicine) or nutrients.

punch biopsy Removal of a small disk-shaped sample of tissue using a sharp, hollow device. The tissue is then examined under a microscope.

Purinethol A drug used to treat acute lymphatic leukemia. It belongs to the family of drugs called antimetabolites. Also called mercaptopurine.

purple clover Trifolium pratense. A plant with flowers that has been used in some cultures to treat certain medical problems. It is being studied in the relief of menopausal symptoms and may have anticancer effects. Also called red clover, wild clover and Trifolium pratense.

purple coneflower An herb native to North America that has been used to prevent and treat the common cold and other respiratory infections. Purple coneflower may interfere with treatment that uses the immune system to fight cancer. The scientific names are Echinacea purpurea and Echinacea angustifolia. Also called echinacea.

PUVA therapy Psoralen and ultraviolet A therapy. A type of photodynamic therapy used to treat skin conditions such as psoriasis, vitiligo, and skin nodules of cutaneous T-cell lymphoma. The patient receives psoralen (a drug that becomes active when it is exposed to light) by mouth or applied to the skin, followed by ultraviolet A radiation. PUVA therapy may increase the risk of getting skin cancer. Also called psoralen and ultraviolet A therapy.

PV701 A virus that is being studied in the treatment of cancer. It belongs to the family of viruses that cause Newcastle disease in birds.

PXD101 A substance being studied in the treatment of certain blood diseases, blood cancers, and other types of cancer. PXD101 may block the growth of tumors and the growth of blood vessels from surrounding tissue to the tumor. It may also make tumor cells more sensitive to other anticancer drugs. PXD101 is a type of histone deacetylase (HDAC) inhibitor and angiogenesis inhibitor.

pyrazine diazohydroxide A substance that is being studied in the treatment of cancer.

pyrazoloacridine A substance that is being studied in the treatment of cancer. It belongs to the family of drugs called acridines.

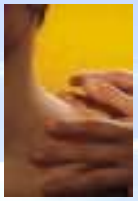
pyridoxine A key nutrient that the body needs to break down proteins, carbohydrates, and fats in food for healthy blood, skin, and nerves. It is found in many foods, including meats, bananas, legumes, eggs and whole grains. Pyridoxine is being studied in the prevention of hand-foot syndrome (a disorder sometimes caused by certain anticancer drugs). Hand-foot syndrome is marked by pain, swelling, numbness, tingling or redness of the hands or feet. Also called vitamin B6.

pyroxamide A substance that is being studied in the treatment of cancer. It belongs to the family of drugs called histone deacetylase inhibitors.

Research • Education • Clinical Delivery

Inside Integrative Medicine





A Newsletter for Staff, Participants and Friends of Integrative Medicine & Place … of wellness February/March 2010

Benefits of Dark Chocolate

"The great news this Valentine's Day is that in addition to being decadent and delicious, moderate amounts of dark chocolate may play a role in cancer prevention," said Sally Scroggs, M.S., R.D., L.D., health education manager at The University of Texas M. D. Anderson Cancer Center's Cancer Prevention Center.

Recent research indicates that dark chocolate's chemicals, which act as antioxidants, have been shown to play a role in reducing cancer risks by helping to combat cell damage that can lead to tumor growth. These antioxidants occur naturally in the plant-based cacao bean, the base of all chocolate products. Cacao beans are, in fact, one of the most concentrated natural sources of antioxidants that exist.

"Dark chocolate has a higher percentage of healthy antioxidants, without the increased sugar and saturated fats added to milk chocolate," Scroggs said.

Chocolate has been a favorite food for centuries, according to the American Dietetic Association. "It has become a symbol for love, indulgence, temptation and now, we can justify it for its health attributes," Scroggs said.

"The main reason that eating dark chocolate, versus milk or white chocolate, reduces cancer risks is because it has a higher percentage of cacao, and thus antioxidants," Scroggs said.

As the cacao content goes up, there also is less room for sugar. According to the American Institute for Cancer Research, people should aim for pure dark chocolate that contains at least 65 percent cacao, as opposed to the kind of chocolate commonly used in cakes and cookies, which contain more calories, sugar and unhealthy fats.

When eating chocolate, looking at portion size and calorie content also is crucial. Recommended servings for dark chocolate are seven ounces per week, which is about one ounce per day.

"Savoring a small amount of dark chocolate is much better than gulping soft drinks or eating doughnuts," Scroggs said.

"Remember, dark chocolate is still a calorie-dense food that can be high in fat. You can enjoy it daily as part of a balanced diet, as long as you keep your portion size in check."

Dark Chocolate Gift Guide

- Choose dark chocolate with at least 65 percent cacao.
- Buy chocolate that can be eaten in small portions, such as individually wrapped 1 oz per servings
- Check the ingredients. Make sure they don't contain fats, such as palm and coconut oils, and they are made without the use of 'hydrogenated' or 'partially hydrogenated' oils.

For additional information, visit Focused on Health

New at Place … of wellness

New Aromatherapy Video Available

Aromatherapy is the use of essential oils to achieve psychological and physical benefits.

Learn more about the safe uses and possible benefits of aromatherapy from a new video on demand.

This video and others are available on M. D. Anderson's iTunes account now and will be available at mdanderson.org/placeofwellness soon.

Exercise 101Returns to PW

If you have questions about starting a fitness program safely or how to restart your exercise plan, join us for Exercise 101 returning to the program schedule starting in March.

This is a fun and fact-filled class designed to teach cancer survivors the principles needed to establish and participate in a fitness program. Wear loose clothing and sturdy shoes as part of the class includes demonstration with class participation

> ***"You can't do anything about the length of your life, but you can do something about its width and depth."***
>
> Evan Esar

Dark Chocolate Drizzled Pears

4 small pears
4 ounces dark chocolate (preferably at least 70 percent cacao), finely chopped

Melt chocolate in a heatproof bowl set over simmering water, stirring until smooth. Let cool slightly.

Remove the core from the bottom of each pear, leaving stem at top intact. Dip each pear in the melted dark chocolate or drizzle from the top. Place coated pears on a parchment-lined dish and refrigerate until the chocolate sets (15 minutes up to 2 hours). Bring to room temperature before serving.

As always, please be mindful of any food allergies or dietary restrictions you may have. Please consult with your medical provider if you have any questions.

Effects of Chlorophyllin

Reprinted with permission from Natural Standard.com

A laboratory study suggests that a compound derived from chlorophyll, the green pigment in most plants, may hold promise for treating colon cancer.

Researchers at the Linus Pauling Institute at Oregon State University examined the activity of chlorophyllin, a water-soluble derivative of chlorophyll. They found that, on a dose-by-dose basis, it was 10 times more effective at killing colon cancer cells than the chemotherapy drug hydroxyurea.

The researchers also reported that chlorophyllin caused colon cancer cells to spend more time than normal in their "synthesis phase," in which DNA is duplicated. This disruption started a process that ultimately led to cell death. Like hydroxyurea, cholorophyllin greatly reduced the level of ribonucleotide reductase, an enzyme important to DNA synthesis.

More research is needed in laboratory and animal studies before human trials could begin. Chlorophyllin is not well absorbed from the human gastrointestinal tract, so it is not clear what levels might be needed for therapeutic purposes or how well they would work.

For more information about chlorophyllin, please visit Natural Standard's Foods, Herbs & Supplements database.

Chimploy K, Díaz GD, Li Q, et al. E2F4 and ribonucleotide reductase mediate S-phase arrest in colon cancer cells treated with chlorophyllin. Int J Cancer. 2009 Nov 1;125(9):2086-94. View Abstract

Anticancer Effects of Pomegranate

Reprinted with permission from Natural Standard.com

Phytochemicals in pomegranate may suppress aromatase, an enzyme that converts androgen into estrogen and that has been implicated in hormone-receptor-positive breast cancer, researchers report.

Aromatase inhibitors, such as anastrozole (Arimidex®), exemestane (Aromasin®) and letrozole (Femara®), are sometimes prescribed to postmenopausal women with hormone-receptor-positive breast cancer. Estrogen promotes the growth of these cancer cells, but aromatase inhibitors lower estrogen levels in the body.

Pomegranate is rich in vitamin C and antioxidants, and some early evidence suggests that it may have preventative effects against prostate cancer.

The researchers tested 10 ellagitannin-derived phytochemicals from pomegranates in cultured breast cancer cells. They found that all 10 compounds, particularly urolithin B, inhibited breast cancer cell growth.

Although promising, these findings are preliminary, and it is unclear if similar beneficial effects would be observed in animal or human trials. Patients are encouraged to talk with their healthcare providers before trying any new therapies.

Pomegranate juice is also commonly used to help prevent atherosclerosis; however, evidence of effectiveness is inconclusive in this area. Early research also suggests that pomegranate may be beneficial as a treatment for erectile dysfunction and high cholesterol. However, more data are needed before a conclusion can be made.

Adams LS, Zhang Y, Seeram NP, et al. Pomegranate ellagitannin-derived compounds exhibit antiproliferative and antiaromatase activity in breast cancer cells in vitro. Cancer Prev Res (Phila Pa). 2010 Jan;3(1):108-13. View Abstract

Natural Standard: The Authority on Integrative Medicine. www.naturalstandard.com

Integrative Medicine Program Lecture Series

February 18, 2010 – **Biobehavioral Mechanisms and Tumor Progression in Ovarian Cancer**
Susan K. Lutgendorf, PhD, Professor, Department of Psychology, Obstetrics and Gynecology, and Urology
Member of Holden Comprehensive Cancer Center, Fellow of the Academy of Behavioral Science, University of Iowa
Iowa City, IA

March 18, 2010 – **Current Issues and Trends in the Field of Herbal Dietary Supplements: Market Data, Regulation and Research**
Mark Blumenthal, Founder and Executive Director, American Botanical Council (ABC), Editor/Publisher of HerbalGram, Austin, TX

Lectures take place at 12:00 – 1:00 p.m. in Hickey Auditorium (R11.1400). For more information about the lecture series, please visit the Complementary/Integrative Medicine Education Resources website at www.mdanderson.org/CIMER

Missed a lecture? Selected lectures from the IM Lecture Series are now are available on DVD at The Learning Center.

THE UNIVERSITY OF TEXAS MD ANDERSON CANCER CENTER
Making Cancer History®

Integrative Medicine Center
1515 Holcombe, Unit 16 Houston, TX 77030
mdanderson.org/departments/intmedprogram 713-794-4700

Best Hospitals 2011-12: the Honor Roll

For clinical excellence, these 17 hospitals possess a rare blend of breadth and depth

By U.S. News Staff

July 18, 2011

A place on the Best Hospitals Honor Roll is reserved for medical centers that demonstrate unusually high expertise across multiple specialties, scoring at or near the top in at least six of 16 specialties. Just 17 of the nearly 5,000 hospitals evaluated for the 2011-12 rankings qualified. Hospitals with the highest scores in a given specialty received 2 Honor Roll points; those with slightly lower scores received 1 point.* Honor Roll standing was determined by the total number of Honor Roll points across all 16 specialties.

Rank	Hospital	Points	Specialties
1	Johns Hopkins Hospital, Baltimore	30	15
2	Massachusetts General Hospital, Boston	29	15
3	Mayo Clinic, Rochester, Minn.	28	15
4	Cleveland Clinic	26	13
5	Ronald Reagan UCLA Medical Center, Los Angeles	25	14
6	New York-Presbyterian University Hospital of Columbia and Cornell, N.Y.	22	12
7	UCSF Medical Center, San Francisco	20	11
8	Brigham and Women's Hospital, Boston	18	12
9	Duke University Medical Center, Durham, N.C.	18	10
10	Hospital of the University of Pennsylvania, Philadelphia	17	12
11	Barnes-Jewish Hospital/Washington University, St. Louis	16	11
12	UPMC-University of Pittsburgh Medical Center	14	8
13	University of Washington Medical Center, Seattle	13	9
14	University of Michigan Hospitals and Health Centers, Ann Arbor	10	6
14	Vanderbilt University Medical Center, Nashville	10	6
16	Mount Sinai Medical Center, New York	8	6
17	Stanford Hospital and Clinics, Stanford, Calif.	7	6

* 2 points for scores 4 or more standard deviations above the mean, 1 point for scores from 3 to 4 standard deviations above the mean.

See rankings in all 16 specialties:

- Cancer
- Cardiology & Heart Surgery
- Diabetes & Endocrinology
- Ear, Nose & Throat
- Gastroenterology
- Geriatrics
- Gynecology
- Nephrology
- Neurology & Neurosurgery
- Ophthalmology
- Orthopedics
- Psychiatry
- Pulmonology
- Rehabilitation
- Rheumatology
- Urology

Tags: hospitals

U.S. Department of Health & Human Services

U.S. Food & Drug Administration

For Consumers

Fast Track, Accelerated Approval and Priority Review

Accelerating Availability of New Drugs for Patients with Serious Diseases

Speeding the development and availability of drugs that treat serious diseases are in everyone's interest, especially when the drugs are the first available treatment or have advantages over existing treatments. The Food and Drug Administration (FDA) has developed three distinct and successful approaches to making such drugs available as rapidly as possible: *Priority Review, Accelerated Approval, and Fast Track*. Because each of these approaches implies speed, there can be confusion about the specific meaning of each and the distinctions among them.

The following summary describes each element, how they differ, and how they complement each other.

Fast Track

Fast track is a **process** designed to facilitate the development, and expedite the review of drugs to treat serious diseases **and** fill an unmet medical need. The purpose is to get important new drugs to the patient earlier. *Fast Track* addresses a broad range of serious diseases.

Determining whether a disease is *serious* is a matter of judgment, but generally is based on whether the drug will have an impact on such factors as survival, day-to-day functioning, or the likelihood that the disease, if left untreated, will progress from a less severe condition to a more serious one. AIDS, Alzheimer's, heart failure and cancer are obvious examples of serious diseases. However, diseases such as epilepsy, depression and diabetes are also considered to be serious diseases.

Filling an *unmet medical need* is defined as providing a therapy where none exists or providing a therapy which may be potentially superior to existing therapy.

Any drug being developed to treat or prevent a disease with no current therapy obviously is directed at an unmet need. If there are existing therapies, a fast track drug must show some advantage over available treatment, such as:

- Showing superior effectiveness
- Avoiding serious side effects of an available treatment
- Improving the diagnosis of a serious disease where early diagnosis results in an improved outcome
- Decreasing a clinically significant toxicity of an accepted treatment

A drug that receives *Fast Track* designation is eligible for some or all of the following:

- More frequent meetings with FDA to discuss the drug's development plan and ensure collection of appropriate data needed to support drug approval
- More frequent written correspondence from FDA about such things as the design of the proposed clinical trials
- Eligibility for *Accelerated Approval,* i.e., approval on an effect on a surrogate, or substitute endpoint reasonably likely to predict clinical benefit
- *Rolling Review*, which means that a drug company can submit completed sections of its New Drug Application (NDA) for review by FDA, rather than waiting until every section of the application is completed before the entire application can be reviewed. NDA review usually does not begin until the drug company has submitted the entire application to the FDA, and
- Dispute resolution if the drug company is not satisfied with an FDA decision not to grant Fast Track status.

In addition, most drugs that are eligible for Fast Track designation are likely to be considered appropriate to receive a *Priority Review*. *Fast Track* designation must be requested by the drug company. The request can be initiated at any time during the drug development process. FDA will review the request and make a decision within
sixty days based on whether the drug fills an unmet medical need in a serious disease.

Once a drug receives *Fast Track* designation, early and frequent communication between the FDA and a drug company is encouraged throughout the entire drug development and review process. The frequency of communication assures that questions and issues are resolved quickly, often leading to earlier drug approval and access by patients.

Accelerated Approval

When studying a new drug, it can take a long time - sometimes many years - to learn whether a drug actually provides real improvement for patients – such as living longer or feeling better. This real improvement is known as a "clinical outcome." Mindful of the fact that obtaining data on clinical outcomes can take a long time, in 1992 FDA instituted the *Accelerated Approval* regulation, allowing earlier approval of drugs to treat serious diseases, and that fill an unmet medical need based on a surrogate endpoint.

A surrogate endpoint is a marker - a laboratory measurement, or physical sign - that is used in clinical trials as an indirect or substitute

measurement that represents a clinically meaningful outcome, such as survival or symptom improvement. The use of a surrogate endpoint can considerably shorten the time required prior to receiving FDA approval.

Approval of a drug based on such endpoints is given on the condition that post marketing clinical trials verify the anticipated clinical benefit.

The FDA bases its decision on whether to accept the proposed surrogate endpoint on the scientific support for thatendpoint. The studies that demonstrate the effect of the drug on the surrogate endpoint must be "adequate and well controlled" studies, the only basis under law, for a finding that a drug is effective.

Use of a surrogate can save valuable time in the drug approval process. For example, instead of having to wait to learn if a drug actually can extend the survival of cancer patients, the FDA might now approve a drug based on evidence that the drug shrinks tumors because tumor shrinkage is considered *reasonably likely to predict* a real clinical benefit. In this example, an approval based upon tumor shrinkage can occur far sooner than waiting to learn whether patients actually lived longer. The drug company will still need to conduct studies to confirm that tumor shrinkage actually does predict that patients will live longer. These studies are known as phase 4 confirmatory trials.

If the confirmatory trial shows that the drug actually provides a clinical benefit, then the FDA grants traditional approval for the drug. If the confirmatory trial does not show that the drug provides clinical benefit for patients, FDA has regulatory procedures in place that could lead to removing the drug from the market.

Priority Review

Prior to approval, each drug marketed in the United States must go through a detailed FDA review process. In 1992, under the Prescription Drug User Act (PDUFA), FDA agreed to specific goals for improving the drug review time and created a two-tiered system of review times – *Standard Review* and *Priority Review*.

Standard Review is applied to a drug that offers at most, only minor improvement over existing marketed therapies. The 2002 amendments to PDUFA set a goal that a *Standard Review* of a new drug application be accomplished within a *ten-month* time frame.

A *Priority Review* designation is given to drugs that offer major advances in treatment, or provide a treatment where no adequate therapy exists. A *Priority Review* means that the time it takes FDA to review a new drug application is reduced. The goal for completing a Priority Review is *six months*.

Priority Review status can apply both to drugs that are used to treat serious diseases and to drugs for less serious illnesses. The FDA goal for reviewing a drug with Priority Review status is six months.

The distinction between priority and standard review times is that additional FDA attention and resources will be directed to drugs that have the potential to provide significant advances in treatment.
Such advances can be demonstrated by, for example:

- evidence of increased effectiveness in treatment, prevention, or diagnosis of disease;
- elimination or substantial reduction of a treatment-limiting drug reaction;
- documented enhancement of patient willingness or ability to take the drug according to the required schedule and dose; or
- evidence of safety and effectiveness in a new subpopulation, such as children.

A request for *Priority Review* must be made by the drug company. It does not affect the length of the clinical trial period. FDA determines within 45 days of the drug company's request whether a *Priority* or *Standard Review* designation will be assigned. Designation of a drug as "Priority" does not alter the scientific/medical standard for approval or the quality of evidence necessary.

SUMMARY

Fast Track, *Accelerated Approval* and *Priority Review* are approaches that are intended to make therapeutically important drugs available at an earlier time. They do not compromise the standards for the safety and effectiveness of the drugs that become available through this process.

These revitalized FDA drug review approaches have yielded tangible results in bringing safe and effective drugs to patients with serious diseases more quickly. For example, since 1996, 68 drugs for cancer therapies have received priority review and approval.

FDA reviewed Gleevec, a treatment for chronic myeloid leukemia, in four months. Shortened review times have also brought promising treatments to patients with HIV/AIDS more quickly. Kaletra for the treatment of HIV/AIDS was reviewed and approved in 3.5 months. Pegasys, a combination product for the treatment of Hepatitis C was approved for marketing in 4 months.

The table below illustrates the improvement in FDA review times in the years between 1993 to 2003. The median time required to review a priority review drug was reduced from 13.9 months to 6.7 months.

Fast Track, *Accelerated Approval*, and *Priority Review* have evolved over time. FDA has been vigilant in assuring that reducing the time necessary for drug development has not compromised the safety and effectiveness of drugs for patients with serious diseases.

Comparison of Approval Times for Priority and Standard Review Drugs

Calendar Years 1993-2003

	Priority		Standard	
Calendar Year	Number Approved	Median FDA Review Time (months)	Number Approved	Median FDA Review Time (months)
1993	13	13.9	12	27.2
1994	13	15.0	9	22.2
1995	9	6.0	19	15.9
1996	18	7.7	35	14.6
1997	9	6.4	30	14.4
1998	16	6.2	14	12.3
1999	19	6.3	16	14.0
2000	9	6.0	18	15.4
2001	7	6.0	17	15.7
2002	7	13.8	10	12.5
2003	9	6.7	12	13.8

U.S. Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993
Ph. 1-888-INFO-FDA (1-888-463-6332)

Disclaimer

INTEGRATIVE MEDICINE

Our Expertise

Therapies, Classes & Workshops

About Herbs, Botanicals & Other Products

Search About Herbs

Herbs, Botanicals & Other Products: FAQs

E-mail Us

For Older Patients

Our Research

Our Clinical Trials

Additional Resources

Bendheim Integrative Medicine Center

This Web site — *Information About Herbs, Botanicals and Other Products* — is for general health information only. This Web site is not to be used as a substitute for medical advice, diagnosis or treatment of any health condition or problem. Users of this Web site should not rely on information provided on this Web site for their own health problems. Any questions regarding your own health should be addressed to your own physician or other healthcare provider.

Memorial Sloan-Kettering Cancer Center makes no warranties nor express or implied representations whatsoever regarding the accuracy, completeness, timeliness, comparative or controversial nature, or usefulness of any information contained or referenced on this Web site. Memorial Sloan-Kettering does not assume any risk whatsoever for your use of this website or the information contained herein. Health-related information changes frequently and therefore information contained on this Web site may be outdated, incomplete or incorrect. Statements made about products have not been evaluated by the Food and Drug Administration. Use of this Web site does not create an expressed or implied physician-patient relationship.

Memorial Sloan-Kettering does not record specific website user information and does not contact users of this website. You are hereby advised to consult with a physician or other professional health-care provider prior to making any decisions, or undertaking any actions or not undertaking any actions related to any health care problem or issue you might have at any time, now or in the future. In using this website you agree that neither Memorial Sloan-Kettering nor any other party is or will be liable or otherwise responsible for any decision made or any action taken or any action not taken due to your use of any information presented at this website.

- I accept all of the above terms by clicking here or by any further use of this service.
- I do not accept all of the above terms.

Glossary Print Download E-mail Share

Home > Cancer Care > Cancer & Treatment > Symptom Management > Integrative Medicine > About Herbs, Botanicals & Other Products

Cancer & Treatment
Adult Cancers
Pediatric Cancers
Clinical Trials
Blood & Marrow Stem Cell Transplantation
Pathology Consultations

For New Patients
Becoming a Patient: The First Steps
Your Cancer Care Team
FAQs for New Patients
For International Patients

Counseling & Support
Counseling
Support Programs
Sexual Health & Reproductive Programs
Patient Services
Help for Older Patients

Survivorship Center
When Treatment Ends
Our Survivorship Services
Survivorship Experts Videos
Survivor Experiences
Survivorship Research

Hospital Information
Why Memorial Sloan-Kettering for Cancer Care?
Patient Care Facilities
Visiting Us
Helpful Phone Numbers

Making an Appointment
Preparing for Your First Appointment
Referring a Patient

Symptom Management
Risk Assessment & Screening
For Healthcare Professionals

Help for Caregivers, Families & Friends
Educational Resources
Online Services

Survivorship for Healthcare Professionals
Upcoming Programs

Insurance & Billing
Financial Assistance

About Memorial Sloan-Kettering
Learn More
Contact Us
Find a Doctor

Making an Appointment
800-525-2225
Monday–Friday
8:30 AM–5:30 PM, ET

Patient Portal MYMSKCC
About MYMSKCC
Login

Online Support
Virtual Groups
Online Community

Memorial Sloan-Kettering Cancer Center | Memorial Hospital for Cancer and Allied Diseases | Sloan-Kettering Institute
Gerstner Sloan-Kettering Graduate School of Biomedical Sciences | Memorial Sloan-Kettering Cancer Center Library

Legal Disclaimer | Privacy Practices | Public Notices

About Herbs, Botanicals & Other Products

INTEGRATIVE MEDICINE

Our Expertise

Therapies, Classes & Workshops

About Herbs, Botanicals & Other Products

Search About Herbs

Herbs, Botanicals & Other Products: FAQs

E-mail Us

For Older Patients

Our Research

Our Clinical Trials

Additional Resources

Bendheim Integrative Medicine Center

Search Herbs, Botanicals & Other Products

All # A B C D E F G H I J K L M N O P Q R S T U V W X Y Z

Pomegranate

Healthcare Professional | Consumer

- Scientific Name
- Common Name
- Clinical Summary
- Food Sources
- Purported Uses
- Constituents
- Mechanism of Action
- Pharmacokinetics
- Warnings
- Adverse Reactions
- Herb-Drug Interactions
- Literature Summary and Critique
- References

Scientific Name

Punica granatum L.

Top

Common Name

Chinese apple

Top

Clinical Summary

Pomegranate is a small fruit-bearing tree native to Asia but is cultivated in many parts of the world including the United States. The fruit juice extracted from the arils of the seeds is used in drinks and as a dietary supplement. Several studies have shown that pomegranate has antioxidant and antiatherosclerotic properties attributed to the presence of multiple polyphenols such as tannins, flavonols, anthocyanins and ellagic acid [1] [2]. Pomegranate juice has been shown to suppress inflammatory cell signaling [1], inhibit prostate tumor growth and lower serum PSA levels [3] [4], and also inhibit aromatase activity, endogenous estrogen biosynthesis and breast cancer cell proliferation [5] in vitro.

Consumption of pomegranate juice was found to benefit patients with carotid artery stenosis [6], in those with hypertension [7], hyperlipidemia [21], mild to moderate erectile dysfunction [19], and in patients with coronary heart disease (CHD) [8], but had no effect in patients with chronic obstructive pulmonary disease (COPD) [9]. Pomegranate juice appears to slow the rate of increase of PSA in men with high PSA levels [2]. But this needs to be confirmed in large scale clinical trials.

Adverse effects associated with use of pomegranate juice are rare. There is, however, a concern that pomegranate juice can inhibit cytochrome P450 enzymes similar to grapefruit juice [10] [11]. But other studies yielded mixed results [12].

Patients should be aware that pomegranate is not an approved cancer treatment.

Top

Food Sources
Whole fruit, juice

Top

Purported Uses
- Cancer treatment and prevention
- Atherosclerosis
- Coronary heart Disease
- Hypercholesterolemia
- Hyperlipidemia
- Hypertension
- HIV

Top

Constituents
- Tannins
- Flavonols
- Anthocyanins
- Ellagic acid

Top

Mechanism of Action
Several studies have indicated that pomegranate juice has antioxidant and antiatherosclerotic properties due to the presence of multiple polyphenols such as tannins, flavonols, anthocyanins and ellagic acid. Punicalagin, an ellagitannin, is the most abundant polyphenol that accounts for >50% of the antioxidant activity [1] [2]. Some commercial pomegranate juices are marketed with claims of higher antioxidant activity than green tea and red wine [13]. However such effects could be due to colonic microflora metabolites and not the polyphenols present in the juice [14]. Pomegranate extract can inhibit aromatase activity and decrease the endogenous synthesis of estrogen [5].

Top

Pharmacokinetics
Studies in rats suggest that most punicalagin is absorbed but only 3-6% is excreted in the feces and urine suggesting that the majority is converted to CO^2 or other undetectable metabolites [15]. The metabolites that are present in urine in both rats and humans, 6H-dibenzo[b,d]pyran-6-one derivatives, are the products of intestinal microflora metabolizing the pomegranate tannins. A recent human study has shown that ellagic acid is absorbed from pomegranate juice and detected in plasma samples. It is unclear whether free ellagic acid is due to hydrolysis of the pomegranate ellagitannins, physiological pH, or gut microflora activity [16].

Top

Warnings
Pomegranate juice may increase the risk of rhabdomyolysis for patients on statin therapy possibly due to the inhibition of CYP 450 enzymes [17].
Diabetic patients should be careful because of the sugar content of pomegranate.

Top

Adverse Reactions
No significant adverse effects were seen with daily consumption of 8 ounces of pomegranate juice in men for over two years [2].

Top

Herb-Drug Interactions
- **Cytochrome P4503A substrates:** Studies in rats indicate that pomegranate juice may inhibit cytochrome P450 3A (CYP3A) activity similar to grapefruit juice [10] [11]. But a study in humans demonstrated that pomegranate juice did not alter clearance of intravenous or oral midazolam, whereas grapefruit juice is known to have this effect [12].
- **CYP 2C9 substrates:** A study done in rats showed that pomegranate juice inhibited CYP2C9 activity and increased tolbutamide bioavailability [18].
- **Warfarin:** According to a case report, pomegranate juice may interact with warfarin [20].

Top

Literature Summary and Critique

Cerda B, Soto C, Albaladejo MD, et al. Pomegranate juice supplementation in chronic obstructive pulmonary disease: a 5-week randomized, double-blind, placebo-controlled trial. *Eur J Clin Nutr* 2006;60(2):245-253.Thirty men with COPD were given either pomegranate juice (providing 2.66 grams of polyphenols) or placebo for five weeks. No significant differences were found between the two groups for any of the study parameters including urinary 8-iso-PGF, respiratory function, hematological and serobiochemical markers, and clinical symptoms of COPD. The authors noted that none of the polyphenols present in pomegranate juice were detected in the plasma or urine of the patients. Instead, the major metabolites found were dibenzopyranone derivatives resulting from the pomegranate ellagitannins metabolized by colonic microflora. The authors suggest that understanding the different bioavailabilities of dietary polyphenols is essential before making claims of antioxidant-based health benefits.

Pantuck AJ, Leppert JT, Zomorodian N, et al. Phase II study of pomegranate juice for men with rising prostate-specific antigen following surgery or radiation for prostate cancer. *Clin Cancer Res.* 2006;12(13):4018-4026.
A phase II clinical trial was conducted with 46 men with rising PSA following surgery or radiotherapy. Subjects were given 240ml (8 ounces) of pomegranate juice daily until progression of disease. Researchers found a significant increase in the mean PSA doubling time following the study period. These results warrant further testing via a placebo-controlled study.

Sumner MD, Elliott-Eller M, Weidner G, et al. Effects of pomegranate juice consumption on myocardial perfusion in patients with coronary heart disease. *Am J Cardiol* 2005;96(6):810-814.
Forty-five patients with stable coronary heart disease (CHD) received 240mL/day of pomegranate juice or placebo for three months. After three months, stress-induced ischemia decreased in the pomegranate group (SDS -0.8 +/- 2.7), but an increase was observed in the placebo group. The authors conclude that pomegranate juice may be of benefit in improving stress-induced myocardial ischemia in CHD patients.

Top

References

1. Adams LS, Seeram NP, Aggarwal BB, Takada Y, Sand D, Heber D. Pomegranate juice, total pomegranate ellagitannins, and punicalagin suppress inflammatory cell signaling in colon cancer cells. *J Agric Food Chem.* Feb 8 2006;54(3):980-985.
2. Pantuck AJ, Leppert JT, Zomorodian N, et al. Phase II study of pomegranate juice for men with rising prostate-specific antigen following surgery or radiation for prostate cancer. *Clin Cancer Res.* Jul 1 2006;12(13):4018-4026.
3. Lansky EP, Jiang W, Mo H, et al. Possible synergistic prostate cancer suppression by anatomically discrete pomegranate fractions. *Invest New Drugs.* Jan 2005;23(1):11-20.
4. Malik A, Afaq F, Sarfaraz S, Adhami VM, Syed DN, Mukhtar H. Pomegranate fruit juice for chemoprevention and chemotherapy of prostate cancer. *Proc Natl Acad Sci* U S A. Oct 11 2005;102 (41):14813-14818.
5. Kim ND, Mehta R, Yu W, et al. Chemopreventive and adjuvant therapeutic potential of pomegranate (Punica granatum) for human breast cancer. *Breast Cancer Res Treat.* Feb 2002;71(3):203-217.
6. Aviram M, Rosenblat M, Gaitini D, et al. Pomegranate juice consumption for 3 years by patients with carotid artery stenosis reduces common carotid intima-media thickness, blood pressure and LDL oxidation. *Clin Nutr.* Jun 2004;23(3):423-433.
7. Aviram M, Dornfeld L. Pomegranate juice consumption inhibits serum angiotensin converting enzyme activity and reduces systolic blood pressure.*Atherosclerosis.* Sep 2001;158(1):195-198.
8. Sumner MD, Elliott-Eller M, Weidner G, et al. Effects of pomegranate juice consumption on myocardial perfusion in patients with coronary heart disease. *Am J Cardiol.* Sep 15 2005;96(6):810-814.
9. Cerda B, Soto C, Albaladejo MD, et al. Pomegranate juice supplementation in chronic obstructive pulmonary disease: a 5-week randomized, double-blind, placebo-controlled trial. *Eur J Clin Nutr.* Feb 2006;60(2):245-253.
10. Summers KM. Potential drug-food interactions with pomegranate juice. *Ann Pharmacother.* Jul-Aug 2006;40(7-8):1472-1473.
11. Hidaka M, Okumura M, Fujita K, et al. Effects of pomegranate juice on human cytochrome p450 3A (CYP3A) and carbamazepine pharmacokinetics in rats.*Drug Metab Dispos.* May 2005;33(5):644-648.
12. Farkas D, Oleson LE, Zhao Y, et al. Pomegranate juice does not impair clearance of oral or intravenous midazolam, a probe for cytochrome P450-3A activity: comparison with grapefruit juice.*J Clin Pharmacol.* Mar 2007;47(3):286-294.
13. Gil MI, Tomas-Barberan FA, Hess-Pierce B, Holcroft DM, Kader AA. Antioxidant activity of pomegranate juice and its relationship with phenolic composition and processing. *J Agric Food Chem.* Oct 2000;48(10):4581-4589.

14. Cerda B, Espin JC, Parra S, Martinez P, Tomas-Barberan FA. The potent in vitro antioxidant ellagitannins from pomegranate juice are metabolised into bioavailable but poor antioxidant hydroxy-6H-dibenzopyran-6-one derivatives by the colonic microflora of healthy humans. *Eur J Nutr.* Aug 2004;43(4):205-220.

15. Cerda B, Llorach R, Ceron JJ, Espin JC, Tomas-Barberan FA. Evaluation of the bioavailability and metabolism in the rat of punicalagin, an antioxidant polyphenol from pomegranate juice. *Eur J Nutr.* Jan 2003;42(1):18-28.

16. Seeram NP, Lee R, Heber D. Bioavailability of ellagic acid in human plasma after consumption of ellagitannins from pomegranate (Punica granatum L.) juice. *Clin Chim Acta.* Oct 2004;348(1-2):63-68.

17. Sorokin AV, Duncan B, Panetta R, Thompson PD. Rhabdomyolysis associated with pomegranate juice consumption. *Am J Cardiol.* Sep 1 2006;98(5):705-706.

18. Nagata M, Hidaka M, Sekiya H, et al. Effects of pomegranate juice on human cytochrome P450 2C9 and tolbutamide pharmacokinetics in rats. *Drug Metab Dispos.* Feb 2007;35(2):302-305.

19. Forest CP, Padma-Nathan H, Liker HR. Efficacy and safety of pomegranate juice on improvement of erectile dysfunction in male patients with mild to moderate erectile dysfunction: a randomized, placebo-controlled, double-blind, crossover study. *Int J Impot Res.* 2007 Nov-Dec;19(6):564-7.

20. Komperda KE. Potential interaction between pomegranate juice and warfarin. *Pharmacotherapy.* 2009 Aug;29(8):1002-6.

21. Mirmiran P, Fazeli MR, Asghari G, Shafiee A, Azizi F. Effect of pomegranate seed oil on hyperlipidaemic subjects: a double-blind placebo-controlled clinical trial. *Br J Nutr.* 2010 Aug;104 (3):402-6.

Top

E-mail your questions and comments to aboutherbs@mskcc.org.

Last updated: April 18, 2011

New Treatments and Research

Physician researchers at the Johns Hopkins Kimmel Cancer Center are actively pursuing new therapies and combinations of therapies for men with all stages of prostate cancer. Studying genetics, biology/immunotherapy, radiation techniques and natural therapies, at any given time our team runs 20 to 25 clinical trials for patients across the continuum, including perioperative cancers and more advanced disease. Several therapies being evaluated today, including the prostate cancer vaccine GVAX and the blood vessel-blocking drug tasquinimod, were developed right here in our laboratories.

Following is a sampling of some of our ongoing work:

Translational Research

In the laboratory of pathologist Angelo DeMarzo, researchers are focusing on the molecular development of prostate cancer. Dr. DeMarzo and colleagues are interested in determining the cell type of origin and the molecular mechanisms involved in early formation of prostate cancers. They also perform translational research in which they interrogate biomarker expression in human prostate tissues to help pathologists make diagnoses, help predict patient outcomes, help determine whether a given pathway alteration is present, or help determine whether a drug has hit its target.

One area of interest lately has been the MYC (“mick”) oncogene, which works like a gas pedal, causing cancer cells to grow and proliferate as it ramps up. Researchers have detected MYC in prostate cancers from its precursor lesions to metastatic disease. A study by Dr. DeMarzo, researcher Cheryl Koh and colleagues, published in the April 2011 issue of the American Journal of Pathology, found for the first time that overexpression of MYC increases the number and size of nucleoles, structures composed of proteins and acids found within the center of cells. Increased size and number of nucleoles are some of the earliest signs of physical changes associated with the development of premalignant prostate intraepithelial (PIN) lesions and invasive cancers; scientists previously had not known the cause of these changes.

Nucleoles produce ribosomes, which are important for cellular growth and proliferation. Additional studies could help better define the development of prostate cancers, which could lead the way to additional preventive treatments.

In basic science research, Dr. DeMarzo’s team has created mice that overexpress MYC in the prostate. Working with researchers at the University of Maryland, Dr. DeMarzo and colleagues have mixed the mice overexpressing MYC with mice missing the P10 tumor suppressor gene. The resulting mice have an explosion of cancers that metastasize to other organs. By studying these models, researchers hope to understand the mechnanisms behind how cancer cells break free of the original tumors and metastasize, and test new drug compounds.

Immunotherapy

Michael Carducci, Mario Eisenberger, Emmanuel Antonarakis, Charles Drake, and other investigators have been directing new combined immunotherapy studies in men with prostate and related cancers. Here is a description of a few of the studies. To find out more about these and other studies you may qualify for, speak with your physician or visit Kimmel's Clinical Trials page.

PD-1

One area of study is a molecule on immune system T cells called PD-1 (programmed death-1), which, when activated by cancers, works like a brake and slows T cells' ability to kill cancer cells. A study published by researchers at Johns Hopkins and other institutions in the July 1, 2010, issue of the Journal of Clinical Oncology showed that an antibody against PD-1 called MDX1106, infused in 39 patients with metastatic prostate cancer, kidney cancer, melanoma, non-small-cell lung cancer and colorectal cancer was well tolerated and in some patients helped T cells re-gain function and start destroying cancer cells. The antibody had lasting effects in a few patients, including one man with kidney cancer who received three doses of the antibody and was still alive three years later.

Additional studies of the antibody in patients with advanced kidney cancers will to try to determine why some patients respond to the drug and some do not, and how the medication works.

In patients with high-risk prostate cancers, a research team led by Drs. Drake and Antonarakis, will compare the effects of the PD-1 blockade drug alone or when given with the prostate cancer vaccine GVAX. They think patients will have a better immune response with the combined therapy.

Immunotherapy and Surgery

Drs. Drake and Antonarakis are conducting a pilot study to assess the antitumor immune effects of the prostate cancer GVAX given alone versus with a low dose of the drug cyclophosphamide in men with localized prostate cancer. These treatments also will be administered three weeks prior to surgery to remove the prostate in men with intermediate- and high-risk disease. Researchers aim to determine the immune effects of GVAX, and whether cylophosphamide given a day before GVAX strengthens the immune infiltration in to the prostate.

Androgen Ablation

Androgen ablation, a hormone therapy that removes or suppresses testosterone, can "wake up" the immune system; it has been shown to be helpful for many patients with prostate cancers. A trial led by Drs. Antonarakis and Drake, along with researchers at the Cleveland Clinic, will compare the effects of androgen ablation on the immune system when combined with the prostate cancer vaccine Provenge. The team also will look at the response of PSA. Half of patients in the trial will get the vaccine before androgen ablation, and half after.

Immunotherapy and PSA levels

Dr. Drake and colleagues at Johns Hopkins are participating in a trial run by the Eastern Cooperative Oncology Group (ECOG) to compare whether men with metastatic prostate cancers fare better and have lower PSA levels when they receive chemotherapy before the prostate cancer vaccine Prostvac or after. Immune therapies alone don't necessarily drop men's PSA levels or shrink tumors; one theory is that they set the body up so that chemotherapy works more

effectively by killing more tumor cells and ratcheting up the body's immune system, Dr. Drake says.

New Drug Studies

- Dr. Carducci is leading a study of the drug Disulfiram, which may benefit prostate cancer patients by restoring tumor suppressor genes, in men with recurrent prostate cancer.
- Drs. Carducci and Antonarakis are directing Hopkins' participation in a multi-center study of Itraconazole, an anti-fungal medication, in patients with metastatic castration-resistant prostate cancer. Early results indicate the drug can prevent prostate cancer from worsening and delay the need for chemotherapy in men with advanced disease. Please read for more information.
- Dr. Carducci is chairing a national phase III study evaluating the combination of the chemotherapy drugs docetaxel and prednisone with bevacizumab (a drug that blocks the growth of new blood vessels), versus just docetaxel and prednisone, in men with prostate cancer that did not respond to hormone therapy.
- Dr. Carducci is principal investigator of an international study evaluating the drug tasquinimod, which blocks the growth of new blood vessels, in men with metastatic castrate-resistant prostate cancer. A phase II study conducted at Johns Hopkins and other centers across the country showed the drug significantly slowed progression and improved progression-free survival in this population.
- Dr. Carducci is leading Hopkins' participation in a multi-center study of the drug KX2-391, an inhibitor of Src kinase (a key regulator of tumor growth, blood vessel development and metastasis), in men with bone-metastatic castrate-resistant prostate cancer.

Alternative Medicine/Natural Product Therapies

Dr. Carducci is leading several studies of natural products, including pomegranate extract, Muscadine grape skin extract and Chinese coix-seed oil in men who have been treated for prostate cancer but still have rising PSA levels:

- In a phase II study, researchers found that pomegranate extract capsules slowed PSA doubling time by more than six months in a group of men with rising PSA levels following treatment for prostate cancer, with no effects on testosterone.
- Extract taken from the skin of Muscadine grapes has been shown to inhibit cell growth in lab studies; in an ongoing phase II study, Dr. Carducci and colleagues are comparing the effects of two doses of extract capsules on PSA doubling time.
- Dr. Carducci and colleagues are participating in a multi-center trial comparing two doses of Kanglaite gelcaps. The gelcaps contain oil from the coix grass plant, which has been used for therapeutic purposes in China for thousands of years. Anecdotally, the gelcaps have been reported to decrease PSA among prostate cancer patients. The extract also has been demonstrated to inhibit prostate tumor growth in animal models

Recent News

- Antifungal Drug Delays Need for Chemo in Advanced Prostate Cancer.
- Closely Monitoring Low-risk Prostate Cancer Does Not Raise Risk of Death.
- Heart Drug Cuts Prostate Cancer Risk.
- Prostate Cancer Updates from AACR 2010: Obesity Near Prostate Cancer Surgery Doubles Risk of Recurrence, Biomarkers Predict Candidates for Prostate Cancer Treatment.
- Drug that Restricts Blood Supply to Prostate Tumors Delays Disease Progression.
- Predicting the Return of Prostate Cancer.
- Autopsy Study Links Prostate Cancer to Single Rogue Cell.
- Radiation Therapy Prolongs Life in Men with Recurrent Prostate Cancer.
- Gene Markers Located for Hereditary Prostate Cancer.

WELCOME TO JOHNS HOPKINS HEALTH ALERTS!

This free public service from Johns Hopkins Medicine helps keep you up to date on the latest breakthroughs for the most common medical conditions which prevent healthy aging. Browse all the articles via the Health Alert Topics navigation bar on the right, or read the headlines below.

Get the latest news sent straight to your Inbox. Register now for your FREE Johns Hopkins Health Alerts. Check the boxes below for all the topics you are interested in, enter your email address, and click "Send." It's fast, easy, and FREE. Benefits of Being A Registered User

Anxiety	Digestion	Memory	Stroke
Arthritis	Enlarged Prostate (BPH)	Nutrition	Vision
Back Pain	Healthy Living	Osteoporosis	Weight Control
Colon Cancer	Heart Health	Prescription Drugs	
Depression	Hypertension	Prostate Cancer	
Diabetes	Lung	Prostatitis	

Enter your email here: (Example: yourname@domain.com)

Please send my alerts as: HTML Text Send my FREE Health Alerts!

We value your privacy and will never rent your email address.Already a Member? Manage your Health Alerts

Print this page Email this to a friend

Prostate Disorders Special Report

Simple Steps to Protect Yourself Against Prostate Cancer

Reducing your risk of prostate cancer begins with the big picture, those well-publicized major lifestyle changes that are widely recommended but often difficult to accomplish. Then there are the smaller details: cancer-protective foods, supplements, and medications. A serious prostate cancer risk-reduction program encompasses both approaches.

Achieving a healthy weight, committing to regular exercise, and altering long-ingrained dietary habits are the most important steps you can take to protect yourself from prostate cancer. And their payoff goes far beyond the prostate. These lifestyle changes could reduce your risk of nearly all the most devastating diseases: heart disease, stroke, diabetes, Alzheimer's disease, and many other forms of cancer. What's more, they work together to improve your health. Here are some strategies to consider:

Weight management.
The links between obesity and prostate cancer continue to strengthen. Fat cells churn out a slew of substances that fuel the development and progression of cancer. These include estrogen, testosterone, and insulin-like growth factor. Men who are obese also are more likely to be diagnosed with advanced prostate cancer. The possible reasons are that obese men tend to have larger prostates (making tumor detection more difficult), and their prostate specific antigen (PSA) scores are often deceptively low.

Regular exercise.
Vigorous physical activity appears to protect against prostate cancer. Men who exercise regularly are less likely to be diagnosed with advanced or fatal prostate cancer. Some evidence suggests that vigorous physical activity may also slow its progression.

Dietary changes.
Adopting a plant-based diet can reduce your risk of prostate cancer and improve your overall health. This dietary approach focuses on fruits, vegetables, legumes (like beans and peas), whole grains, seeds, and nuts. Soy foods (like soy nuts and tofu) also appear to be protective. Aim for at least nine fruits and vegetables a day.

To get all the cancer-fighting nutrients you need, try to include a "rainbow" of fruits and vegetables each day -- reds, oranges, yellows, greens, and blues/purples. Brightly colored fruits and vegetables are rich in carotenoids, cancer-fighting substances that serve as coloring agents in plant foods. Also be sure to include at least one serving per day of a cruciferous vegetable (like broccoli, cabbage, or

cauliflower). These vegetables contain other types of cancer-fighting chemicals.

Specific Foods, Supplements, and Medications. Ongoing research into prostate cancer prevention has identified a number of individual substances that may be protective:

Lycopene. The carotenoid lycopene is found in tomatoes, pink grapefruit, and watermelon. Cooked tomato products such as spaghetti sauce and ketchup are the richest source.

Pomegranates. Pomegranates and pomegranate juice have recently been found to cause prostate cancer cells to self destruct. Among men with prostate cancer, daily glasses of pomegranate juice have slowed the increase in PSA levels after treatment.

Omega-3 fatty acids. Omega- 3 fatty acids are a type of polyunsaturated fat found abundantly in fatty fish (like salmon, sardines, tuna, and halibut) and fish oil. Flaxseeds, walnuts, and canola oil contain a weaker, but still beneficial, plant-based form of these healthful fats. Omega-3s have anti-inflammatory and anticancer effects. Several studies have suggested that men who eat fish two or more times per week have a lower risk of developing prostate cancer.

Selenium and vitamin E. These two nutrients are being tested for their potential protective effects in SELECT (Selenium and Vitamin E Cancer Prevention Trial) -- the largest clinical study ever launched about prostate cancer prevention, coordinated by the U.S. National Cancer Institute. Several smaller studies have shown benefits, but until the SELECT results are in, doctors recommend against taking large amounts of either nutrient. A multivitamin that includes both is the best bet for now.

Calcium. High calcium intake may also be a risk factor for prostate cancer. A sensible approach is to limit calcium consumption to no more than 1,200 mg daily through food sources.

Vitamin D. Vitamin D plays an important role in regulating cell growth and has been associated with a reduced risk of prostate cancer. The dietary sources of vitamin D include fortified milk and fatty fish. The way to boost your body's natural production of vitamin D is to spend about 15 minutes a day (without sunscreen) in the sun.

Finasteride. Used to treat benign prostatic hyperplasia, finasteride (Proscar) has been shown to reduce the overall incidence of prostate cancer, but it is not clear if it reduces the risk of death or increases life expectancy. It may also increase the risk of developing higher-grade more aggressive cancers (Gleason score 7-10). While some doctors support the use of finasteride to prevent prostate cancer, others do not.

Statins. Prostate cancer researchers are discovering the important role inflammation plays in the development of prostate cancer. High cholesterol levels also may increase the risk. The cholesterol-lowering medications known as statins tackle both problems. In a study that Johns Hopkins researchers participated in, men who took statins had half the risk of developing prostate cancer compared with nonusers.

NSAIDs. Nonsteroidal anti-inflammatory drugs (NSAIDs) also reduce inflammation and appear to lower the risk of prostate cancer. These medications target a protein called COX-2, which is believed to help prostate cancer cells spread.

Posted in Prostate Disorders on May 29, 2008

Prostate cancer

With Mayo Clinic urologist

Erik P. Castle, M.D.

read biography

Question

Pomegranate juice: A cure for prostate cancer?

Is it true that pomegranate juice may slow the growth of prostate cancer? How much should I drink?

Answer

from Erik P. Castle, M.D.

Some research suggests that drinking pomegranate juice may slow the progression of prostate cancer.

For example, in one study, the length of time it took for prostate-specific antigen (PSA) to double after surgery or radiation for prostate cancer was significantly longer in men who drank 8 ounces (237 milliliters) of pomegranate juice daily for up to two years. A longer PSA doubling time indicates that the cancer may be progressing less rapidly. Other studies have found that certain compounds in pomegranate juice inhibited growth of prostate cancer cells in the laboratory.

Although these results are encouraging, they're only preliminary. Clinical trials are under way, and it's too early to say if pomegranate juice can definitely slow the growth of prostate cancer. It's also unclear whether drinking pomegranate juice alters the course of prostate cancer overall so that men live longer or better.

If you choose to drink pomegranate juice, talk with your doctor first. Although pomegranate juice is generally safe, there is evidence that it affects the metabolism of several prescription medications, including the blood thinner warfarin (Coumadin) and some drugs used to treat high blood pressure and high cholesterol.

Next question
Frequent sex: Does it protect against prostate cancer?

References

Nov. 30, 2010 AN01477

THE UNIVERSITY OF CHICAGO MEDICAL CENTER

AT THE FOREFRONT OF MEDICINE®

Michael H. Davidson, MD

Clinical Professor of Medicine
Director, Preventive Cardiology

Michael H. Davidson, MD, is a nationally recognized expert on statins, novel lipid-lowering drugs and the reduction of coronary artery disease risk through diet and exercise. He specializes in heart disease prevention--teaching patients to take a proactive approach in managing cardiac risk factors.

An active researcher, Dr. Davidson's clinical research background encompasses both pharmaceutical and nutritional clinical trials. His extensive research on statins, novel lipid-lowering drugs, and nonpharmacologic risk factor reduction has established him as a key opinion leader in this area.

A prolific author and lecturer on lipid disorders, nutrition, and atherosclerosis, Dr. Davidson has coordinated more than 1,000 clinical trials in areas of preventive cardiology. He has published more than 250 articles for leading medical journals and has written 3 books on Lipidology.

Dr. Davidson has been named one of "The Best Doctors in America" by Best Doctors Inc. for the past 10 years and was named Father of the Year by the American Diabetes Association, 2010. He currently serves as president of the National Lipid Association.

Practice Locations

150 E. Huron Street
Suite 900
Chicago, IL 60611

Year Started Practice

1986

Board Certifications

Internal Medicine
Cardiology
Lipidology

Clinical Interests

- Cardiology
- Preventive cardiology
- Cardiovascular lipid management
- Cardiovascular risk factor modification

Request an Appointment

150 E. Huron Street
Request an appointment online
or call **(773) 834-4150**

Physicians, contact the
Referring Physician Access Line
at **1-877-DOM-2730**

Selected Publications

View a partial list of Dr. Davidson's publications through the National Library of Medicine's PubMed online database.

Medical School

Ohio State University, Columbus, OH

Internship, Residency & Fellowship

Rush-Presbyterian-St. Luke's Medical Center, Chicago

Memberships

American College of Cardiology
American College of Chest Physicians
American Medical Association
Midwest Lipid Association
National Lipid Association

Language Spoken

English

Email

mdavidso@bsd.uchicago.edu

Office Phone

(773) 702-1717

Office Fax

(773) 834-7300

Office Postal Address

Michael H. Davidson, MD
University of Chicago Medical Center
5841 S. Maryland Avenue, MC 6080
Chicago, IL 60637

The University of Chicago Medical Center
5841 S. Maryland Avenue
Chicago, IL 60637 | 773-702-1000

Appointments: 1-888-UCH-0200

The National Institutes of Health (NIH), a part of the U.S. Department of Health and Human Services , is the nation's medical research agency—making important discoveries that improve health and save lives.

Thanks in large part to NIH-funded medical research, Americans today are living longer and healthier. Life expectancy in the United States has jumped from 47 years in 1900 to 78 years as reported in 2009, and disability in people over age 65 has dropped dramatically in the past 3 decades. In recent years, nationwide rates of new diagnoses and deaths from all cancers combined have fallen significantly.

SCIENTIFIC LEADERSHIP

NIH is the largest source of funding for medical research in the world, creating hundreds of thousands of high-quality jobs by funding thousands of scientists in universities and research institutions in every state across America and around the globe.

NIH is made up of 27 Institutes and Centers, each with a specific research agenda, often focusing on particular diseases or body systems. NIH leadership plays an active role in shaping the agency's research planning, activities, and outlook.

The Office of the Director is the central office at NIH, responsible for setting policy for NIH and for planning, managing, and coordinating the programs and activities of all the NIH components. The NIH Director, with a unique and critical perspective on the entire agency, is responsible for providing leadership to the Institutes and for constantly identifying needs and opportunities, especially for efforts that involve multiple Institutes. The NIH Director is assisted by the NIH Deputy Directors including the Principal Deputy Director, who shares in the overall direction of the agency's activities.

NIH is responsive to Congressional legislation that adjusts NIH's programs to meet changing research needs. As a result of the NIH reauthorization process, NIH is able to respond strategically in an era when medical research requires constant innovation and increased interdisciplinary efforts.

More than 80% of the NIH's budget goes to more than 300,000 research personnel at over 3,000 universities and research institutions. In addition, about 6,000 scientists work in NIH's own Intramural Research laboratories, most of which are on the NIH main campus in Bethesda, Maryland. The main campus is also home to the NIH Clinical Center, the largest hospital in the world totally dedicated to clinical research.

Successful biomedical research depends on the talent and dedication of the scientific workforce. NIH supports many innovative training programs and funding mechanisms that foster scientific creativity and exploration. The goal is to strengthen our nation's research capacity, broaden our research base, and inspire a passion for science in current and future generations of researchers.

NIH encourages and depends on public involvement in federally supported research and activities. NIH's wide-ranging public efforts include outreach and education, nationwide events, requests for public input on NIH projects, and special programs designed specifically to involve public representatives in clinical research.

A History of Health

For over a century, NIH scientists have paved the way for important discoveries that improve health and save lives. In fact, more than 130 Nobel Prize winners have received support from NIH. Their studies have led to the development of MRI, understanding of how viruses can cause cancer, insights into cholesterol control, and knowledge of how our brain processes visual information, among dozens of other advances.

Read more about NIH history

NIH at a Glance

NIH Facts
Common Questions
Mission & Goals

NIH Director
Francis S. Collins, M.D., Ph.D.

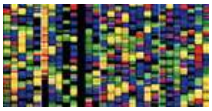
Headquarters
Bethesda, Maryland, USA

NIH...Turning Discovery Into Health

Revolutionary ideas often come from unexpected directions. Here are some of the main research areas that NIH supports.


Chronic Diseases


Infectious Diseases


Personalized Medicine & New Technologies


Health at All Ages

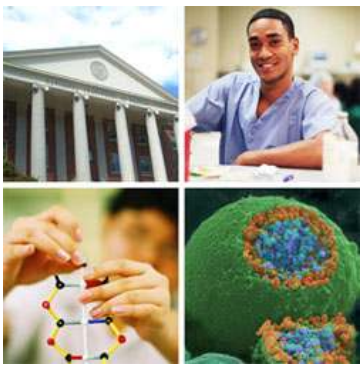

Print the full brochure
(PDF - 4.1 MB)

This page last reviewed on December 5, 2011

National Institutes of Health (NIH), 9000 Rockville Pike, Bethesda, Maryland 20892

Mission

NIH's mission is to seek fundamental knowledge about the nature and behavior of living systems and the application of that knowledge to enhance health, lengthen life, and reduce the burdens of illness and disability.



The goals of the agency are:

- to foster fundamental creative discoveries, innovative research strategies, and their applications as a basis for ultimately protecting and improving health;
- to develop, maintain, and renew scientific human and physical resources that will ensure the Nation's capability to prevent disease;
- to expand the knowledge base in medical and associated sciences in order to enhance the Nation's economic well-being and ensure a continued high return on the public investment in research; and
- to exemplify and promote the highest level of scientific integrity, public accountability, and social responsibility in the conduct of science.

In realizing these goals, the NIH provides leadership and direction to programs designed to improve the health of the Nation by conducting and supporting research:

- in the causes, diagnosis, prevention, and cure of human diseases;
- in the processes of human growth and development;
- in the biological effects of environmental contaminants;
- in the understanding of mental, addictive and physical disorders; and
- in directing programs for the collection, dissemination, and exchange of information in medicine and health, including the development and support of medical libraries and the training of medical librarians and other health information specialists.

This page last reviewed on March 3, 2011

National Institutes of Health (NIH), 9000 Rockville Pike, Bethesda, Maryland 20892

U.S. Food & Drug Administration

For Consumers

Fast Track, Accelerated Approval and Priority Review

Accelerating Availability of New Drugs for Patients with Serious Diseases

Speeding the development and availability of drugs that treat serious diseases are in everyone's interest, especially when the drugs are the first available treatment or have advantages over existing treatments. The Food and Drug Administration (FDA) has developed three distinct and successful approaches to making such drugs available as rapidly as possible: *Priority Review, Accelerated Approval, and Fast Track*. Because each of these approaches implies speed, there can be confusion about the specific meaning of each and the distinctions among them.

The following summary describes each element, how they differ, and how they complement each other.

Fast Track

Fast track is a **process** designed to facilitate the development, and expedite the review of drugs to treat serious diseases **and** fill an unmet medical need. The purpose is to get important new drugs to the patient earlier. *Fast Track* addresses a broad range of serious diseases.

Determining whether a disease is *serious* is a matter of judgment, but generally is based on whether the drug will have an impact on such factors as survival, day-to-day functioning, or the likelihood that the disease, if left untreated, will progress from a less severe condition to a more serious one. AIDS, Alzheimer's, heart failure and cancer are obvious examples of serious diseases. However, diseases such as epilepsy, depression and diabetes are also considered to be serious diseases.

Filling an *unmet medical need* is defined as providing a therapy where none exists or providing a therapy which may be potentially superior to existing therapy.

Any drug being developed to treat or prevent a disease with no current therapy obviously is directed at an unmet need. If there are existing therapies, a fast track drug must show some advantage over available treatment, such as:

- Showing superior effectiveness
- Avoiding serious side effects of an available treatment
- Improving the diagnosis of a serious disease where early diagnosis results in an improved outcome
- Decreasing a clinically significant toxicity of an accepted treatment

A drug that receives *Fast Track* designation is eligible for some or all of the following:

- More frequent meetings with FDA to discuss the drug's development plan and ensure collection of appropriate data needed to support drug approval
- More frequent written correspondence from FDA about such things as the design of the proposed clinical trials
- Eligibility for *Accelerated Approval,* i.e., approval on an effect on a surrogate, or substitute endpoint reasonably likely to predict clinical benefit
- *Rolling Review*, which means that a drug company can submit completed sections of its New Drug Application (NDA) for review by FDA, rather than waiting until every section of the application is completed before the entire application can be reviewed. NDA review usually does not begin until the drug company has submitted the entire application to the FDA, and
- Dispute resolution if the drug company is not satisfied with an FDA decision not to grant Fast Track status.

In addition, most drugs that are eligible for Fast Track designation are likely to be considered appropriate to receive a *Priority Review*. *Fast Track* designation must be requested by the drug company. The request can be initiated at any time during the drug development process. FDA will review the request and make a decision within
sixty days based on whether the drug fills an unmet medical need in a serious disease.

Once a drug receives *Fast Track* designation, early and frequent communication between the FDA and a drug company is encouraged throughout the entire drug development and review process. The frequency of communication assures that questions and issues are resolved quickly, often leading to earlier drug approval and access by patients.

Accelerated Approval

When studying a new drug, it can take a long time - sometimes many years - to learn whether a drug actually provides real improvement for patients – such as living longer or feeling better. This real improvement is known as a "clinical outcome." Mindful of the fact that obtaining data on clinical outcomes can take a long time, in 1992 FDA instituted the *Accelerated Approval* regulation, allowing earlier approval of drugs to treat serious diseases, and that fill an unmet medical need based on a surrogate endpoint.

A surrogate endpoint is a marker - a laboratory measurement, or physical sign - that is used in clinical trials as an indirect or substitute

measurement that represents a clinically meaningful outcome, such as survival or symptom improvement. The use of a surrogate endpoint can considerably shorten the time required prior to receiving FDA approval.

Approval of a drug based on such endpoints is given on the condition that post marketing clinical trials verify the anticipated clinical benefit.

The FDA bases its decision on whether to accept the proposed surrogate endpoint on the scientific support for thatendpoint. The studies that demonstrate the effect of the drug on the surrogate endpoint must be "adequate and well controlled" studies, the only basis under law, for a finding that a drug is effective.

Use of a surrogate can save valuable time in the drug approval process. For example, instead of having to wait to learn if a drug actually can extend the survival of cancer patients, the FDA might now approve a drug based on evidence that the drug shrinks tumors because tumor shrinkage is considered *reasonably likely to predict* a real clinical benefit. In this example, an approval based upon tumor shrinkage can occur far sooner than waiting to learn whether patients actually lived longer. The drug company will still need to conduct studies to confirm that tumor shrinkage actually does predict that patients will live longer. These studies are known as phase 4 confirmatory trials.

If the confirmatory trial shows that the drug actually provides a clinical benefit, then the FDA grants traditional approval for the drug. If the confirmatory trial does not show that the drug provides clinical benefit for patients, FDA has regulatory procedures in place that could lead to removing the drug from the market.

Priority Review

Prior to approval, each drug marketed in the United States must go through a detailed FDA review process. In 1992, under the Prescription Drug User Act (PDUFA), FDA agreed to specific goals for improving the drug review time and created a two-tiered system of review times – *Standard Review* and *Priority Review*.

Standard Review is applied to a drug that offers at most, only minor improvement over existing marketed therapies. The 2002 amendments to PDUFA set a goal that a *Standard Review* of a new drug application be accomplished within a *ten-month* time frame.

A *Priority Review* designation is given to drugs that offer major advances in treatment, or provide a treatment where no adequate therapy exists. A *Priority Review* means that the time it takes FDA to review a new drug application is reduced. The goal for completing a Priority Review is *six months*.

Priority Review status can apply both to drugs that are used to treat serious diseases and to drugs for less serious illnesses. The FDA goal for reviewing a drug with Priority Review status is six months.

The distinction between priority and standard review times is that additional FDA attention and resources will be directed to drugs that have the potential to provide significant advances in treatment.
Such advances can be demonstrated by, for example:

- evidence of increased effectiveness in treatment, prevention, or diagnosis of disease;
- elimination or substantial reduction of a treatment-limiting drug reaction;
- documented enhancement of patient willingness or ability to take the drug according to the required schedule and dose; or
- evidence of safety and effectiveness in a new subpopulation, such as children.

A request for *Priority Review* must be made by the drug company. It does not affect the length of the clinical trial period. FDA determines within 45 days of the drug company's request whether a *Priority* or *Standard Review* designation will be assigned. Designation of a drug as "Priority" does not alter the scientific/medical standard for approval or the quality of evidence necessary.

SUMMARY

Fast Track, *Accelerated Approval* and *Priority Review* are approaches that are intended to make therapeutically important drugs available at an earlier time. They do not compromise the standards for the safety and effectiveness of the drugs that become available through this process.

These revitalized FDA drug review approaches have yielded tangible results in bringing safe and effective drugs to patients with serious diseases more quickly. For example, since 1996, 68 drugs for cancer therapies have received priority review and approval.

FDA reviewed Gleevec, a treatment for chronic myeloid leukemia, in four months. Shortened review times have also brought promising treatments to patients with HIV/AIDS more quickly. Kaletra for the treatment of HIV/AIDS was reviewed and approved in 3.5 months. Pegasys, a combination product for the treatment of Hepatitis C was approved for marketing in 4 months.

The table below illustrates the improvement in FDA review times in the years between 1993 to 2003. The median time required to review a priority review drug was reduced from 13.9 months to 6.7 months.

Fast Track, *Accelerated Approval*, and *Priority Review* have evolved over time. FDA has been vigilant in assuring that reducing the time necessary for drug development has not compromised the safety and effectiveness of drugs for patients with serious diseases.

Comparison of Approval Times for Priority and Standard Review Drugs

Calendar Years 1993-2003

	Priority		Standard	
Calendar Year	Number Approved	Median FDA Review Time (months)	Number Approved	Median FDA Review Time (months)
1993	13	13.9	12	27.2
1994	13	15.0	9	22.2
1995	9	6.0	19	15.9
1996	18	7.7	35	14.6
1997	9	6.4	30	14.4
1998	16	6.2	14	12.3
1999	19	6.3	16	14.0
2000	9	6.0	18	15.4
2001	7	6.0	17	15.7
2002	7	13.8	10	12.5
2003	9	6.7	12	13.8

U.S. Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993
Ph. 1-888-INFO-FDA (1-888-463-6332)

Centers for Disease Control and Prevention
CDC 24/7: Saving Lives. Protecting People. Saving Money through Prevention.

Highlights: How Smoking Harms People of All Ages

- Toxic ingredients in cigarette smoke travel throughout the body, causing damage in several different ways. (p. 616)
- Nicotine reaches the brain within 10 seconds after smoke is inhaled. It has been found in every part of the body and in breast milk. (p. 616)
- Carbon monoxide binds to hemoglobin in red blood cells, preventing affected cells from carrying a full load of oxygen. (p. 616)
- Cancer-causing agents (carcinogens) in tobacco smoke damage important genes that control the growth of cells, causing them to grow abnormally or to reproduce too rapidly. (pp. 44–45)
- The carcinogen benzo[a]pyrene binds to cells in the airways and major organs of smokers. (p. 616)
- Smoking affects the function of the immune system and may increase the risk for respiratory and other infections. (p. 616)
- There are several likely ways that cigarette smoke does its damage. One is oxidative stress that mutates DNA, promotes atherosclerosis, and leads to chronic lung injury. Oxidative stress is thought to be the general mechanism behind the aging process, contributing to the development of cancer, cardiovascular disease, and COPD. (p. 619)
- The body produces antioxidants to help repair damaged cells. Smokers have lower levels of antioxidants in their blood than do nonsmokers. (pp. 618–619)
- Smoking is associated with higher levels of chronic inflammation, another damaging process that may result from oxidative stress. (p. 619)

Disclaimer: Data and findings provided on this page reflect the content of this particular Surgeon General's Report. More recent information may exist elsewhere on the Smoking & Tobacco Use Web site (for example, in fact sheets, frequently asked questions, or other materials that are reviewed on a regular basis and updated accordingly).

Historical content
Page last updated: May 27, 2004
Content source: Office on Smoking and Health, National Center for Chronic Disease Prevention and Health Promotion

Centers for Disease Control and Prevention 1600 Clifton Rd. Atlanta, GA 30333, USA
800-CDC-INFO (800-232-4636) TTY: (888) 232-6348, New Hours of Operation 8am-8pm ET/Monday-Friday
Closed Holidays - cdcinfo@cdc.gov

USA.gov Government Made Easy






The 2004
Surgeon General's Report

The Health Consequences of Smoking

what it means to you

U.S. DEPARTMENT
OF HEALTH AND
HUMAN SERVICES

about
the surgeon general's report

The Surgeon General is appointed by the President of the United States to help promote and protect the health of our citizens. As the nation's highest-ranking public health officer, the Surgeon General can direct studies on health risks—such as smoking.

The 2004 *Surgeon General's Report on the Health Consequences of Smoking* was prepared by 19 of the country's top scientists, doctors, and public health experts. The full report is nearly 1,000 pages long and took more than 3 years to complete. It is written for a scientific audience. However, the Surgeon General believes that the findings are very important to everyone and asked that this booklet be created. This booklet explains what the report says and what it means to you.

Suggested Citation:

U.S. Department of Health and Human Services. The Health Consequences of Smoking: what it means to you. U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health, 2004.

Since the first Surgeon General's report on smoking and health in 1964, medical experts have written 27 more reports for the Surgeon General on tobacco use. In each report, leading scientists have found that using tobacco causes people to become sick, disabled, or to die.

This report goes even further in detailing the bad health effects of smoking. Everyone knows smoking hurts you. This report shows that it is worse than you know.

Costs of Smoking in Dollars and Lives

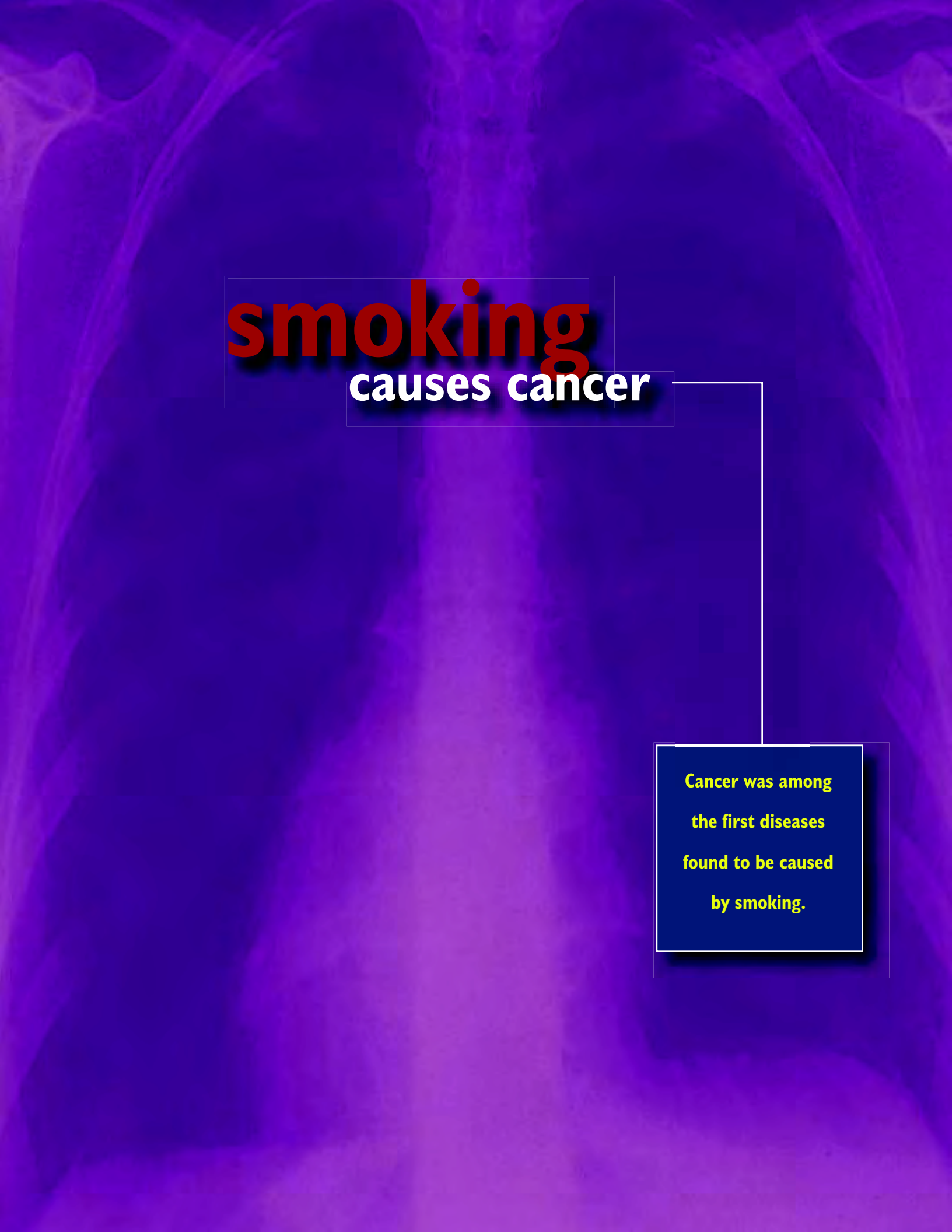
Deaths Since 1964	12 Million Americans Dead
Costs to the Nation	$157.7 Billion Each Year
Number of Adults and High School Students Who Smoke	About 1 Out of Every 4 Adults and Students
Number of Young People Who Smoke Their 1st Cigarette	More Than 4,000 Each Day

The Surgeon General of the United States, working with a team of leading experts on smoking and health, released a new report in 2004. After reviewing scientific evidence, researchers reached these important conclusions:

- **Smoking harms nearly every organ of your body. It causes diseases and worsens your health.**
- **Quitting smoking has many benefits. It lowers your risk for diseases and death caused by smoking and improves your health.**
- **Low-tar and low-nicotine cigarettes are not safer to smoke.**
- **The list of diseases that we know are caused by smoking has grown even longer. The list now includes cancers of the cervix, pancreas, kidneys, and stomach, aortic aneurysms, leukemia, cataracts, pneumonia, and gum disease.**

The 2004 Surgeon General's report has new information about how smoking harms your health. A new database of more than 1,600 articles cited in this report is available on the Internet. By going to the CDC Web site at **www.cdc.gov/tobacco/sgr/sgr_2004/** you can search many of the studies cited in this report. Topics

include cancer, cardiovascular diseases, respiratory diseases, reproductive effects, and other harmful health effects.



smoking causes cancer

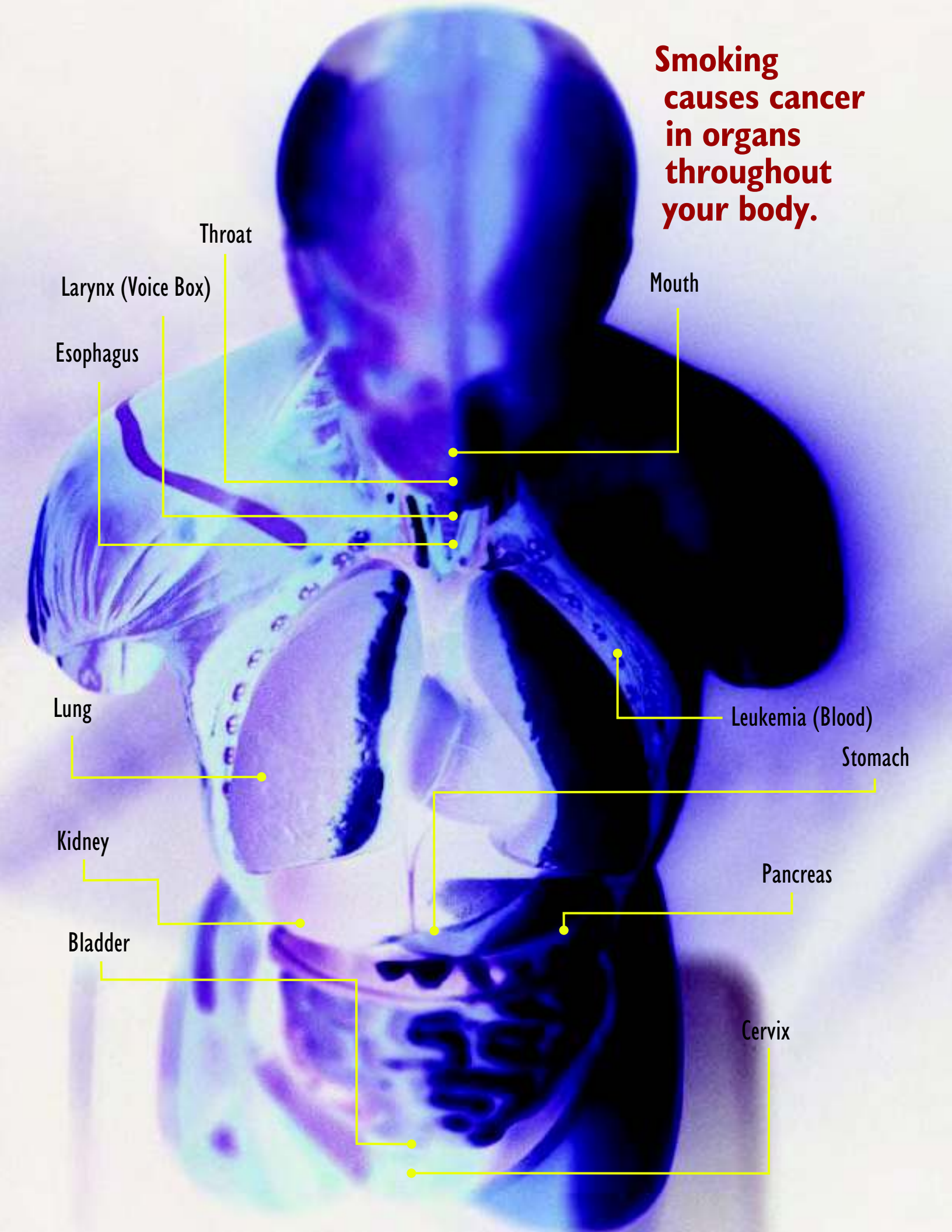
Cancer was among the first diseases found to be caused by smoking.

Cancer is the second leading cause of death in the United States. One out of every four people in this country dies because of cancer. In 2003, researchers estimated that more than half a million Americans—that's over 1,500 people a day—would die of cancer. The cost of treating cancer in the United States is overwhelming. In 2002, cancer cost our nation over $170 billion. This included more than $110 billion in lost work by people who were disabled or who died, and at least $60 billion for medical treatments.

Cancer was among the first diseases found to be caused by smoking. The earliest major studies, carried out in the 1950s and 1960s, focused on lung cancer. The number of lung cancer cases among smokers reached very high levels during that time.

Since the first Surgeon General's report on smoking in 1964 concluded that smoking causes lung cancer, the list of diseases linked to smoking has grown to include cancers in organs throughout the body. Your risk for these cancers increases with the number of cigarettes you smoke and the number of years you smoke. Your risk decreases after quitting completely.

Your risk for cancer increases with the number of cigarettes you smoke and the number of years you smoke.


Smoking causes cancer in organs throughout your body.
Throat
Larynx (Voice Box)
Esophagus
Mouth
Lung
Leukemia (Blood)
Stomach
Kidney
Pancreas
Bladder
Cervix

facts you should know

- Smoking causes cancers of the mouth, throat, larynx (voice box), lung, esophagus, pancreas, kidney, and bladder.
- Smoking causes cancers of the stomach, cervix, and acute myeloid leukemia, which is a cancer of the blood.
- Cigarette smoking causes most cases of lung cancer. Smokers are about 20 times more likely to develop lung cancer than nonsmokers. Smoking causes about 90 percent of lung cancer deaths in men and almost 80 percent in women.
- Using both cigarettes and alcohol causes most cases of larynx cancer.
- Certain agents in tobacco smoke can damage important genes that control the growth of cells and lead to cancer.
- Smoking low-tar cigarettes does not reduce your risk for lung cancer.

Smoking causes

90% of lung cancer

deaths in men and

80% in women.

smoking

causes cardiovascular diseases

Cigarette smoke damages the cells lining your blood vessels and heart.

Heart disease and stroke are cardiovascular (heart and blood vessel) diseases caused by smoking. Heart disease and stroke are also the first and third leading causes of death in the United States.

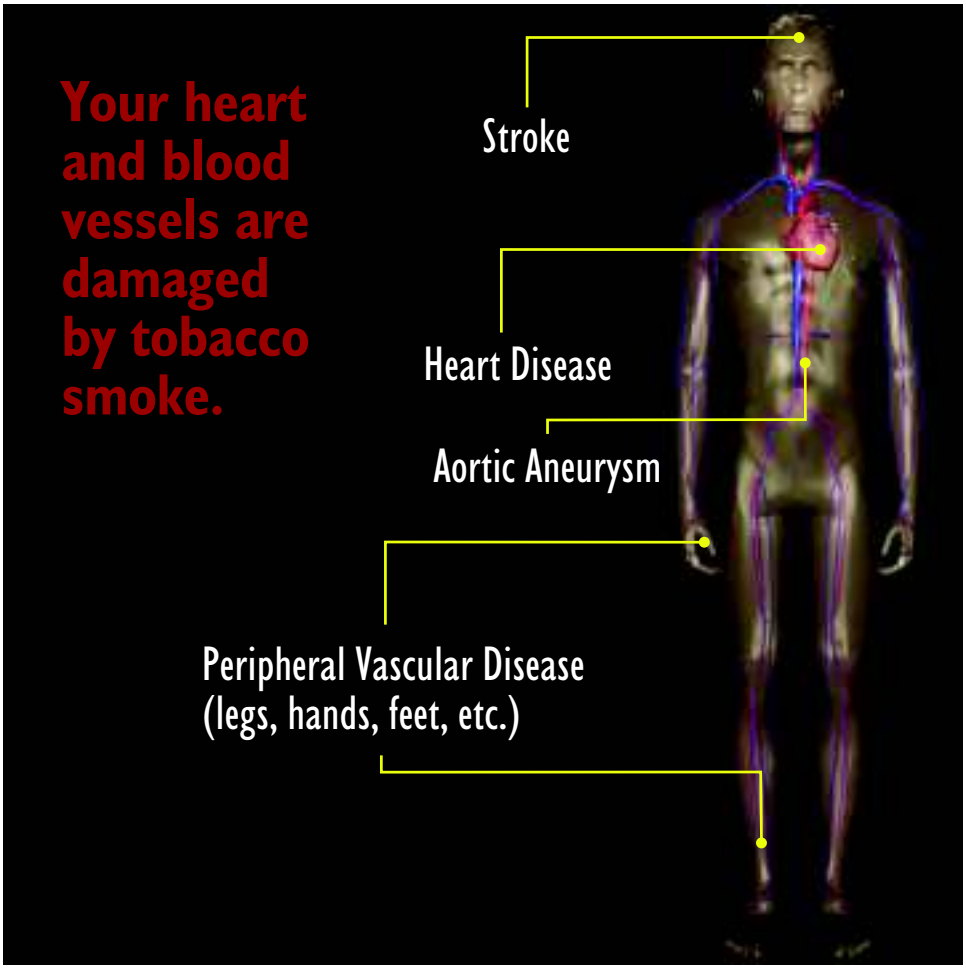
More than 61 million people in the United States suffer from some form of heart and blood vessel disease. This includes high blood pressure, coronary heart disease, stroke, and congestive heart failure. Nearly 2,600 Americans die every day as a result of cardiovascular diseases. This is about 1 death every 33 seconds. You are up to four times more likely to die from heart disease if you smoke. In 2003, heart disease and stroke cost the United States an estimated $351 billion in health care costs and lost productivity from death and disability.

The link between smoking and heart disease was noted in the first Surgeon General's report in 1964. Later reports revealed a much stronger connection. Researchers found that smoking is a major cause of diseases of blood vessels inside and outside the heart.

Most cases of these diseases are caused by atherosclerosis, a hardening and narrowing of the arteries. Damage to your arteries and blood clots that block blood flow can cause heart attacks or strokes.

Cigarette smoking speeds up this process even in smokers in their 20s. Cigarette smoke damages the cells lining the blood vessels and heart. The damaged tissue swells. This makes it hard for blood vessels to get enough oxygen to cells and tissues. Your heart and all parts of your body must have oxygen. Perhaps most important, cigarette smoking can increase your risk of dangerous blood clots, both because of swelling and redness and by causing blood platelets to clump together.

Cigarettes aren't the only dangerous kind of tobacco. Even smokeless tobacco can lead to heart and blood vessel disease.



facts you should know

- Coronary heart disease is the leading cause of death in the United States.
- You are up to four times more likely to die from coronary heart disease if you smoke.
- In 2000, about 1.1 million Americans had heart attacks.
- Even with treatment, 25 percent of men and 38 percent of women die within one year of a heart attack.
- Smoking causes atherosclerosis, or hardening and narrowing of your arteries.
- Smoking causes coronary heart disease.
- Smoking low-tar or low-nicotine cigarettes rather than regular cigarettes does not reduce the risk of coronary heart disease.
- Smoking causes strokes.
- Smoking causes abdominal aortic aneurysm, a dangerous weakening and ballooning of the major artery near your stomach.

smoking

causes respiratory diseases

Smoking causes more than 90 percent of deaths from COPD each year.

Smoking harms your lungs. If you smoke, your lungs can't fight infection well and this causes injuries to lung tissues. Tissue injury leads to chronic obstructive pulmonary disease (COPD), sometimes called emphysema, and other respiratory diseases. People with COPD slowly start to die from lack of air.

COPD is the fourth leading cause of death in the United States. It is responsible for more than 100,000 deaths per year. Smoking causes more than 90 percent of these deaths.

Most sudden respiratory illnesses, such as bronchitis or pneumonia, are caused by viral or bacterial infections. They are usually diagnosed as upper respiratory tract infections (nose, throat, and larynx) or lower respiratory tract infections (below the larynx). Smokers have more upper and lower respiratory tract infections than nonsmokers. This happens because smoking damages your body's defenses against infections.

Normally, your body helps keep dangerous viruses and bacteria out by clearing your nose with mucus. But this defense takes almost twice as long in smokers as in nonsmokers. Once viruses and bacteria are inside your body, cells in your immune system usually kill them and prevent infection. But in smokers, some of the cells that destroy germs are decreased while others are increased. This imbalance makes a smoker's immune system weaker.

Mothers who smoke during pregnancy hurt their babies' lungs.

Chronic lung diseases are long lasting. They usually affect your airways and the tiny sacs where oxygen is absorbed into your lungs. Lung injury in smokers begins when smoke causes lung tissues to become red and swollen. This releases unwanted oxygen molecules that damage the lung. It also causes enzymes to be released that can eat delicate lung tissue.

Normally, your body fights damaging oxygen molecules with antioxidants. It fights the destructive enzymes with defensive enzymes. Smoking makes antioxidants and defensive enzymes less effective. Over time, redness and swelling cause scarring and destroy your lungs, causing COPD.

Smoking harms people of all ages.

Infants. Effects of smoking on lung development can begin before birth. When mothers smoke during pregnancy, it hurts their babies' lungs.

Children. Children and teens who smoke are less physically fit and have more breathing problems. Smoking at this age can slow lung growth. If you smoke as a teenager, your lung function begins to decline years earlier than nonsmokers. This hurts you when you want to be active.

All Ages. At any age, smoking damages your lungs. The more cigarettes you smoke, the faster this happens. Air pollution, being overweight, and not eating enough fresh fruit increase your risk of lung disease even more if you smoke. However, if you quit smoking, your lungs can gradually return to normal for your age.

facts you should know

Smoking causes injury to the airways and lungs, leading to a deadly lung condition.

Smokers are more likely than nonsmokers to have upper and lower breathing tract infections.

Mothers who smoke during pregnancy hurt the lungs of their babies.

If you smoke during childhood and teenage years, it slows your lung growth and causes your lungs to decline at a younger age.

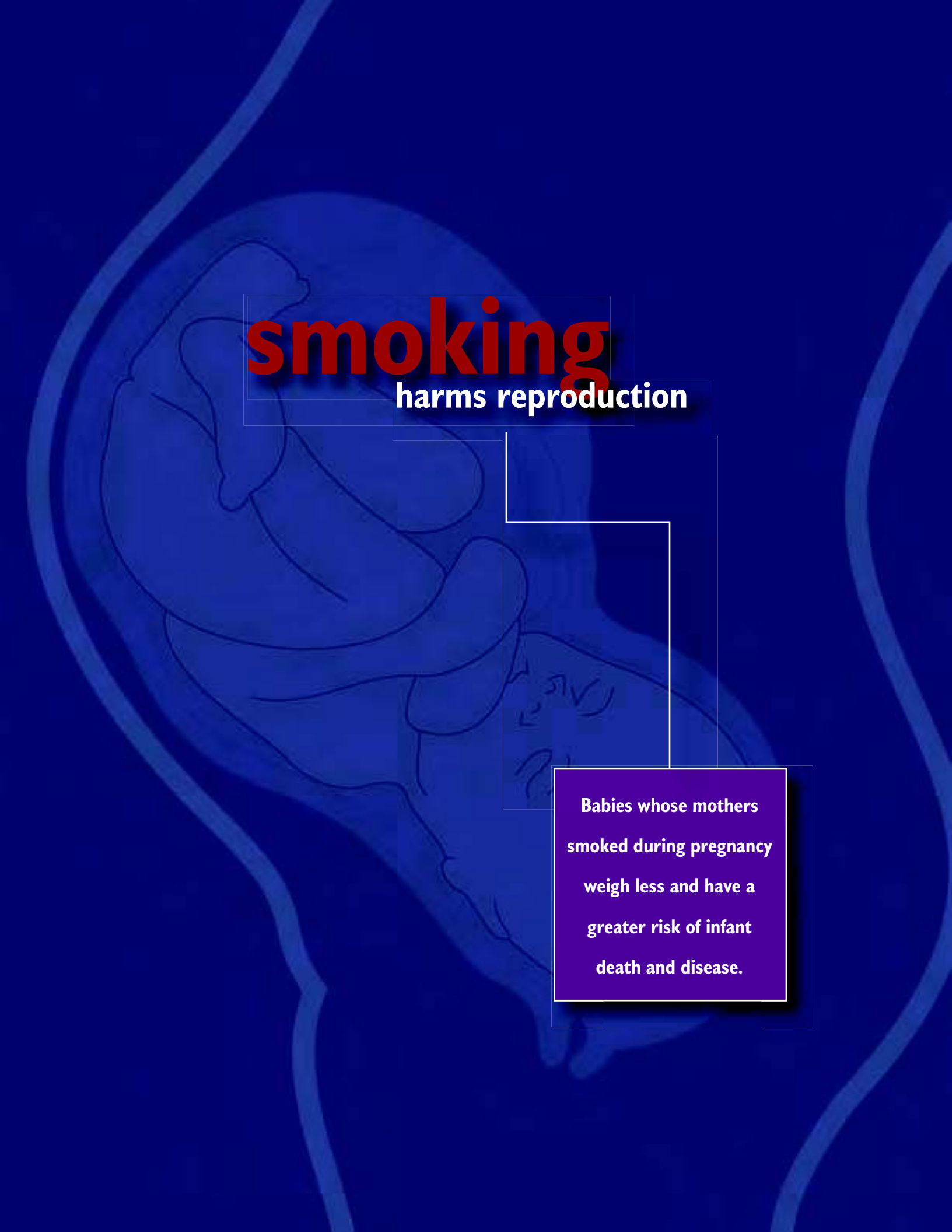
Smoking is related to chronic coughing, wheezing, and asthma among children and teens.

Smoking is related to chronic coughing and wheezing among adults.

After stopping smoking, former smokers eventually return to normal age-related lung function.

think about it

Do you know anyone who has been diagnosed with COPD? Do you know if they smoked cigarettes?



smoking

harms reproduction

Babies whose mothers smoked during pregnancy weigh less and have a greater risk of infant death and disease.

Smoking harms every phase of reproduction. Women who smoke have more difficulty becoming pregnant and have a higher risk of never becoming pregnant. Women who smoke during pregnancy have a greater chance of complications, premature birth, low birth weight infants, stillbirth, and infant mortality.

Low birth weight is a leading cause of infant deaths. Many of these deaths are linked to smoking. Even though we now know the danger of smoking during pregnancy, fewer than one out of four women quit smoking once they become pregnant.

High Risk Pregnancy. Smoking makes it more difficult for women to become pregnant. Once they are pregnant, women who smoke have more complications. One complication is *placenta previa*, a condition where the placenta (the organ that nourishes the baby) grows too close to the opening of the womb. This condition frequently requires delivery by caesarean section. Pregnant women who smoke are also more likely to have *placental abruption*. In this condition, the placenta separates from the wall of the womb earlier than it should. This can lead to preterm delivery, stillbirth, and early infant death. If you smoke while you are pregnant, you are also at a

higher risk that your water will break before labor begins. All these conditions make it more likely that, if you smoke, your baby will be born too early.

Babies whose mothers smoke before and after birth are 3 to 4 times more likely to die from sudden infant death syndrome.

Low Birth Weight Babies. Babies of mothers who smoked during pregnancy have lower birth weights, often weighing less than 5.5 pounds. Low birth weight babies are at greater risk for childhood and adult illnesses and even death. Babies of smokers have less muscle mass and more fat than babies of nonsmokers. Nicotine causes the blood vessels to constrict in the umbilical cord and womb. This decreases the amount of oxygen to the unborn baby. This can lead to low birth weight. It also reduces the amount of blood in the baby's system. Pregnant smokers actually eat more than pregnant nonsmokers, yet their babies weigh less. If you quit smoking before your third trimester (the last 3 months), your baby is more likely to be close to normal weight.

Sudden Infant Death Syndrome. The death rate from sudden infant death syndrome (SIDS) has fallen by more than half since the "Back to Sleep" campaign began in the 1990s. This campaign reminds parents that babies should lie on their backs while sleeping. Yet more can be done. Babies exposed to secondhand smoke after birth have double the risk of SIDS. Babies whose mothers smoke before and after birth are three to four times more likely to die from SIDS.

facts you should know

- Smoking causes lower fertility in women.
- Babies of women who smoke are more likely to be born too early.
- Smoking during pregnancy causes *placenta previa* and *placental abruption*. These conditions can cause a baby to be born too early and then be sick.
- The nicotine in cigarette smoke reduces the amount of oxygen reaching the fetus.
- Smoking causes reduced fetal growth and low birth weight.
- Smoking by the mother can cause SIDS.

think about it

If you were a woman who smokes, would you quit smoking to help protect the life of your child?

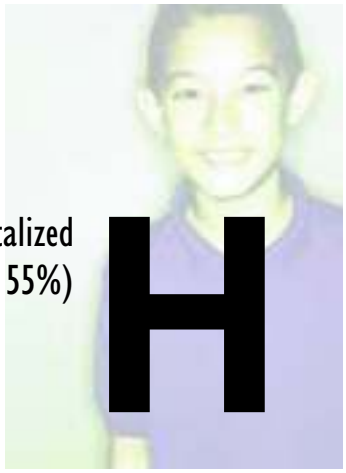
other effects of smoking

Overall health in smokers is poorer than in nonsmokers.

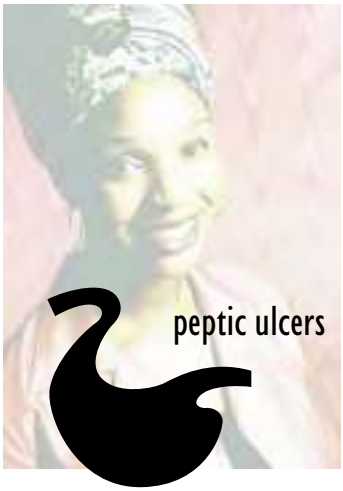
Smoking damages your health in many other ways. Smokers are less healthy overall than nonsmokers. Smoking harms your immune system and increases your risk of infections. The toxic ingredients in cigarette smoke travel throughout your body. For example, nicotine reaches your brain within 10 seconds after you inhale smoke. It has been found in every organ of the body, as well as in breast milk. If you smoke, your cells will not get the amount of oxygen needed to work properly. This is because carbon monoxide keeps red blood cells from carrying a full load of oxygen. Carcinogens, or cancer-causing poisons, in tobacco smoke bind to cells in your airways and throughout your body.

Smoking harms your whole body. It increases your risk of fractures, dental diseases, sexual problems, eye diseases, and peptic ulcers. If you smoke, your illnesses last longer and you are more likely to be absent from work. In a study of U.S. military personnel, those who smoked were hospitalized 28 percent to 55 percent longer than nonsmokers. And the more cigarettes they smoked, the longer their hospitalization. Smokers also use more medical services than nonsmokers.

Among people younger than 65 enrolled in a health maintenance organization, or HMO, health care costs for smokers were 25 percent higher than for nonsmokers.

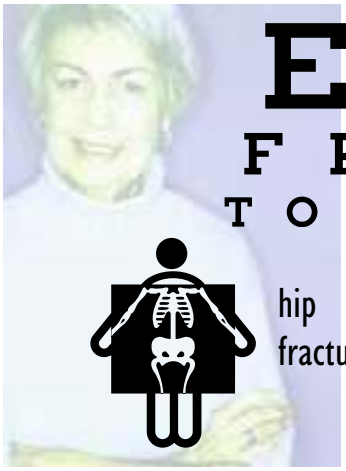


being hospitalized (by up to 55%)



peptic ulcers

sexual and reproductive problems



cataracts

hip fractures

smoking also increases your risk of...

respiratory infections

complications after surgery

gum disease and tooth loss (half of all cases)

facts you should know

Smokers are less healthy than nonsmokers.

Smokers are more likely to be absent from work than nonsmokers.

Smokers use medical care services more often than nonsmokers.

After surgery, smokers have more problems with wound healing and more respiratory complications.

For women, smoking causes your bones to lose density after menopause.

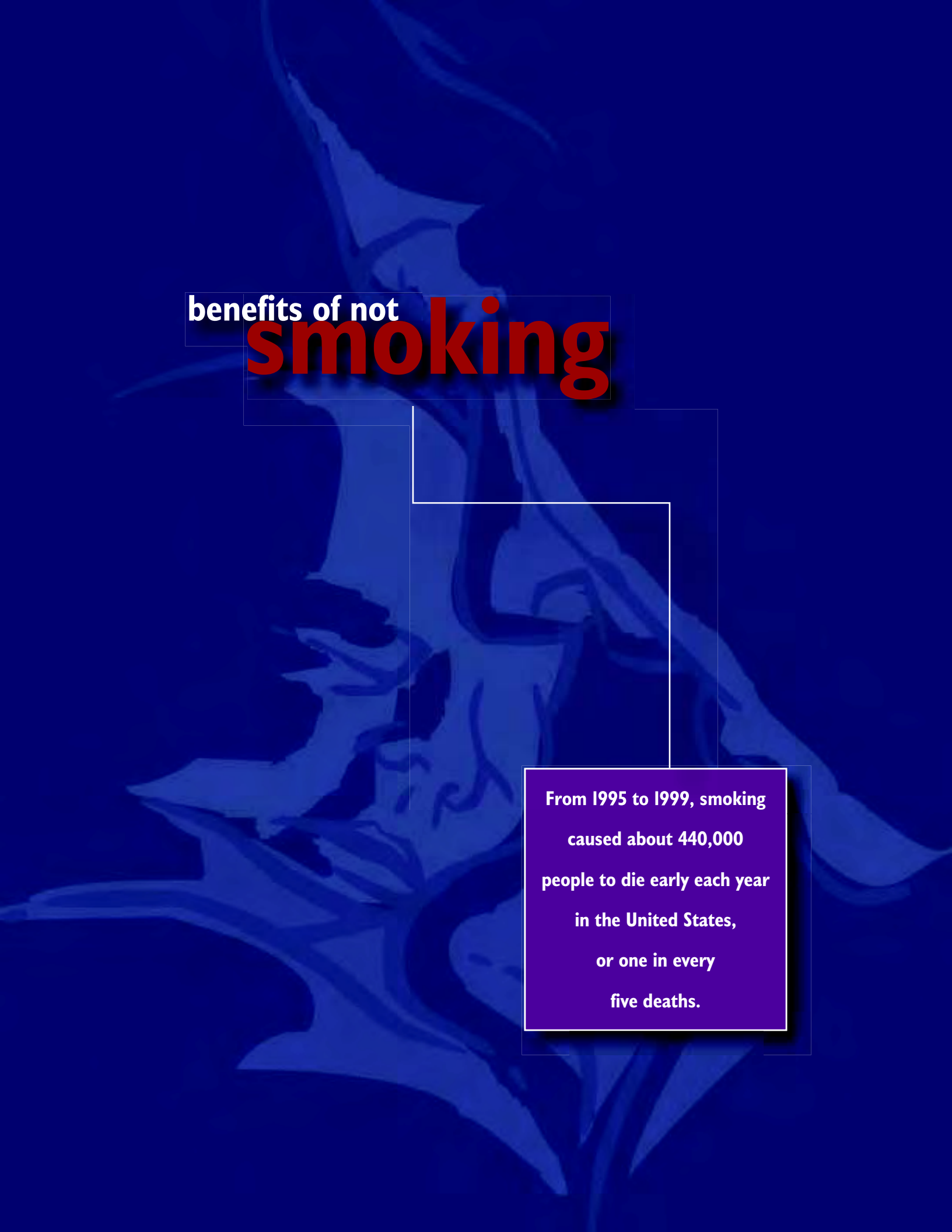
Smoking increases your risk of hip fractures.

Smoking causes half of all cases of adult periodontitis, a serious gum infection that can cause pain and tooth loss.

For men, smoking may cause sexual problems.

Smoking increases your risk for cataracts, a leading cause of blindness in the United States and worldwide. Smokers are two to three times more likely to develop cataracts than nonsmokers.

Smoking causes peptic ulcers in smokers with *Helicobacter pylori* infections. Compared with nonsmokers, smokers with this infection are more likely to develop ulcers and to have complications of an ulcer. In severe cases, this condition can lead to death.


benefits of not
smoking
From 1995 to 1999, smoking
caused about 440,000
people to die early each year
in the United States,
or one in every
five deaths.

Cigarette smoking is the leading cause of preventable disease and death in the United States. It is also costly to our nation.

Cigarette smoking has caused an estimated 12 million deaths since the first Surgeon General's report on smoking in 1964. These include

- **4.1 million deaths from cancer**
- **5.5 million deaths from cardiovascular (heart and blood vessel) diseases**
- **1.1 million deaths from respiratory diseases, and**
- **94,000 fetal and infant deaths.**

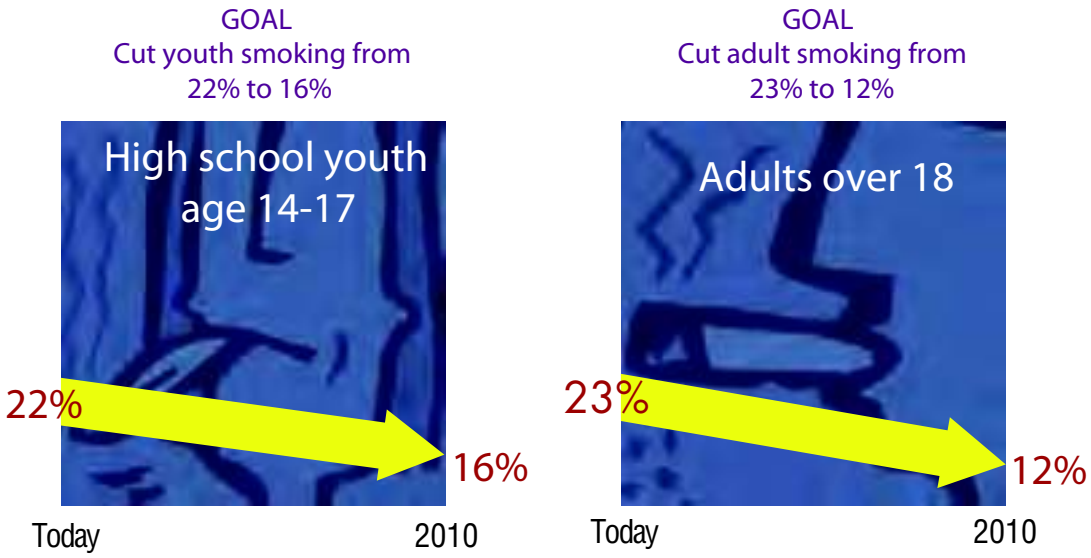
From 1995 to 1999, smoking caused about 440,000 people to die early each year in the United States. That was one in every five deaths. Adults who smoke die an average of 13 to 14 years early.

The U.S. Public Health Service has set goals to reduce smoking in our country by the year 2010. The first goal is to cut smoking rates among

The economic burden of cigarette use is enormous. From 1995 to 1999, smoking-related costs totaled $157.7 billion each year. This figure includes more than $75 billion in direct medical costs for adults (ambulatory care, hospital care, prescription drugs, nursing homes, and other care), about $82 billion in indirect costs from lost productivity, and $366 million for neonatal care. This equals an estimated $3,000 per smoker per year.

high school aged youth from 22 percent to 16 percent. Among adults, the goal is to reduce smoking from 23 percent to 12 percent.

If these goals are met, about 7.1 million early deaths will be prevented after 2010. Although adult and youth smoking rates have gone down in recent years, the diseases caused by smoking will continue for many years.



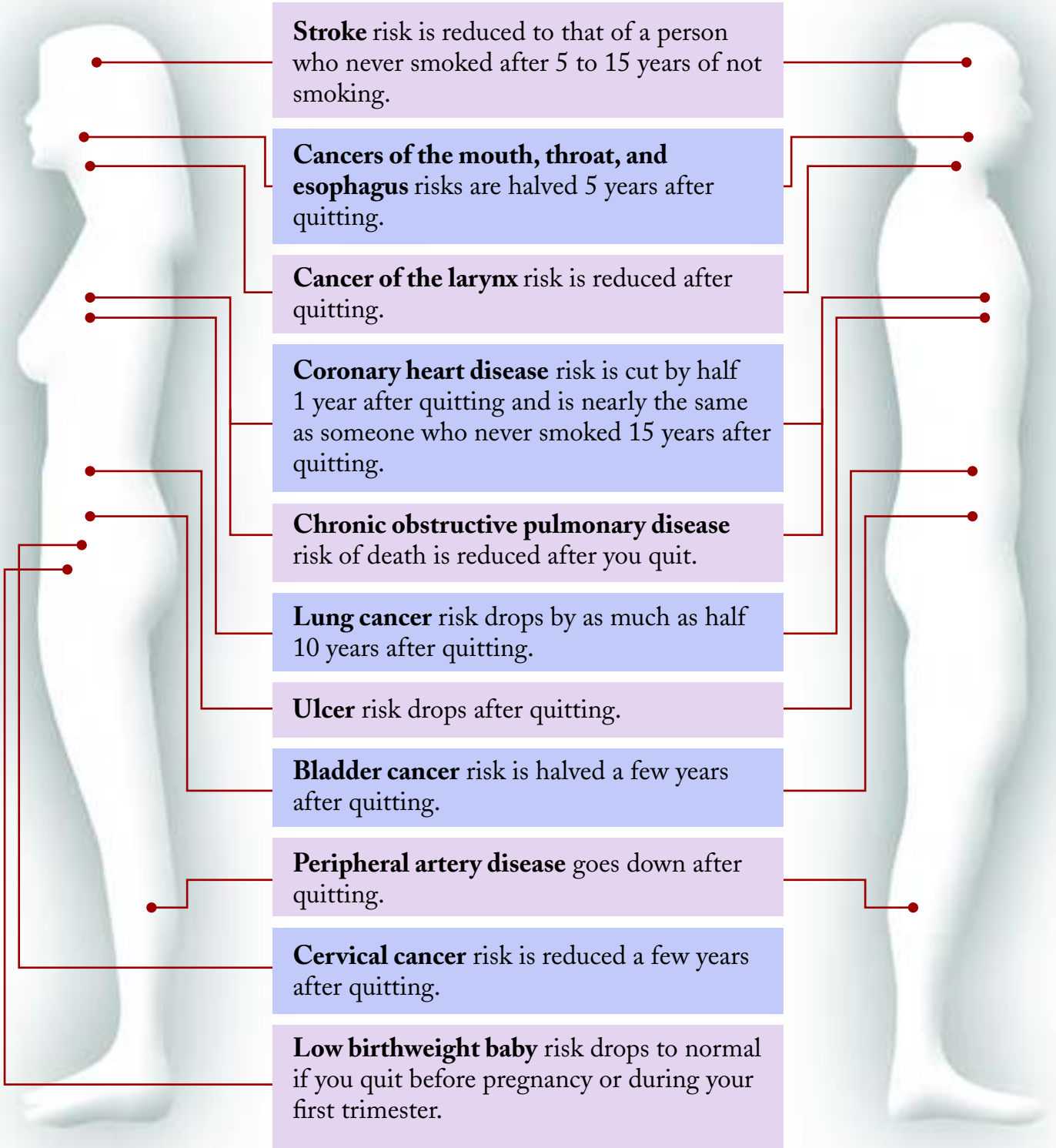
The numbers shown in this chart are the latest from CDC Surveillance Summaries on May 21, 2004. They show that fewer kids are smoking now than last year.

facts you should know

- More than 12 million deaths have been caused by smoking since the first published Surgeon General's report on smoking in 1964.
- Cigarette smoking has caused about 440,000 early deaths each year from 1995 to 1999, or more than 1,200 people every day.
- One half of all lifetime smokers will die early because of their decisions to smoke.
- The economic costs of smoking in the United States each year from 1995 to 1999 were $157.7 billion.
- Meeting our national health goals for reducing smoking will prevent 7.1 million early deaths after 2010.
- Adults who smoke lose an average of 13 to 14 years of their lives.

the benefits of quitting

Compared to smokers, your…



Stroke risk is reduced to that of a person who never smoked after 5 to 15 years of not smoking.

Cancers of the mouth, throat, and esophagus risks are halved 5 years after quitting.

Cancer of the larynx risk is reduced after quitting.

Coronary heart disease risk is cut by half 1 year after quitting and is nearly the same as someone who never smoked 15 years after quitting.

Chronic obstructive pulmonary disease risk of death is reduced after you quit.

Lung cancer risk drops by as much as half 10 years after quitting.

Ulcer risk drops after quitting.

Bladder cancer risk is halved a few years after quitting.

Peripheral artery disease goes down after quitting.

Cervical cancer risk is reduced a few years after quitting.

Low birthweight baby risk drops to normal if you quit before pregnancy or during your first trimester.

quitting isn't easy

- Most ex-smokers try to quit several times before succeeding. About one-third of smokers who quit for a year may start again. However, the longer you stay quit, the less likely you are to start smoking again.

- According to polls, nearly three out of four smokers say that they would like to quit.

- Only 19 percent of people who smoke have **never** tried to quit.

- Each year, about 15 million smokers quit for at least a day, but fewer than 5 percent of them are able to stay tobacco-free for 3 to 12 months.

- Remember, smokers often try to quit more than once before they succeed.

within 20 minutes of quitting...

Within 20 minutes after you smoke that last cigarette, your body begins a series of changes that continue for years.

20 Minutes After Quitting
Your heart rate drops.

12 Hours After Quitting
Carbon monoxide level in your blood drops to normal.

2 Weeks to 3 Months After Quitting
Your heart attack risk begins to drop.
Your lung function begins to improve.

1 to 9 Months After Quitting
Your coughing and shortness of breath decrease.

1 Year After Quitting
Your added risk of coronary heart disease is half that of a smoker's.

5 Years After Quitting
Your stroke risk is reduced to that of a nonsmoker's 5-15 years after quitting.

10 Years After Quitting
Your lung cancer death rate is about half that of a smoker's.
Your risk of cancers of the mouth, throat, esophagus, bladder, kidney, and pancreas decreases.

15 Years After Quitting
Your risk of coronary heart disease is back to that of a nonsmoker's.

quit tips

- Nibble on low-calorie snacks like carrot sticks, celery, and apples.
- Chew gum.
- Stretch out your meals. Eat slowly and pause between bites.
- After dinner, instead of a cigarette, suck on a hard candy or sip your favorite beverage.
- Take a deep breath and exhale slowly. Remember, the desire to smoke will pass.

basic strategies

- See your doctor, call a telephone quitline, or join a group program to learn new skills and behaviors to deal with situations where you want to smoke.
- Get ready and set a quit date.
- Get support and encouragement from family and friends.
- Get medication and use it correctly.
- Be prepared for relapse or difficult situations.

about weight gain

- Nearly 80 percent of those who quit smoking gain weight. But 56 percent of people who continue to smoke gain weight, too.
- The average weight gain after quitting smoking is just 5 pounds.
- The bottom line: The health benefits of quitting far exceed any risks from the average weight gain that may follow quitting.

helpful hints

To limit weight gain after you quit smoking, eat a well-balanced diet and avoid extra calories in sugary and fatty foods. If you crave sweets, eat small pieces of fruit. Have low-calorie snacks on hand for nibbling. Drink 6 to 8 glasses of water each day. Build exercise into your life by walking 30 minutes per day, or choose another exercise like running, swimming, cycling, or gardening. Talk to your doctor about an exercise program that is right for you.

acknowledgments

Project Leads and Writers
Sarah Gregory, Health Communications Specialist, Centers for Disease Control and Prevention
Pete Xiques, Science Applications International Corporation

Graphic Design
C. Mark Van Hook, Denton Lesslie, Science Applications International Corporation

Editorial Assistance
Vickie Reddick, Science Applications International Corporation

A special thank you to Surgeon General Dr. Richard Carmona for his commitment to health literacy and his commissioning of this public document.

Additional thanks to the many people who provided expert advice and suggestions: Dr. Jonathan Samet, Senior Scientific Editor of the 2004 Surgeon General's Report and Professor and Chairman, Department of Epidemiology, Bloomberg School of Public Health, Johns Hopkins University; Dr. Allan Noonan, Senior Advisor, Office of the Surgeon General, DHHS; Craig Stevens, Director of Communications, Office of the Surgeon General, DHHS; Jennifer Cabe, Speechwriter, Office of Public Health and Science, DHHS; Campbell Gardett, Director, News Division, Office of the Secretary, DHHS; Leslie Norman, Managing Editor of the 2004 Surgeon General's Report, CDC; Peggy Williams, Writer-Editor, Constella Health Sciences; Lynn Hughley, Lead Graphics Specialist, Northrop Grumman Corporation; the CDC Health Literacy Workgroup, co-chaired by Suzi Gates and Dr. P. Lynne Stockton, CDC, Kelly Holton, Lockheed Martin Corporation; Dr. Ruth Parker, Associate Professor of Medicine, Emory University School of Medicine; Dr. Julie Gazmararian, Research Associate Professor, Rollins School of Public Health, Emory University; and the scientific and communications staff of the Office on Smoking and Health, CDC.

For more information on smoking and your health, or for advice on how to quit smoking, talk to your doctor.

More facts and advice are available from CDC's Office on Smoking and Health or on the Web at:

Office on Smoking and Health
Mail Stop K-50
4770 Buford Highway, NE
Atlanta, GA 30341-3717
770-488-5705, press 3

or

www.cdc.gov/tobacco

To find out if your state has a telephone quitline, or to talk to a trained counselor from the National Cancer Institute, call

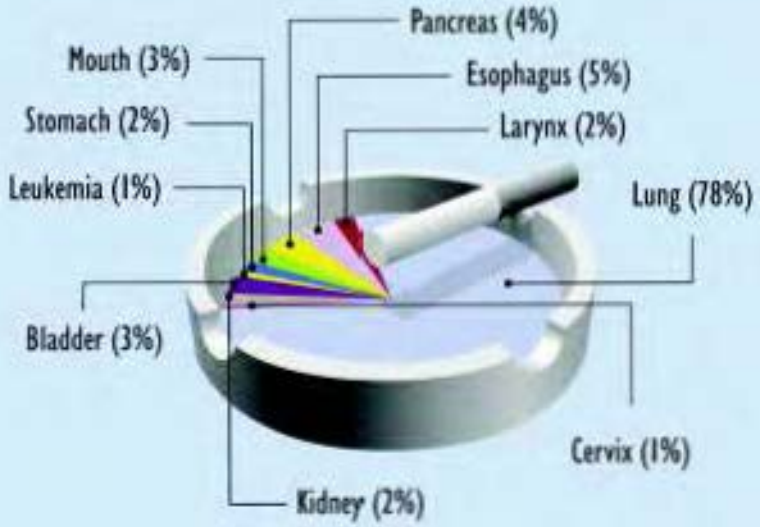
1-877-44U-QUIT

or visit the Web at

www.smokefree.gov

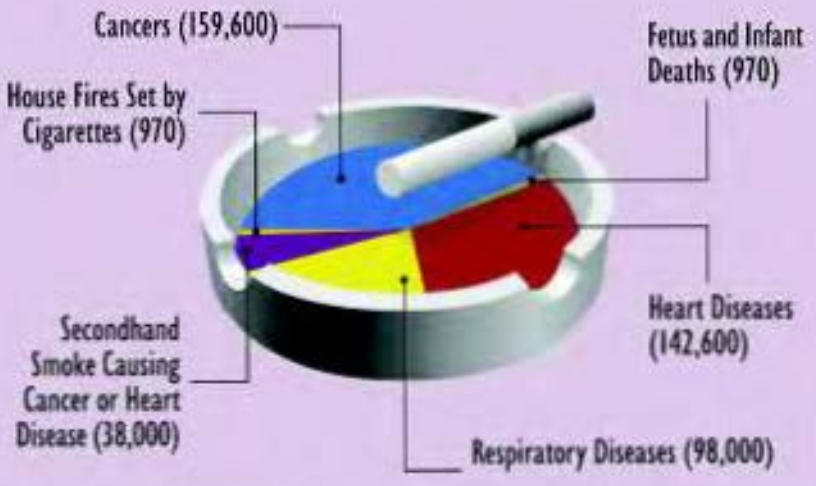
Smoking
cancer, death, and you

Cancers You Get From Smoking



Percentage of total 159,600 individual cases
All numbers are rounded.

440,000 Deaths Each Year Caused by Smoking



All numbers are rounded.

Centers for Disease Control and Prevention
CDC 24/7: Saving Lives. Protecting People. Saving Money through Prevention.

Health Across Lifespan

Infancy and Childhood (Birth to Age 18)

In the United States, the most prevalent disabling childhood conditions are vision disorders including amblyopia, strabismus, and significant refractive errors. Early detection increases the likelihood of effective treatment; however, less than 15% of all preschool children receive an eye exam, and less than 22% of preschool children receive some type of vision screening. Vision screening for children scored on par with breast cancer screening for women. Other eye diseases affecting this age group include retinopathy of prematurity (ROP), congenital defects, diabetic retinopathy (DR), and cancers such as retinoblastoma.

Adults Younger Than Age 40

Vision impairments in people younger than age 40 are mainly caused by refractive errors, which affect 25% of children and adolescents, and accidental eye injury. Approximately 1 million eye injuries occur each year, and 90% of these injuries are preventable. More than half (52%) of all patients treated for eye injuries are between ages 18 and 45 and almost 30% of those are 30–40 years (McGwin, Aiyuan, & Owsley, 2005). Additionally, diabetes affects this age group and is the leading cause of blindness among the working-age group 20–74. Racial disparities occur in prevalence and incidence of some eye conditions. For example, among specific high-risk groups such as African Americans, early signs of glaucoma may begin in this age group, particularly if there is a family history for glaucoma. Lifestyle choices adopted during this period may adversely affect vision and eye health in later years (e.g., smoking, sunlight exposure).

Adults Older Than Age 40

American adults aged 40 years and older are at greatest risk for eye diseases; as a result, extensive population-based study data are available for this age group. The major eye diseases among people aged 40 years and older are cataract, diabetic retinopathy, glaucoma, and age-related macular degeneration. These diseases are often asymptomatic in the early treatable stages. The prevalence of blindness and vision impairment increases rapidly with age among all racial and ethnic groups, particularly after age 75 (Prevent Blindness America, 2002). Although aging is unavoidable, evidence is mounting to show the association between some modifiable risk factors (i.e., smoking, ultraviolet light exposure, avoidable trauma, etc.) and these leading eye diseases affecting older Americans. Additional modifiable factors that might lend themselves to improved overall ocular health include a diet rich in antioxidants and maintenance of normal levels of blood sugar, lipids, total cholesterol, body weight, and blood pressure combined with regular exercise.

References

Bailey RN, Indian RW, Zhang X, Geiss LS, Duenas MR, Saaddine JB (2006). Visual impairment and eye care among older adults—five states. *MMWR* 2005:55:49; 1321–1325.

Centers for Disease Control and Prevention. Prevalence of disabilities and associated health conditions among adults—United States. *MMWR* 2001:50(7):120–5.

Prevent Blindness America, National Eye Institute. *Vision Problems in the U. S.—Prevalence of Adult Vision Impairment and Age-Related Eye Disease in America* [PDF–2.32MB] . Schaumburg, IL: Prevent Blindness America, 2002.

McGwin G, Aiyuan X, Owsley C. Rate of eye injury in the United States. *Arch of Ophthalmol* 2005:123;970–976.

Yawn BP, Kurland M, Butterfield L, Johnson B. Barriers to seeking care following school vision screening in Rochester, Minnesota, *J Sch Health* 1998:68:8; 319–324.

Page last reviewed: September 28, 2009
Page last updated: September 28, 2009
Content source: Division of Diabetes Translation, National Center for Chronic Disease Prevention and Health Promotion

Centers for Disease Control and Prevention 1600 Clifton Rd. Atlanta, GA 30333, USA
800-CDC-INFO (800-232-4636) TTY: (888) 232-6348, New Hours of Operation 8am-8pm ET/Monday-Friday
Closed Holidays - cdcinfo@cdc.gov

Alice Hamilton Award Winners and Honorable Mentions: Descriptions, 2003

NOTE: This page is archived for historical purposes and is no longer being maintained or updated.

Biological Science Category:

—Winner:

TITLE: **A Role of tumor necrosis factor (TNF) in toluene diisocyanate (TDI) asthma**

AUTHORS: **Joanna Matheson, Ranulfo Lamus, Robert W. Lange, Meryl H. Karol, Michael I. Luster**

SOURCE: **American Journal of Respiratory Cell and Molecular Biology 2002; 27:396-405**

ABSTRACT: Nearly 9 million workers are exposed to chemical agents associated with occupational asthma, with isocyanates representing the chemical class most responsible. Isocyanate-induced asthma has been difficult to diagnose and control, in part because the biologic mechanisms responsible for the disease and the determinants of exposure have not been well defined. Isocyanate-induced asthma is characterized by airway inflammation, and we hypothesized that inflammation is a prerequisite of isocyanate-induced asthma, with tumor necrosis factor (TNF)-α being critical to this process. To explore this hypothesis, wildtype mice, athymic mice, TNF-α receptor knockout (TNFR), and anti-TNF-α antibody-treated mice were sensitized by subcutaneous injection (20μ .l on Day 1; 5μl, Days 4 and 11), and challenged 7 d later by inhalation (100 ppb; Days 20, 22, and 24) with toluene diisocyanate (TDI). Airway inflammation, goblet cell metaplasia, epithelial cell damage, and nonspecific airtent way reactivity to methacholine challenge, measured 24 h folcific lowing the last challenge, were reduced to baseline levels in TNF-α null mice and athymic mice. TNF-α deficiency also merktrophils, edly abrogated TDI-induced Th2 cytokines in airway tissues, indicating a role in the development of Th2 responses. Despite abrogation of all indicators of asthma pathology, TNF-α neutralization had no effect on serum IgE levels or IgG-specific TDI antibodies, suggesting the lack of importance of a humoral response in the manifestation of TDI-induced asthma. Instillation studies with fluorescein-conjugated isothiocyanate and TDI suggested that TNF-α deficiency also resulted in a significant reduction in the migration of airway dendritic cells to the draining lymph nodes. Taken together, these results suggest that, unlike protein antigens, TNF-α has multiple and central roles in TDI-induced asthma, influencing both nonspecific inflammatory processes and specific immune events.

Link to abstract in NIOSHTIC-2.

—Honorable Mention:

TITLE: **Chemoprotection by phenolic antioxidants: Inhibition of tumor mecrosis factor alpha induction in macrophages**

AUTHORS: **Qiang Ma, Krista Kinneer**

SOURCE: **The Journal Of Biological Chemistry 2002;277:2477-2484**

ABSTRACT: Phenolic antioxidants exhibit anti-inflammatory activity in protection against chemical toxicity and cancer. To investigate the molecular mechanism of antiinflammation, we analyzed the regulation of tumor necrosis factor a (TNF-α) expression in macrophages, a key step in inflammation, by the antioxidants. Whereas lipopolysaccharide (LPS), an inflammatory inducer, stimulates rapid synthesis of TNF-a protein, phenolic antioxidants, exemplified by *tert*-butyl hydroquinone and 1,4-dihydroquinone, block LPS-induced production of TNF-αprotein in a time- and dose-dependent manner. Inhibition of TNF-α induction correlates with the capacity of the antioxidants to undergo oxidation-reduction cycling, implicating oxidative signaling in the inhibition. The antioxidants blocked LPS-induced increase of the steady-state mRNA of TNF-α but did not affect the half-life of the mRNA. Electrophoretic mobility shift assay reveals a total inhibition of LPS-induced formation of nuclear factor κB.DNA binding complexes by phenolic antioxidants. Finally, 1,4-dihydroquinone blocks the induction of TNF-α target genes interleukin 1β and interleukin 6 at both mRNA and protein levels. Our findings demonstrate that phenolic antioxidants potently inhibit signal-induced TNF-α transcription and suggest a mechanism of anti-inflammation by the antioxidants through control of cytokine induction during inflammation.

Go to journal site to view full paper.

Engineering and Physical Sciences Category:

—Winner:

TITLE: **A random walk model of skin permeation**

AUTHORS: **H. Frederick Frasch**

SOURCE: **Risk Analysis 2002; 22:265-276**

ABSTRACT: A new mathematical model for permeability of chemicals in aqueous vehicle through skin is presented. The rationale for this model is to represent diffusion by its fundamental molecular mechanism, i.e., random thermal motion. Diffusion is modeled as a twodimensional random walk through the biphasic (lipid and corneocyte) stratum corneum (SC). This approach permits calculations of diffusion phenomena in a morphologically realistic SC structure. Two concepts are key in the application of the model to the prediction of steady-state skin permeability coefficients: "effective diffusivity" and "effective path length," meaning the diffusivity and thickness of a homogeneous membrane having identical permeation properties as the stratum corneum. Algebraic expressions for these two variables are developed as

functions of the molecular weight and octanol-water partition coefficient of the diffusing substance. Combining these with expressions for membrane-vehicle partition coefficient and permeability of the aqueous epidermis enables the calculation of steady-state skin permeability coefficients. The resulting four-parameter algebraic model was regressed against the "Flynn data base" with excellent results (R^2 = 0.84; SE = 0.0076; F = 154; N = 94). The model provides insight into the contributions of stratum corneum diffusivity and effective path lengths to overall skin permeability and may prove useful in the prediction of non-steady-state diffusion phenomena.

Go to journal site to view full paper.

—Honorable Mention:

TITLE: **Studies of the measurement of respirable coal dusts and diesel particulate matter**

AUTHORS: **Charles D. Litton**

SOURCE: **Measurement Science and Technology 2002;13:365-374**

ABSTRACT: Experiments were conducted to determine the optical scattering properties of respirable coal dusts and diesel particulate matter (DPM) at discrete angles in the forward direction and at light source wavelengths of 632.8 and 635 nm. In addition to the scattering data, simultaneous measurements were made of the total mass concentration of dust, DPM or mixtures of the two, and the responses of a unipolar ion chamber and a simpler, more common bipolar ion chamber typical of residential smoke detectors. The results of these experiments indicate, for respirable coal dusts, that the intensity per unit mass concentration at discrete angles in the range of 15–30 varies linearly with mass concentration independent of the volatility of the dust, but that at larger scattering angles, intensities per unit mass concentration are affected by dust volatility. For DPM, the intensities per unit mass concentration are significantly lower. The results also indicate that the ion chambers respond significantly to DPM while there is no response to respirable coal dust, and that when mixtures of the two are present, the ion chambers respond to the DPM mass fraction only. In addition, it was found that the angular intensity distribution for respirable dusts is adequately described by classical Mie scattering theory, while for DPM classical Mie scattering is inadequate, and treatment of the particles as fractal-like aggregates yields much better agreement with the experimental data. This paper describes the experiments and their results.

Go to journal site to view full paper.

—Honorable Mention:

TITLE: **A derived association between ambient aerosol surface area and excess mortality using historic time series data**

AUTHOR: **Andrew D. Maynard, Robert L. Maynard**

SOURCE: **. Atmospheric Environment 2002;36:5561-5567**

ABSTRACT: Although aerosol mass concentration is widely associated with ill health following inhalation; there is increasing evidence that it is a poor indicator of .ne and ultra.ne particle toxicity.

Research has indicated that biological response to such particles is closely associated with particulate surface area; although no epidemiology data currently exist to validate the association. By applying a simple model to historic mass-based time series data, we have been able to estimate mortality rate as a function of ambient aerosol surface area. Within the simplifying assumptions of the model, a linear association is indicated between mortality rate and surface area concentration for coalescing particles. The analysis also indicates the existence of a threshold aerosol concentration, below which particulate mass and surface area are linearly related. Below this threshold, we suggest that mass concentration measurements may provide a good indicator of health effects, although for high exposures found in the developing world and industry, the model indicates that aerosol exposure may be more appropriately characterized by surface area. Further experimental validation of the model should establish the applicability of derived relationships between aerosol mass and surface area concentration to ambient and occupational exposures.

Go to journal site to view full paper.

Human Studies Category:

—Winner:

TITLE: **The impact of mental processing and pacing on spine loading**

AUTHOR: **Kermit G. Davis, William S. Marras, Catherine A. Heaney, Thomas R.Waters, Purnendu Gupta**

SOURCE: **Spine 2002;27:2645-2653**

ABSTRACT: *Study Design*
The impact of various levels of mental processing and pacing (during lifting) on spine loading was monitored under laboratory conditions.
Objectives
To explore how mental demands and pacing influence the biomechanical response and subsequent spine loading and, to determine whether individual characteristics have a modifying role in the responses.
Summary of Background Data
Modern work often requires rapid physical exertions along with demands of mental processing (both psychosocial stressors). While the effect of physical workplace factors on spine loading has been widely documented, few studies have investigated the impact that interaction of psychosocial factors and individual factors has on spine loads.
Methods
For this study, 60 subjects lifted boxes while completing two types of mental processing tasks: 1) series tasks with decisions occurring before the act of lifting, and 2) simultaneous tasks with decisions occurring concurrently with the lift. For both of these mental processing conditions, two intensities of mental load were evaluated: simple and complex. Task pacing was also adjusted under slow and fast conditions. Finally, individual characteristics (personality and gender) were evaluated as potential modifiers. An electromyographically assisted model evaluated the three-dimensional spine loads under the experimental conditions.
Results
Simultaneous mental processing had the largest impact on the spine loads, with the complex intensity resulting in increases of 160 N with lateral shear, 80 N with anteroposterior shear, and 700 N with compression. Increased task pace produced greater lateral shear (by 20 N), anteroposterior shear (by 60 N), and compression loads (by 410 N). Gender and personality also influenced loadings by as much as 17%.

Conclusions
Mental processing stress acted as a catalyst for the biomechanical responses, leading to intensified spine loading. Mental stress appeared to occur as a function of time pressures on task performance and resulted in less controlled movements and increases in trunk muscle coactivation. These adjustments significantly increased spine loading. These results suggest a potential mechanism for the increase in low back pain risk resulting from psychosocial stress caused by modern work demands.

Go to journal site to view full paper.

—Honorable Mention:

TITLE: **Clinical bronchiolitis obliterans in workers at a microwave-popcorn plant**

AUTHORS: **Kathleen Kreiss, Ahmed Gomaa, Greg Kullman, Kathleen Fedan, Eduardo J.Simoes, Paul L. Enright**

SOURCE: **The New England Journal of Medicine 2002;347:330-338**

ABSTRACT: *Background*
In May 2000, eight persons who had formerly worked at a microwave-popcorn production plant were reported to have severe bronchiolitis obliterans. No recognized cause was identified in the plant. Therefore, we medically evaluated current employees and assessed their occupational exposures.
Methods
Questionnaire responses and spirometric findings in participating workers were compared with data from the third National Health and Nutrition Examination Survey, after adjustment for age and smoking status. We evaluated the relation between exposures and health-related outcomes by analyzing the rates of symptoms and abnormalities according to current and cumulative exposure to diacetyl, the predominant ketone in artificial butter flavoring and in the air at the plant.
Results
Of the 135 current workers at the plant, 117 (87 percent) completed the questionnaire. These 117 workers had 2.6 times the expected rates of chronic cough and shortness of breath, according to comparisons with the national data, and twice the expected rates of physician-diagnosed asthma and chronic bronchitis. Overall, the workers had 3.3 times the expected rate of airway obstruction; those who had never smoked had 10.8 times the expected rate. Workers directly involved in the production of microwave popcorn had higher rates of shortness of breath on exertion and skin problems that had developed since they started work than workers in other parts of the plant. There was a strong relation between the quartile of estimated cumulative exposure to diacetyl and the frequency and extent of airway obstruction.
Conclusions
The excess rates of lung disease and lung-function abnormalities and the relation between exposure and outcomes in this working population indicate that they probably had occupational bronchiolitis obliterans caused by the inhalation of volatile butter-flavoring ingredients. (N Engl J Med 2002;347:330-8.)

Go to journal site to view full paper.

Back to Alice Hamilton Awards

Page last updated: April 28, 2011
Page last reviewed: October 19, 2011
Content Source: National Institute for Occupational Safety and Health (NIOSH)

NIOSH Home | NIOSH Search | Site Index | Topic List | Contact Us

MedlinePlus®
Trusted Health Information for You

U.S. National Library of Medicine
NIH National Institutes of Health

Antioxidants

URL of this page: http://www.nlm.nih.gov/medlineplus/antioxidants.html

Antioxidants are substances that may protect your cells against the effects of free radicals. Free radicals are molecules produced when your body breaks down food, or by environmental exposures like tobacco smoke and radiation. Free radicals can damage cells, and may play a role in heart disease, cancer and other diseases.

Antioxidant substances include

- Beta-carotene
- Lutein
- Lycopene
- Selenium
- Vitamin A
- Vitamin C
- Vitamin E

Antioxidants are found in many foods. These include fruits and vegetables, nuts, grains, and some meats, poultry and fish.

Start Here

- Antioxidant Supplements for Health: An Introduction [http://nccam.nih.gov/health/antioxidants/introduction.htm] *NIH* (National Center for Complementary and Alternative Medicine)

Overviews

- Antioxidants: Beyond the Hype [http://www.hsph.harvard.edu/nutritionsource/what-should-you-eat/antioxidants/] (Harvard School of Public Health)

Latest News

- Health Perk [http://www.nlm.nih.gov/medlineplus/videos/news/health_perk_122111.html] (12/21/2011, HealthDay)
- Veggies, Fruit May Lower Women's Stroke Risk [http://www.nlm.nih.gov/medlineplus/news/fullstory_119276.html] (12/01/2011, HealthDay)
- Study Links Coffee to Lower Risk of Endometrial Cancer [http://www.nlm.nih.gov/medlineplus/news/fullstory_118984.html] (11/22/2011, HealthDay)
- Red Wine Antioxidant Could Give Metabolism a Boost [http://www.nlm.nih.gov/medlineplus/news/fullstory_118197.html] (11/01/2011, HealthDay)

Specific Conditions

- Cranberry [http://nccam.nih.gov/health/cranberry/ataglance.htm] *NIH* (National Center for Complementary and Alternative Medicine)
- Grape Seed Extract [http://nccam.nih.gov/health/grapeseed/ataglance.htm] *NIH* (National Center for Complementary and Alternative Medicine)
- Lycopene: An Antioxidant for Good Health [http://www.eatright.org/Public/content.aspx?id=3542&terms=Lycopene%3a+An+Antioxidant+for+Good+Health] (Academy of Nutrition and Dietetics)
- Noni [http://nccam.nih.gov/health/noni/] *NIH* (National Center for Complementary and Alternative Medicine)

- Selenium [http://ods.od.nih.gov/factsheets/selenium/] *NIH* (National Institutes of Health, Office of Dietary Supplements)
- Vitamin A and Carotenoids [http://ods.od.nih.gov/factsheets/vitamina/] *NIH* (National Institutes of Health, Office of Dietary Supplements)
- Vitamin C [http://www.merckmanuals.com/home/print/disorders_of_nutrition/vitamins/vitamin_c.html] (Merck & Co., Inc.)
- Vitamin E [http://ods.od.nih.gov/factsheets/VitaminE-QuickFacts/] *NIH* (National Institutes of Health, Office of Dietary Supplements)
  Also available in Spanish [http://ods.od.nih.gov/factsheets/VitaminE-DatosEnEspanol/]
- Zinc [http://ods.od.nih.gov/factsheets/Zinc-QuickFacts/] *NIH* (National Institutes of Health, Office of Dietary Supplements)
  Also available in Spanish [http://ods.od.nih.gov/factsheets/Zinc-DatosEnEspanol/]

Related Issues

- Chocolate: Temptation or Health Food? [http://www.intelihealth.com/IH/ihtPrint/WSIHW000/24479/408/432358.html?d=dmtHMSContent&hide=t&k=basePrint] (InteliHealth, Harvard Medical School)
- Coenzyme Q10 (PDQ) [http://www.cancer.gov/cancertopics/pdq/cam/coenzymeQ10/patient] *NIH* (National Cancer Institute)
- Fighting Heart Disease: Should You Be "Pro" or "Anti" Antioxidants? [http://my.clevelandclinic.org/heart/disorders/cad/vitamin_e.aspx] (Cleveland Clinic Foundation)
- Lutein and Zeaxanthin [http://www.aoa.org/x11815.xml] (American Optometric Association)

Clinical Trials

- ClinicalTrials.gov: Antioxidants [http://clinicaltrials.gov/search/open/intervention=antioxidants] *NIH* (National Institutes of Health)

Research

- Claims about Cocoa: Can Chocolate Really Be Good for You? [http://newsinhealth.nih.gov/issue/Aug2011/Feature1] *NIH* (National Institutes of Health)
- Selenium and Vitamin E Cancer Prevention Trial (SELECT): Questions and Answers [http://www.cancer.gov/newscenter/qa/2008/selectqa] *NIH* (National Cancer Institute)
  Also available in Spanish [http://www.cancer.gov/espanol/noticias/SELECTQandA]

Journal Articles

References and abstracts from MEDLINE/PubMed (National Library of Medicine)

- Article: Can you recommend anything for dysthymia? [http://www.ncbi.nlm.nih.gov/pubmed/22125827?tool=MedlinePlus]
- Article: Systematic review: generating evidence-based guidelines on the concurrent use of... [http://www.ncbi.nlm.nih.gov/pubmed/22085269?tool=MedlinePlus]
- Article: Glucocorticoids plus N-acetylcysteine in severe alcoholic hepatitis. [http://www.ncbi.nlm.nih.gov/pubmed/22070475?tool=MedlinePlus]
- Antioxidants – see more articles [http://www.ncbi.nlm.nih.gov/pubmed?term=(antioxidants/ae[mh]+OR+antioxidants/tu[majr])+AND+(english[la]+AND+review[pt]+OR+guideline[pt]+OR+clinical+trial[pt]+OR+jsubsetk[text]+OR+jsubsetaim[text]+OR+jsubsetn[text]+OR+patient+education+handout[pt])+NOT+(letter[pt]+OR+editorial[pt])+AND+%22last+1+Year%22[edat]&tool=MedlinePlus]

Directories

- Find a Registered Dietitian [http://www.eatright.org/iframe/FindRD.aspx?] (Academy of Nutrition and Dietetics)
- Nutrient Lists [http://www.ars.usda.gov/Main/docs.htm?docid=15869] (Dept. of Agriculture) - PDF

Organizations

- Food and Nutrition Information Center [http://fnic.nal.usda.gov/]
- National Institutes of Health, Office of Dietary Supplements [http://ods.od.nih.gov/] *NIH*

You may also be interested in these related MedlinePlus topics:

- Vitamin A [http://www.nlm.nih.gov/medlineplus/vitamina.html]
- Vitamin C [http://www.nlm.nih.gov/medlineplus/vitaminc.html]
- Vitamin E [http://www.nlm.nih.gov/medlineplus/vitamine.html]
- Vitamins [http://www.nlm.nih.gov/medlineplus/vitamins.html]
- Food and Nutrition [http://www.nlm.nih.gov/medlineplus/foodandnutrition.html]

Date last updated: 09 January 2012
Topic last reviewed: 04 October 2011

APPENDIX OF ADVERTISEMENTS

1. For ease of reference, Respondents include this separate Appendix of Advertisements, which is an advertisement-by-advertisement analysis of the exhibits listed in the chart set forth in paragraph 2252 of the RFF, with the exception of the "outlier" ads, website materials, press releases, and the interviews of Mrs. Resnick and Mr. Tupper, which have been thoroughly addressed in the RFF XVII(D)(4).

2. Additionally, as set for the in the Proposed Findings of Fact, each of the ads analyzed below also fall into one or more of the three categories: (a) specific study; (b) "backed by" and (c) antioxidant, and are supported by competent and reliable scientific evidence. (*See* RFF XVII(G)(1)).

24 SCIENTIFIC STUDIES NOW IN ONE EASY-TO SWALLOW PILL - (CX0348)

3. Complaint Counsel claim that on April 1, 2010, POM ran an advertisement with the headline "24 Scientific Studies" with the body copy that appears on (CX0348_0001.)

4. Complaint Counsel failed to present any other definitive information regarding this ad's dissemination.

5. Complaint Counsel failed to present any evidence that Respondents would run this ad in the future, let alone whether it is probable they would do so.

6. Complaint Counsel's expert, Professor Mazis, testified that Complaint Counsel is not challenging POM's ads for POM Juice that ran after December 2008. (Mazis, Tr. 2753-54). Accordingly, based on these representations, Complaint Counsel cannot now challenge this ad.

7. Nowhere in this ad do Respondents expressly (*i.e.*, unequivocally and directly) state that (a) taking one POMx Pill per day "prevents," "treats," or "reduces the risk" of heart disease or prostate cancer; or (b) taking one POMx Pill per day is "clinically proven" to "prevent," "treat," or "reduce the risk" of heart disease or prostate cancer. (CX0348_0001).

8. Complaint Counsel's assertion that the ad conveys the message that (a) taking one POMx Pill per day "prevents," "treats," or "reduces the risk" of heart disease or prostate cancer; or (b) taking one POMx Pill per day is "clinically proven" to "prevent," "treat," or "reduce the risk" of heart disease or prostate cancer is not conspicuous, self-evident, or reasonably clear from the face of the ad. (CX0348_0001).

9. Consequently, because the above-referenced challenged implied claim may not be determined with confidence from the face of the ad, extrinsic evidence must be examined.

10. The overall net impression of this ad is not that not that taking one POMx Pill per day prevents, treats or reduces the risk of certain diseases, such as heart disease or prostate cancer; or (b) taking one POMx Pill per day is "clinically proven" to prevent, treat or reduce the risk of certain diseases, such as heart disease or prostate cancer. (CX0348_0001). Even the language of the ad itself uses such qualifiers as "emerging science suggests," "help protect," "promising results," "initial UCLA study," "hopeful results" and "preliminary study." (CX0348_0001).

11. To the extent a "reduce the risk" claim can be implied from this ad, the overall net impression is not that taking one POMx Pill per day "reduces the risk" of certain diseases, such as heart disease or prostate cancer, like a drug with a single target of action, but "reduces the risk," like a healthy diet of fruits and vegetables and exercise "reduces the risk" of disease. (CX0348_0001).

12. To the extent a "treat" claim can be implied from this ad (which it cannot), the overall net impression of any ad is not that POMx Pills are a substitute for conventional medical treatment. (Butters, Tr. 2821-22; Appendix of Advertisements).

13. To the extent a "proven" claim can be implied from this ad (which it cannot), the overall impression of this ad is not that POMx Pills are "proven" to be 100% effective in preventing, treating or reducing the risk of heart disease or prostate cancer because (1) all of the qualifying language contradicts an implied "clinically proven" interpretation, and (2) "proven" in science means the "average person in the study benefitted," not that "everyone in the study necessarily benefitted." (Heber, Tr. 2011; Butters, Tr. 2893-2894; PX0361 (Sacks, Dep. at 81)).

14. Mrs. Resnick testified that the purpose of including the amount of money related to medical research in the advertising was a "very direct way of communicating to the consumer that here was a natural food that had gone through rigorous scientific testing and that we cared enough to do this and we wanted to tell people that we had and continue to do scientific research." (L. Resnick, Tr. 249-53).

15. Professor Butters testified that this advertisement conveys "the sense that pomegranate juice is healthy and that pomegranate juice contains the same antioxidants that are found in the POMx super pill, the antioxidant super pill." (Butters, Tr. 2939).

16. Professor Butters also testified that the ad also communicates that one of the benefits of POMx Pills is that they may help with prostate health. Professor Butters does not believe that it is reasonable for viewers to equate hopeful results for prostate health to mean hopeful results for preventing prostate cancer though. (Butters, Tr. 2940-43).

17. Further, Professor Butters testified that the ad never states that it will treat a disease and that reasonable consumers cannot infer from this advertisement that POMx Pills treat disease, prevent or reduce the risk of prostate cancer or heart disease, like a drug, as distinguished from the way a healthy diet of fruits and vegetables and exercise maintain health and reduce the risk of disease. (PX0350 (Butters, Dep. at 139)).

18. Professor Butters also testified that the advertisement could not communicate to reasonable consumers or more than just outliers that scientific studies document that POMx Pills treat, prevent or reduce the risk of prostate cancer or heart disease like a drug may. (PX0350 (Butters, Dep. at 137-38)).

19. Viewing the "24 Scientific Studies" ad as a whole, including the interaction of the words and visual imagery, the overall net impression of the ad is that POMx Pills are healthy and that they may help with prostate health. (PX0350 (Butters, Dep. at 141); (PX0158-0033)).

20. Complaint Counsel presented no extrinsic evidence or expert opinion on this ad's meaning, consumer perceptions of this ad, or consumer interpretations regarding this ad. (PX0357 (Stewart, Dep. at 49, 52)).

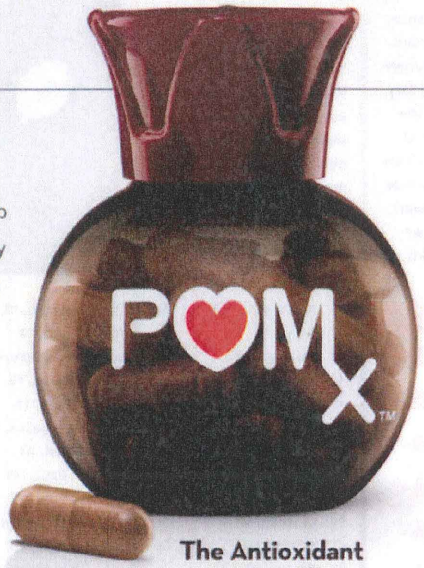
21. Complaint Counsel failed to present any evidence that the claims in this ad reasonably convey that the Challenged Products are "clinically proven" to prevent, treat or reduce the risk of heart disease, prostate cancer or erectile dysfunction.

22. Complaint Counsel failed to present any evidence regarding the number of exposures consumers had to this ad or any particular POM advertisement. (Mazis, Tr. 2752).

VMS ID: 100400591
RUN DATE: 04/01/2010

24 SCIENTIFIC STUDIES
NOW IN ONE EASY-TO-SWALLOW PILL.

FREE SHIPPING!



The Antioxidant Superpill.™

Antioxidants 101.

Emerging science suggests that antioxidants are critically important to maintaining good health because they protect you from free radicals, which can damage your body. Taking one POMx pill a day will help protect you from free radicals. It's just that simple.

The antioxidant power of our 8oz juice.

POMx is powerful. Naturally.

POMx is an all-natural, ultra-potent antioxidant extract. Containing a full spectrum of pomegranate polyphenols, POMx is so concentrated that a single capsule has the anti-oxidant power of a full glass of POM Wonderful® 100% Pomegranate Juice.

$32 million in medical research. Science. Not fiction.

POMx is made from the only pomegranates backed by $32 million in medical research at the world's leading universities. Not only has this research documented the unique and superior antioxidant power of pomegranates, it has revealed promising results for prostate and cardiovascular health.

Complicated studies. Simplified.

Our POMx pills are made from the same pomegranates we use to make our POM Wonderful 100% Pomegranate Juice, on which each of the following medical studies was conducted.

An initial UCLA study on our juice found hopeful results for prostate health, reporting "statistically significant prolongation of PSA doubling times," according to Dr. Allen J. Pantuck in *Clinical Cancer Research*, 2006.[1,2,3]

Additional preliminary study on our juice showed promising results for heart health. "Stress-induced ischemia (restricted blood flow to the heart) decreased in the pomegranate group," Dr. Dean Ornish reported in the *American Journal of Cardiology*, 2005.[1,2,4]

Try POMx Monthly FREE for ONE MONTH.

We'll even pay for the shipping.*

Order Now: 888-766-7455
or pompills.com/mh Use discount code: MH30

*SIGN UP FOR POMx MONTHLY, AND WE'LL SEND YOUR FIRST BOTTLE FREE. AFTER THAT, YOU'LL CONTINUE TO RECEIVE MONTHLY SHIPMENTS FOR $29.95 WITH COMPLIMENTARY SHIPPING. Offer expires 8/31/10 and applies only to the purchase price for the first bottle of POMx Monthly. Following months will be $29.95 per bottle. One discount per customer. Cannot be combined with other offers. No substitutions, transfer rights or cash equivalents. We reserve the right to discontinue this promotion, change product price or shipping charge at any time. Valid only at pompills.com or 1-888-766-7455. Not valid on POMx Trial or other POM products.

POM WONDERFUL®

[1]pompills.com/research. [2]These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure or prevent any disease. [3]45 men with rising PSA after surgery or radiotherapy drank 8oz 100% pomegranate juice daily for two years. [4]45 patients with coronary heart disease and myocardial ischemia drank 8oz 100% pomegranate juice daily for three months.

24 SCIENTIFIC STUDIES NOW IN ONE EASY-TO SWALLOW PILL - (CX0350)

23. Complaint Counsel claim that on April 26, 2010, POM ran an advertisement with the headline "24 Scientific Studies" with the body copy that appears on CX0350_0001.

24. Complaint Counsel failed to present any other definitive information regarding this ad's dissemination.

25. Complaint Counsel failed to present any evidence that Respondents would run this ad in the future, let alone whether it is probable they would do so.

26. Complaint Counsel's expert, Professor Mazis, testified that Complaint Counsel is not challenging POM's ads for POM Juice that ran after December 2008. (Mazis, Tr. 2753-54). Accordingly, based on these representations, Complaint Counsel cannot now challenge this ad.

27. Nowhere in this ad do Respondents expressly (*i.e.*, unequivocally and directly) state that (a) taking one POMx Pill per day "prevents," "treats," or "reduces the risk" of heart disease or prostate cancer; or (b) taking one POMx Pill per day is "clinically proven" to "prevent," "treat," or "reduce the risk" of heart disease or prostate cancer. (CX0350_0001).

28. Complaint Counsel's assertion that the ad conveys the message that (a) taking one POMx Pill per day "prevents," "treats," or "reduces the risk" of heart disease or prostate cancer; or (b) taking one POMx Pill per day is "clinically proven" to "prevent," "treat," or "reduce the risk" of heart disease or prostate cancer is conveyed in this ad is not conspicuous, self-evident, or reasonably clear from the face of the ad. (CX0350_0001).

29. Consequently, because the above-referenced challenged implied claim may not be determined with confidence from the face of the ad, extrinsic evidence must be examined.

30. The overall net impression of this ad is not that not that taking one POMx Pill per day prevents, treats or reduces the risk of certain diseases, such as heart disease or prostate cancer; or (b) taking one POMx Pill per day is "clinically proven" to prevent, treat or reduce the risk of certain diseases, such as heart disease or prostate cancer. (CX0350_0001). Even the language of the ad itself uses such qualifiers as "emerging science suggests," "help protect," "promising results," "initial UCLA study," "hopeful results" and "preliminary study." (CX0350_0001).

31. To the extent a "reduce the risk" claim can be implied from this ad, the overall net impression is not that taking one POMx Pill per day "reduces the risk" of certain diseases, such as heart disease or prostate cancer, like a drug with a single target of action, but "reduces the risk," like a healthy diet of fruits and vegetables and exercise "reduces the risk" of disease. (CX0350_0001).

32. To the extent a "treat" claim can be implied from this ad (which it cannot), the overall net impression of any ad is not that POMx Pills are a substitute for conventional medical treatment. (Butters, Tr. 2821-22; Appendix of Advertisements).

33. To the extent a "proven" claim can be implied from this ad (which it cannot), the overall impression of this ad is not that POMx Pills are "proven" to be 100% effective in preventing, treating or reducing the risk of heart disease or prostate cancer because (1) all of the qualifying language contradicts an implied "clinically proven" interpretation, and (2) "proven" in science means the "average person in the study benefitted," not that "everyone in the study necessarily benefitted." (Heber, Tr. 2011; Butters, Tr. 2893-2894; PX0361 (Sacks, Dep. at 81)).

34. Mrs. Resnick testified that the purpose of including the amount of money in medical research in the advertising was a "very direct way of communicating to the consumer that here was a natural food that had gone through rigorous scientific testing and that we cared enough to do this and we wanted to tell people that we had and continue to do scientific research." (L. Resnick, Tr. 249-53).

35. Butters testified that this advertisement conveys "the sense that pomegranate juice is healthy and that pomegranate juice contains the same antioxidants that are found in the POMx super pill, the antioxidant super pill." (Butters, Tr. 2939).

36. Professor Butters also testified that the ad also communicates that one of the benefits of POMx Pills is that they may help with prostate health. Professor Butters does not believe that it is reasonable for viewers to equate hopeful results for prostate health to mean hopeful results for preventing prostate cancer though. (Butters, Tr. 2940-43).

37. Further, Professor Butters testified that the ad never states that it will treat a disease and that reasonable consumers cannot infer from this advertisement that POMx Pills treats disease, prevents or reduces the risk of prostate cancer or heart disease, like a drug, as distinguished from the way a healthy diet of fruits and vegetables and exercise maintain health and reduce the risk of disease. (PX0350 (Butters, Dep. at 139)).

38. Professor Butters also testified that the advertisement could not communicate to reasonable consumers or more than just outliers that scientific studies document

that POMx Pills treat, prevent or reduce the risk of prostate cancer or heart disease like a drug may. (PX0350 (Butters, Dep. at 137-38)).

39. Viewing the "24 Scientific Studies" ad as a whole, including the interaction of the words and visual imagery, the overall net impression of the ad is that POMx Pills are healthy and that they may help with prostate health. (PX0350 (Butters, Dep. at 141); (PX0158-0033)).

40. Complaint Counsel presented no extrinsic evidence or expert opinion on this ad's meaning, consumer perceptions of this ad, or consumer interpretations regarding this ad. (PX0357 (Stewart, Dep. at 49, 52)).

41. Complaint Counsel failed to present any evidence that the claims in this ad reasonably convey that the Challenged Products are "clinically proven" to prevent, treat or reduce the risk of heart disease, prostate cancer or erectile dysfunction.

42. Complaint Counsel failed to present any evidence regarding the number of exposures consumers had to this ad or any particular POM advertisement. (Mazis, Tr. 2752).

VMS ID: 100411090
RUN DATE: 04/26/2010

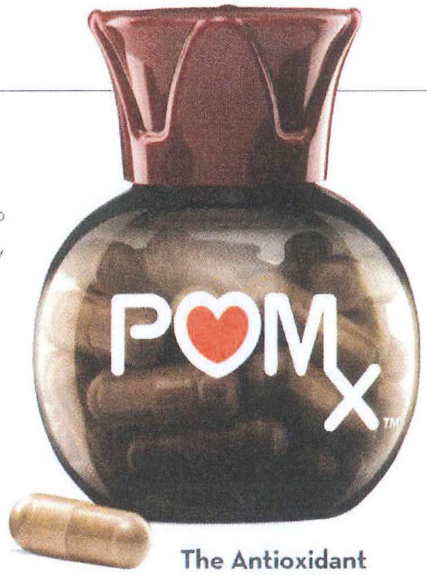
24 SCIENTIFIC STUDIES.
NOW IN ONE EASY-TO-SWALLOW PILL.

FREE SHIPPING!

Antioxidants 101.

Emerging science suggests that antioxidants are critically important to maintaining good health because they protect you from free radicals, which can damage your body. Taking one POMx pill a day will help protect you from free radicals. It's just that simple.

The antioxidant power of our 8oz juice.



The Antioxidant Superpill.™

POMx is powerful. Naturally.

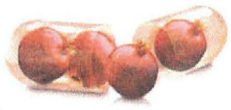
POMx is an all-natural, ultra-potent antioxidant extract. Containing a full spectrum of pomegranate polyphenols, POMx is so concentrated that a single capsule has the anti-oxidant power of a full glass of POM Wonderful® 100% Pomegranate Juice.

$34 million in medical research. Science. Not fiction.

POMx is made from the only pomegranates backed by $34 million in medical research at the world's leading universities. Not only has this research documented the unique and superior antioxidant power of pomegranates, it has revealed promising results for prostate and cardiovascular health.

Complicated studies. Simplified.

Our POMx pills are made from the same pomegranates we use to make our POM Wonderful 100% Pomegranate Juice, on which each of the following medical studies was conducted.



An initial UCLA study on our juice found hopeful results for prostate health, reporting "statistically significant prolongation of PSA doubling times," according to Dr. Allen J. Pantuck in *Clinical Cancer Research*, 2006.[1,2,3]

Additional preliminary study on our juice showed promising results for heart health. "Stress-induced ischemia (restricted blood flow to the heart) decreased in the pomegranate group," Dr. Dean Ornish reported in the *American Journal of Cardiology*, 2005.[1,2,4]

Try POMx Pills FREE FOR ONE MONTH

when you sign up for POMx Monthly delivery.*

Cancel Anytime.

Order Now: 888-766-7455
or pompills.com/t Use discount code: T30

*SIGN UP FOR POMx MONTHLY AND WE'LL SEND YOUR FIRST BOTTLE FREE. AFTER THAT, YOU'LL CONTINUE TO RECEIVE MONTHLY SHIPMENTS FOR $29.95 WITH COMPLIMENTARY SHIPPING. Offer expires 7/31/10 and applies only to the purchase price for the first bottle of POMx Monthly. Following months will be $29.95 per bottle. One discount per customer. Cannot be combined with other offers. No substitutions, transfer rights or cash equivalents. We reserve the right to modify or discontinue this promotion, change the product price or change the shipping charge at any time. Valid only at pompills.com or 1-888-766-7455. Not valid on POMx Trial or other POM products. Credit or debit card required. POM WONDERFUL®

[illegible] health-improvement claims. These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure or prevent any disease. [illegible] years. [illegible] patients with [illegible] drank 8oz 100% pomegranate juice daily for three months. [illegible] Pom Wonderful LLC. All rights reserved. POM Wonderful, POMx and the Superpill are trademarks of Pom Wonderful LLC. Printed [illegible]

VMS-0000313

CX0350_0001

100% PURE pomegranate juice to the rescue! - (CX0380_0006; CX0372_0004)

43. Complaint Counsel claim that, on September 10, 2009, POM ran an advertisement with the headline "100% PURE pomegranate juice to the rescue!" with this body copy:

> Will POM Wonderful 100% purity be enough to help save your health? Does its lack of added sugar, colorants and cheap filler juice make it superior to its competitors? Can POM products' $32 million in medical research truly make a difference in the current state of your health?* Do superheroes wear tights?
>
> *visit POM Wonderful.com/health/research to review published studies

(CX0380_0006; CX0372_0004).

44. Complaint Counsel failed to present any definitive information regarding this ad's dissemination.

45. Complaint Counsel failed to present any evidence that Respondents would run this ad in the future, let alone whether it is probable they would do so.

46. Mrs. Resnick testified that she does not remember seeing "100% pure pomegranate juice to the rescue" as an ad but the headline sounds familiar to her. The ad may never have happened. If the ad did run, she does not think that POM ran this ad much. (L. Resnick, Tr. 118-20).

47. Complaint Counsel's assertion that the ad conveys the message that (a) POM Juice "prevents," "treats," or "reduces the risk" of certain diseases; or (b) POM Juice is "clinically proven" to "prevent," "treat," or "reduce the risk" of certain diseases is not conspicuous, self-evident, or reasonably clear from the face of the ad. (CX0380_0006; CX0372_0004).

48. Consequently, because the above-referenced challenged implied claim may not be determined with confidence from the face of the ad, extrinsic evidence must be examined.

49. The overall net impression of this ad is not that (a) drinking eight ounces of POM Juice prevents, treats or reduces the risk of certain diseases; or (b) drinking eight ounces of POM Juice is "clinically proven" to prevent, treat or reduce the risk of certain diseases. (CX0380_0006; CX0372_0004).

50. To the extent a "reduce the risk" claim can be implied from ad, the overall net impression is not that drinking eight ounces of POM Juice "reduces the risk" of certain diseases, like a drug with a single target of action, but "reduces the risk," like a healthy diet of fruits and vegetables and exercise "reduces the risk" of disease. (CX0380_0006; CX0372_0004).

51. To the extent a "treat" claim can be implied from this ad (which it cannot), the overall net impression of any ad is not that POM Juice is a substitute for conventional medical treatment. (Butters, Tr. 2821-22).

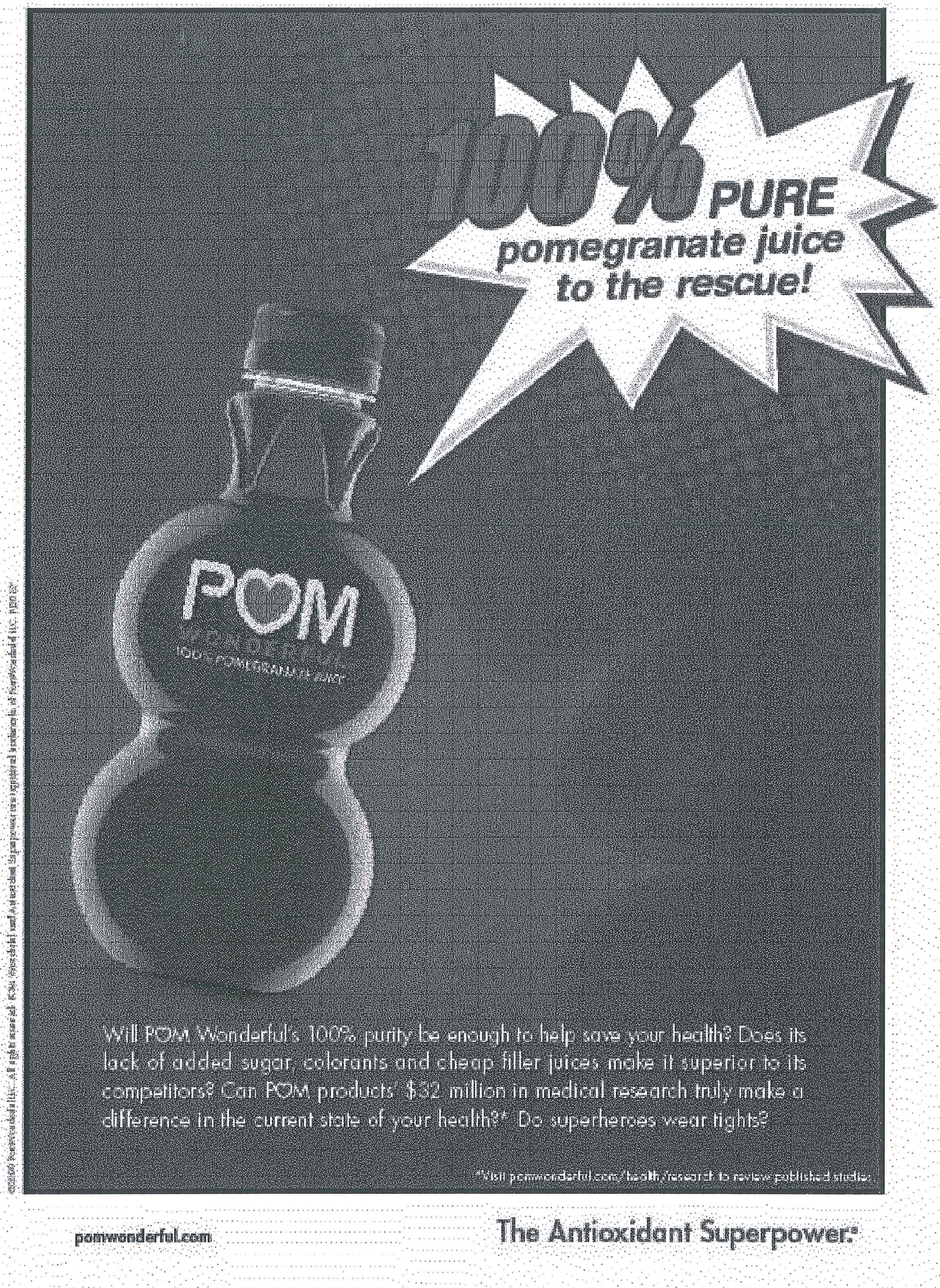
52. To the extent a "proven" claim can be implied from this ad (which it cannot), the overall impression of this ad is not that POM Juice is "proven" to be 100% effective in preventing, treating or reducing the risk of certain diseases because (1) all of the qualifying language contradicts an implied "clinically proven" interpretation, and (2) "proven" in science means the "average person in the study benefitted," not that "everyone in the study necessarily benefitted." (Heber, Tr. 2011; Butters, Tr. 2893-2894; PX0361 (Sacks, Dep. at 81)).

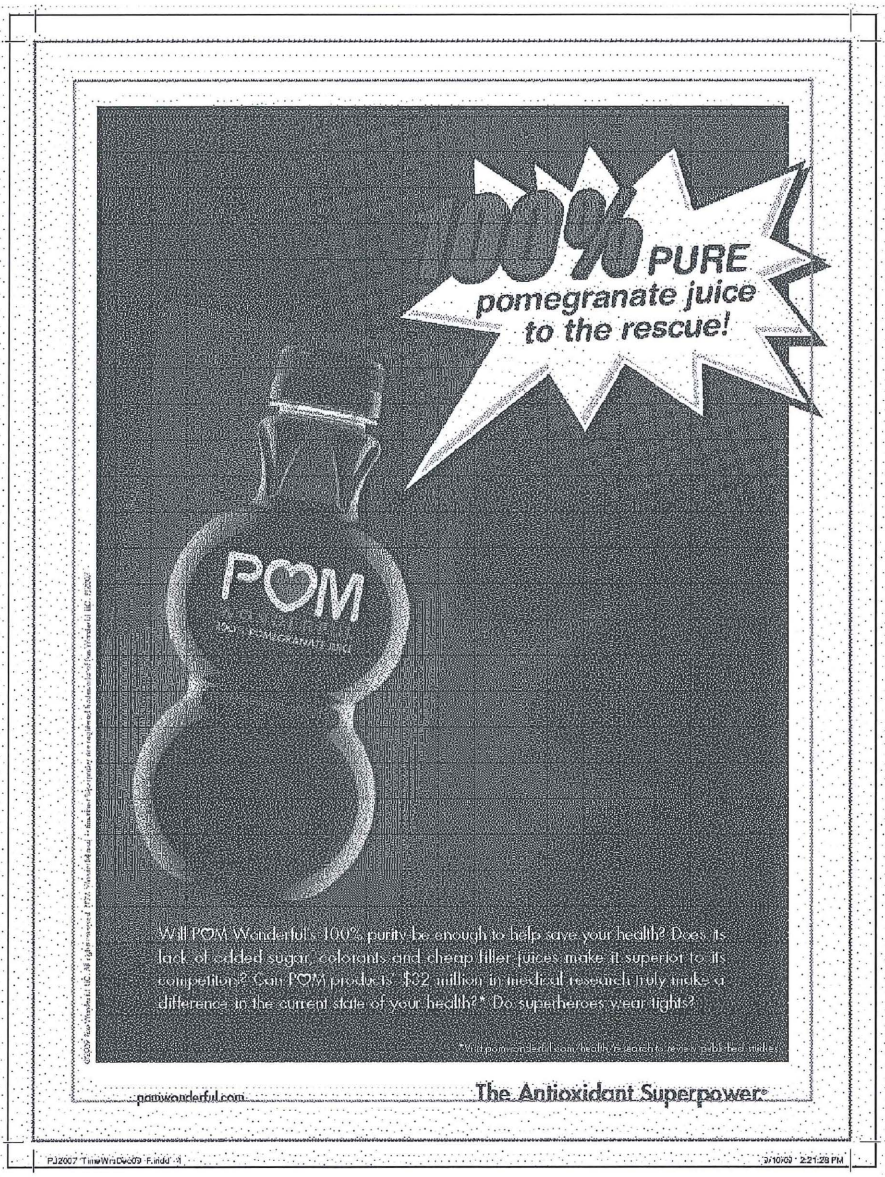
53. Professor Butters concluded that POM's ads in general depend on parody, exaggeration and humor to bring their message to the potential consumer; including the following messages: 1) POM is the best pomegranate that anyone can buy; 2) POM Juice is healthy; 3) POM Juice is tasty; 4) POM Juice is arguably the best source of antioxidants of any of the comparable beverages available; 5) medical research has suggested that antioxidants combat free radicals, which are unhealthy, and may contribute to diseases of the heart, arteries, and prostate, as well as erectile dysfunction; and 6) POM also offers concentrated forms of pomegranate extract for those who wish to ingest antioxidants in even more concentrated form than pomegranate juice itself. (PX0158-0033).

54. Complaint Counsel presented no extrinsic evidence or expert opinion on this ad's meaning, consumer perceptions of this ad, or consumer interpretations regarding this ad. (PX0357 (Stewart, Dep. at 49, 52)).

55. Further, Complaint Counsel presented no evidence that the claims in Respondents' ads reasonably conveyed that the Challenged Products are "clinically proven" to prevent, treat or reduce the risk of heart disease, prostate cancer or erectile dysfunction.

56. Complaint Counsel failed to present any evidence regarding the number of exposures consumers had to this ad or any particular POM advertisement. (Mazis, Tr. 2752).


100% PURE
pomegranate juice
to the rescue!
POM
Will POM Wonderful's 100% purity be enough to help save your health? Does its lack of added sugar, colorants and cheap filler juices make it superior to its competitors? Can POM products' $32 million in medical research truly make a difference in the current state of your health?* Do superheroes wear tights?
*Visit pomwonderful.com/health/research to review published studies.
pomwonderful.com
The Antioxidant Superpower.



PJ2007 TimeWrapDec09 F.indd 1 2/10/09 2:21:28 PM

JOB NO.: PJ2007	TRIM: 7.875" x 10.5"	COLOR: 4/C PROS	DATE IN: 9-02-09	CREATIVE: CJ
PROJECT: Time Magazine Wrap - Dec 09	LIVE: 7.125" x 9.75"	LIVE: TRIM: BLEED (DO NOT PRINT)	CLIENT SIGN OFF: 00-00-00	PRODUCTION: MS
SCALE: 1 : 1	BLEED: 8.375" x 11.0"	PRINT OUT SIZE: 100%	RELEASE DATE: 9-10-09	PROOF: F

*PLEASE MARK ALL CHANGES ON INSITE DOCUMENT *NO CHANGES ON PRINTED FLAT WILL BE MADE

Amaze your urologist - (CX1426_00036, Exh. G; CX0468_0001)

57. Complaint Counsel claim that POM ran an advertisement with the headline "Amaze your urologist" with this body copy:

> The Antioxidant Superpower. Learn More. (CX1426_0036, Exh. G; CX0468_0001).

58. Complaint Counsel failed to present any definitive information regarding this ad's dissemination.

59. Complaint Counsel failed to present any evidence that Respondents would run this ad in the future, let alone whether it is probable they would do so.

60. Complaint Counsel's assertion that the ad conveys the message that (a) POM Juice "prevents," "treats," or "reduces the risk" of prostate cancer; or (b) POM Juice is "clinically proven" to "prevent," "treat," or "reduce the risk" of prostate cancer is not conspicuous, self-evident, or reasonably clear from the face of the ad. (CX1426_0036, Exh. G; CX0468_0001).

61. Consequently, because the above-referenced challenged implied claim may not be determined with confidence from the face of the ad, extrinsic evidence must be examined.

62. The overall net impression of this ad is not that (a) drinking eight ounces of POM Juice prevents, treats or reduces the risk of certain diseases, such as prostate cancer; or (b) drinking eight ounces of POM Juice is "clinically proven" to prevent, treat or reduce the risk of certain diseases, such as prostate cancer. (CX1426_0036, Exh. G; CX0468_0001).

63. To the extent a "reduce the risk" claim can be implied from ad, the overall net impression is not that drinking eight ounces of POM Juice "reduces the risk" of certain diseases, such as prostate cancer, like a drug with a single target of action, but "reduces the risk," like a healthy diet of fruits and vegetables and exercise "reduces the risk" of disease. (CX1426_0036, Exh. G; CX0468_0001).

64. To the extent a "treat" claim can be implied from this ad (which it cannot), the overall net impression of any ad is not that POM Juice is a substitute for conventional medical treatment. (Butters, Tr. 2821-22).

65. To the extent a "proven" claim can be implied from this ad (which it cannot), the overall impression of this ad is not that POM Juice is "proven" to be 100% effective in preventing, treating or reducing the risk of prostate cancer because (1) all of the qualifying language contradicts an implied "clinically proven" interpretation, and (2) "proven" in science means the "average person in the study

benefitted," not that "everyone in the study necessarily benefitted." (Heber, Tr. 2011; Butters, Tr. 2893-2894; PX0361 (Sacks, Dep. at 81)).

66. Mr. Perdigao testified that he does not know when this advertisement ran or what internet sites the advertisement ran on. He testified that Fire Station wrote a copy stating "Amaze your urologist," because pomegranate juice is a healthy product and there have been studies that suggested it is good for prostate health. (CX1373 (Perdigao, Dep. at 290-93)).

67. Professor Butters concluded that POM's ads in general depend on parody, exaggeration and humor to bring their message to the potential consumer; including the following messages: 1) POM is the best pomegranate that anyone can buy; 2) POM Juice is healthy; 3) POM Juice is tasty; 4) POM Juice is arguably the best source of antioxidants of any of the comparable beverages available; 5) medical research has suggested that antioxidants combat free radicals, which are unhealthy, and may contribute to diseases of the heart, arteries, and prostate, as well as erectile dysfunction; and 6) POM also offers concentrated forms of pomegranate extract for those who wish to ingest antioxidants in even more concentrated form than pomegranate juice itself. (PX0158-0033).

68. Viewing the "Amaze your urologist" ad as a whole, including the interaction of the words and visual imagery, the overall net impression of the ad is that POM Juice is a healthy product. (CX1373 (Perdigao, Dep. at 290-93)).

69. Complaint Counsel presented no extrinsic evidence or expert opinion on this ad's meaning, consumer perceptions of this ad, or consumer interpretations regarding this ad. (PX0357 (Stewart, Dep. at 49, 52)).

70. Complaint Counsel failed to present any evidence that the claims in this ad reasonably convey that the Challenged Products are "clinically proven" to prevent, treat or reduce the risk of heart disease, prostate cancer or erectile dysfunction.

71. Complaint Counsel failed to present any evidence regarding the number of exposures consumers had to this ad or any particular POM advertisement. (Mazis, Tr. 2752).

Amaze your
urologist

The
Antioxidant
Superpower.

LEARN MORE ›

Exhibit G

VMS-0000115

CX0468_0001

Antioxidant Superpill - (CX1426_0038-0042, Exh. I)

72. Complaint Counsel claim that POM ran an advertisement with the headline "Antioxidant Superpill" with the body copy that appears on CX1426_0038-0042, Exh. I.

73. Complaint Counsel failed to present any definitive information regarding this ad's dissemination.

74. Complaint Counsel failed to present any evidence that Respondents would run this ad in the future, let alone whether it is probable they would do so.

75. Nowhere in this ad do Respondents expressly (*i.e.*, unequivocally and directly) state that (a) taking one POMx Pill per day "prevents," "treats," or "reduces the risk" of heart disease or prostate cancer; or (b) taking one POMx Pill per day is "clinically proven" to "prevent," "treat," or "reduce the risk" of heart disease or prostate cancer. (CX01426_0038-0042, Exh. I).

76. Complaint Counsel's assertion that the ad conveys the message that (a) taking one POMx Pill per day "prevents," "treats," or "reduces the risk" of heart disease or prostate cancer; or (b) taking one POMx Pill per day is "clinically proven" to "prevent," "treat," or "reduce the risk" of heart disease or prostate cancer is not conspicuous, self-evident, or reasonably clear from the face of the ad. (CX1426_0038-0042, Exh. I).

77. Consequently, because the above-referenced challenged implied claim may not be determined with confidence from the face of the ad, extrinsic evidence must be examined.

78. The overall net impression of this ad is not that not that taking one POMx Pill per day prevents, treats or reduces the risk of certain diseases, such as heart disease or prostate cancer; or (b) taking one POMx Pill per day is "clinically proven" to prevent, treat or reduce the risk of certain diseases, such as heart disease or prostate cancer. (CX1426_0038-0042, Exh. I). Even the language of the ad itself uses such qualifiers as "emerging science," may be linked," helping to prevent," "can lead," "can disrupt," "findings from a small study suggest," "may one day prove," "potential ability," "basic studies indicate," and "may have the same effect." (CX1426_0038-0042, Exh. I).

79. To the extent a "reduce the risk" claim can be implied from this ad, the overall net impression is not that taking one POMx Pill per day "reduces the risk" of certain diseases, such as heart disease or prostate cancer, like a drug with a single target of action, but "reduces the risk," like a healthy diet of fruits and vegetables and exercise "reduces the risk" of disease. (CX1426_0038-0042, Exh. I).

80. To the extent a "treat" claim can be implied from this ad (which it cannot), the overall net impression of any ad is not that POMx Pills are a substitute for conventional medical treatment. (Butters, Tr. 2821-22).

81. To the extent a "proven" claim can be implied from this ad (which it cannot), the overall impression of this ad is not that POMx Pills are "proven" to be 100% effective in preventing, treating or reducing the risk of heart disease or prostate cancer because (1) all of the qualifying language contradicts an implied "clinically proven" interpretation, and (2) "proven" in science means the "average person in the study benefitted," not that "everyone in the study necessarily benefitted." (Heber, Tr. 2011; Butters, Tr. 2893-2894; PX0361 (Sacks, Dep. at 81)).

82. Complaint Counsel presented no extrinsic evidence or expert opinion on this ad's meaning, consumer perceptions of this ad, or consumer interpretations regarding this ad. (PX0357 (Stewart, Dep. at 49, 52)).

83. Complaint Counsel failed to present any evidence that the claims in this ad reasonably convey that the Challenged Products are "clinically proven" to prevent, treat or reduce the risk of heart disease, prostate cancer or erectile dysfunction.

84. Complaint Counsel failed to present any evidence regarding the number of exposures consumers had to this ad or any particular POM advertisement. (Mazis, Tr. 2752).


POMx
Antioxidant Superpill™
The most concentrated source
of pomegranate antioxidants available.
POMx
POM IN A PILL
1.888.POM.PILL (1.888.766.7455)
pompills.com
© 2007 POM Wonderful LLC. All rights reserved. POM Wonderful, POMx, Antioxidant Superpill,
POMx in a pill and The power of POM. Now in one little pill are trademarks of POM Wonderful LLC

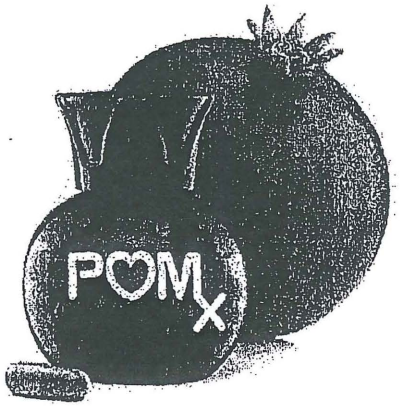
POMx™ is the first and only pomegranate antioxidant supplement reviewed for safety by the FDA.

POMx™ is a highly concentrated, incredibly powerful blend of all-natural polyphenol antioxidants made from the very same pomegranates in POM Wonderful 100% Pomegranate Juice. In fact, our method of harnessing astonishing levels of antioxidants is so extraordinary, it's patent-pending.

The power of POM. Now in one little pill.™

All of the antioxidant power of an 8oz glass of POM Wonderful 100% Pomegranate Juice is now available in the convenience of a single calorie-free pill. Take one daily. Each bottle contains a one-month supply of 30 pills.

Our antioxidants make other antioxidants feel inferior.



fact. 1 More polyphenol antioxidants than any other 100% pomegranate supplement

fact. 2 The antioxidant power of an 8oz glass of our juice, in a calorie-free pill

fact. 3 An astonishing 1000mg of natural pomegranate polyphenol extract in every pill

fact. 4 Made from the same California pomegranates in POM Wonderful 100% Pomegranate Juice

Why take an antioxidant supplement?

Let's start with the problem: free radicals. Emerging science tells us these unstable molecules aggressively destroy healthy cells in your body and may be linked to everything from the wrinkles we get as we age to more serious health threats like cancer and heart disease. In fact, scientists have already linked free radicals to as many as 60 different types of diseases.

Fighting free radicals.

Where do free radicals come from? Everywhere. They're formed by exposure to alcohol, sunlight, tobacco smoke, air pollution, pesticides and even fried foods. That's where antioxidants come in. Science tells us that pomegranate antioxidants neutralize free radicals, helping to prevent the damage that can lead to disease. In the fight against free radicals, POMx is the Antioxidant Superpill.™

Not all antioxidants are equal.

POMx is made from pomegranates only—nothing else. When other supplements add non-pomegranate ingredients or even other antioxidants, they can disrupt the balance of molecules that nature intended the pomegranate to have. The polyphenol antioxidants in POMx are as natural and unadulterated as those in our fresh, California-grown POM Wonderful Pomegranates.

"Findings from a small study suggest that pomegranate juice may one day prove an effective weapon against prostate cancer."

The New York Times (July 4, 2006)

Prostate health.

Prostate cancer is the most commonly diagnosed cancer among men in the United States and the second-leading cause of cancer death in men after lung cancer.[1]

Time pill.

Stable levels of prostate-specific antigens (or PSA levels) are critical for men with prostate cancer. Patients with quick PSA doubling times are more likely to die from their cancer.[2] According to a UCLA study of 46 men age 65 to 70 with advanced prostate cancer, drinking an 8oz glass of POM Wonderful 100% Pomegranate Juice every day slowed their PSA doubling time by nearly 350%.[3]

83% of those who participated in the study showed a significant decrease in their cancer regrowth rate.[3]

One small pill for mankind.

New studies are under way to further investigate the possibilities of POM Wonderful pomegranate antioxidants and their potential ability to slow the rise of PSA levels in patients with prostate cancer.

To learn more, visit pompills.com/research.

"The most abundant and most active ingredients in pomegranate juice are also found in POMx. Basic studies indicate that POMx and POM Wonderful Pomegranate Juice may have the same effects on prostate health."

David Heber, MD, PhD, Professor of Medicine and Director, UCLA Center for Human Nutrition

These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure or prevent any disease.

[1] American Cancer Society [2] *Vital Signs* newsletter, UCLA Healthcare, April 2007 [3] pompills.com/research [4] Data on file

"POM Wonderful Pomegranate Juice has been proven to promote cardiovascular health, and we believe that POMx may have the same health benefits."

Dr. Michael Aviram, Lipid Research Laboratory, Technion Faculty of Medicine, Haifa, Israel

Heart health.

In two groundbreaking preliminary studies, patients who drank POM Wonderful 100% Pomegranate Juice experienced impressive cardiovascular results. A pilot study at the Rambam Medical Center in Israel included 19 patients with atherosclerosis (clogged arteries). After a year, arterial plaque decreased 30% for those patients who consumed 8oz of POM Wonderful 100% Pomegranate Juice daily.[3]

An additional study at the University of California, San Francisco included 45 patients with impaired blood flow to the heart. Patients who consumed 8oz of POM Wonderful 100% Pomegranate Juice daily for three months experienced a 17% improvement in blood flow.[3] Initial studies on POMx share similar promise for heart health, and our research continues.

fig.1 THE HEART

The POMx Difference

Ultra-Potent:

- 1000mg of natural pomegranate polyphenol extract in every pill
- More antioxidants than any other pomegranate supplement
- One POMx pill = the antioxidant power of 8oz of POM Wonderful 100% Pomegranate Juice
- Your daily antioxidants in a single pill
- A full spectrum of pomegranate polyphenol antioxidants

Natural:

- Made from pomegranates and nothing else
- No synthetic or other antioxidants added
- No sugar, artificial colors or preservatives
- Calorie-free, vegan, kosher

Science, Not Fiction:

- Made from the only pomegranates backed by $20 million in medical research and the POM Wonderful brand
- Promotes heart and prostate health
- Guards your body against free radicals[4]
- Proven to be easily absorbed[4]
- Clinically tested on adults[4]

To access the original published studies mentioned, visit pompills.com/research.

Cheat death - (CX0188)

85. Complaint Counsel claim that, on April 1, 2008, POM ran an advertisement with the headline "Cheat death" with this body copy:

> You need more than luck to live longer. You need antioxidants. And POM Wonderful 100% Pomegranate Juice is loaded with them. It helps guard your body against free radicals, unstable molecules that emerging science suggests aggressively destroy healthy cells in your body and contribute to disease. POM Wonderful 100% Pomegranate Juice is supported by $23 million of medical scientific research from leading universities, which has uncovered encouraging results in prostate and cardiovascular health. So drink a glass a day and cheat death. Live life.
>
> **POM Wonderful 100% Pomegranate Juice. The Antioxidant Superpower.**

(CX0188_0001).

86. Complaint Counsel failed to present any other definitive information regarding this ad's dissemination.

87. Complaint Counsel failed to present any evidence that Respondents would run this ad in the future, let alone whether it is probable they would do so.

88. Mrs. Resnick testified that she does not recall bringing back the "Cheat death" headline for use in 2008. (L. Resnick, Tr. 191-92).

89. Complaint Counsel presented no evidence to contradict Mrs. Resnick's testimony regarding the use of this ad in 2008.

90. Complaint Counsel's assertion that the ad conveys the message that (a) POM Juice "prevents," "treats," or "reduces the risk" of heart disease or prostate cancer; or (b) POM Juice is "clinically proven" to "prevent," "treat," or "reduce the risk" of heart disease or prostate cancer is not conspicuous, self-evident, or reasonably clear from the face of the ad. (CX0188_0001).

91. Consequently, because the above-referenced challenged implied claim may not be determined with confidence from the face of the ad, extrinsic evidence must be examined.

92. The overall net impression of this ad is not that (a) drinking eight ounces of POM Juice prevents, treats or reduces the risk of certain diseases, such as heart disease

or prostate cancer; or (b) drinking eight ounces of POM Juice is "clinically proven" to prevent, treat or reduce the risk of certain diseases, such as heart disease or prostate cancer. (CX0188_0001). Even the language of the ad itself uses such qualifiers as "helps guard," "emerging science suggests," "contribute," and "encouraging results." (CX0188_0001).

93. To the extent a "reduce the risk" claim can be implied from ad, the overall net impression is not that drinking eight ounces of POM Juice "reduces the risk" of certain diseases, such as heart disease or prostate cancer, like a drug with a single target of action, but "reduces the risk," like a healthy diet of fruits and vegetables and exercise "reduces the risk" of disease. (CX0188_0001).

94. To the extent a "treat" claim can be implied from this ad (which it cannot), the overall net impression of any ad is not that POM Juice is a substitute for conventional medical treatment. (Butters, Tr. 2821-22).

95. To the extent a "proven" claim can be implied from this ad (which it cannot), the overall impression of this ad is not that POM Juice is "proven" to be 100% effective in preventing, treating or reducing the risk of heart disease or prostate cancer because (1) all of the qualifying language contradicts an implied "clinically proven" interpretation, and (2) "proven" in science means the "average person in the study benefitted," not that "everyone in the study necessarily benefitted." (Heber, Tr. 2011; Butters, Tr. 2893-2894; PX0361 (Sacks, Dep. at 81)).

96. Mrs. Resnick testified that the idea of the ad is to "make you laugh. And what we're saying here essentially with puffery is that you'll live longer if you -- you can cheat death, which we all know you can't." (L. Resnick, Tr. 194-95).

97. Mrs. Resnick further testified that the intent of the ad is to get the attention of the reader, make the reader read the ad, remember the shape of the bottle and the fact that POM has a healthy message. (L. Resnick, Tr. 195-97).

98. Professor Butters concluded that POM's ads in general depend on parody, exaggeration and humor to bring their message to the potential consumer; including the following messages: 1) POM is the best pomegranate that anyone can buy; 2) POM Juice is healthy; 3) POM Juice is tasty; 4) POM Juice is arguably the best source of antioxidants of any of the comparable beverages available; 5) medical research has suggested that antioxidants combat free radicals, which are unhealthy, and may contribute to diseases of the heart, arteries, and prostate, as well as erectile dysfunction; and 6) POM also offers concentrated forms of pomegranate extract for those who wish to ingest antioxidants in even more concentrated form than pomegranate juice itself. (PX0158-0033).

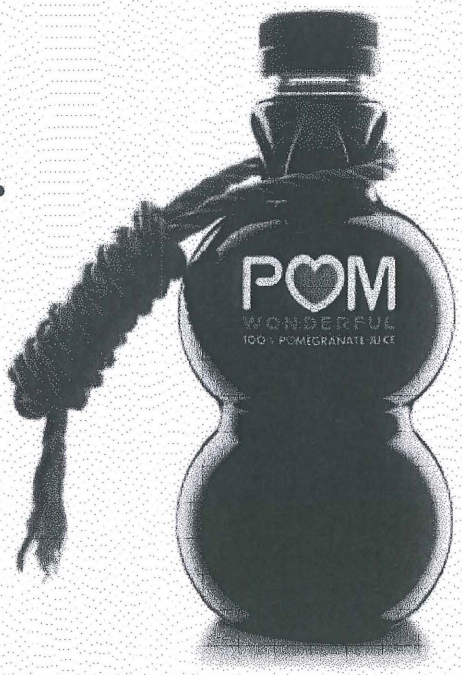
99. Viewing the "Cheat death" ad as a whole, including the interaction of the words and visual imagery, the overall net impression of the ad is that it is a humorous ad that uses puffery and that POM Juice is a healthy product. (L. Resnick, Tr. 195-97).

100. Complaint Counsel presented no extrinsic evidence or expert opinion on this ad's meaning, consumer perceptions of this ad, or consumer interpretations regarding this ad. (PX0357 (Stewart, Dep. at 49, 52)).

101. Complaint Counsel failed to present any evidence that the claims in this ad reasonably convey that the Challenged Products are "clinically proven" to prevent, treat or reduce the risk of heart disease, prostate cancer or erectile dysfunction.

102. Complaint Counsel failed to present any evidence regarding the number of exposures consumers had to this ad or any particular POM advertisement. (Mazis, Tr. 2752).

Cheat death.



You need more than luck to live longer. You need antioxidants. And POM Wonderful 100% Pomegranate Juice is loaded with them. It helps guard your body against free radicals, unstable molecules that emerging science suggests aggressively destroy healthy cells in your body and contribute to disease. POM Wonderful 100% Pomegranate Juice is supported by $23 million of medical scientific research from leading universities, which has uncovered encouraging results in prostate and cardiovascular health. So drink a glass a day and cheat death. Live life.

POM Wonderful 100% Pomegranate Juice. The Antioxidant Superpower.

POM WONDERFUL®
pomegranatetruth.com

JOB NO.: PJ8516	TRIM : 7" x 10.125"	COLOR : 4/C PROC	DATE IN : 03-27-08
PROJECT: PJ Advocate Print Ad CheatDeath June08	LIVE : n/a	TRIM (DO NOT PRINT)	DATE OUT : 04-1-08
SCALE: 1 : 1	BLEED : n/a	PRINTOUT SIZE : 100%	PROOF ROUND : F

Drink to prostate health - (CX0260; CX1426_0028, Exh. B)

103. Complaint Counsel claim that, on December 1, 2008, POM ran an advertisement with the headline "Drink to prostate health."

> Sometimes, good medicine can taste great. Case in point: POM Wonderful. A recently published preliminary medical study followed 46 men previously treated for prostate cancer, either with surgery or radiation. After drinking 8 ounces of POM Wonderful 100% Pomegranate Juice daily for at least two years, these men experienced significantly longer PSA doubling times. Want to learn more about the results of this study? Visit pomwonderful.com/prostate. **Trust in POM.**

(CX260_0001; CX1426_0028, Exh. B).

104. Complaint Counsel failed to present any definitive information regarding this ad's dissemination.

105. Complaint Counsel failed to present any evidence that Respondents would run this ad in the future, let alone whether it is probable they would do so.

106. Nowhere in this ad do Respondents expressly (*i.e.*, unequivocally and directly) state that (a) POM Juice "prevents," "treats," or "reduces the risk" of prostate cancer; or (b) POM Juice is "clinically proven" to "prevent," "treat," or "reduce the risk" of prostate cancer. (CX260_0001; CX1426_0028, Exh. B).

107. Mrs. Resnick testified that she does not recall this specific advertisement, is not familiar with it, and does not know when it ran. (L. Resnick, Tr. 243-44).

108. Mrs. Resnick testified that she does not know if this specific advertisement actually ran. (CX1359 (L. Resnick, Dep. at 125)).

109. Complaint Counsel's assertion that the ad impliedly conveys the message that (a) POM Juice "prevents," "treats," or "reduces the risk" of prostate cancer, like a drug; or (b) POM Juice is "clinically proven" to "prevent," "treat," or "reduce the risk" of prostate cancer, like a drug, is not conspicuous, self-evident, or reasonably clear from the face of the ad. (CX260_0001; CX1426_0028, Exh. B).

110. Consequently, because the above-referenced challenged implied claim may not be determined with confidence from the face of the ad, extrinsic evidence must be examined.

111. The overall net impression of this ad is not that (a) drinking eight ounces of POM Juice prevents, treats or reduces the risk of certain diseases, such as prostate

cancer, like a drug; or (b) drinking eight ounces of POM Juice is "clinically proven" to prevent, treat or reduce the risk of certain diseases, such as prostate cancer, like a drug. (CX260_0001; CX1426_0028, Exh. B). Even the language of the ad itself uses the qualifier "preliminary medical study." (CX260_0001; CX1426_0028, Exh. B).

112. To the extent a "reduce the risk" claim can be implied from ad, the overall net impression is not that drinking eight ounces of POM Juice "reduces the risk" of certain diseases, such as prostate cancer, like a drug with a single target of action, but "reduces the risk," like a healthy diet of fruits and vegetables and exercise "reduces the risk" of disease. (CX260_0001; CX1426_0028, Exh. B).

113. To the extent a "treat" claim can be implied from this ad (which it cannot), the overall net impression of any ad is not that POM Juice is a substitute for conventional medical treatment. (Butters, Tr. 2821-22).

114. To the extent a "proven" claim can be implied from this ad (which it cannot), the overall impression of this ad is not that POM Juice is "proven" to be 100% effective in preventing, treating or reducing the risk of prostate cancer because (1) all of the qualifying language contradicts an implied "clinically proven" interpretation, and (2) "proven" in science means the "average person in the study benefitted," not that "everyone in the study necessarily benefitted." (Heber, Tr. 2011; Butters, Tr. 2893-2894; PX0361 (Sacks, Dep. at 81)).

115. Professor Butters testified that this advertisement employs humor and references an alcoholic beverage toast. (PX0350 (Butters, Dep. at 119-20)). He does not believe that any reasonable viewer could find that the advertisement communicates that it could treat, prevent, or reduce the risk of disease. (PX0350 (Butters, Dep. at 121-124)). Professor Butters testified that there may be some outliers that may interpret the ad as making a health claim but those outliers would, by definition, not be ordinary or normal. (PX0350 (Butters, Dep. at 124-25)).

116. Professor Butters concluded that POM's ads in general depend on parody, exaggeration and humor to bring their message to the potential consumer; including the following messages: 1) POM is the best pomegranate that anyone can buy; 2) POM Juice is healthy; 3) POM Juice is tasty; 4) POM Juice is arguably the best source of antioxidants of any of the comparable beverages available; 5) medical research has suggested that antioxidants combat free radicals, which are unhealthy, and may contribute to diseases of the heart, arteries, and prostate, as well as erectile dysfunction; and 6) POM also offers concentrated forms of pomegranate extract for those who wish to ingest antioxidants in even more concentrated form than pomegranate juice itself. (PX0158-0033).

117. Ms. Leow testified that this ad was part of the "Trust in Pom" campaign and that the campaign's message was to let people know that POM Juice is healthy and is made with 100 percent pomegranate juice from California-grown pomegranates. (PX0330 (Leow, Dep. at 102-04)).

118. Viewing the "Drink to prostate health" ad as a whole, including the interaction of the words and visual imagery, the overall net impression of the ad is that it is a humorous reference to an alcoholic toast, that POM Juice is healthy and is made with 100 percent pomegranate juice from California-grown pomegranates. (PX0350 (Butters, Dep. at 124-25); (PX0330 (Leow, Dep. at 104)).

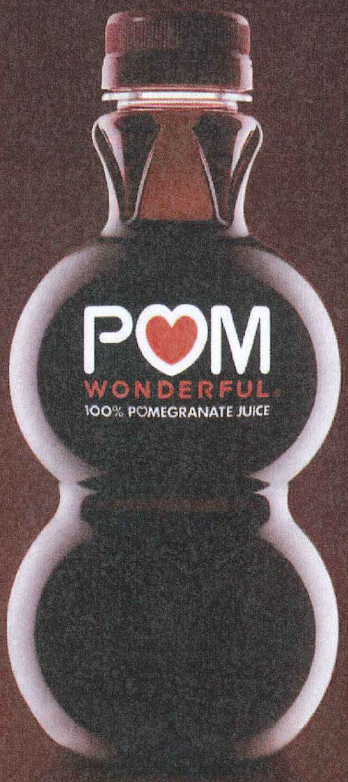
119. Complaint Counsel presented no extrinsic evidence or expert opinion on this ad's meaning, consumer perceptions of this ad, or consumer interpretations regarding this ad. (PX0357 (Stewart, Dep. at 49, 52)).

120. Complaint Counsel failed to present any evidence that the claims in this ad reasonably convey that the Challenged Products are "clinically proven" to prevent, treat or reduce the risk of heart disease, prostate cancer or erectile dysfunction.

121. Complaint Counsel failed to present any evidence regarding the number of exposures consumers had to this ad or any particular POM advertisement. (Mazis, Tr. 2752).

VMS ID: 081200704
RUN DATE: 12/01/2008

Drink to prostate health.



Sometimes, good medicine can taste great. Case in point: POM Wonderful®. A recently published preliminary medical study followed 46 men previously treated for prostate cancer, either with surgery or radiation. After drinking 8 ounces of POM Wonderful 100% Pomegranate Juice daily for at least two years, these men experienced significantly longer PSA doubling times. Want to learn more about the results of this study? Visit pomwonderful.com/prostate. **Trust in POM.**

pomwonderful.com

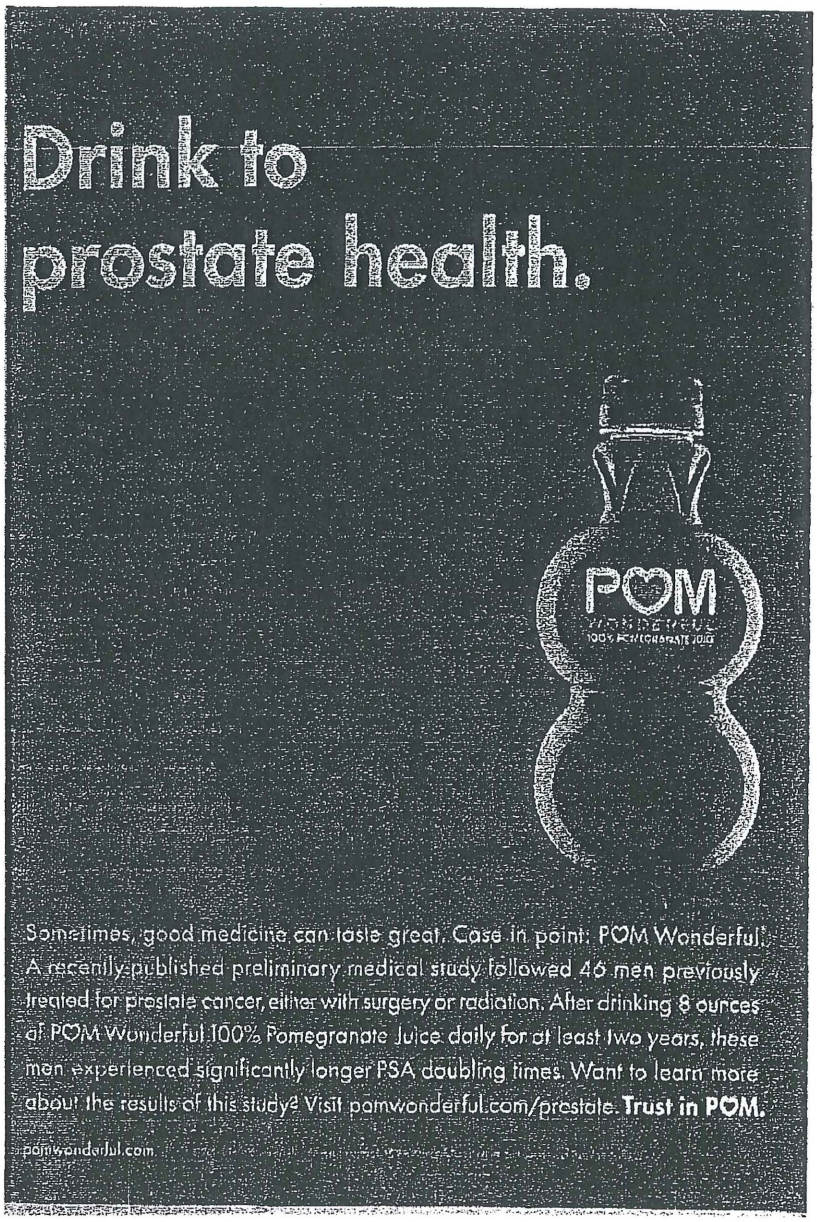

Drink to prostate health.
POM
Sometimes, good medicine can taste great. Case in point: POM Wonderful. A recently-published preliminary medical study followed 46 men previously treated for prostate cancer, either with surgery or radiation. After drinking 8 ounces of POM Wonderful 100% Pomegranate Juice daily for at least two years, these men experienced significantly longer PSA doubling times. Want to learn more about the results of this study? Visit pomwonderful.com/prostate. Trust in POM.
pomwonderful.com

Exhibit B

Drink to Prostate Health - (CX0314_0003; CX0314_0007)

122. Complaint Counsel claim that, on September 9, 2008, POM ran an advertisement with the headline "Drink to prostate health." without body copy. (CX0314_0003; CX0314_0007).

123. Complaint Counsel failed to present any other definitive information regarding this ad's dissemination.

124. Complaint Counsel failed to present any evidence that Respondents would run this ad in the future, let alone whether it is probable they would do so.

125. Complaint Counsel's assertion that the ad impliedly conveys the message that (a) POM Juice "prevents," "treats," or "reduces the risk" of prostate cancer, like a drug; or (b) POM Juice is "clinically proven" to "prevent," "treat," or "reduce the risk" of prostate cancer, like a drug, is not conspicuous, self-evident, or reasonably clear from the face of the ad. (CX0314_0003; CX0314_0007).

126. Consequently, because the above-referenced challenged implied claim may not be determined with confidence from the face of the ad, extrinsic evidence must be examined.

127. The overall net impression of this ad is not that (a) drinking eight ounces of POM Juice prevents, treats or reduces the risk of certain diseases, such as prostate cancer like a drug; or (b) drinking eight ounces of POM Juice is "clinically proven" to prevent, treat or reduce the risk of certain diseases, such as prostate cancer, like a drug. (CX0314_0003; CX0314_0007).

128. To the extent a "reduce the risk" claim can be implied from ad, the overall net impression is not that drinking eight ounces of POM Juice "reduces the risk" of certain diseases, such as prostate cancer, like a drug with a single target of action, but "reduces the risk," like a healthy diet of fruits and vegetables and exercise "reduces the risk" of disease. (CX0314_0003; CX0314_0007).

129. To the extent a "treat" claim can be implied from this ad (which it cannot), the overall net impression of any ad is not that POM Juice is a substitute for conventional medical treatment. (Butters, Tr. 2821-22).

130. To the extent a "proven" claim can be implied from this ad (which it cannot), the overall impression of this ad is not that POM Juice is "proven" to be 100% effective in preventing, treating or reducing the risk of prostate cancer because (1) all of the qualifying language contradicts an implied "clinically proven" interpretation, and (2) "proven" in science means the "average person in the study

benefitted," not that "everyone in the study necessarily benefitted." (Heber, Tr. 2011; Butters, Tr. 2893-2894; PX0361 (Sacks, Dep. at 81)).

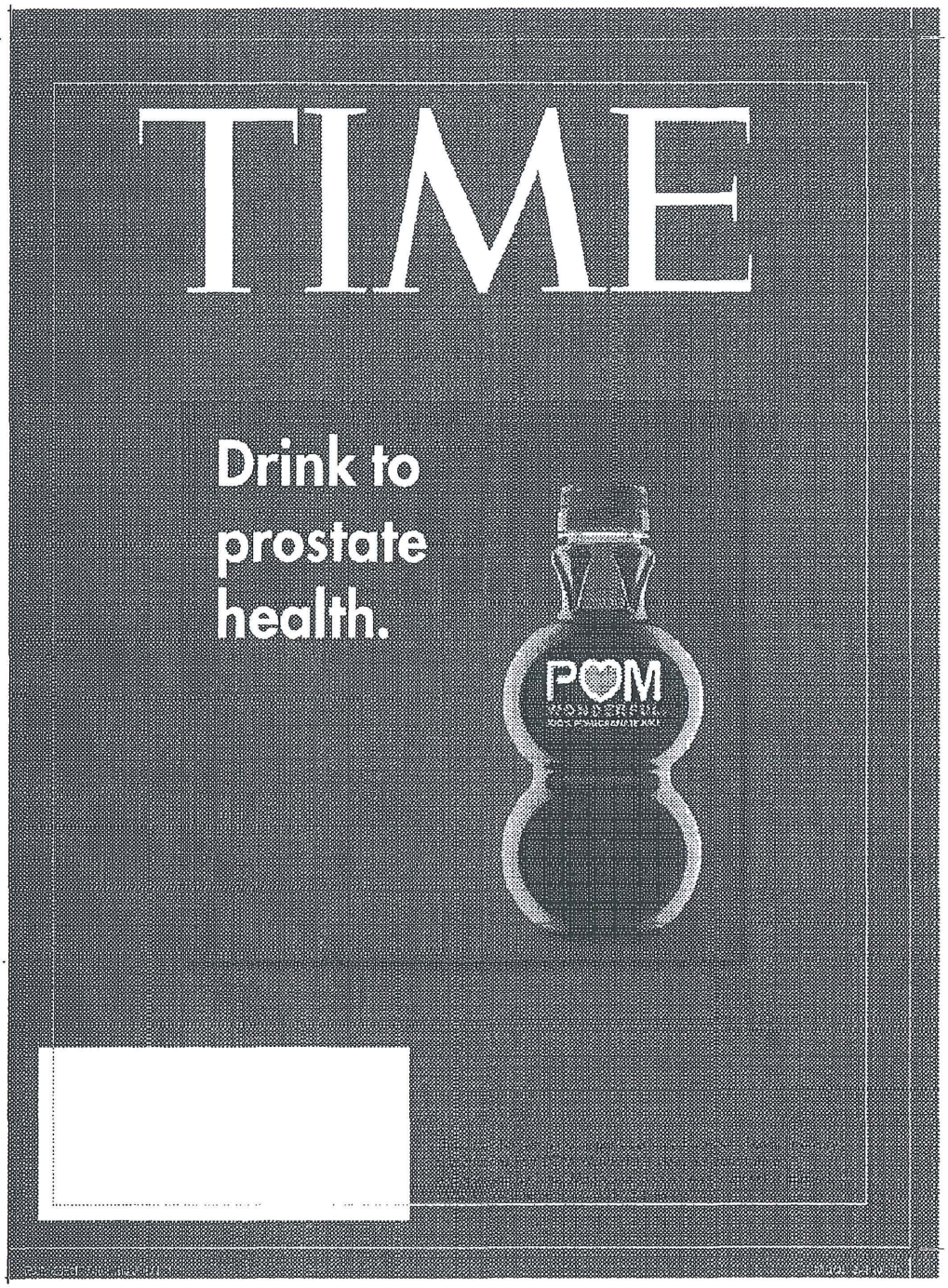
131. Professor Butters concluded that POM's ads in general depend on parody, exaggeration and humor to bring their message to the potential consumer; including the following messages: 1) POM is the best pomegranate that anyone can buy; 2) POM Juice is healthy; 3) POM Juice is tasty; 4) POM Juice is arguably the best source of antioxidants of any of the comparable beverages available; 5) medical research has suggested that antioxidants combat free radicals, which are unhealthy, and may contribute to diseases of the heart, arteries, and prostate, as well as erectile dysfunction; and 6) POM also offers concentrated forms of pomegranate extract for those who wish to ingest antioxidants in even more concentrated form than pomegranate juice itself. (PX0158-0033).

132. Viewing the "Drink to prostate health" ad as a whole, including the interaction of the words and visual imagery, the overall net impression of the ad is that it is a humorous reference to an alcoholic toast, that POM Juice is healthy and is made with 100 percent pomegranate juice from California-grown pomegranates. (PX0350 (Butters, Dep. at 124-25); (PX0330 (Leow, Dep. at 104)).

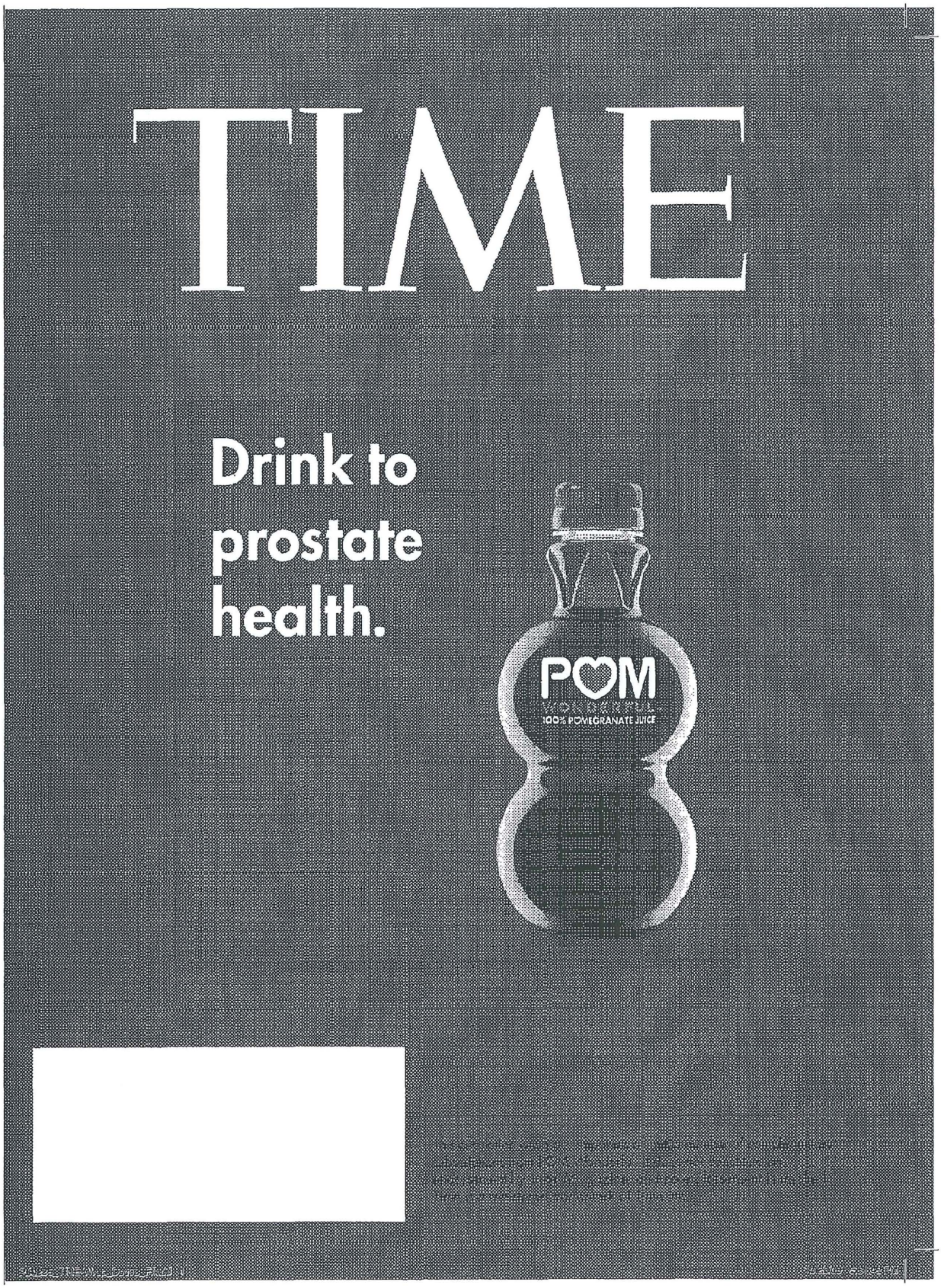
133. Complaint Counsel presented no extrinsic evidence or expert opinion on this ad's meaning, consumer perceptions of this ad, or consumer interpretations regarding this ad. (PX0357 (Stewart, Dep. at 49, 52)).

134. Complaint Counsel failed to present any evidence that the claims in this ad reasonably convey that the Challenged Products are "clinically proven" to prevent, treat or reduce the risk of heart disease, prostate cancer or erectile dysfunction.

135. Complaint Counsel failed to present any evidence regarding the number of exposures consumers had to this ad or any particular POM advertisement. (Mazis, Tr. 2752).



JOB NO.: PJ9745	TRIM: 7.875"x10.5"	COLOR: 4/C PROS	DATE IN: 08-25-08
PROJECT: NY Times Magazine Wrap	LIVE: 7.125" x 9.75"	BLEED: TRIM, BLEED (DO NOT PRINT)	DATE OUT: 09-09-08
SCALE: 1 : 1	MATCH: 8.375" x 11"	PRINTOUT SIZE: 100%	PROOF ROUND: F


TIME
Drink to prostate health.
POM
WONDERFUL
100% POMEGRANATE JUICE

Have no health fear . . . POM IS HERE! - (CX0380_0004)

136. Complaint Counsel claim that, on September 10, 2009, POM ran an advertisement with the headline "Have no health fear … POM IS HERE!" and the body copy:

> It's a champion of superior health…It's a medical marvel…It's the Antioxidant Superpower, POM Wonderful® 100% pure pomegranate juice. Unpolluted by cheap filler juices, added sugars or colorants. Backed by published medical research.* Devoted to keeping you alive and well for a good, long time!
>
> *Visit pomwonderful.com/health/research to review published studies.

(CX0380_0004).

137. Complaint Counsel failed to present any other definitive information regarding this ad's dissemination.

138. Complaint Counsel failed to present any evidence that Respondents would run this ad in the future, let alone whether it is probable they would do so.

139. Complaint Counsel's expert, Professor Mazis, testified that Complaint Counsel is not challenging POM's ads for POM Juice that ran after December 2008. (Mazis, Tr. 2753-54). Accordingly, based on these representations, Complaint Counsel cannot now challenge this ad.

140. Complaint Counsel's assertion that the ad conveys the message that (a) POM Juice "prevents," "treats," or "reduces the risk" of certain diseases; or (b) POM Juice is "clinically proven" to "prevent," "treat," or "reduce the risk" of certain diseases is not conspicuous, self-evident, or reasonably clear from the face of the ad. (CX0380_0004).

141. Consequently, because the above-referenced challenged implied claim may not be determined with confidence from the face of the ad, extrinsic evidence must be examined.

142. The overall net impression of this ad is not that (a) drinking eight ounces of POM Juice prevents, treats or reduces the risk of certain diseases; or (b) drinking eight ounces of POM Juice is "clinically proven" to prevent, treat or reduce the risk of certain diseases. (CX0380_0004).

143. To the extent a "reduce the risk" claim can be implied from ad, the overall net impression is not that drinking eight ounces of POM Juice "reduces the risk" of

certain diseases, like a drug with a single target of action, but "reduces the risk," like a healthy diet of fruits and vegetables and exercise "reduces the risk" of disease. (CX0380_0004).

144. To the extent a "treat" claim can be implied from this ad (which it cannot), the overall net impression of any ad is not that POM Juice is a substitute for conventional medical treatment. (Butters, Tr. 2821-22).

145. To the extent a "proven" claim can be implied from this ad (which it cannot), the overall impression of this ad is not that POM Juice is "proven" to be 100% effective in preventing, treating or reducing the risk of certain diseases because (1) all of the qualifying language contradicts an implied "clinically proven" interpretation, and (2) "proven" in science means the "average person in the study benefitted," not that "everyone in the study necessarily benefitted." (Heber, Tr. 2011; Butters, Tr. 2893-2894; PX0361 (Sacks, Dep. at 81)).

146. Professor Butters concluded that POM's ads in general depend on parody, exaggeration and humor to bring their message to the potential consumer; including the following messages: 1) POM is the best pomegranate that anyone can buy; 2) POM Juice is healthy; 3) POM Juice is tasty; 4) POM Juice is arguably the best source of antioxidants of any of the comparable beverages available; 5) medical research has suggested that antioxidants combat free radicals, which are unhealthy, and may contribute to diseases of the heart, arteries, and prostate, as well as erectile dysfunction; and 6) POM also offers concentrated forms of pomegranate extract for those who wish to ingest antioxidants in even more concentrated form than pomegranate juice itself. (PX0158-0033).

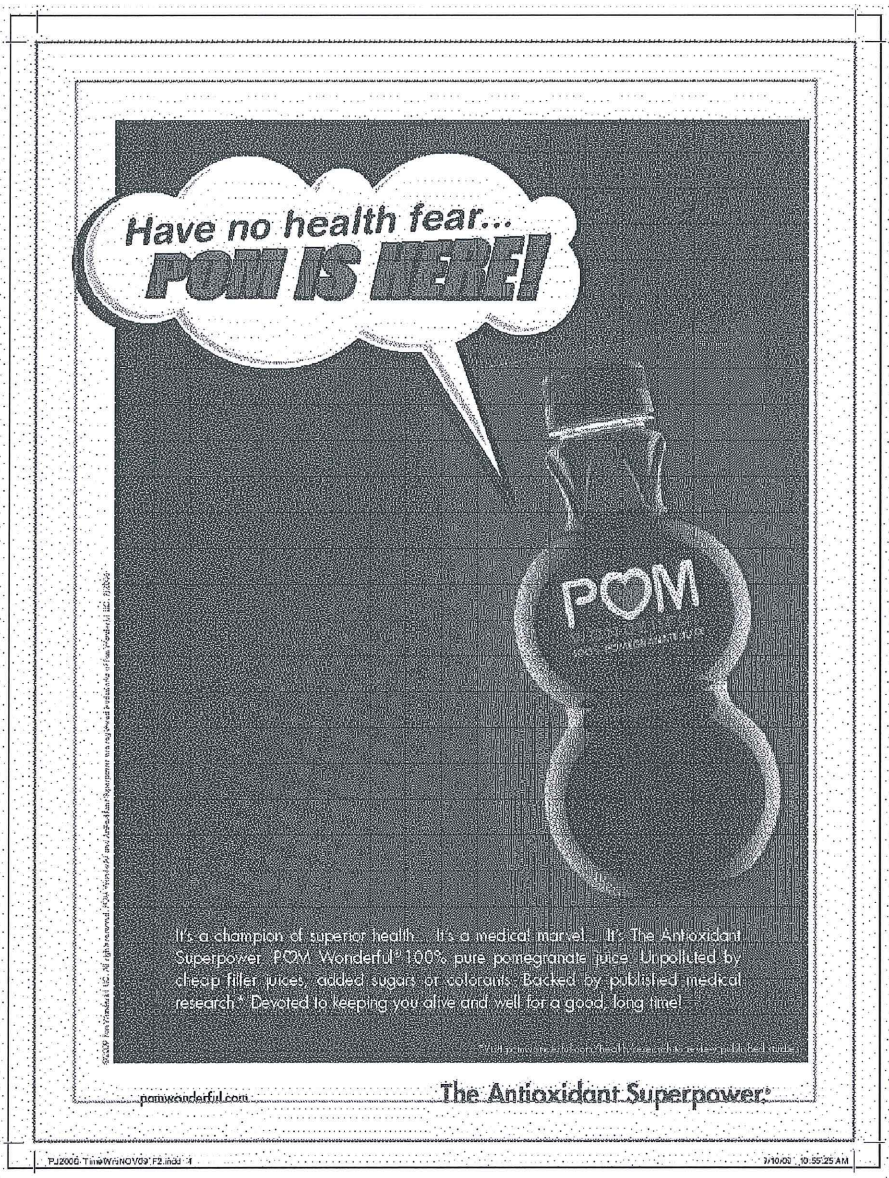
147. Ms. Kuyoomijian testified that this ad's headline is a "broad claim," meaning that it is not addressing any specific health benefit but just conveying that the product is generally healthy. (CX1357 (Kuyoomijian, Dep. at 195-96)).

148. Viewing the "Have no health fear … POM IS HERE!"ad as a whole, including the interaction of the words and visual imagery, the overall net impression of the ad is that it is a humorous reference to a superhero, that POM Juice is a healthy product. ((PX0158-0033); (PX0329 (Kuyoomijian, Dep. at 195-96)).

149. Complaint Counsel presented no extrinsic evidence or expert opinion on this ad's meaning, consumer perceptions of this ad, or consumer interpretations regarding this ad. (PX0357 (Stewart, Dep. at 49, 52)).

150. Complaint Counsel failed to present any evidence that the claims in this ad reasonably convey that the Challenged Products are "clinically proven" to prevent, treat or reduce the risk of heart disease, prostate cancer or erectile dysfunction.

151. Complaint Counsel failed to present any evidence regarding the number of exposures consumers had to this ad or any particular POM advertisement. (Mazis, Tr. 2752).



PJ2006 Time Wrap NOV09 F2.indd 1 9/10/09 10:55:25 AM

JOB NO.: PJ2006	TRIM: 7.875" x 10.5"	COLOR: 4/C PROS	DATE IN: 9-01-09	CREATIVE: CJ
PROJECT: Time Magazine Wrap - Nov 09	LIVE: 7.125" x 9.75"	LIVE, TRIM, BLEED (DO NOT PRINT)	CLIENT SIGN OFF: 00-00-00	PRODUCTION: MS
SCALE: 1 : 1	BLEED: 8.375" x 11.0"	PRINTOUT SIZE: 100%	RELEASE DATE: 9-10-09	PROOF: FZ

*PLEASE MARK ALL CHANGES ON INSITE DOCUMENT *NO CHANGES ON PRINTED FLAT WILL BE MADE

Healthy, ~~Wealthy~~ & Wise - (CX0331, CX1426_0043, Exh. J)

152. Complaint Counsel claim that, on September 27, 2009, POM ran an advertisement with the headline "Healthy, ~~Wealthy~~ & Wise" with the body copy that appears on CX0331_0001 and CX1426_0043, Exh. J.

153. Complaint Counsel failed to present any other definitive information regarding this ad's dissemination.

154. Complaint Counsel failed to present any evidence that Respondents would run this ad in the future, let alone whether it is probable they would do so.

155. Complaint Counsel's expert, Professor Mazis, testified that Complaint Counsel is not challenging POM's ads for POM Juice that ran after December 2008. (Mazis, Tr. 2753-54). Accordingly, based on these representations, Complaint Counsel cannot now challenge this ad.

156. Nowhere in this ad do Respondents expressly (*i.e.*, unequivocally and directly) state that (a) taking one POMx Pill per day "prevents," "treats," or "reduces the risk" of heart disease or prostate cancer; or (b) taking one POMx Pill per day is "clinically proven" to "prevent," "treat," or "reduce the risk" of heart disease or prostate cancer. (CX0331_0001; CX1426_0043, Exh. J).

157. Complaint Counsel's assertion that the ad conveys the message that (a) taking one POMx Pill per day "prevents," "treats," or "reduces the risk" of heart disease or prostate cancer; or (b) taking one POMx Pill per day is "clinically proven" to "prevent," "treat," or "reduce the risk" of heart disease or prostate cancer is not conspicuous, self-evident, or reasonably clear from the face of the ad. (CX0331_0001; CX1426_0043, Exh. J).

158. Consequently, because the above-referenced challenged implied claim may not be determined with confidence from the face of the ad, extrinsic evidence must be examined.

159. The overall net impression of this ad is not that not that taking one POMx Pill per day prevents, treats or reduces the risk of certain diseases, such as heart disease or prostate cancer; or (b) taking one POMx Pill per day is "clinically proven" to prevent, treat or reduce the risk of certain diseases, such as heart disease or prostate cancer. (CX0331_0001; CX1426_0043, Exh. J). Even the language of the ad itself uses such qualifiers as "emerging science suggests," "help protect," "promising results," "initial UCLA study," "hopeful results" and "preliminary studies." (CX0331_0001; CX1426_0043, Exh. J).

160. To the extent a "reduce the risk" claim can be implied from this ad, the overall net impression is not that taking one POMx Pill per day "reduces the risk" of certain diseases, such as heart disease or prostate cancer, like a drug with a single target of action, but "reduces the risk," like a healthy diet of fruits and vegetables and exercise "reduces the risk" of disease. (CX0331_0001; CX1426_0043, Exh. J).

161. To the extent a "treat" claim can be implied from this ad (which it cannot), the overall net impression of any ad is not that POMx Pills are a substitute for conventional medical treatment. (Butters, Tr. 2821-22).

162. To the extent a "proven" claim can be implied from this ad (which it cannot), the overall impression of this ad is not that POMx Pills are "proven" to be 100% effective in preventing, treating or reducing the risk of heart disease or prostate cancer because (1) all of the qualifying language contradicts an implied "clinically proven" interpretation, and (2) "proven" in science means the "average person in the study benefitted," not that "everyone in the study necessarily benefitted." (Heber, Tr. 2011; Butters, Tr. 2893-2894; PX0361 (Sacks, Dep. at 81)).

163. Professor Butters concluded that POM's ads in general depend on parody, exaggeration and humor to bring their message to the potential consumer; including the following messages: 1) POM is the best pomegranate that anyone can buy; 2) POM Juice is healthy; 3) POM Juice is tasty; 4) POM Juice is arguably the best source of antioxidants of any of the comparable beverages available; 5) medical research has suggested that antioxidants combat free radicals, which are unhealthy, and may contribute to diseases of the heart, arteries, and prostate, as well as erectile dysfunction; and 6) POM also offers concentrated forms of pomegranate extract for those who wish to ingest antioxidants in even more concentrated form than pomegranate juice itself. (PX0158-0033).

164. Professor Butters describes the headline of this ad as "light hearted," "kind of a joke," and "a bit of, if not self parody, at least confession of the high price of POM products." He further testified that this advertisement tells the consumer that the POM "products are not cheap, but they're really good." (PX0350 (Butters, Dep. at 135)).

165. Viewing the "Healthy, ~~Wealthy~~ & Wise" ad as a whole, including the interaction of the words and visual imagery, the overall net impression of the ad is that it is a humorous ad and that POMx Pills are healthy. (PX0350 (Butters, Dep. at 135); (PX0158-0033))).

166. Complaint Counsel presented no extrinsic evidence or expert opinion on this ad's meaning, consumer perceptions of this ad, or consumer interpretations regarding this ad. (PX0357 (Stewart, Dep. at 49, 52)).

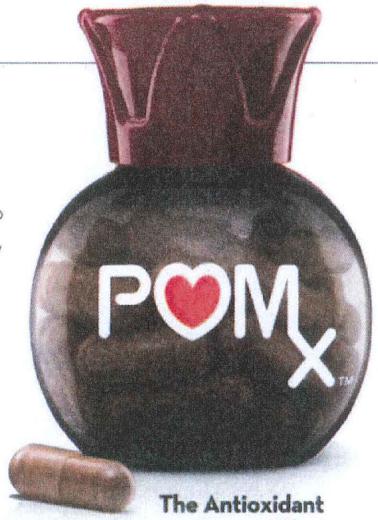
167. Complaint Counsel failed to present any evidence that the claims in this ad reasonably convey that the Challenged Products are "clinically proven" to prevent, treat or reduce the risk of heart disease, prostate cancer or erectile dysfunction.

168. Complaint Counsel failed to present any evidence regarding the number of exposures consumers had to this ad or any particular POM advertisement. (Mazis, Tr. 2752).

VMS ID: 090921830
RUN DATE: 09/27/2009

HEALTHY. ~~WEALTHY.~~ AND WISE.

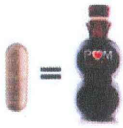
(2 OUT OF 3 IN THIS ECONOMY AIN'T BAD.)



The Antioxidant Superpill.™

Antioxidants are a necessity. Not a luxury.

Emerging science suggests that antioxidants are critically important to maintaining good health because they protect you from free radicals, which can damage your body. Taking one POMx pill a day will help protect you from free radicals and keep you at your healthy best. Even when you're going through the worst.



The antioxidant power of our 8oz juice.

Recession-proof your health with POMx.

POMx is an all-natural, ultra-potent antioxidant extract. Containing a full spectrum of pomegranate polyphenols, POMx is so concentrated that a single capsule has the anti-oxidant power of a full glass of POM Wonderful® 100% Pomegranate Juice.

$32 million in medical research. A sound investment.

POMx is made from the only pomegranates backed by $32 million in medical research at the world's leading universities. Not only has this research documented the unique and superior antioxidant power of pomegranates, it has revealed promising results for prostate and cardiovascular health.

Hope for the future. Yours.

Our POMx pills are made from the same pomegranates we use to make our POM Wonderful 100% Pomegranate Juice, on which each of the following medical studies was conducted.

An initial UCLA study on our juice found hopeful results for prostate health, reporting "statistically significant prolongation of PSA doubling times," according to Dr. Allen J. Pantuck in *Clinical Cancer Research*, '06.[1,2,3]

Two additional preliminary studies on our juice showed promising results for heart health. "Stress-induced ischemia (restricted blood flow to the heart) decreased in the pomegranate group," Dr. Dean Ornish reported in the *American Journal of Cardiology*, '05.[1,2,4]

"Pomegranate juice consumption resulted in significant reduction in IMT[5] (thickness of arterial plaque) by up to 30% after one year," said Dr. Michael Aviram in *Clinical Nutrition*, '04.[1,2,5,6]

Try POMx Monthly FREE for ONE MONTH.
We'll even pay for the shipping.*

Order Now: 888-766-7455 or pompills.com/ph
Use discount code: PH30

*SIGN UP FOR POMx MONTHLY, AND WE'LL SEND YOUR FIRST BOTTLE FREE. AFTER THAT, YOU'LL CONTINUE TO RECEIVE MONTHLY SHIPMENTS FOR $29.95 WITH COMPLIMENTARY SHIPPING. Offer expires 12/15/09 and applies only to the purchase price for the first bottle of POMx Monthly. Following months will be $29.95 per bottle. One discount per customer. Cannot be combined with other offers. No substitutions, transfer rights or cash equivalents. We reserve the right to discontinue this promotion, change product price or shipping charge at any time. Valid only at pompills.com/ph or 1-888-766-7455. Not valid on POMx Trial or other POM products.

POM WONDERFUL®

[1]pompills.com/research [2]These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure or prevent any disease. [3]46 men with rising PSA after surgery or radiotherapy drank 8oz 100% pomegranate juice daily for two years. [4]45 patients with coronary heart disease and myocardial ischemia drank 8oz 100% pomegranate juice daily for three months. [5]Study measured intima-media thickness (IMT). [6]19 patients aged 65-75 years with severe atherosclerosis drank 8oz 100% pomegranate juice daily for one year.

VMS-0000299

CX0331_0001

HEALTHY. ~~WEALTHY~~. AND WISE.

(2 OUT OF 3 IN THIS ECONOMY AIN'T BAD.)

The Antioxidant Superpill.™

Antioxidants are a necessity. Not a luxury.

Emerging science suggests that antioxidants are critically important to maintaining good health because they protect you from free radicals, which can damage your body. Taking one POMx pill a day will help protect you from free radicals and keep you at your healthy best. Even when you're going through the worst.

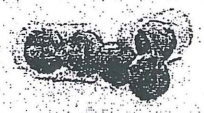
The antioxidant power of our 8oz juice.

Recession-proof your health with POMx.

POMx is an all-natural, ultra-potent antioxidant extract. Containing a full spectrum of pomegranate polyphenols, POMx is so concentrated that a single capsule has the antioxidant power of a full glass of POM Wonderful® 100% Pomegranate Juice.

$32 million in medical research. A sound investment.

POMx is made from the only pomegranates backed by $32 million in medical research at the world's leading universities.



Not only has this research documented the unique and superior antioxidant power of pomegranates, it has revealed promising results for prostate and cardiovascular health.

Hope for the future. Yours.

Our POMx pills are made from the same pomegranates we use to make our POM Wonderful 100% Pomegranate Juice, on which each of the following medical studies was conducted.

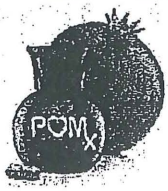
An initial UCLA study on our juice found hopeful results for prostate health, reporting "statistically significant prolongation of PSA doubling times," according to Dr. Allen J. Pantuck in *Clinical Cancer Research*, '06.[1,2,3]

Two additional preliminary studies on our juice showed promising results for heart health. "Stress-induced ischemia (restricted blood flow to the heart) decreased in the pomegranate group," Dr. Dean Ornish reported in the *American Journal of Cardiology*, '05.[1,2,4]

"Pomegranate juice consumption resulted in significant reduction in IMT[5] (thickness of arterial plaque) by up to 30% after one year," said Dr. Michael Aviram in *Clinical Nutrition*, '04.[1,2,5,6]

Try POMx Monthly FREE for ONE MONTH.

We'll even pay for the shipping.*



Order Now: 888-766-7455 or pompills.com/ph

Use discount code: PH30

*SIGN UP FOR POMx MONTHLY, AND WE'LL SEND YOUR FIRST BOTTLE FREE. AFTER THAT, YOU'LL CONTINUE TO RECEIVE MONTHLY SHIPMENTS FOR $29.95 WITH COMPLIMENTARY SHIPPING. Offer expires 12/15/09 and applies only to the purchase price for the first bottle of POMx Monthly. Following months will be $29.95 per bottle. One discount per customer. Cannot be combined with other offers. No substitutions, transfer rights or cash equivalents. We reserve the right to discontinue this promotion, change product price or shipping charge at any time. Valid only at pompills.com/ph or 1-888-766-7455. Not valid on POMx Trial or other POM products.

POM WONDERFUL

[1]pompills.com/research [2]These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure or prevent any disease. [3]28 men with rising PSA after surgery or radiotherapy drank 8oz 100% pomegranate juice daily for two years. [4]45 patients with coronary heart disease and myocardial ischemia drank 8oz 100% pomegranate juice daily for three months. [5]Study measured intima-media thickness (IMT). [6]39 patients aged 65-75 years with severe atherosclerosis drank 8oz 100% pomegranate juice daily for one year. ©2009 PomWonderful LLC. All rights reserved. POM Wonderful, POMx and Antioxidant Superpills are trademarks of PomWonderful LLC. PP332

Exhibit J

Heart Therapy - (CX0109)

169. Complaint Counsel claim that, on April 1, 2007, POM ran an advertisement with the headline "Heart Therapy" with this body copy:

> Seek professional help for your heart. Drink POM Wonderful Pomegranate Juice. It helps guard your body against free radicals, unstable molecules that emerging science suggests aggressively destroy and weaken healthy cells in your body and contribute to disease. POM Wonderful Pomegranate Juice is supported by $20 million of initial scientific research from leading universities, which has uncovered encouraging results in prostate and cardiovascular health. Keep your heart healthy and drink 8 ounces a day.

(CX0109_0001).

170. Complaint Counsel failed to present any other definitive information regarding this ad's dissemination.

171. Complaint Counsel failed to present any evidence that Respondents would run this ad in the future, let alone whether it is probable they would do so.

172. This ad cannot provide a basis for injunctive relief because (a) it ran almost five years ago; and (b) no evidence exists to show that Respondents are likely to run this ad in the future.

173. Complaint Counsel's assertion that that the ad conveys the message that (a) POM Juice "prevents," "treats," or "reduces the risk" of heart disease or prostate cancer; or (b) POM Juice is "clinically proven" to "prevent," "treat," or "reduce the risk" of heart disease or prostate cancer is not conspicuous, self-evident, or reasonably clear from the face of the ad. (CX0109_0001).

174. Consequently, because the above-referenced challenged implied claim may not be determined with confidence from the face of the ad, extrinsic evidence must be examined.

175. The overall net impression of this ad is not that (a) drinking eight ounces of POM Juice prevents, treats or reduces the risk of certain diseases, such as heart disease or prostate cancer; or (b) drinking eight ounces of POM Juice is "clinically proven" to prevent, treat or reduce the risk of certain diseases, such as heart disease or prostate cancer. (CX0109_0001). Even the language of the ad itself uses such qualifiers as "helps guard," "emerging science suggests," "initial scientific research" and "encouraging results." (CX0109_0001).

176. To the extent a "reduce the risk" claim can be implied from this ad, the overall net impression is not that drinking eight ounces of POM Juice "reduces the risk" of certain diseases, such as heart disease or prostate cancer, like a drug with a single target of action, but "reduces the risk," like a healthy diet of fruits and vegetables and exercise "reduces the risk" of disease. (CX0109_0001).

177. To the extent a "treat" claim can be implied from this ad (which it cannot), the overall net impression of any ad is not that POM Juice is a substitute for conventional medical treatment. (Butters, Tr. 2821-22; Appendix of Advertisements).

178. To the extent a "proven" claim can be implied from this ad (which it cannot), the overall impression of this ad is not that POM Juice is "proven" to be 100% effective in preventing, treating or reducing the risk of heart disease or prostate cancer because (1) all of the qualifying language contradicts an implied "clinically proven" interpretation, and (2) "proven" in science means the "average person in the study benefitted," not that "everyone in the study necessarily benefitted." (Heber, Tr. 2011; Butters, Tr. 2893-2894; PX0361 (Sacks, Dep. at 81)).

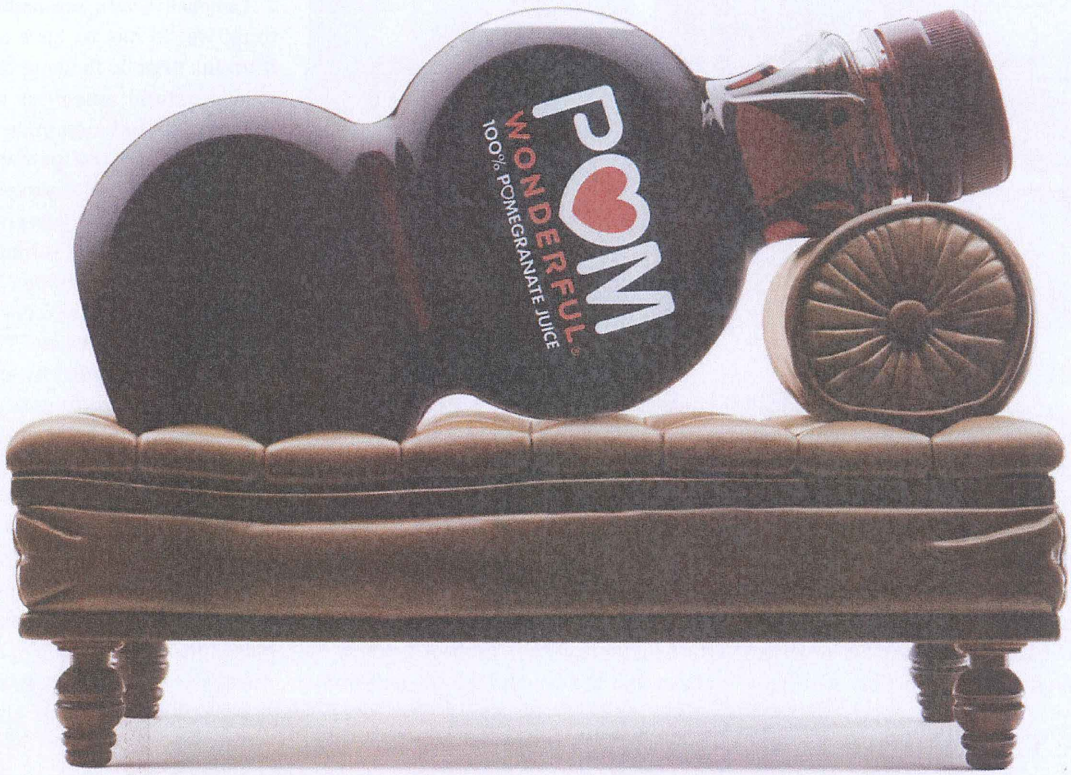
179. Professor Butters concluded that POM's ads in general depend on parody, exaggeration and humor to bring their message to the potential consumer; including the following messages: 1) POM is the best pomegranate that anyone can buy; 2) POM Juice is healthy; 3) POM Juice is tasty; 4) POM Juice is arguably the best source of antioxidants of any of the comparable beverages available; 5) medical research has suggested that antioxidants combat free radicals, which are unhealthy, and may contribute to diseases of the heart, arteries, and prostate, as well as erectile dysfunction; and 6) POM also offers concentrated forms of pomegranate extract for those who wish to ingest antioxidants in even more concentrated form than pomegranate juice itself. (PX0158-0033).

180. Complaint Counsel presented no extrinsic evidence or expert opinion on this ad's meaning, consumer perceptions of this ad, or consumer interpretations regarding this ad. (PX0357 (Stewart, Dep. at 49, 52)).

181. Complaint Counsel failed to present any evidence that the claims in this ad reasonably convey that the Challenged Products are "clinically proven" to prevent, treat or reduce the risk of heart disease, prostate cancer or erectile dysfunction.

182. Complaint Counsel failed to present any evidence regarding the number of exposures consumers had to this ad or any particular POM advertisement. (Mazis, Tr. 2752).

VMS ID: 070420398
RUN DATE: 04/01/2007



Heart therapy.

Seek professional help for your heart. Drink POM Wonderful Pomegranate Juice. It helps guard your body against free radicals, unstable molecules that emerging science suggests aggressively destroy and weaken healthy cells in your body and contribute to disease. POM Wonderful Pomegranate Juice is supported by $20 million of initial scientific research from leading universities, which has uncovered encouraging results in prostate and cardiovascular health. Keep your heart healthy and drink 8 ounces a day.

POM WONDERFUL®
pomwonderful.com

POM Wonderful Pomegranate Juice. The Antioxidant Superpower.™

HOLY HEALTH! $25 million in medical research - (CX1426_0030, Exh. D)

183. Complaint Counsel claim that POM ran an advertisement with the headline "Holy Health! $25 Million In Medical Research" with this body copy:

> In a time of major health problems, one 16-ounce hero will unleash its incredible healing powers: POM Wonderful® 100% pure pomegranate juice. Backed by an unheard-of $25 million in medical research, The Antioxidant Superwpower® sweeps into action to help fight for heart and prostate health. Ka-POM!

(CX1426_0030, Exh. D).

184. Complaint Counsel failed to present any definitive information regarding this ad's dissemination.

185. Complaint Counsel failed to present any evidence that Respondents would run this ad in the future, let alone whether it is probable they would do so.

186. Complaint Counsel's assertion that the ad conveys the message that (a) POM Juice "prevents," "treats," or "reduces the risk" of heart disease or prostate cancer; or (b) POM Juice is "clinically proven" to "prevent," "treat," or "reduce the risk" of heart disease or prostate cancer is not conspicuous, self-evident, or reasonably clear from the face of the ad. (CX1426_0030, Exh. D).

187. Consequently, because the above-referenced challenged implied claim may not be determined with confidence from the face of the ad, extrinsic evidence must be examined.

188. The overall net impression of this ad is not that (a) drinking eight ounces of POM Juice prevents, treats or reduces the risk of certain diseases, such as heart disease or prostate cancer; or (b) drinking eight ounces of POM Juice is "clinically proven" to prevent, treat or reduce the risk of certain diseases, such as heart disease or prostate cancer. (CX1426_0030, Exh. D). Even the language of the ad itself uses such qualifiers as "help" and "fight for." (CX1426_0030, Exh. D).

189. To the extent a "reduce the risk" claim can be implied from ad, the overall net impression is not that drinking eight ounces of POM Juice "reduces the risk" of certain diseases, such as heart disease or prostate cancer, like a drug with a single target of action, but "reduces the risk," like a healthy diet of fruits and vegetables and exercise "reduces the risk" of disease. (CX1426_0030, Exh. D).

190. To the extent a "treat" claim can be implied from this ad (which it cannot), the overall net impression of any ad is not that POM Juice is a substitute for conventional medical treatment. (Butters, Tr. 2821-22).

191. To the extent a "proven" claim can be implied from this ad (which it cannot), the overall impression of this ad is not that POM Juice is "proven" to be 100% effective in preventing, treating or reducing the risk of heart disease or prostate cancer because (1) all of the qualifying language contradicts an implied "clinically proven" interpretation, and (2) "proven" in science means the "average person in the study benefitted," not that "everyone in the study necessarily benefitted." (Heber, Tr. 2011; Butters, Tr. 2893-2894; PX0361 (Sacks, Dep. at 81)).

192. Mrs. Resnick testified that she does not recall approving the print headline, "HOLY HEALTH!" for print use. (L. Resnick, Tr. 120).

193. Professor Butters concluded that POM's ads in general depend on parody, exaggeration and humor to bring their message to the potential consumer; including the following messages: 1) POM is the best pomegranate that anyone can buy; 2) POM Juice is healthy; 3) POM Juice is tasty; 4) POM Juice is arguably the best source of antioxidants of any of the comparable beverages available; 5) medical research has suggested that antioxidants combat free radicals, which are unhealthy, and may contribute to diseases of the heart, arteries, and prostate, as well as erectile dysfunction; and 6) POM also offers concentrated forms of pomegranate extract for those who wish to ingest antioxidants in even more concentrated form than pomegranate juice itself. (PX0158-0033).

194. Complaint Counsel presented no extrinsic evidence or expert opinion on this ad's meaning, consumer perceptions of this ad, or consumer interpretations regarding this ad. (PX0357 (Stewart, Dep. at 49, 52)).

195. Complaint Counsel failed to present any evidence that the claims in this ad reasonably convey that the Challenged Products are "clinically proven" to prevent, treat or reduce the risk of heart disease, prostate cancer or erectile dysfunction.

196. Complaint Counsel failed to present any evidence regarding the number of exposures consumers had to this ad or any particular POM advertisement. (Mazis, Tr. 2752).

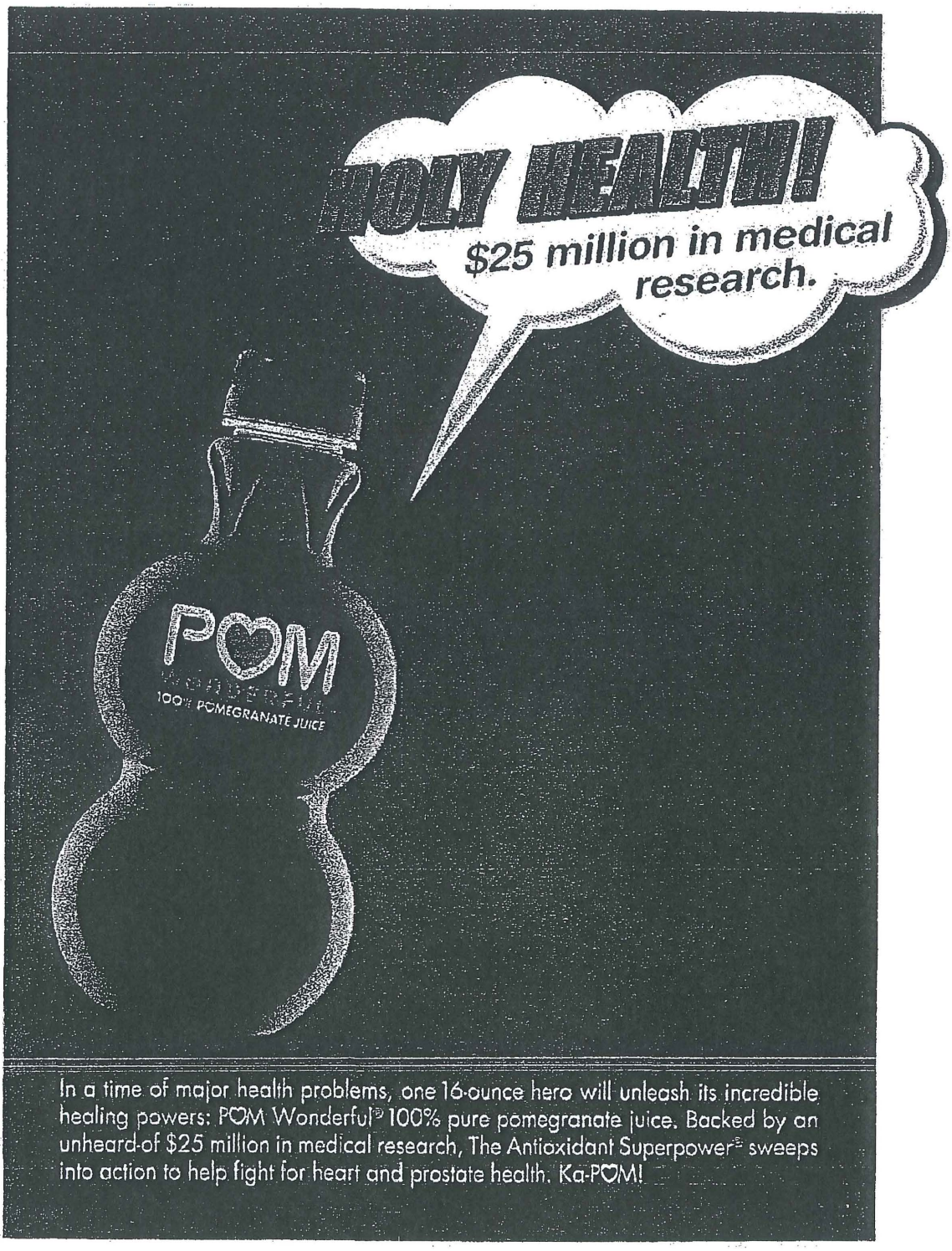

HOLY HEALTH!
$25 million in medical research.
POM
100% POMEGRANATE JUICE
In a time of major health problems, one 16-ounce hero will unleash its incredible healing powers: POM Wonderful® 100% pure pomegranate juice. Backed by an unheard-of $25 million in medical research, The Antioxidant Superpower® sweeps into action to help fight for heart and prostate health. Ka-POM!
pomwonderful.com
The Antioxidant Superpower.®

Exhibit D

HOLY HEALTH! $32 Million In Medical Research - (CX0379_0002; CX0372_0002; CX00380_0002)

197. Complaint Counsel claim that, on August 20, 2009 and September 10, 2009, POM ran an advertisement with the headline "Holy Health! $32 million in medical research" with the body copy that appears on CX0379_0002, CX0372_0002 and CX00380_0002.

198. Complaint Counsel failed to present any other definitive information regarding this ad's dissemination.

199. Complaint Counsel failed to present any evidence that Respondents would run this ad in the future, let alone whether it is probable they would do so.

200. Complaint Counsel's expert, Professor Mazis, testified that Complaint Counsel is not challenging POM's ads for POM Juice that ran after December 2008. (Mazis, Tr. 2753-54). Accordingly, based on these representations, Complaint Counsel cannot now challenge this ad.

201. Mrs. Resnick testified that she did not approve this headline for use. (L. Resnick, Tr. 120).

202. Complaint Counsel presented no evidence to contradict Mrs. Resnick's testimony that she never approved the headline of this ad for use.

203. Nowhere in this ad do Respondents expressly (*i.e.*, unequivocally and directly) state that (a) POM Juice "prevents," "treats," or "reduces the risk" of prostate cancer; or (b) POM Juice is "clinically proven" to "prevent," "treat," or "reduce the risk" of prostate cancer. (CX0379_0002; CX0372_0002; CX00380_0002.)

204. Complaint Counsel's assertion that the ad conveys the message that (a) POM Juice "prevents," "treats," or "reduces the risk" of heart disease or prostate cancer; or (b) POM Juice is "clinically proven" to "prevent," "treat," or "reduce the risk" of prostate cancer is not conspicuous, self-evident, or reasonably clear from the face of the ad. (CX0379_0002; CX0372_0002; CX00380_0002).

205. Consequently, because the above-referenced challenged implied claim may not be determined with confidence from the face of the ad, extrinsic evidence must be examined.

206. The overall net impression of this ad is not that (a) drinking eight ounces of POM Juice prevents, treats or reduces the risk of certain diseases, such as prostate cancer; or (b) drinking eight ounces of POM Juice is "clinically proven" to prevent, treat or reduce the risk of certain diseases, such as heart disease or prostate cancer. (CX0379_0002; CX0372_0002; CX00380_0002). Even the

language of the ad itself uses such qualifiers as "pilot study," "may indicate," "emerging science suggests," "may be able," "promising," and "further investigate." (CX0379_0002; CX0372_0002; CX00380_0002).

207. To the extent a "reduce the risk" claim can be implied from ad, the overall net impression is not that drinking eight ounces of POM Juice "reduces the risk" of certain diseases, such as prostate cancer, like a drug with a single target of action, but "reduces the risk," like a healthy diet of fruits and vegetables and exercise "reduces the risk" of disease. (CX0379_0002; CX0372_0002; CX00380_0002).

208. To the extent a "treat" claim can be implied from this ad (which it cannot), the overall net impression of any ad is not that POM Juice is a substitute for conventional medical treatment. (Butters, Tr. 2821-22).

209. To the extent a "proven" claim can be implied from this ad (which it cannot), the overall impression of this ad is not that POM Juice is "proven" to be 100% effective in preventing, treating or reducing the risk of prostate cancer because (1) all of the qualifying language contradicts an implied "clinically proven" interpretation, and (2) "proven" in science means the "average person in the study benefitted," not that "everyone in the study necessarily benefitted." (Heber, Tr. 2011; Butters, Tr. 2893-2894; PX0361 (Sacks, Dep. at 81)).

210. Professor Butters concluded that POM's ads in general depend on parody, exaggeration and humor to bring their message to the potential consumer; including the following messages: 1) POM is the best pomegranate that anyone can buy; 2) POM Juice is healthy; 3) POM Juice is tasty; 4) POM Juice is arguably the best source of antioxidants of any of the comparable beverages available; 5) medical research has suggested that antioxidants combat free radicals, which are unhealthy, and may contribute to diseases of the heart, arteries, and prostate, as well as erectile dysfunction; and 6) POM also offers concentrated forms of pomegranate extract for those who wish to ingest antioxidants in even more concentrated form than pomegranate juice itself. (PX0158-0033).

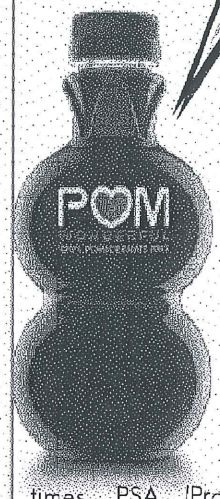
211. Complaint Counsel presented no extrinsic evidence or expert opinion on this ad's meaning, consumer perceptions of this ad, or consumer interpretations regarding this ad. (PX0357 (Stewart, Dep. at 49, 52)).

212. Complaint Counsel failed to present any evidence that the claims in this ad reasonably convey that the Challenged Products are "clinically proven" to prevent, treat or reduce the risk of heart disease, prostate cancer or erectile dysfunction.

213. Complaint Counsel failed to present any evidence regarding the number of exposures consumers had to this ad or any particular POM advertisement. (Mazis, Tr. 2752).

POM WONDERFUL

HOLY HEALTH!
$32 million in medical research.



A recently published pilot study* involving POM Wonderful 100% Pomegranate Juice followed 46 men previously treated for prostate cancer either with surgery or radiation.

After drinking eight ounces of POM Wonderful 100% Pomegranate Juice daily for at least two years, these men experienced significantly slower average PSA doubling times. PSA (Prostate-Specific Antigen) is a biomarker that indicates the presence of prostate cancer. PSA doubling time is a measure of how long it takes for PSA levels to double. A longer doubling time may indicate slower progression of the disease.

At the beginning of the study, PSA levels doubled on average every 15 months. By the end of the study, doubling time had slowed to 54 months – nearly a four-fold improvement. *"This is a big increase. I was surprised when I saw such an improvement in PSA numbers," said Dr. Allan Pantuck, lead author of the UCLA Study.*

One important note: All of the patients drank the same POM Wonderful 100% Pomegranate Juice which is available in your supermarket produce section.

Prostate cancer is the most commonly diagnosed cancer in men in the United States. After lung cancer, it's the second leading cause of cancer death in men. However, emerging science suggests that diet and lifestyle may be able to significantly improve prostate health.

The Research Continues Results from this study were so promising that many of the original patients continued to drink pomegranate juice daily, and their PSA doubling times remained suppressed. Three more clinical studies are now underway to further investigate the effects of POM on prostate health.

Learn why POM Wonderful is the only pomegranate juice you can trust. *(See inside back cover of this wrap.)*

pomwonderful.com

POM WONDERFUL

* Pantuck et al., Phase II study of pomegranate juice for men with rising prostate specific antigen following surgery or radiation for prostate cancer, *Clinical Cancer Research* (2006)
Visit pomwonderful.com/health/research to review this and other published studies.

PJ2005_TimeWrapOct09_F2.indd 2 8/20/09 3:47:27 PM

JOB NO.: PJ2005	TRIM: 7.875"x10.5"	COLOR: 4/C PROCESS	DATE IN: 7-22-09
PROJECT: TimeWrap Oct09	LIVE: 7.125" x 9.75"	LIVE, TRIM, BLEED (DO NOT PRINT)	DATE OUT: 8-20-09
SCALE: 1 : 1	BLEED: 8.375" x 11"	PRINTOUT SIZE: 100%	PROOF ROUND: F2

POM WONDERFUL

NOW WE'RE TALKING!
$32 million in medical research.

A recently published pilot study* involving POM Wonderful 100% Pomegranate Juice followed 46 men previously treated for prostate cancer either with surgery or radiation.

After drinking eight ounces of POM Wonderful 100% Pomegranate Juice daily for at least two years, these men experienced significantly slower average PSA doubling times. PSA (Prostate-Specific Antigen) is a biomarker that indicates the presence of prostate cancer. PSA doubling time is a measure of how long it takes for PSA levels to double. A longer doubling time may indicate slower progression of the disease.

At the beginning of the study, PSA levels doubled on average every 15 months. By the end of the study, doubling time had slowed to 54 months – nearly a four-fold improvement. *"This is a big increase. I was surprised when I saw such an improvement in PSA numbers," said Dr. Allan Pantuck, lead author of the UCLA Study.*

One important note: All of the patients drank the same POM Wonderful 100% Pomegranate Juice which is available in your supermarket produce section.

Prostate cancer is the most commonly diagnosed cancer in men in the United States. After lung cancer, it's the second leading cause of cancer death in men. However, emerging science suggests that diet and lifestyle may be able to significantly improve prostate health.

The Research Continues Results from this study were so promising that many of the original patients continued to drink pomegranate juice daily, and their PSA doubling times remained suppressed. Three more clinical studies are now underway to further investigate the effects of POM on prostate health.

Learn why POM Wonderful is the only pomegranate juice you can trust. *(See inside back cover of this wrap.)*

pomwonderful.com

POM WONDERFUL

* Pantuck et al., "Pomegranate juice delays PSA doubling time in humans," *Clinical Cancer Research* (2006)
Visit pomwonderful.com/health/research to review this and other published studies.

PJ2007 TimeWrap0909 F.indd 2 9/10/09 2:20:45 PM

JOB NO.: PJ2007	TRIM: 7.875" x 10.5"	COLOR: 4/C PROS	DATE IN: 9-02-09	CREATIVE: CJ
PROJECT: Time Magazine Wrap - Dec 09	LIVE: 7.125" x 9.75"	LIVE, TRIM, BLEED (DO NOT PRINT)	CLIENT SIGN OFF: 00-00-00	PRODUCTION: MS
SCALE: 1 : 1	BLEED: 8.375" x 11.0"	PRINTOUT SIZE: 100%	RELEASE DATE: 9-10-09	PROOF: F

•PLEASE MARK ALL CHANGES ON INSITE DOCUMENT •NO CHANGES ON PRINTED FLAT WILL BE MADE

POM WONDERFUL

NOW WE KNOW!

$32 million in medical research.

A recently published pilot study* involving POM Wonderful 100% Pomegranate Juice followed 46 men previously treated for prostate cancer either with surgery or radiation.

After drinking eight ounces of POM Wonderful 100% Pomegranate Juice daily for at least two years, these men experienced significantly slower average PSA doubling times. PSA (Prostate-Specific Antigen) is a biomarker that indicates the presence of prostate cancer. PSA doubling time is a measure of how long it takes for PSA levels to double. A longer doubling time may indicate slower progression of the disease.

At the beginning of the study, PSA levels doubled on average every 15 months. By the end of the study, doubling time had slowed to 54 months – nearly a four-fold improvement. *"This is a big increase. I was surprised when I saw such an improvement in PSA numbers," said Dr. Allan Pantuck, lead author of the UCLA Study.*

One important note: All of the patients drank the same POM Wonderful 100% Pomegranate Juice which is available in your supermarket produce section.

Prostate cancer is the most commonly diagnosed cancer in men in the United States. After lung cancer, it's the second leading cause of cancer death in men. However, emerging science suggests that diet and lifestyle may be able to significantly improve prostate health.

The Research Continues Results from this study were so promising that many of the original patients continued to drink pomegranate juice daily, and their PSA doubling times remained suppressed. Three more clinical studies are now underway to further investigate the effects of POM on prostate health.

Learn why POM Wonderful is the only pomegranate juice you can trust. *(See inside back cover of this wrap.)*

pomwonderful.com

POM WONDERFUL

* Pantuck et al., Phase II study of pomegranate juice for men with rising prostate specific antigen following surgery or radiation for prostate cancer, Clinical Cancer Research (2006)
Visit pomwonderful.com/health/research to review this and other published studies.

PJ2009 TimeWrstNOV09_F2.indd 2 9/10/09 10:51:55 AM

JOB NO.: PJ2006	TRIM: 7.875" x 10.5"	COLOR: 4/C PROS	DATE IN: 9-01-09	CREATIVE: CJ
PROJECT: Time Magazine Wrap - Nov 09	LIVE: 7.125" x 9.75"	LIVE, TRIM, BLEED (DO NOT PRINT)	CLIENT SIGN OFF: 00-00-00	PRODUCTION: MS
SCALE: 1 : 1	BLEED: 8.375" x 11.0"	PRINTOUT SIZE: 100%	RELEASE DATE: 9-10-09	PROOF: F2

•PLEASE MARK ALL CHANGES ON INSITE DOCUMENT •NO CHANGES ON PRINTED FLAT WILL BE MADE

I'm off to save PROSTATES! - (CX0274_0001; CX1426_0029, Exh. C)

214. Complaint Counsel claim that, on February 1, 2009, POM ran an advertisement with the headline "I'm off to save PROSTATES!" with this body copy:

> Man by man, gland by gland, The Antioxidant Superpower® is 100% committed to defending healthy prostates. Powered by pure pomegranate juice…backed by $25 million in vigilant medical research*…there's no telling just how far it will go to improve prostate health in the future
>
> *Prostate study details at http://www.pomwonderful.com/health_benefits.html

(CX0274_0001; CX1426_0029, Exh. C).

215. Complaint Counsel failed to present any other definitive information regarding this ad's dissemination.

216. Complaint Counsel failed to present any evidence that Respondents would run this ad in the future, let alone whether it is probable they would do so.

217. Mrs. Resnick testified that she does not recall this advertisement, is not familiar with it, and does not know when it ran. (L. Resnick, Tr. 243-44).

218. Mrs. Resnick testified that she does not know if the advertisement actually ran. (CX1359 (L. Resnick, Dep. at 125)).

219. Complaint Counsel's expert, Professor Mazis, testified that Complaint Counsel is not challenging POM's ads for POM Juice that ran after December 2008. (Mazis, Tr. 2753-54). Accordingly, based on these representations, Complaint Counsel cannot now challenge this ad.

220. Complaint Counsel's assertion that the ad conveys the message that (a) POM Juice "prevents," "treats," or "reduces the risk" of heart disease or prostate cancer; or (b) POM Juice is "clinically proven" to "prevent," "treat," or "reduce the risk" of prostate cancer is not conspicuous, self-evident, or reasonably clear from the face of the ad. (CX0274_0001; CX1426_0029, Exh. C).

221. Consequently, because the above-referenced challenged implied claim may not be determined with confidence from the face of the ad, extrinsic evidence must be examined.

222. The overall net impression of this ad is not that (a) drinking eight ounces of POM Juice prevents, treats or reduces the risk of certain diseases, such as prostate

cancer; or (b) drinking eight ounces of POM Juice is "clinically proven" to prevent, treat or reduce the risk of certain diseases, such as prostate cancer. (CX0274_0001; CX1426_0029, Exh. C). Even the language of the ad itself uses such qualifiers as "committed to defending," and "improve." (CX0274_0001; CX1426_0029, Exh. C).

223. To the extent a "reduce the risk" claim can be implied from ad, the overall net impression is not that drinking eight ounces of POM Juice "reduces the risk" of certain diseases, such as prostate cancer, like a drug with a single target of action, but "reduces the risk," like a healthy diet of fruits and vegetables and exercise "reduces the risk" of disease. (CX0274_0001; CX1426_0029, Exh. C).

224. To the extent a "treat" claim can be implied from this ad (which it cannot), the overall net impression of any ad is not that POM Juice is a substitute for conventional medical treatment. (Butters, Tr. 2821-22).

225. To the extent a "proven" claim can be implied from this ad (which it cannot), the overall impression of this ad is not that POM Juice is "proven" to be 100% effective in preventing, treating or reducing the risk of prostate cancer because (1) all of the qualifying language contradicts an implied "clinically proven" interpretation, and (2) "proven" in science means the "average person in the study benefitted," not that "everyone in the study necessarily benefitted." (Heber, Tr. 2011; Butters, Tr. 2893-2894; PX0361 (Sacks, Dep. at 81)).

226. Mrs. Resnick testified that the message that was intended by the ad was that POM Juice is good for prostates. She testified that the headline, "I'm off to save PROSTATES!" would absolutely not mean that POM Juice would prevent prostate cancer. Mrs. Resnick further testified that the copy below the image means that POM Juice is backed by research and that POM Juice improves prostate health; however, the ad does not say anything about preventing prostate cancer. Mrs. Resnick explained that the intent of the ad was not to communicate to consumers that POM would treat prostate cancer; it was meant to communicate that POM Juice is good for your prostate. (L. Resnick, Tr. 217-19).

227. Professor Butters testified that "'I'm off to save PROSTATES!" could be interpreted by outliers, unreasonable viewers of the ad, to mean I'm going to somehow protect them or rescue them from disease but that he believes that such an interpretation is unlikely. (Butters, Tr. 2895-01).

228. Professor Butters also testified that he concluded in his report that the use of the humor in this ad indicates to the reader that this is not serious medical advice; that this is a general suggestion that POM Juice is healthy, looking at the context of the entire ad. (Butters, Tr. 2905-06).

229. Further, Professor Butters testified that the personification in the ad is the literal personification of the pomegranate bottle, which is being compared "frivolously and extravagantly" to a superhero, which in itself is a work of fiction and that "the extraordinary powers" of POM Wonderful has to do with the high level of antioxidants. The copy in the ad "there's just no telling how far it will go to improve prostate health in the future," is a strong suggestion that what is going on has been undecided. Professor Butters further explained that he views the word "vigilant" as an odd word choice in the ad, because vigilant is something that refers to the superhero rather than to what you would normally say about medical research, and that keeps viewers from seeing this as any kind of a definitive medical statement. The statement does not suggest that the $25 million in vigilant medical research is anything other than what it is when you look at the web site or when you look at the footnote. (Butters, Tr. 2906-10).

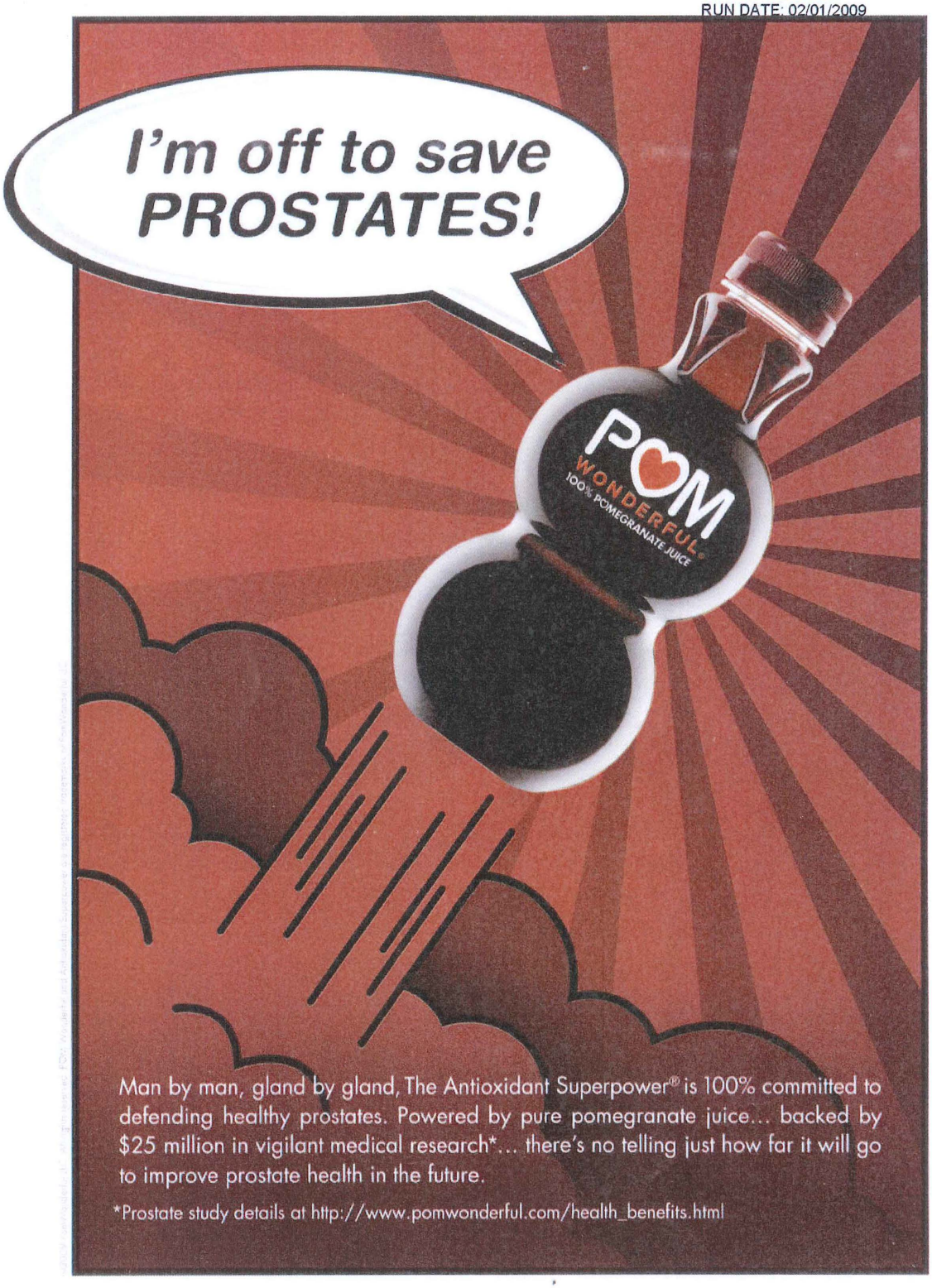
230. Professor Butters further testified that the hyperbole in the POM ads and the humor in the visual representations blocks literal interpretation of many of the headings, such as "I'm off to save prostates." These are absurd terms and will not be viewed as indicating claims. However, Professor Butters stated that the humor does not block the serious statements that are made in the text and footnotes. He testified that when you say a product is committed to defend against something, a reasonable person would not infer that they definitely succeed in eliminating that something, that disease. "Committed" is a -- is a word like "fight for," which does not necessarily guarantee the success of the outcome. (Butters, Tr. 2958-60).

231. Viewing the "I'm off to save PROSTATES!" ad as a whole, including the interaction of the words and visual imagery, the overall net impression of the ad is that it is a humorous reference to a superhero, that POM Juice is healthy and that POM Juice is good for prostate health, not that it would treat or prevent prostate cancer. ((Butters, Tr. 2905-06); (L. Resnick, Tr. 217-19)).

232. Complaint Counsel failed to present any evidence that the claims in this ad reasonably convey that the Challenged Products are "clinically proven" to prevent, treat or reduce the risk of heart disease, prostate cancer or erectile dysfunction.

233. Complaint Counsel failed to present any evidence regarding the number of exposures consumers had to this ad or any particular POM advertisement. (Mazis, Tr. 2752).

VMS ID: 090200523
RUN DATE: 02/01/2009



pomwonderful.com

The Antioxidant Superpower.®

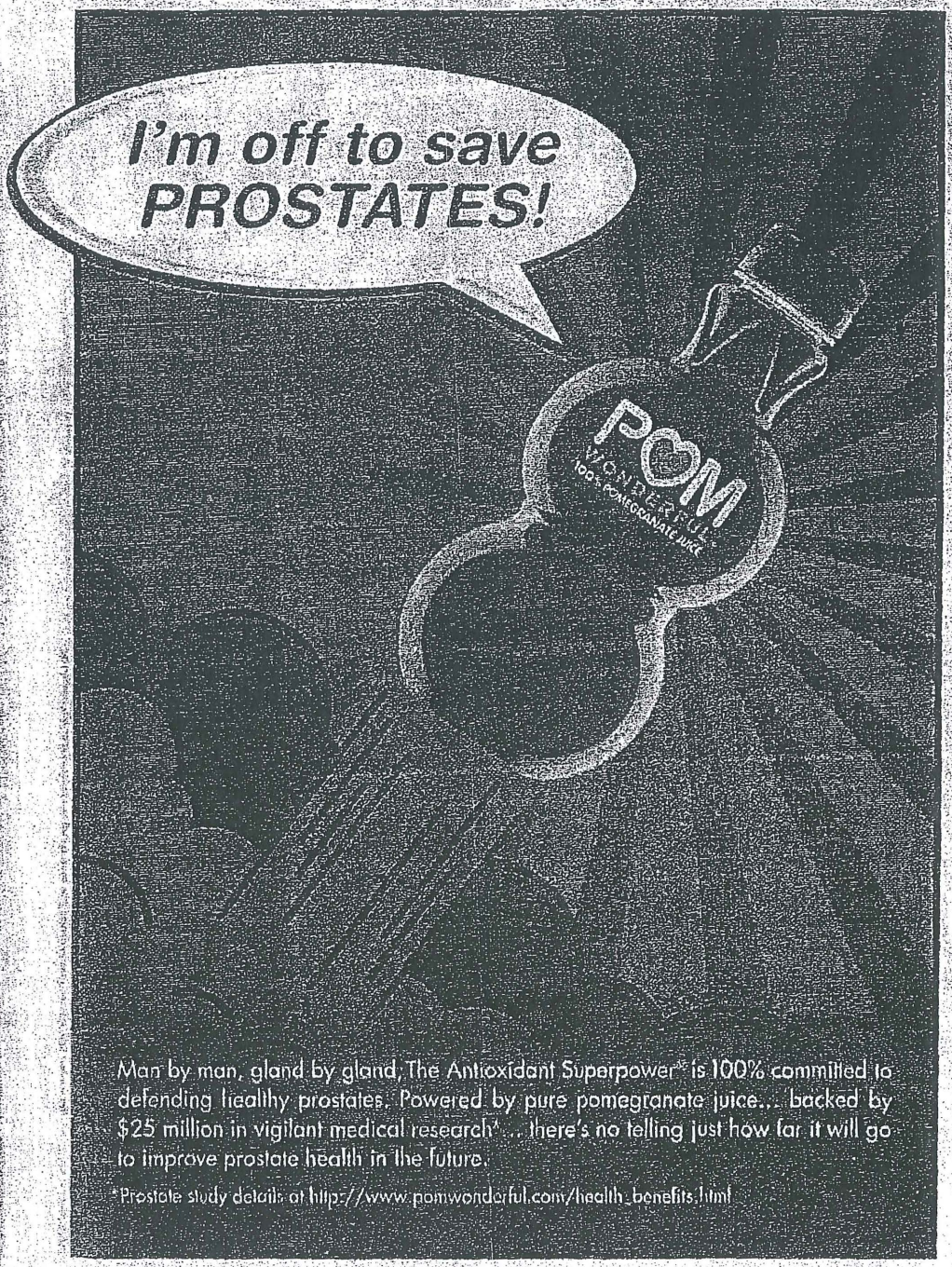

I'm off to save PROSTATES!
POM WONDERFUL
100% POMEGRANATE JUICE
Man by man, gland by gland, The Antioxidant Superpower* is 100% committed to defending healthy prostates. Powered by pure pomegranate juice... backed by $25 million in vigilant medical research*... there's no telling just how far it will go to improve prostate health in the future.
*Prostate study details at http://www.pomwonderful.com/health_benefits.html
pomwonderful.com
The Antioxidant Superpower.®

Exhibit C

I'm off to save PROSTATES! - (CX1426_0037, Exh. H)

234. Complaint Counsel claim that POM ran an advertisement with the headline "I'm off to save PROSTATES!" with this body copy:

> The Antioxidant Superpower. Learn More. (CX1426_0037, Exh. H).

235. Complaint Counsel failed to present any definitive information regarding this ad's dissemination.

236. Complaint Counsel failed to present any evidence that Respondents would run this ad in the future, let alone whether it is probable they would do so.

237. Mr. Resnick testified that this ad is another execution of the "I'm off to save prostates" theme that likely appeared on the website since it says "Learn more." Mr. Resnick testified that the statement "I'm off to save prostates" is a "tongue-in-cheek" approach to communicate that POM Juice is healthy for prostates. (CX1376 (S. Resnick, Dep. at 150-51)).

238. Complaint Counsel's assertion that the ad conveys the message that (a) POM Juice "prevents," "treats," or "reduces the risk" of prostate cancer; or (b) POM Juice is "clinically proven" to "prevent," "treat," or "reduce the risk" of prostate cancer is not conspicuous, self-evident, or reasonably clear from the face of the ad. (CX1426_0037, Exh. H).

239. Consequently, because the above-referenced challenged implied claim may not be determined with confidence from the face of the ad, extrinsic evidence must be examined.

240. The overall net impression of this ad is not that (a) drinking eight ounces of POM Juice prevents, treats or reduces the risk of certain diseases, such as prostate cancer; or (b) drinking eight ounces of POM Juice is "clinically proven" to prevent, treat or reduce the risk of certain diseases, such as prostate cancer. (CX1426_0037, Exh. H).

241. To the extent a "reduce the risk" claim can be implied from ad, the overall net impression is not that drinking eight ounces of POM Juice "reduces the risk" of certain diseases, such as prostate cancer, like a drug with a single target of action, but "reduces the risk," like a healthy diet of fruits and vegetables and exercise "reduces the risk" of disease. (CX1426_0037, Exh. H).

242. To the extent a "treat" claim can be implied from this ad (which it cannot), the overall net impression of any ad is not that POM Juice is a substitute for conventional medical treatment. (Butters, Tr. 2821-22).

243. To the extent a "proven" claim can be implied from this ad (which it cannot), the overall impression of this ad is not that POM Juice is "proven" to be 100% effective in preventing, treating or reducing the risk of prostate cancer because (1) all of the qualifying language contradicts an implied "clinically proven" interpretation, and (2) "proven" in science means the "average person in the study benefitted," not that "everyone in the study necessarily benefitted." (Heber, Tr. 2011; Butters, Tr. 2893-2894; PX0361 (Sacks, Dep. at 81)).

244. Professor Butters concluded that POM's ads in general depend on parody, exaggeration and humor to bring their message to the potential consumer; including the following messages: 1) POM is the best pomegranate that anyone can buy; 2) POM Juice is healthy; 3) POM Juice is tasty; 4) POM Juice is arguably the best source of antioxidants of any of the comparable beverages available; 5) medical research has suggested that antioxidants combat free radicals, which are unhealthy, and may contribute to diseases of the heart, arteries, and prostate, as well as erectile dysfunction; and 6) POM also offers concentrated forms of pomegranate extract for those who wish to ingest antioxidants in even more concentrated form than pomegranate juice itself. (PX0158-0033).

245. Viewing the "I'm off to save PROSTATES!" ad as a whole, including the interaction of the words and visual imagery, the overall net impression of the ad is that it is a humorous reference to a superhero, that POM Juice is healthy, that POM Juice is good for prostate health. (CX1376 (S. Resnick, Dep. at 150-51); (PX0158-0033)).

246. Complaint Counsel presented no extrinsic evidence or expert opinion on this ad's meaning, consumer perceptions of this ad, or consumer interpretations regarding this ad. (PX0357 (Stewart, Dep. at 49, 52)).

247. Complaint Counsel failed to present any evidence that the claims in this ad reasonably convey that the Challenged Products are "clinically proven" to prevent, treat or reduce the risk of heart disease, prostate cancer or erectile dysfunction.

248. Complaint Counsel failed to present any evidence regarding the number of exposures consumers had to this ad or any particular POM advertisement. (Mazis, Tr. 2752).

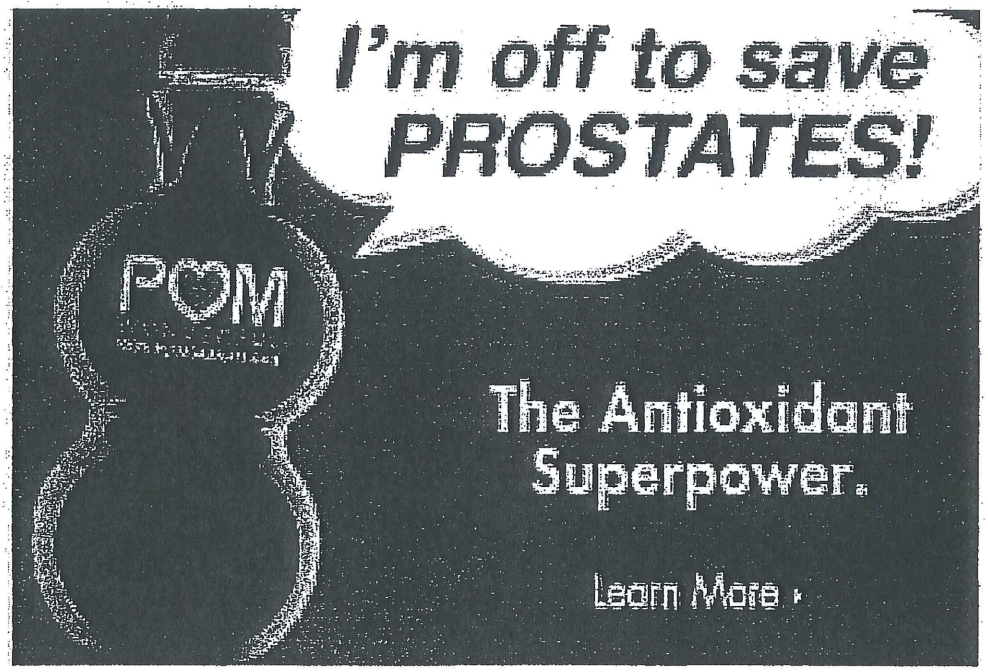

I'm off to save PROSTATES!
POM
The Antioxidant Superpower.
Learn More ›

Exhibit H

KA-POM! - (CX0379_0003; CX0372_0003; CX0380_0003)

249. Complaint Counsel claim that, on August 20, 2009 and September 10, 2009, POM ran an advertisement with the headline "KA POM!" with the body copy that appears on CX0379_0003, CX0372_0003 and CX380_0003.

250. Complaint Counsel failed to present any other definitive information regarding this ad's dissemination.

251. Complaint Counsel failed to present any evidence that Respondents would run this ad in the future, let alone whether it is probable they would do so.

252. Complaint Counsel's expert, Professor Mazis, testified that Complaint Counsel is not challenging POM's ads for POM Juice that ran after December 2008. (Mazis, Tr. 2753-54). Accordingly, based on these representations, Complaint Counsel cannot now challenge this ad.

253. Complaint Counsel's assertion that the ad conveys the message that (a) POM Juice "prevents," "treats," or "reduces the risk" of heart disease or prostate cancer; or (b) POM Juice is "clinically proven" to "prevent," "treat," or "reduce the risk" of heart disease, prostate cancer or erectile dysfunction is not conspicuous, self-evident, or reasonably clear from the face of the ad. (CX0379_0003; CX0372_0003; CX380_0003).

254. Consequently, because the above-referenced challenged implied claim may not be determined with confidence from the face of the ad, extrinsic evidence must be examined.

255. The overall net impression of this ad is not that (a) drinking eight ounces of POM Juice prevents, treats or reduces the risk of certain diseases, such as heart disease, prostate cancer or erectile dysfunction; or (b) drinking eight ounces of POM Juice is "clinically proven" to prevent, treat or reduce the risk of certain diseases, such as heart disease, prostate cancer or erectile dysfunction. (CX0379_0003; CX0372_0003; CX380_0003).

256. To the extent a "reduce the risk" claim can be implied from ad, the overall net impression is not that drinking eight ounces of POM Juice "reduces the risk" of certain diseases, such as heart disease, prostate cancer or erectile dysfunction, like a drug with a single target of action, but "reduces the risk," like a healthy diet of fruits and vegetables and exercise "reduces the risk" of disease. (CX0379_0003; CX0372_0003; CX380_0003).

257. To the extent a "treat" claim can be implied from this ad (which it cannot), the overall net impression of any ad is not that POM Juice is a substitute for conventional medical treatment. (Butters, Tr. 2821-22).

258. To the extent a "proven" claim can be implied from this ad (which it cannot), the overall impression of this ad is not that POM Juice is "proven" to be 100% effective in preventing, treating or reducing the risk of heart disease, prostate cancer or erectile dysfunction because (1) all of the qualifying language contradicts an implied "clinically proven" interpretation, and (2) "proven" in science means the "average person in the study benefitted," not that "everyone in the study necessarily benefitted." (Heber, Tr. 2011; Butters, Tr. 2893-2894; PX0361 (Sacks, Dep. at 81)).

259. Complaint Counsel presented no extrinsic evidence or expert opinion on this ad's meaning, consumer perceptions of this ad, or consumer interpretations regarding this ad. (PX0357 (Stewart, Dep. at 49, 52)).

260. Complaint Counsel failed to present any evidence that the claims in this ad reasonably convey that the Challenged Products are "clinically proven" to prevent, treat or reduce the risk of heart disease, prostate cancer or erectile dysfunction.

261. Complaint Counsel failed to present any evidence regarding the number of exposures consumers had to this ad or any particular POM advertisement. (Mazis, Tr. 2752).

POM WONDERFUL

KA-POM!

100% Authentic

POM is the only brand guaranteed to contain 100% real pomegranate juice. We wish other brands were as honest. In fact, according to recent independent tests, nine out of ten so-called "pomegranate" juices were found to have added sugar, colorants and other low-grade fruit juices.

Tree to Bottle

POM is the only brand that controls its juice from tree to bottle, batch to batch, year to year. We only grow "Wonderful" variety pomegranates, renowned for their superior antioxidants and delicious taste. And every 16oz bottle contains the juice of five whole pomegranates.

The Antioxidant Superpower®

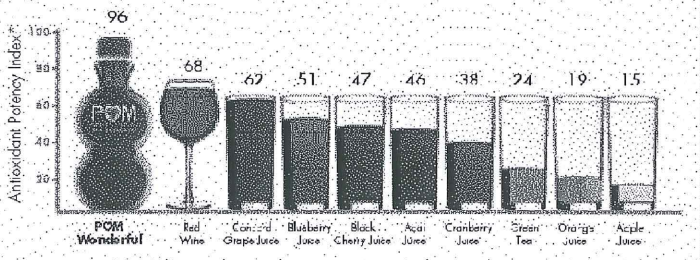
With uniquely high levels of powerful antioxidants, POM Wonderful 100% Pomegranate Juice has demonstrated superior ability to neutralize harmful free radicals and to inhibit excess inflammation.

Backed by Science

Only POM products are backed by $32 million in medical research conducted at the world's leading universities, primarily in the areas of cardiovascular, prostate and erectile function.

More Antioxidants

Sip for sip, POM Wonderful 100% Pomegranate Juice has more polyphenol antioxidants than red wine, green tea and other juices.



POM WONDERFUL® pomwonderful.com

*Index combines results from four leading antioxidant tests (ORAC, DPPH, FRAP, TEAC). N. Seeram, et al., Comparison of Antioxidant Potency of Commonly Consumed Polyphenol-Rich Beverages in the United States, Journal of Agricultural and Food Chemistry (2008). Study found at pomwonderful.com/compare.

PJ2005_TimeWrapOct09_F2.indd 3 8/20/09 3:47:28 PM

JOB NO.: PJ2005	TRIM: 7.875"x10.5"	COLOR: 4/C PROCESS	DATE IN: 7-22-09
PROJECT: TimeWrap Oct09	LIVE: 7.125" x 9.75"	LIVE, TRIM, BLEED (DO NOT PRINT)	DATE OUT: 8-20-09
SCALE: 1 : 1	BLEED: 8.375" x 11"	PRINTOUT SIZE: 100%	PROOF ROUND: F2

POM WONDERFUL

EX-POM!

100% Authentic

POM is the only brand guaranteed to contain 100% real pomegranate juice. We wish other brands were as honest. In fact, according to recent independent tests, nine out of ten so-called "pomegranate" juices were found to have added sugar, colorants and other low-grade fruit juices.

Tree to Bottle

POM is the only brand that controls its juice from tree to bottle, batch to batch, year to year. We only grow "Wonderful" variety pomegranates, renowned for their superior antioxidants and delicious taste. And every 16oz bottle contains the juice of five whole pomegranates.

The Antioxidant Superpower*

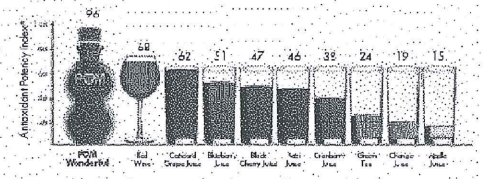
With uniquely high levels of powerful antioxidants, POM Wonderful 100% Pomegranate Juice has demonstrated superior ability to neutralize harmful free radicals and to inhibit excess inflammation.

Backed by Science

Only POM products are backed by $32 million in medical research conducted at the world's leading universities, primarily in the areas of cardiovascular, prostate and erectile function.

More Antioxidants

Sip for sip, POM Wonderful 100% Pomegranate Juice has more polyphenol antioxidants than red wine, green tea and other juices.



POM WONDERFUL pomwonderful.com

*Index combines results from four leading antioxidant tests (ORAC, DPPH, FRAP, TEAC). N. Seeram, et al., Comparison of Antioxidant Potency of Commonly Consumed Polyphenol-Rich Beverages in the United States, Journal of Agricultural and Food Chemistry (2008). Study funded at pomwonderful.com/research

PJ2007 TimeWrapDec09_F.indd 3 2/10/09 2:20:10 PM

JOB NO.: PJ2007	TRIM: 7.875" x 10.5"	COLOR: 4/C PROS	DATE IN: 9-02-09	CREATIVE: CJ
PROJECT: Time Magazine Wrap - Dec 09	LIVE: 7.125" x 9.75"	LIVE, TRIM, BLEED (DO NOT PRINT)	CLIENT SIGN OFF: 00-00-00	PRODUCTION: MS
SCALE: 1 : 1	BLEED: 8.375" x 11.0"	PRINTOUT SIZE: 100%	RELEASE DATE: 9-10-09	PROOF: F

*PLEASE MARK ALL CHANGES ON INSITE DOCUMENT *NO CHANGES ON PRINTED FLAT WILL BE MADE

POM WONDERFUL

EX-POM!

100% Authentic

POM is the only brand guaranteed to contain 100% real pomegranate juice. We wish other brands were as honest. In fact, according to recent independent tests, nine out of ten so-called "pomegranate" juices were found to have added sugar, colorants and other low-grade fruit juices.

Tree to Bottle

POM is the only brand that controls its juice from tree to bottle, batch to batch, year to year. We only grow "Wonderful" variety pomegranates, renowned for their superior antioxidants and delicious taste. And every 16oz bottle contains the juice of five whole pomegranates.

The Antioxidant Superpower*

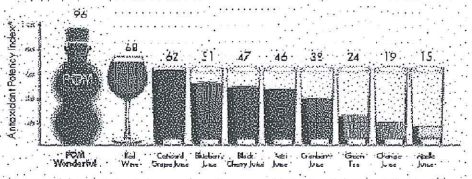
With uniquely high levels of powerful antioxidants, POM Wonderful 100% Pomegranate Juice has demonstrated superior ability to neutralize harmful free radicals and to inhibit excess inflammation.

Backed by Science

Only POM products are backed by $32 million in medical research conducted at the world's leading universities, primarily in the areas of cardiovascular, prostate and erectile function.

More Antioxidants

Sip for sip, POM Wonderful 100% Pomegranate Juice has more polyphenol antioxidants than red wine, green tea and other juices.



POM WONDERFUL pomwonderful.com

*Index combines results from four leading antioxidant tests (ORAC, DPPH, FRAP, TEAC). N. Seeram, et al., Comparison of Antioxidant Potency of Commonly Consumed Polyphenol-Rich Beverages in the United States, Journal of Agricultural and Food Chemistry (2008). Study found at pomwonderful.com/compare

PJ2006 TimeWrapNOV09_F2.indd 3 9/10/09 10:51:55 AM

JOB NO.: PJ2006	TRIM: 7.875" x 10.5"	COLOR: 4/C PROS	DATE IN: 9-01-09	CREATIVE: CJ
PROJECT: Time Magazine Wrap - Nov 09	LIVE: 7.125" x 9.75"	LIVE, TRIM, BLEED (DO NOT PRINT)	CLIENT SIGN OFF: 00-00-00	PRODUCTION: MS
SCALE: 1 : 1	BLEED: 8.375" x 11.0"	PRINTOUT SIZE: 100%	RELEASE DATE: 9-10-09	PROOF: F2

*PLEASE MARK ALL CHANGES ON INSITE DOCUMENT *NO CHANGES ON PRINTED FLAT WILL BE MADE

Life Support - (CX0033)

262. Complaint Counsel claim that, on December 30, 2004, POM ran an advertisement with the headline "Life Support" with this body copy:

> POM Wonderful Pomegranate Juice fills your body with what it needs. On top of being refreshing and delicious, this amazing juice has more naturally occurring antioxidants than any other drink. These antioxidants fight hard against free radicals that can cause heart disease, premature aging, Alzheimer's, even cancer. Just drink eight ounces a day and you'll be on life support – in a good way. (CX0033_0001).

263. Complaint Counsel failed to present any other definitive information regarding this ad's dissemination.

264. Complaint Counsel failed to present any evidence that Respondents would run this ad in the future, let alone whether it is probable they would do so.

265. This ad cannot provide a basis for injunctive relief because (a) it ran seven years ago; and (b) no evidence exists to show that Respondents are likely to run this ad in the future.

266. Complaint Counsel's assertion that the ad conveys the message that (a) POM Juice "prevents," "treats," or "reduces the risk" of heart disease or prostate cancer; or (b) POM Juice is "clinically proven" to "prevent," "treat," or "reduce the risk" of heart disease or prostate cancer is not conspicuous, self-evident, or reasonably clear from the face of the ad. (CX0033_0001).

267. Consequently, because the above-referenced challenged implied claim may not be determined with confidence from the face of the ad, extrinsic evidence must be examined.

268. The overall net impression of this ad is not that (a) drinking eight ounces of POM Juice prevents, treats or reduces the risk of certain diseases, such as heart disease or prostate cancer; or (b) drinking eight ounces of POM Juice is "clinically proven" to prevent, treat or reduce the risk of certain diseases, such as heart disease or prostate cancer. (CX0033_0001). Even the language of the ad itself uses such qualifiers as "can cause" and "fight." (CX0033_0001).

269. To the extent a "reduce the risk" claim can be implied from ad, the overall net impression is not that drinking eight ounces of POM Juice "reduces the risk" of certain diseases, such as heart disease or prostate cancer, like a drug with a single

target of action, but "reduces the risk," like a healthy diet of fruits and vegetables and exercise "reduces the risk" of disease. (CX0033_0001).

270. To the extent a "treat" claim can be implied from this ad (which it cannot), the overall net impression of any ad is not that POM Juice is a substitute for conventional medical treatment. (Butters, Tr. 2821-22).

271. To the extent a "proven" claim can be implied from this ad (which it cannot), the overall impression of this ad is not that POM Juice is "proven" to be 100% effective in preventing, treating or reducing the risk of heart disease or prostate cancer because (1) all of the qualifying language contradicts an implied "clinically proven" interpretation, and (2) "proven" in science means the "average person in the study benefitted," not that "everyone in the study necessarily benefitted." (Heber, Tr. 2011; Butters, Tr. 2893-2894; PX0361 (Sacks, Dep. at 81)).

272. Mr. Tupper testified that the meaning of this "Life Support" ad is that POM Juice is an incredibly healthful product that helps support a healthy life driven by the antioxidant content of the juice. (CX1364 (Tupper, Dep. at 281)).

273. Professor Butters concluded that POM's ads in general depend on parody, exaggeration and humor to bring their message to the potential consumer; including the following messages: 1) POM is the best pomegranate that anyone can buy; 2) POM Juice is healthy; 3) POM Juice is tasty; 4) POM Juice is arguably the best source of antioxidants of any of the comparable beverages available; 5) medical research has suggested that antioxidants combat free radicals, which are unhealthy, and may contribute to diseases of the heart, arteries, and prostate, as well as erectile dysfunction; and 6) POM also offers concentrated forms of pomegranate extract for those who wish to ingest antioxidants in even more concentrated form than pomegranate juice itself. (PX0158-0033).

274. Viewing the "Life Support" ad a whole, including the interaction of the words and visual imagery, the overall net impression of this ad is that POM Juice is a healthy product. (CX1364 (Tupper, Dep. at 281)).

275. Complaint Counsel presented no extrinsic evidence or expert opinion on this ad's meaning, consumer perceptions of this ad, or consumer interpretations regarding this ad. (PX0357 (Stewart, Dep. at 49, 52)).

276. Complaint Counsel failed to present any evidence that the claims in this ad reasonably convey that the Challenged Products are "clinically proven" to prevent, treat or reduce the risk of heart disease, prostate cancer or erectile dysfunction.

277. Complaint Counsel failed to present any evidence regarding the number of exposures consumers had to this ad or any particular POM advertisement. (Mazis, Tr. 2752).

POM Wonderful Pomegranate Juice fills your body with what it needs. On top of being refreshing and delicious, this amazing juice has more naturally occurring antioxidants than any other drink. These antioxidants fight hard against free radicals that can cause heart disease, premature aging, Alzheimer's, even cancer. Just drink eight ounces a day and you'll be on life support—in a good way.

POM Wonderful Pomegranate Juice. The Antioxidant Superpower.™

POM WONDERFUL®

pomwonderful.com

Live Long Enough To Watch Your 401(k) Recover - (CX0280)

278. Complaint Counsel, claim that, on March 12, 2009, POM ran an advertisement with the headline "Live Long Enough To Watch Your 401(k) Recover" with the body copy that appears on CX0280_0001.

279. Complaint Counsel failed to present any other definitive information regarding this ad's dissemination.

280. Complaint Counsel failed to present any evidence that Respondents would run this ad in the future, let alone whether it is probable they would do so.

281. Complaint Counsel's expert, Professor Mazis, testified that Complaint Counsel is not challenging POM's ads for POM Juice that ran after December 2008. (Mazis, Tr. 2753-54). Accordingly, based on these representations, Complaint Counsel cannot now challenge this ad.

282. Nowhere in this ad do Respondents expressly (*i.e.*, unequivocally and directly) state that (a) taking one POMx Pill per day "prevents," "treats," or "reduces the risk" of heart disease or prostate cancer; or (b) taking one POMx Pill per day is "clinically proven" to "prevent," "treat," or "reduce the risk" of heart disease or prostate cancer. (CX0280_0001).

283. Complaint Counsel's assertion that the ad conveys the message that (a) taking one POMx Pill per day "prevents," "treats," or "reduces the risk" of heart disease or prostate cancer; or (b) taking one POMx Pill per day is "clinically proven" to "prevent," "treat," or "reduce the risk" of heart disease or prostate cancer is not conspicuous, self-evident, or reasonably clear from the face of the ad. (CX0280_0001).

284. Consequently, because the above-referenced challenged implied claim may not be determined with confidence from the face of the ad, extrinsic evidence must be examined.

285. The overall net impression of this ad is not that not that taking one POMx Pill per day prevents, treats or reduces the risk of certain diseases, such as heart disease or prostate cancer; or (b) taking one POMx Pill per day is "clinically proven" to prevent, treat or reduce the risk of certain diseases, such as heart disease or prostate cancer. (CX0280_0001). Even the language of the ad itself uses such qualifiers as "initial UCLA MEDICAL STUDY," "hopeful results," "fight," "preliminary studies," and "promising results." (CX0280_0001).

286. To the extent a "reduce the risk" claim can be implied from this ad, the overall net impression is not that taking one POMx Pill per day "reduces the risk" of certain

diseases, such as heart disease or prostate cancer, like a drug with a single target of action, but "reduces the risk," like a healthy diet of fruits and vegetables and exercise "reduces the risk" of disease. (CX0280_0001).

287. To the extent a "treat" claim can be implied from this ad (which it cannot), the overall net impression of any ad is not that POMx Pills are a substitute for conventional medical treatment. (Butters, Tr. 2821-22).

288. To the extent a "proven" claim can be implied from this ad (which it cannot), the overall impression of this ad is not that POMx Pills are "proven" to be 100% effective in preventing, treating or reducing the risk of heart disease or prostate cancer because (1) all of the qualifying language contradicts an implied "clinically proven" interpretation, and (2) "proven" in science means the "average person in the study benefitted," not that "everyone in the study necessarily benefitted." (Heber, Tr. 2011; Butters, Tr. 2893-2894; PX0361 (Sacks, Dep. at 81)).

289. Professor Butters testified that this headline of this ad is not irreverent but "kind of joking" and "gallows humor"; the ad is a "joking reference to a very serious issue." (PX0350 (Butters, Dep. at 141)).

290. Professor Butters concluded that POM's ads in general depend on parody, exaggeration and humor to bring their message to the potential consumer; including the following messages: 1) POM is the best pomegranate that anyone can buy; 2) POM Juice is healthy; 3) POM Juice is tasty; 4) POM Juice is arguably the best source of antioxidants of any of the comparable beverages available; 5) medical research has suggested that antioxidants combat free radicals, which are unhealthy, and may contribute to diseases of the heart, arteries, and prostate, as well as erectile dysfunction; and 6) POM also offers concentrated forms of pomegranate extract for those who wish to ingest antioxidants in even more concentrated form than pomegranate juice itself. (PX0158-0033).

291. Viewing the "Live Long Enough To Watch Your 401(k) Recover" ad as a whole, including the interaction of the words and visual imagery, the overall net impression of the ad is that it is a humorous ad and that POM Juice is healthy. (PX0350 (Butters, Dep. at 141); (PX0158-0033)).

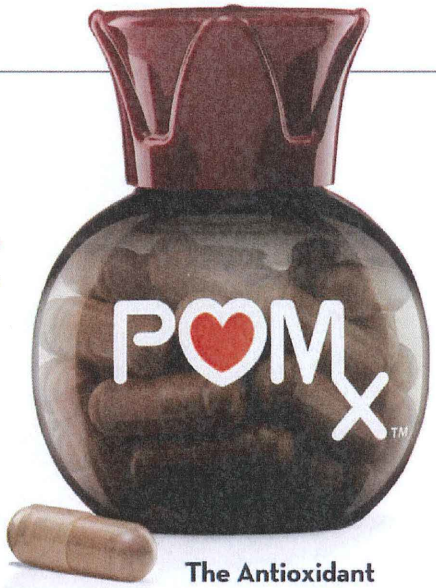
292. Complaint Counsel presented no extrinsic evidence or expert opinion on this ad's meaning, consumer perceptions of this ad, or consumer interpretations regarding this ad. (PX0357 (Stewart, Dep. at 49, 52)).

293. Complaint Counsel failed to present any evidence that the claims in this ad reasonably convey that the Challenged Products are "clinically proven" to prevent, treat or reduce the risk of heart disease, prostate cancer or erectile dysfunction.

294. Complaint Counsel failed to present any evidence regarding the number of exposures consumers had to this ad or any particular POM advertisement. (Mazis, Tr. 2752).

VMS ID: 090312940
RUN DATE: 03/12/2009

LIVE LONG ENOUGH TO WATCH YOUR 401(K) RECOVER.



The Antioxidant Superpill.™

Antioxidants are a necessity. Not a luxury.

Emerging science suggests that antioxidants are critically important to maintaining good health because they protect you from free radicals, which can damage your body. Taking one POMx pill a day will help protect you from free radicals and keep you at your healthy best. Even when you're going through the worst.

Recession-proof your health with POMx.

POMx – an ultra-potent antioxidant extract made from the same pomegranates as POM Wonderful® 100% Pomegranate Juice – is the most potent natural antioxidant supplement available. Each 1000mg POMx pill has the antioxidant power of a full glass of POM Wonderful 100% Pomegranate Juice.

The antioxidant power of our 8oz juice.

$25 million in medical research. A sound investment.

POMx is made from the only pomegranates backed by $25 million in medical research at the world's leading universities.

Not only has this research documented the unique and superior antioxidant power of pomegranates, it has revealed promising results for prostate and cardiovascular health.

Hope for the future. Yours.

Our POMx pills are made from the same pomegranates we use to make our POM Wonderful 100% Pomegranate Juice, on which each of the following medical studies was conducted.

An initial UCLA study on our juice found hopeful results for prostate health, reporting "statistically significant prolongation of PSA doubling times," according to Dr. Allen J. Pantuck in *Clinical Cancer Research*, '06.[1,2,3]

Two additional preliminary studies on our juice showed promising results for heart health. "Stress-induced ischemia (restricted blood flow to the heart) decreased in the pomegranate group," Dr. Dean Ornish reported in the *American Journal of Cardiology*, '05.[1,2,4]

"Pomegranate juice consumption resulted in significant reduction in IMT[5] (thickness of arterial plaque) by up to 30% after one year," said Dr. Michael Aviram in *Clinical Nutrition*, '04.[1,2,5,6]

Try POMx Monthly FREE for ONE MONTH.
We'll even pay for the shipping.*

Order Now: 888-766-7455 or pompills.com/n3
Use discount code: N330

*SIGN UP FOR POMx MONTHLY, AND WE'LL SEND YOUR FIRST BOTTLE FREE. AFTER THAT, YOU'LL CONTINUE TO RECEIVE MONTHLY SHIPMENTS FOR $29.95 WITH COMPLIMENTARY SHIPPING. Offer expires 5/30/09 and applies only to the purchase price for the first bottle of POMx Monthly. Following months will be $29.95 per bottle. One discount per customer. Cannot be combined with other offers. No substitutions, transfer rights or cash equivalents. We reserve the right to discontinue this promotion, change product price or shipping charge at any time. Valid only at pompills.com or 1-888-766-7455. Not valid on POMx Trial or other POM products.

POM WONDERFUL®

[1]pompills.com/research [2]These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure or prevent any disease. [3]45 men with rising PSA after surgery or radiotherapy drank 8oz 100% pomegranate juice daily for two years. [4]45 patients with coronary heart disease and myocardial ischemia drank 8oz 100% pomegranate juice daily for three months. [5]Study measured intima-media thickness (IMT). [6]19 patients aged 65-75 years with severe atherosclerosis drank 8oz 100% pomegranate juice daily for one year.

Lucky I have super HEALTH POWERS! - (CX0379_0001; CX0372_0001; CX0380_0001; CX0380_0005; CX0380_0007)

295. Complaint Counsel claim that, on August 20, 2009 and September 10, 2009 POM ran an advertisement with the headline "Lucky I have super HEALTH POWERS!" (CX0379_0001; CX0372_0001; CX0380_0001; CX0380_0005; CX0380_0007).

296. Complaint Counsel failed to present any other definitive information regarding this ad's dissemination.

297. Complaint Counsel failed to present any evidence that Respondents would run this ad in the future, let alone whether it is probable they would do so.

298. Complaint Counsel's expert, Professor Mazis, testified that Complaint Counsel is not challenging POM's ads for POM Juice that ran after December 2008. (Mazis, Tr. 2753-54). Accordingly, based on these representations, Complaint Counsel cannot now challenge this ad.

299. Mrs. Resnick testified that she did not approve this headline for use. (L. Resnick, Tr. 117).

300. Complaint Counsel presented no evidence to contradict Mrs. Resnick's testimony that she never approved the headline of this ad for use.

301. Nowhere in this ad do Respondents expressly (*i.e.*, unequivocally and directly) state that (a) POM Juice "prevents," "treats," or "reduces the risk" of certain diseases; or (b) POM Juice is "clinically proven" to "prevent," "treat," or "reduce the risk" of certain diseases. (CX0379_0001; CX0372_0001; CX0380_0001; CX0380_0005; CX0380_0007).

302. Complaint Counsel's assertion that the ad conveys the message that (a) POM Juice "prevents," "treats," or "reduces the risk" of certain diseases; or (b) POM Juice is "clinically proven" to "prevent," "treat," or "reduce the risk" of certain diseases is not conspicuous, self-evident, or reasonably clear from the face of the ad. (CX0379_0001; CX0372_0001; CX0380_0001; CX0380_0005; CX0380_0007).

303. Consequently, because the above-referenced challenged implied claim may not be determined with confidence from the face of the ad, extrinsic evidence must be examined.

304. The overall net impression of this ad is not that (a) drinking eight ounces of POM Juice prevents, treats or reduces the risk of certain diseases, such as heart disease or prostate cancer; or (b) drinking eight ounces of POM Juice is "clinically proven" to prevent, treat or reduce the risk of certain diseases, such as heart

disease or prostate cancer. (CX0379_0001; CX0372_0001; CX0380_0001 CX0380_0005; CX0380_0007).

305. To the extent a "reduce the risk" claim can be implied from ad, the overall net impression is not that drinking eight ounces of POM Juice "reduces the risk" of certain diseases, such as heart disease or prostate cancer, like a drug with a single target of action, but "reduces the risk," like a healthy diet of fruits and vegetables and exercise "reduces the risk" of disease. (CX0379_0001; CX0372_0001; CX0380_0001 CX0380_0005; CX0380_0007).

306. To the extent a "treat" claim can be implied from this ad (which it cannot), the overall net impression of any ad is not that POM Juice is a substitute for conventional medical treatment. (Butters, Tr. 2821-22).

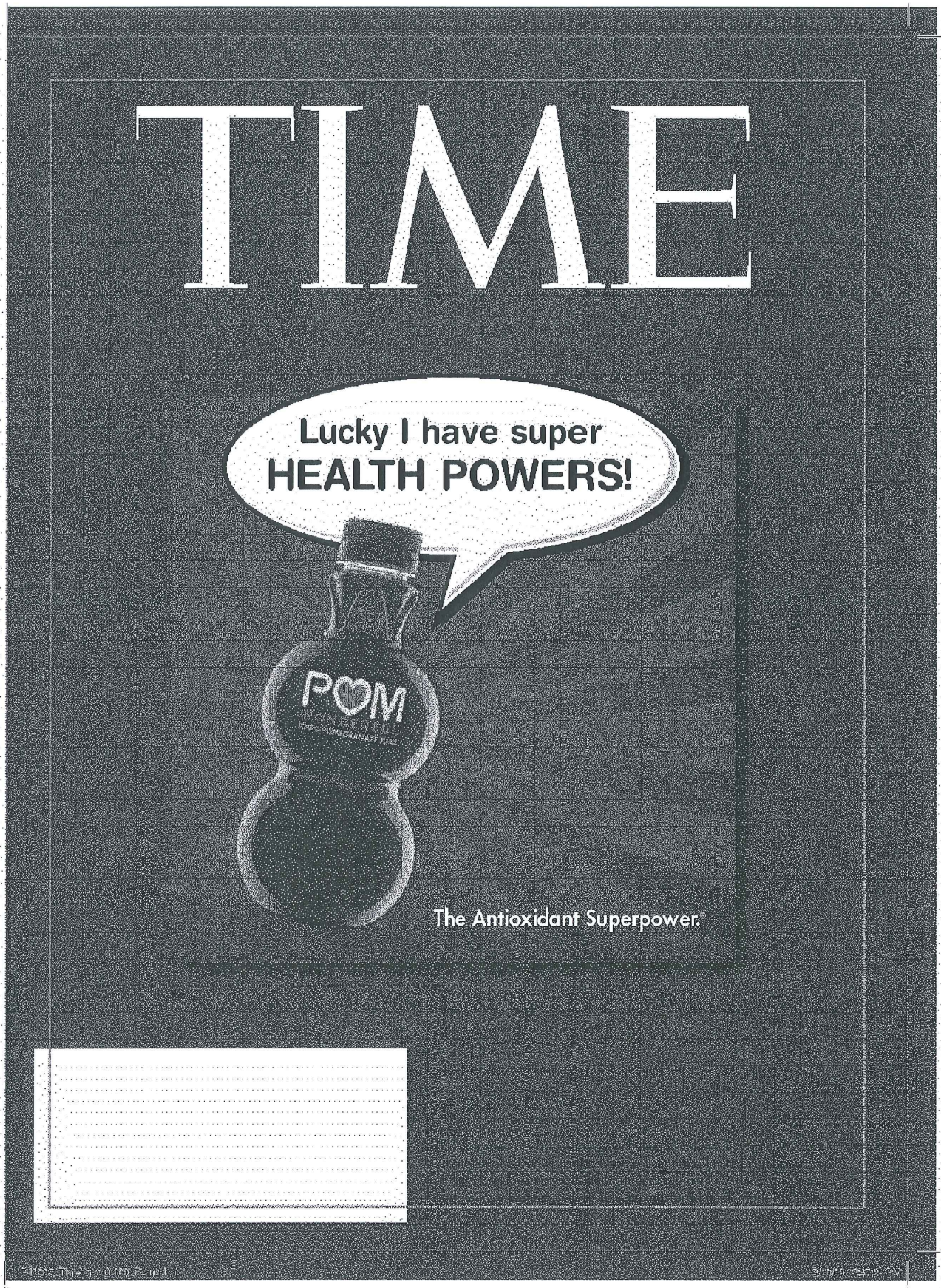
307. To the extent a "proven" claim can be implied from this ad (which it cannot), the overall impression of this ad is not that POM Juice is "proven" to be 100% effective in preventing, treating or reducing the risk of heart disease or prostate cancer because (1) all of the qualifying language contradicts an implied "clinically proven" interpretation, and (2) "proven" in science means the "average person in the study benefitted," not that "everyone in the study necessarily benefitted." (Heber, Tr. 2011; Butters, Tr. 2893-2894; PX0361 (Sacks, Dep. at 81)).

308. Professor Butters concluded that POM's ads in general depend on parody, exaggeration and humor to bring their message to the potential consumer; including the following messages: 1) POM is the best pomegranate that anyone can buy; 2) POM Juice is healthy; 3) POM Juice is tasty; 4) POM Juice is arguably the best source of antioxidants of any of the comparable beverages available; 5) medical research has suggested that antioxidants combat free radicals, which are unhealthy, and may contribute to diseases of the heart, arteries, and prostate, as well as erectile dysfunction; and 6) POM also offers concentrated forms of pomegranate extract for those who wish to ingest antioxidants in even more concentrated form than pomegranate juice itself. (PX0158-0033).

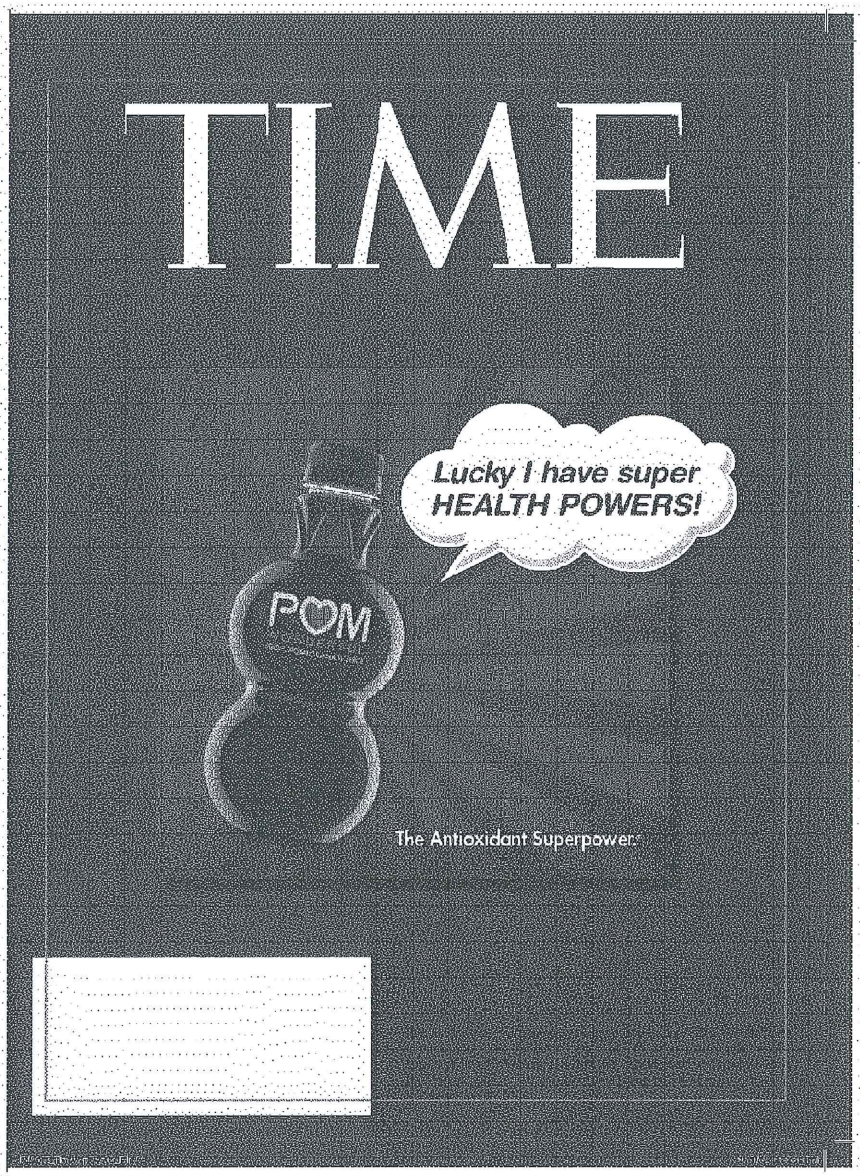
309. Complaint Counsel presented no extrinsic evidence or expert opinion on this ad's meaning, consumer perceptions of this ad, or consumer interpretations regarding this ad. (PX0357 (Stewart, Dep. at 49, 52)).

310. Complaint Counsel failed to present any evidence that the claims in this ad reasonably convey that the Challenged Products are "clinically proven" to prevent, treat or reduce the risk of certain diseases, such as heart disease or prostate cancer.

311. Complaint Counsel failed to present any evidence regarding the number of exposures consumers had to this ad or any particular POM advertisement. (Mazis, Tr. 2752).

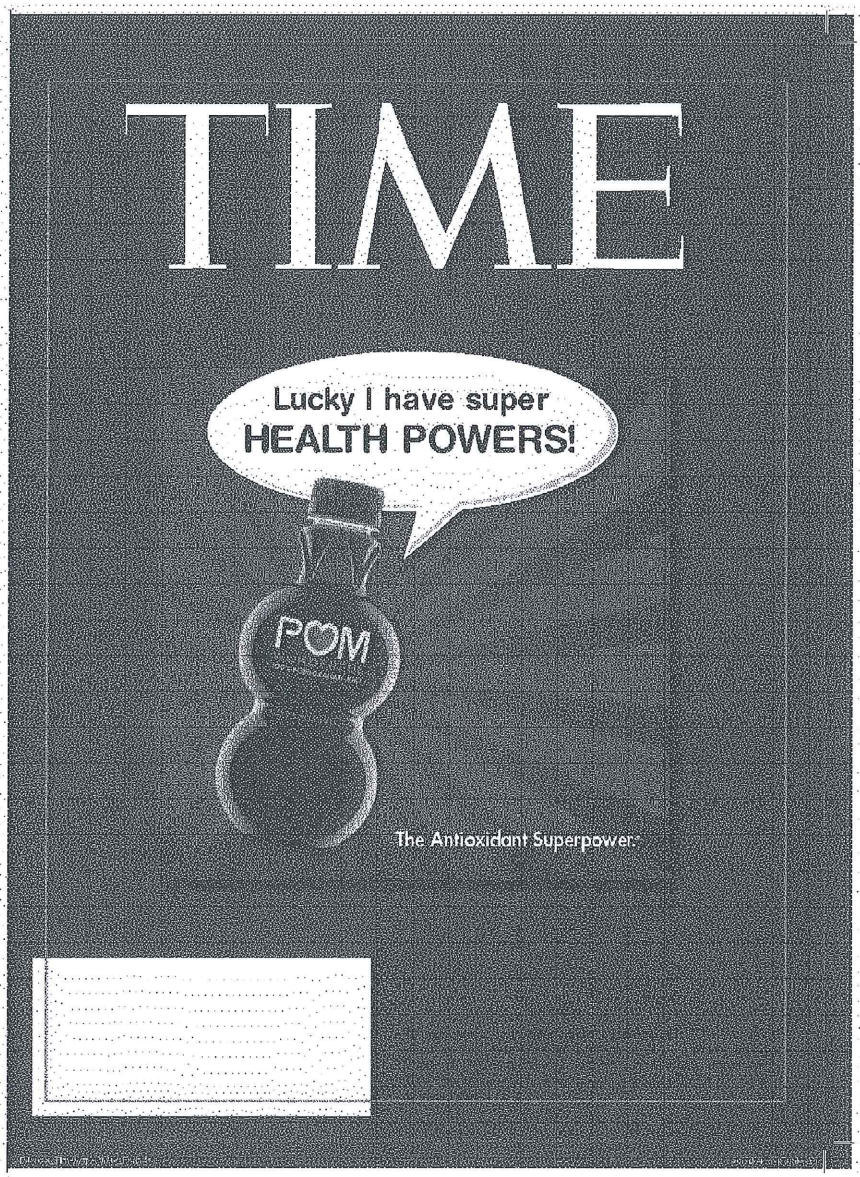


JOB NO.: PJ2005	TRIM: 7.875"x10.5"	COLOR: 4/C PROCESS	DATE IN: 7-22-09
PROJECT: TimeWrap Oct09	LIVE: 7.125" x 9.75"	LIVE, TRIM, BLEED (DO NOT PRINT)	DATE OUT: 8-20-09
SCALE: 1 : 1	BLEED: 8.375" x 11"	PRINTOUT SIZE: 100%	PROOF ROUND: F2



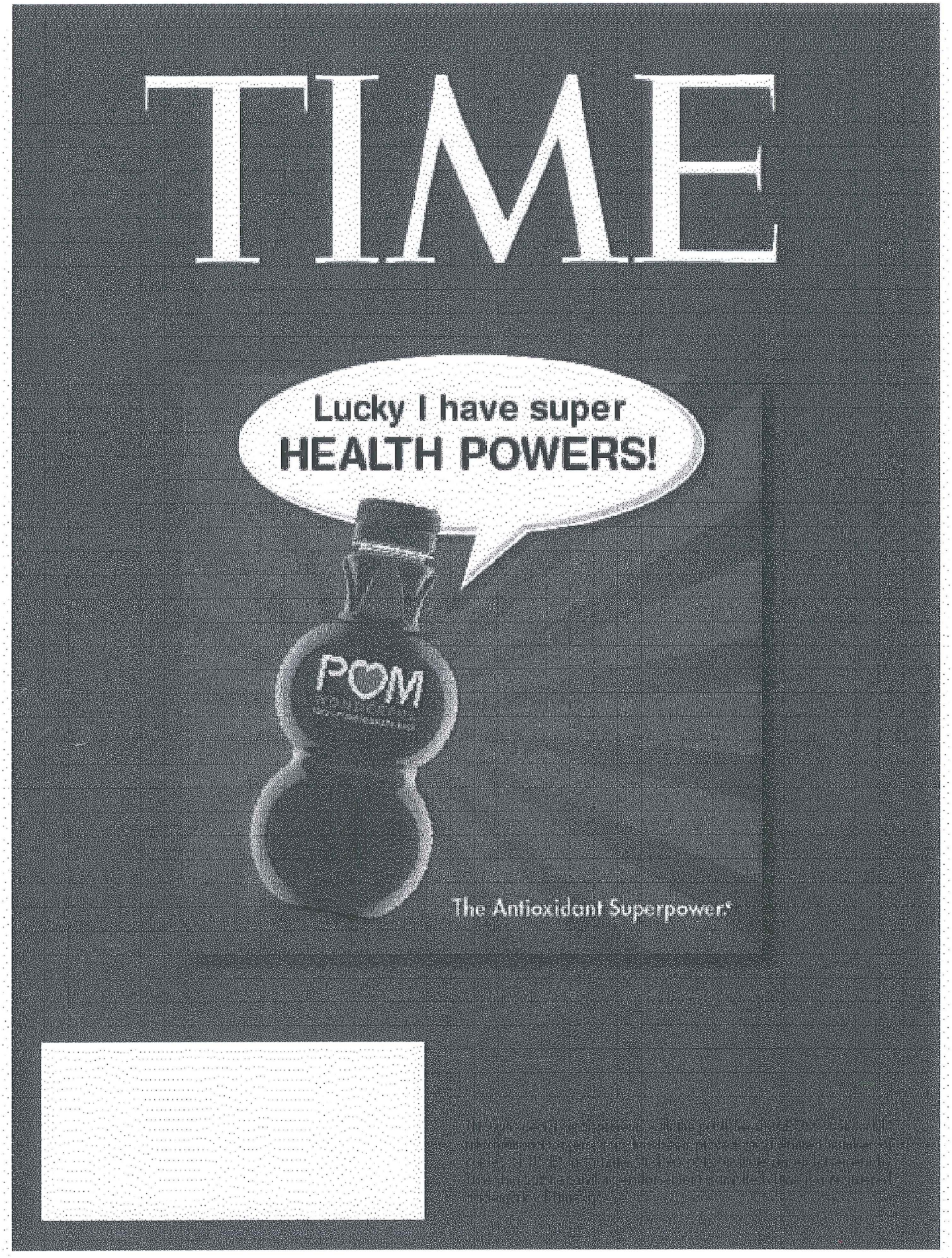
JOB NO.: PJ2097	TRIM: 7.875" x 10.5"	COLOR: 4/C PROS	DATE IN: 9-02-09	CREATIVE: CJ
PROJECT: Time Magazine Wrap - Dec 09	LIVE: 7.125" x 9.75"	LIVE, TRIM, BLEED (DO NOT PRINT)	CLIENT SIGN OFF: 00-00-00	PRODUCTION: MS
SCALE: 1 : 1	BLEED: 8.375" x 11.0"	PRINTOUT SIZE: 100%	RELEASE DATE: 9-10-09	PROOF: F

•PLEASE MARK ALL CHANGES ON INSITE DOCUMENT •NO CHANGES ON PRINTED FLAT WILL BE MADE



JOB NO.: PJ2006	TRIM: 7.875" x 10.5"	COLOR: 4/C PROS	DATE IN: 9-01-09	CREATIVE: CJ
PROJECT: Time Magazine Wrap - Nov 09	LIVE: 7.125" x 9.75"	DIVE: TRIM, BLEED (DO NOT PRINT)	CLIENT SIGN OFF: 00-00-00	PRODUCTION: MS
SCALE: 1 : 1	BLEED: 8.375" x 11.0"	PRINTOUT SIZE: 100%	RELEASE DATE: 9-10-09	PROOF: F2

*PLEASE MARK ALL CHANGES ON INSITE DOCUMENT *NO CHANGES ON PRINTED FLAT WILL BE MADE


TIME
Lucky I have super
HEALTH POWERS!
POM
The Antioxidant Superpower.*

One small pill for mankind. – (CX0120)

312. Complaint Counsel claim that, on May 28, 2007, POM ran an advertisement with the headline "One small pill for mankind" with this body copy:

> Introducing POMx – a highly concentrated, incredibly powerful blend of all natural polyphenol antioxidants made from the very same pomegranates in **POM Wonderful 100% Pomegranate Juice**. Our method of harnessing astonishing levels of antioxidants is so extraordinary, it's patent-pending. So now you can get all the antioxidant power of an 8oz glass of juice in the convenience of a calorie-free capsule.
>
> Ready to take on free radicals? Put up your POMx and fight them with a mighty 1000mg capsule – that's more concentrated pomegranate polyphenol antioxidants than any other 100% pomegranate supplement. An initial UCLA medical study on POM Wonderful 100% Pomegranate Juice showed hopeful results for men with prostate cancer.[1,3] And preliminary human research suggests that our California-grown pomegranate juice also promotes heart health.[2,3] Take your antioxidants into your own hands. **Call 1-888-POM-PILL now, or visit pompills.com/fort and get your first monthly shipment for just ~~$29.95~~ $24.95 with coupon.**
>
> [1]**pomwonderful.com/cancer.html**
> [2]**pomwonderful.com/heart_health.html** [3] These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure or prevent any disease.

(CX0120_0001) (emphasis in original).

313. Complaint Counsel failed to present any other definitive information regarding this ad's dissemination.

314. Complaint Counsel failed to present any evidence that Respondents would run this ad in the future, let alone whether it is probable they would do so.

315. Complaint Counsel's assertion that the ad conveys the message that (a) taking one POMx Pill per day "prevents," "treats," or "reduces the risk" of heart disease or prostate cancer; or (b) taking one POMx Pill per day is "clinically proven" to "prevent," "treat," or "reduce the risk" of heart disease or prostate cancer is not

conspicuous, self-evident, or reasonably clear from the face of the ad. (CX0120_0001).

316. Consequently, because the above-referenced challenged implied claim may not be determined with confidence from the face of the ad, extrinsic evidence must be examined.

317. The overall net impression of this ad is not that not that taking one POMx Pill per day prevents, treats or reduces the risk of certain diseases, such as heart disease or prostate cancer; or (b) taking one POMx Pill per day is "clinically proven" to prevent, treat or reduce the risk of certain diseases, such as heart disease or prostate cancer. (CX0120_0001). Even the language of the ad itself uses such qualifiers as "suggest," "may one day prove an effective weapon," "initial UCLA medical study," "hopeful results," "fight" and "preliminary human research suggests." (CX0120_0001).

318. To the extent a "reduce the risk" claim can be implied from this ad, the overall net impression is not that taking one POMx Pill per day "reduces the risk" of certain diseases, such as heart disease or prostate cancer, like a drug with a single target of action, but "reduces the risk," like a healthy diet of fruits and vegetables and exercise "reduces the risk" of disease. (CX0120_0001).

319. To the extent a "treat" claim can be implied from this ad (which it cannot), the overall net impression of any ad is not that POMx Pills are a substitute for conventional medical treatment. (Butters, Tr. 2821-22; Appendix of Advertisements).

320. To the extent a "proven" claim can be implied from this ad (which it cannot), the overall impression of this ad is not that POMx Pills are "proven" to be 100% effective in preventing, treating or reducing the risk of heart disease or prostate cancer because (1) all of the qualifying language contradicts an implied "clinically proven" interpretation, and (2) "proven" in science means the "average person in the study benefitted," not that "everyone in the study necessarily benefitted." (Heber, Tr. 2011; Butters, Tr. 2893-2894; PX0361 (Sacks, Dep. at 81)).

321. Professor Butters testified that this ad is humorous and is an "irreverent re-appropriation" of what was said by the first man on the moon. (PX0350 (Butters, Dep. at 141)).

322. Mr. Tupper testified that this ad indicated that there were "hopeful results for men with prostate cancer." (Tupper, Tr. 1004).

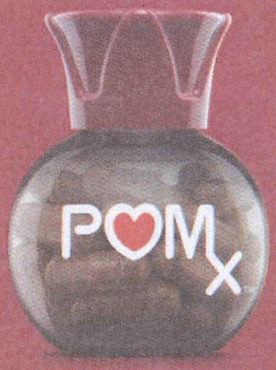
323. Viewing the "One pill for mankind" ad as a whole, including the interaction of the words and visual imagery, the overall net impression of this ad is that the headline

is humorous and that there are hopeful results regarding testing of POM Juice for men with prostate cancer. (PX0350 (Butters, Dep. at 141); (CX1364 (Tupper, Dep. at 1004)).

324. Complaint Counsel presented no extrinsic evidence or expert opinion on this ad's meaning, consumer perceptions of this ad, or consumer interpretations regarding this ad. (PX0357 (Stewart, Dep. at 49, 52)).

325. Complaint Counsel failed to present any evidence that the claims in this ad reasonably convey that the Challenged Products are "clinically proven" to prevent, treat or reduce the risk of heart disease, prostate cancer or erectile dysfunction.

326. Complaint Counsel failed to present any evidence regarding the number of exposures consumers had to this ad or any particular POM advertisement. (Mazis, Tr. 2752).



One small pill for mankind.

"Findings from a small study suggest that pomegranate juice may one day prove an effective weapon against prostate cancer."

The New York Times (July 4, 2006).

Introducing POMx™ – a highly concentrated, incredibly powerful blend of all-natural polyphenol antioxidants made from the very same pomegranates in **POM Wonderful 100% Pomegranate Juice**. Our method of harnessing astonishing levels of antioxidants is so extraordinary, it's patent-pending. So now you can get all the antioxidant power of an 8oz glass of juice in the convenience of a calorie-free capsule.

Ready to take on free radicals? Put up your POMx and fight them with a mighty 1000mg capsule – that's more concentrated pomegranate polyphenol antioxidants than any other 100% pomegranate supplement. An initial UCLA medical study on POM Wonderful 100% Pomegranate Juice showed hopeful results for men with prostate cancer.[1,3] And preliminary human research suggests that our California-grown pomegranate juice also promotes heart health.[2,3] Take your antioxidants into your own hands. **Call 1-888-POM-PILL now, or visit pompills.com/fort and get your first monthly shipment for just ~~$29.95~~ $24.95 with coupon.**

POM IN A PILL™

CALL 1-888-POM-PILL now, or visit pompills.com/fort

Not available in stores | 100% money-back guarantee

SAVE $5 ON YOUR FIRST ORDER.

Call 1-888-POM-PILL or visit pompills.com/fort and mention or enter code **FORT5** at checkout. To pay by check, call 1-888-POM-PILL for instructions. Hurry, offer expires July 31, 2007.

CONSUMER: This offer expires July 31, 2007. Mention or enter coupon code FORT5 at checkout. This coupon can only be used on POMx products. One coupon redemption per customer. Cannot be combined with other offers. No substitutions, transfer rights or cash equivalents will be given. We reserve the right to modify or discontinue this promotion at any time. Coupon code valid only at pompills.com/fort or 1-888-POM-PILL.

[1] **pomwonderful.com/cancer.html** [2] **pomwonderful.com/heart_health.html** [3] These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure or prevent any disease.

POM Wonderful and Prostate Health - (CX0314_0004; CX0314_0008)

327. Complaint Counsel claim that, on September 9, 2008 and October 23, 2008, POM ran an advertisement with the headline "POM Wonderful and Prostate Health." with the body copy that appears on CX0314_0004 and CX0314_0008.

328. Complaint Counsel failed to present any other definitive information regarding this ad's dissemination.

329. Complaint Counsel failed to present any evidence that Respondents would run this ad in the future, let alone whether it is probable they would do so.

330. Nowhere in this ad do Respondents expressly (*i.e.*, unequivocally and directly) state that (a) POM Juice "prevents," "treats," or "reduces the risk" of prostate cancer; or (b) POM Juice is "clinically proven" to "prevent," "treat," or "reduce the risk" of prostate cancer. (CX0314_0004; CX0314_0008).

331. Complaint Counsel's assertion that the ad conveys the message that (a) POM Juice "prevents," "treats," or "reduces the risk" of prostate cancer; or (b) POM Juice is "clinically proven" to "prevent," "treat," or "reduce the risk" of prostate cancer is not conspicuous, self-evident, or reasonably clear from the face of the ad. (CX0314_004; CX0314_0008).

332. Consequently, because the above-referenced challenged implied claim may not be determined with confidence from the face of the ad, extrinsic evidence must be examined.

333. The overall net impression of this ad is not that (a) drinking eight ounces of POM Juice prevents, treats or reduces the risk of certain diseases, such as prostate cancer; or (b) drinking eight ounces of POM Juice is "clinically proven" to prevent, treat or reduce the risk of certain diseases, such as prostate cancer. (CX0314_0004; CX0314_0008). Even the language of the ad itself uses such qualifiers as "emerging science suggests," and "may be able." (CX0314_0004; CX0314_0008).

334. To the extent a "reduce the risk" claim can be implied from ad, the overall net impression is not that drinking eight ounces of POM Juice "reduces the risk" of certain diseases, such as prostate cancer, like a drug with a single target of action, but "reduces the risk," like a healthy diet of fruits and vegetables and exercise "reduces the risk" of disease. (CX0314_0004; CX0314_0008).

335. To the extent a "treat" claim can be implied from this ad (which it cannot), the overall net impression of any ad is not that POM Juice is a substitute for conventional medical treatment. (Butters, Tr. 2821-22).

336. To the extent a "proven" claim can be implied from this ad (which it cannot), the overall impression of this ad is not that POM Juice is "proven" to be 100% effective in preventing, treating or reducing the risk of prostate cancer because (1) all of the qualifying language contradicts an implied "clinically proven" interpretation, and (2) "proven" in science means the "average person in the study benefitted," not that "everyone in the study necessarily benefitted." (Heber, Tr. 2011; Butters, Tr. 2893-2894; PX0361 (Sacks, Dep. at 81)).

337. Complaint Counsel presented no extrinsic evidence or expert opinion on this ad's meaning, consumer perceptions of this ad, or consumer interpretations regarding this ad. (PX0357 (Stewart, Dep. at 49, 52)).

338. Complaint Counsel failed to present any evidence that the claims in this ad reasonably convey that the Challenged Products are "clinically proven" to prevent, treat or reduce the risk of heart disease, prostate cancer or erectile dysfunction.

339. Complaint Counsel failed to present any evidence regarding the number of exposures consumers had to this ad or any particular POM advertisement. (Mazis, Tr. 2752).

POM Wonderful and Prostate Health

A recently published medical study involving POM Wonderful 100% Pomegranate Juice followed 46 men previously treated for prostate cancer either with surgery or radiation.

After drinking eight ounces of POM Wonderful 100% Pomegranate Juice daily for at least two years, these men experienced significantly slower PSA doubling times. PSA (Prostate-Specific Antigen) is a biomarker that indicates the presence of prostate cancer. "PSA doubling time" is a measure of how long it takes for PSA levels to double. A longer doubling time may indicate slower progression of the disease.

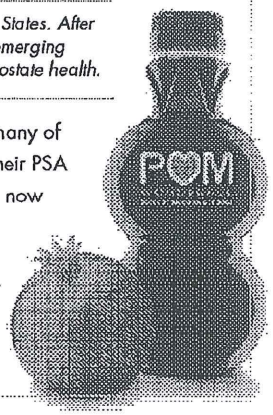
At the beginning of the study, PSA levels doubled on average every 15 months. By the end of the study, doubling time had slowed to 54 months – nearly a four-fold improvement.

"This is a big increase. I was surprised when I saw such an improvement in PSA numbers," said Dr. Allan Pantuck, lead author of the UCLA Study.

In addition, in-vitro testing using blood serum from the patients who drank pomegranate juice showed a 17% increase in prostate cancer cell death and a 12% decrease in cancer cell growth.

One important note: All patients drank the same POM Wonderful 100% Pomegranate Juice which is available in your supermarket produce section.

Prostate Cancer is the most commonly diagnosed cancer in men in the United States. After lung cancer, it's the second leading cause of cancer death in men. However, emerging science suggests that diet and lifestyle may be able to significantly improve prostate health.



The Research Continues Results from this study were so promising that many of the original patients continued to drink pomegranate juice daily, and their PSA doubling times remained suppressed. Three more clinical studies are now underway to further investigate the effects of POM on prostate health.

Learn why POM Wonderful is the only pomegranate juice you can trust.
(See inside back cover of this wrap.)

POM WONDERFUL pomwonderful.com

PJ9745_POMtime wrap_F.indd 2 9/10/08 9:24:12 AM

JOB NO.: PJ9745	TRIM: 7.875"x10.5"	COLOR: 4/C PROS	DATE IN: 08-25-08
PROJECT: NY Times Magazine Wrap	LIVE: 7.125" x 9.75"	LIVE, TRIM, BLEED (DO NOT PRINT)	DATE OUT: 09-09-08
SCALE: 1 : 1	BLEED: 8.375" x 11"	PRINTOUT SIZE: 100%	PROOF NUMBER: F

POM Wonderful® and Prostate Health

POM WONDERFUL

A recently published medical study involving POM Wonderful 100% Pomegranate Juice followed 46 men previously treated for prostate cancer either with surgery or radiation.

After drinking eight ounces of POM Wonderful 100% Pomegranate Juice daily for at least two years, these men experienced significantly slower PSA doubling times. PSA (Prostate-Specific Antigen) is a biomarker that indicates the presence of prostate cancer. "PSA doubling time" is a measure of how long it takes for PSA levels to double. A longer doubling time may indicate slower progression of the disease.

At the beginning of the study, PSA levels doubled on average every 15 months. By the end of the study, doubling time had slowed to 54 months – nearly a four-fold improvement.

"This is a big increase. I was surprised when I saw such an improvement in PSA numbers," said Dr. Allan Pantuck, lead author of the UCLA Study.

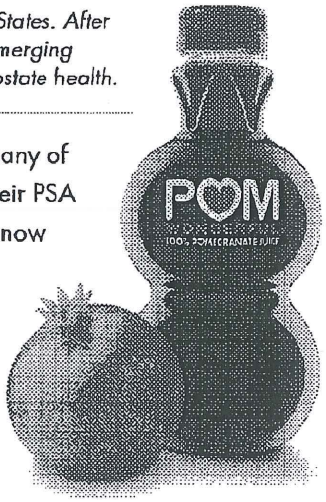
In addition, in-vitro testing using blood serum from the patients who drank pomegranate juice showed a 17% increase in prostate cancer cell death and a 12% decrease in cancer cell growth.

One important note: All patients drank the same POM Wonderful 100% Pomegranate Juice which is available in your supermarket produce section.

Prostate Cancer is the most commonly diagnosed cancer in men in the United States. After lung cancer, it's the second leading cause of cancer death in men. However, emerging science suggests that diet and lifestyle may be able to significantly improve prostate health.

The Research Continues Results from this study were so promising that many of the original patients continued to drink pomegranate juice daily, and their PSA doubling times remained suppressed. Three more clinical studies are now underway to further investigate the effects of POM on prostate health.

Learn why POM Wonderful is the only pomegranate juice you can trust.
(See inside back cover of this wrap.)



POM WONDERFUL **pomwonderful.com**

Risk your health in this economy? NEVER! - (CX0379_0004)

340. Complaint Counsel claim that, on August 20, 2009, POM ran an advertisement with the headline "Risk your health in this economy? NEVER!" with this body copy:

> In a time of financial distress, one 16-ounce hero has devoted itself to maintaining the world's health: POM Wonderful®. One of the POM products backed by $32 million in medical research,* the Antioxidant Superpower will defend you with the full force of its 100% pure pomegranate juice. And you will survive.
>
> (CX0379_0004).

341. Complaint Counsel failed to present any other definitive information regarding this ad's dissemination.

342. Complaint Counsel failed to present any evidence that Respondents would run this ad in the future, let alone whether it is probable they would do so.

343. Complaint Counsel's expert, Professor Mazis, testified that Complaint Counsel is not challenging POM's ads for POM Juice that ran after December 2008. (Mazis, Tr. 2753-54). Accordingly, based on these representations, Complaint Counsel cannot now challenge this ad.

344. Complaint Counsel's assertion that the ad conveys the message that (a) POM Juice "prevents," "treats," or "reduces the risk" of certain diseases; or (b) POM Juice is "clinically proven" to "prevent," "treat," or "reduce the risk" of heart disease or prostate cancer is not conspicuous, self-evident, or reasonably clear from the face of the ad. (CX0379_0004).

345. Consequently, because the above-referenced challenged implied claim may not be determined with confidence from the face of the ad, extrinsic evidence must be examined.

346. The overall net impression of this ad is not that (a) drinking eight ounces of POM Juice prevents, treats or reduces the risk of certain diseases; or (b) drinking eight ounces of POM Juice is "clinically proven" to prevent, treat or reduce the risk of certain diseases. (CX0379_0004). Even the language of the ad itself uses the qualifier "defend." (CX0379_0004).

347. To the extent a "reduce the risk" claim can be implied from ad, the overall net impression is not that drinking eight ounces of POM Juice "reduces the risk" of certain diseases, like a drug with a single target of action, but "reduces the risk,"

like a healthy diet of fruits and vegetables and exercise "reduces the risk" of disease. (CX0379_0004).

348. To the extent a "treat" claim can be implied from this ad (which it cannot), the overall net impression of any ad is not that POM Juice is a substitute for conventional medical treatment. (Butters, Tr. 2821-22).

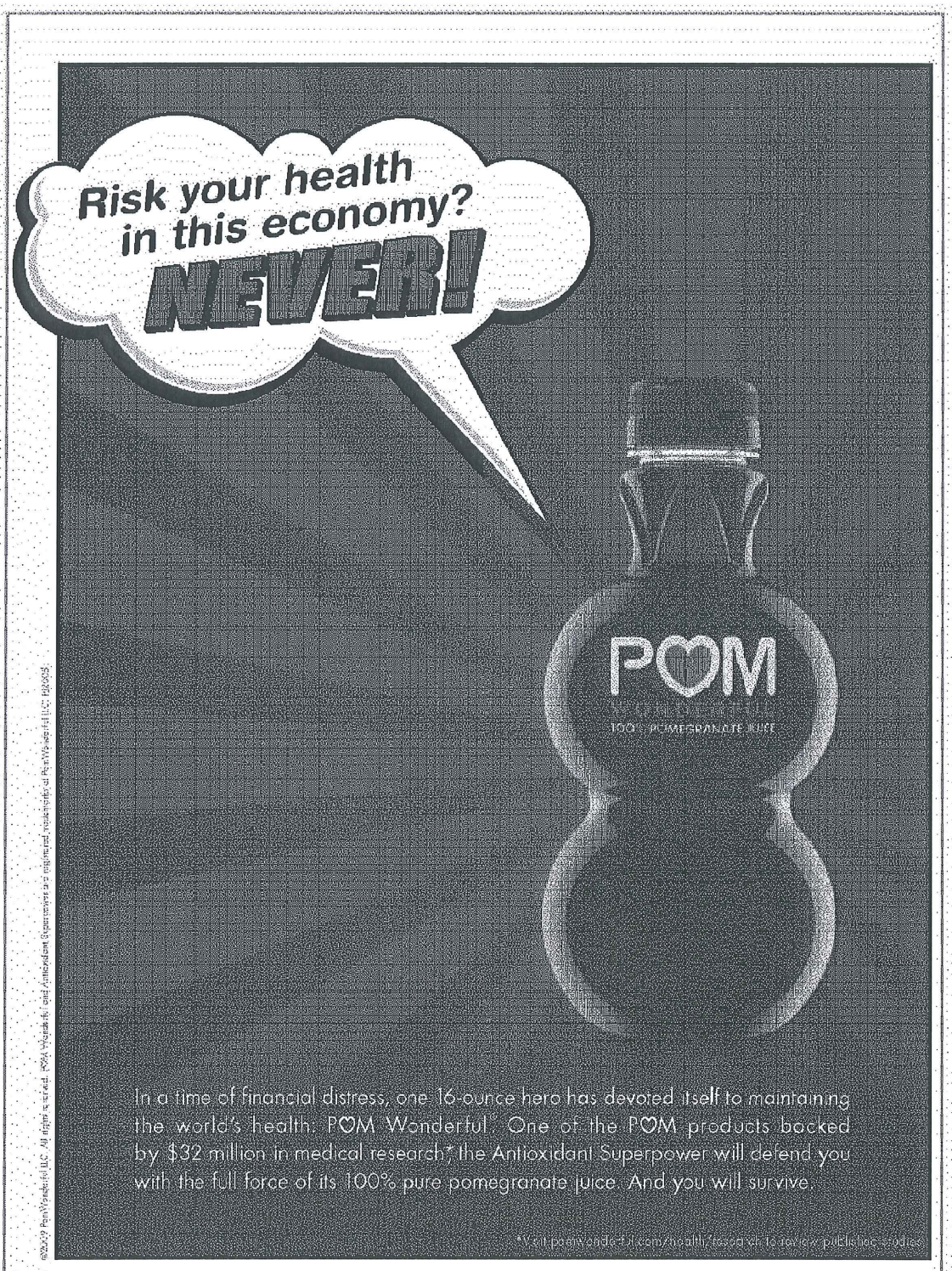
349. To the extent a "proven" claim can be implied from this ad (which it cannot), the overall impression of this ad is not that POM Juice is "proven" to be 100% effective in preventing, treating or reducing the risk of certain diseases because (1) all of the qualifying language contradicts an implied "clinically proven" interpretation, and (2) "proven" in science means the "average person in the study benefitted," not that "everyone in the study necessarily benefitted." (Heber, Tr. 2011; Butters, Tr. 2893-2894; PX0361 (Sacks, Dep. at 81)).

350. Professor Butters concluded that POM's ads in general depend on parody, exaggeration and humor to bring their message to the potential consumer; including the following messages: 1) POM is the best pomegranate that anyone can buy; 2) POM Juice is healthy; 3) POM Juice is tasty; 4) POM Juice is arguably the best source of antioxidants of any of the comparable beverages available; 5) medical research has suggested that antioxidants combat free radicals, which are unhealthy, and may contribute to diseases of the heart, arteries, and prostate, as well as erectile dysfunction; and 6) POM also offers concentrated forms of pomegranate extract for those who wish to ingest antioxidants in even more concentrated form than pomegranate juice itself. (PX0158-0033).

351. Complaint Counsel presented no extrinsic evidence or expert opinion on this ad's meaning, consumer perceptions of this ad, or consumer interpretations regarding this ad. (PX0357 (Stewart, Dep. at 49, 52)).

352. Complaint Counsel failed to present any evidence that the claims in this ad reasonably convey that the Challenged Products are "clinically proven" to prevent, treat or reduce the risk of heart disease, prostate cancer or erectile dysfunction.

353. Complaint Counsel failed to present any evidence regarding the number of exposures consumers had to this ad or any particular POM advertisement. (Mazis, Tr. 2752).



PJ2005_TimeWrapOct09_F2.indd 4 8/20/09 3:47:46 PM

JOB NO.: PJ2005	TRIM: 7.875"x10.5"	COLOR: 4/C PROCESS	DATE IN: 7-22-09
PROJECT: TimeWrap Oct09	LIVE: 7.125" x 9.75"	LIVE, TRIM, BLEED (DO NOT PRINT)	DATE OUT: 8-20-09
SCALE: 1 : 1	BLEED: 8.375" x 11"	PRINTOUT SIZE: 100%	PROOF ROUND: F2

Science, not fiction - (CX0122)

354. Complaint Counsel claim that, on June 1, 2007, POM ran an advertisement with the headline "Science, not fiction" with this body copy:

> Introducing POMx – a highly concentrated, incredibly powerful blend of all natural polyphenol antioxidants made from the very same pomegranates in **POM Wonderful 100% Pomegranate Juice**. Our method of harnessing astonishing levels of antioxidants is so extraordinary, it's patent-pending. So now you can get all the antioxidant power of an 8oz glass of juice in the convenience of a calorie-free capsule.
>
> Ready to take on free radicals? Put up your POMx and fight them with a mighty 1000mg capsule – that's more concentrated pomegranate polyphenol antioxidants than any other 100% pomegranate supplement. An initial UCLA medical study on POM Wonderful 100% Pomegranate Juice showed hopeful results for men with prostate cancer.[1,3] And preliminary human research suggests that our California-grown pomegranate juice also promotes heart health.[2,3] Take your antioxidants into your own hands. **Call 1-888-POM-PILL now, or visit pompills.com/dvr and get your first monthly shipment for just ~~$29.95~~ $24.95 with coupon.**
>
> [1]**pomwonderful.com/cancer.html**
> [2]**pomwonderful.com/heart_health.html** [3] These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure or prevent any disease.

(CX0122_0001) (emphasis in original).

355. Complaint Counsel failed to present any other definitive information regarding this ad's dissemination.

356. Complaint Counsel failed to present any evidence that Respondents would run this ad in the future, let alone whether it is probable they would do so.

357. Complaint Counsel's assertion that the ad conveys the message that (a) taking one POMx Pill per day "prevents," "treats," or "reduces the risk" of heart disease or prostate cancer; or (b) taking one POMx Pill per day is "clinically proven" to "prevent," "treat," or "reduce the risk" of heart disease or prostate cancer is not

conspicuous, self-evident, or reasonably clear from the face of the ad. (CX0122_0001).

358. Consequently, because the above-referenced challenged implied claim may not be determined with confidence from the face of the ad, extrinsic evidence must be examined.

359. The overall net impression of this ad is not that not that taking one POMx Pill per day prevents, treats or reduces the risk of certain diseases, such as heart disease or prostate cancer; or (b) taking one POMx Pill per day is "clinically proven" to prevent, treat or reduce the risk of certain diseases, such as heart disease or prostate cancer. (CX0122_0001). Even the language of the ad itself uses such qualifiers as "initial UCLA medical study," "hopeful results," "fight," "preliminary studies" and "promising results." (CX0122_0001).

360. To the extent a "reduce the risk" claim can be implied from this ad, the overall net impression is not that taking one POMx Pill per day "reduces the risk" of certain diseases, such as heart disease or prostate cancer, like a drug with a single target of action, but "reduces the risk," like a healthy diet of fruits and vegetables and exercise "reduces the risk" of disease. (CX0122_0001).

361. To the extent a "treat" claim can be implied from this ad (which it cannot), the overall net impression of any ad is not that POMx Pills are a substitute for conventional medical treatment. (Butters, Tr. 2821-22; Appendix of Advertisements).

362. To the extent a "proven" claim can be implied from this ad (which it cannot), the overall impression of this ad is not that POMx Pills are "proven" to be 100% effective in preventing, treating or reducing the risk of heart disease or prostate cancer because (1) all of the qualifying language contradicts an implied "clinically proven" interpretation, and (2) "proven" in science means the "average person in the study benefitted," not that "everyone in the study necessarily benefitted." (Heber, Tr. 2011; Butters, Tr. 2893-2894; PX0361 (Sacks, Dep. at 81)).

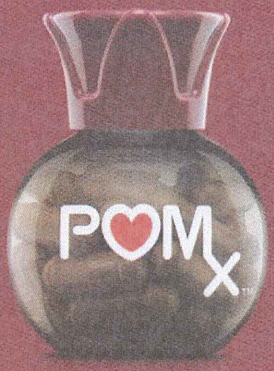
363. Professor Butters testified that this ad is a parody or pun on "science fiction" that constitutes a humorous introduction to the ad. (PX0350 (Butters, Dep. at 140)).

364. Viewing the "Science, not fiction" ad as a whole, including the interaction of the words and visual imagery, the overall net impression of this ad is that the headline is humorous and that there were hopeful results regarding testing of POM Juice for men with prostate cancer. (PX0350 (Butters, Dep. at 140); (PX0158-0033)).

365. Complaint Counsel presented no extrinsic evidence or expert opinion on this ad's meaning, consumer perceptions of this ad, or consumer interpretations regarding this ad. (PX0357 (Stewart, Dep. at 49, 52)).

366. Complaint Counsel failed to present any evidence that the claims in this ad reasonably convey that the Challenged Products are "clinically proven" to prevent, treat or reduce the risk of heart disease, prostate cancer or erectile dysfunction.

367. Complaint Counsel failed to present any evidence regarding the number of exposures consumers had to this ad or any particular POM advertisement. (Mazis, Tr. 2752).



Science, not fiction.

Made from the only pomegranates backed by $20 million in medical research.

Introducing POMx™– a highly concentrated, incredibly powerful blend of all-natural polyphenol antioxidants made from the very same pomegranates in **POM Wonderful 100% Pomegranate Juice**. Our method of harnessing astonishing levels of antioxidants is so extraordinary, it's patent-pending. So now you can get all the antioxidant power of an 8oz glass of juice in the convenience of a calorie-free pill.

Ready to take on free radicals? Put up your POMx and fight them with a mighty 1000mg capsule – that's more concentrated pomegranate polyphenol antioxidants than any other 100% pomegranate supplement. An initial UCLA medical study on POM Wonderful 100% Pomegranate Juice showed hopeful results for men with prostate cancer.[1,3] And preliminary human research suggests that our California-grown pomegranate juice also promotes heart health.[2,3] Take your antioxidants into your own hands. **Call 1-888-POM-PILL now, or visit pompills.com/dvr and get your first monthly shipment for just ~~$29.95~~ $24.95 with coupon.**

POM IN A PILL™

CALL 1-888-POM-PILL now, or visit pompills.com/dvr

Not available in stores | 100% money-back guarantee

SAVE $5 ON YOUR FIRST ORDER.

Call 1-888-POM-PILL or visit pompills.com/dvr and mention or enter code **DVR5** at checkout. To pay by check, call 1-888-POM-PILL for instructions. Hurry, offer expires July 31, 2007.

CONSUMER: This offer expires July 31, 2007. This coupon can only be used on POMx products. One coupon redemption per customer. Cannot be combined with other offers. No substitutions, transfer rights or cash equivalents will be given. We reserve the right to modify or discontinue this promotion at any time. Coupon code valid only at pompills.com/dvr or 1-888-POM-PILL.

[1] **pomwonderful.com/cancer.html** [2] **pomwonderful.com/heart_health.html** [3] These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure or prevent any disease.

Science, not fiction - (CX0279)

368. Complaint Counsel claim that, on March 1, 2009, POM ran an advertisement with the headline "Science, not fiction." with the body copy that appears on CX0279_0001.

369. Complaint Counsel failed to present any other definitive information regarding this ad's dissemination.

370. Complaint Counsel failed to present any evidence that Respondents would run this ad in the future, let alone whether it is probable they would do so.

371. Complaint Counsel's expert, Professor Mazis, testified that Complaint Counsel is not challenging POM's ads for POM Juice that ran after December 2008. (Mazis, Tr. 2753-54). Accordingly, based on these representations, Complaint Counsel cannot now challenge this ad.

372. Nowhere in this ad do Respondents expressly (*i.e.*, unequivocally and directly) state that (a) taking one POMx Pill per day "prevents," "treats," or "reduces the risk" of heart disease or prostate cancer; or (b) taking one POMx Pill per day is "clinically proven" to "prevent," "treat," or "reduce the risk" of heart disease or prostate cancer. (CX0279_0001).

373. Complaint Counsel's assertion that the ad conveys the message that (a) taking one POMx Pill per day "prevents," "treats," or "reduces the risk" of heart disease or prostate cancer; or (b) taking one POMx Pill per day is "clinically proven" to "prevent," "treat," or "reduce the risk" of heart disease or prostate cancer is not conspicuous, self-evident, or reasonably clear from the face of the ad. (CX0279_0001).

374. Consequently, because the above-referenced challenged implied claim may not be determined with confidence from the face of the ad, extrinsic evidence must be examined.

375. The overall net impression of this ad is not that not that taking one POMx Pill per day prevents, treats or reduces the risk of certain diseases, such as heart disease or prostate cancer; or (b) taking one POMx Pill per day is "clinically proven" to prevent, treat or reduce the risk of certain diseases, such as heart disease or prostate cancer. (CX0279_0001). Even the language of the ad itself uses such qualifiers as "initial UCLA MEDICAL STUDY," "hopeful results," "fight," "preliminary studies," and "promising results." (CX0279_0001).

376. To the extent a "reduce the risk" claim can be implied from this ad, the overall net impression is not that taking one POMx Pill per day "reduces the risk" of certain

diseases, such as heart disease or prostate cancer, like a drug with a single target of action, but "reduces the risk," like a healthy diet of fruits and vegetables and exercise "reduces the risk" of disease. (CX0279_0001).

377. To the extent a "treat" claim can be implied from this ad (which it cannot), the overall net impression of any ad is not that POMx Pills are a substitute for conventional medical treatment. (Butters, Tr. 2821-22).

378. To the extent a "proven" claim can be implied from this ad (which it cannot), the overall impression of this ad is not that POMx Pills are "proven" to be 100% effective in preventing, treating or reducing the risk of heart disease or prostate cancer because (1) all of the qualifying language contradicts an implied "clinically proven" interpretation, and (2) "proven" in science means the "average person in the study benefitted," not that "everyone in the study necessarily benefitted." (Heber, Tr. 2011; Butters, Tr. 2893-2894; PX0361 (Sacks, Dep. at 81)).

379. Complaint Counsel presented no extrinsic evidence or expert opinion on this ad's meaning, consumer perceptions of this ad, or consumer interpretations regarding this ad. (PX0357 (Stewart, Dep. at 49, 52)).

380. Complaint Counsel failed to present any evidence that the claims in this ad reasonably convey that the Challenged Products are "clinically proven" to prevent, treat or reduce the risk of heart disease, prostate cancer or erectile dysfunction.

381. Complaint Counsel failed to present any evidence regarding the number of exposures consumers had to this ad or any particular POM advertisement. (Mazis, Tr. 2752).

VMS ID: 090300701
RUN DATE: 03/01/2009

Science, not fiction.

Made from the only pomegranates backed by $25 million in medical research.

Ready to take your antioxidants into your own hands? Introducing POMx™ – a highly concentrated, incredibly powerful blend of all-natural polyphenol antioxidants made from the same pomegranates as **POM Wonderful®** **100% Pomegranate Juice.**

100% All-natural.

POMx fights free radicals with a powerful 1000 milligrams. That's more concentrated polyphenol antioxidants than any other pomegranate supplement. And POMx is the first and only antioxidant supplement reviewed for safety by the FDA.

The antioxidant power of our 8oz juice.

POMx is made from the only pomegranates backed by $25 million in medical research, the same pomegranates we use to make our POM Wonderful 100% Pomegranate Juice. An initial UCLA MEDICAL STUDY on POM Wonderful 100% Pomegranate Juice found *hopeful results for prostate health.* The study reports "statistically significant prolongation of PSA doubling times," according to Dr. Allen J. Pantuck in Clinical Cancer Research, 2006.[1,2,3] Two additional preliminary studies on our juice showed *promising results for heart health.* "Stress-induced ischemia decreased in the pomegranate group," Dr. Dean Ornish reported in the American Journal of Cardiology, 2005.[1,2,4] "Pomegranate juice consumption resulted in a significant IMT[5] reduction by up to 30% after one year," said Dr. Michael Aviram, referring to reduced arterial plaque in Clinical Nutrition, 2004.[1,2,6]

ORDER NOW: 1-888-POM-PILL (766-7455) or pompills.com/pop

Try POMx for one month – FREE!

We'll even pay for the shipping. Visit pompills.com/pop or call 1-888-POM-PILL. Use discount code: POP30

SIGN UP FOR POMx MONTHLY, AND WE'LL SEND YOUR FIRST BOTTLE FREE. AFTER THAT, YOU'LL CONTINUE TO RECEIVE MONTHLY SHIPMENTS FOR $29.95 WITH COMPLIMENTARY SHIPPING. Offer expires June 30, 2009. The first month free plus free shipping offer applies only to the purchase price for the first month of POMx Monthly. Following months will be $29.95 per bottle. This discount can only be used on POMx products. One discount per customer. Cannot be combined with other offers. No substitutions, transfer rights or cash equivalents will be given. We reserve the right to modify or discontinue this promotion at any time. We reserve the right to change product price or shipping charge at any time. Offer valid only at pompills.com or 1-888-POM-PILL. Discount code is not valid on POMx trial.

[1] pompills.com/research [2] These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure or prevent any disease. [3] 45 men with rising PSA after surgery or radiotherapy drank 8oz 100% pomegranate juice daily for two years. [4] 45 patients with coronary heart disease and myocardial ischemia drank 8oz 100% pomegranate juice daily for three months. [5] Study measured intima-media thickness (IMT). [6] 19 patients aged 65-75 years with severe atherosclerosis drank 8oz 100% pomegranate juice daily for one year.

POM WONDERFUL®

VMS-0000291

CX0279_0001

Studies Show: 10 out of 10 don't want to die - (CX0029)

382. Complaint Counsel claim that, on November 1, 2004, POM ran an advertisement with the headline "Studies Show That 10 Out Of 10 People Don't Want To Die" with this body copy:

POMEGRANATE JUICE

STUDIES SHOW THAT 10 OUT OF 10
PEOPLE DON'T WANT TO DIE

IT'S NOT EASY BEING ALIVE IN TODAY'S POLLUTED, STRESSED OUT WORLD. Here's a tip: with more naturally occurring antioxidant power than any other drink, a glass of POM Wonderful Pomegranate Juice a day might be just what the doctor ordered.

Fighting Free Radicals

Let's start with the problem: free radicals…unstable little molecules that can accelerate aging, lead to heart disease and stroke, and have even been implicated in cancer. Where do they come from? Everywhere. Free radicals are formed by exposure to air pollution alcohol, pesticides, sunlight, tobacco smoke, drugs, even fried foods. Of course, when you're very young, your body's self-repair mechanism can neutralize the activity of many free radicals. But by the time you're in your twenties, those mechanisms just don't work as well. That's where antioxidants come in. They neutralize free radicals, helping to prevent the cell and tissue damage that leads to disease. Which brings us back to POM Wonderful Pomegranate Juice.

Not All Antioxidants are Equal

Since our bodies don't produce enough antioxidants to do the job on their own, we need a little outside help. POM Wonderful Pomegranate Juice, with a higher level of antioxidants than any other drink, is a real Antioxidant Superpower.

Our Research: Heartening

We've been working with a number of top scientists, including a Nobel Laureate, for 6 years now and our seven

published, peer-reviewed papers reveal heartening results. Here's the story: Free radicals are the culprits that turn LDL – or "bad" cholesterol – into that sticky stuff that becomes the plaque that clogs your arteries. Our scientific research shows that pomegranate juice is 8 times better than green tea at preventing formation of oxidized (sticky) LDL.[1] And a clinical pilot study shows that an 8 oz. glass of POM Wonderful 100% Pomegranate Juice, consumed daily, reduces plaque in the arteries up to 30%.[2]

The Heart Stopping Truth

Remember: heart disease is America's number one killer. For women as well as men. 98% of heart attacks are due to atherosclerosis, or too much plaque in the arteries. That same plaque increases your chance of stroke. One final scary statistic: half of patients who have a severe heart attack have normal cholesterol levels. In other words, we're all at risk.

Just a Glass a Day

To keep your heart healthy: exercise regularly. Eat a healthy diet. And drink 8 ounces of POM Wonderful Pomegranate Juice. Make every day a good to be alive.

[1]Aviram M., Drugs Under Experimental and Clinical Research, 2002. Indexed values based on relative amount of oxidized LDL created. [2]Aviram M., Clinical Nutrition 2004.

(CX0029_0001-0002).

383. Complaint Counsel failed to present any other definitive information regarding this ad's dissemination.

384. Complaint Counsel failed to present any evidence that Respondents would run this ad in the future, let alone whether it is probable they would do so.

385. This ad cannot provide a basis for injunctive relief because (a) it ran over seven years ago; and (b) no evidence exists to show that Respondents are likely to run this ad in the future.

386. Nowhere in this ad do Respondents expressly (*i.e.*, unequivocally and directly) state that (a) POM Juice "prevents," "treats," or "reduces the risk" of heart

disease; or (b) POM Juice is "clinically proven" to "prevent," "treat," or "reduce the risk" of heart disease. (CX0029_0001).

387. Complaint Counsel's assertion that the ad conveys the message that (a) POM Juice "prevents," "treats," or "reduces the risk" of heart disease; or (b) POM Juice is "clinically proven" to "prevent," "treat," or "reduce the risk" of heart disease is not conspicuous, self-evident, or reasonably clear from the face of the ad. (CX0029_0001-0002).

388. Consequently, because the above-referenced challenged implied claim may not be determined with confidence from the face of the ad, extrinsic evidence must be examined.

389. The overall net impression of this ad is not that (a) drinking eight ounces of POM Juice prevents or treats heart disease; or (b) drinking eight ounces of POM Juice is "clinically proven" to prevent, treat or reduce the risk of certain diseases, such as heart disease. (CX0029_0001-0002). Even the language of the ad itself uses such qualifiers as "might be," "heartening results," and "pilot study." (CX0029_0001-0002).

390. To the extent a "reduce the risk" claim can be implied from this ad, the overall net impression is not that drinking eight ounces of POM Juice "reduces the risk" of certain diseases, such as heart disease or prostate cancer, like a drug with a single target of action, but "reduces the risk," like a healthy diet of fruits and vegetables and exercise "reduces the risk" of disease. (CX0029_0001-0002).

391. To the extent a "treat" claim can be implied from this ad (which it cannot), the overall net impression of any ad is not that POM Juice is a substitute for conventional medical treatment. (Butters, Tr. 2821-22).

392. To the extent a "proven" claim can be implied from this ad (which it cannot), the overall impression of "this ad is not that POM Juice is "proven" to be 100% effective in preventing, treating or reducing the risk of heart disease because (1) all of the qualifying language contradicts an implied "clinically proven" interpretation, and (2) "proven" in science means the "average person in the study benefitted," not that "everyone in the study necessarily benefitted." (Heber, Tr. 2011; Butters, Tr. 2893-2894; PX0361 (Sacks, Dep. at 81)).

393. Complaint Counsel presented no extrinsic evidence or expert opinion on this ad's meaning, consumer perceptions of this ad, or consumer interpretations regarding this ad. (PX0357 (Stewart, Dep. at 49, 52)).

394. Complaint Counsel failed to present any evidence that the claims in this ad reasonably convey that the Challenged Products are "clinically proven" to prevent, treat or reduce the risk of heart disease, prostate cancer or erectile dysfunction.

395. Complaint Counsel failed to present any evidence regarding the number of exposures consumers had to this ad or any particular POM advertisement. (Mazis, Tr. 2752).

advertisement

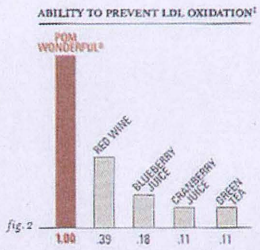


fig. 2

level of antioxidants than any other drink, is a real Antioxidant Superpower.™

Our Research: Heartening

We've been working with a number of top scientists, including a Nobel Laureate, for 6 years now and our seven published, peer-reviewed papers reveal heartening results. Here's the story: Free radicals are the culprits that turn LDL – or "bad" cholesterol – into that sticky stuff that becomes the plaque that clogs your arteries. Our scientific research shows that pomegranate juice is 8 times better than green tea at preventing formation of oxidized (sticky) LDL.[1] And a clinical pilot study shows that an 8 oz. glass of POM Wonderful 100% Pomegranate Juice, consumed daily, reduces plaque in the arteries up to 30%.[2]

The Heart Stopping Truth

Remember: heart disease is America's number one killer. For women as well as men. 98% of heart attacks are due to atherosclerosis, or too much plaque in the arteries. That same plaque increases your chance of stroke. One final scary statistic: half of patients who have a severe heart attack have normal cholesterol levels. In other words, we're all at risk.

Just a Glass a Day

To keep your heart healthy: exercise regularly. Eat a healthy diet. And drink 8 ounces of POM Wonderful Pomegranate Juice. Make every day a good day to be alive.

[1]Aviram, M., Drugs Under Experimental and Clinical Research, 2002. Indexed values, based on relative amount of oxidized LDL created. [2]Aviram, M., Clinical Nutrition, 2004.

POM Wonderful Pomegranate Juice is the Antioxidant Superpower.™ Drink a glass a day!

For more medical research on the Antioxidant Superpower, visit pomwonderful.com

Super HEALTH Powers! - (CX1426_0027, Exh. A)

396. Complaint Counsel claim that POM ran an advertisement with the headline "Super HEALTH Powers!" with this body copy:

> **100% PURE POMEGRANATE JUICE.** It's 100% pure! It's heroically healthy! It's The Antioxidant Superpower, POM Wonderful 100% authentic pomegranate juice. Backed by $25 million in medical research. Proven to fight for cardiovascular, prostate and erectile health. Committed to keeping you healthy for a good, long time!

(CX1426_0027, Exh. A).

397. Complaint Counsel failed to present any definitive information regarding this ad's dissemination.

398. Complaint Counsel failed to present any evidence that Respondents would run this ad in the future, let alone whether it is probable they would do so.

399. Complaint Counsel's assertion that the ad conveys the message that (a) POM Juice "prevents," "treats," or "reduces the risk" of heart disease or prostate cancer; or (b) POM Juice is "clinically proven" to "prevent," "treat," or "reduce the risk" of heart disease or prostate cancer is not conspicuous, self-evident, or reasonably clear from the face of the ad. (CX1426_0027, Exh. A).

400. Consequently, because the above-referenced challenged implied claim may not be determined with confidence from the face of the ad, extrinsic evidence must be examined.

401. The overall net impression of this ad is not that (a) drinking eight ounces of POM Juice prevents, treats or reduces the risk of certain diseases, such as heart disease, prostate cancer or erectile dysfunction; or (b) drinking eight ounces of POM Juice is "clinically proven" to prevent, treat or reduce the risk of certain diseases, such as heart disease, prostate cancer or erectile dysfunction. (CX1426_0027, Exh. A). Even the language of the ad itself uses such qualifiers as "fight for" and "committed." (CX1426_0027, Exh. A).

402. To the extent a "reduce the risk" claim can be implied from ad, the overall net impression is not that drinking eight ounces of POM Juice "reduces the risk" of certain diseases, such as heart disease, prostate cancer or erectile dysfunction, like a drug with a single target of action, but "reduces the risk," like a healthy diet of fruits and vegetables and exercise "reduces the risk" of disease. (CX1426_0027, Exh. A).

403. To the extent a "treat" claim can be implied from this ad (which it cannot), the overall net impression of any ad is not that POM Juice is a substitute for conventional medical treatment. (Butters, Tr. 2821-22).

404. To the extent a "proven" claim can be implied from this ad (which it cannot), the overall impression of this ad is not that POM Juice is "proven" to be 100% effective in preventing, treating or reducing the risk of heart disease, prostate cancer or erectile dysfunction because (1) all of the qualifying language contradicts an implied "clinically proven" interpretation, and (2) "proven" in science means the "average person in the study benefitted," not that "everyone in the study necessarily benefitted." (Heber, Tr. 2011; Butters, Tr. 2893-2894; PX0361 (Sacks, Dep. at 81)).

405. Professor Butters concluded that because hangtags are small and will engage the concerted attention of relatively few potential purchasers, a hangtag offers limited opportunity for public communication (as compared to, newspaper ads or television commercials). (Butters, Tr. 2868-69).

406. Professor Butters testified that the hangtag is considered a form of point-of-sale marketing and in his opinion, hangtags are less important than print advertisements. (Butters, Tr. 2869-70).

407. Professor Butters further testified that the dominant theme of the hangtag is that POM Juice has super health powers and that the overall messaging of the hangtag reflects the tone and spirit of POM's superhero advertising campaign. Professor Butters testified that one message that is being conveyed by the hangtag is that POM Wonderful juice is extremely healthy. (Butters, Tr. 2870-73).

408. Professor Butters testified that it is necessary to view the hangtag as a whole. In his opinion, the hangtag does not make any medical claims; readers would not take away that it is proven that if you drink pomegranate juice, it is going to treat cardiovascular, prostate, and erectile disease, or even give you cardiovascular, prostate, and erectile health. The hangtag only makes claims "within the framework of the superhero and the verb 'fight for,' which is not something that people are going to take as anything other than -- than hyperbolic, … It will merely 'fight for.'" (Butters, Tr. 2884-85).

409. Professor Butters testified that the message suggested by the phrase "proven to fight for cardiovascular, prostate, and erectile health" is that you have a better cardiovascular, prostate, and erectile health -- not that POM has a cure. "Fight for" doesn't necessarily mean that you are going to win, not does it mean that POM Juice is going to treat or cure diseases. (Butters, Tr. 2893-94).

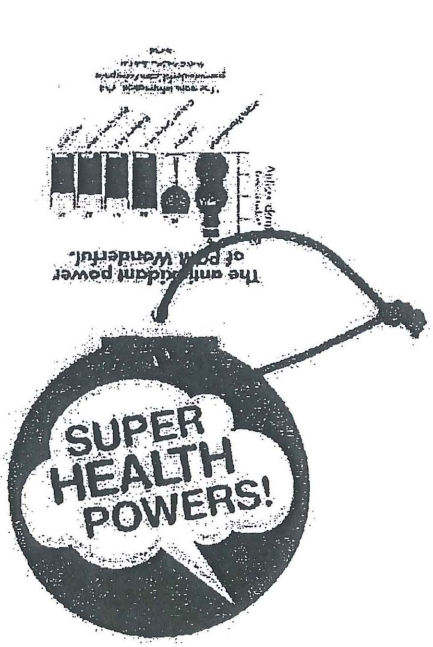
410. Professor Butters testified that "in describing Pom Juice as extremely 'healthy,'" the hangtag merely repeats and references conventional wisdom with respect to fruit juices in general. (PX0350 (Butters, Dep. at 178-79)).

411. Viewing the "Super HEALTH Powers!" ad as a whole, including the interaction of the words and visual imagery, the overall net impression of this ad is that the ad is hyperbolic, POM Juice is a healthy product, and POM Juice "fights" for cardiovascular, prostate, and erectile health. (Butters, Tr. 2870-73; 2884-85; 2893-94).

412. Complaint Counsel presented no extrinsic evidence or expert opinion on this ad's meaning, consumer perceptions of this ad, or consumer interpretations regarding this ad. (PX0357 (Stewart, Dep. at 49, 52)).

413. Complaint Counsel failed to present any evidence that the claims in this ad reasonably convey that the Challenged Products are "clinically proven" to treat like a drug or reduce the risk of or prevent heart disease, prostate cancer or erectile dysfunction like a drug.

414. Complaint Counsel failed to present any evidence regarding the number of exposures consumers had to this ad or any particular POM advertisement. (Mazis, Tr. 2752).


SUPER
HEALTH
POWERS!

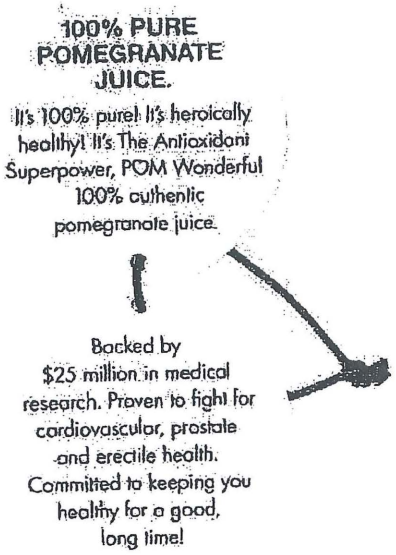

100% PURE
POMEGRANATE
JUICE.
It's 100% pure! It's heroically
healthy! It's The Antioxidant
Superpower, POM Wonderful
100% authentic
pomegranate juice.
Backed by
$25 million in medical
research. Proven to fight for
cardiovascular, prostate
and erectile health.
Committed to keeping you
healthy for a good,
long time!

Exhibit A

Take Out A Life Insurance Supplement - (CX0342)

415. Complaint Counsel claim that on February 22, 2010, POM ran an advertisement with the headline "Take Out A Life Insurance Supplement" with the body copy that appears on CX0342_0001.

416. Complaint Counsel failed to present any other definitive information regarding this ad's dissemination.

417. Complaint Counsel failed to present any evidence that Respondents would run this ad in the future, let alone whether it is probable they would do so.

418. Complaint Counsel's expert, Professor Mazis, testified that Complaint Counsel is not challenging POM's ads for POM Juice that ran after December 2008. (Mazis, Tr. 2753-54). Accordingly, based on these representations, Complaint Counsel cannot now challenge this ad.

419. Nowhere in this ad do Respondents expressly (*i.e.*, unequivocally and directly) state that (a) taking one POMx Pill per day "prevents," "treats," or "reduces the risk" of heart disease or prostate cancer; or (b) taking one POMx Pill per day is "clinically proven" to "prevent," "treat," or "reduce the risk" of heart disease or prostate cancer. (CX0342_0001).

420. Complaint Counsel's assertion that the ad conveys the message that (a) taking one POMx Pill per day "prevents," "treats," or "reduces the risk" of heart disease or prostate cancer; or (b) taking one POMx Pill per day is "clinically proven" to "prevent," "treat," or "reduce the risk" of heart disease or prostate cancer is not conspicuous, self-evident, or reasonably clear from the face of the ad. (CX0342_0001).

421. Consequently, because the above-referenced challenged implied claim may not be determined with confidence from the face of the ad, extrinsic evidence must be examined.

422. The overall net impression of this ad is not that not that taking one POMx Pill per day prevents, treats or reduces the risk of certain diseases, such as heart disease or prostate cancer; or (b) taking one POMx Pill per day is "clinically proven" to prevent, treat or reduce the risk of certain diseases, such as heart disease or prostate cancer. (CX0342_0001). Even the language of the ad itself uses such qualifiers as "emerging science suggests," "help protect," "promising results," "initial UCLA study," "hopeful results" and "preliminary studies." (CX0342_0001).

423. To the extent a "reduce the risk" claim can be implied from this ad, the overall net impression is not that taking one POMx Pill per day "reduces the risk" of certain diseases, such as heart disease or prostate cancer, like a drug with a single target of action, but "reduces the risk," like a healthy diet of fruits and vegetables and exercise "reduces the risk" of disease. (CX0342_0001).

424. To the extent a "treat" claim can be implied from this ad (which it cannot), the overall net impression of any ad is not that POMx Pills are a substitute for conventional medical treatment. (Butters, Tr. 2821-22; Appendix of Advertisements).

425. To the extent a "proven" claim can be implied from this ad (which it cannot), the overall impression of this ad is not that POMx Pills are "proven" to be 100% effective in preventing, treating or reducing the risk of heart disease or prostate cancer because (1) all of the qualifying language contradicts an implied "clinically proven" interpretation, and (2) "proven" in science means the "average person in the study benefitted," not that "everyone in the study necessarily benefitted." (Heber, Tr. 2011; Butters, Tr. 2893-2894; PX0361 (Sacks, Dep. at 81)).

426. Professor Butters testified that this ad employs humor as it is a "joking reference to death." (PX0350 (Butters, Dep. at 141)).

427. Professor Butters concluded that POM's ads in general depend on parody, exaggeration and humor to bring their message to the potential consumer; including the following messages: 1) POM is the best pomegranate that anyone can buy; 2) POM Juice is healthy; 3) POM Juice is tasty; 4) POM Juice is arguably the best source of antioxidants of any of the comparable beverages available; 5) medical research has suggested that antioxidants combat free radicals, which are unhealthy, and may contribute to diseases of the heart, arteries, and prostate, as well as erectile dysfunction; and 6) POM also offers concentrated forms of pomegranate extract for those who wish to ingest antioxidants in even more concentrated form than pomegranate juice itself. (PX0158-0033).

428. Viewing the "Take Out A Life Insurance Supplement" ad as a whole, including the interaction of the words and visual imagery, the overall net impression of the ad is that it is a humorous ad and that POMx Pills are healthy. (PX0350 (Butters, Dep. at 141); (PX0158-0033)).

429. Complaint Counsel presented no extrinsic evidence or expert opinion on this ad's meaning, consumer perceptions of this ad, or consumer interpretations regarding this ad. (PX0357 (Stewart, Dep. at 49, 52)).

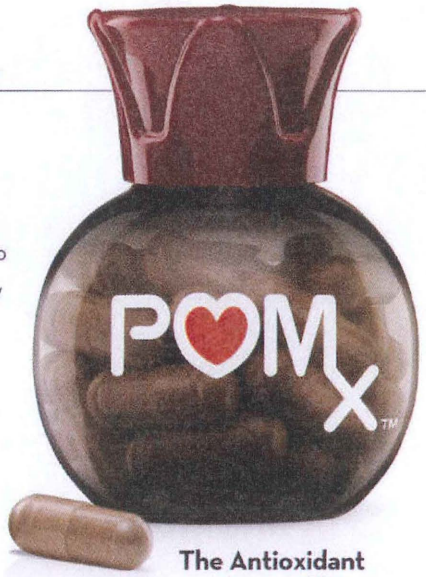
430. Complaint Counsel failed to present any evidence that the claims in this ad reasonably convey that the Challenged Products are "clinically proven" to prevent, treat or reduce the risk of heart disease, prostate cancer or erectile dysfunction.

431. Complaint Counsel failed to present any evidence regarding the number of exposures consumers had to this ad or any particular POM advertisement. (Mazis, Tr. 2752).

VMS ID: 100208568
RUN DATE: 02/22/2010

TAKE OUT A LIFE INSURANCE SUPPLEMENT.

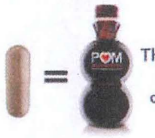
TRY POMx MONTHLY FREE!



The Antioxidant Superpill.™

Antioxidants? We've got you covered.

Emerging science suggests that antioxidants are critically important to maintaining good health because they protect you from free radicals, which can damage your body. Taking one POMx pill a day will help protect you from free radicals and keep you at your healthy best. (Just the way insurers like you to be.)



The antioxidant power of our 8oz juice.

POMx. Now that's a plan.

POMx is an all-natural, ultra-potent antioxidant extract. Containing a full spectrum of pomegranate polyphenols, POMx is so concentrated that a single capsule has the anti-oxidant power of a full glass of POM Wonderful® 100% Pomegranate Juice.

$32 million in medical research. No deductible.

POMx is made from the only pomegranates backed by $32 million in medical research at the world's leading universities. Not only has this research documented the unique and superior antioxidant power of pomegranates, it has revealed promising results for prostate and cardiovascular health.

Get the maximum benefits.

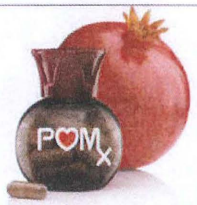
Our POMx pills are made from the same pomegranates we use to make our POM Wonderful 100% Pomegranate

Juice, on which each of the following medical studies was conducted.

An initial UCLA study on our juice found hopeful results for prostate health, reporting "statistically significant prolongation of PSA doubling times," according to Dr. Allen J. Pantuck in *Clinical Cancer Research*, 2006.[1,2,3]

Additional preliminary study on our juice showed promising results for heart health. "Stress-induced ischemia (restricted blood flow to the heart) decreased in the pomegranate group," Dr. Dean Ornish reported in the *American Journal of Cardiology*, 2005.[1,2,4]

FREE ONE MONTH TRIAL



We'll even pay for the shipping.*

Order Now: 888-766-7455

or pompills.com/t Use discount code: T30

*SIGN UP FOR POMx MONTHLY, AND WE'LL SEND YOUR FIRST BOTTLE FREE. AFTER THAT, YOU'LL CONTINUE TO RECEIVE MONTHLY SHIPMENTS FOR $29.95 WITH COMPLIMENTARY SHIPPING. Offer expires 6/30/10 and applies only to the purchase price for the first bottle of POMx Monthly. Following months will be $29.95 per bottle. One discount per customer. Cannot be combined with other offers. No substitutions, transfer rights or cash equivalents. We reserve the right to discontinue this promotion, change product price or shipping charge at any time. Valid only at pompills.com or 1-888-766-7455. Not valid on POMx Trial or other POM products. POM WONDERFUL®

[1]pompills.com/research [2]These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure or prevent any disease. [3]46 men with rising PSA after surgery or radiotherapy drank 8oz 100% pomegranate juice daily for two years. [4]45 patients with coronary heart disease and myocardial ischemia drank 8oz 100% pomegranate juice daily for three months.

VMS-0000306

CX0342_0001

Take Out A Life Insurance Supplement - (CX0353)

432. Complaint Counsel claim that on June 14, 2010, POM ran an advertisement with the headline "Take Out A Life Insurance Supplement" with the body copy that appears on CX0353_0001.

433. Complaint Counsel failed to present any other definitive information regarding this ad's dissemination.

434. Complaint Counsel failed to present any evidence that Respondents would run this ad in the future, let alone whether it is probable they would do so.

435. Complaint Counsel's expert, Professor Mazis, testified that Complaint Counsel is not challenging POM's ads for POM Juice that ran after December 2008. (Mazis, Tr. 2753-54). Accordingly, based on these representations, Complaint Counsel cannot now challenge this ad.

436. Nowhere in this ad do Respondents expressly (*i.e.*, unequivocally and directly) state that (a) taking one POMx Pill per day "prevents," "treats," or "reduces the risk" of heart disease or prostate cancer; or (b) taking one POMx Pill per day is "clinically proven" to "prevent," "treat," or "reduce the risk" of heart disease or prostate cancer. (CX0353_0001).

437. Complaint Counsel's assertion that the ad conveys the message that (a) taking one POMx Pill per day "prevents," "treats," or "reduces the risk" of heart disease or prostate cancer; or (b) taking one POMx Pill per day is "clinically proven" to "prevent," "treat," or "reduce the risk" of heart disease or prostate cancer is not conspicuous, self-evident, or reasonably clear from the face of the ad. (CX0353_0001).

438. Consequently, because the above-referenced challenged implied claim may not be determined with confidence from the face of the ad, extrinsic evidence must be examined.

439. The overall net impression of this ad is not that not that taking one POMx Pill per day prevents, treats or reduces the risk of certain diseases, such as heart disease or prostate cancer; or (b) taking one POMx Pill per day is "clinically proven" to prevent, treat or reduce the risk of certain diseases, such as heart disease or prostate cancer. (CX0353_0001). Even the language of the ad itself uses such qualifiers as "emerging science suggests," "help protect," "promising results," "initial UCLA study," "hopeful results" and "preliminary studies." (CX0353_0001).

440. To the extent a "reduce the risk" claim can be implied from this ad, the overall net impression is not that taking one POMx Pill per day "reduces the risk" of certain diseases, such as heart disease or prostate cancer, like a drug with a single target of action, but "reduces the risk," like a healthy diet of fruits and vegetables and exercise "reduces the risk" of disease. (CX0353_0001).

441. To the extent a "treat" claim can be implied from this ad (which it cannot), the overall net impression of any ad is not that POMx Pills are a substitute for conventional medical treatment. (Butters, Tr. 2821-22; Appendix of Advertisements).

442. To the extent a "proven" claim can be implied from this ad (which it cannot), the overall impression of this ad is not that POMx Pills are "proven" to be 100% effective in preventing, treating or reducing the risk of heart disease or prostate cancer because (1) all of the qualifying language contradicts an implied "clinically proven" interpretation, and (2) "proven" in science means the "average person in the study benefitted," not that "everyone in the study necessarily benefitted." (Heber, Tr. 2011; Butters, Tr. 2893-2894; PX0361 (Sacks, Dep. at 81)).

443. Professor Butters testified that this ad employs humor as it is a "joking reference to death." (PX0350 (Butters, Dep. at 141)).

444. Professor Butters concluded that POM's ads in general depend on parody, exaggeration and humor to bring their message to the potential consumer; including the following messages: 1) POM is the best pomegranate that anyone can buy; 2) POM Juice is healthy; 3) POM Juice is tasty; 4) POM Juice is arguably the best source of antioxidants of any of the comparable beverages available; 5) medical research has suggested that antioxidants combat free radicals, which are unhealthy, and may contribute to diseases of the heart, arteries, and prostate, as well as erectile dysfunction; and 6) POM also offers concentrated forms of pomegranate extract for those who wish to ingest antioxidants in even more concentrated form than pomegranate juice itself. (PX0158-0033).

445. Viewing the "Take Out A Life Insurance Supplement" ad as a whole, including the interaction of the words and visual imagery, the overall net impression of the ad is that it is a humorous ad and that POMx Pills are healthy. (PX0350 (Butters, Dep. at 141); (PX0158-0033)).

446. Complaint Counsel presented no extrinsic evidence or expert opinion on this ad's meaning, consumer perceptions of this ad, or consumer interpretations regarding this ad. (PX0357 (Stewart, Dep. at 49, 52)).

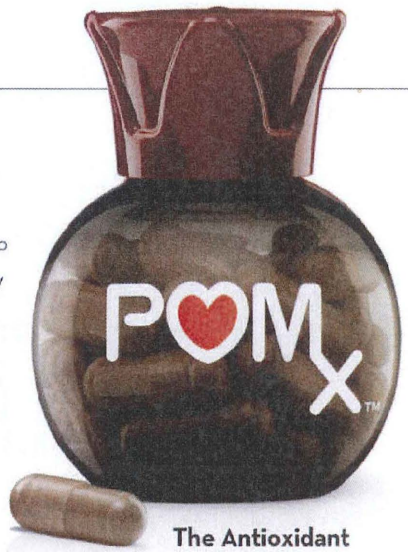
447. Complaint Counsel failed to present any evidence that the claims in this ad reasonably convey that the Challenged Products are "clinically proven" to prevent, treat or reduce the risk of heart disease, prostate cancer or erectile dysfunction.

448. Complaint Counsel failed to present any evidence regarding the number of exposures consumers had to this ad or any particular POM advertisement. (Mazis, Tr. 2752).

VMS ID: 100608485
RUN DATE: 06/14/2010

TAKE OUT A LIFE INSURANCE SUPPLEMENT.

TRY POMx MONTHLY FREE!



The Antioxidant Superpill.™

Antioxidants? We've got you covered.

Emerging science suggests that antioxidants are critically important to maintaining good health because they protect you from free radicals, which can damage your body. Taking one POMx pill a day will help protect you from free radicals and keep you at your healthy best. (Just the way insurers like you to be.)

The antioxidant power of our 8oz juice.

POMx. Now that's a plan.

POMx is an all-natural, ultra-potent antioxidant extract. Containing a full spectrum of pomegranate polyphenols, POMx is so concentrated that a single capsule has the anti-oxidant power of a full glass of POM Wonderful® 100% Pomegranate Juice.

$34 million in medical research. No deductible.

POMx is made from the only pomegranates backed by $34 million in medical research at the world's leading universities. Not only has this research documented the unique and superior antioxidant power of pomegranates, it has revealed promising results for prostate and cardiovascular health.

Get the maximum benefits.

Our POMx pills are made from the same pomegranates we use to make our POM Wonderful 100% Pomegranate Juice, on which each of the following medical studies was conducted.

An initial UCLA study on our juice found hopeful results for prostate health, reporting "statistically significant prolongation of PSA doubling times," according to Dr. Allen J. Pantuck in *Clinical Cancer Research*, 2006.[1,2,3]

An additional preliminary study on our juice showed promising results for heart health. "Stress-induced ischemia (restricted blood flow to the heart) decreased in the pomegranate group," Dr. Dean Ornish reported in the *American Journal of Cardiology*, 2005.[1,2,4]

Try POMx Monthly FREE for ONE MONTH.

We'll even pay for the shipping.*

Order Now: 888-766-7455
or pompills.com/sm Use discount code: SM30

*SIGN UP FOR POMx MONTHLY, AND WE'LL SEND YOUR FIRST BOTTLE FREE. AFTER THAT, YOU'LL CONTINUE TO RECEIVE MONTHLY SHIPMENTS FOR $29.95 WITH COMPLIMENTARY SHIPPING. Offer expires 10/31/10 and applies only to the purchase price for the first bottle of POMx Monthly. Following months will be $29.95 per bottle. One discount per customer. Cannot be combined with other offers. No substitutions, transfer rights or cash equivalents. We reserve the right to modify or discontinue this promotion, change the product price or change the shipping charge at any time. Valid only at pompills.com or 1-888-766-7455. Not valid on POMx Trial or other POM products. Credit or debit card required. POM WONDERFUL®

[1]pompills.com/research [2]These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure or prevent any disease. [3]45 men with rising PSA after surgery or radiotherapy drank 8oz 100% pomegranate juice daily for two years. [4]45 patients with coronary heart disease and myocardial ischemia drank 8oz 100% pomegranate juice daily for three months.

VMS-0000320

CX0353_0001

The antioxidant superpill - (CX0180; CX1426_044, Exh. K)

449. Complaint Counsel claim that, on February 3, 2008, POM ran an advertisement with the headline "The antioxidant superpill" with the body copy that appears on CX0180_0001 and CX1426_044, Exh. K.

450. Complaint Counsel failed to present any other definitive information regarding this ad's dissemination.

451. Complaint Counsel failed to present any evidence that Respondents would run this ad in the future, let alone whether it is probable they would do so.

452. Nowhere in this newsletter do Respondents expressly (i.e., unequivocally and directly) state that (a) taking one POMx Pill per day "prevents," "treats," or "reduces the risk" of heart disease or prostate cancer; or (b) taking one POMx Pill per day is "clinically proven" to "prevent," "treat," or "reduce the risk" of heart disease or prostate cancer. (CX0180_0001; CX1426_044, Exh. K).

453. Complaint Counsel's assertion that the ad conveys the message that (a) taking one POMx Pill per day "prevents," "treats," or "reduces the risk" of heart disease or prostate cancer; or (b) taking one POMx Pill per day is "clinically proven" to "prevent," "treat," or "reduce the risk" of heart disease or prostate cancer is not conspicuous, self-evident, or reasonably clear from the face of the ad. (CX0180_0001; CX1426_044, Exh. K).

454. Consequently, because the above-referenced challenged implied claim may not be determined with confidence from the face of the ad, extrinsic evidence must be examined.

455. The overall net impression of this ad is not that not that taking one POMx Pill per day prevents or treats certain diseases, such as heart disease or prostate cancer; or (b) taking one POMx Pill per day is "clinically proven" to prevent, treat or reduce the risk of certain diseases, such as heart disease or prostate cancer. (CX0180_0001; CX1426, Exh. K). Even the language of the ad itself uses such qualifiers as "fights," "initial UCLA MEDICAL STUDY," "hopeful results," "promising results" and "preliminary studies." (CX018_0001; CX1426_044, Exh. K).

456. To the extent a "reduce the risk" claim can be implied from this ad, the overall net impression is not that taking one POMx Pill per day "reduces the risk" of certain diseases, such as heart disease or prostate cancer, like a drug with a single target of action, but "reduces the risk," like a healthy diet of fruits and vegetables and exercise "reduces the risk" of disease. (CX018_0001; CX1426_044, Exh. K).

457. To the extent a "treat" claim can be implied from this ad (which it cannot), the overall net impression of any ad is not that POMx Pills are a substitute for conventional medical treatment. (Butters, Tr. 2821-22; Appendix of Advertisements).

458. To the extent a "proven" claim can be implied from this ad (which it cannot), the overall impression of this ad is not that POMx Pills are "proven" to be 100% effective in preventing, treating or reducing the risk of heart disease or prostate cancer because (1) all of the qualifying language contradicts an implied "clinically proven" interpretation, and (2) "proven" in science means the "average person in the study benefitted," not that "everyone in the study necessarily benefitted." (Heber, Tr. 2011; Butters, Tr. 2893-2894; PX0361 (Sacks, Dep. at 81)).

459. Complaint Counsel presented no extrinsic evidence or expert opinion on this ad's meaning, consumer perceptions of this ad, or consumer interpretations regarding this ad. (PX0357 (Stewart, Dep. at 49, 52)).

460. Complaint Counsel failed to present any evidence that the claims in this ad reasonably convey that the Challenged Products are "clinically proven" to prevent, treat or reduce the risk of heart disease, prostate cancer or erectile dysfunction.

461. Complaint Counsel failed to present any evidence regarding the number of exposures consumers had to this ad or any particular POM advertisement. (Mazis, Tr. 2752).

VMS ID: 080203607
RUN DATE: 02/03/2008

The antioxidant superpill.™

1000 milligrams. 0 calories.

Ready to take your antioxidants into your own hands? Introducing POMx™ – a highly concentrated, incredibly powerful blend of all-natural polyphenol antioxidants made from the same pomegranates as **POM Wonderful® 100% Pomegranate Juice.**

POMx fights free radicals with a powerful 1000 milligrams. That's more concentrated polyphenol antioxidants than any other pomegranate supplement. And POMx is the first and only antioxidant supplement reviewed for safety by the FDA.

100% All-natural.

The antioxidant power of our 8 oz. juice.

POMx is made from the only pomegranates backed by $23 million in medical research, the same pomegranates we use to make our POM Wonderful 100% Pomegranate Juice. An initial UCLA MEDICAL STUDY on POM Wonderful 100% Pomegranate Juice found *hopeful results for prostate health.* The study reports "statistically significant prolongation of PSA doubling times," according to Dr. Allen J. Pantuck in Clinical Cancer Research, 2006.[1,2,3] Two additional preliminary studies on our juice showed *promising results for heart health.* "Stress-induced ischemia decreased in the pomegranate group," Dr. Dean Ornish reported in the American Journal of Cardiology, 2005.[1,2,4] "Pomegranate juice consumption resulted in a significant IMT[5] reduction by up to 30% after one year," said Dr. Michael Aviram, referring to reduced arterial plaque in Clinical Nutrition, 2004.[1,2,6]

CALL 1-888-POM-PILL (766-7455) now or visit pompills.com/la

Try POMx for one month – FREE!

We'll even pay for the shipping. Visit pompills.com/la or call 1-888-POM-PILL. Use discount code: LA30

SIGN UP FOR POMx MONTHLY, AND WE'LL SEND YOUR FIRST BOTTLE FREE. AFTER THAT, YOU'LL CONTINUE TO RECEIVE MONTHLY SHIPMENTS FOR $29.95 WITH COMPLIMENTARY SHIPPING. Offer expires April 15, 2008. The first month free plus free shipping offer applies only to the purchase price for the first month of POMx Monthly. Following months will be $29.95 per bottle. This discount can only be used on POMx products. One discount per customer. Cannot be combined with other offers. No substitutions, transfer rights or cash equivalents will be given. We reserve the right to modify or discontinue this promotion at any time. We reserve the right to change product price or shipping charge at any time. Offer valid only at pompills.com/la or 1-888-POM-PILL. Discount code is not valid on POMx trial.

[1] pompills.com/research [2] These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure or prevent any disease. [3] 45 men with rising PSA after surgery or radiotherapy drank 8 oz. 100% pomegranate juice daily for two years. [4] 45 patients with coronary heart disease and myocardial ischemia drank 8 oz. 100% pomegranate juice daily for three months. [5] Study measured intima-media thickness (IMT). [6] 19 patients aged 65-75 years with severe atherosclerosis drank 8 oz. 100% pomegranate juice daily for one year.

POM WONDERFUL®

VMS-0000261

CX0180_0001

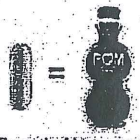
The antioxidant superpill.™

1000 milligrams. 0 calories.

Ready to take your antioxidants into your own hands? Introducing POMx® – a highly concentrated, incredibly powerful blend of all-natural polyphenol antioxidants, made from the same pomegranates as POM Wonderful® 100% Pomegranate Juice.

POMx fights free radicals with a powerful 1000 milligrams. That's more concentrated polyphenol antioxidants than any other pomegranate supplement. And POMx is the first and only antioxidant supplement reviewed for safety by the FDA.

100% All-natural.



The antioxidant power of our 8oz juice.

POMx is made from the only pomegranates backed by $32 million in medical research. These are the same pomegranates we use to make our POM Wonderful 100% Pomegranate Juice, on which each of the following medical studies was conducted. An initial UCLA MEDICAL STUDY on POM Wonderful 100% Pomegranate Juice found *hopeful results for prostate health.* The study reports "statistically significant prolongation of PSA doubling times," according to Dr. Allen J. Pantuck in Clinical Cancer Research, 2006.[1,2,3] Two additional preliminary studies on our juice found *promising results for heart health.* "Stress-induced ischemia decreased in the pomegranate group," Dr. Dean Ornish reported in the American Journal of Cardiology, 2005.[1,2,4] "Pomegranate juice consumption resulted in a significant IMT[5] reduction by up to 30% after one year," said Dr. Michael Aviram, referring to reduced arterial plaque in Clinical Nutrition, 2004.[1,2,5]

ORDER NOW: 1-888-POM-PILL (766-7455) or www.pompills.com/fsin

Try POMx for one month – FREE!

We'll even pay for the shipping.

Visit pompills.com/fsin or call 1-888-POM-PILL. Use discount code: FN30

SIGN UP FOR POMx MONTHLY, AND WE'LL SEND YOUR FIRST BOTTLE FREE. AFTER THAT, YOU'LL CONTINUE TO RECEIVE MONTHLY SHIPMENTS FOR $29.95 WITH COMPLIMENTARY SHIPPING. Offer expires April 15, 2010. The first month free plus shipping offer applies only to the purchase price for the first month of POMx Monthly. Following months will be $34.95 per bottle. This discount can only be used on POMx products. One discount per customer. Cannot be combined with other offers. No substitutions, transfer rights, or cash equivalents will be given. We reserve the right to modify or discontinue promotion at any time. We reserve the right to change product price or shipping charge at any time. Offer valid only on pompills.com/fsin or 1-888-POM-PILL. Discount code is not valid on POMx Trio.

[1] pompills.com/research [2] These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure or prevent any disease. [3] 45 men with rising PSA after surgery or radiotherapy drank 8oz 100% pomegranate juice daily for two years. [4] 45 patients with coronary heart disease and myocardial ischemia (insufficient blood flow to the heart) drank 8oz 100% pomegranate juice daily for three months. [5] Study measured intima-media thickness (IMT), which increases plaque buildup in the carotid artery [6] 19 patients aged 65-75 years with severe atherosclerosis drank 8oz 100% pomegranate juice daily for one year. ©2010 PomWonderful LLC. All rights reserved. POM Wonderful, POMx and "antioxidant superpill" are trademarks of PomWonderful LLC. PP2815

POM WONDERFUL®

Exhibit K

The Antioxidant Superpower. - (CX0314_0006)

462. Complaint Counsel claim that, on September 9, 2008, POM ran an advertisement with the headline "The Antioxidant Superpower." with this body copy:

> What's it like to have a personal superhero? Find out by drinking delicious and refreshing POM Wonderful 100% Pomegranate Juice. It has more naturally occurring antioxidants than other drinks. Antioxidants fight free radicals, villainous little molecules that may cause premature aging, heart disease, stroke, Alzheimer's, even cancer. All you need is eight ounces to save the day. Every day.
>
> **The Antioxidant Superpower 100% Pure Pomegranate Juice.**

(CX0314_0006).

463. Complaint Counsel failed to present any other definitive information regarding this ad's dissemination.

464. Complaint Counsel failed to present any evidence that Respondents would run this ad in the future, let alone whether it is probable they would do so.

465. Complaint Counsel's assertion that the ad conveys the message that (a) POM Juice "prevents," "treats," or "reduces the risk" of heart disease or prostate cancer; or (b) POM Juice is "clinically proven" to "prevent," "treat," or "reduce the risk" of heart disease or prostate cancer is not conspicuous, self-evident, or reasonably clear from the face of the ad. (CX0314_0006).

466. Consequently, because the above-referenced challenged implied claim may not be determined with confidence from the face of the ad, extrinsic evidence must be examined.

467. The overall net impression of this ad is not that (a) drinking eight ounces of POM Juice prevents, treats or reduces the risk of certain diseases, such as heart disease or prostate cancer; or (b) drinking eight ounces of POM Juice is "clinically proven" to prevent, treat or reduce the risk of certain diseases, such as heart disease or prostate cancer. (CX0314_0006). Even the language of the ad itself uses the qualifier "may cause." (CX0314_0006).

468. To the extent a "reduce the risk" claim can be implied from ad, the overall net impression is not that drinking eight ounces of POM Juice "reduces the risk" of certain diseases, such as heart disease or prostate cancer, like a drug with a single target of action, but "reduces the risk," like a healthy diet of fruits and vegetables and exercise "reduces the risk" of disease. (CX0314_0006).

469. To the extent a "treat" claim can be implied from this ad (which it cannot), the overall net impression of any ad is not that POM Juice is a substitute for conventional medical treatment. (Butters, Tr. 2821-22).

470. To the extent a "proven" claim can be implied from this ad (which it cannot), the overall impression of this ad is not that POM Juice is "proven" to be 100% effective in preventing, treating or reducing the risk of heart disease or prostate cancer because (1) all of the qualifying language contradicts an implied "clinically proven" interpretation, and (2) "proven" in science means the "average person in the study benefitted," not that "everyone in the study necessarily benefitted." (Heber, Tr. 2011; Butters, Tr. 2893-2894; PX0361 (Sacks, Dep. at 81)).

471. Mrs. Resnick testified that the term "Antioxidant Superpower," means that POM Juice is full of polyphenol antioxidants and that when tested against orange, blueberry and cranberry juice and green tea and many other juices, POM Juice is the most impressive in polyphenol antioxidants. (CX1375 (L. Resnick, Dep. at 85-86)).

472. Professor Butters concluded that POM's ads in general depend on parody, exaggeration and humor to bring their message to the potential consumer; including the following messages: 1) POM is the best pomegranate that anyone can buy; 2) POM Juice is healthy; 3) POM Juice is tasty; 4) POM Juice is arguably the best source of antioxidants of any of the comparable beverages available; 5) medical research has suggested that antioxidants combat free radicals, which are unhealthy, and may contribute to diseases of the heart, arteries, and prostate, as well as erectile dysfunction; and 6) POM also offers concentrated forms of pomegranate extract for those who wish to ingest antioxidants in even more concentrated form than pomegranate juice itself. (PX0158-0033).

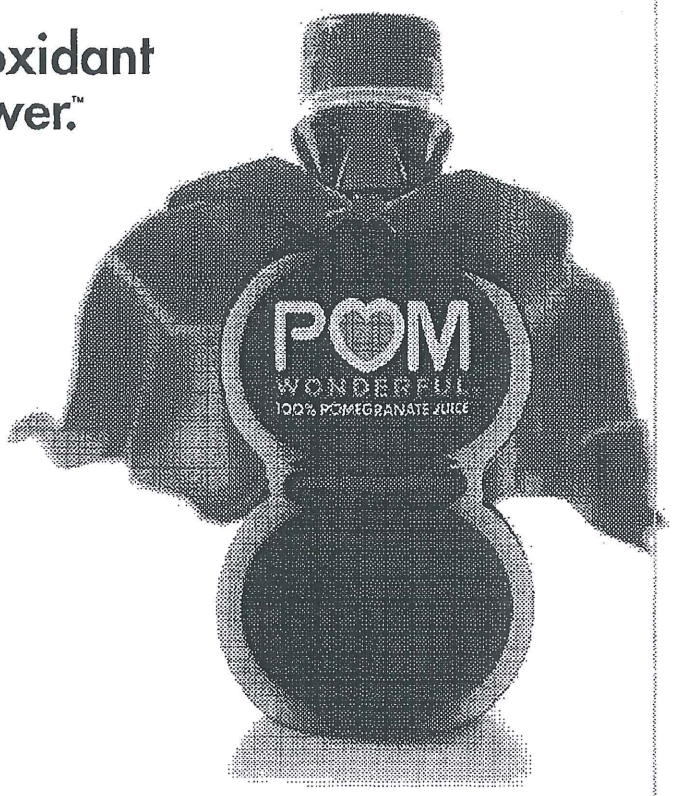
473. Viewing the "The Antioxidant Superpower" ad as a whole, including the interaction of the words and visual imagery, the overall net impression of the ad is the ad is humorous and that POM Juice has antioxidants. ((PX0158-0033); (CX1375 (L. Resnick, Dep. at 85-86))).

474. Complaint Counsel presented no extrinsic evidence or expert opinion on this ad's meaning, consumer perceptions of this ad, or consumer interpretations regarding this ad. (PX0357 (Stewart, Dep. at 49, 52)).

475. Complaint Counsel failed to present any evidence that the claims in this ad reasonably convey that the Challenged Products are "clinically proven" to prevent, treat or reduce the risk of heart disease, prostate cancer or erectile dysfunction.

476. Complaint Counsel failed to present any evidence regarding the number of exposures consumers had to this ad or any particular POM advertisement. (Mazis, Tr. 2752).

The Antioxidant Superpower.™



What's it like to have a personal superhero? Find out by drinking delicious and refreshing POM Wonderful® 100% Pomegranate Juice. It has more naturally occurring antioxidants than other drinks. Antioxidants fight free radicals, villainous little molecules that may cause premature aging, heart disease, stroke, Alzheimer's, even cancer. All you need is eight ounces to save the day. Every day.

POM WONDERFUL
pomwonderful.com

The Antioxidant Superpower. 100% Pure Pomegranate Juice.

PJ9745_POM time wrap_F.indd 4 9/10/08 9:24:19 AM

JOB NO.: PJ9745	TRIM: 7.875"x10.5"	COLOR: 4/C PROS	DATE IN: 08-25-08
PROJECT: NY Times Magazine Wrap	LIVE: 7.125" x 9.75"	LIVE, TRIM, BLEED (DO NOT PRINT)	DATE OUT: 09-09-08
SCALE: 1 : 1	BLEED: 8.375" x 11"	PRINTOUT SIZE: 100%	PROOF ROUND: F

The First Bottle You Should Open In 2010 - (CX0337)

477. Complaint Counsel claim that on January 3, 2010, POM ran an advertisement with the headline "The First Bottle You Should Open In 2010" with the body copy that appears on CX0337_0001.

478. Complaint Counsel failed to present any other definitive information regarding this ad's dissemination.

479. Complaint Counsel failed to present any evidence that Respondents would run this ad in the future, let alone whether it is probable they would do so.

480. Complaint Counsel's expert, Professor Mazis, testified that Complaint Counsel is not challenging POM's ads for POM Juice that ran after December 2008. (Mazis, Tr. 2753-54). Accordingly, based on these representations, Complaint Counsel cannot now challenge this ad.

481. Nowhere in this ad do Respondents expressly (*i.e.*, unequivocally and directly) state that (a) taking one POMx Pill per day "prevents," "treats," or "reduces the risk" of heart disease or prostate cancer; or (b) taking one POMx Pill per day is "clinically proven" to "prevent," "treat," or "reduce the risk" of heart disease or prostate cancer. (CX0337_0001).

482. Complaint Counsel's assertion that the ad conveys the message that (a) taking one POMx Pill per day "prevents," "treats," or "reduces the risk" of heart disease or prostate cancer; or (b) taking one POMx Pill per day is "clinically proven" to "prevent," "treat," or "reduce the risk" of heart disease or prostate cancer is not conspicuous, self-evident, or reasonably clear from the face of the ad. (CX0337_0001).

483. Consequently, because the above-referenced challenged implied claim may not be determined with confidence from the face of the ad, extrinsic evidence must be examined.

484. The overall net impression of this ad is not that not that taking one POMx Pill per day prevents, treats or reduces the risk of certain diseases, such as heart disease or prostate cancer; or (b) taking one POMx Pill per day is "clinically proven" to prevent, treat or reduce the risk of certain diseases, such as heart disease or prostate cancer. (CX0337_0001). Even the language of the ad itself uses such qualifiers as "emerging science suggests," "help protect," "promising results," "initial UCLA study," "hopeful results" and "preliminary studies." (CX0337_0001).

485. To the extent a "reduce the risk" claim can be implied from this ad, the overall net impression is not that taking one POMx Pill per day "reduces the risk" of certain diseases, such as heart disease or prostate cancer, like a drug with a single target of action, but "reduces the risk," like a healthy diet of fruits and vegetables and exercise "reduces the risk" of disease. (CX0337_0001).

486. To the extent a "treat" claim can be implied from this ad (which it cannot), the overall net impression of any ad is not that POMx Pills are a substitute for conventional medical treatment. (Butters, Tr. 2821-22; Appendix of Advertisements).

487. To the extent a "proven" claim can be implied from this ad (which it cannot), the overall impression of this ad is not that POMx Pills are "proven" to be 100% effective in preventing, treating or reducing the risk of heart disease or prostate cancer because (1) all of the qualifying language contradicts an implied "clinically proven" interpretation, and (2) "proven" in science means the "average person in the study benefitted," not that "everyone in the study necessarily benefitted." (Heber, Tr. 2011; Butters, Tr. 2893-2894; PX0361 (Sacks, Dep. at 81)).

488. Professor Butters testified that this ad employs parody; it is a parody on "the self-importance of POMx itself," that POMx Pills "should be the first bottle you open" and that POMx Pills are "as important as champagne on New Year's." (PX0350 (Butters, Dep. at 141)).

489. Professor Butters concluded that POM's ads in general depend on parody, exaggeration and humor to bring their message to the potential consumer; including the following messages: 1) POM is the best pomegranate that anyone can buy; 2) POM Juice is healthy; 3) POM Juice is tasty; 4) POM Juice is arguably the best source of antioxidants of any of the comparable beverages available; 5) medical research has suggested that antioxidants combat free radicals, which are unhealthy, and may contribute to diseases of the heart, arteries, and prostate, as well as erectile dysfunction; and 6) POM also offers concentrated forms of pomegranate extract for those who wish to ingest antioxidants in even more concentrated form than pomegranate juice itself. (PX0158-0033).

490. Viewing the "The First Bottle You Should Open In 2010" ad as a whole, including the interaction of the words and visual imagery, the overall net impression of the ad is that it is a humorous ad and that POMx Pills are healthy. (PX0350 (Butters, Dep. at 141); (PX0158-0033)).

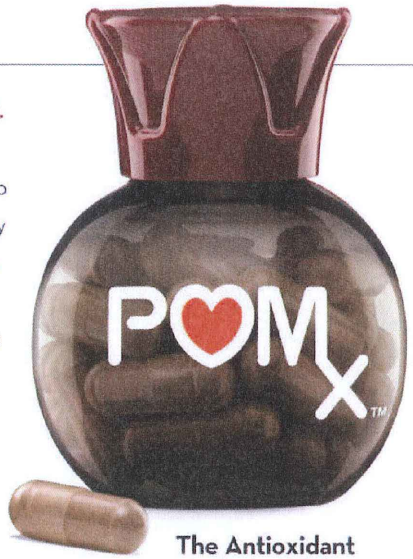
491. Complaint Counsel presented no extrinsic evidence or expert opinion on this ad's meaning, consumer perceptions of this ad, or consumer interpretations regarding this ad. (PX0357 (Stewart, Dep. at 49, 52)).

492. Complaint Counsel failed to present any evidence that the claims in this ad reasonably convey that the Challenged Products are "clinically proven" to prevent, treat or reduce the risk of heart disease, prostate cancer or erectile dysfunction.

493. Complaint Counsel failed to present any evidence regarding the number of exposures consumers had to this ad or any particular POM advertisement. (Mazis, Tr. 2752).

VMS ID: 100101214
RUN DATE: 01/03/2010

THE FIRST BOTTLE YOU SHOULD OPEN IN 2010.



The Antioxidant Superpill.™

2010, Year of the Antioxidant.

Emerging science suggests that antioxidants are critically important to maintaining good health because they protect you from free radicals, which can damage your body. Taking one POMx pill a day will help protect you from free radicals and keep you at your healthy best. Make it your first New Year's resolution.

The antioxidant power of our 8oz juice.

POMx: Ultra-potent. Hangover-free.

POMx is an all-natural, ultra-potent antioxidant extract. Containing a full spectrum of pomegranate polyphenols, POMx is so concentrated that a single capsule has the antioxidant power of a full glass of POM Wonderful® 100% Pomegranate Juice.

$32 million in medical research. Cheers.

POMx is made from the only pomegranates backed by $32 million in medical research at the world's leading universities.

Not only has this research documented the unique and superior antioxidant power of pomegranates, it has revealed promising results for prostate and cardiovascular health.

Our bottle. Your health.

Our POMx pills are made from the same pomegranates we use to make our POM Wonderful 100% Pomegranate Juice, on which each of the following medical studies was conducted.

An initial UCLA study on our juice found hopeful results for prostate health, reporting "statistically significant prolongation of PSA doubling times," according to Dr. Allen J. Pantuck in *Clinical Cancer Research*, '06.[1,2,3]

Two additional preliminary studies on our juice showed promising results for heart health. "Stress-induced ischemia (restricted blood flow to the heart) decreased in the pomegranate group," Dr. Dean Ornish reported in the *American Journal of Cardiology*, '05.[1,2,4]

"Pomegranate juice consumption resulted in significant reduction in IMT[5] (thickness of arterial plaque) by up to 30% after one year," said Dr. Michael Aviram, in *Clinical Nutrition*, '04.[1,2,5,6]

Try POMx Monthly FREE for ONE MONTH.
We'll even pay for the shipping.*

Order Now: 888-766-7455 or pompills.com/n3
Use discount code: N330

*SIGN UP FOR POMx MONTHLY, AND WE'LL SEND YOUR FIRST BOTTLE FREE. AFTER THAT, YOU'LL CONTINUE TO RECEIVE MONTHLY SHIPMENTS FOR $29.95 WITH COMPLIMENTARY SHIPPING. Offer expires 3/31/10 and applies only to the purchase price for the first bottle of POMx Monthly. Following months will be $29.95 per bottle. One discount per customer. Cannot be combined with other offers. No substitutions, transfer rights or cash equivalents. We reserve the right to discontinue this promotion, change product price or shipping charge at any time. Valid only at pompills.com or 1-888-766-7455. Not valid on POMx Trial or other POM products.

POM WONDERFUL®

[1]pompills.com/research [2]These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure or prevent any disease. [3]46 men with rising PSA after surgery or radiotherapy drank 8oz 100% pomegranate juice daily for two years. [4]45 patients with coronary heart disease and myocardial ischemia drank 8oz 100% pomegranate juice daily for three months. [5]Study measured intima-media thickness (IMT). [6]19 patients aged 65-75 years with severe atherosclerosis drank 8oz 100% pomegranate juice daily for one year.

VMS-0000304

CX0337_0001

The Only Antioxidant Supplement Rated X - (CX0351)

494. Complaint Counsel claim that on June 1, 2010, POM ran an advertisement with the headline "The Only Antioxidant Supplement Rated X" with the body copy that appears on CX0351_0001.

495. Complaint Counsel failed to present any other definitive information regarding this ad's dissemination.

496. Complaint Counsel failed to present any evidence that Respondents would run this ad in the future, let alone whether it is probable they would do so.

497. Complaint Counsel's expert, Professor Mazis, testified that Complaint Counsel is not challenging POM's ads for POM Juice that ran after December 2008. (Mazis, Tr. 2753-54). Accordingly, based on these representations, Complaint Counsel cannot now challenge this ad.

498. Nowhere in this ad do Respondents expressly (*i.e.*, unequivocally and directly) state that (a) taking one POMx Pill per day "prevents," "treats," or "reduces the risk" of heart disease, prostate cancer or erectile dysfunction; or (b) taking one POMx Pill per day is "clinically proven" to "prevent," "treat," or "reduce the risk" of heart disease, prostate cancer or erectile dysfunction. (CX0351_0001).

499. Complaint Counsel's assertion that the ad conveys the message that (a) taking one POMx Pill per day "prevents," "treats," or "reduces the risk" of heart disease, prostate cancer or erectile dysfunction; or (b) taking one POMx Pill per day is "clinically proven" to "prevent," "treat," or "reduce the risk" of heart disease, prostate cancer or erectile dysfunction is not conspicuous, self-evident, or reasonably clear from the face of the ad. (CX0351_0001).

500. Consequently, because the above-referenced challenged implied claim may not be determined with confidence from the face of the ad, extrinsic evidence must be examined.

501. The overall net impression of this ad is not that not that taking one POMx Pill per day prevents, treats or reduces the risk of certain diseases, such as heart disease, prostate cancer or erectile dysfunction; or (b) taking one POMx Pill per day is "clinically proven" to prevent, treat or reduce the risk of certain diseases, such as heart disease, prostate cancer or erectile dysfunction. (CX0351_0001). Even the language of the ad itself uses such qualifiers as "emerging science suggests," "help protect," "promising results," "initial UCLA study," "potential," "hopeful results" and "preliminary study." (CX0351_0001).

502. To the extent a "reduce the risk" claim can be implied from this ad, the overall net impression is not that taking one POMx Pill per day "reduces the risk" of certain diseases, such as heart disease, prostate cancer or erectile dysfunction, like a drug with a single target of action, but "reduces the risk," like a healthy diet of fruits and vegetables and exercise "reduces the risk" of disease. (CX0351_0001).

503. To the extent a "treat" claim can be implied from this ad (which it cannot), the overall net impression of any ad is not that POMx Pills are a substitute for conventional medical treatment. (Butters, Tr. 2821-22; Appendix of Advertisements).

504. To the extent a "proven" claim can be implied from this ad (which it cannot), the overall impression of this ad is not that POMx Pills are "proven" to be 100% effective in preventing, treating or reducing the risk of heart disease, prostate cancer or erectile dysfunction because (1) all of the qualifying language contradicts an implied "clinically proven" interpretation, and (2) "proven" in science means the "average person in the study benefitted," not that "everyone in the study necessarily benefitted." (Heber, Tr. 2011; Butters, Tr. 2893-2894; PX0361 (Sacks, Dep. at 81)).

505. Mrs. Resnick testified the purpose of this ad was "just meant to give you a chuckle." (L. Resnick, Tr. 266-67).

506. Professor Butters' testified that part of his conclusion in his report regarding this POMx Pills ad was that "preliminary initial studies suggest that pomegranate extract, a strong source of antioxidants, could help alleviate erectile dysfunction." (Butters, Tr. 2943).

507. Professor Butters concluded that POM's ads in general depend on parody, exaggeration and humor to bring their message to the potential consumer; including the following messages: 1) POM is the best pomegranate that anyone can buy; 2) POM Juice is healthy; 3) POM Juice is tasty; 4) POM Juice is arguably the best source of antioxidants of any of the comparable beverages available; 5) medical research has suggested that antioxidants combat free radicals, which are unhealthy, and may contribute to diseases of the heart, arteries, and prostate, as well as erectile dysfunction; and 6) POM also offers concentrated forms of pomegranate extract for those who wish to ingest antioxidants in even more concentrated form than pomegranate juice itself. (PX0158-0033).

508. Viewing the "The Only Antioxidant Supplement Rated X" ad as a whole, including the interaction of the words and visual imagery, the overall net impression of the ad is that it is a humorous ad, that POMx Pills are healthy and that they may help with erectile dysfunction. ((L. Resnick, Tr. 266-67); (PX0350 (Butters, Dep. at 141); (PX0158-0033)).

509. Complaint Counsel presented no extrinsic evidence or expert opinion on this ad's meaning, consumer perceptions of this ad, or consumer interpretations regarding this ad. (PX0357 (Stewart, Dep. at 49, 52)).

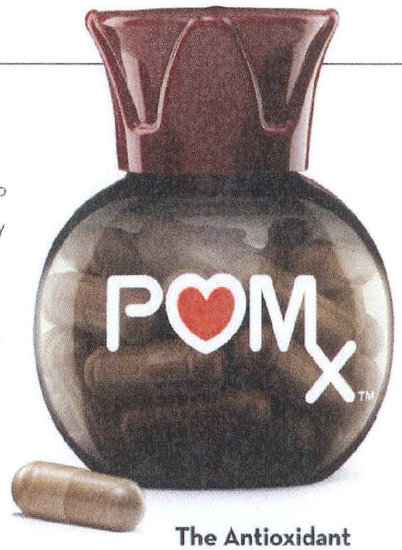
510. Complaint Counsel failed to present any evidence that the claims in this ad reasonably convey that the Challenged Products are "clinically proven" to prevent, treat or reduce the risk of heart disease, prostate cancer or erectile dysfunction.

511. Complaint Counsel failed to present any evidence regarding the number of exposures consumers had to this ad or any particular POM advertisement. (Mazis, Tr. 2752).

VMS ID: 100600955
RUN DATE: 06/01/2010

THE ONLY ANTIOXIDANT SUPPLEMENT RATED X.

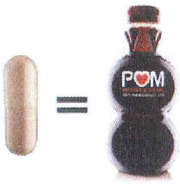
FREE SHIPPING!



The Antioxidant Superpill.™

Always use protection.

Emerging science suggests that antioxidants are critically important to maintaining good health because they protect you from free radicals, which can damage your body. Taking one POMx pill a day will help protect you from free radicals and keep you at your healthy best.



The antioxidant power of our 8oz juice.

POMx. Super-potent. Like you.

POMx is an all-natural, ultra-potent antioxidant extract. Containing a full spectrum of pomegranate polyphenols, POMx is so concentrated that a single capsule has the anti-oxidant power of a full glass of POM Wonderful® 100% Pomegranate Juice.

$32 million in research. We're not just playing doctor.

POMx is made from the only pomegranates backed by $32 million in medical research at the world's leading universities. Not only has this research documented the unique and superior antioxidant power of pomegranates, it has revealed promising results for erectile, prostate and cardiovascular health.

Is that POMx in your pocket?

Our POMx pills are made from the same pomegranates we use to make our POM Wonderful 100% Pomegranate Juice, on which each of the following medical studies was conducted.

In a preliminary study on erectile function, men who consumed POM Juice reported a 50% greater likelihood of improved erections as compared to placebo. "As a powerful antioxidant, enhancing the actions of nitric oxide in vascular endothelial cells, POM has potential in the management of ED... further studies are warranted." *International Journal of Impotence Research*, '07.[1,2,3]

An initial UCLA study on our juice found hopeful results for prostate health, reporting "statistically significant prolongation of PSA doubling times." *Clinical Cancer Research*, '06.[1,2,4]

A preliminary study on our juice showed promising results for heart health. "Stress-induced ischemia (restricted blood flow to the heart) decreased in the pomegranate group." *American Journal of Cardiology*, '05.[1,2,5]

Try POMx Pills FREE FOR ONE MONTH

when you sign up for POMx Monthly delivery.*
(cancel anytime)

Order Now: 888-766-7455
or pompills.com/adv Use discount code: ADV30

*SIGN UP FOR POMx MONTHLY, AND WE'LL SEND YOUR FIRST BOTTLE FREE. AFTER THAT, YOU'LL CONTINUE TO RECEIVE MONTHLY SHIPMENTS FOR $29.95 WITH COMPLIMENTARY SHIPPING. Offer expires 9/30/10 and applies only to the purchase price for the first bottle of POMx Monthly. Following months will be $29.95 per bottle. One discount per customer. Cannot be combined with other offers. No substitutions, transfer rights or cash equivalents. We reserve the right to modify or discontinue this promotion or change the product price or change the shipping charge at any time. Valid only at pompills.com or 1-888-766-7455. Not valid on POMx Trial or other POM products. Credit or debit card required.

POM WONDERFUL®

[1] pompills.com/research. [2] These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure or prevent any disease. [3] 53 men with mild/moderate erectile dysfunction drank 8oz 100% pomegranate juice daily for one month. [4] 46 men with rising PSA after surgery or radiotherapy drank 8oz 100% pomegranate juice daily for two years. [5] 45 patients with coronary heart disease and myocardial ischemia drank 8oz 100% pomegranate juice daily for three months. PP3423

VMS-0000319

CX0351_0001

The Only Antioxidant Supplement Rated X - (CX0355)

512. Complaint Counsel claim that on July1, 2010, POM ran an advertisement with the headline "The Only Antioxidant Supplement Rated X" with the body copy that appears on CX0355_0001.

513. Complaint Counsel failed to present any other definitive information regarding this ad's dissemination.

514. Complaint Counsel failed to present any evidence that Respondents would run this ad in the future, let alone whether it is probable they would do so.

515. Complaint Counsel's expert, Professor Mazis, testified that Complaint Counsel is not challenging POM's ads for POM Juice that ran after December 2008. (Mazis, Tr. 2753-54). Accordingly, based on these representations, Complaint Counsel cannot now challenge this ad.

516. Nowhere in this ad do Respondents expressly (*i.e.*, unequivocally and directly) state that (a) taking one POMx Pill per day "prevents," "treats," or "reduces the risk" of heart disease, prostate cancer or erectile dysfunction; or (b) taking one POMx Pill per day is "clinically proven" to "prevent," "treat," or "reduce the risk" of heart disease, prostate cancer or erectile dysfunction. (CX0355_0001).

517. Complaint Counsel's assertion that the ad conveys the message that (a) taking one POMx Pill per day "prevents," "treats," or "reduces the risk" of heart disease, prostate cancer or erectile dysfunction; or (b) taking one POMx Pill per day is "clinically proven" to "prevent," "treat," or "reduce the risk" of heart disease, prostate cancer or erectile dysfunction is not conspicuous, self-evident, or reasonably clear from the face of the ad. (CX0355_0001).

518. Consequently, because the above-referenced challenged implied claim may not be determined with confidence from the face of the ad, extrinsic evidence must be examined.

519. The overall net impression of this ad is not that not that taking one POMx Pill per day prevents, treats or reduces the risk of certain diseases, such as heart disease, prostate cancer or erectile dysfunction; or (b) taking one POMx Pill per day is "clinically proven" to prevent, treat or reduce the risk of certain diseases, such as heart disease, prostate cancer or erectile dysfunction. (CX0355_0001). Even the language of the ad itself uses such qualifiers as "emerging science suggests," "help protect," "promising results," "initial UCLA study," "potential," "hopeful results" and "preliminary study." (CX0355_0001).

520. To the extent a "reduce the risk" claim can be implied from this ad, the overall net impression is not that taking one POMx Pill per day "reduces the risk" of certain diseases, such as heart disease, prostate cancer or erectile dysfunction, like a drug with a single target of action, but "reduces the risk," like a healthy diet of fruits and vegetables and exercise "reduces the risk" of disease. (CX0355_0001).

521. To the extent a "treat" claim can be implied from this ad (which it cannot), the overall net impression of any ad is not that POMx Pills are a substitute for conventional medical treatment. (Butters, Tr. 2821-22; Appendix of Advertisements).

522. To the extent a "proven" claim can be implied from this ad (which it cannot), the overall impression of this ad is not that POMx Pills are "proven" to be 100% effective in preventing, treating or reducing the risk of heart disease, prostate cancer or erectile dysfunction because (1) all of the qualifying language contradicts an implied "clinically proven" interpretation, and (2) "proven" in science means the "average person in the study benefitted," not that "everyone in the study necessarily benefitted." (Heber, Tr. 2011; Butters, Tr. 2893-2894; PX0361 (Sacks, Dep. at 81)).

523. Mrs. Resnick testified the purpose of this ad was "just meant to give you a chuckle." (L. Resnick, Tr. 266-67).

524. Professor Butters' testified that part of his conclusion in his report regarding this POMx Pills ad was that "preliminary initial studies suggest that pomegranate extract, a strong source of antioxidants, could help alleviate erectile dysfunction." (Butters, Tr. 2943).

525. Professor Butters concluded that POM's ads in general depend on parody, exaggeration and humor to bring their message to the potential consumer; including the following messages: 1) POM is the best pomegranate that anyone can buy; 2) POM Juice is healthy; 3) POM Juice is tasty; 4) POM Juice is arguably the best source of antioxidants of any of the comparable beverages available; 5) medical research has suggested that antioxidants combat free radicals, which are unhealthy, and may contribute to diseases of the heart, arteries, and prostate, as well as erectile dysfunction; and 6) POM also offers concentrated forms of pomegranate extract for those who wish to ingest antioxidants in even more concentrated form than pomegranate juice itself. (PX0158-0033).

526. Viewing the "The Only Antioxidant Supplement Rated X" ad as a whole, including the interaction of the words and visual imagery, the overall net impression of the ad is that it is a humorous ad, that POMx Pills are healthy and that they may help with erectile dysfunction. ((L. Resnick, Tr. 266-67); (PX0350 (Butters, Dep. at 141); (PX0158-0033)).

527. Complaint Counsel presented no extrinsic evidence or expert opinion on this ad's meaning, consumer perceptions of this ad, or consumer interpretations regarding this ad. (PX0357 (Stewart, Dep. at 49, 52)).

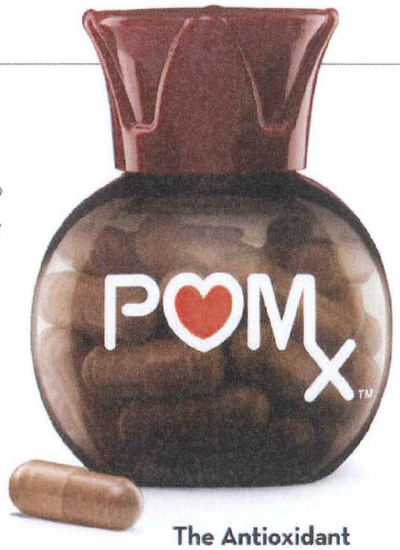
528. Complaint Counsel failed to present any evidence that the claims in this ad reasonably convey that the Challenged Products are "clinically proven" to prevent, treat or reduce the risk of heart disease, prostate cancer or erectile dysfunction.

529. Complaint Counsel failed to present any evidence regarding the number of exposures consumers had to this ad or any particular POM advertisement. (Mazis, Tr. 2752).

VMS ID: 100700683
RUN DATE: 07/01/2010

THE ONLY ANTIOXIDANT SUPPLEMENT RATED X.

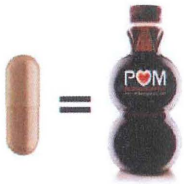
FREE SHIPPING!



The Antioxidant Superpill.™

Always use protection.

Emerging science suggests that antioxidants are critically important to maintaining good health because they protect you from free radicals, which can damage your body. Taking one POMx pill a day will help protect you from free radicals and keep you at your healthy best.



The antioxidant power of our 8oz juice.

POMx. Super-potent. Like you.

POMx is an all-natural, ultra-potent antioxidant extract. Containing a full spectrum of pomegranate polyphenols, POMx is so concentrated that a single capsule has the anti-oxidant power of a full glass of POM Wonderful® 100% Pomegranate Juice.

$34 million in research. We're not just playing doctor.

POMx is made from the only pomegranates backed by $34 million in medical research at the world's leading universities. Not only has this research documented the unique and superior antioxidant power of pomegranates, it has revealed promising results for erectile, prostate and cardiovascular health.

Is that POMx in your pocket?

Our POMx pills are made from the same pomegranates we use to make our POM Wonderful 100% Pomegranate Juice, on which each of the following medical studies was conducted.

In a preliminary study on erectile function, men who consumed POM Juice reported a 50% greater likelihood of improved erections as compared to placebo. "As a powerful antioxidant, enhancing the actions of nitric oxide in vascular endothelial cells, POM has potential in the management of ED... further studies are warranted." *International Journal of Impotence Research*, '07. [1,2,3]

An initial UCLA study on our juice found hopeful results for prostate health, reporting "statistically significant prolongation of PSA doubling times." *Clinical Cancer Research*, '06. [1,2,4]

A preliminary study on our juice showed promising results for heart health. "Stress-induced ischemia (restricted blood flow to the heart) decreased in the pomegranate group." *American Journal of Cardiology*, '05. [1,2,5]

Try POMx Monthly FREE for ONE MONTH

We'll even pay for the shipping.*

Order Now: 888-766-7455 or pompills.com/ga Use discount code: GA30

*SIGN UP FOR POMx MONTHLY, AND WE'LL SEND YOUR FIRST BOTTLE FREE. AFTER THAT, YOU'LL CONTINUE TO RECEIVE MONTHLY SHIPMENTS FOR $29.95 WITH COMPLIMENTARY SHIPPING. Offer expires 9/30/10 and applies only to the purchase price for the first bottle of POMx Monthly. Following months will be $29.95 per bottle. One discount per customer. Cannot be combined with other offers. No substitutions, transfer rights or cash equivalents. We reserve the right to modify or discontinue this promotion, change the product price or change the shipping charge at any time. Valid only at pompills.com or 1-888-766-7455. Not valid on POMx Trial or other POM products. Credit or debit card required.

POM WONDERFUL®

[1] pompills.com/research. [2] These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure or prevent any disease. [3] 53 men with mild/moderate erectile dysfunction drank 8oz 100% pomegranate juice daily for one month. [4] 46 men with rising PSA after surgery or radiotherapy drank 8oz 100% pomegranate juice daily for two years. [5] 45 patients with coronary heart disease and myocardial ischemia drank 8oz 100% pomegranate juice daily for three months.

VMS-0000323

CX0355_0001

The power of POM, in one little pill - (CX0169; CX1426_0045 Exh. L)

530. Complaint Counsel claim that, on January 6, 2008, POM ran an advertisement with the headline "The power of POM, in one little pill" with the body copy that appears on CX0169_0001.

531. CX1426_0045, Exh. L appears to be identical to CX0169_0001. (CX1426_0045, Exh. L; CX0169_0001).

532. Complaint Counsel failed to present any other definitive information regarding this ad's dissemination.

533. Complaint Counsel failed to present any evidence that Respondents would run this ad in the future, let alone whether it is probable they would do so.

534. This ad cannot provide a basis for injunctive relief because (a) it ran five years ago; and (b) no evidence exists to show that Respondents are likely to run this ad in the future.

535. Nowhere in this ad do Respondents expressly (*i.e.*, unequivocally and directly) state that (a) taking one POMx Pill per day "prevents," "treats," or "reduces the risk" of heart disease or prostate cancer; or (b) taking one POMx Pill per day is "clinically proven" to "prevent," "treat," or "reduce the risk" of heart disease or prostate cancer. (CX1426_0045, Exh. L; CX0169_0001).

536. Complaint Counsel's assertion that the ad conveys the message that (a) taking one POMx Pill per day "prevents," "treats," or "reduces the risk" of heart disease or prostate cancer; or (b) taking one POMx Pill per day is "clinically proven" to "prevent," "treat," or "reduce the risk" of heart disease or prostate cancer is not conspicuous, self-evident, or reasonably clear from the face of the ad. (CX1426_0045, Exh. L; CX0169_0001).

537. Consequently, because the above-referenced challenged implied claim may not be determined with confidence from the face of the ad, extrinsic evidence must be examined.

538. The overall net impression of this ad is not that not that taking one POMx Pill per day prevents, treats or reduces the risk of certain diseases, such as heart disease or prostate cancer; or (b) taking one POMx Pill per day is "clinically proven" to prevent, treat or reduce the risk of certain diseases, such as heart disease or prostate cancer. (CX1426_0045, Exh. L; CX0169_0001). Even the language of the ad itself uses such qualifiers as "emerging science suggests," "contributing," "fights," "initial UCLA MEDICAL STUDY," "hopeful results," "preliminary studies" and "pilot research suggests." (CX1426_0045, Exh. L; CX0169_0001).

539. To the extent a "reduce the risk" claim can be implied from this ad, the overall net impression is not that taking one POMx Pill per day "reduces the risk" of certain diseases, such as heart disease or prostate cancer, like a drug with a single target of action, but "reduces the risk," like a healthy diet of fruits and vegetables and exercise "reduces the risk" of disease. (CX1426_0045, Exh. L; CX0169_0001).

540. To the extent a "treat" claim can be implied from this ad (which it cannot), the overall net impression of any ad is not that POMx Pills are a substitute for conventional medical treatment. (Butters, Tr. 2821-22; Appendix of Advertisements).

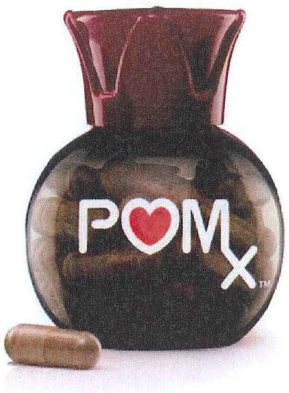
541. To the extent a "proven" claim can be implied from this ad (which it cannot), the overall impression of this ad is not that POMx Pills are "proven" to be 100% effective in preventing, treating or reducing the risk of heart disease or prostate cancer because (1) all of the qualifying language contradicts an implied "clinically proven" interpretation, and (2) "proven" in science means the "average person in the study benefitted," not that "everyone in the study necessarily benefitted." (Heber, Tr. 2011; Butters, Tr. 2893-2894; PX0361 (Sacks, Dep. at 81)).

542. Complaint Counsel presented no extrinsic evidence or expert opinion on this ad's meaning, consumer perceptions of this ad, or consumer interpretations regarding this ad. (PX0357 (Stewart, Dep. at 49, 52)).

543. Complaint Counsel failed to present any evidence that the claims in this ad reasonably convey that the Challenged Products are "clinically proven" to prevent, treat or reduce the risk of heart disease, prostate cancer or erectile dysfunction.

544. Complaint Counsel failed to present any evidence regarding the number of exposures consumers had to this ad or any particular POM advertisement. (Mazis, Tr. 2752).

VMS ID: 080106753
RUN DATE: 01/06/2008



The power of POM, in one little pill.

The easy, portable, calorie-free way to get your daily antioxidants.

Antioxidant Superpill.™ Not all antioxidants are created equal. POMx™ fights free radicals with a mighty 1000mg in every pill. That's more concentrated antioxidants than any other pomegranate antioxidant supplement. There are antioxidants, and then there are POMx antioxidants.

Peace of Mind in a Pill. POMx is a highly concentrated, powerful blend of polyphenol antioxidants made from the very same pomegranates as POM Wonderful® 100% Pomegranate Juice. The same pomegranates we grow exclusively in California, where they're hand-picked on site.

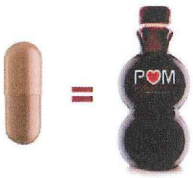
Safe and Natural. POMx is made from pure pomegranates. So there are no added sugars, preservatives or any other ingredients – just 100% pomegranate polyphenol antioxidants. So naturally, POMx is absorbed safely into your body. In fact, POMx is the first and only antioxidant supplement reviewed for safety by the FDA.

Backed by Science. POMx is made from the only pomegranates supported by $23 million in medical research. Emerging science suggests that free radicals aggressively destroy healthy cells in your body – contributing to premature aging and even disease. The good news is POM Wonderful pomegranate antioxidants neutralize free radicals. An initial UCLA MEDICAL STUDY on POM Wonderful 100% Pomegranate Juice found *hopeful results for prostate health.* "Pomegranate juice delays PSA doubling time in humans," according to AJ Pantuck, et al, in Clinical Cancer Research, 2006.[1,2,3] Two additional preliminary studies on our juice showed *promising results for heart health.* "Pomegranate juice improves myocardial perfusion in coronary heart patients," per D. Ornish, et al, in the American Journal of Cardiology, 2005.[1,2,4] "Pomegranate juice pilot research suggests anti-atherosclerosis benefits," according to M. Aviram, et al, in Clinical Nutrition, 2004.[1,2,5]

California-grown.

One a Day, For Life. Ready to take on free radicals? A daily POMx pill is all you need. Invest in your health and order your 30-day supply today. Call now to get your first monthly shipment.

Call 1-888-POM-PILL (766-7455) or visit pompills.com/nb and enter NB30 at checkout.



The antioxidant power of our 8 oz. juice.

Reviewed for Safety by the FDA.

100% Natural Pomegranate Extract.

Try POMx for one month – FREE!

We'll even pay for the shipping. Visit pompills.com/nb or call 1-888-POM-PILL. Use discount code: NB30

SIGN UP FOR POMx MONTHLY, AND WE'LL SEND YOUR FIRST BOTTLE FREE. AFTER THAT, YOU'LL CONTINUE TO RECEIVE MONTHLY SHIPMENTS FOR $29.95 WITH COMPLIMENTARY SHIPPING. Offer expires April 15, 2008. The first month free plus free shipping offer applies only to the purchase price for the first month of POMx Monthly. Following months will be $29.95 per bottle. This discount can only be used on POMx products. One discount per customer. Cannot be combined with other offers. No substitutions, transfer rights or cash equivalents will be given. We reserve the right to modify or discontinue this promotion at any time. We reserve the right to change product price or shipping charge at any time. Offer valid only at pompills.com/nb or 1-888-POM-PILL. Discount code is not valid on POMx trial.

[1] pompills.com/research [2] These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure or prevent any disease. [3] 45 men with rising PSA after surgery or radiotherapy drank 8 oz. 100% pomegranate juice daily for two years. [4] 45 patients with coronary heart disease and myocardial ischemia drank 8 oz. 100% pomegranate juice daily for three months. [5] 19 patients aged 65-75 years with severe atherosclerosis drank 8 oz. 100% pomegranate juice daily for one year.

POM WONDERFUL®

VMS-0000255

CX0169_0001

New York Times Magazine
Issue: January 6th, 2008
In Home: 1/6/08

The easy, portable, calorie-free way to get your daily antioxidants.

The power of POM, in one little pill.

Antioxidant Superpill.™ Not all antioxidants are created equal. POMx™ fights free radicals with a mighty 1000mg in every pill. That's more concentrated antioxidants than any other pomegranate antioxidant supplement. There are antioxidants, and then there are POMx antioxidants.

Peace of Mind in a Pill. POMx is a highly concentrated, powerful blend of polyphenol antioxidants made from the very same pomegranates as POM Wonderful® 100% Pomegranate Juice. The same pomegranates we grow exclusively in California, where they're hand-picked on site.

Safe and Natural. POMx is made from pure pomegranates. So there are no added sugars, preservatives or any other ingredients – just 100% pomegranate polyphenol antioxidants. So naturally, POMx is absorbed safely into your body. In fact, POMx is the first and only antioxidant supplement reviewed for safety by the FDA.

Backed by Science. POMx is made from the only pomegranates supported by $23 million in medical research. Emerging science suggests that free radicals aggressively destroy healthy cells in your body – contributing to premature aging and even disease. The good news is POM Wonderful pomegranate antioxidants neutralize free radicals. An initial UCLA MEDICAL STUDY on POM Wonderful 100% Pomegranate Juice found *hopeful results for prostate health.* "Pomegranate juice delays PSA doubling time in humans," according to AJ Pantuck, et al, in Clinical Cancer Research, 2006.[1,2,3] Two additional preliminary studies on our juice showed *promising results for heart health.* "Pomegranate juice improves myocardial perfusion in coronary heart patients," per D. Ornish, et al, in the American Journal of Cardiology, 2005.[4,5,6] "Pomegranate juice pilot research suggests anti-atherosclerosis benefits," according to M. Aviram, et al, in Clinical Nutrition, 2004.[7,8,9]

California-grown.

One a Day, For Life. Ready to take on free radicals? A daily POMx pill is all you need. Invest in your health and order your 30-day supply today. Call now to get your first monthly shipment.

Call 1-888-POM-PILL (766-7455) or visit pompills.com/nb and enter NB30 at checkout.

The antioxidant power of our 8 oz. juice.

Reviewed for Safety by the FDA.

100% Natural Pomegranate Extract.

Try POMx for one month – FREE!

We'll even pay for the shipping. Visit pompills.com/nb or call 1-888-POM-PILL. Use discount code: NB30

SIGN UP FOR POMx MONTHLY, AND WE'LL SEND YOUR FIRST BOTTLE FREE. AFTER THAT, YOU'LL CONTINUE TO RECEIVE MONTHLY SHIPMENTS FOR $29.95 WITH COMPLIMENTARY SHIPPING. Offer expires April 15, 2008. The first month free plus free shipping offer applies only to the purchase price for the first month of POMx Monthly. Following months will be $29.95 per bottle. This discount can only be used on POMx products. One discount per customer. Cannot be combined with other offers. No substitutions. Sample rights or similar requirements will be given. We reserve the right to modify or discontinue this promotion at any time. We reserve the right to change product prices or shipping charges at any time. Offer void where prohibited or restricted by law. To order by phone, call 1-888-POM-PILL. Discount code is not valid on POMx plus.

[1] pompills.com/research [2] These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure or prevent any disease. [3] 45 men with rising PSA after surgery or radiotherapy drank 8 oz. 100% pomegranate juice daily for two years. [4] 46 patients with coronary heart disease and myocardial ischemia drank 8 oz. 100% pomegranate juice daily for three months. [5] 15 patients aged 65-75 years with severe atherosclerosis drank 8 oz. 100% pomegranate juice daily for one year. ©2008 PomWonderful LLC. All rights reserved. POM Wonderful, POMx and "Antioxidant Superpill" are trademarks of PomWonderful LLC.

POM WONDERFUL

Exhibit L

The proof is in the POM - (CX0314_0005)

545. Complaint Counsel claim that, on September 9, 2008, POM ran an advertisement with the headline "The proof is in the POM" with the body copy that appears on CX0314_0005.

546. Complaint Counsel failed to present any other definitive information regarding this ad's dissemination.

547. Complaint Counsel failed to present any evidence that Respondents would run this ad in the future, let alone whether it is probable they would do so.

548. Nowhere in this ad do Respondents expressly (*i.e.*, unequivocally and directly) state that (a) POM Juice "prevents," "treats," or "reduces the risk" of heart disease or prostate cancer; or (b) POM Juice is "clinically proven" to "prevent," "treat," or "reduce the risk" of heart disease or prostate cancer. (CX0314_0005).

549. Complaint Counsel's assertion that the ad conveys the message that (a) POM Juice "prevents," "treats," or "reduces the risk" of heart disease or prostate cancer; or (b) POM Juice is "clinically proven" to "prevent," "treat," or "reduce the risk" of heart disease or prostate cancer is not conspicuous, self-evident, or reasonably clear from the face of the ad. (CX0314_0005).

550. Consequently, because the above-referenced challenged implied claim may not be determined with confidence from the face of the ad, extrinsic evidence must be examined.

551. The overall net impression of this ad is not that (a) drinking eight ounces of POM Juice prevents, treats or reduces the risk of certain diseases, such as heart disease or prostate cancer; or (b) drinking eight ounces of POM Juice is "clinically proven" to prevent, treat or reduce the risk of certain diseases, such as heart disease or prostate cancer. (CX0314_0005).

552. To the extent a "reduce the risk" claim can be implied from ad, the overall net impression is not that drinking eight ounces of POM Juice "reduces the risk" of certain diseases, such as heart disease or prostate cancer, like a drug with a single target of action, but "reduces the risk," like a healthy diet of fruits and vegetables and exercise "reduces the risk" of disease. (CX0314_0005).

553. To the extent a "treat" claim can be implied from this ad (which it cannot), the overall net impression of any ad is not that POM Juice is a substitute for conventional medical treatment. (Butters, Tr. 2821-22).

554. To the extent a "proven" claim can be implied from this ad (which it cannot), the overall impression of this ad is not that POM Juice is "proven" to be 100%

effective in preventing, treating or reducing the risk of heart disease or prostate cancer because (1) all of the qualifying language contradicts an implied "clinically proven" interpretation, and (2) "proven" in science means the "average person in the study benefitted," not that "everyone in the study necessarily benefitted." (Heber, Tr. 2011; Butters, Tr. 2893-2894; PX0361 (Sacks, Dep. at 81)).

555. Complaint Counsel presented no extrinsic evidence or expert opinion on this ad's meaning, consumer perceptions of this ad, or consumer interpretations regarding this ad. (PX0357 (Stewart, Dep. at 49, 52)).

556. Complaint Counsel failed to present any evidence that the claims in this ad reasonably convey that the Challenged Products are "clinically proven" to prevent, treat or reduce the risk of heart disease, prostate cancer or erectile dysfunction.

557. Complaint Counsel failed to present any evidence regarding the number of exposures consumers had to this ad or any particular POM advertisement. (Mazis, Tr. 2752).

The proof is in the POM

100% Authentic

POM is the only brand guaranteed to contain 100% real pomegranate juice. We wish other brands were as honest. In fact, according to recent independent tests, nine out of ten so-called "pomegranate" juices were found to have added sugar, colorants and other low-grade fruit juices.

Tree to Bottle

POM is the only brand that controls its juice from tree to bottle, batch to batch, year to year. We only grow "Wonderful" variety pomegranates, renowned for their superior antioxidants and delicious taste. And every 16oz bottle contains the juice of five whole pomegranates.

The Antioxidant Superpower*

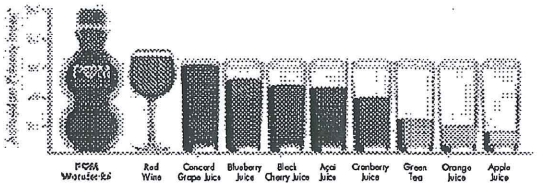
With uniquely high levels of powerful antioxidants, POM Wonderful 100% Pomegranate Juice has demonstrated superior ability to neutralize harmful free radicals and to inhibit excess inflammation.

Backed by Science

Only POM is backed by $25 million in medical research conducted at the world's leading universities. Clinical studies have documented the benefits of drinking POM Wonderful 100% Pomegranate Juice, including improved cardiovascular and prostate health.

More Antioxidants

Sip for sip, POM Wonderful 100% Pomegranate Juice has more polyphenol antioxidants than red wine, green tea and other juices.



POM WONDERFUL pomwonderful.com

*Index combines results from four leading antioxidant tests (ORAC, DPPH, FRAP, TEAC). N. Seeram, et al., "Comparison of Antioxidant Potency of Commonly Consumed Polyphenol-Rich Beverages in the United States," Journal of Agricultural Food and Chemistry (2008).

PJ9745_POM time wrap_F.indd 3 9/10/08 9:24:12 AM

JOB NO.: PJ9745	TRIM: 7.875"x10.5"	COLOR: 4/C PROS	DATE IN: 08-25-08
PROJECT: NY Times Magazine Wrap	LIVE: 7.125" x 9.75"	LIVE, TRIM, BLEED (DO NOT PRINT)	DATE OUT: 09-09-08
SCALE: 1 : 1	BLEED: 8.375" x 11"	PRINTOUT SIZE: 100%	PROOF READER: F

What Gets Your Heart Pumping - (CX0192)

558. Complaint Counsel claim that, on May 1, 2008, POM ran an advertisement with the headline "What gets your heart pumping?" with this body copy:

> Supermodels or beaches? 36-24-36? Or perhaps healthy arteries. Drink POM Wonderful 100% Pomegranate Juice. It helps guard your body against free radicals, unstable molecules that emerging science suggests aggressively destroy healthy cells in your body and contribute to disease. POM Wonderful 100% Pomegranate Juice is supported by $23 million of initial scientific research from leading universities, which has uncovered encouraging results in prostate and cardiovascular health. Eight ounces a day is enough to keep your heart pumping, even if you're not dating a supermodel.
>
> **POM Wonderful 100% Pomegranate Juice. The Antioxidant Superpower**

(CX0192_0001).

559. Complaint Counsel failed to present any other definitive information regarding this ad's dissemination.

560. Complaint Counsel failed to present any evidence that Respondents would run this ad in the future, let alone whether it is probable they would do so.

561. Complaint Counsel's assertion that the ad conveys the message that (a) POM Juice "prevents," "treats," or "reduces the risk" of heart disease or prostate cancer; or (b) POM Juice is "clinically proven" to "prevent," "treat," or "reduce the risk" of heart disease or prostate cancer is not conspicuous, self-evident, or reasonably clear from the face of the ad. (CX0192_0001).

562. Consequently, because the above-referenced challenged implied claim may not be determined with confidence from the face of the ad, extrinsic evidence must be examined.

563. The overall net impression of this ad is not that (a) drinking eight ounces of POM Juice prevents, treats or reduces the risk of certain diseases, such as heart disease or prostate cancer; or (b) drinking eight ounces of POM Juice is "clinically proven" to prevent, treat or reduce the risk of certain diseases, such as heart disease or prostate cancer. (CX0192_0001). Even the language of the ad itself uses such qualifiers as "helps guard," "emerging science," and "initial scientific research" and "encouraging results." (CX0192_0001).

564. To the extent a "reduce the risk" claim can be implied from ad, the overall net impression is not that drinking eight ounces of POM Juice "reduces the risk" of certain diseases, such as heart disease or prostate cancer, like a drug with a single target of action, but "reduces the risk," like a healthy diet of fruits and vegetables and exercise "reduces the risk" of disease. (CX0192_0001).

565. To the extent a "treat" claim can be implied from this ad (which it cannot), the overall net impression of any ad is not that POM Juice is a substitute for conventional medical treatment. (Butters, Tr. 2821-22).

566. To the extent a "proven" claim can be implied from this ad (which it cannot), the overall impression of this ad is not that POM Juice is "proven" to be 100% effective in preventing, treating or reducing the risk of heart disease or prostate cancer because (1) all of the qualifying language contradicts an implied "clinically proven" interpretation, and (2) "proven" in science means the "average person in the study benefitted," not that "everyone in the study necessarily benefitted." (Heber, Tr. 2011; Butters, Tr. 2893-2894; PX0361 (Sacks, Dep. at 81)).

567. Mr. Tupper testified that this ad portrays a take on the female anatomy and conveys that the juice is a healthy product. (CX1364 (Tupper, Dep. at 293-94)).

568. Professor Butters concluded that POM's ads in general depend on parody, exaggeration and humor to bring their message to the potential consumer; including the following messages: 1) POM is the best pomegranate that anyone can buy; 2) POM Juice is healthy; 3) POM Juice is tasty; 4) POM Juice is arguably the best source of antioxidants of any of the comparable beverages available; 5) medical research has suggested that antioxidants combat free radicals, which are unhealthy, and may contribute to diseases of the heart, arteries, and prostate, as well as erectile dysfunction; and 6) POM also offers concentrated forms of pomegranate extract for those who wish to ingest antioxidants in even more concentrated form than pomegranate juice itself. (PX0158-0033).

569. Viewing the "What gets your heart pumping?" ad a whole, including the interaction of the words and visual imagery, the overall net impression of this ad is that it is a humorous ad and that POM Juice is a healthy product. ((PX0158-0033); (CX1364 (Tupper, Dep. at 293-94))).

570. Complaint Counsel presented no extrinsic evidence or expert opinion on this ad's meaning, consumer perceptions of this ad, or consumer interpretations regarding this ad. (PX0357 (Stewart, Dep. at 49, 52)).

571. Complaint Counsel failed to present any evidence that the claims in this ad reasonably convey that the Challenged Products are "clinically proven" to prevent, treat or reduce the risk of heart disease, prostate cancer or erectile dysfunction.

572. Complaint Counsel failed to present any evidence regarding the number of exposures consumers had to this ad or any particular POM advertisement. (Mazis, Tr. 2752).

VMS ID: 080505048
RUN DATE: 05/01/2008

What gets your heart pumping?

Supermodels or beaches? 36-24-36? Or perhaps healthy arteries. Drink POM Wonderful 100% Pomegranate Juice. It helps guard your body against free radicals, unstable molecules that emerging science suggests aggressively destroy healthy cells in your body and contribute to disease. POM Wonderful 100% Pomegranate Juice is supported by $23 million of initial scientific research from leading universities, which has uncovered encouraging results in prostate and cardiovascular health. Eight ounces a day is enough to keep your heart pumping, even if you're not dating a supermodel.

POM WONDERFUL®

pomegranatetruth.com

POM Wonderful 100% Pomegranate Juice. The Antioxidant Superpower.™

Your New Health Care Plan - (CX0328)

573. Complaint Counsel claim that on November 8, 2009, POM ran an advertisement with the headline "Your New Health Care Plan" with the body copy that appears on CX0328_0001.

574. Complaint Counsel failed to present any other definitive information regarding this ad's dissemination.

575. Complaint Counsel failed to present any evidence that Respondents would run this ad in the future, let alone whether it is probable they would do so.

576. Complaint Counsel's expert, Professor Mazis, testified that Complaint Counsel is not challenging POM's ads for POM Juice that ran after December 2008. (Mazis, Tr. 2753-54). Accordingly, based on these representations, Complaint Counsel cannot now challenge this ad.

577. Nowhere in this ad do Respondents expressly (*i.e.*, unequivocally and directly) state that (a) taking one POMx Pill per day "prevents," "treats," or "reduces the risk" of heart disease or prostate cancer; or (b) taking one POMx Pill per day is "clinically proven" to "prevent," "treat," or "reduce the risk" of heart disease or prostate cancer. (CX0328_0001).

578. Complaint Counsel's assertion that the ad conveys the message that (a) taking one POMx Pill per day "prevents," "treats," or "reduces the risk" of heart disease or prostate cancer; or (b) taking one POMx Pill per day is "clinically proven" to "prevent," "treat," or "reduce the risk" of heart disease or prostate cancer is not conspicuous, self-evident, or reasonably clear from the face of the ad. (CX0328_0001).

579. Consequently, because the above-referenced challenged implied claim may not be determined with confidence from the face of the ad, extrinsic evidence must be examined.

580. The overall net impression of this ad is not that not that taking one POMx Pill per day prevents, treats or reduces the risk of certain diseases, such as heart disease or prostate cancer; or (b) taking one POMx Pill per day is "clinically proven" to prevent, treat or reduce the risk of certain diseases, such as heart disease or prostate cancer. (CX0328_0001). Even the language of the ad itself uses such qualifiers as "emerging science suggests," "help protect," "promising results," "initial UCLA study," "hopeful results" and "preliminary studies." (CX0328_0001).

581. To the extent a "reduce the risk" claim can be implied from ad, the overall net impression is not that drinking eight ounces of POM Juice "reduces the risk" of certain diseases, such as heart disease or prostate cancer, like a drug with a single target of action, but "reduces the risk," like a healthy diet of fruits and vegetables and exercise "reduces the risk" of disease. (CX0328_0001).

582. To the extent a "treat" claim can be implied from this ad (which it cannot), the overall net impression of any ad is not that POM Juice is a substitute for conventional medical treatment. (Butters, Tr. 2821-22).

583. To the extent a "proven" claim can be implied from this ad (which it cannot), the overall impression of this ad is not that POM Juice is "proven" to be 100% effective in preventing, treating or reducing the risk of heart disease or prostate cancer because (1) all of the qualifying language contradicts an implied "clinically proven" interpretation, and (2) "proven" in science means the "average person in the study benefitted," not that "everyone in the study necessarily benefitted." (Heber, Tr. 2011; Butters, Tr. 2893-2894; PX0361 (Sacks, Dep. at 81)).

584. Professor Butters concluded that POM's ads in general depend on parody, exaggeration and humor to bring their message to the potential consumer; including the following messages: 1) POM is the best pomegranate that anyone can buy; 2) POM Juice is healthy; 3) POM Juice is tasty; 4) POM Juice is arguably the best source of antioxidants of any of the comparable beverages available; 5) medical research has suggested that antioxidants combat free radicals, which are unhealthy, and may contribute to diseases of the heart, arteries, and prostate, as well as erectile dysfunction; and 6) POM also offers concentrated forms of pomegranate extract for those who wish to ingest antioxidants in even more concentrated form than pomegranate juice itself. (PX0158-0033).

585. Mr. Tupper testified that this advertisement references the healthcare reform debate that was going on at the time the ad was released. He further testified that the language in the ad, "no town hall meeting required," is also a reference to the health care reform debate. (Tupper, Tr. 969).

586. Professor Butters describes this advertisement as a "joking reference to a very serious matter." (PX0350 (Butters, Dep. at 142)).

587. Viewing the "Your New Health Care Plan" ad as a whole, including the interaction of the words and visual imagery, the overall net impression of the ad is that it is a humorous ad that references the debate on health care reform that was taking place when the ad ran and that POMx Pills are healthy. (PX0350 (Butters, Dep. at 135); (PX0158-0033))).

588. Complaint Counsel presented no extrinsic evidence or expert opinion on this ad's meaning, consumer perceptions of this ad, or consumer interpretations regarding this ad. (PX0357 (Stewart, Dep. at 49, 52))).

589. Complaint Counsel failed to present any evidence that the claims in this ad reasonably convey that the Challenged Products are "clinically proven" to prevent, treat or reduce the risk of heart disease, prostate cancer or erectile dysfunction.

590. Complaint Counsel failed to present any evidence regarding the number of exposures consumers had to this ad or any particular POM advertisement. (Mazis, Tr. 2752).

VMS ID: 091107449
RUN DATE: 11/08/2009

YOUR NEW HEALTH CARE PLAN.

(NO TOWN HALL MEETING REQUIRED.)

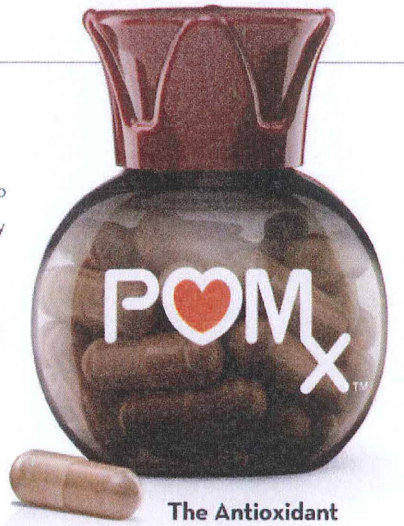
Antioxidant Health Insurance.

Emerging science suggests that antioxidants are critically important to maintaining good health because they protect you from free radicals, which can damage your body. Taking one POMx pill a day will help protect you from free radicals and keep you at your healthy best. Better yet, it's a health plan that's open to everyone.

The antioxidant power of our 8oz juice.

All-natural. Non-political.

POMx is an all-natural, ultra-potent antioxidant extract. Containing a full spectrum of pomegranate polyphenols, POMx is so concentrated that a single capsule has the anti-oxidant power of a full glass of POM Wonderful® 100% Pomegranate Juice.



The Antioxidant Superpill.™

$32 million in medical research. Zero deductible.

POMx is made from the only pomegranates backed by $32 million in medical research at the world's leading universities. Not only has this research documented the unique and superior antioxidant power of pomegranates, it has revealed promising results for prostate and cardiovascular health.

A health care plan for a healthy future.

Our POMx pills are made from the same pomegranates we use to make our POM Wonderful 100% Pomegranate Juice, on which each of the following medical studies was conducted.

An initial UCLA study on our juice found hopeful results for prostate health, reporting "statistically significant prolongation of PSA doubling times," according to Dr. Allen J. Pantuck in *Clinical Cancer Research*, '06.[1,2,3]

Two additional preliminary studies on our juice showed promising results for heart health. "Stress-induced ischemia (restricted blood flow to the heart) decreased in the pomegranate group," Dr. Dean Ornish reported in the *American Journal of Cardiology*, '05.[1,2,4]

"Pomegranate juice consumption resulted in significant reduction in IMT[5] (thickness of arterial plaque) by up to 30% after one year," said Dr. Michael Aviram, in *Clinical Nutrition*, '04.[1,2,5,6]

Try POMx Monthly FREE for ONE MONTH.
We'll even pay for the shipping.*

Order Now: 888-766-7455 or pompills.com/wp
Use discount code: WP30

*SIGN UP FOR POMx MONTHLY, AND WE'LL SEND YOUR FIRST BOTTLE FREE. AFTER THAT, YOU'LL CONTINUE TO RECEIVE MONTHLY SHIPMENTS FOR $29.95 WITH COMPLIMENTARY SHIPPING. Offer expires 4/30/10 and applies only to the purchase price for the first bottle of POMx Monthly. Following months will be $29.95 per bottle. One discount per customer. Cannot be combined with other offers. No substitutions, transfer rights or cash equivalents. We reserve the right to discontinue this promotion, change product price or shipping charge at any time. Valid only at pompills.com or 1-888-766-7455. Not valid on POMx Trial or other POM products.

POM WONDERFUL®

[1]pompills.com/research [2]These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure or prevent any disease. [3]46 men with rising PSA after surgery or radiotherapy drank 8oz. 100% pomegranate juice daily for two years. [4]45 patients with coronary heart disease and myocardial ischemia drank 8oz 100% pomegranate juice daily for three months. [5]Study measured intima-media thickness (IMT). [6]19 patients aged 66-75 years with severe atherosclerosis drank 8oz 100% pomegranate juice daily for one year.

VMS-0000303

CX0328_0001

Your Partner In Promoting Lifelong Health, Volume 1, Issue 1: For Your Heart ("Dreher Heart Newsletter") - (CX1426_0048-0048, Exh. M)

591. Complaint Counsel claim that in the Summer of 2007, Respondents disseminated a newsletter with the title "Your Partner In Promoting Lifelong Health" with the body copy that appears on CX01426_0046-0048, Exh. M.

592. Complaint Counsel failed to present any other definitive information regarding this newsletter's dissemination.

593. Complaint Counsel failed to present any evidence that Respondents would run this newsletter in the future, let alone whether it is probable they would do so.

594. This newsletter cannot provide a basis for injunctive relief because (a) it ran over five years ago; and (b) no evidence exists to show that Respondents are likely to run this ad in the future.

595. Nowhere in this newsletter do Respondents expressly (*i.e.*, unequivocally and directly) state that (a) taking one POMx Pill per day "prevents," "treats," or "reduces the risk" of heart disease; or (b) taking one POMx Pill per day is "clinically proven" to "prevent," "treat," or "reduce the risk" of heart disease. (CX01426_0046-0048, Exh. M).

596. Complaint Counsel's assertion that the ad conveys the message that (a) taking one POMx Pill per day "prevents," "treats," or "reduces the risk" of heart disease; or (b) taking one POMx Pill per day is "clinically proven" to "prevent," "treat," or "reduce the risk" of heart disease is conveyed in this newsletter is not conspicuous, self-evident, or reasonably clear from the face of it. (CX01426_0046-0048, Exh. M).

597. Consequently, because the above-referenced challenged implied claim may not be determined with confidence from the face of the newsletter, extrinsic evidence must be examined.

598. The overall net impression of this Dreher Heart Newsletter is not that not that taking one POMx Pill per day prevents, treats or reduces the risk of certain diseases, such as heart disease or prostate cancer; or (b) taking one POMx Pill per day is "clinically proven" to prevent, treat or reduce the risk of certain diseases, such as heart disease or prostate cancer. (CX1426_0046-0048, Exh. M). Even the language of the ad itself uses such qualifiers as "pipeline of research suggesting," "initial findings," "can lead," "may help," "pilot study," "initial scientific research," "encouraging results," "aim," "promotes" and "promising information." (CX1426_0046-0048, Exh. M).

599. To the extent a "may reduce the risk" or "reduce the risk" claim can be implied from this newsletter, the overall net impression is not that taking one POMx Pill per day "reduces the risk" of heart disease, like a drug with a single target of action, but "may reduce the risk" or "reduces the risk," like a healthy diet of fruits and vegetables and exercise "reduces the risk" of heart disease. (CX1426_0046-0048, Exh. M).

600. To the extent a "treat" claim can be implied from this newsletter (which it cannot), the overall net impression of any ad is not that POMx Pills are a substitute for conventional medical treatment. (Butters, Tr. 2821-22; Appendix of Advertisements).

601. To the extent a "proven" claim can be implied from this newsletter (which it cannot), the overall impression of this ad is not that POMx Pills are "proven" to be 100% effective in preventing, treating or reducing the risk of heart disease because (1) all of the qualifying language contradicts an implied "clinically proven" interpretation, and (2) "proven" in science means the "average person in the study benefitted," not that "everyone in the study necessarily benefitted." (Heber, Tr. 2011; Butters, Tr. 2893-2894; PX0361 (Sacks, Dep. at 81)).

602. Complaint Counsel presented no extrinsic evidence or expert opinion on this newsletter's meaning, consumer perceptions of this newsletter, or consumer interpretations regarding this newsletter. (PX0357 (Stewart, Dep. at 49, 52)).

603. Complaint Counsel failed to present any evidence that the claims in this newsletter reasonably convey that the Challenged Products are "clinically proven" to prevent, treat or reduce the risk of heart disease, prostate cancer or erectile dysfunction.

604. Complaint Counsel failed to present any evidence regarding the number of exposures consumers had to this newsletter or any particular POM advertisement. (Mazis, Tr. 2752).

POMx Heart Newsletter
Pills and Liquid
Monthly
2nd Continuity Shipment
Summer '07 - present (ongoing)

POMx YOUR PARTNER IN PROMOTING LIFELONG HEALTH

VOLUME 1, ISSUE 1: FOR YOUR HEART

What's New in the Lab by Dr. Mark Dreher

Mark Dreher, PhD
Chief Science Officer
POMWonderful, LLC

Hi, I'm Dr. Mark Dreher, Chief Science Officer at POM, and your guide to continuing new research on the benefits of POMx and POM Wonderful pomegranates as they relate to your health. Welcome to Your First Issue of the POMx Newsletter! There's more to come, so please stay tuned in the coming months for:...

Future newsletters will contain content derived from these questions and reader feedback. We look forward to hearing from you!

♥ ♥ ♥

Enjoy Your Life With a Healthy Heart

According to the American Heart Association (AHA), at least 58.8 million Americans suffer from some form of heart disease. Maintaining a healthy heart by reducing your risk for cardiovascular disease should be at the core of every lifelong

POMx YOUR PARTNER IN PROMOTING LIFELONG HEALTH

VOLUME 1, ISSUE 1: FOR YOUR HEART

What's New in the Lab by Dr. Mark Dreher

Mark Dreher, PhD
Chief Science Officer
POMWonderful, LLC

Hi, I'm Dr. Mark Dreher, Chief Science Officer at POM, and your guide to continuing new research on the benefits of POMx and POM Wonderful pomegranates as they relate to your health. Welcome to Your First Issue of the POMx Newsletter! There's more to come, so please stay tuned in the coming months for...

- POM Wonderful's latest research
- Health tips
- Pomegranate facts
- New product information

There's a strong pipeline of research supporting initial findings that POM Wonderful 100% Pomegranate Juice and its counterpart, POMx, are successfully fulfilling their promise for promoting heart health. We are committed to continually testing our products, not only prior to market release but at every step in their evolution. Various patient studies across a wide variety of health concerns are in the works, and we look forward to sharing the results of this research with you.

At POM Wonderful, we aim to be your partner in the promotion of good health that lasts a lifetime. It is our commitment to you and our mission as a company. If you have any questions and/or concerns please send them directly to me at: chiefsciencesofficer@pomwonderful.com

Future newsletters will contain content derived from these questions and reader feedback. We look forward to hearing from you!

♥ ♥ ♥

Did You Know?

POLYPHENOLS

Polyphenols are antioxidants that naturally occur in pomegranates. These antioxidants neutralize free radicals, helping to prevent the cell and tissue damage that can lead to disease. The heart health benefits associated with California grown, Wonderful variety pomegranates are due to their very high levels of polyphenols.

Enjoy Your Life With a Healthy Heart

According to the American Heart Association (AHA), at least 58.8 million Americans suffer from some form of heart disease. Maintaining a healthy heart by reducing your risk for cardiovascular disease should be at the core of every lifelong wellness plan. A nutrient-rich diet and active lifestyle are the best weapons you have for combatting heart disease and enhancing your vitality at any age.

The AHA recommends eating plenty of fruits and vegetables loaded with the vitamins, minerals and fiber your body requires, without the extra calories it doesn't need. But even though you may be eating enough of the right foods, your body still may not be getting all the nutrients it needs to keep you heart truly healthy.

ANTIOXIDANTS: YOUR ALLY IN FIGHTING HEART DISEASE

In order to keep your body in tip-top shape and your heart beating to the rhythm of all you wish to do in life, you need help in the prevention of cell and tissue damage that can lead to disease.

Science tells us that antioxidants neutralize the free radicals that can aggressively destroy healthy cells in your body. But not all antioxidants are equal – some are better at neutralizing free radicals than others. And because your body may not always produce enough of the antioxidants required to neutralize all the free radicals that can lead to cell damage, we have developed POMx to harness and deliver the most potent antioxidants around.

THE FREE RADICAL FIGHTER

Pomegranates contain polyphenols – powerful antioxidants that are important as part of a balanced diet. Published research has shown that the unique polyphenol antioxidants

(please turn to back)

Healthy Heart (from front)
in POMx and POM Wonderful 100% Pomegranate Juice are superior fighters in the battle against free radicals. Each dose of POMx contains the same amount of antioxidant polyphenols found in 8oz of POM Wonderful 100%

The antioxidants in POMx are supported by $20 million in initial scientific research

Pomegranate Juice, and POMx is the *most* concentrated source of pomegranate polyphenol antioxidants available.

POM Wonderful is committed to understanding the effects of POM Wonderful Pomegranate Juice on cardiovascular health. To date, our scientists have found that pomegranate juice may help counteract factors leading to arterial plaque build up, as well as inhibit a number of factors associated with heart disease.

NEW RESEARCH OFFERS FURTHER PROOF OF THE HEART-HEALTHY BENEFITS OF POM WONDERFUL JUICE

30% DECREASE IN ARTERIAL PLAQUE

After one year of a pilot study conducted at the Technion Institute in Israel involving 19 patients with atherosclerosis (clogged arteries),

> In his 2006 POMx study, Dr. Michael Aviram, one of the world's pre-eminent cardiovascular researchers from the Technion Institute in Israel, remarked that *"POMx is as potent an antioxidant as pomegranate juice and just like pomegranate juice, POMx may promote cardiovascular health."*

those patients who consumed 8oz of POM Wonderful 100% Pomegranate Juice daily saw a 30% decrease in arterial plaque.

17% IMPROVED BLOOD FLOW

A recent study at the University of California, San Francisco (UCSF) included 45 patients with impaired blood flow to the heart. Patients who consumed 8oz of POM Wonderful 100% Pomegranate Juice daily for three months experienced 17% improved blood flow. Those who drank a placebo experienced an 18% decline.

PROMOTES HEALTHY BLOOD VESSELS

An in vitro study at the University of California, Los Angeles (UCLA) showed that pomegranate juice uniquely possesses enough antioxidant activity to protect nitric oxide (an important biochemical that helps maintain healthy blood vessels for proper blood flow) against oxidative destruction thereby enhancing its biological activity. In other words, pomegranate juice by protecting nitric oxide promotes healthy blood flow.

THE POWER OF POMX

The antioxidants in POMx are supported by $20 million in initial scientific research from leading universities and so far we've uncovered encouraging results.

POMx supplements your diet without adding calories, allowing you to more easily maintain a healthy weight while still getting the necessary antioxidants

Due to this promising information, our studies on POMx and heart health continue. It is our mission to deliver the latest information on our research to you in this newsletter as soon as studies are completed. At POM Wonderful we are committed to learning all we can about the health benefits of this miraculous fruit and sharing them with you.

♥ ♥ ♥

NEXT ISSUE: PROSTATE HEALTH

One out of every six men will get prostate cancer, but only one out of 34 will die from the disease. In our newsletter next month, we will discuss preventative measures all men need to know to manage their prostate health.

1.888.POMPILL
WWW.POMPILLS.COM

POM WONDERFUL

Your Partner In Promoting Lifelong Health, Volume 1, Issue 2: For Your Prostate ("Dreher Prostate Newsletter") - (CX1426_0049-0051, Exh. N)

605. Complaint Counsel claim that, in the Fall of 2007, POM ran a newsletter with the title "Your partner in promoting lifelong health" with the body copy that appears on CX01426_0049-0051, Exh. N.

606. Complaint Counsel failed to present any other definitive information regarding this newsletter's dissemination.

607. Complaint Counsel failed to present any evidence that Respondents would run this newsletter in the future, let alone whether it is probable they would do so.

608. This newsletter cannot provide a basis for injunctive relief because (a) it ran over five years ago; and (b) no evidence exists to show that Respondents are likely to run this newsletter in the future.

609. Nowhere in this newsletter do Respondents expressly (*i.e.*, unequivocally and directly) state that (a) taking one POMx Pill per day "prevents," "treats," or "reduces the risk" of prostate cancer; or (b) taking one POMx Pill per day is "clinically proven" to "prevent," "treat," or "reduce the risk" of prostate cancer. (CX01426_0049-0051, Exh. N).

610. Complaint Counsel's assertion that the ad conveys the message that (a) taking one POMx Pill per day "prevents," "treats," or "reduces the risk" of prostate cancer; or (b) taking one POMx Pill per day is "clinically proven" to "prevent," "treat," or "reduce the risk" of prostate cancer is conveyed in this newsletter is not conspicuous, self-evident, or reasonably clear from the face of it. (CX1426_0049-0051, Exh. N).

611. Consequently, because the above-referenced challenged implied claim may not be determined with confidence from the face of the newsletter, extrinsic evidence must be examined.

612. The overall net impression of this Dreher Prostate Newsletter is not that not that taking one POMx Pill per day prevents, treats or reduces the risk of certain diseases, such as prostate cancer; or (b) taking one POMx Pill per day is "clinically proven" to prevent, treat or reduce the risk of certain diseases, such as prostate cancer. (CX1426_0049-0051, Exh. N). Even the language of the ad itself uses such qualifiers as "preliminary UCLA medical study," "promising news," "aim," "may indicate," "promising results," "preliminary studies," "potential," "initial scientific research," "encouraging results and information." (CX1426_0049-0051, Exh. N).

613. To the extent a "reduce the risk" or "may reduce the risk" claim can be implied from this newsletter, the overall net impression is not that taking one POMx Pill per day "reduces the risk" of certain diseases, such as prostate cancer, like a drug with a single target of action, but "reduces the risk" or "may reduce the risk," like a healthy diet of fruits and vegetables and exercise "reduces the risk" of disease. (CX1426_0049-0051, Exh. N).

614. To the extent a "treat" claim can be implied from this ad (which it cannot), the overall net impression of any newsletter is not that POMx Pills are a substitute for conventional medical treatment. (Butters, Tr. 2821-22; Appendix of Advertisements).

615. To the extent a "proven" claim can be implied from this newsletter (which it cannot), the overall impression of this newsletter is not that POMx Pills are "proven" to be 100% effective in preventing, treating or reducing the risk of prostate cancer because (1) all of the qualifying language contradicts an implied "clinically proven" interpretation, and (2) "proven" in science means the "average person in the study benefitted," not that "everyone in the study necessarily benefitted." (Heber, Tr. 2011; Butters, Tr. 2893-2894; PX0361 (Sacks, Dep. at 81)).

616. Complaint Counsel presented no extrinsic evidence or expert opinion on this newsletter's meaning, consumer perceptions of this newsletter, or consumer interpretations regarding this newsletter. (PX0357 (Stewart, Dep. at 49, 52)).

617. Complaint Counsel failed to present any evidence that the claims in this newsletter reasonably convey that the Challenged Products are "clinically proven" to prevent, treat or reduce the risk of heart disease, prostate cancer or erectile dysfunction.

618. Complaint Counsel failed to present any evidence regarding the number of exposures consumers had to this newsletter or any particular POM advertisement. (Mazis, Tr. 2752).

POMx Prostate Newsletter
Pills and Liquid
Monthly
3rd Continuity Shipment
Fall '07 - present (ongoing)

POMx YOUR PARTNER IN PROMOTING LIFELONG HEALTH

VOLUME 1, ISSUE 2: PROSTATE HEALTH

Prostate Cancer Affects 1 Out of Every 6 Men

Prostate cancer is the second leading cause of cancer related death in men in the United States according to the National Cancer Institute. Prostate cancer incidence rates rose dramatically in the late 1980's with improved detection and diagnosis through widespread use of prostate-specific antigen (PSA) testing.

Prostate cancer is the second leading cause of

fruits and vegetables. Doctors are not sure which of these factors causes the risk to go up but the best advice is to consume daily the equivalent of five or

(continued on back)

What's New in the Lab by Dr. Mark Dreher

Mark Dreher, PhD
Chief Science Officer
POMWonderful, LLC

Research studies like the ones discussed in this newsletter and

POMx YOUR PARTNER IN PROMOTING LIFELONG HEALTH

VOLUME 1, ISSUE 2: PROSTATE HEALTH

Prostate Cancer Affects 1 Out of Every 6 Men

Prostate cancer is the second leading cause of cancer related death in men in the United States according to the National Cancer Institute. Prostate cancer incidence rates rose dramatically in the late1980's with improved detection and diagnosis through widespread use of prostate-specific antigen (PSA) testing.

Prostate cancer is the second leading cause of cancer related to death in men in the United States according to the National Cancer Institute

Since the early 1990's, prostate cancer incidence and deaths have been declining, but the American Cancer Society estimates that there will still be about 218,890 new cases of prostate cancer and 27,050 deaths in the United States in 2007.

According to the American Cancer Society, some of the risk factors for prostate cancer include:

Age – Growing older raises a man's risk of prostate cancer. About two of every three prostate cancers are found in men over the age of 65.

Family History – Men with close family members (father or brother) who have had prostate cancer are more likely to get it themselves, especially if their relatives were young when they got the disease.

Diet – One risk factor that can be changed is diet. The National Cancer Institute's research suggest that obesity and weight gain is linked to increased prostate cancer mortality.

Men who eat a lot of red meat or high-fat dairy products seem to have a greater chance of getting prostate cancer. These men also tend to eat fewer fruits and vegetables. Doctors are not sure which of these factors causes the risk to go up but the best advice is to consume daily the equivalent of five or

(continued on back)

What's New in the Lab by Dr. Mark Dreher

Mark Dreher, PhD
Chief Science Officer
POMWonderful, LLC

Research studies like the ones discussed in this newsletter and conducted by UCLA (my alma mater) serve to validate the many reasons I am proud to be affiliated with POM Wonderful and POMx.

POM Wonderful 100% Pomegranate Juice and POMx are backed by a $25 million dollar investment in world-class scientific research. This includes ten clinical studies published in top peer-reviewed medical journals that document the pomegranate's antioxidant health benefits such as heart and prostate health.

Working at POM Wonderful gives me the unique opportunity to really make a difference in the world. That's what gets me up every morning! I get to work with renowned scientists, including a Nobel Laureate, at leading

Studies funded by POM represent the vast majority of medical research ever conducted on pomegranates.

universities around the world. In fact, studies funded by POM represent the vast majority of human medical research ever conducted on pomegranates. No other company that I know of is as dedicated as POM in pursuing the truth and keeping our customers informed.

At POM Wonderful, we aim to be your partner in the promotion of good health that lasts a lifetime. It is our commitment to you, our mission as a company.

Prostate Cancer (from front)

more servings of vegetables and fruits rich in antioxidants and to eat less red meat and high-fat foods.

EARLY DETECTION SEEN AS KEY TO INCREASING SURVIVAL RATES"

The prostate-specific antigen (PSA) test and rectal exam can be used to detect the presence of prostate cancer when no symptoms are present. They may help catch the disease at an early stage when treatment is more effective.

During a PSA test, a small amount of blood is drawn and the level of PSA (a protein produced by the prostate) is measured to determine the level of risk. When prostate cancer is found and treated, the PSA test may also measure the potential risk for the cancer to return.

"Please talk to your doctor for more specific prostate cancer information.

NEW POMEGRANATE RESEARCH OFFERS HOPE TO PROSTATE CANCER PATIENTS

A preliminary UCLA medical study involving POM Wonderful 100% Pomegranate Juice revealed promising news. 46 men who had been treated for prostate cancer with surgery or radiation were given 8oz of POM Wonderful 100% Pomegranate Juice to drink daily. A

Patients with prostate cancer showed a prolongation of PSA doubling time, coupled with corresponding lab effects on reduced prostate cancer as well as reduced oxidated stress.

majority of the patients experienced a significantly extended PSA doubling time. Doubling time is an indicator of prostate cancer progression – extended doubling time may indicate slower disease progression.

Before the study, the mean doubling time was 15 months. After drinking 8oz of pomegranate juice daily for two years, the mean PSA doubling time increased to 54 months. Testing on patient blood serum showed a 12% decrease in cancer cell proliferation and a 17% increase in cancer cell death (apoptosis).

In another study, in vitro laboratory testing at UCLA showed that POMx significantly decreased human prostate cancer cell growth and increased cancer cell death.

Based on the promising results of these preliminary studies, two additional studies are underway to more fully investigate the potential of POMx to extend PSA doubling time.

According to Dr. David Heber, Director of UCLA's Center for Human Nutrition, "The most abundant and most active ingredients in pomegranate juice are also found in POMx. Basic studies in our laboratory so far indicate that POMx and pomegranate juice may have the same effects."

SEND US YOUR QUESTIONS AND COMMENTS

We encourage you to participate in our commitment to a lifetime of good health by sending your questions and/or concerns to chiefscienceofficer@pompills.com Future newsletters will contain content derived from these questions and reader feedback. We look forward to hearing from you!

♥ ♥ ♥

NEXT ISSUE: POMEGRANATE SUPPLEMENT COMPARISONS

How does POMx compare with other pomegranate supplements for antioxidant potency?

♥ ♥ ♥

1.888.POMPILL
WWW.POMPILLS.COM

POM WONDERFUL®

RX5007 Appendix

Rx5007	Blumberg, Jeffery, et al. *Evidence-based Criteria in the Nutritional Context.* Nutrition Reviews Vol. 68(8), 478-484 (2010)

Evidence-based criteria in the nutritional context

Jeffrey Blumberg, Robert P Heaney, Michael Huncharek, Theresa Scholl, Meir Stampfer, Reinhold Vieth, Connie M Weaver, and Steven H Zeisel

During the last decade, approaches to evidence-based medicine, with its heavy reliance on the randomized clinical trial (RCT), have been adapted to nutrition science and policy. However, there are distinct differences between the evidence that can be obtained for the testing of drugs using RCTs and those needed for the development of nutrient requirements or dietary guidelines. Although RCTs present one approach toward understanding the efficacy of nutrient interventions, the innate complexities of nutrient actions and interactions cannot always be adequately addressed through any single research design. Because of the limitations inherent in RCTs, particularly of nutrients, it is suggested that nutrient policy decisions will have to be made using the totality of the available evidence. This may mean action at a level of certainty that is different from what would be needed in the evaluation of drug efficacy. Similarly, it is judged that the level of confidence needed in defining nutrient requirements or dietary recommendations to prevent disease can be different from that needed to make recommendations to treat disease. In brief, advancing evidence-based nutrition will depend upon research approaches that include RCTs but go beyond them. Also necessary to this advance is the assessing, in future human studies, of covariates such as biomarkers of exposure and response, and the archiving of samples for future evaluation by emerging technologies.

INTRODUCTION

In a Medline search of article titles, the term "evidence-based" occurred less than 100 times in articles published in 1995. Since then, citations have risen steadily to nearly 7,900 in 2009 alone. This level of occurrence provides ample documentation of a substantial shift in both awareness and vocabulary in the community of scientists and policymakers involved with the clinical sciences. Evidence-based medicine (EBM) was established for the evaluation of medical interventions. It provides a hierarchy of research designs, with the results of randomized, placebo-controlled trials (RCTs) considered the highest level of evidence.[1,2] EBM and its underlying concepts and

Affiliations: *J Blumberg* is with the Jean Mayer USDA Human Nutrition Research Center on Aging at Tufts University, Boston, Massachusetts, USA. *RP Heaney* is with Creighton University, Omaha, Nebraska, USA. *M Huncharek* is with the Division of Radiation Oncology at St. Louis Veterans Administration Medical Center, St. Louis, Missouri, USA. *T Scholl* is with the Department of Obstetrics and Gynecology at the University of Medicine and Dentistry of New Jersey, Stratford, New Jersey, USA. *M Stampfer* is with the Departments of Epidemiology and Nutrition at the Harvard School of Public Health, Boston, Massachusetts, USA. *R Vieth* is with the Departments of Nutritional Sciences and Laboratory Medicine and Pathobiology at the University of Toronto, Toronto, Ontario, Canada. *CM Weaver* is with the Department of Foods and Nutrition at Purdue University, West Lafayette, Indiana, USA. *SH Zeisel* is with the Department of Nutrition and Nutrition Research Institute, University of North Carolina, Chapel Hill, North Carolina, USA.

Correspondence: *RP Heaney*, Creighton University, 601 North 30th Street, Suite 4841, Omaha, NE 68131, USA. E-mail: rheaney@creighton.edu, Phone: +1-402-280-4029, Fax: +1-402-280-4751.

The authors have worked in nutritional science, policy, and practice throughout most of their professional careers, serving, for example, on the US Dietary Guidelines Committee and various advisory panels of the Institute of Medicine concerned with dietary reference intakes. Several have chaired National Institutes of Health study sections and have been recipients of major nutrition awards of the American Society for Nutrition and the United States Department of Agriculture.

Key words: benefit, evidence-based, nutritional policy, randomized clinical trials, risk

doi:10.1111/j.1753-4887.2010.00307.x

methods were soon directly extended to the field of clinical nutritional science as evidence-based nutrition (EBN). Beginning with the 1997 Dietary Reference Intakes,[3] the Institute of Medicine explicitly sought to provide the evidence base for its recommendations. A similar approach was used in developing the DHHS Dietary Guidelines for Americans, beginning with the 2005 edition.[4] Similarly, the U.S. Food and Drug Administration has put forth a set of evidence criteria for nutrient-related health claims[5,6] and professional associations such as the American Dietetic Association[7] have promulgated EBN guidelines for their own policies and publications. A popular approach has been the use of evidence-based systematic reviews and meta-analyses; their application to nutrition questions has been recently reviewed.[8–11] Adherence to EBN guidelines is increasingly required by peer-reviewed nutrition journals.

While multiple research approaches in nutrition science afford evidence of nutrient effects, there often appears to be an almost exclusive reliance on the RCT as the only type of evidence worthy of such consideration (e.g., references[12–16]). However, certain features of EBM seem ill-suited to the nutrition context.[17–19] Some of the differences between the evaluation of drugs and nutrients cited previously[18] are as follows: (i) medical interventions are designed to cure a disease *not* produced by their absence, while nutrients prevent dysfunction that would result from their inadequate intake; (ii) it is usually not plausible to summon clinical equipoise for basic nutrient effects, thus creating ethical impediments to many trials; (iii) drug effects are generally intended to be large and with limited scope of action, while nutrient effects are typically polyvalent in scope and, in effect size, are typically within the "noise" range of biological variability; (iv) drug effects tend to be monotonic, with response varying in proportion to dose, while nutrient effects are often of a sigmoid character, with useful response occurring only across a portion of the intake range; (v) drug effects can be tested against a nonexposed (placebo) contrast group, whereas it is impossible and/or unethical to attempt a zero intake group for nutrients; and (vi) therapeutic drugs are intended to be efficacious within a relatively short term while the impact of nutrients on the reduction of risk of chronic disease may require decades to demonstrate – a difference with significant implications for the feasibility of conducting pertinent RCTs.

Nevertheless, it is indisputable that the RCT, in one of its variant forms, is the clinical study design that best permits strong causal inference concerning the relationship between an administered agent (whether drug or nutrient) and any specific outcome. Both drug indications and health claims for nutrients that are backed by one or more well-conducted RCTs are appropriately considered to have a more persuasive evidence base than corresponding claims based primarily upon observational data.[20] However, it is also generally understood, if not often acknowledged, that it can be difficult to implement RCTs correctly. For certain types of questions, such as those concerning epigenetic effects (which seem increasingly likely for several nutrients), RCTs would often be precluded on both ethical and feasibility grounds. Or, when trying to assess the potential benefits of conditionally essential nutrients (e.g., α-lipoic acid and ubiquinone, which are synthesized in vivo) and putatively nonessential nutrients (e.g., carotenoids and flavonoids, which are nearly ubiquitous dietary constituents), the problem of providing this evidence through RCTs becomes even more challenging. Additionally, a poorly executed RCT may have no more (or even less) inferential power than a cohort study.[21,22]

For all these reasons, it seemed useful to suggest some ways to advance the current approach to EBN, ways which better reflect the unique features of nutrients and dietary patterns, and which also recognize the need to deal with uncertainty in situations in which evidence from RCTs might never be obtained. The perspective that follows constitutes a summary of the deliberations on these issues that took place at an invitational workshop convened in Omaha, Nebraska, September 3–4, 2008, by Tufts and Creighton Universities. In approaching this issue here, a few key questions are asked and an attempt is made to define the evidence needed to support nutritional policy decisions. Instances of some of the details, as well as brief allusions to the background science, are included in the Supporting Information available online.

PROOF OF WHAT BENEFIT?

By definition, an essential nutrient is a substance that an organism needs for optimal function and which must be obtained from the environment because it cannot be adequately synthesized in vivo. That nutrients produce benefits is a truism enshrined in the Dietary Reference Intakes of the Institute of Medicine,[23] and in the intake recommendations of most nations of the world. Contrariwise, inadequate intakes produce dysfunction or disease. Hence, the association of inadequate intake with disease is not so much a matter of proof as of definition. A substance would not be an essential nutrient if low intake were not harmful; i.e., a null hypothesis analogous to that for a drug ("nutrient *X* confers no health benefit") is not tenable for most nutrients. Instead the questions clinical nutrition scientists must ask are: (i) What is the full spectrum of dysfunctions or diseases produced by low intake of a nutrient? and (ii) How high an intake is required to ensure optimal physiological function or reduced risk for disease across *all* body systems and endpoints?

Among the many advances of modern nutritional science are (i) the recognition of long-latency deficiency diseases and (ii) the understanding that nutrients often act through several distinct mechanisms within the organism.[24] Thus, inadequate intake of a single nutrient can result in multiple dysfunctions, some of which may be quite slow to manifest. Further, there often is not a sharp transition between health and disease, but a multidimensional continuum, with different organ systems in the same individual exhibiting varying sensitivities, and with individuals varying among themselves in sensitivity. The Recommended Dietary Allowances (RDAs) are designed to account for interindividual differences in requirements[3] but, as implemented, they largely focus on single organ system endpoints, and do not usually deal with the multiplicity of a nutrient's effects throughout the body. Typically, policy-making bodies have tended to adopt the default position of defining the intake requirement mainly for prevention of the disease for which there is the clearest evidence or at least a clear consensus, i.e., the "index" disease.

This approach raises questions regarding the adequacy of such recommendations, since prevention of the nonindex diseases may require more than the intake needed to prevent the index disease. For example, the intake of dietary folate necessary to reduce the risk of neural tube birth defects is greater than that necessary to prevent macrocytic anemia,[25] and the amount of vitamin D required to reduce the risk of falls and hip fracture in the elderly is greater than that required to prevent rickets or osteomalacia.[3]

For several nutrients, RCTs have been conducted with nonindex diseases as the outcome measure, but they have most often failed to show a significant effect on the occurrence of the selected disease endpoint (e.g., references[26–31]). Such RCTs are often flawed, not so much in their conduct as in their design; for example, they do not provide a sufficiently low intake of the nutrient for the control group[26,27] or they do not ensure adequate intake of other essential nutrients needed for the test nutrient to manifest its own proper effect.[32–34] It is worth noting that, in this latter respect, such nutrient RCTs emulate drug RCTs, which usually strive to eliminate all confounding variables and effect modifiers, rather than to optimize them.

ARE RANDOMIZED CONTROLLED TRIALS AVAILABLE TO TEST NUTRIENT EFFECTS?

In order to conduct a RCT that adequately tests the efficacy of a nutrient for a specific chronic disease, it will usually be important to ensure an adequate contrast in intake between the intervention and the control groups. The control intake is an approximate analog of the placebo control in drug RCTs. However, since sufficiently low intakes are associated with significant disease in some body systems, doing so can lead to serious ethical problems, particularly if the disease outcome is serious and/or irreversible, e.g., preeclampsia, hip fracture, neural tube defect, or myocardial infarction. In contrast to observational studies, which typically assess nutrient exposures ranging from low to high, most RCTs of nutrient effects have employed a control group receiving an intake typical of the population, oftentimes near the RDA, and certainly above the thresholds for many deficiency states, while the intervention group receives even more. This approach transforms the hypothesis ostensibly being tested to one of "more is better". Such trials are ethical and feasible, but they often do not test the hypothesis that low intake of nutrient *A* causes (or increases the risk of) disease *X*. This is not to question the value of asking such secondary questions, but simply to stress that they are different questions.

EBN thus departs from the situation of EBM, where, for most interventions, the use of a no-intake control group is usually quite appropriate. In EBM, the hypothesis is that *adding* an intervention ameliorates a disease, whereas in EBN it is that *reducing* the intake of a nutrient causes (or increases the risk of) disease. This distinction is critical. No one proposes in EBM that a disease is caused by the absence of its remedy; whereas for nutrients the hypothesis is precisely that malfunction is caused by deficiency. A hypothesis about disease causation can rarely, if ever, be directly tested in humans using the RCT design. This is because in the RCT the disease/dysfunction occurs in at least some of the study participants, and the investigators must ensure that this will happen. Instead where EBN must operate is with respect to two related, but different questions: (i) In addition to disease *X*, does the inadequate intake of nutrient *A* also contribute to other diseases? and (ii) At what level of intake of nutrient *A* is risk of *all* related disease minimized or all related functions optimized?

In brief, it is unlikely that RCT evidence could feasibly or appropriately be produced with respect to the role of a nutrient for many nonindex-disease endpoints. Therefore, the majority of the evidence with respect to nutrients and nonindex diseases will continue, of necessity, to be derived from observational studies. That does not mean that action must be suspended. Over 30 years ago, Hill[35] described guidelines to assess causation under such circumstances (see Supporting Information).

HOW MUCH CERTAINTY IS NECESSARY?

RCTs, if well designed and well executed, provide a high level of certainty that a specific intervention can reliably be counted on to produce a specific effect in a selected

population. As a society, we have determined that a high level of certainty is required for the evaluation of efficacy for therapeutic drugs. Such a standard is justified by the usually high cost of such medical treatment, by the risk that therapeutic decisions based on inadequate evidence would shift treatment away from possibly more efficacious therapies, and from the need to balance benefit against the risks that accompany pharmacotherapy. These same concerns are substantially less pressing for nutrients. Nutrients are orders of magnitude less expensive than drugs and often exhibit a broader margin between efficacy and toxicity. Is the same high level of certainty required regarding the nutrient intake recommendations to *prevent* disease as is needed for drugs used to *treat* disease?

There is no simple answer to this question. Nevertheless, it seems clear that requiring RCT-level evidence to answer questions for which the RCT may not be an available study design will surely impede the application of nutrition research to public health issues. Moreover, to fail to act in the absence of conclusive RCT evidence increases the risk of forgoing benefits that might have been achieved with little risk and at low cost. This is not to suggest that the standards of what constitutes proof ought to be relaxed for nutrients, but to propose instead that nutrient-related decisions could be made at a level of certainty somewhat below that required for drugs. Under such circumstances, confidence in the correctness of a decision would necessarily be lower.

Figures 1 and 2 present these considerations graphically, where confidence in the correctness of a certain recommendation (vertical axis) is the dependent variable, expressed as a function of the following: i) the level of certainty (or strength of the evidence) relating a given intake to any specific effect; and ii) the benefit-to-risk ratio that follows from acting. "Acting" here means specifying an intake level as a recommendation for the general public (or approving a drug for a given indication). In EBN, the strength of the evidence, ranging from high to low, might be quantified in an ordinal fashion, such as "established", "probable", "likely", and "unclear." Here, "unclear" means simply no ability to decide one way or the other, i.e., the null position.

As Figure 1 shows, confidence in the correctness of a decision to act rises as a function of both certainty and benefit : risk, reaching its maximum only when the levels of both certainty and benefit : risk are high. This would be typical of the drug decision context (Figure 2A). By contrast, Figure 2B depicts what would seem to be appropriate for nutrients, for which a lower level of certainty would be acceptable; i.e., the confidence needed to act would be less than that needed for drugs.

As inspection of Figure 2B shows, the intersection of the cut-point plane with the three-dimensional surface is

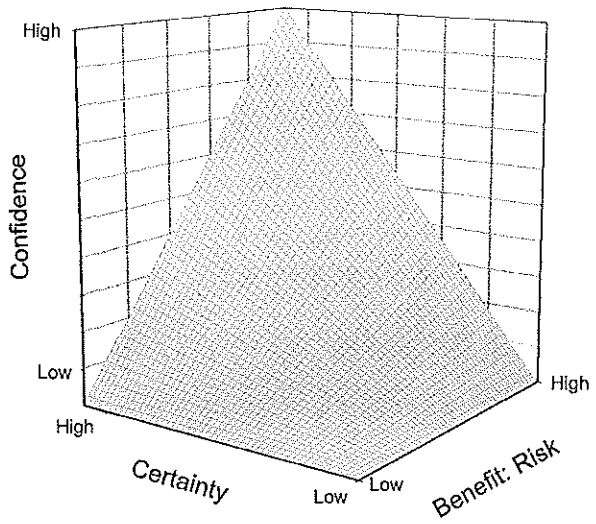


Figure 1 **Three-dimensional plot depicting the relation between *confidence* that a decision to act or to implement a nutrient recommendation is the correct thing to do (the vertical axis), and the degree of *certainty* about efficacy (*strength* of the evidence) of the nutrient (left horizontal-plane axis), and the ratio of *benefit to risk* of the change in intake (right horizontal-plane axis).** The surface represented by the grid illustrates a confidence outcome, incorporating the full range of inputs of efficacy and benefit : risk. (Copyright Robert P. Heaney, 2010. Used with permission.)

a curved line. This line itself is a reflection of an inverse relation between certainty and benefit : risk for any given degree of confidence in the correctness of an action. Thus, for nutrients with high benefit : risk, less certainty might be adequate to permit action, whereas for nutrients with less potential benefit (or more potential risk), a higher certainty of efficacy would be needed.

Importantly, these figures are simply illustrative; their use here is not intended to propose a rigid, mathematical approach that could be applied robotically to such questions. The purpose is simply to illustrate a potential willingness to act for low-risk interventions with probable benefit and at a level of certainty below what would be needed for approval of medical interventions.

WHAT FEATURES AFFECT CERTAINTY?

It is interesting to note that while regulatory agencies from around the world rely on RCTs, there is a high degree of discordance regarding how different jurisdictions evaluate the strength of the evidence produced by the same studies for the substantiation of health claims for nutrients and foods. Thus, in advancing approaches

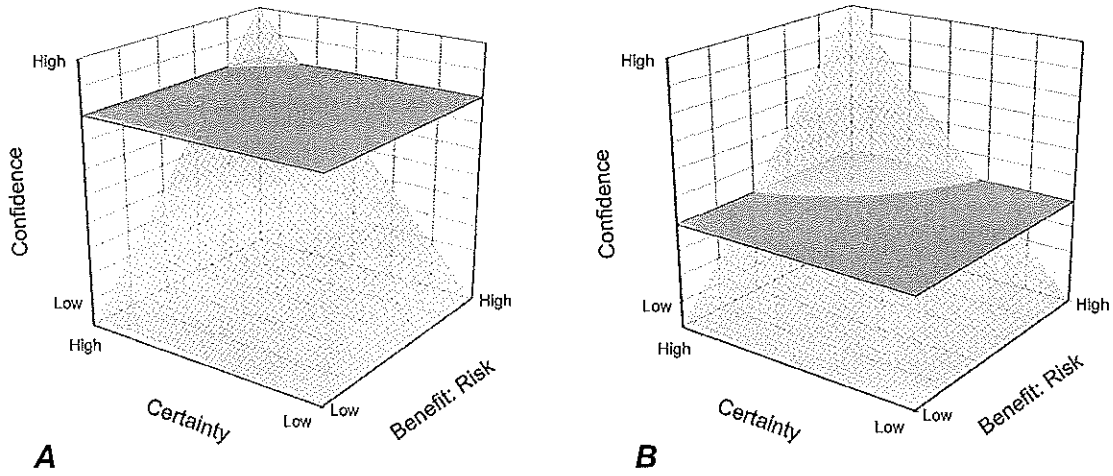


Figure 2 **The decision plot for the relationship of Figure 1, as implemented for drugs (*A*) and for nutrients (*B*). Any value above the cut-plane would permit action.** Notice that a high benefit : risk ratio would permit action at a lower level of evidential certainty and vice versa. (Copyright Robert P. Heaney, 2010. Used with permission.)

Table 1 **Factors affecting the level of certainty of evidence provided by various study designs.**

Study type	Factors
Randomized controlled trial	Control group (or period) with sufficiently low intake
	Accuracy of intake assessment
	Minimal losses of sampling units
	Replication
	Adherence/compliance
	Optimization/control of conutrient intakes
	Effect size (e.g., relative risk >2.0 [or <0.5])
Cohort design	Low intake control group
	Intake estimate validation
	Correct temporal sequence
	Dose-response relationship
	Replication/multiplicity of studies
	Low between-subject variance
	Biological plausibility
	Adequate control for conutrient intake
	Adequate control for other confounding factors
	Effect size (e.g., relative risk >2.0 [or <0.5])
Case-control design	Low intake control group
	Contrast groups randomly derived from population
	Biological plausibility
	Adequate control for conutrient intakes
	Effect size (e.g., odds ratio >2.0 [or <0.5])

to EBN, it will be useful to set forth some of the factors that we judge will affect the level of *certainty* (evidential strength) that various study designs offer (Table 1), as well as the factors that affect the level of *confidence* in a decision that may flow from any given degree of certainty (i.e., high benefit : risk ratio; important consequences of possible Type II error; low deployment cost; low opportunity cost; multiplicity of lines of supporting evidence).

Additionally, certainty can be enhanced by ancillary measurements. Discussion of these features is further developed in the Supporting Information.

As listed in Table 1, an RCT gains or loses certainty depending upon whether or not the following apply: i) there is an adequate contrast in intake between the intervention and control group; ii) it has been replicated; iii) it suffered only minimal losses of sampling units; iv) it measured and controlled adequately for conutrient intakes;

and (v) its estimate of effect size is large. While not all of those factors are absolutely necessary, each contributes a degree of certainty in its own right. These features are developed at greater length in the Supporting Information.

As RCT-based evidence may not be available ethically or feasibly to answer many nutrient-related questions, it is important to attend to the factors needed to support action when evidential certainty is less than perfect. The factors affecting confidence, as listed above, represent a start at this effort. Perhaps the most compelling concern regarding this issue is the fact that benefits may be forgone when action is deferred, i.e., the consequence of the type II error when the conclusion from available evidence is "not proven". Offsetting that risk are the costs associated with action when the true effect is actually negligible or null. Therefore, low deployment cost and low opportunity cost should be important considerations. Any change in nutritional policy creates work for both industry and regulators, efforts that have a cost and that may displace other action that might have been more productive. There is no single or simple correct answer to these questions about cost, but it is worthwhile to stress that they must be factored into the decision matrix on a case-by-case basis.

CONCLUSION

Inadequate intakes of nutrients result in a variety of dysfunctions and diseases. The full spectrum of those untoward effects is unknown. Because deliberately reducing intake to deficient levels in humans is ethically impermissible, the RCT will often not be available as a means of elucidating many potential nutrient-disease relationships. The general principles of EBN can provide a sufficient foundation for establishing nutrient requirements and dietary guidelines in the absence of RCTs for every nutrient and food group. Sackett et al.,[36] among the intellectual fathers of EBM, stressed nearly 15 years ago that EBM was "not restricted to randomized trials and meta-analyses", a counsel that has been shunted aside in recent years. A general approach to acting in the absence of ultimate certainty should include a broader consideration of other research strategies along with revised estimates of the certainty level of the evidence and the confidence needed to act in support of public health. In such judgments, it will be important to assess the balance between the potential harm of making any given recommendation and the potential harm of not making it. Additionally, a key challenge will be to find appropriate educational strategies to convey varying levels of strength of evidence for a given recommendation.

Acknowledgments

This paper is the product of an invited workshop convened at Creighton University, Omaha, Nebraska, USA, September 3–4, 2008. It was supported by Creighton University research funds and by unrestricted grants from ConAgra Foods Inc., Omaha, Nebraska; Dairy Management Incorporated, Rosemont, Illinois; and the Council for Responsible Nutrition, Washington, DC.

Each author had a role in generating the concepts and preparing the manuscript.

Declaration of interest. *CW* has received research grants from Dairy Management Incorporated, Preisland Foods, General Mills, and Tate & Lyle. None of the other authors has relevant interests to declare.

REFERENCES

1. Harris RP, Helfand M, Woolf SH, Lohr KN. Current methods of the U.S. Preventive Services Task Force: a review of the process. Am J Prev Med. 2001;20:21–35.
2. Woolf SH, DiGuiseppi CG, Atkins D, Kamerow DB. Developing evidence-based clinical practice guidelines: lessons learned by the U.S. Preventive Services Task Force. Ann Rev Public Health. 1996;17:511–538.
3. Food and Nutrition Board, Institute of Medicine. *Dietary Reference Intakes for Calcium, Magnesium, Phosphorus, Vitamin D, and Fluoride*. Washington, DC: National Academy Press; 1997.
4. U.S. Department of Health and Human Services and U.S. Department of Agriculture. *Dietary Guidelines for Americans*, 6th edn. Washington, DC: U.S. Government Printing Office; 2005.
5. Center for Food Safety and Applied Nutrition. *Guidance for Industry: Evidence-Based Review System for the Scientific Evaluation of Health Claims – Final*. College Park, MD: FDA. Center for Food Safety and Applied Nutrition; 2009.
6. Schneeman B. FDA's review of scientific evidence for health claims. J Nutr. 2007;137:493–494.
7. American Dietetic Association. ADA Evidence Analysis Manual. 2005. Available at: http://www.adaevidencelibrary.com/topic.cfm?cat=1155. Accessed 12 June 2010.
8. Balk EM, Horsley TA, Newberry SJ, Lichtenstein AH. A collaborative effort to apply the evidence-based review process to the field of nutrition: challenges, benefits, and lessons learned. Am J Clin Nutr. 2007;85:1448–1456.
9. Lichtenstein AH, Yetley EA, Lau J. Application of systematic review methodology to the field of nutrition. J Nutr. 2008; 138:2297–2306.
10. Moher D, Tricco AD. Issues related to the conduct of systematic reviews: a focus on the nutrition field. Am J Clin Nutr. 2008;88:1191–1199.
11. Jew S, Vanstone CA, Antoine J-M, Jones PJH. Generic and product-specific health claim processes for functional foods across global jurisdictions. J Nutr. 2008;138(Suppl):S1228–S1236.
12. Bjelakovic G, Nikolova D, Gluud LL, Simonetti RG, Gluud C. Antioxidant supplements for prevention of mortality in healthy participants and patients with various diseases. The Cochrane Library. 2008;2:1–188.

13. Shea B, Wells G, Cranney A, et al. Meta-analyses of therapies for postmenopausal osteoporosis. VII. Meta-analysis of calcium supplementation for the prevention of postmenopausal osteoporosis. Endocr Rev. 2002;23:552–559.
14. Coates PM, Dwyer JT, Thurn AL, eds. Supplement: multivitamin/mineral supplements and chronic disease prevention. Am J Clin Nutr. 2007;85(Suppl):S254–S327.
15. Bleys J, Miller ER III, Pastor-Barriuso R, Appel LJ, Guallar E. Vitamin-mineral supplementation and the progression of atherosclerosis: a meta-analysis of randomized controlled trials. Am J Clin Nutr. 2006;84:880–887.
16. Miller ER 3rd, Pastor-Barriuso R, Dalal D, Riemersma RA, Appel LJ, Guallar E. Meta-analysis: high-dosage vitamin E supplementation may increase all-cause mortality. Ann Intern Med. 2005;142:37–46.
17. Heaney RP. Nutrition, chronic disease, and the problem of proof. Am J Clin Nutr. 2006;84:471–472.
18. Heaney RP. 2008 W.O. Atwater Memorial Lecture: nutrients, endpoints, and the problem of proof. J Nutr. 2008;138:1591–1595.
19. Feinstein AR. Epidemiologic analyses of causation: the unlearned scientific lessons of randomized trials. J Clin Epidemiol. 1989;42:481–489.
20. Katz DL. *Clinical Epidemiology & Evidence-Based Medicine: Fundamental Principles of Clinical Reasoning & Research.* Thousand Oaks, CA: Sage Publications; 2001.
21. Hornberger J, Wrone E. When to base clinical policies on observational versus randomized trial data. Ann Intern Med. 1997;127:697–703.
22. Feinstein AR, Horwitz RI. Problems in the "evidence" of "evidence-based medicine". Am J Med. 1997;103:529–535.
23. Institute of Medicine. *How Should the Recommended Dietary Allowances Be Revised?* Washington, DC: National Academy Press; 1994.
24. Heaney RP. Long-latency deficiency disease: insights from calcium and vitamin D. Am J Clin Nutr. 2003;78:912–919.
25. Food and Nutrition Board, Institute of Medicine. *Dietary Reference Intakes for Thiamin, Riboflavin, Niacin, Vitamin B6, Folate, Vitamin B12, Pantothenic Acid, Biotin, and Choline.* Washington, DC: National Academy Press; 1998.
26. Jackson RD, LaCroix AZ, Gass M, et al. for the Women's Health Initiative Investigators. Calcium plus vitamin D supplementation and the risk of fractures. N Engl J Med. 2006;354:669–683.
27. Levine RJ, Hauth JC, Curet LB, et al. Trial of calcium to prevent preeclampsia. N Engl J Med. 1997;337:69–76.
28. Bischoff-Ferrari H, Willett WC, Wong JB, Giovannucci E, Dietrich T, Dawson-Hughes B. Fracture prevention with vitamin D supplementation: a meta-analysis of randomized controlled trials. JAMA. 2005;293:2257–2264.
29. Sesso HD, Buring JE, Christen WG, et al. Vitamins E and C in the prevention of cardiovascular disease in men: the Physicians' Health Study II randomized controlled trial. JAMA. 2008;300:2123–2133.
30. Zhang SM, Cook NR, Albert CM, Gaziano JM, Buring JE, Manson JE. Effect of combined folic acid, vitamin B6, and vitamin B12 on cancer risk in women. A randomized trial. JAMA. 2008;300:2012–2021.
31. Bonaa KH, Njolstad I, Ueland PM, et al. NORVIT Trial Investigators. Homocysteine lowering and cardiovascular events after acute myocardial infarction. N Engl J Med. 2006;354:1578–1588.
32. Dawson-Hughes B, Harris S. Calcium intake influences the association of protein intake with rates of bone loss in elderly men and women. Am J Clin Nutr. 2002;75:773–779.
33. Heaney RP. Effects of protein on the calcium economy. In: Burckhardt P, Heaney RP, Dawson-Hughes B, eds. *Nutritional Aspects of Osteoporosis 2006.* Amsterdam: Elsevier Inc; 2007:191–197.
34. Heaney RP. Vitamin D: role in the calcium economy. In: Feldman D, Glorieux FH, Pike JW, eds. *Vitamin D,* 2nd edn. San Diego, CA: Academic Press; 2005:773–787.
35. Hill AB. The environment and disease: association or causation? Proc R Soc Med. 1965;58:295–300.
36. Sackett DL, Rosenberg WMC, Gray JAM, et al. Evidence-based medicine: what it is and what it isn't. BMJ. 1996;312:71–72.

SUPPORTING INFORMATION

Additional Supporting Information may be found in the online version of this article:

Appendix S1. Amplification on certain of the points discussed in the paper "Evidence-Based Criteria in the Nutritional Context", by Blumberg et al. [*Nutr Rev* 2010;68(8):478–484].

Figure S1. Plateau diagrams illustrating the difference in measurable response for studies in which the low intake contrast group falls above or below the plateau intake. As Fig. A1*A* depicts, at least one of the contrast intakes must be below the response plateau if a measurable effect is to be produced. With both intakes at an above the threshold of the plateau (i.e, A1*B*), response would be expected to be minimal or absent entirely. (Copyright Robert P. Heaney, 2008. Used with permission.)

Please note: Wiley-Blackwell are not responsible for the content or functionality of any supporting materials supplied by the authors. Any queries (other than missing material) should be directed to the corresponding author for the article.

POM WONDERFUL

Health Benefits

POM Wonderful 100% Pomegranate Juice is the only pomegranate juice backed by $25 million in medical research. Actually, we are the only pomegranate juice backed by any medical research at all.

There has been a lot of talk lately about the role of pomegranates in promoting heart health, prostate health, and proper erectile function. But while these results are promising, keep in mind that all of the research has been done on POM Wonderful 100% Pomegranate Juice. Our juice comes from a unique pomegranate variety (the Wonderful), which is grown in a unique location (California), and which is juiced with proprietary technology (ours!). No other pomegranate juice can claim these distinctions, and no other brand has been clinically tested.

So what are the medical results on POM Wonderful 100% Pomegranate Juice?

Cardiovascular

- A 2005 study published in the American Journal of Cardiology showed improved blood flow to the heart in patients drinking 8oz. daily of POM Wonderful 100% Pomegranate Juice for 3 months. Researchers studied a total of 45 patients with coronary heart disease who had reduced blood flow to the heart. Patients drinking POM Wonderful 100% Pomegranate Juice experienced a 17% improvement in blood flow, compared to a 18% worsening in patients drinking a placebo...Read more

- One pilot study on 19 patients with atherosclerosis (clogged arteries) at the Technion Institute in Israel demonstrated a reduction in arterial plaque growth. After one year, arterial plaque decreased 30% for those patients who consumed 8oz of POM Wonderful 100% Pomegranate Juice daily, compared to a 9% worsening for patients who drank a placebo. ..Read more.

Prostate Health

- A preliminary UCLA medical study, published by The American Association for Cancer Research, found hopeful results for prostate health. The study followed 46 men previously treated for prostate cancer either with surgery or radiation. After drinking 8 oz POM Wonderful 100% Pomegranate Juice daily for two years, these men experienced significantly slower PSA doubling times – from 15 months at the beginning of the study to 54 months at the end. PSA is a biomarker for prostate cancer, and slower PSA doubling time may indicate slower disease progression.

POM WONDERFUL

The truth about our pomegranates.

The proof is in the POM.

POM is the only pomegranate juice you can trust for real pomegranate health benefits and superior taste. There are many imitators, but only one POM.

100% Authentic.

POM is the only brand guaranteed to contain 100% authentic pomegranate juice. Unfortunately, not all brands are as honest. According to recent tests conducted by three independent labs, nine out of ten so-called "pomegranate juices" had added sugar, colorants and other low-grade fruit juices. Why is this? Two reasons: (1) because there is currently a worldwide shortage of pomegranate juice; and (2) because pomegranate juice is very expensive to produce. By using non-pomegranate ingredients, unscrupulous exporters to the U.S. make their "pomegranate juice" cheaper and more readily available. As a result, what's missing are the unique antioxidants that make pomegranate juice so healthy.

Read more.

Read the label.

Beware of filler juices! Other companies try to sell you "100% juice" with the word "Pomegranate" next to pretty pictures of pomegranate fruit. These companies want you to believe their products contain all the health benefits of real pomegranate juice. Don't be fooled. These products are loaded with highly processed filler juices like white grape, apple and pear, all of which are little better than sugar water when it comes to antioxidant benefits. Read more.

Backed by science.

POM is the only pomegranate juice backed by $25 million in medical research. To date numerous published clinical studies have documented the benefits of drinking pomegranate juice, benefits that include improved heart and prostate health and better erectile function. **All of these studies featured patients who drank POM Wonderful 100% Pomegranate Juice, not any other brands.** Since POM is totally different from other pomegranate juices (see below), that means ours is the only one you can trust to deliver genuine pomegranate health benefits. Read more.

Tree to bottle.

POM is the only brand that controls its pomegranate juice from tree to bottle. We grow the fruit in our own orchards, hand-pick the pomegranates when perfectly ripe, squeeze them in our own specially designed presses, and even manufacture our own bottles. Unlike other brands, we never buy pomegranate juice from outside vendors. This is how we guarantee pomegranate perfection in each bottle. Read more.

Wonderfully superior.

POM is the only pomegranate juice guaranteed to be made exclusively from Wonderful variety pomegranates. There are over a hundred different pomegranate varieties, but only the Wonderful variety is known for its unique combination of superior antioxidants, incredible taste and brilliant red color. That's why we chose to grow only the Wonderful variety because it's simply the best. Read more.

Grown in California, U.S.A.

POM is the only pomegranate juice guaranteed to come from pomegranates grown exclusively in the U.S.A. All of our pomegranate orchards are located in Central California's fertile and sunny San Joaquin Valley. Other brands contain pomegranate juice from Turkey, India, Iran and other countries where agricultural and food processing practices are far less strict.

Read more.

With POM, our 100% pure and authentic pomegranate juice comes from fruit grown on our own trees right here in California. POM may cost more than other brands, but you get what you pay for. If superior antioxidants and real pomegranate taste are important to you, then POM is the only brand you can trust.

Research Study Synopses - POM Health - Windows Internet Explorer

http://pomwonderful.com/health/research/

File Edit View Favorites Tools Help

Favorites

Research Study Synopses « POM Health

SEARCH POM'S PUBLISHED STUDIES GO

COMMUNITY

REGISTER SIGN IN

Research Study Synopses

Published studies are on POM Wonderful 100% Pomegranate Juice and POMx Polyphenol Extract. Patients received a minimum of 8 ounces of POM Wonderful 100% Pomegranate Juice or 850mg total pomegranate polyphenols per day.

Cardiovascular

ATHEROSCLEROSIS:

• A randomized, placebo-controlled, double-blind clinical trial followed 289 subjects at moderate risk for coronary heart disease. These subjects consumed 8 ounces per day of either POM Wonderful 100% Pomegranate Juice or a placebo beverage. After 18 months, there was no reduction in the progression of intima-media thickness of the carotid artery (CIMT) in the group as a whole. However, further analysis revealed an indication that the rate of CIMT progression slowed in nearly one third of patients, those with elevated cardiovascular disease risk factors. Read the Study.

DID YOU KNOW?

Since 1860, the British Medical Association has displayed pomegranates on its crest, depicting fertility, profilicacy and the persistence of life.

CONTRIBUTE

Do you have a positive experience with POM Wonderful? Share your story with us.

YOUTUBE

Done Internet 100%

start

POM IS THE ANTIOXIDANT SUPERPOWER

WHAT ARE ANTIOXIDANTS?

POM'S UNIQUE ANTIOXIDANTS

OTHER ANTIOXIDANT BENEFITS

OTHER RESOURCES

GLOSSARY

RELATED ARTICLES & RESOURCES

Pomegranate juice or 300mg total pomegranate polyphenols per day.

Cardiovascular

ATHEROSCLEROSIS:

• A randomized, placebo-controlled, double-blind clinical trial followed 289 subjects at moderate risk for coronary heart disease. These subjects consumed 8 ounces per day of either POM Wonderful 100% Pomegranate Juice or a placebo beverage. After 18 months, there was no reduction in the progression of intima-media thickness of the carotid artery (CIMT) in the POM group as a whole. However, further analysis revealed that the rate of CIMT progression slowed in nearly one third of POM patients, those with elevated cardiovascular disease risk factors. Read the Study. • In a pilot study of 19 subjects with carotid artery stenosis (plaque buildup), patients who consumed 8 ounces of POM Wonderful 100% Pomegranate Juice daily for a one-year period experienced a 30% reduction in intima-media thickness of the carotid artery vs. a 9% increase for the placebo group. Read the study. • In 13 healthy male volunteers who drank POM Wonderful 100% Pomegranate Juice for 2 weeks, the amount of LDL cholesterol oxidation decreased by 20% and antioxidant activity in the blood increased by 9%. Read the study.

BLOOD FLOW / PRESSURE:

• In 45 subjects with ischemic coronary heart disease (reduced blood supply to the heart), coronary blood flow increased by 17% in the group consuming 8 ounces of pomegranate juice over a three-month period vs. 18% decrease in placebo group. Read the study. • In a pilot study of 10 subjects with hypertension, reduction in ACE (angiotensin converting enzyme) activity and a slight decrease in systolic blood pressure was experienced after consuming POM Wonderful 100% Pomegranate Juice daily for two weeks. Read the study.

Prostate Cancer

• In a clinical study involving 46 men with rising PSA after prostate cancer treatment (surgery or radiation) who consumed 8 ounces of POM Wonderful 100% Pomegranate Juice daily over two years, PSA doubling time increased from 15 to 54 months ($p < 0.001$).5 A longer term (6-year) continued evaluation of active sub-group patients showed a further increase in PSA doubling time to 88 months. Read the study. * PSA doubling time is an indicator of prostate cancer progression.

Diabetes - Type II

Alternative Fuel: Powered by Plants
James Herrera

176 4

Pomegranates for a Healthy Holiday Season
Janet Ovrut

74 2

CONTRIBUTE

Do you have a positive experience with POM Wonderful?

RECENT SUBMISSION

Tell Us Your Health Story.
POM Wonderful

92 4

Share your story with us.

POM TESTIMONIALS

Just wanted to let you know that your Pomegranate peach passion white tea is just about the best thing I've ever tasted!

Betsy

DID YOU KNOW?

Author and scientist Pliny the Elder (AD 23-79) recommended pomegranates for easing nausea in pregnant women.
POM Wonderful

80 0

http://www.pomwonderful.com/health_benefits.html

File Edit View Favorites Tools Help

POM Wonderful - Health Benefits Home

POM WONDERFUL

POM's Blog | History & Legend | Club POM | Store Locator

Search

Products | Health Benefits | Recipes | Decorations | POM in the News | POM Ads | Store Locator

- Antioxidants
- Published Research
- Glossary

Health Benefits

POM Wonderful 100% Pomegranate Juice is the only pomegranate juice backed by $25 million in medical research. Actually, we are the only pomegranate juice backed by any medical research at all.

There has been a lot of talk lately about the role of pomegranates in promoting heart health, prostate health, and proper erectile function. But while these results are promising, keep in mind that all of the research has been done on POM Wonderful 100% Pomegranate Juice. Our juice comes from a unique pomegranate variety (the Wonderful), which is grown in a unique location (California), and which is juiced with proprietary technology (ours!). No other pomegranate juice can claim these distinctions, and no other brand has been clinically tested.

So what are the medical results on POM Wonderful 100% Pomegranate Juice?

Cardiovascular

- A 2005 study published in the American Journal of Cardiology showed improved blood flow to the heart in patients drinking 8oz. daily of POM Wonderful 100% Pomegranate Juice for 3 months. Researchers studied a total of 45 patients with coronary heart disease who had reduced blood flow to the heart. Patients drinking POM Wonderful 100% Pomegranate Juice experienced a 17% improvement in blood flow, compared to a 18% worsening in patients drinking a placebo...Read more

- One pilot study on 19 patients with atherosclerosis (clogged arteries) at the Technion Institute in Israel demonstrated a reduction in arterial plaque growth. After one year, arterial plaque decreased 30% for those patients who consumed 8oz of POM Wonderful 100% Pomegranate Juice daily, compared to a 9% worsening for patients who drank a placebo. ..Read more.

Prostate Health

- A preliminary UCLA medical study, published by The American Association for Cancer Research, found hopeful results for prostate health. The study followed 46 men previously treated for prostate cancer either with surgery or radiation. After drinking 8 oz POM Wonderful 100% Pomegranate Juice daily for two years, these men experienced significantly slower PSA doubling times – from 15 months at the beginning of the study to 54 months at the end. PSA is a biomarker for prostate cancer, and slower PSA doubling time may indicate slower disease progression.

Internet

RUSHTON_001

The truth about our pomegranates.

The proof is in the POM.

POM is the only pomegranate juice you can trust for real pomegranate health benefits and superior taste. There are many imitators, but only one POM.

100% Authentic.

POM is the only brand guaranteed to contain 100% authentic pomegranate juice. Unfortunately, not all brands are as honest. According to recent tests conducted by three independent labs, nine out of ten so-called "pomegranate juices" had added sugar, colorants and other low-grade fruit juices. Why is this? Two reasons: (1) because there is currently a worldwide shortage of pomegranate juice; and (2) because pomegranate juice is very expensive to produce. By using non-pomegranate ingredients, unscrupulous exporters to the U.S. make their "pomegranate juice" cheaper and more readily available. As a result, what's missing are the unique antioxidants that make pomegranate juice so healthy.

Read more.

Read the label.

Beware of filler juices! Other companies try to sell you "100% juice" with the word "Pomegranate" next to pretty pictures of pomegranate fruit. These companies want you to believe their products contain all the health benefits of real pomegranate juice. Don't be fooled. These products are loaded with highly processed filler juices like white grape, apple and pear, all of which are little better than sugar water when it comes to antioxidant benefits. Read more.

Backed by science.

POM is the only pomegranate juice backed by $25 million in medical research. To date numerous published clinical studies have documented the benefits of drinking pomegranate juice, benefits that include improved heart and prostate health and better erectile function. All of these studies featured patients who drank POM Wonderful 100% Pomegranate Juice, not any other brands. Since POM is totally different from other pomegranate juices (see below), that means ours is the only one you can trust to deliver genuine pomegranate health benefits. Read more.

Tree to bottle.

POM is the only brand that controls its pomegranate juice from tree to bottle. We grow the fruit in our own orchards, hand-pick the pomegranates when perfectly ripe, squeeze them in our own specially designed presses, and even manufacture our own bottles. Unlike other brands, we never buy pomegranate juice from outside vendors. This is how we guarantee pomegranate perfection in each bottle. Read more.

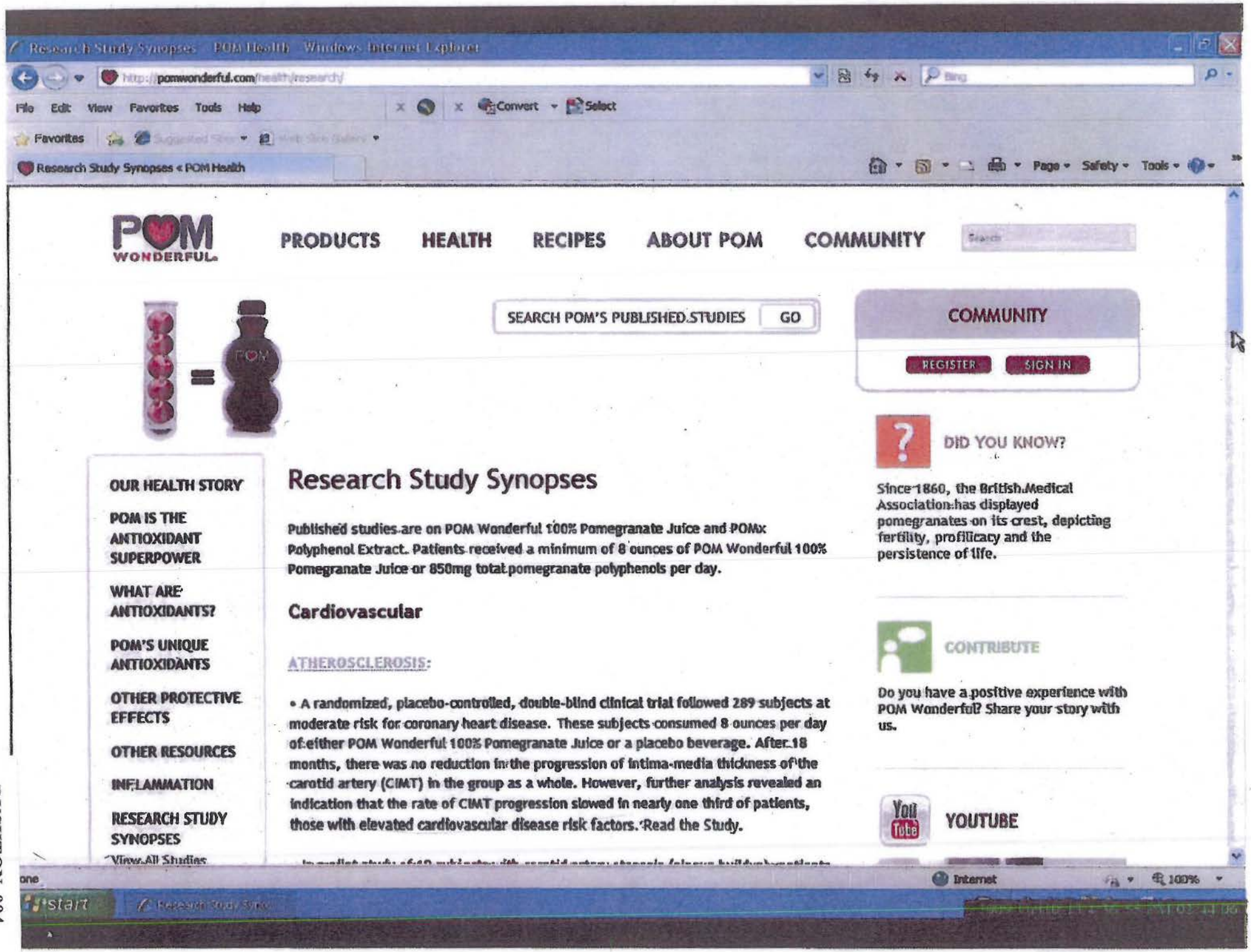
Wonderfully superior.

POM is the only pomegranate juice guaranteed to be made exclusively from Wonderful variety pomegranates. There are over a hundred different pomegranate varieties, but only the Wonderful variety is known for its unique combination of superior antioxidants, incredible taste and brilliant red color. That's why we chose to grow only the Wonderful variety because it's simply the best. Read more.

Grown in California, U.S.A.

POM is the only pomegranate juice guaranteed to come from pomegranates grown exclusively in the U.S.A. All of our pomegranate orchards are located in Central California's fertile and sunny San Joaquin Valley. Other brands contain pomegranate juice from Turkey, India, Iran and other countries where agricultural and food processing practices are far less strict. Read more.

With POM, our 100% pure and authentic pomegranate juice comes from fruit grown on our own trees, right here in California. POM may cost more than other brands, but you get what you pay for. If superior antioxidants and real pomegranate taste are important to you, then POM is the only brand you can trust.


Research Study Synopses - POM Health - Windows Internet Explorer
http://pomwonderful.com/health/research/
File Edit View Favorites Tools Help
Convert Select
Favorites
Research Study Synopses « POM Health
Page Safety Tools
POM WONDERFUL
PRODUCTS HEALTH RECIPES ABOUT POM COMMUNITY
SEARCH POM'S PUBLISHED STUDIES GO
COMMUNITY
REGISTER SIGN IN
OUR HEALTH STORY
POM IS THE ANTIOXIDANT SUPERPOWER
WHAT ARE ANTIOXIDANTS?
POM'S UNIQUE ANTIOXIDANTS
OTHER PROTECTIVE EFFECTS
OTHER RESOURCES
INFLAMMATION
RESEARCH STUDY SYNOPSES
View All Studies
Research Study Synopses
Published studies are on POM Wonderful 100% Pomegranate Juice and POMx Polyphenol Extract. Patients received a minimum of 8 ounces of POM Wonderful 100% Pomegranate Juice or 850mg total pomegranate polyphenols per day.
Cardiovascular
ATHEROSCLEROSIS:
• A randomized, placebo-controlled, double-blind clinical trial followed 289 subjects at moderate risk for coronary heart disease. These subjects consumed 8 ounces per day of either POM Wonderful 100% Pomegranate Juice or a placebo beverage. After 18 months, there was no reduction in the progression of intima-media thickness of the carotid artery (CIMT) in the group as a whole. However, further analysis revealed an indication that the rate of CIMT progression slowed in nearly one third of patients, those with elevated cardiovascular disease risk factors. Read the Study.
DID YOU KNOW?
Since 1860, the British Medical Association has displayed pomegranates on its crest, depicting fertility, profilicacy and the persistence of life.
CONTRIBUTE
Do you have a positive experience with POM Wonderful? Share your story with us.
YOUTUBE
Internet
100%
start

RUSHTON_004

pomegranate juice or 850mg total pomegranate polyphenols per day.

Cardiovascular

ATHEROSCLEROSIS:

• A randomized, placebo-controlled, double-blind clinical trial followed 289 subjects at moderate risk for coronary heart disease. These subjects consumed 8 ounces per day of either POM Wonderful 100% Pomegranate Juice or a placebo beverage. After 18 months, there was no reduction in the progression of intima-media thickness of the carotid artery (CIMT) in the POM group as a whole. However, further analysis revealed that the rate of CIMT progression slowed in nearly one third of POM patients, those with elevated cardiovascular disease risk factors. Read the Study. • In a pilot study of 19 subjects with carotid artery stenosis (plaque buildup), patients who consumed 8 ounces of POM Wonderful 100% Pomegranate Juice daily for a one-year period experienced a 30% reduction in intima-media thickness of the carotid artery vs. a 9% increase for the placebo group. Read the study. • In 13 healthy male volunteers who drank POM Wonderful 100% Pomegranate Juice for 2 weeks, the amount of LDL cholesterol oxidation decreased by 20% and antioxidant activity in the blood increased by 9%. Read the study.

BLOOD FLOW / PRESSURE:

• In 45 subjects with ischemic coronary heart disease (reduced blood supply to the heart), coronary blood flow increased by 17% in the group consuming 8 ounces of pomegranate juice over a three-month period vs. 18% decrease in placebo group. Read the study. • In a pilot study of 10 subjects with hypertension, reduction in ACE (angiotensin converting enzyme) activity and a slight decrease in systolic blood pressure was experienced after consuming POM Wonderful 100% Pomegranate Juice daily for two weeks. Read the study.

Prostate Cancer

• In a clinical study involving 46 men with rising PSA after prostate cancer treatment (surgery or radiation) who consumed 8 ounces of POM Wonderful 100% Pomegranate Juice daily over two years, PSA doubling time increased from 15 to 54 months ($p < 0.001$).5 A longer term (6-year) continued evaluation of active sub-group patients showed a further increase in PSA doubling time to 88 months. Read the study. * PSA doubling time is an indicator of prostate cancer progression.

Diabetes - Type II

Alternative Fuel: Powered by Plants
James Herrera

176 4

Pomegranates for a Healthy Holiday Season
Janet Ovrut

74 2

CONTRIBUTE

Do you have a positive experience with POM Wonderful?

RECENT SUBMISSION

Tell Us Your Health Story.
POM Wonderful

92 4

Share your story with us. >

POM TESTIMONIALS

Just wanted to let you know that your Pomegranate peach passion white tea is just about the best thing I've ever tasted!

Betsy

DID YOU KNOW?

Author and scientist Pliny the Elder (AD 23-79) recommended pomegranates for easing nausea in pregnant women.
POM Wonderful

80 0

RUSHTON_006