FEDERAL TRADE COMMISSION

I N D E X

IN RE POM WONDERFUL LLC, ET AL.

TRIAL VOLUME 9

PUBLIC RECORD

JUNE 13, 2011

EXHIBITS	FOR ID	IN EVID	IN CAMERA	STRICKEN/REJECTED
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UNITED STATES OF AMERICA

BEFORE THE 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
STEWART A. RESNICK,	)	
LYNDA RAE RESNICK, and	)	
MATTHEW TUPPER, individually	)	
and as officers of the	)	
companies.	)	
	)	
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Monday, June 13, 2011

9:33 a.m.

TRIAL VOLUME 9

PUBLIC RECORD

BEFORE THE HONORABLE D. MICHAEL CHAPPELL

Administrative Law Judge

Federal Trade Commission

600 Pennsylvania Avenue, N.W.

Washington, D.C.

Reported by: Josett F. Whalen, RMR-CRR

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P R O C E E D I N G S

- - - - -

JUDGE CHAPPELL: Back on the record Docket 9344.

Next witness.

MS. EVANS: Good morning, Your Honor.

JUDGE CHAPPELL: Good morning.

MS. EVANS: Dr. Frank Sacks, could you please go to the stand.

- - - - -

Whereupon --

FRANK M. SACKS, M.D.

a witness, called for examination, having been first duly sworn, was examined and testified as follows:

DIRECT EXAMINATION

BY MS. EVANS:

Q. Dr. Sacks, could you please state your full name for the record.

A. Frank M. Sacks.

Q. And could you spell the word "Sacks."

A. S-A-C-K-S.

Q. Thank you.

On the table before you is a binder containing various exhibits. Could you please turn to CX 1292 behind tab 1, which I believe is your CV.

A. Yes.

Q. Could you identify this document.

A. Yes. That is my CV.

Q. Could you please summarize your education after high school.

A. Yes. Well, I went to Brown University where I was an undergraduate, graduated with a bachelor of science in biology, really biochemistry. And then I switched fields for a time. I wanted to explore music, and I started again as an undergraduate at the New England Conservatory of Music in Boston from 1970 to 1972 and then got sort of inspired by the idea of a career in nutrition as a physician and went to medical school at Columbia University in New York.

Q. And where are you currently employed?

A. I'm employed at two places, at Harvard -- well, I'm employed by Harvard University, and I work at Harvard School of Public Health as a professor of cardiovascular disease prevention in the Department of Nutrition, and I also have a dual appointment as professor, as a professor of medicine at Harvard Medical School.

And then my -- then I also am employed by Brigham and Women's Hospital, which is one of the big teaching hospitals of Harvard Medical School.

Q. Thank you.

And these are all associated with Harvard University.

A. Well, yes. Harvard School of Public Health and Harvard Medical School are schools in Harvard University. And Brigham and Women's Hospital is its own entity. It's a hospital, but it's one of the major teaching hospitals providing clinical training to Harvard medical students.

Q. Thank you.

Now, in connection with your teaching responsibilities at Harvard Medical School and the Harvard School of Public Health, what courses have you taught?

A. Well, at Harvard School of Public Health I teach the science of nutrition to graduate students. These are students that are either getting a master's in public health, master of science, or who are getting a Ph.D. or equivalent degree.

I teach -- I teach a seminar in scientific writing for advanced Ph.D. students, in other words, teaching them how to write a scientific paper and how to submit it in to a scientific journal. The whole publication process I teach to advanced Ph.D. students.

Then I give lectures often at Harvard Medical School. I teach nutrition to -- nutrition -- mostly

nutrition and cardiovascular disease, diabetes, obesity, to Harvard medical students, give lectures there. Then I do the same at Brigham and Women's Hospital to medical residents or fellows in cardiology training.

Q. Have you also in the course of your career taught nutritional epidemiology?

A. I teach -- yes. I give lectures in nutrition, nutritional epidemiology.

Q. And do you teach about nutrition and disease?

A. Yes. Well, in the nutrition lectures in the nutrition course, the science of nutrition that I mentioned and nutritional epidemiology, yes, the focus is definitely nutrition as it relates to disease, particularly cardiovascular disease, obesity, diabetes.

Q. And have you also taught clinical epidemiology, including clinical trials?

A. Yes. I've given lectures at the medical school on that.

Q. Now, during your career have you engaged in scholarly research?

A. Yes.

Q. And is that research related to cardiovascular disease, including coronary heart disease, the relationship between nutrition and these risk factors, including lipids, hypertension, obesity and diabetes?

A. Yes. That's really where my research started. It started in nutrition back when I was a medical student in the '70s, and it's been a major theme of my research career up to the present time.

Q. And has your research also included the effects on coronary heart disease or cardiovascular disease and various risk factors of modifying diets, foods, food components and drugs?

A. Yes.

Q. Has your research resulted in published articles?

A. Yes.

Q. About how many published articles?

A. Well -- okay. So research articles in the peer-reviewed science literature certainly some -- about 170 of those. And then I've also written review articles on topics such as the ones you mentioned, and I've written editorials and position papers, and so forth, and those also get published in major scientific journals, and I have about 60 or 70 of those.

Q. On the table before you is a document that's been marked CX 1291. Could you identify that document. It's in the left-hand side of your binder.

A. Yes. That's my expert report.

Q. Okay. Now, on pages 2 and 3 of this report you

have listed some publications; is that correct?

A. Correct.

Q. Do those -- the articles listed there, do they report on original research that you have conducted?

A. Yes.

Q. Okay. I want to ask you about the research underlying some of these articles.

For example, could you talk about the study that's identified in paragraph (e).

A. Paragraph (e), yes.

Well, this was a randomized, controlled study. It was a comparative effectiveness study of different diets to promote weight loss in people who were overweight or obese. It was a two-year study. It was the largest of its kind. Eight hundred -- over 800 overweight or obese participants were randomized to one of four weight loss diets, and the results over two years were studied.

It was a study -- the research was sponsored by the National Institutes of Health, actually the National Heart, Lung and Blood Institute, and it was published in the New England Journal of Medicine in 2009.

Q. And is the New England Journal of Medicine a high-end journal?

A. The New England Journal is considered to be the top.

Q. Could you describe the research that's listed in paragraph -- I believe this is paragraph (l).

A. (l), yes. Okay.

Well, this was a randomized, placebo-controlled trial of a drug, pravastatin, which is a statin drug. It lowers cholesterol levels. And it was a study to determine whether pravastatin reduced heart disease in patients who had average cholesterol levels.

And that was a big issue in the late '80s and early '90s. The issue was whether an average cholesterol level was really too high and should be lowered via drug treatment.

This was a study in 4,159 patients, and the duration was five years, and indeed we found that pravastatin significantly reduced heart attacks, strokes, related conditions in these patients.

Q. And with regard to the study that's listed and described in paragraph (j), could you discuss that.

A. Yes. Okay. (j).

Now -- so this was a meta-analysis of cholesterol-lowering effects of dietary fibers, meaning, for example, oat bran or fruit pectin, guar gum that's used in some -- in foods.

So the issue at that point was that individual studies were very inconsistent in results about whether these fibers lowered cholesterol, some studies showing yes and some studies saying no.

So when that happens, the standard procedure is to combine all of these studies together in what's called a meta-analysis to determine what the overall impact of fiber is on cholesterol levels. And indeed, there was a small real effect of fiber on cholesterol levels that was identified by the meta-analysis technique.

And that was published in the American Journal of Clinical Nutrition. In fact when I checked a few years ago, a couple of years ago, when I was an associate editor of that journal, this paper was the most widely cited of all the AJCN papers over the years.

Q. And turning to paragraph (m) of your expert report, could you describe the research that underlie that report.

A. Yes. Okay. Well, this was the well-known DASH diet. Now, DASH is a diet that was designed to lower blood pressure, and it utilized all the evidence available on foods and nutrients to lower blood pressure. I led -- I was the chair of the study design

committee that designed the DASH diet and the DASH study.

This study -- so this study showed that diets that are high in fruits and vegetables, high in whole grains, fish, reduced in sugar and sugar-sweetened beverages, reduced in refined carbohydrates and red meats, that diet, the diet that is now called the DASH diet, substantially lowered blood pressure compared to the control diet, which was sort of what people eat, what an average -- an average American diet.

And that study was published in New England Journal of Medicine, and in fact the DASH diet and its modified -- modifications or improvements over the years is in fact the standard used for U.S. dietary goals and the American Heart Association's nutrition guidelines, and so forth.

Q. Thank you.

Now, during your career you've conducted both observational research and randomized clinical trials; correct?

A. Correct.

Q. Can you conclude from observational research that there's a causal effect between an intervention and reduction of heart disease?

A. No. That cannot be proven from an observational

study.

Q. Does that mean that observational research is bad?

A. Oh, no. Observational research is very, very important. Particularly well-conducted, well-executed observational research is very important. It's just one important modality in the progress of evaluating foods, nutrients or anything.

Q. Have you offered -- and you mentioned earlier that you've also offered review articles relating to cardiovascular disease, coronary heart disease and the relationship between nutrition and these diseases or other risk factors?

A. Yes.

Q. Are some of them identified on page 5 of your report?

A. Yes.

Q. For example, could you describe what the publication that's marked as -- on page 5 as paragraph (a), could you identify the substance of that article.

A. Yes, paragraph (a).

Well, paragraph (a) is a scientific statement from the American Heart Association on dietary sugars and cardiovascular health. I was a member of the

writing group and participated in discussions and editing, drafting of that, of that article.

So that article is published in Circulation. It's the leading heart journal that's -- it's produced by the American Heart Association, and it's where the American Heart Association publishes its scientific statements.

So we -- the -- you know, the bottom line was that we certainly had concern about this high amount of sugar intake causing obesity and other metabolic problems.

And also that actually -- that statement came out of the nutrition committee of the American Heart Association of which I am currently the chair.

Q. Could you describe what paragraph (b) is.

A. Okay. Paragraph (b) is also a scientific statement from the American Heart Association. The Heart Association was quite concerned that the scientific discussion on polyunsaturated fatty acids was getting skewed in a particular direction favoring the omega-3 fatty acids, whereas the scientific evidence was very strongly that both the omega-3 and the omega-6 polyunsaturated fats were beneficial.

We wanted to set the record straight, and we

organized a writing group led by the first author, Harris, William Harris, who has built his reputation on omega-3 fatty acids, so here we had a top researcher in omega-3 fatty acids writing a statement emphasizing that omega-6 fatty acids are very beneficial. As you can see, I was the senior author of that statement.

Q. With regard to the publication identified in paragraph (d), could you discuss that document.

A. Yes. Okay. Now, that's a -- the Heart Association wanted to have an update of effects of soy protein, isoflavones, and cardiovascular health.

At that time I was a member of the nutrition committee -- I was not in the leadership at that time -- and the leadership asked if I could study the evidence and lead the writing group.

And in fact the evidence in fact was very much balanced between benefit and no benefit of soy protein and isoflavones with actually the potential that there could be some harm on the cancer side.

So we felt that was extremely important to summarize for the public because again the public was getting in some ways a skewed concept of the benefits of soy protein and the soy isoflavones. Particularly for women's health we felt the message was getting a little bit away from the scientific evidence.

Q. Now, have you also served as the principal investigator in federally funded studies relating to nutrition and cardiovascular disease?

A. Yes.

Q. And could you describe some of these studies.

A. Yes. I mean, really it went back many years. I've been a principal investigator, meaning, I applied for and was awarded grants from the peer review system at the National Institutes of Health on nutritional topics.

And for example, in the '80s, that included nutrition and blood pressure.

And the DASH study, for example, the DASH sodium study, which really established the powerful dose effects of dietary sodium on blood pressure, I was principal investigator of that. It was funded by National Heart, Lung and Blood Institute in the late '90s.

And then in -- as noted by lowercase (a), this is the diet study in weight loss that I described earlier that ended in 2009.

And currently I have two NIH grants in the nutrition field. One is by (b), listed by lowercase (b). It's what we call the OMNI-Carb study. It's a refinement of the DASH diet.

We're constantly trying to extend our understanding of whole diets and cardiovascular health, so the OMNI-Carb study is trying to find out the effects of types of carbohydrate, for example, fruit versus juice or -- as part of a total diet, carbohydrate-containing foods that are absorbed quicker or absorbed slowly.

And that's a controlled feeding study. We feed -- like the DASH study, we feed people complete diets. It's very, very carefully controlled. And we compare -- in this study we're comparing four different diets.

Also in lowercase (c) this is a new grant I got in the middle of last year, and that's to study how dietary fat affects the metabolism of HDL. HDL is the good cholesterol, commonly called good cholesterol. And dietary fat raises the good cholesterol. High-carbohydrate, low-fat diets lower the good cholesterol.

So we're trying to understand what's at the basis of this. I mean, is this a problem of low-fat diets that they lower -- it lowers good cholesterol? Well, it might be. We're trying to understand the metabolism in that.

JUDGE CHAPPELL: Hold on a second.

MS. EVANS: Are we having problems with...

(Pause in the proceedings due to technical difficulties.)

JUDGE CHAPPELL: Next question.

BY MS. EVANS:

Q. Do you keep current on developments and research in the areas of nutrition, cardiovascular disease, cholesterol disorders and hypertension?

A. Yes.

Q. How?

A. Well, by reading the literature as it comes out, by attending and participating in scientific conferences in these fields.

Q. And do you have any experience as an editor of medical journals?

A. I didn't catch that. Sorry.

Q. Do you have experience as an editor of medical journals?

A. Yes. For three years I was an associate editor of the American Journal of Clinical Nutrition; which means, the associate editors have responsibility for evaluating the quality and importance of submitted research manuscripts and making the decision actually whether to accept the manuscript for publication or not.

Q. In an average year about how many manuscripts do you review?

A. Two to three hundred.

Q. And do many of these papers involve randomized clinical trials and other clinical studies?

A. Yes.

Q. And do you review these for the adequacy of the design and the conduct of the clinical research?

A. Each one.

Q. And do you review them for the appropriateness and adequacy of the statistical analysis?

A. Yes.

Q. Now, what portion of the studies you review involve cardiovascular disease or coronary heart disease?

A. Well, most of them. That's my -- that's a major area of my expertise, and that's what the editor in chief wanted me on the -- as an associate editor, to evaluate studies related to cardiovascular health or obesity and sometimes diabetes.

JUDGE CHAPPELL: Hold it.

(Pause in the proceedings due to technical difficulties.)

BY MS. EVANS:

Q. Do you also serve as an adviser to federal and

nonprofit entities related to nutrition, cardiovascular disease and coronary heart disease?

A. Yes.

Q. I think you mentioned already the Heart Association, one of your responsibilities there?

A. Well, I'm the chair of the Heart Association's nutrition committee, which is the committee that advises the Heart Association on nutrition, on nutrition-related science and public health.

Q. And you mentioned the National Heart, Lung and Blood Institute.

What is your relationship with that organization?

A. I serve or advise on their committees.

For example, they're involved in the U.S. dietary goals, the 2010 U.S. dietary goals, and I was asked to be an adviser to the 2010 dietary goals.

Secondly, the National Heart, Lung and Blood Institute generates guidelines for cholesterol treatment, and I am currently on that panel that is revising the cholesterol treatment guidelines for the United States.

I'm also on the lifestyle working group, which is a cross-cutting group that goes -- that advises the cholesterol treatment, the obesity treatment group,

regarding guidelines.

JUDGE CHAPPELL: Hold it.

(Pause in the proceedings due to technical difficulties.)

BY MS. EVANS:

Q. Do you have a relationship with the National Kidney Foundation?

A. Yes. The National Kidney Foundation produces guidelines for patients with chronic kidney disease or kidney failure, and they have a guidelines committee on treating cholesterol or lipid disorders because kidney patients get disorders of -- cholesterol-related disorders, and they've asked me to serve on their guidelines panel.

Q. And what is The Endocrine Society?

A. The Endocrine Society is one of the top professional organizations for endocrinologists.

Endocrinologists treat diabetes and thyroid disorders and things like that.

And they -- they also convened a group to study hypertriglyceridemia, in other words, high levels of blood fats, and they asked me to be on that panel to advise them on guideline information to advise endocrinologists on how to treat patients with high triglycerides.

Q. Finally, did you serve as an invited adviser in connection with the 2010 revisions to the dietary guidelines for America?

A. Yes, I did. I actually mentioned that a few -- a minute ago, but yes, that is true.

Q. Now, are you a member of professional societies relating to cardiovascular and coronary health?

A. Yes.

Q. Could you describe these.

A. Well, the major society that I'm involved with is the American Heart Association.

Q. And have you -- are you regularly asked to serve as a guest lecturer or panelist at professional meetings?

A. Yes, I am.

Actually also I'll just mention the American Society of Nutrition I'm a member and fellow of.

And yes, I'm asked to give presentations at workshops and scientific meetings on nutrition-related topics.

Q. And do many of these focus on heart disease and cholesterol disorders and blood pressure?

A. Yes.

Q. About how many panels have you or invited

lectures have you done since 2004?

A. About 60.

Q. Now, based on your education, training and experience, you have many areas of expertise; correct?

A. Correct.

Q. Would you consider yourself to be an expert in the field of nutrition?

A. Yes.

Q. Cardiovascular disease, including coronary heart disease?

A. Yes.

Q. Cholesterol disorders?

A. Yes.

Q. Hypertension?

A. Yes.

Q. Analysis of clinical studies?

A. Yes.

MS. EVANS: Okay. Now, based on Dr. Sacks' education, training and experience, complaint counsel moves for Dr. Sacks to be accepted as an expert in nutrition, cardiovascular disease, including coronary heart disease, cholesterol disorders, hypertension and analysis of clinical studies.

MR. FIELDS: No objection, Your Honor.

MS. EVANS: Thank you, sir.

JUDGE CHAPPELL: Any opinions that meet the proper legal standards will be considered.

MS. EVANS: Thank you.

BY MS. EVANS:

Q. Now, Dr. Sacks, based on your experience, do you have an opinion with regard to what kind of evidence is needed to support a claim that a product like pomegranate juice or pomegranate extract prevents or reduces the risk of cardiovascular disease?

A. Yes.

Q. And what is that -- if you could bring up -- I'd like to refer you to paragraph 20 of your report.

Does that state your opinion with regard to the evidence needed to show a prevention or reduced risk of cardiovascular disease?

A. Yes.

Q. And so could you read that paragraph.

A. Yes.

"In my opinion, 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 the appropriately analyzed results of well-designed, well-conducted, randomized, double-blinded, controlled human clinical studies (referred to by experts in the

field of clinical testing as 'RCTs'), demonstrating significant changes in valid surrogate markers of cardiovascular health. The population can be persons with or without established CVD or CHD. The studies, research, and/or trials would need strong 'p' values. I should further note that, in my opinion, 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."

Q. Now, based on your experience, do you have an opinion with regard to what kind of evidence is needed to support a claim that a product like pomegranate juice or pomegranate extract treats cardiovascular disease?

A. Yes.

Q. In what manner would this evidence need to differ from the evidence to support a prevention claim?

A. Well, it would require patients who have established cardiovascular disease.

Q. Now, you used a lot of terms in your opinion about the level of evidence required, and I'd like to explore those further.

What do you mean by a controlled clinical study?

A. Okay. A controlled study is a study in which

the -- there are at least two groups, and one group gets the agent that's being tested, such as pomegranate product, and the other gets an alternative, which could be a placebo or some control substance or nothing. That would be -- that would be a control, a control group, so a controlled study has a group that gets the active drug or an active food or a control group that gets something else.

Q. In paragraph 22 of your report, you talk about methodological drift. What does that mean?

A. Methodological drift, well, it's a change in the conditions of measurement, for example, a change in calibration of instrumentation. Sometimes it could be due to seasonal changes, and they cause just changes in anything that a study is attempting to measure.

Q. Is it sufficient if a study is self-controlled?

A. Well, "self-controlled" is actually not a term that we use in clinical trials research very often. Occasionally you see it.

So self-controlled research, if it refers to a randomized crossover study, it's fine. In that case the self-controlled research is that both the control substance and the active agent is given to the same people in random order, so that is a good type of self-controlled research.

Now, occasionally self-controlled research is -- self-controlled is applied to just a before-after study where patients are studied before a treatment is given or -- and then after a treatment is given, and there's no control group in that type of study and occasionally called self-controlled. Well, that study is simply not controlled at all. It's not correct to even use the term "controlled" in that kind of a study.

Q. That's just a before-and-after study?

A. Correct.

Q. Now, you've indicated that randomization is an important part of a clinical trial. Why is this?

A. Well, randomization creates -- it creates a randomized -- creates a clinical trial. It distinguishes a clinical trial from an observational study.

So in an observational study, people choose what foods or activities they're going to engage in. In a trial, the research chooses for the patients what they're going to take.

So randomization ensures that the choice of treatment or placebo is not influenced by the biases or preferences of either the patient or the researcher or treating physician.

So in other words, the assignment of, let's say,

an active agent or a placebo is done entirely via chance with no bias whatsoever, so it creates two groups, a control group and a treated treatment group that are identical in all characteristics as produced by the randomization process.

Q. And does it create a statistical likelihood that the two groups will be similar on both measured and unmeasured factors?

A. Well, if a study is large, then randomization has a greater chance of being effective. If a study is small, let's say you have twenty patients and you randomize ten to one group and ten to another, well, just by chance those groups could be quite different.

Q. Now, what is the importance of blinding to a clinical trial?

A. Well, blinding is -- well, there are different types of blinding, but blinding is important to ensure an unbiased -- unbiased measurements, unbiased analysis.

So just in brief, it's very important, it's most essential that the researchers taking the measurements and analyzing the data are blinded to the treatment assignment.

So in other words, a researcher who measures -- let's say he's measuring blood pressure -- really

absolutely cannot know whether that the person who's getting the measurement is on active agent or placebo. That's what's -- that's the most essential part of blinded research.

Now, the other aspect then is that the patient or the research subject also should be blinded as much as -- as much as a particular study can permit, so the patient or research subject is not told that he or she is getting an active agent or a control agent or placebo.

Q. Now, are there instances when blinding of the patients is not possible?

A. Well, for example, if you're -- I mean, you know, one could do a study comparing apples and oranges, literally, in which case it's impossible to blind, you know, an apple and an orange.

Q. You can blind the fruit, but with people that's different.

A. Exactly. Or you can test -- in other words, I did a study of salt content, for example, the DASH sodium study that I mentioned earlier, and in that study -- well, we tested diets that had different levels of salt in them.

So we did not tell the research subject, Now you're going to get the low-sodium diet or now you're

going to get the high-sodium diet. We just said, You're going to get diet A and diet B. But of course it tastes different, so realistically, you know, many of the research subjects could -- you know, could, you know, taste the difference in sodium, so strictly speaking, you know, they weren't entirely blinded to the intervention.

Q. But in that case were the investigators kept blinded?

A. Right.

So in that case the investigators were kept blinded by very careful procedures, essentially a firewall between the measurement team and analytic team and the nutritional team. The nutritional team obviously have to know what they're putting in the food, but there's a firewall between the measurers and the interventionists.

Q. Now, once research has been completed and all the data has been collected, how should the data be evaluated?

A. Okay. Well, the data in a randomized, controlled trial, the changes in the outcome variables in the treated group have to be compared to the changes in the control group.

Q. And should the protocol -- should there have

been a protocol for a good trial?

A. Yes.

So the standard procedure is that a protocol is written describing the essential features of the research, and it also states the analysis plan and importantly states the primary outcome variable.

In other words, to give an example, let's say the purpose of a study is to evaluate an agent on blood pressure, so to treat hypertension, so the protocol would state that the primary outcome variable of this study is systolic blood pressure or, you know, carotid intima-media thickness of the posterior wall, et cetera, et cetera.

Q. Are you familiar with the term "per-protocol analysis"?

A. Yes.

Q. And what does it mean?

A. Well, per-protocol analysis is usually a secondary type of analysis in a randomized clinical trial.

So to back up a bit, the primary type of analysis is called intention to treat. What this means is that all randomized participants, all participants entered into the trial need to be analyzed, whether they adhere or don't adhere or whether they drop out or

whether they disappear or whatnot. There are procedures to deal with missing data, and intention to treat involves all the participants who were randomized in the study.

Now, that is absolutely critical, the intention-to-treat analysis is absolutely critical, and it's the only truly valid way to analyze a randomized clinical trial. If you don't do an intention to treat, then a clinical trial becomes more like an observational study because, as I mentioned earlier, in an observational study the participants choose for themselves whether they -- you know, whether they -- you know, choose their treatment or foods or what have you.

In a randomized trial, the participants don't choose. If you let the participants drop out and you don't count their data, then essentially you're creating out of a beautiful randomized clinical trial more of a, you know, less precise observational study.

So that's the standard.

Now, your question was per-protocol, so "per-protocol" is used to refer to an analysis only of the subjects in the study who adhered to the protocol, did not drop out, did not -- you know, had a certain specified level of adherence. Now, that's fine to do a secondary analysis.

Q. So are you saying that the intention-to-treat analysis is the standard for scientific research?

A. It is.

Q. Now, what's the importance of a between-group analysis?

A. Okay. So between-group analysis is the correct way to analyze a randomized, controlled trial.

So in a randomized, controlled trial participants are assigned -- are put in the active treatment group or the control group, so it is -- it's essential to analyze the changes in the active treatment group compared to the changes in the control group. Essentially the changes in the active treatment group are subtracted from the -- the changes in the control group are subtracted from the changes in the active treatment group. And that's the way to determine whether the active treatment actually, actually has an effect beyond methodologic drift, seasonal effects, other secular effects.

Q. Now, what's the meaning of the term "p-value"?

A. P-value. Well, p-value is probability, is the probability that the changes that occur in the outcome variables are more than simply chance. And the p-value itself is a sort of level of probability defined by the protocol, usually .05, but it could be something

different.

Q. Now, is statistical significance alone sufficient?

A. Statistical significance establishes whether the change in the active treatment group is due to something more than chance, is real.

Q. Uh-huh.

A. But the change, for example, could be very, very small and might not be clinically important, so we often ask whether the -- whether statistical significance is similar to clinical significance, and it's really clinical significance is -- you know, follows from statistical significance. You need statistical significance to tell whether a change is real, and then you look at the change and say, well, is it meaningful to the clinical course of a patient.

Q. Now, do the endpoints that are measured -- do they affect the persuasiveness in terms of whether a study suggests a benefit to heart health?

Are you familiar with the term "endpoint"?

A. Yes.

Q. So in the case of heart disease, what are the relevant direct endpoints?

A. Well, the direct element -- the direct endpoints are heart attacks, unstable angina, the need for a

coronary stent or coronary bypass surgery, death.

Q. And are there relevant and reliable surrogate markers of heart disease that are recognized by the Food and Drug Administration and clinical guidelines?

A. Yes.

Q. What would they be?

A. Well, they're the blood pressure and LDL cholesterol.

Q. And are there also some additional markers that at least some experts in the field of cardiovascular disease consider to be reliable surrogate markers?

A. Yes. For example, C-reactive protein as a measure of inflammation, high triglyceride levels or low HDL cholesterol levels.

Q. So do some guidelines permit these to be used as targets in clinical trials?

A. Yes.

Q. Now, are you familiar with the term "carotid intima-media thickness"?

A. Yes.

Q. And what is this?

A. Carotid intima-media thickness. Okay. Well, "carotid" refers to the carotid artery, which is an artery -- there are several of them -- arteries in the neck that feed the brain.

Now, the intima-media thickness. Now, the lining of the carotid artery -- the lining of the carotid artery is -- well, just under the lining of the carotid artery is an area called intima, and that's where cholesterol goes in, that's where the blood vessel gets blocked, where inflammation occurs. And then deeper, beyond this intima, intimal layer, is the media, which is a muscular layer.

So intima-media thickness includes the intima, the layer where atherosclerosis, cholesterol, inflammation occurs, and the muscular layer, which is irrelevant to atherosclerosis and disease, so intima-media thickness is the sum of the thickness of the intima and the media.

Q. So the fact that it also measures the media, is that kind of noise in the measurement?

A. Yes. So actually carotid intima-media thickness is composed of the disease process plus some noise in the -- it's not a purely a disease, a disease imaging technique.

Q. Now, do you have an opinion on the reliability of CIMT, carotid intima-media thickness, as a measure of change in cardiovascular disease?

A. Yes.

Q. And what is this?

A. I think it's moderately -- it's moderately reliable. If one sees a reduction in the intima-media thickness, then it's reasonable -- it's reasonable evidence, moderately good evidence, that there is a reduction in atherosclerosis, although I just add the proviso that if there isn't a -- it's not a very tight connection. It's a moderate -- in my opinion, it's a moderate connection, and it can be a useful technique.

Q. Would you be reluctant to rely on CIMT improvements alone if that was the only evidence that an intervention prevented or treated coronary heart disease?

A. Yes. I would be reluctant to rely only on CIMT for reasons that I mentioned, and some other -- some other imaging technique it would be important to also have.

Q. Now, what would be an example of a second imaging study?

A. Well, for example, coronary arteriography. That's where the coronary arteries are directly visualized. That's a -- I mean, that's a -- or, you know, some special new imaging technique of coronary arteries that actually looks at inflammatory plaque in the artery, some other imaging technique.

Q. Now -- and was there a recent published article

that evaluated whether or not reductions in CIMT were in fact directly associated with improvements in heart disease?

A. Yes.

Q. And what did that study show?

A. Well, that article actually was, in my -- for me, that was rather surprising that the article really showed there was -- that the relationship between reduction in CIMT and reduction in coronary incidence was actually rather small.

Q. Now, does the number of tested subjects and their characteristics play a role in your evaluation of the methodological soundness of a study?

A. Yes.

Q. And how is that?

A. Well, generally the more subjects, the more subjects, the better. It -- and for many reasons.

I mean, one reason is that it just reduces the chance of a null effect, increases the chance of actually detecting real effects. It generally studies a wider range of people, so it would be more generalizable. Larger studies are often conducted with higher quality or supervision because they involve multiple sites.

So there are a number of reasons why big studies

are better.

Q. When you talked about the diversity of the population, is there a -- are there instances where diverse, different populations have different heart disease risk?

A. Oh, absolutely. There's quite a lot of difference in heart disease risk across populations.

I mean, for example, I'll just give you -- and actually there are differences in response to treatment.

I mean, for example, triglyceride levels. You know, high triglyceride levels are a risk factor for heart disease. Now, African Americans have low triglyceride levels compared to Caucasians or South Asians, for example. And in fact diet has only a minimal effect on triglyceride levels in African Americans compared to Caucasians and other racial ethnic groups, so it is important, you know, to have enough of a study population with different groups to be able to be confident that the results are generalizable.

Q. Does the length of a trial or study play a role in your evaluation of its methodological soundness?

A. Yes. Well, the length of the trial -- the length of the trial must be selected so that a new --

you know, a new baseline or a new steady state is achieved by the treatment.

So, for example, in the field of blood pressure lowering, you know, one likes to see at least four weeks of treatment to see, you know, to be confident that a new steady state is reached.

Q. And is replication important to the credibility of studies?

A. Yes. It's very, very important. In fact, two well-controlled, well-conducted, randomized clinical trials are needed or a meta-analysis of many smaller studies with a definitive outcome are needed.

Q. And should they have been conducted by independent researchers?

A. Yes.

Q. Now, do you believe that most scientists in the fields of nutrition, epidemiology and the prevention and treatment of cardiovascular disease would require that this evidence that you've just described is the kind of evidence required to show the efficacy of products like pomegranate juice and the POMx?

A. Yes.

Q. And why is it that you believe that other experts would agree with you?

A. Well, I'm just articulating the standard of

scientific evidence in medical research.

Q. Okay. And do you discuss those standards, for example, at conferences and in consultation with others?

A. Oh, absolutely. I mean, it's also how we grade manuscripts when we evaluate them for -- in peer review or evaluate them on the editorial level.

Q. Thank you.

Now, did there come a time when you were asked by the Federal Trade Commission to review the scientific evidence relating to POM juice and POMx?

A. Yes.

Q. And in connection with this request, did the FTC provide you with materials?

A. Yes.

Q. Now, did we just advise you that they been provided by the respondents?

A. Yes.

Q. Now, if you could look at CX 1292, appendices 2, 3 and 4.

A. Okay.

Q. Are you familiar with those?

A. Yes.

Q. Do they show the documents that were provided by you -- to you by complaint counsel in 2010?

A. Yes.

Q. And there's about -- there's over 200 documents there?

A. Yes.

Q. And in addition, did you review the transcripts of the fact deposition of Dr. Sumner, Dr. Heber, Dr. Ornish and the exhibits attached to those depositions?

A. Yes.

Q. And about how many more documents was that?

A. Including the attachments?

Q. Yes.

A. Twenty or thirty perhaps.

Q. And in forming -- did you review these materials with an eye towards forming an opinion regarding whether they constituted reliable scientific evidence that POM juice or the POMx extract products prevent, reduce the risk of or treat cardiovascular disease?

A. Yes.

Q. And in forming your opinions, did you also rely on your education, experience and knowledge of developments in the fields of nutrition, cardiovascular disease, including coronary health (sic) disease, cholesterol disorders, hypertension, and analysis of clinical studies?

A. Yes.

Q. And did you also review of the expert reports of Dr. Ornish and Dr. Heber?

A. Yes.

Q. And the documents attached to those expert reports.

A. Yes.

Q. Okay. Were there included in the materials that complaint counsel provided to you a large number of articles reported on in vitro studies?

A. Yes.

Q. Did you review these articles?

A. Yes.

Q. And did this review include the articles mentioned in paragraph 30 of your report?

A. Yes.

Q. And -- but you reviewed many more than the ones you mention in paragraph 30.

A. Yes.

Q. Now, for example, did you review articles reporting on the results of studies that reported on the behavior of human plasma in vitro or studies on foam cells and microphages?

A. Yes.

Q. And at the transcript, did the transcript of

your deposition call foam cells "cell phones"?

A. Yes, actually.

Q. Just a little correction there.

Is it your opinion that human metabolism and disease processes are very complicated and cannot be replicated in model systems such as the petri dish or test tube?

A. Yes. They are very complicated and they cannot be replicated like that in a petri dish or in an animal model.

Q. So, for example, if you find a mechanism of action in an in vitro test, can you tell if the human body may have other mechanisms that counteract that?

A. Yes. I mean, that's the -- that's the fundamental problem of in vitro research. In vitro research studies single mechanisms. Now, those mechanisms may or may not actually work or be active in intact people. And furthermore, there are many other mechanisms that are affected by nutrients or drugs or whatnot that can either amplify, counteract, nullify the mechanism that study did in vitro.

Q. And did the materials that you reviewed include the results of animal testing?

A. Yes.

Q. For example, did you -- were there several

articles on tests in animals, including mice?

A. Yes.

Q. Why do researchers conduct animal studies?

A. Well, there are two reasons. One is one has to do toxicology testing, so animal studies are absolutely essential for safety testing. Then animal studies are useful for what we would call proof of principle.

For example, a biochemical or molecular or gene target is identified, and that target is manipulated in animals, and one can see whether an agent or a food or whatever, a nutrient or a drug affects that target by creating, you know, elegant animal models that manipulate the target, the expression of the target.

So that's fine, but it doesn't say what will happen when the same product or agent is given to an intact human. The animal models for proof of principle are actually poorly predictive of what actually happens in a human being.

Q. And so, in your opinion, are the results from in vitro and animal testing alone enough to prevent reasonable scientists to conclude that a tested product will prevent or treat heart disease in humans?

A. In vitro studies and animal models are never sufficient alone to prove a benefit in humans.

Q. What if there's dozens and dozens of them?

A. Well, I mean, no. I mean, you can have a mountain of evidence in animals and in vitro studies that don't amount to anything with regard to whether that same agent is effective in humans.

Q. Thank you.

You can turn in your binder to CX 542.

A. Okay.

Q. Is this one of the human studies that you were provided by complaint counsel?

A. Yes.

Q. Could you identify it.

A. Okay. The title of it is Pomegranate Juice Consumption Inhibits Serum Angiotensin Converting Enzyme Activity and Reduces Systolic Blood Pressure. The authors are Michael Aviram and Leslie Dornfeld, published in Atherosclerosis in 2001.

Q. Could you summarize what was done in this study.

A. Okay. Well, ten elderly patients with high blood pressure drank 50 -- were given 50 milliliters per day of pomegranate juice product for two weeks, so this was -- this was simply a before-after study. There was no control group in this study. And they measured serum angiotensin converting enzyme activity and blood pressure.

Q. What were the -- is blood pressure a recognized surrogate for heart disease?

A. Yes, it is.

Q. And what about -- can I call this ACE, angiotensin converter enzyme? Is that called ACE?

A. ACE.

Well, that's not a recognized surrogate of cardiovascular disease.

Q. Now, what results were provided in this report?

A. Well, it was stated that serum ACE activity went down by 36 percent, and then it was also stated that seven out of the ten -- that the ten patients experienced a 5 percent reduction in systolic blood pressure.

Q. Was this a randomized, blinded or placebo-controlled trial?

A. No, it was not.

Q. So in your view, does this study provide reliable evidence of an improvement in ACE or blood pressure?

A. No, it doesn't.

Q. Why not?

A. Well, because there's no control group.

Q. Is blood pressure something that can change over time without an intervention?

A. Blood pressure is one of those measurements that's notorious for changing over time.

For example, there are seasonal effects on blood pressure. Blood pressure goes up in the winter and down in the summer.

Secondly, blood pressure typically goes down during the course of the first few weeks of measuring, so especially in a study like this, it's a two-week study, you expect blood pressure to go down somewhat. Anxiety, new situations raise blood pressure, and over time participants, patients, get used to the circumstances, and their blood pressure decreases. And we have a term for that, "white coat hypertension."

So blood pressure is one of those measurements that without a control group, changes are really meaningless.

Q. Could you turn to CX 611.

A. Okay.

Q. Is this also one of the studies that you reviewed for complaint counsel?

A. Yes.

Q. Could you identify it, please.

A. Okay. This is a study. The first author is Michael Aviram, and the title is Pomegranate Juice Consumption for Three Years by Patients with

Coronary (sic) Artery Stenosis Reduces Common Carotid Intima Media Thickness, Blood Pressure and LDL Oxidation. It was published in the journal called Clinical Nutrition in 2004.

Q. Is Clinical Nutrition a well-regarded journal?

A. Clinical Nutrition is not a top-tier journal.

Q. Now, can you summarize what was done in this study.

A. Okay. So again he selected ten patients, and they were given pomegranate juice for one year. Five of them continued for up to three years. And then he had a control group that did not consume pomegranate juice.

Q. And does he call this a placebo group on some occasions?

A. In some occasions he calls it a placebo group.

Q. And did you read Dr. Aviram's transcript?

A. Yes.

Q. And did he indicate in his transcript, his deposition transcript, that in fact it was -- the study was not placebo-controlled?

A. Correct. That he stated that there was actually no -- nothing given to the control group, so it was not -- what he stated in this research article was actually untrue.

Q. And did he also say that he didn't randomize the patients, he just tried to match them up?

A. Right.

So in the paper -- in the published article he said that he randomized them, but in the other document, the transcript, it said he said that he didn't, he just selected them and tried to match them.

Q. What tests were conducted in this study?

A. Carotid intima-media thickness, blood pressure, LDL oxidation.

Q. Did he also do some serum measurements such as paraoxonase and paroxidation (sic)?

A. Peroxidation.

Q. Yeah.

A. Yes.

Q. And so what were the results that were provided?

A. Well, he said that blood pressure went down by 12 percent in the treated group but not in the un- -- control group and also that carotid intima-media thickness went down, decreased, in the treated group.

Q. And he said it went down by, what, 35 percent?

A. Thirty -- yes, yes.

Q. Now, was all the data that was provided in this trial before-and-after data?

A. Yes. Actually, yes.

Q. Was there any between-group statistical analysis?

A. No.

So what -- Dr. Aviram just made statements that blood pressure went down in the treated group but not in the control group, or carotid intima-media thickness went down by 30 percent in the treated group, went up by 9 percent in the untreated group, so he never did the proper statistics, which was to ask whether, for example, that 12 percent drop in systolic blood pressure in the treated group was actually different from the change in the control group.

Q. And to do that analysis you'd need the measures of -- well, what the range of the data and at different points in time?

A. Yes. What you'd need to do is to compute the change and the standard deviation of the change between the groups.

Q. Now, one of the things that Dr. Aviram did in this study was to compare carotid lesions from people in the POM juice group to carotid lesions for people in the third group; correct?

A. Correct.

Q. Now, what's a carotid lesion?

A. Well, a carotid lesion, it's a -- it's -- you might say it's a growth in the intimal part of the artery.

So right under the lining of the blood vessel is the intimal layer. It gets loaded with cholesterol, with different cells, fibrous elements, calcium, crystalline cholesterol, things like that, inflammatory cells, clots and what have you, very complicated, very complicated lesion. And in that -- and -- and those lesions will block the flow of blood, or they'll rupture and cause a clot, and that -- in the carotid artery, that can cause a stroke, for example, so it's a lesion.

Q. So did some of the people in the pomegranate juice group have to have a carotidectomy?

A. Yes. So -- that's correct. So -- yes. Some of the pomegranate -- patients in the pomegranate juice group had to get a carotid endarterectomy. That's essentially a surgical clean-out of the lesions in the carotid artery.

Q. A Roto-Rooter?

A. Right. Kind of.

Q. Did he compare those carotid lesions that he took from the POM juice patients -- I believe it was two of them -- to carotid lesions from just a totally

group -- different group of people?

A. Yes, he did.

Q. Okay. And what did he find?

A. Well, what he found was that the cholesterol content of the lesion -- of the lesions in the pomegranate group was less than the cholesterol content of the lesions in the other patients, the comparison group.

Q. And based on this, what did Dr. Aviram conclude?

A. Well, he concluded that pomegranate juice had some favorable effect at reducing cholesterol in the carotid artery lesions.

Q. And in your opinion, was that a reasonable conclusion?

A. Well, first of all, no. On its face it's not a reasonable conclusion. And that's -- I mean, that's -- that's because the patients -- the patients taking pomegranate juice were not compared to a random -- there was no randomized control group at all, so he just had some comparison group that's unspecified as to what their characteristics were, how they were selected and what have you, and -- but -- you know, so I wouldn't even grant him that pomegranate juice reduced cholesterol content in the lesions.

But even more so, there's another reason why his assertions of benefit make no sense, because here these people who were drinking pomegranate juice had deterioration in their atherosclerosis of the carotid arteries that required them to have surgery, so how can he claim that those patients were benefited by any of the measurements he took.

Q. Now, in your opinion, do these two human studies by Dr. Aviram -- so that would be the ACE blood pressure study that's marked as CX 542 and the IMT blood pressure study that's marked as CX 611 -- do they have sufficient evidence that they're reliable and can warrant serious consideration in light of their quality and benefits measure?

A. No.

Q. If you could please turn to CX 1198.

A. Okay.

Q. Is this one of the studies that you were provided by complaint counsel?

A. Yes.

Q. And could you identify this document.

A. Yes. This is a document. The first author was Michael Sumner and the last or senior author was Dean Ornish. The title is Effects of Pomegranate Juice Consumption on Myocardial Perfusion in Patients with

Coronary Heart Disease. It was published in the American Journal of Cardiology in 2005.

Q. Now, how many patients were involved in this study?

A. Okay. There were 45 patients.

Q. And what product was tested?

A. Pomegranate juice.

Q. And was this a randomized, double-blind, placebo-controlled study?

A. Yes.

Q. And what tests were conducted?

A. Coronary perfusion was measured and then -- yes, coronary measure was measured.

Q. Were lipids and blood pressure also measured?

A. Yes.

Q. Now, turning to table 2, does table 2 report the results of the IMT -- excuse me -- the myocardial perfusion testing?

A. Yes.

Q. Now, what does it show -- looking at the summed rest score, the summed stress score and the summed difference score -- that's the SRS, the SSS and the SDS -- what do they show about these two groups at baseline, the pomegranate --

A. So at baseline the placebo group has a high --

has -- well, it has a 3.8 score and the pomegranate juice has a 1.9 score.

Q. So does that mean that the pomegranate juice people started off with a healthier summed rest score?

A. Yes.

Q. And what does this table show with regard to the end of the trial?

A. The end of -- in the summed rest score?

Q. Uh-huh.

A. So in the pomegranate juice group the summed rest score at three months was 2.2, a little bit higher than 1.9 at baseline, and in placebo it was 3.8 at baseline and went down to 3.1.

Q. So does this indicate a statistically significant difference in the summed rest score at the end of the trial?

A. At the end of the trial?

Q. Uh-huh.

A. Well, he does not indicate that it's significant, so I'm assuming it's not significant.

Q. What about the data for the summed rest score -- excuse me -- the summed stress score?

A. So in the summed stress score a similar problem occurred, that at baseline the score in the pomegranate juice group was 6.4 and the sum in the placebo group was

quite a bit higher, was 9.6, so 50 percent higher. And for the summed stress score, in the pomegranate group the baseline of 6.4 went down a little bit to 6.0, in the placebo group the 9.6 at baseline went up a little bit to 10.2.

Q. And then did you discuss the summed difference score yet?

A. No, I didn't.

So the summed difference is the -- it's the difference between the summed rest score -- I mean, summed stress score and summed rest score. And that difference at baseline in the pomegranate juice group that went from 4.5 to 3.7, in the placebo group 5.9 at baseline went up to 7.1, and that was noted as statistically significant.

Q. Now, if you turn to page 3, the right-hand column, there's a discussion -- it's on the right-hand column. It's the last full sentence in the first full paragraph.

A. Okay. Is that the sentence that begins with --

Q. "Angina."

A. Yes, I see that.

Q. And what is angina?

A. Well, angina is chest pain due to insufficient blood flow to the heart.

Q. And did the study report there were no statistically significant changes in angina?

A. That's correct. It reported the angina episodes and stated that this difference is not -- was not statistically significant.

Q. And with regard to blood pressure, does table 3 of this report provide blood pressure results?

A. Yes.

Q. And what does it show?

A. That showed no effect.

Q. Now, do you believe that this study suffers from limitations on its face?

A. Yes, it does.

Q. Is use of myocardial perfusion data as an endpoint a significant limitation?

A. Yes. Well, it's a -- I mean, it's a biologically interesting process. It's certainly a biologically clinically interesting process, myocardial perfusion. But myocardial perfusion is not used as the primary outcome in studies of drug treatment in coronary heart disease. It's just an interesting mechanistic study to use and to add to clinical trials that use more -- you know, more recognized, more solid clinical outcomes, or it's a clinical test to try to evaluate chest pain in people.

Q. Now, would the summed stress score, the SSS, would that tell you, for example, if someone had angina?

A. Well, I mean, clinically it's a value that -- yes. I mean, clinically it's used to evaluate patients who have chest pain, you know, but if patients don't have chest pain, it doesn't necessarily indicate angina.

Q. Well, if you have a really bad summed score, does that predict a natural history outcome?

A. Yes. That predicts a natural history outcome, so a bad stress score is certainly a prognostic indicator of cardiac problems down the road.

Q. And of the three summed scores reported in Dr. Ornish's report, is the SSS particularly validated to predict natural history outcomes such as myocardial infusion (sic)?

A. Infarction.

Q. Infarction?

A. Correct. The SSS score in -- yes, is -- according to the leading textbook of cardiology, Braunwald's textbook, the chapter on nuclear cardiology states that, that SSS is particularly the most validated measure that has prognostic information in cardiac patients. That only makes sense because SSS is

composed -- is composed of essentially infarcted myocardium or dead heart muscle plus heart muscle that -- plus areas that are -- that have a functional deficit, so it's a combination of the effects of myocardial infarction and functional deficits.

Q. But the changes in summed scores over time, have they been validated as a reliable surrogate endpoint?

A. Well, those really are not used in clinical outcome studies when you're evaluating treatments that prevent or treat heart disease.

Q. So Dr. Ornish reports on three myocardial perfusion outcomes, the SSS, the SDS and the SRS; is that correct?

A. Correct.

Q. Now, when there are three possible outcomes, is a p-value of .05 or close to .05 generally considered to be a statistically significant effect?

A. Correct.

Q. There was --

A. Yes, a .05 is generally the standard for demonstrating an effect.

Q. But where there are three possible outcomes, in that instance -- three possible primary outcomes, in that case is a p-value of .05 statistically

significant?

A. Oh, okay. I'm sorry. I didn't get your question.

So yeah, I mean that -- when there are primary multiple primary -- well, when there are multiple outcomes, you get -- then a p-value of .05 is not, you know, really the same thing as -- it doesn't convey the same level of confidence than in a situation where there is one primary outcome.

You see, a p-value of .05 means a 1 in 20 chance of -- you know, a 1 in 20 chance that the result is false and due to chance -- okay -- a 1 in 20 chance, so if you have one outcome, you've got one shot at that 1 in 20 chance. If you've got three outcomes, you've got three tries or three throws of your 1 in 20 dice. If you've got ten outcomes, you've got ten choices -- you've got ten chances, so if you've got ten chances, you know, it's most -- it's very likely that one is going to hit. That's the problem of an unadjusted p-value.

So if you have three outcomes like in this case, none of which are specified as a primary outcome, you've got SSS, SRS and SDS, then a p-value of exactly .05, which is what they found, is not -- is really not as impressive as a p-value of 5 percent.

Q. Now -- and here, where there are changes in the SDS but not in clinical outcomes such as angina, is it clear that the SDS change would be clinically meaningful?

A. Well, that's the whole question about the SDS. SDS is a functional -- it's sort of a functional test. And like the textbook said, that really is the combination of structural and functional that has the closest relation to prognostic information. And again, it only makes sense because the SSS includes dead tissue.

So let's say a patient during the study has a silent myocardial infarction. That causes dead heart tissue, dead heart muscle, and that would be seen in the SSS. It would not be seen in the SDS, so you'd never want to take out -- you know, I mean, more dead heart tissue is bad. You don't want to take that out of your results by only relying on this SDS, which is functional.

Q. Okay. In this study was there an inconsistency of the number of patients discussed?

A. Yes.

Q. How many were enrolled?

A. Well, 45 were enrolled.

Q. And then four dropped out or had unreadable

data.

A. That's correct.

Q. And when you -- turning back to -- excuse me -- table 2, how many patients did they give data for?

A. 39.

Q. Okay. So --

A. Two that are unaccounted for it seems.

Q. Now, where there's a p-value very close to .05, is an alteration of the sample size potentially critical?

A. Oh, absolutely. I mean, there are two -- you know, two subjects who are just unaccounted for, it could easily change that p-value, well, in either direction, to make it stronger or to make it weaker.

Q. Now, in a situation like this, would you typically expect to see results for all of the patients that were originally randomized to treatment or control?

A. Yes.

Q. So Dr. Ornish's study did not follow the intention-to-treat analysis that is the standard for clinical trials?

A. It did not.

Q. Now, given the differences between the juice and placebo members in this trial, would you have

predicted that -- the baseline differences -- would you have predicted that the control group was going to get sicker?

A. Yes. In other words, the -- you know, the control group I assume by chance just had a worse, you know, worse perfusion, so they had a more severe disease to begin with. And I mean, how do they get more severe disease? Well, they have progressive accelerated disease, so you'd certainly expect as you follow them that they would continue to get worse at a more rapid rate than the other, than the pomegranate group.

Q. And at your deposition I believe that you discussed with respondent's counsel the concept of regression to the mean?

A. Correct.

Q. And they suggested that regression of the mean would have narrowed the differences?

A. Yeah, that was suggested.

Q. And what was your response to this?

A. Well, I think that's unlikely. I think -- I mean, regression to the mean, it's a statistical phenomenon that arises sort of out of chance when, you know -- after randomization.

So what happens is, with statistical regression to the mean, by chance, people who have higher values at

baseline will have a -- will show some decrease in those higher values over time. In other words, it regresses or decreases toward the average value, the typical value.

That happens a lot with something like blood pressure, which is there's a lot of bouncing around in an individual's blood pressure, so if you catch somebody at a high point, then the chances are they'll sort of move down.

But, you know, a myocardial perfusion score you wouldn't assume since this is an accurate, carefully done measurement, which it certainly looks like it was in Dr. Ornish's study, so that measurement, you know, was higher probably for something other than chance because it was a good measurement, so I wouldn't expect that this regression to the mean hypothesis to be accurate. Rather, it's more biology, as I mentioned, rather than statistics.

Q. And also at your deposition did opposing counsel ask you if it was true that the baseline differences between the juice and placebo groups were fully addressed through the statistical analysis?

A. No. I certainly did not see that in the statistical plan.

Q. What is your opinion about whether the baseline

differences were addressed through the statistical analysis?

A. No, I don't see any evidence that that occurred.

Q. Okay. Now, in your report you state that this study suffers from limitations on its face.

Are the issues that we just discussed, that is, the use of myocardial perfusion data, inconsistent number of patients, focus on the SDS score rather than the SRS and the SSS, use of a p-value of .05 when there were three potential outcomes, are those the limitations on the face of this study?

A. Correct.

Q. Now, given these limitations, do you have an opinion with regard to whether experts in the field of cardiovascular disease would consider the results of this study to reliably support the proposition that pomegranate juice provides a prevention -- a benefit in the prevention or treatment of heart disease?

A. Let me -- I mean, the conclusion is that pomegranate juice did not have those beneficial effects.

Q. Did you review additional documents related to this study?

A. Yes.

Q. Did they include the study protocol, Dr. Ornish's fact testimony, and other related documents?

A. Yes.

Q. Could you turn to CX 599.

A. Okay.

Q. Could you identify this document.

A. Yeah. This is the Beverage Study I protocol. That's the perfusion study.

Q. And what did this document reveal in terms of the planned duration of the study?

A. That it would be one year, twelve months.

Q. And did you also review CX 633?

A. Yes.

Q. Could you identify that document.

A. Okay. This is -- these are notes from a team meeting, Dr. Ornish's team meeting, research team meeting.

Q. What did this document show you?

A. Well, you know, the upper part, the upper panel in that document summarizes a discussion that occurred, and what it says is that -- well, I'll just read it:

"Dean says the good news is, after reviewing data, the research shows that ischemia is reduced with the sum difference score of 4.33 to 3.63. Dean wants to

quit while we are ahead and wants to call the Resnicks with the news" and then, et cetera.

Q. Now, you read Dr. Ornish's transcript; correct?

A. Correct.

Q. And he said that his funding had been cut?

A. Yes.

Q. Now, if his funding was cut, would you expect him to pay for the research himself?

A. No.

Q. It is reasonable to stop research if your funding is cut; correct?

A. Well, you have to. There's no choice in that situation. Correct.

Q. What should a researcher do in that circumstance?

A. Well, just close out the study I guess. I mean, that's an unusual circumstance. I guess you would have to close out the study as -- when the money runs out I suppose is -- you know, just try to keep the money going as long as you possibly can to complete as much of the protocol as you possibly can and then stop if you can't get more funding.

Q. Now, if you then publish a report about the study, should the fact that it was cut short be reported in the article?

A. Yes. Of course.

Q. And why is that important?

A. Well, again, it's important, in a controlled trial, it's essential to state what was the original plan and what was actually done. The original plan is the unbiased statement of what -- of the intentions of the researcher. What was actually done needs to be in line with what was planned. Otherwise, the study could have -- could develop biases. And readers have to know that, have to know, okay, if the study was not twelve months, why wasn't it and at what point and on what basis was the study stopped.

Q. Now, turning back to the protocol, CX 599, does that -- and turning to pages 4 and 5 of that, of that study, does that talk about the endpoints to be measured?

A. Yes.

Q. And does it expressly state anywhere that SDS was the primary endpoint?

A. No.

Q. Does this study anywhere -- does this protocol state anything about the statistical analysis to be conducted?

A. No.

Q. Okay. Now, did any of the documents that you

reviewed, including Dr. Ornish's testimony, relate to whether patients in the placebo group were unblinded before their three-month data was collected?

A. Yes.

Q. And what did his -- what did the testimony show?

A. Well, there was a group of subjects that -- well, they and the staff actually learned of their treatment assignment, in other words, both staff and patients. Now, of course staff really can't, really have to be blind. That's the most important part of blinding, is that the staff is blinded.

So yeah, there was unblinding.

Q. And it was about seven or eight people?

A. Correct.

Q. Now, did any of the documents -- and that was before their three-month myocardial perfusion data was collected?

A. Correct.

Q. Now, did any of the documents, including Dr. Ornish's transcript, that you reviewed relate to whether or not some of the placebo group patients in fact received a placebo treatment?

A. Yeah. There was -- there was information on that. Some did not receive a placebo treatment.

Q. So two of the patients were randomized placebo -- to placebo, but they never sent them any placebo product and they measured them at three months anyway?

A. Correct.

Q. And -- thank you.

Now, did any of the documents that you received that you reviewed suggest -- turning to CX 701 and looking at the -- there's a paragraph on the first page that's got the number 8 in front of it.

Did this document suggest significant baseline differences between the pomegranate and placebo group patients?

A. Yes.

Q. And should this statistically significant difference in the SS measures of the baseline patients at the beginning of the trial, which apparently was a p is less than .04, should that have been revealed in the published report?

A. Yes.

Q. Now, did any of -- turning to CX 664, is this a document you reviewed in connection with your testimony in this matter?

A. Yes.

Q. Now, in this document were they engaging in

various statistical analyses of the study results?

A. Yes.

Q. And they had -- they had the study results -- in the first paragraph they talk about study results involving 24 experimental patients and 16 control patients; correct?

A. Correct.

Q. Then they do -- at the bottom of the page they do the same study results, but they pull out one patient?

A. Correct.

Q. Correct.

And once they pull that patient out, there are 23 experimental patients and 16 control patients; is that correct?

A. Correct.

Q. And when they actually published the study results, were there also 23 experimental patients and 16 control patients?

A. Correct.

Q. So this person that they pulled out of the data, what was -- what was his health status?

A. Well, it sounded like -- it seemed -- reading the documents, it seemed like that patient had a silent myocardial infarction, a silent heart attack.

Q. And he was in the experimental group --

A. Correct.

Q. -- so -- and did pomegranate juice appear to have prevented his myocardial infarction?

A. Well, apparently not if he got his silent MI during the time he was drinking the juice.

Q. Okay. Turning to -- well, considering everything we've just discussed, do you have a conclusion about whether the results of the Bev I myocardial perfusion study support a conclusion that pomegranate juice had a favorable effect on coronary perfusion?

A. Yes, I have an opinion.

Q. And what is that conclusion?

A. Well, that the data do not support a benefit of pomegranate juice on cardiovascular health.

Q. Are you familiar with Dr. Ornish?

A. Correct.

Q. And you guys have actually published together?

A. Yes, we did.

Q. What's your opinion of Dr. Ornish?

A. Well, I knew him in the very early '80s when -- before he moved to Boston. He did his medical residency at Massachusetts General Hospital, and he was very interested -- he contacted me in the late '70s because

he was very interested in my research in vegetarians that I had published. That was my first -- my first scientific research was on vegetarian diets and cardiovascular health, so he was very interested in that and struck up a relationship and moved to Boston, and we did some research.

We did some research together at this yoga ashram in Connecticut where he was a member of that group, Swami Satchidananda's ashram in Connecticut. He was a member of that group, and he arranged for my boss and I to go out there and measure blood pressure and study their diets, which was an interesting study. Eventually we published the results together.

So that's how I originally knew him, and then he wanted to plan -- well, he had this really -- he had this great vision that I really shared, nutrition and the potential of nutrition to prevent and treat heart disease, that really so much of our heart disease is due to -- is due to our diet and lifestyle.

And he -- he pursued that vision and conducted his landmark coronary arteriographic study -- it's a landmark study -- when he -- after he moved to San Francisco. And he proved that his diet, as part of his program, not just the diet, but the whole improved lifestyle program could reverse coronary artery disease,

so that was his landmark study published in The Lancet, so give him a lot of credit for that.

But as things evolved, he got very -- sort of very dogmatic about a low-fat diet, which -- that a low-fat diet was superior to diets that were lower -- a low-fat, high-carb diet was superior to diets that were higher in fat or lower in carbohydrate, and that opinion became -- got further and further away from evolving scientific evidence that lower carbohydrate is actually better for cardiovascular health. And that -- some I think -- yeah.

And so -- so that sort of had kind of marginalized his impact because he didn't consider the evolving evidence, for example, on Mediterranean diets and, you know, being very healthy and the unwillingness of many people to eat a very -- a very, very low-fat diet that he recommended.

And I have to say I've been a bit disappointed in going through all these materials and seeing all the problems that -- you know, self-inflicted problems that occurred with this particular research.

MS. EVANS: Your Honor, is it a good time to take a break?

JUDGE CHAPPELL: How much more time do you need?

MS. EVANS: At least an hour, perhaps an hour and twenty minutes.

JUDGE CHAPPELL: Okay. We will take our morning break. We'll reconvene at 11:35.

(Recess)

JUDGE CHAPPELL: Back on the record Docket 9344.

Next question.

BY MS. EVANS:

Q. Dr. Sacks, could you please refer to CX 754.

A. Okay.

Q. Is this one of the studies you were provided by complaint counsel?

A. Yes.

Q. Could you identify this document.

A. Yes. This is the summary of the Bev 2 study.

Q. And who's it from?

A. This is from Dr. Ornish.

Q. And what does this document purport to be?

A. I'm sorry?

Q. If you read on in the text of the message, it says "attached is a summary of the Bev 2 results which should have been included in my prior e-mail."

A. Okay.

Q. And is there attached to it a document entitled Bev 2 Summary?

A. Yes.

Q. And what does that -- what does that document refer to?

A. Okay. This refers to a second study that Dr. Ornish conducted on pomegranate juice, and this study involved measurements of carotid intima-media thickness.

Q. And did you also review the protocol for this study?

A. Yes.

Q. And was that CX 597?

A. Yes.

Q. And according to the protocol, what was the purpose of the study?

A. The purpose was to determine the effect of pomegranate juice on carotid intima-media thickness and additional mechanistic blood measurements.

Q. And how many patients -- according to this protocol, turning to page 4, how many patients were in the target sample?

A. How many patients were in the -- you mean what was the -- I don't understand that question.

Q. Okay. It says -- does it indicate that the target sample was 50 participants?

A. Correct.

Q. Okay. And what product was tested?

A. Pomegranate juice.

Q. Okay. And how long was the duration of the study?

A. That was one year.

Q. Okay. Now, returning to CX 754, were there in fact 73 patients randomized in the study?

A. Yes, there were 73 patients.

Q. And have you summarized what was done in this study?

A. Okay. So this study was a randomized, placebo-controlled, blinded study. And it -- the participants were randomized either to pomegranate juice or to placebo. And CIMT and other measurements were taken at baseline, six months and one year.

Q. Was elasticity and blood pressure also measured?

A. Correct.

Q. And what were the results of this study?

A. The results were there were no significant changes to any of the measurements.

Q. And that looked -- and if you turn to page 4 of CX 754, does it identify baseline, six-month and twelve-month data for the IMT common carotid artery on the left, the IMT common carotid artery on the right,

and the IMT combined?

A. That's table 2?

Q. Yes.

A. Correct.

Q. And are the relevant results contained in the last column on that page?

A. The last column is the p-value for the results, yes.

Q. And we need to look at the time versus group data?

A. Correct.

Q. And did that -- so did that -- do those results show no statistically significant group at the end of the trial in the left common carotid artery, the right --

(Admonition by the court reporter.)

BY MS. EVANS:

Q. What do these results show?

A. Okay. The results showed no significant effect of pomegranate juice on any of these measurements, the common carotid artery on the left, the right, the combined, or these various measurements of carotid artery stiffness.

Q. And turning to page 5, do these provide information with regard to blood pressure results?

A. Correct.

Q. And what does it show?

A. There was no significant effect of pomegranate juice on any of these measurements: blood pressure, body mass index, cholesterol, HDL, triglycerides.

Q. Now, you're aware that at his deposition Dr. Ornish stated that he originally wanted to measure 200 patients in this study?

A. Correct.

Q. And his -- his budget got cut?

A. Correct.

Q. So did he argue that his -- the results of this study are not relevant to an analysis of whether PJ offers benefits -- pomegranate juice offers benefits to the heart?

A. Right.

Q. And did he argue that it was -- since it was underpowered, you couldn't pay any attention to the results?

A. Yes. He did say that.

Q. And if there were 200 people in the study, it would have been statistically significant?

A. That's what he indicated, yeah.

Q. And is that a reasonable argument?

A. No, it is not.

Q. Why?

A. Why.

Well, Dr. Ornish has only been -- would only accept a positive result, is what he's saying. He's saying he only accepts a positive result, a negative result is meaningless.

So that's not the way to do clinical trial research. In clinical trial research you have to have a position of equipoise, meaning that you can accept the fact that your agent can be effective or not effective. And you never do a study that excludes one of those possibilities at the outset, and that's apparently what he's saying. He doesn't care if the results are negative, because if they're negative, the study is too small. If they're positive, obviously, in his mind, they would be -- they would be credible.

So I mean, just on its face, that's not really a scientific way to go about conducting a clinical trial.

Now, another thing, if -- he may just flat-out be wrong anyway. I mean, a result that's negative in a smaller sample could be negative because there's no effect of the agent. I mean, that's a pretty -- I mean, that's a pretty obvious alternative.

And he could do a study of a million people and

find -- and not find any -- not find any effect as well. I mean, that's simply the way it could have turned out.

Q. Now, he's saying here, as I understand it -- and correct me if I'm wrong -- that if you had, you know, basically cloned these 73 people and tripled the size of the study, then there would have been a statistically significant result.

Can you -- can we assume that the extra 130 studies that were recruited for the trial would have had the same characteristics and the same response to the treatment as they did with this first 73 people?

A. I mean, not -- not at all. I mean, he's unable -- nobody can predict what would happen if you, you know, added 127 patients to the 73 patients. It's impossible. One alternative is, well, maybe there could be a significant effect in the 200. Maybe there would not be a significant effect.

Q. And would you characterize the results of this study as convincingly null?

A. Well, in the context of the study, 73-patient study, performed and executed well -- this is a well-executed study. I didn't see problems in this particular study -- the results are convincingly null.

Q. And do the results of this study have to be

considered as a part of the body of evidence relating to pomegranate juice and POMx on heart health?

A. Well, they must be considered. I mean, there's no other proper way to deal with these results. And results of any clinical trial have to be considered when -- you know, when evaluating or analyzing evidence on the effectiveness of any agent. You can never throw a whole study out just because it didn't show the desired positive effect that the investigator wanted to see.

Q. Now, could you turn to CX 1065.

A. Okay.

Q. Is this one of the documents you reviewed for complaint counsel?

A. Yes.

Q. And have discussed in your report?

A. Yes.

Q. Could you identify this document.

A. Okay. This is a research report by Michael Davidson and colleagues. It's titled Effect of Consumption of Pomegranate Juice on Carotid Intima-Media Thickness in Men and Women at Moderate Risk for Coronary Heart Disease. It was published in the American Journal of Cardiology in 2009.

Q. And you're familiar with Dr. Davidson?

A. Yes. I know Dr. Davidson very well.

Q. And what's your opinion of Dr. Davidson?

A. Dr. Davidson is one of the foremost clinical trialists in the cardiovascular field; meaning, he has a superb reputation for top-quality clinical trial research in cardiovascular disease.

Q. Can you summarize what's done in this study.

A. Okay. In this study -- in this study they -- the patients were randomized to pomegranate juice or to placebo, and they -- and they were studied -- their carotid intima-media thickness was studied at baseline and at 12 and 18 months.

Q. And how many patients were included in the intention-to-treat analysis?

A. I just want to make sure we get the exact number here.

It looks like there were 146 in the pomegranate juice and 143 in the control, in the control group.

Q. So 289?

A. Yes.

Q. Okay. And what product was tested?

A. Excuse me?

Q. What product was tested?

A. Pomegranate juice.

Q. And was this a randomized, double-blind,

placebo-controlled trial?

A. Yes.

Q. In addition to measuring IMT, did they measure blood pressure and markers of inflammation and oxidative stress?

A. Yes.

Q. Now, if you'd turn to table 3.

A. Okay.

Q. Does this table report on the results of the study?

A. Yes.

Q. Okay. And what does it show with regard to IMT?

A. Okay. Well, I mean, it shows no -- it shows no significant effect of pomegranate juice on IMT, either the anterior or the posterior or the composite carotid artery.

Q. At the end of the trial.

A. At the end of treatment, correct. At the end of -- correct.

Q. Now, looking at the anterior results alone -- and that's the top line -- does this right here provide a good example of why it's important to have a control group?

A. Well, yes.

Q. So the pomegranate juice group did have reduced progression of their IMT at the end of the year; right?

A. Correct.

Q. But so did the control group?

A. Correct.

Q. So if we hadn't had a control group, we wouldn't know what would have happened to that control group; correct?

A. Correct. We would not know whether the change in the pomegranate juice group would have occurred anyway.

Q. Now, looking at CX 1065 page 5.

A. Okay.

Q. In the first full paragraph, what does this paragraph show with regard to the blood pressure data?

A. Well, it said there are no significant differences between the pomegranate juice group and the control group in blood pressure, blood pressure and other risk markers.

Q. And that's at the end of the trial?

A. Correct.

Q. And did it also show that both groups gained weight?

A. Yes.

Q. How much?

A. It says one to two kilograms.

Q. Is this a meaningful weight gain?

A. Yes. Over 18 months.

Q. And if you refer to table 2, does that provide the results of the study on the measures of inflammation and oxidative stress?

A. Yes.

Q. And what does it show?

A. Again, no significant effect of the pomegranate juice compared to the control.

Q. And that is -- does that include measures of TBARS?

A. Correct.

Q. Now, returning to table 3 -- oh, strike that for a second.

How was compliance measured, compliance with the protocol measured in this study?

A. It was measured by subject report, diaries of intake.

Q. And is that indicated on page 2 in the right-hand column at the end of the second full paragraph?

A. Correct.

Q. And did Dr. Davidson report any problems with compliance?

A. No, he did not.

Q. Now, now we'll turn to table 3.

A. Okay.

Q. Does table 3 identify IMT results at 12 months?

A. Yes.

Q. And what were these results in terms of the anterior or posterior and composite results?

A. What were the results?

Q. Uh-huh. At 12 months.

A. Well, if you look at the anterior, in the pomegranate juice group the baseline was 0.84 millimeters and at -- at baseline and at 12 months it was 0.82, and in the control group it started at 0.85 and went to 0.84.

Q. Uh-huh.

Was that a statistically significant difference in the measurement?

A. You mean the 0.82 versus the 0.84?

Q. Uh-huh.

A. The p-value -- I don't know why they would report a p-value for that anyway, but they did. It's .02 -- it's 0.024.

Q. And with regard to the posterior measurement, what happened at 12 months?

A. So the pomegranate juice group at baseline

was .77, at 12 months it was .78, so it increased by .01 millimeters. In the control group it was 0.77 at baseline, went up to 0.79. It went up by 0.02 millimeters.

Q. Okay. And was the difference between those two significantly different?

A. No. The p-value is 0.128.

Q. And then finally on the composite measure, what does that show between baseline and 12 months?

A. Okay. So on the composite measure the baseline was 0.78 and the 12-month was 0.79, so it went up by .01, and in the control group it was 0.79 and went up -- at baseline and went to 0.81, and so it went up by 0.02.

Q. Now, they report a p-value for that; correct?

A. Correct.

Q. Now, is that p-value, is that reflecting progression of intima-media thickness?

A. No. It's -- you see how I narrated the results. I narrated the results by stating the baseline, the 12-month, and the change in each group. Okay? It's the change in each group that's key. We're looking at an intervention. We're then evaluating a change. It's the change that counts. And there is no statistical testing of that change in that table. However, in another part

of this document it states that there were no significant effects on changes at any time point.

Q. In fact -- I'm sorry.

A. So -- so that's the right way to analyze it, analyze the changes. That's exactly what they did at the end of the treatment. You see the last line on that table, progression at the end of treatment in millimeters per year. That's how they analyzed the end of treatment. That's appropriate. But they didn't present that analysis at the 12 months.

Q. In looking at the first line of the abstract in this study, it says that there -- that the study assessed the influence of pomegranate juice on anterior and posterior CIMT progression rates; correct?

A. Correct.

Q. Now, is there any scientific merit to saying that pomegranate juice can reduce IMT because the composite carotid arteries have smaller values at 12 months?

A. Absolutely not.

Q. And why not?

A. Well, it treats the data as a cross-sectional study, as just a -- it doesn't treat the data as it got produced. It got produced out of an intervention study. In an intervention study one has to look at the

change.

So the way I'm narrating these results, I'm narrating them in terms of change, and change is what has to be analyzed at 12 months as well as at the end of treatment, so it's an entirely -- this p-value on this table at 12 months composite of 0.022 is a totally meaningless p-value.

Q. Now -- and also in Dr. Ornish's scientific study, he looked at combined IMT results at 12 months; correct?

A. Correct.

Q. And there was no statistically significant difference there?

A. Correct.

Q. Okay. Now, turning to CX 716.

A. Okay.

Q. Did you also review this protocol in connection with your review of the available documents?

A. Yes.

Q. And in your opinion, is this a well-designed protocol?

A. Yes.

Q. And if you'd turn to page 28.

A. I'm sorry. Which page?

Q. Page 28.

A. 28.

Okay.

Q. Does this protocol identify the primary outcome variable?

A. It does.

Q. And what is that?

A. Okay. It says, "The primary outcome variable will be the difference between placebo and POM Wonderful juice groups in the posterior wall common carotid IMT progression rate in millimeter per year using (sic) noncontrast images."

Q. And did he also identify a number of secondary outcome variables?

A. Yes.

Q. Was the combination of the anterior and posterior walls, the combined -- the composite index, was that one of the secondary outcomes that he identified?

A. Yes.

Q. Well, looking down -- I'm sorry.

A. Yes. The bullet -- the second to the last bullet: Difference between placebo and POM Wonderful juice groups in the composite measure.

Q. Well, it says common and internal and the carotid bifurcation.

Did he measure the carotid bifurcation?

A. Oh, okay. I misunderstood your question. Yes. No. I -- the composite measure reported in the paper, in the article, is not what the composite measure stated here, which would include the internal carotid artery and the carotid bifurcation.

Q. Now, at your deposition, respondent's counsel asked you about Dr. Ornish's argument that the combined endpoints should have been the primary variable; correct?

A. Correct.

Q. Okay. Now, do you believe it's appropriate to analyze clinical trials in this manner?

A. No.

Q. Why is that?

A. Well, Dr. -- I mean, Dr. Davidson, first of all, he does these studies. He does carotid intima-media thickness studies in many of his clinical trials. He's very experienced in this kind of technique, so I'm not going to -- first of all, I wouldn't challenge Dr. Davidson's selection of the primary endpoint for carotid intima-media thickness in any way.

But that is -- Dr. Davidson stated clearly in what we have right up here on the screen what the primary outcome was. That was his best judgment of the

most important, relevant CIMT measurement to test the effect of pomegranate juice at the beginning of the study before it was analyzed.

So that is his best scientific -- best expression of his scientific judgment as to what's the most important thing to measure, and that's what the study must be judged upon. It's not right to go back and say, well, oh, I should have picked something else because what he picked didn't turn out to be significant.

Q. Okay. Now, does this report -- does this medical journal article, does it also report on a post hoc subgroup analysis?

A. Yes.

Q. And you discuss this in your report at paragraph 53?

A. Yes.

Q. And what is a post hoc analysis?

A. A post hoc analysis is -- it's an analysis that is not stated in the protocol, so it's -- so it's an analysis that's conceived after the researchers have seen the data.

So it's generally less -- it's a less valid approach than to -- than -- than analyses that are based on what you state up-front, so it's more subject to

bias.

Q. Now, what were the results of the post hoc analysis in this case?

A. Well, in this case the post hoc analysis consisted of patients who had high levels of risk factors, and so let's take a look at that, so I'll able to --

Q. Nice cue.

So we're looking at CX 1065 page 5, second -- third full paragraph?

A. Okay. And that's what I was --

Q. Is that correct?

A. That's what I was -- I was looking for that in figure 1 so we can all see what I'll be talking about.

So the groups that he looked at -- let's say we look up at the top panel here -- the groups that he looked at were --

Q. Are you referring to figure 3?

A. Yes. I'm sorry. I'm referring to figure 3.

Q. Could we bring figure 3 up.

A. Well, I can work from this. I could work from this.

Q. Okay.

A. Okay. Figure 3 has three panels. The top panel is the anterior wall, and so what these bars mean is

the -- the open bars is the change in progression rate in the control group, and the solid bars are the change in the pomegranate juice group.

So, for example, you see downward bars for several of these categories that are on the X axis, you know, for example, HDL or L -- HDL or apolipoprotein B and total cholesterol ratio, ratio, triglycerides.

So what he's saying is he thinks he's seeing or he thinks he's observing a pattern of results where higher-risk groups, people with high triglycerides or high cholesterol-to-HDL ratios, show a reduction, a diminished progression rate in the CIMT in the pomegranate juice compared to the control group.

So that's what he sees in the anterior, and then the middle panel is posterior, which, you know, that's his primary outcome, he doesn't see any trend toward that at all in the posterior. And in the composite there are -- that's the lower panel -- there are some trends that the pomegranate juice group, well, had less worsening or less than the control group in some of these high-risk patients.

Q. So when you look then, if you're looking at the graphs on the top table, these categories here, the first graphs would show the results from the total population?

A. Yes.

Q. Okay. And then the next one is excluding statin users, and the third one is metabolic syndrome?

A. Yes.

Q. The fourth is people who are smokers?

A. Yes.

Q. And then each of those others categories is a specific subgroup?

A. Yes.

Q. And so in the anterior wall measures -- and that's the data on the graphs that are marked as A -- there were a couple of statistically significant changes; correct?

A. Correct.

Q. And that was -- that was those data on the right-hand side?

A. Yes.

Q. And then I'm looking -- so -- and then the second set of data is marked as B, so in this one they do the same breakdown of all the subjects; correct?

A. Correct.

Q. But there's no statistically significant change in the posterior wall measures?

A. Correct. In other words, in each of these categories the posterior wall CIMT progressed just as

much as in the pomegranate juice group and in the control group.

Q. And then in the last column that's C, that's the composite wall measures?

A. Correct.

Q. And those composite wall measures were not identified as being a primary or secondary endpoint in the protocol?

A. Correct.

Q. Okay. Now, if you turn to CX 1065 at page 6, under the word -- under the heading Discussion, if you read down one, two, three and then you go to the fourth sentence, could you read that sentence that starts with the word "because."

A. I'm just counting sentences. I'm sorry. What did the sentence start with?

Q. "Because the decrease in CIMT."

A. Okay.

"Because the decrease in CIMT progression in these subgroups was based on analyses that were not preplanned and had no correction for multiple comparisons (increasing the possibility of type I errors), these findings will need to be confirmed in future investigations."

Q. And do you agree with Dr. Davidson's assessment

of the data?

A. Yes.

Q. And what does it mean to say "no correction for multiple comparisons"?

A. Well, if you recall on the figure we just looked at, there were many subgroups and -- and with each additional subgroup the chances are higher and higher and higher that one or more will turn out to be -- will have a p-value of less than .05.

So a p-value of less than .05 becomes almost meaningless when many, many subgroups are measured. I mean, you know, if you have a die with -- if you have some roulette wheel with twenty categories and spin it twenty times, the chances are something will hit. I mean, that's a bad analogy, but it's just -- it is a probabilistic thing, so that's why the p-value of .05 really needs to be adjusted downward when you take multiple shots at the target.

And so that's what he -- what we call correcting for multiple comparisons, and he very appropriately recognized that and wrote about it.

Q. And he said that these results will need to be confirmed in future investigations?

A. Correct.

Q. Now, at your deposition was there a discussion

of whether clinical trials always correct for multiple comparisons? Correct?

A. There was a discussion.

Q. Okay. Now, if you're just doing a mechanistic study, do you need to do a correction?

A. Okay. Correction for multiple comparisons, it's especially important when a high degree of confidence in the results is needed. Now, when is that? Well, you need a high degree of confidence in the results when you want to make a public health recommendation or to recommend that -- you know, that -- you know, that people change their behavior, like drink a particular kind of juice to improve their health. Then you need to adhere to a high standard, and a high standard requires correcting for multiple comparisons.

Now, if you do an exploratory study of various mechanisms, then that -- then it's not -- it's not so critical. A lot of folks, including myself from time to time, will not correct for multiple comparisons in a mechanistic study from which we're not going to make public policy -- public health recommendations.

Q. But was this a mechanistic study?

A. No, this was not.

Q. Would a qualified scientist reasonably conclude that the post hoc subgroup analysis in this study

supports claims that POM juice or POMx prevent, reduce the risk of or treat cardiovascular disease or coronary heart disease in the subpopulations identified in figure 3 of Dr. Davidson's IMT report?

A. No. The data are not adequate to make that kind of statement.

Q. Now, you noted earlier that some of Dr. Aviram's studies showed improvements in LDL oxidation; correct?

A. Correct.

Q. And they also showed increased paraoxonase activity and decreased TBARS?

A. Correct.

Q. Were these results replicated in Dr. Davidson's study?

A. They were not -- well, they were measured, but the results were not replicated.

Q. Now, turning to the first page of Dr. Davidson's article, one of the authors on this study is Harley Liker M.D.?

A. Yes.

Q. Is that correct?

A. I see that.

Q. And according to the footnote F, Dr. Liker is with the David Geffen School of Medicine at the

University of California?

A. Correct.

Q. If Dr. Liker has a title at POM, should that have been revealed in this report?

A. I'm sorry. I didn't hear that question.

Q. If Dr. Liker has a title at one of the respondents' companies, should that have been reported in this report?

A. Yes.

Q. If we could turn to CX 684.

A. Okay.

Q. Did you review this article in connection with this study?

A. Yes, I reviewed that article, that document.

Q. Okay. And can you summarize what was done in this study?

A. Okay. So in this study, 45 patients were enrolled in a study of brachial artery reactivity.

Q. And were these -- was this a group of people who were also in Dr. Davidson's larger study?

A. Yes. A subset of those patients.

Q. Okay. It was a subset that was identified at the beginning?

A. I'm sorry?

Q. There was a subset identified in the protocol?

A. I have to -- I'd have to check that.

Q. And actually I can refer you back to CX 716 at page 74.

A. Okay.

Q. So there's a protocol here for the brachial artery reactivity testing contained in Dr. Davidson's protocol?

A. Yes. I see that.

Q. Excuse me for a second.

Now, how many patients were enrolled in this study?

A. 45.

Q. And what product was tested?

A. Pomegranate juice.

Q. Was this a randomized, double-blind, placebo-controlled study?

A. Yes.

Q. And what tests -- you said this was brachial artery reactivity testing?

A. Yes.

Q. Is this also known as flow-mediated dilation?

A. Yes.

Q. And so what does this study measure?

A. Well, this study measures the -- sort of the ability of the brachial artery to dilate in response to

some stress. And the brachial artery is a major artery in the arm, the forearm, and -- well, so it's an easily accessible artery, and that's why it's used.

Q. And in this study did they also measure blood pressure?

A. Yes.

Q. And what was the duration of this study?

A. 13 weeks.

Q. And what were the results of the BART testing?

A. The brachial artery reactivity testing, the results, there was no significance difference between the pomegranate juice and control.

Q. And in your view, is flow-mediated dilation a reasonable, reliable marker of heart health?

A. No, it is not.

Q. And why is that?

A. Well, I mean, first of all, it's fine to measure. It's a measure of nitric oxide reduction in the brachial artery, so it's a good -- it's -- it's absolutely fine as a mechanistic measure of an important function in arteries. However, it's performed in the arm, and the arteries in the arm do not get atherosclerosis, so right off the bat it's a -- it has a limited relevance to arteries in the heart that do get atherosclerosis or arteries in the neck.

So -- and it -- and brachial artery reactivity is not so closely connected to coronary atherosclerosis progression or clinical coronary events. Originally there was a lot of excitement about that, which has only been, let's say, partially borne out by recent data.

Q. And -- but I believe at the deposition you discussed the potential for BART testing to show nitric oxide activity?

A. Yes.

So nitric oxide production by arteries is a, you know, very -- is an important, very important function of arteries because dilation of arteries is important. Now, is nitric oxide production in an artery in the arm that does not get atherosclerosis really relevant to human disease? Well, that's really the essential flaw or limit -- not really a flaw. It's an essential limitation of brachial artery reactivity testing.

Q. And if POM meaningfully affected nitric oxide metabolism and activity, would you have expected to see a positive result in Dr. Davidson's BART/FMD testing?

A. Right.

So in fact actually, I mean, brachial artery reactivity testing has relevance to the in vitro

studies that were -- that -- you know, that -- that were reported with -- with -- so it really shows that when you take an in vitro result and you put it to an in vivo or an intact human test, you don't always get the same results. And in fact the results are quite null for brachial artery reactivity testing, in other words, nitric oxide effects in humans, but though they might have been in in vitro studies.

Q. Turning to page 19 of this study?

A. Of the protocol or --

Q. Excuse me. Of CX 684.

A. Okay.

Okay.

Q. Does this -- does this page report the results of the blood pressure testing in this study in the intention to treat population?

A. Yes.

Q. And what does it show?

A. It shows no effect on blood pressure.

Q. And turning to page 11?

A. Okay.

Q. Does this page report results of angiotensin converting enzyme --

A. Yes.

Q. -- or ACE?

And what does it show?

A. No significant effects.

Q. Is this consistent or inconsistent with the results of Dr. Aviram's testing?

A. Inconsistent.

Q. Now, at pages 32 to 35 of the report, you talk about documents relating to two studies on persons with elevated waist circumference?

A. Yes.

Q. And was one of these studies conducted in Denver and the other in San Diego?

A. Yes.

Q. Okay. Now, if you look at CX 839.

A. Okay.

Q. Is this the protocol for the Denver study?

A. Yes.

Q. And what product was to be tested there?

A. POMx, a pill.

Q. And was that designed as a blinded or controlled study?

A. That one was unblinded and uncontrolled.

Q. And what was the duration of the study?

A. 28 days.

Q. And it states on page 7 of this protocol that up to 50 subjects would be randomized or recruited and

enrolled; is that correct?

A. Correct.

Q. And on page 7 do they identify a variety of parameters to be measured from the blood samples?

A. Yes, they identify them.

Q. And what would they be?

A. It says a metabolic and lipid panel, hs-CRP, TBARS, serum paraoxonase, IL-1, IL-2, IL-6, FFA, C-peptide and fructosamine.

Q. And what are the ILs?

A. IL is interleukin. Those are molecules that involve inflammation, involved in inflammation.

Q. And turning to CX 877, are these the results of the testing at the Denver site?

A. Yes.

Q. And does it say how many patients were actually enrolled on page 2?

A. It says that we enrolled 24 adults.

Q. And turning to -- also on page 2, do they indicate that they found a significant decrease in TBARS measures?

A. Yes.

Q. And what's TBARS?

A. TBARS is a measure of oxidation in the blood.

Q. And then if you could turn to CX 825.

A. Okay.

Q. I'll give counsel a minute to pull up that exhibit.

(Pause in the proceedings.)

Is this the protocol for the San Diego site?

A. Yes.

Q. And does it indicate that the lead -- the principal investigator is Dr. David Heber?

A. Yes.

Q. And what's the title of this protocol?

A. A Placebo-Controlled, Randomized, Double-Blind Study to Compare Antioxidant Levels in Normal Subjects with Elevated Waist Circumference When Administered One or Two Pomegranate Dietary Supplement Capsules for Four Weeks.

Q. So this was a study of pomegranate dietary supplement capsules?

A. Correct.

Q. And was this described -- if you turn to -- if you turn to page 3, does it indicate that the subjects would be randomized to one of three treatment groups?

I'm sorry. Page 6.

A. 6. Okay.

Yes, three groups.

Q. So some people got a placebo, some got one

pomegranate dietary supplement and one placebo, and some got two pomegranate dietary supplements for four weeks?

A. Yes.

Q. Okay. And if you turn to -- and was this a 28-day study or designed as that?

A. Yes.

Q. And turning to CX 825 at page 23.

A. Okay.

Q. Under Special Assays or Procedures, does it identify what parameters were to be measured?

A. Yes.

Q. And what were they?

A. Okay. It says oxidized phospholipids, oxidized LDL/HDL ratio, ex vivo serum lipoprotein oxidation, serum nitric oxide, serum paraoxonase, lipid peroxidation, urinary and plasma isoprostane, hs-CRP, DNA damage assay and serum insulin level.

Q. Now, if you'd turn to CX 859.

Does this identify the clinical study report for the placebo-controlled, randomized, double-blinded study to compare antioxidant levels in normal subjects with elevated waist circumference?

A. Yes.

Q. And what does it find -- if you turn to page 21,

what did you find were the results of this study on blood pressure?

A. Okay. So it -- I mean, they just present the change -- they present the changes from baseline. They don't indicate whether there's any statistical significance or not. And usually when there's no indication in the table of statistical significance it means there isn't.

Q. Okay.

A. So once daily pomegranate -- with once daily pomegranate extract blood pressure went down minus 0.2. I mean, that's not a change.

Q. Okay.

A. And then in twice daily minus 2.7 and in placebo minus 0.1.

Q. And turning to page 20 of CX 859?

A. Okay.

Q. Do they conclude that there were no apparent treatment-related changes in weight, systolic blood pressure?

A. Right. Yes. Okay.

So there they state that in the previous table there were no significant effects. Okay.

Q. Now, does this document, CX 859, provide the results of the testing on oxidized phospholipids,

oxidized LDL/HDL, nitric oxide or those other inflammatory antioxidant parameters?

A. Well, I'm looking just to make sure.

(Pause in the proceedings.)

As I recall, it's -- they did not. I don't see it here

Q. If you turn to CX 859 at page 4, does it state, "Results of antioxidant and anti-inflammatory levels are reported separately"?

A. Yes. Yes. Exactly.

Q. And also talking about -- if you refer to CX 859 and page 5, does it indicate that the name of the finished medical -- medicinal product is POMx?

A. I'm sorry. I couldn't hear with the echo.

Q. I'm sorry. I'm tired.

A. Would you repeat that, please. I'm sorry.

Q. At page 859 -- at CX 859 at page 5 --

A. Okay.

Q. -- does it indicate that the name of the finished medicinal product is POMx?

A. Oh, okay. I see it. Yeah. Okay. Exactly. Yes.

Q. Okay. Now, if you could turn to CX 1254.

A. Okay.

Q. Does this document provide the results of the

inflammatory markers and antioxidant markers from the San Diego site?

A. Yes.

Q. And what does it find?

A. Well, it doesn't find any change -- any -- any changes.

Q. And does it say at CX 1254 page 26 that in this study there were no changes in the groups receiving one or two POMx capsules per day in markers of antioxidant stress or inflammation that were studied?

A. Correct.

Q. And turning to the page before that, pages before that measure isoprostanes, and looking at page CX 1254 at pages 19 to 21 which shows measures of nitric oxide --

A. Yes.

Q. -- et cetera?

And none of these shows any statistically significant difference?

A. Correct.

Q. Okay. Now, if you could please turn to CX 934.

A. Okay.

Q. Is this a published report by Dr. Heber?

A. Yes.

Q. Could you identify this document.

A. Okay. Dr. Heber is the first author, and the title is Safety and Antioxidant Activity of a Pomegranate Ellagitannin-Enriched Polyphenol Dietary Supplement in Overweight Individuals with Increased Waist Size. It was published in the Journal of Agricultural and Food Chemistry in 2007.

Q. Is the Journal of Agricultural and Food Chemistry considered to be a competitive publication?

A. No. It's not a competitive journal for human nutritional studies at least.

Q. Now, does this document provide the results of the research at the Denver site, the unblinded site?

A. Yes.

Q. And does it conclude that the reduction of TBARS seen there shows that it was efficacious for heart health?

A. Yes. Well, that's the implication.

Q. And does it provide the results of research at the San Diego site?

A. Yes.

Q. Does it provide the negative results of the San Diego site in terms of the inflammatory and antioxidant markers?

A. No.

Q. With regard to the conclusions that Dr. Heber

reaches, do you -- in this report, what are those conclusions?

A. Well, the conclusion as stated in the abstract, for example, it says -- this is five lines from the bottom -- "There was evidence of antioxidant activity through a significant reduction in TBARS linked with cardiovascular disease risk," so that's what I mean there's the -- the implication he gives is that there is cardiovascular benefit.

Q. But that data was only obtained at the unblinded site?

A. Correct.

Q. Did you also review some studies that purported to evaluate the effect of consuming pomegranate products on diabetes, diabetic patients?

A. Yes.

Q. And do you analyze these at pages 36 to 37 of your report?

A. Yes.

Q. Now, for example, did you look at two reports by -- and I'm going to massacre this -- Dr. Esmaillzadeh, E-S-M-A-I-L-L-Z-A-D-E-H?

A. Yes. They are my students.

Q. And one of those reports has since been marked as PX 38?

A. Yes.

Q. And is this an unblinded, unrandomized and uncontrolled study?

A. Correct.

Q. Did you also look at a study by force -- the lead author is Wasseem Rock that has been since marked as PX 127?

A. Yes.

Q. And was this study also unblinded, unrandomized or uncontrolled?

A. Yes.

Q. What did this product test?

A. It tested pomegranate juice and extract in diabetic patients.

Q. And did you also look at a study by Dr. Rosenblat that has since been marked as CX 765?

A. Yes.

Q. Now, in this study there were two groups; correct?

A. Correct.

Q. And one of them was a group of diabetics and the other was a group of people without diabetes?

A. Correct. Without diabetes, correct.

Q. Can that be described as a randomized trial?

A. No.

Q. So would such a study design be basically -- with that study design, are you also going to get -- just get before and after results --

A. Yes --

Q. -- for each group?

A. -- before and after.

Q. So were any of the studies, any of the diabetes studies, randomized clinical trials?

A. No.

Q. Okay. Can a qualified scientist conclude whether the changes reported in these studies are due to pomegranate juice or POMx consumption?

A. No.

Q. Okay. And why not?

A. Well, again, without a control group you never know whether the changes observed are due to the pomegranate agent or just would have happened anyway.

Q. Okay. And supposing the respondent has dozens of these single-blinded, one-arm studies -- excuse me -- not single-blinded but one-arm studies on diabetic patients, would that -- would that increase the level of confidence in the results?

A. No. I mean, if you -- I mean, it's a bad study design, you know, to omit a control group unfortunately, so many, many bad studies don't equal a

good study.

Q. Okay. Do any of the published studies on the use of pomegranates -- pomegranate products by diabetics provide scientific support for claims that POM juice or POMx prevents, reduces the risk of or treats heart disease?

A. No.

Q. You were asked at your deposition whether POM juice and the POMx products are bioequivalent; is that correct?

A. Correct.

Q. And did you state that you question whether they are bioequivalent given that POM juice contains anthocyanins?

A. Correct.

Q. And this is because there is some preliminary research on -- suggesting that anthocyanins may have effects on vascular functions?

A. Correct.

Q. So they would be biologically meaningful components of pomegranate juice?

A. Possibly, yes.

Q. But at the same time, there is not competent, reliable scientific evidence to support the conclusion that anthocyanins prevent or reduce the risk of

cardiovascular disease?

A. That is correct also.

Q. Now, also during your deposition you were asked if the pomegranate products are safe; correct?

A. Correct.

Q. And did you testify that the safety of pomegranate juice and the POMx products has not been proven?

A. Correct.

Q. Did you further testify that there are safety signals in some of the test results?

A. Correct.

Q. For example, did you state that some of the safety signals include transient increases in blood glucose, triglycerides, lipoprotein A and gamma GT?

A. Correct.

Q. And was the weight gain of the Davidson study a potential safety signal?

A. Correct.

Q. Now, are you familiar with the term "generally recognized as safe"?

A. Yes.

Q. Is this an FDA designation?

A. Yes.

Q. If FDA grants a product a GRAS status, meaning,

generally recognized as safe, does that mean the product is proven to be safe?

A. No.

Q. If could bring up a demonstrative exhibit.

And are you familiar with this document?

A. Yes.

Q. Does this document accurately reflect the results of the studies that we've just discussed except for the diabetes studies?

A. Yes.

Q. Now, based on your review of the evidence in this matter, including all the discussions -- all the data we've discussed above, does competent and reliable scientific evidence show that drinking eight ounces of POM juice daily prevents or reduces the risk of heart disease, including by decreasing arterial plaque, lowering blood pressure and/or improving blood flow to the heart?

A. No.

Q. Based on your review of the evidence in this matter, including the data discussed above, does competent and reliable scientific evidence show that drinking eight ounces of POM juice daily treats heart disease, including by decreasing arterial plaque, lowering blood pressure and/or improving blood flow to

the heart?

A. No.

Q. Based on your review of the evidence in this matter, including the data discussed above, do clinical studies, research and/or trials prove that drinking eight ounces of POM juice daily prevents or reduces the risk of or treats heart disease, including by decreasing arterial plaque, lowering blood pressure and/or improving blood flow to the heart?

A. No.

Q. Based on your review of the evidence in this matter, including the data discussed above, does competent and scientific reliable evidence show that taking one POMx pill or one teaspoon of POMx liquid daily prevents, reduces the risk of or treats heart disease, including by decreasing arterial plaque, lowering blood pressure and/or improving blood flow to the heart?

A. No.

Q. Based on your review of the evidence in this matter, including the data discussed above, do clinical studies, research and/or trials prove that taking one POMx pill or one teaspoon of POMx liquid daily prevents, reduces the risk of or treats heart disease, including by decreasing arterial plaque, lowering blood pressure

or improving blood flow to the heart?

A. No.

Q. In reaching these conclusions did you consider all of the data available to you, including the in vitro, animal and human study results?

A. Yes.

Q. Focusing on the blood pressure data shown on the heart demonstrative here, what was the weight of the evidence with regard to blood pressure?

A. No effect on blood pressure.

Q. Focusing on the blood flow data, what was the weight of the evidence?

A. No effect on blood flow.

Q. And focusing on the IMT data, what was the weight of the evidence?

A. No effect on IMT.

Q. If you could turn to CX 660 at page 41.

A. We're trying to find 660?

Q. Yeah. It should look like this (indicating).

A. You wouldn't happen to know where -- any idea where --

Q. It would be right after -- it would be very close to Dr. Ornish's myocardial perfusion study results.

A. It would be towards the front then. 660?

Okay.

Q. And turning to -- can you identify that document?

A. Yes. This is a presentation, a PowerPoint presentation by Dr. Gerdi Weidner from the Preventive Medicine Research Institute, Dr. Ornish's institute.

Q. And what's it dated?

A. June 16, 2004.

Q. And turning to page 41 of that report, does that PowerPoint page appear to provide the actual statistical analysis on the summed difference score, the summed rest score and the summed stress score?

A. Yes.

Q. And is a statistically significant difference of .046, is that a robust p-value?

A. No. For reasons we've discussed, that is not a robust p-value.

MS. EVANS: Thank you. I have no further questions.

JUDGE CHAPPELL: Cross?

MR. FIELDS: Just to adjust my timing, Your Honor, what time do you want to try and take the noon recess?

JUDGE CHAPPELL: Sometime just past 1:00, just

past 1:00.

MR. FIELDS: Just past 1:00. Okay.

JUDGE CHAPPELL: Go about 15 minutes.

MR. FIELDS: Yeah.

JUDGE CHAPPELL: How much time do you think you'll need? Do you have an idea?

MR. FIELDS: I would guess an hour and a half to two hours, Your Honor.

JUDGE CHAPPELL: All right.

- - - - -

CROSS-EXAMINATION

BY MR. FIELDS:

Q. Good morning --

A. Good morning.

Q. -- Doctor.

In response to complaint counsel's questions you talked about your affiliations in an advisory capacity with a number of organizations.

Is it correct that you are or have been a consultant for a number of pharmaceutical companies?

A. Correct.

Q. That includes -- correct me if I'm wrong -- Abbott Labs?

A. Correct.

Q. Merck?

A. Correct.

Q. AstraZeneca?

A. Yes.

Q. Eli Lilly?

A. Yes.

Q. Genzyme?

A. Yes.

Q. Isis Pharmaceuticals?

A. Yes.

Q. Aegerion Pharmaceuticals?

A. Yes.

Q. Any others that I've left out?

Sir?

A. Did you say Amgen?

Q. I said, are there any others that I've left out?

A. No. No. I'm thinking. That's a mouthful, isn't it?

Amgen. Did you say Amgen?

Q. I didn't say Amgen.

A. Okay. Well, there's one.

Q. Now, as I understand it, you're a shareholder of Isis Pharmaceuticals.

A. No, no. I'm not a shareholder of any pharmaceutical company.

Q. Well, are you on the advisory board of pharmaceutical companies?

A. Yes. That's the same as consulting. That's how I do the consulting usually.

Q. Well, just to clarify for Your Honor, I want to refer you to Exhibit 5025.

Do we have copies of that?

I believe complaint counsel has copies of that.

5025 is an article in which you are coauthor, and on page it looks like 854 perhaps it's S4 -- yes, it's S4 -- it says "Frank M. Sacks, M.D." and then it says "stock/shareholder of Isis Pharmaceuticals, Inc."

Is that incorrect?

A. No. That's a mistake.

Q. This was your article, sir.

A. Well, you know what I think happened? I think they swapped it. Just above that it says "advisory board Lipid Sciences." I was at some point a shareholder in Lipid Sciences, and I was an adviser in Isis, so I think they got switched (indicating).

Q. Okay. All right. Now, these various advisory board positions for all these companies, you didn't put those in your CV, did you?

A. No.

Q. And you didn't put them in your report.

A. No.

Q. Okay. Did you make a conscious decision not to include that, those relationships with all those pharmaceutical companies?

A. I don't put them in my CV.

Q. I noticed that you don't put them in your CV.

A. Well, that's my decision. I don't include them in my academic CV. That's the CV I have prepared for everything.

Q. Well, this was a CV designed to tell this court and the rest of us what connections you had that might be relevant to this inquiry, and here you have a connection to -- I didn't count them, but it looks like about ten pharmaceutical companies, and you elected not to disclose that; correct?

A. Well, I just never do. I neither elected nor not elected. I just don't. For anything.

Q. Okay. All right. Let's talk a little bit about safety, which is something that you talked about near the end.

I gather you refuse to admit that pomegranate juice is safe; correct?

A. Incorrect. That would mischaracterize my opinion.

Q. Sir?

A. Well, would you mind repeating that question, please.

MR. FIELDS: Can the reporter read it back to save my poor voice, with the court's permission.

JUDGE CHAPPELL: Right, she can read, starting with "I gather."

(The record was read as follows:)

"QUESTION: I gather you refuse to admit that pomegranate juice is safe; correct?"

THE WITNESS: Well, my judgment is that pomegranate juice has not been proven for safety. I wouldn't characterize my opinion as refusing to admit.

Okay?

BY MR. FIELDS:

Q. Okay.

And you don't know whether it's safe or not, according to your testimony; isn't that correct?

A. Correct.

Q. All right. And it can only be proven safe with large double-blind, placebo-based, controlled trials; isn't that your position?

A. Correct.

Q. And those would have to be large studies; correct?

A. Correct.

Q. And in talking about the standard of evidence required to support the claims of respondents, the POM people, did you consider the safety of the product a factor to go into that weighing process?

A. Safety is very important.

Q. Safety is very important.

So if a product is safe, you would be inclined to give it a lower standard of evidence to support claims; correct?

A. Incorrect.

Q. Incorrect.

So it really doesn't matter to you whether it's safe or not so far as what kind of evidence you require; is that right?

A. Correct. Efficacy is efficacy. Safety is safety.

Q. Well --

A. They must stand on their own in terms of testing.

Q. I'm not sure I understand you.

Are you saying that you would require double-blinded, placebo-controlled tests to support the claims for a product that is completely safe?

A. Of course.

Q. All right. And then isn't it correct that you

are not considering safety in evaluating the standard of evidence, you're requiring the same standard of evidence whether it's safe or not safe; isn't that correct?

A. I'm assuming -- when you say "standard of evidence," I'm assuming -- you're using it in the context of efficacy. Am I correct in interpreting your question?

Q. Well, I'm -- I understood that a great part of your testimony this morning was about what kind of evidence was required to support the claims that the Federal Trade Commission is accusing my clients of making, and I understood you to say that the standard of evidence that you required was two RCT trials, large ones.

And I'm asking you if in setting the standard of evidence that I've just described isn't it correct that it wasn't relevant to that determination whether it was safe or not?

A. Okay. I agree with that.

Q. Okay. Good.

And Doctor, isn't it true that the kind of RCT questions that you have -- pardon me -- the kind of RCT studies that you would require are very, very expensive, two "verys"?

A. Well, they're expensive. Very, very expensive? Well, that depends on -- well, I don't know. They're expensive certainly.

Q. Didn't you testify that they would be very, very expensive?

A. Well, I don't know. We'll have to take a look. If I used that, those exact words, then --

Q. I'm having some trouble hearing you, Doctor.

A. My apologies.

Q. It's not your fault. It's some of us get too close and too far from the mikes.

A. We're all having this problem. Okay. I hope this is better.

Well, I'd have to verify that I used "very, very" rather than just "expensive," which I'm using now.

JUDGE CHAPPELL: I'm not sure what good it does to dig a ditch to nowhere, expensive versus very versus very, very. Give the guy a benchmark and let's have something that makes sense if you're going to pursue this.

MR. FIELDS: All right, Your Honor. Sure.

BY MR. FIELDS:

Q. The other day we had a witness who testified to a very, very large RCT trial costing I think he said in

the ballpark of $600 million. And I think you would agree that's very expensive.

Is that the ballpark of really large RCT trials?

A. Well, I think you could go down easily one or two orders of magnitude to test. If you just wanted to do just a straight safety test, I think you could drop down one or two orders of magnitude of that.

I mean, I don't know -- $600 million, certainly some studies do cost that amount, but some studies cost 60 million and some 6 million, and you can get good data at each level.

Q. And suppose you have a -- somebody who has a product and that product -- assume for this moment that the product is safe and it has a potential benefit and this person can't afford even 6 million for RCT trials, much less 60 or 600 million.

Is it your testimony that he simply shouldn't be making a public claim under those circumstances?

A. I'm sorry. I think I'd have to break that down.

So the initial -- your initial phrase was assuming that there is -- that it is safety -- that it is safe? I mean, do we --

Q. Assume it's safe, assume it could create a

potential benefit, and assume that this person simply because of the nature of his business or whatever reason cannot afford to have a -- one, much less two double-blind, placebo-based tests of the kind you required.

Does that mean that he can't get the information out to the public?

A. I think you'd have to spend that money to determine if it was safe in the first place.

Q. I'm not talking now about just safety. I'm talking about the potential benefit to the public.

Assume it is safe. Let's not argue about that. And assume that it has a potential benefit, and assume that he just can't afford 6, 600 or 60 million for this kind of a study.

Is it correct that in your view of what evidence is required he simply can't tell the public about the potential benefit of his product?

A. Well, if he doesn't know it's safe -- I mean, if he doesn't know it's beneficial, then he can't say anything about it.

Q. No. I'm saying to assume it has a potential benefit, but he can't afford that kind of trial.

Is your answer he can't get the information of the potential benefit out to the public because he

hasn't done RCT trials?

A. Well, you could just -- you know, I have -- I'm just having trouble with this.

I mean, if he doesn't do the necessary studies, he doesn't know if it's beneficial, so he can't say anything --

Q. Well, that --

A. -- about it being beneficial, so my answer is no, he shouldn't -- he can't -- he has no basis in your framework for him to be able to make such a statement to the public of benefit because benefit hasn't been established.

Q. So when you set the standard of evidence, you are making your judgment without reference to the cost of these RCTs; isn't that correct?

A. Correct.

MR. FIELDS: Okay. Good.

Is this a convenient stopping point, Your Honor?

JUDGE CHAPPELL: Right, this is a good time.

MR. FIELDS: Thank you.

JUDGE CHAPPELL: Okay. We will reconvene at 2:05.

(Whereupon, at 1:02 p.m., a lunch recess was taken.)

A F T E R N O O N S E S S I O N

(2:08 p.m.)

JUDGE CHAPPELL: Back on the record Docket 9344.

Next question.

MR. FIELDS: Thank you, Your Honor.

BY MR. FIELDS:

Q. Doctor, the two RCT claim tests that you've told us about today as the requirement for making the claims we've been talking about, that's the tests that the FDA applies to drugs; isn't that correct?

A. Correct.

Q. Now, isn't it also correct, sir, that you have clarified your opinion in this case to make an exception to that requirement where you're talking about fruit? Isn't that true?

A. Fruit. I'm not quite sure about that.

Q. You're not quite sure?

A. I'm not quite sure how to answer that statement.

Have I made an exception as regards to fruit.

Q. Yes. An exception to the requirement of two RCT trials.

Haven't you made an exception and haven't you said that in your opinion, in dealing with claims for whole foods like fruit, the standard of evidence is

lowered and we don't need randomized, controlled, blinded trials?

A. Well, I think -- I mean, my point there is that it's hard to blind a fruit, and if --

Q. I'm sorry. I didn't hear you, Doctor.

A. Oh, I'll get this (indicating).

Well, my point is, as I recall, that you don't -- you can't really blind a fruit, and so, you know, for pills and things that can be tested in a blinded way, of course we want a blinded, a double-blind study, but with a fruit we can't really do that.

Q. Well, haven't you said that in your opinion we don't need RCTs to test the benefit of food categories that are included in a diet already tested like the DASH diet?

A. Oh, I remember that. That's from my deposition transcript. Maybe it would be a good idea if I saw the context of that in the deposition transcript.

Q. Well, can you answer my question and then --

A. I think I'd rather see the transcript before I attempt to answer the question because I want to see the context in which you've taken that comment. Is that okay? It's not available?

Q. Oh, it is available, and of course you can see

your entire deposition if you'd like.

I refer to page 141 -- could we get the witness a copy of the deposition.

We can put it on the screen as well and you can take your choice.

JUDGE CHAPPELL: Do you want a hard copy or is on the screen sufficient?

THE WITNESS: I'd prefer a hard copy if that's possible.

JUDGE CHAPPELL: Go ahead.

(Pause in the proceedings.)

THE WITNESS: Okay. If you'd kindly just tell me the page number --

BY MR. FIELDS:

Q. I'm looking at page 141 and I'm looking at lines 1 through 13 particularly. I'll read it to you if you'd like.

"So is it fair to say then, Dr. Sacks, your opinion is that two RCTs would be required for a juice extract or supplement in order to make a public health recommendation?

"Yes. That's right.

"QUESTION: And the only distinction you would draw it would be for a whole food would be a lesser standard?

"ANSWER: A whole food --

"QUESTION: Fruit, sorry.

"ANSWER: Correct. A whole food or fruit if it's contained in a diet already tested. For example, the DASH study."

Now, what you're saying there -- it seems clear to me, but you can correct me if I'm wrong -- is that, A, there is to be a lower standard for something that has already been tested in the DASH diet, and you don't need RCTs for that; isn't that correct?

A. Well, if we continue for another sentence, another two sentences, then that would explain what I, you know -- what I'm trying to -- what my -- what my opinion is, which I have here, so I appreciate the opportunity to review this.

So of course that's correct as -- I mean, that is what I said, but I said: "We tested a diet that had a beneficial effect on that diet that had whole food and also had some juice, but we're not going out from the DASH study recommending any particular component. It's a total approach."

So total approach is fruits and vegetables in the context of this healthy diet is beneficial according to the DASH study, which is a randomized, controlled trial. And -- and that's -- so then you'd say, Well,

what fruit do you recommend? Well, we recommend the fruits that were in the study.

Q. Again, I'm finding it hard to hear you. Could you talk into the mike, because I don't have a monitor at --

A. Oh, okay. Well, again, I'm sorry.

So --

Q. You don't need to repeat what you said --

A. Okay.

Q. -- if you'd just do that for me.

JUDGE CHAPPELL: If you'd like, you can step over and look at realtime, if you want to do that, for that particular response.

MR. FIELDS: That would be helpful.

MR. PADILLA: Can I move that over, Your Honor?

JUDGE CHAPPELL: Yes. Go ahead.

MR. PADILLA: Thank you.

MR. FIELDS: Thank you, Your Honor.

BY MR. FIELDS:

Q. All right. I'm not sure I understood your answer, but let's see if we can clarify it.

Isn't it your opinion that we don't need RCT trials to test the benefit of food categories that are included in a diet already tested, like the DASH diet?

A. I agree.

Q. You agree.

A. Yes.

Q. Okay. Good.

And is it correct that this is because the DASH diet has already included and tested fruit as a category?

A. Correct. Fruits and vegetables.

Q. Yeah, fruit individually.

A. Yes.

Q. And is it correct, sir, that you include as a fruit in that category we just discussed pomegranates?

A. Yes. I would include -- I would include pomegranates.

Q. So they get a lower standard along with pineapples and papayas and bananas, et cetera --

A. Yes.

Q. -- right?

You can --

A. I agree.

Q. Okay. Good. Good. All right.

Now, you appear to draw a line between pomegranates and pomegranate juice, and if I understand your testimony correctly, at your deposition you seemed to say that although pomegranates get a lower standard, they don't need two RCTs, pomegranate juice does; is

that your position?

A. Correct.

Q. Okay. And sir, isn't it true that you testified you were not offering any opinion as to any differences between pomegranates and pomegranate juice? Do you remember that?

A. I have not offered an opinion? I'm sorry. I don't understand the question.

Q. Well, I understood you to testify in your deposition that you were not offering any opinion as to any differences between pomegranates and pomegranate juice. That's at page 77 of your deposition you've got there and you can look at it.

A. Okay.

JUDGE CHAPPELL: Why don't we see if he agrees with you before he needs to look at the deposition.

MR. FIELDS: Okay. Yes.

BY MR. FIELDS:

Q. Do you agree with me that you're not offering any opinion on the differences between pomegranates and pomegranate juice?

A. Well, I certainly have my opinion.

Q. Well, but whether you have one is somewhat different from whether you told us you were not offering an opinion on that, because when you say

you're not offering an opinion, we tend to rely on that.

So can you tell us if in fact that is what you said?

JUDGE CHAPPELL: Let me see if I can clarify this. I think the witness may be confused.

Are you asking him if he's offering an opinion in this case for the FTC or does he have an opinion?

MR. FIELDS: No, no. I'm asking him if he --

JUDGE CHAPPELL: Because I heard him say "I have an opinion," but I'm not sure he understood what you meant by "offering an opinion."

BY MR. FIELDS:

Q. I mean offering an opinion in this case.

Didn't you testify you were not offering an opinion in this case on the differences, if any, between pomegranates and pomegranate juice?

A. Oh, okay. Thank you. I just wasn't requested to --

Q. Sure.

A. -- so I'm not.

Q. All right. And you're not offering any opinion in this case on the physical properties of either pomegranates or pomegranate juice; isn't that correct?

A. Correct.

Q. Okay. Now, you said that pomegranates were exempted from the two-RCT rule because they were part of a category of fruit that had already been tested in the DASH diet.

Isn't it correct, sir, that fruit juice was also tested in the DASH diet as a category rather than separate fruit juices?

A. Well, there was -- I mean, fruit juice was included. That's correct.

Q. Well, fruit juice was treated exactly the same as fruit in the DASH diet; isn't that true, sir?

A. Not really.

Q. Well, let's take a look at the DASH diet.

I'd like you to look at first Exhibit 5020, 5020.

And if my associate can approach the witness?

JUDGE CHAPPELL: Yes. Go ahead.

BY MR. FIELDS:

Q. If you look, sir, on page 6 of that exhibit, you will see the DASH diet.

Now, it says, the third category, fruits, four to five a day, three-quarters of a cup of fruit juice, one medium fruit, one quarter cup dried fruit, one half cup fresh, frozen or canned fruit.

Now, that is what has been tested and included

in the DASH diet, sir. And I think you'll agree that fruit juice, like fruit, was left up to the individual, they could choose whatever fruit they wanted, and as a category fruits were tested and fruit juice was tested.

A. I disagree.

Q. You disagree.

A. I disagree.

I designed that, and so I think I have a right to disagree.

JUDGE CHAPPELL: Well, you can disagree whether you designed it or not.

THE WITNESS: Okay. Thank you.

But I don't have to look at -- I mean, I don't know what this is. This is just some article in some -- oh, this is Nutrition Action published in 1997.

I mean, I don't have to use this to tell me what's in the DASH diet and what our intent was on how to use the DASH diet.

BY MR. FIELDS:

Q. Doctor, I think you were one of the people who contributed to this article. Isn't that correct?

A. No. I never contribute to these articles. I sometimes give an interview.

Q. Okay.

A. But I couldn't remember whether I did in 1997 or

not at this point.

Q. Well, if you'll look on page 2, it says that you were interviewed about this article, and you talk about it, Frank Sacks, a researcher at Harvard Medical School who helped create the DASH study.

But are you denying that the DASH diet simply left fruits as a category and left it up to the individual as to which fruits he or she ate?

A. Yes. But our intent was not to have them consume the entire fruit category as orange juice or apple juice or what have you.

Q. I think we got a confusing answer there. I asked you if you're denying that fruit was left up to the individual so that it wasn't tested as a category, not as an individual kind of fruit.

A. Right. We used several fruits in the fruit -- in the fruit category.

Q. Well, they had their choice of fruit; isn't that correct?

A. Well, when we generalize it to the population, we are -- yes, we're saying that people can choose whatever fruits they like to --

Q. And fruits were tested and approved as a category. You told us that before; isn't that right?

A. Correct.

Q. And fruit juice was treated exactly the same way. They can choose whatever fruit juice they wanted; isn't that right?

A. I'm sorry. That's what you say, but that's not what we say in that study.

Q. Well, that's what this document says, sir.

A. Well, this is not an authoritative document. I didn't pass -- I didn't have anything to do with the construction of that table. I just gave an interview to these -- to these writers.

Q. And let's look at Exhibit 5019.

May we approach to give the witness a hard copy?

JUDGE CHAPPELL: Go ahead.

BY MR. FIELDS:

Q. If you look at 5019, which purports to be a scientific report on the DASH diet --

JUDGE CHAPPELL: Can that guy back there at the command post, can you focus that?

MR. PADILLA: It will focus when we zoom on specific sections.

JUDGE CHAPPELL: Okay.

MR. FIELDS: Can we give Your Honor a hard copy?

JUDGE CHAPPELL: No. That's fine. He's going to zoom it. That's fine.

BY MR. FIELDS:

Q. Zoom. All right.

If you'll look on page 747, sir, you'll see exactly the same thing that was in the other exhibit, fruits, unspecified what kind, under the heading of Fruits, six ounces fruit juice, one medium fruit, one-quarter cup dried fruit, one-half cup fresh, frozen or canned fruit, the same thing.

It gives examples of kinds of fruit, but it doesn't require any particular kind of fruit or juice, it's left up to the individual; right?

A. Well, our intent was not to have people, you know, fill up the fruit category with fruit juice. Our intent was for them to use a whole variety of these different fruits, as stated. And notice we only say orange juice or grapefruit juice and we say to avoid sugar-containing beverages.

JUDGE CHAPPELL: Hold on a second.

You didn't answer his question.

THE WITNESS: I'm sorry.

JUDGE CHAPPELL: He asked you if any particular kind of fruit or juice is left up to the individual. Your answer said what your intent was. That's not what he asked.

THE WITNESS: Okay. I'm sorry, Your Honor.

BY MR. FIELDS:

Q. Regardless of your intent, sir, both of the documents I've shown you, which purport to be the DASH diet, list actually "Table 1, The DASH Diet." It simply says six ounces of fruit juice, one medium fruit.

And your testimony, sir, was that the reason there's a lower standard of evidence for fruit is it was approved as a category, so we don't have to test individual fruits; isn't that correct?

A. Correct.

Q. And the same thing applies to fruit juice. It is treated exactly the same way in the DASH diet, sir, isn't it, regardless of your intent?

A. Well, I mean, I never viewed it that way, so that's best I can do for you.

Q. Thank you.

JUDGE CHAPPELL: Can you answer from the perspective of the person on the diet?

THE WITNESS: Well --

JUDGE CHAPPELL: Do they not see what we're seeing here, that they can pick any of those?

THE WITNESS: They can pick any of those. And we give -- we actually have very detailed menu guides published. The NIH has published that. And I mean, that's what we use for explicit advice for people and

for dieticians, you know, detailed menu guides, which really give a much closer approximation of what we recommend to actually what we tested in the study.

BY MR. FIELDS:

Q. But we're talking about what was tested in the study.

Now, is Dr. Meir Stampfer a cattle -- a colleague of yours?

A. Yes.

Q. And you both work up at Harvard?

A. Yes.

Q. Okay. Now, have you read Dr. Stampfer's article along with Dr. Blumberg, I think it is, called Evidence-Based Criteria in the Nutritional Context?

A. No, I haven't read that article.

Q. All right. Well, I'd like to read you parts of -- from that and ask if you agree with Dr. Stampfer. If I can find it.

This is Exhibit -- and this is in evidence as 5007. If you'd like to have a hard copy --

A. Please.

Q. -- you can receive that.

(Pause in the proceedings.)

All right. Did you get a copy?

A. No.

Q. Oh, we're still -- I have an extra copy I think.

Sorry.

Now --

MR. GRAUBERT: Here we go.

Approach Your Honor?

JUDGE CHAPPELL: I think he has it already.

MR. FIELDS: I already gave him one.

JUDGE CHAPPELL: You can still approach, though.

MR. GRAUBERT: Okay. Next time.

BY MR. FIELDS:

Q. All right. Well, at page 480, Dr. Stampfer says -- and he's talking about food and diet. This is what this whole article is about -- Dr. Stampfer says, "A hypothesis about disease causation can rarely, if ever, be directly tested in humans using the RCT design."

Do you agree with that?

A. Well, not really. It's -- I -- I'd be curious about the context, but just reading this one sentence for the first time in my life, I can't really agree with that.

Q. Okay. He says it's unlikely -- this is at page 480 -- it's unlikely that RCT evidence could

feasibly or appropriately be produced with reference to the role of a nutrient for many nonindex-disease endpoints.

Do you agree with that?

A. Actually I don't know what he's referring to by or when he says "nonindex-disease endpoints." I've never seen that term, so I can't offer you an opinion.

Q. All right.

A. Unless you could -- somebody can educate me on what a nonindex-disease endpoint is.

Q. That's not a term that you've used with Dr. Stampfer, "nonindex disease"?

A. This is the first time I've ever seen it. Now, maybe he has defined it in this document, but...

Q. He says, "... the majority of evidence with respect to nutrients and nonindex diseases will continue, of necessity, to be derived from observational studies." That's at page 480, same page.

Do you agree with that?

A. Well, again, I just don't know what he means by a nonindex disease. I've never seen that word before.

Q. Well, let's substitute the words "some diseases" for "nonindex diseases."

Would you agree that the majority of evidence with respect to nutrients and some diseases will

continue, of necessity, to be derived from observational studies?

A. Well, there are certainly some diseases that that's probably right, yeah.

Q. Okay. And Dr. Stampfer points out, at page 481, the importance of RCT trials in testing drugs, but he says, and I quote, "These concerns are substantially less pressing in nutrients."

Do you agree with that?

A. Well, in the -- I don't know what his context is, but in my context in what I've been talking about here, cardiovascular diseases, there's not so much of a disparity between -- a disparity between what can be done with a drug and what can be done with a nutrient or food or extract.

Q. Except in the case of fruits and fruit juices, which we've discussed; right?

A. Except in -- as we have discussed, granted.

Q. Now, Dr. Stampfer addresses the kind of decision we face here, and he concludes there can be a sufficient foundation for nutrient-related claims in the absence of RCTs. That's at page 483.

Do you agree with that statement?

Sir?

A. Yes. I'm just trying to digest that question.

Q. Oh, I'll read it again.

That there can be a sufficient foundation for nutrient-related claims in the absence of RCTs.

A. Well, I don't -- I mean, we always need RCTs on -- at least on surrogate markers in addition to the observational studies that Dr. Stampfer conducts.

Q. All right. Dr. Stampfer adds -- we're getting to the end of this -- that it's important, and I quote, "to assess the balance between the potential harm of making any given recommendation and the potential harm of not making it."

Do you agree with Dr. Stampfer on that?

A. Fair enough in general.

Q. And that means that we have to weigh the risk that the product will do harm against the potential harm in keeping the information from the public; isn't that what that means?

A. Correct.

Q. Okay. Now, is it true that there are common clinical recommendations today that haven't been proven by RCT trials?

A. Yes.

Q. And you yourself make public health claims that you think will benefit the public even when you don't have RCT trials to substantiate the results; isn't that

correct as well?

A. I'm -- well, let's think of an example. I tell people they should stop smoking, and we don't have, you know, a 10,000-patient smoking cessation trial as far as I know.

I'd say the nutrition-based advice I give, recommendations, does have randomized clinical trial basis for it.

Q. Well, how about your own DASH study on sodium intake? Didn't you tell us that was not a blinded study in reality?

A. Well, it was a single -- it was actually a blinded study, but as I mentioned earlier in direct testimony, something like sodium, the participants get -- will certainly get some idea of whether they're -- whether they're eating a high-sodium or a low-sodium diet, but it is certainly a blinded study with regard to the measurers, the investigators, which is the critical thing. And it is a randomized, controlled trial, the DASH sodium study.

Q. All right. Weren't you criticized by some doctors because these were not major RCT trials supporting what you said?

A. I don't know exactly what you refer to.

Q. Well, let's look at your article on sodium.

I'll give you a number in a minute, and we'll supply you with a copy, I hope.

Yes. It's called The Importance of Population-Wide Reduction as a Means to Prevent Cardiovascular Disease and Stroke.

JUDGE CHAPPELL: Go ahead.

BY MR. FIELDS:

Q. I refer you, with regard to my last question, to page 3, and I quote:

"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."

Did you say that, sir?

A. Yes.

Q. Okay. And when you said they are not feasible because of financial considerations, you were talking about the cost of conducting that kind of major trial; right?

A. Yes.

Q. Okay. Now, you claim that sodium reduction was an integral component of preventing CVD, stroke and kidney disease; isn't that correct?

A. Preventing CVD and -- the last part? I'm sorry.

Q. Stroke and kidney disease.

A. Correct.

Q. Now, let's look at some other examples.

You told the public that the intake of omega-6 reduces the risk of coronary heart disease; isn't that correct?

A. Correct.

Q. And isn't it correct that that was based on what you called flawed and unblinded studies with small sample sizes plus observational studies on animals and humans?

A. I don't recall those words. I'd have to see the context.

Q. All right. Let's look at -- I'll give you the number in a minute. It's the article that you wrote on omega-6. It's Exhibit 5022.

A. Okay. I'm familiar with this article.

Q. All right. I'm looking for the page.

Did you say that the studies that had been done on omega-6 had the inability to double-blind these studies, that they had design limitations such as small sample size, that they had soft endpoints, that they had randomization of sites rather than individuals with open enrollment, that they had a high turnover of subjects,

but nevertheless, based on those studies and some observational trials, you strongly recommended omega-6 and said it reduces the risk of coronary heart disease; right?

A. Correct.

Q. Okay. And your public recommendation of reduced sugar intake was also based on observational studies; isn't that correct?

A. Well, it was based on observational studies and also randomized, controlled trials and just like the omega-6 was, observation and randomized, controlled trials.

I mean, you know, just to go back, I mean, you cited our honest -- our honest writing where we are explaining the limitations of the studies. In contrast, those studies have major strengths. If they're a bunch of lousy studies, we aren't going to use them to form recommendations. There were major strengths to those studies, and that's why we came to that conclusion.

Q. Even if they were not RCTs.

A. Well, I'm going back to the omega-6 --

Q. Yeah.

A. -- and --

Q. Omega-6 --

A. Oh, yes. There were lots of randomized clinical trials.

Q. You said they were unblinded.

A. Some were; some weren't.

Q. Pardon me?

A. Some were; some weren't. Some were small; some were big.

Q. And you heavily criticized them, as I read to you.

A. We wanted to show, as good scientists should, that we recognized the weaknesses as well as the strengths of the studies we're evaluating.

Q. So even though a weakened study with all the problems that I just read to you, that would still support a recommendation if you felt it was in the interest of the public to give that recommendation; isn't that true?

A. Untrue.

Q. Untrue.

You would --

A. Untrue.

Q. You would never recommend something based upon the kind of studies that I read to you?

A. The recommendation -- our decision to go forward with those studies is not due to showing -- is not due

to exposing the public to studies that had a bunch of flaws; it was to expose the public to studies that had major strengths.

Q. But you referred to all those flaws in the studies that you were relying upon, even though are you now telling me with all those flaws they still had major strengths?

A. Well, we have -- we can sit down and discuss all the strengths rather than just discussing the flaws --

Q. Well, is your --

A. -- or the limitations. There are plenty of strengths. Otherwise, we wouldn't be recommending them.

Q. But you'll agree with me I think that the fact that a study has a number of flaws like those that you referred to in this article doesn't disqualify it, it may still have major strengths; correct?

A. Correct.

Q. Okay. Now, let's go back a little bit to what we started this morning, that is, talking about safety.

And you told me that about RCT tests you couldn't go on with saying that a product was safe; right?

A. We need RCTs to make -- we need RCTs to make a

determination of safety.

Q. Yes.

A. Yes, I agree.

Q. And it is -- there again, let's assume that the hypothetical fellow we talked about this morning has a product that has never harmed anyone that he knows about and offers a potential benefit, and he can't afford a 6 or 60 million or 600-million-dollar RCT test to prove the safety of it.

Isn't it just the public just doesn't get that information under the Sacks rule?

A. How does he know whether the thing is safe or not if he doesn't actually do the study?

Q. Well, let's assume nobody has ever been harmed by it and it will create a potential benefit. Let's even assume that the benefit is pretty solid, but he -- you're saying that he can't tell the public about that benefit.

Let's assume that it cures cancer. Because he hasn't measured the safety of it through double-blind, placebo-based claims because he can't afford it -- right? -- it doesn't get out there. The public dies.

A. I don't know -- I find this whole thing a little bit -- well, you know, you have to do -- the assumption that you assume safety and without doing any

studies just -- is just ludicrous. I can't go on -- I can't continue with another assumption after that if I don't buy into the idea that this gentleman knows that his product is safe. How does he know his product is safe if he doesn't do a study to show it's safe?

Q. Well, I asked you to assume, and I get to ask you to assume certain things, and I asked you to assume that nobody has ever been harmed by this product, he has no indication that it isn't safe, and he -- it has a heckuva benefit for mankind, but he can't afford to do a couple of double-blind, placebo-based trials on this, so the answer I take it to my question is the public doesn't get the information; right?

A. The public doesn't get the noninformation, correct.

JUDGE CHAPPELL: Are you saying you can't envision a product that you would assume is safe that someone wants to test? What about something like blueberries? People have been consuming them, cooking with them, eating them. What if somebody wants to do a study with blueberries? Can't you assume they're safe?

THE WITNESS: Well, blueberries are the whole fruit, and I put those in the category of safe, eating whole fruit. That's just fine.

JUDGE CHAPPELL: That's what I was inquiring

into. I thought I heard you say you could not ever assume anything was safe in an assumption in a hypothetical.

Is that what you said?

THE WITNESS: Yeah. I said that an agent could not be assumed to be safe if it actually isn't shown to be, if it actually isn't proven to be safe.

JUDGE CHAPPELL: So I'm just trying to figure out, is that your position even with something that's been consumed or drunk or been around, used in cooking for years? Would that still be true, that you wouldn't assume safety?

THE WITNESS: Well, the historical base doesn't -- I don't feel really tells us anything.

I mean, for example, pomegranates themselves, you know, if we eat a pomegranate, I'd have no problem with that, just like a blueberry. That would -- that as far as I'm concerned could be part of the DASH diet, fruits and -- in the fruit category of the DASH diet, and we're telling people that it's just fine to eat it. But some product made from blueberries, you know, that -- that's a different situation, Your Honor.

JUDGE CHAPPELL: So you're drawing the line at a product made from the naturally occurring food or vegetable or fruit.

THE WITNESS: Correct. I mean apple juice compared to apples.

JUDGE CHAPPELL: Okay.

BY MR. FIELDS:

Q. Let's understand this, sir.

So you're saying that you're satisfied that pomegranates are safe, but pomegranate juice might not be.

A. Correct.

In fact we say in the DASH diet to -- that the DASH diet avoids sugar-containing beverages.

Q. I didn't hear what you said, sir.

A. Okay. We say in the DASH diet that the description of the DASH diet is that it is low, reduced, in sugar-containing beverages and sweets.

Q. Well, you're not talking about fruit juice because we've already shown you in two separate documents that fruit juice was a daily requirement of the DASH diet; right?

A. Well, I wouldn't say it's a daily requirement. It is a component of it.

Q. It is what?

A. Did I say it was a daily requirement? It's a component of the diet.

Q. The document said it's a daily requirement to

take -- I've forgotten the quantity of fruit juice, fruit and those other things I read to you. On two separate documents listing the DASH diet it included fruit juice.

You don't want to tell me that you were discouraging people from having fruit juice, do you?

A. Well, we had fruit juice. We didn't have fruit juice plus added sugar.

Q. Well, we're not talking about added sugar.

Is it your testimony that they add sugar to pomegranate juice when they make it?

A. I don't know that.

Q. You don't know anything about how they make pomegranate juice; isn't that true?

A. No. That is true.

Q. Okay. And you know that pomegranates have been eaten safely for centuries; right?

A. I don't know that.

Q. You don't know that. Okay.

A. You know, it's the "safely" -- when you threw in the "safely," that's something I don't know.

Q. Well, you don't know anybody that ever got harmed by eating pomegranates, do you, over all these centuries?

A. I don't know if I know anybody. I've never

looked into it.

Q. Okay. Thank you.

Well, let's talk a little bit about the science and the studies.

JUDGE CHAPPELL: Hold on a second.

With the benefit of realtime, I heard you use the word "agent," that the agent wouldn't be assumed safe. What do you mean by "agent"?

THE WITNESS: I mean any -- any -- anything that is being -- anything that's being tested, so I mean -- I mean "agent" in a broad context. It could be a food, a supplement, a drug. It's just the thing that is being tested in a study, an agent.

JUDGE CHAPPELL: Okay.

BY MR. FIELDS:

Q. All right. Let's -- I'm not going to go over every one of those studies I don't think. Let's begin with Dr. Aviram at the Technion Institute.

Was it your opinion that Dr. Aviram does good basic science?

A. Yes. I'd agree.

Q. And he's part of the Technion Institute; correct?

A. Correct.

Q. And that's a good research institution, isn't

it?

A. Correct.

Q. And Dr. Aviram did an in vitro study that showed that pomegranate juice inhibited the macrophagic uptake of oxidized LDL; isn't that correct?

A. Correct.

Q. And that's one of the factors that causes plaque and reduces blood flow to the heart?

A. It's one component of atherosclerosis.

Q. Yes.

As a matter of fact, so you and I can be talking about the same thing, I'd like to put up on the screen if we can a -- we have a little heart graphic.

Can we give a copy to the doctor.

JUDGE CHAPPELL: You need to be extremely careful when you don't ask permission. Some people trip.

MR. FIELDS: I'm sorry. I should have said, "May we approach?"

JUDGE CHAPPELL: And it turned out not to be a good idea to allow that.

MR. FIELDS: Can we have a continuing opportunity to approach if we have a document?

JUDGE CHAPPELL: And I'm not going to mention who's blushing that I can see from up here.

THE WITNESS: Okay.

BY MR. FIELDS:

Q. Can you put that on my screen, too? Okay.

Here's where you get a chance to educate me.

This diagram, in very oversimplified terms I'm sure, tells us the -- one of the ways in which a cardiovascular event occurs, and I'll just go through it because we're going to talk about it a little bit and I want to make sure that we understand that we're talking about the same thing.

At the left-hand side you'll see LDL cholesterol.

That's what people call bad cholesterol?

A. Yes.

Q. And what happens in the next thing is that LDL cholesterol oxidizes.

That's a bad thing; right?

Yes?

A. Well, it's a theory. I mean, actually -- honestly, that whole theory has never panned out in any therapeutic way, but go ahead. I mean, you know, people sometimes -- you know, it's sort of a classical view of atherosclerosis, but it's getting more and more passe as we learn a lot more about the processes.

Q. So you no longer believe that the oxidation of

LDL cholesterol indirectly leads to plaque and ultimately to cardiovascular events?

A. Well, whether it's oxidized or not, it's a bad thing in there.

Q. All right. After it oxidizes or whatever it does, things called macrophages come in; isn't that correct?

A. Correct.

Q. And that means big eaters I think, macro- and -phage; right?

A. They're big eaters.

Q. Right.

And they eat the oxidized LDL; is that right?

A. Correct.

Q. And that really results in plaque, which is the next thing on here; is that correct?

A. Well, actually it's a -- it keeps the oxidized LDL from causing more trouble inside the artery wall, so --

Q. Isn't that what we call plaque that builds up on the artery wall?

A. Well, partly from LDL-loaded macrophages. That's a component of plaque.

Q. Yeah. I don't mean to say this is the only way this happens. I don't mean to say it's the only

cardiovascular event causes, but this is one of the principal ways I think that we get a problem with the heart.

So the next -- after we get plaque buildup in the coronary artery, that either clogs the artery or it breaks off in some way and stops or reduces blood flow to the heart; is that correct?

A. Correct.

Q. Okay. And I guess even I know that when you don't get blood flow to the heart, you die or you have a heart attack.

A. Correct.

Q. Okay. So this change is, while certainly oversimplified, it tells us in general what happens with LDL cholesterol, how it works into a cardiovascular event; correct?

A. One can -- well, it's one component of the story.

Q. Yes.

JUDGE CHAPPELL: Is this LDL oxidization the only way that plaque builds up or are there other ways?

THE WITNESS: Yeah, that's quite key. There are other ways as well.

I mean, LDL, whether it's oxidized or not, causes problems inside the blood vessel, inside the

artery wall, and it can aggregate. It can -- it -- macrophages gobble it up whether it's oxidized or not.

In fact, NIH scientists Drs. Kruth and Colley strongly feel that oxidation is not really the primary process of LDL causing atherosclerosis.

JUDGE CHAPPELL: These --

THE WITNESS: Just LDL in there. And also DLDL is also a bad component.

JUDGE CHAPPELL: These LDL-eating macrophages, what are these, enzymes or chemicals? What are they?

THE WITNESS: No, no. A macrophage is a cell, and it's sort of a -- it's a big cell and it's underneath the and sort of in the lining of the artery wall, of the artery wall.

JUDGE CHAPPELL: So these are naturally occurring in every human?

THE WITNESS: Every human has -- macrophages are part of our immune system and also our defense system against -- against, you know, bad things like LDL.

So when the macrophage -- so when the lining of the blood vessel, the artery wall, starts getting a lot of LDL in there, it stimulates macrophages to get in there and eat up the LDL to contain it, because LDL is pretty -- can be toxic if it just hangs around inside

the wall, inside the blood vessel wall.

JUDGE CHAPPELL: So are these well-meaning macrophages doing harm or good by eating the LDL?

THE WITNESS: Well, they're doing good.

In fact, it happens to babies. I mean, babies have this same process. It's just a completely natural process. It's just when there's just too much LDL getting in there or if you add, you know, cigarette smoke or some other insult, then this whole inflammatory process, well, it just gets out of control, and then that's how the macrophages eventually will cause some plaque because they get overloaded.

JUDGE CHAPPELL: Thank you.

BY MR. FIELDS:

Q. So it's the macrophages themselves having devoured the LDL that tend to cause the plaque; is that correct?

A. That's one part of the process. Yes.

Q. I don't mean that there aren't other ways that plaque can get there.

A. What happens is the macrophages get so loaded up with cholesterol, eventually they die. They just break open and spill all this cholesterol into the artery wall, and that sets off a really bad inflammatory reaction.

So it's essentially, like you said, Your Honor, beneficial, a good thing, a protective mechanism that just has just gotten out of control.

Q. Okay. So what Dr. Aviram showed was that pomegranate juice inhibited the macrophagic uptake of the LDL; isn't that correct?

A. Yes.

Q. And in vitro studies like Dr. Aviram's enable us to understand the mechanism by which agents like pomegranate juice have an effect; isn't that correct?

A. They're used to study -- they study actions of agents like pomegranate.

Q. And isn't it correct that they can provide competent and reliable evidence of such an agent's effect on a particular mechanism?

A. Correct.

Q. Okay. Just to make it shorthand, some of respondents' in vitro studies showed favorable effects of pomegranate juice on the mechanisms involved in cardiovascular disease; isn't that correct?

A. Correct.

Q. Now, Dr. Aviram also did animal studies on pomegranate juice at the Technion Institute; isn't that right?

A. Yes.

Q. Okay. And those also showed some favorable effects for the pomegranate juice on this process.

A. Correct.

Q. One such study, for example, showed that pomegranate juice showed a marked decrease in the oxidation of LDL; right?

A. Correct.

Q. And it also caused a significant reduction in atherosclerotic vessels; isn't that right?

A. I think so. If I remember right.

Q. Okay. It's hard to remember all of these studies I agree.

Now, of course animal studies, as you've pointed out, can't always be replicated in humans, but sometimes they can; isn't that true?

A. Well, sometimes they can.

Q. And sometimes we assume that they can, for example, when we do safety studies, we make that assumption, don't we?

A. Well, that's really not true. A safety study, a toxicology study in animals must be done, and agents must pass the tox test in animal studies, but then of course the safety must be very carefully evaluated in humans as well because humans don't have necessarily the same sensitivity that animals do and sometimes they

have sensitivities to agents that the animals don't have.

Q. I understand.

But you've said that animal testing is essential to safety; isn't that right?

A. Correct.

Q. And when we test an animal and the animal study shows that it's safe, we tend to assume that it's safe.

That doesn't mean we're not going to do a human study because, as you pointed out, it may not be the same; is that right?

A. Incorrect. When it passes the animal safety studies, all we say is we can advance it to phase I human testing.

Q. Okay. Now, like in vitro studies, animal studies are very useful; you'd agree with that?

A. Correct.

Q. Another of Dr. Aviram's human studies -- this time it is a human study -- he did a human study on the oxidation stress and atherogenic changes in LDL; isn't that correct?

A. Correct.

Q. And that showed a marked decrease in those factors that contribute ultimately to plaque and reduced blood flow to the heart?

A. Well, actually I'll have to look at that specific study. You know, I don't put -- I mean, what is the study? I have to look at that study to be able to answer your question. I mean, which one of the many Aviram studies are you asking me to opine on?

Q. Well, it's an observational study, so if you were going to apply the RCT test, it flunks, but if you're applying the fruit and fruit juice test, it may be sufficient.

You don't recall whether it shows a marked decrease in those factors that contribute ultimately to plaque.

A. Well, if it's -- if it's uncontrolled, well, then we don't know whether the pomegranate juice really did anything or not. We just know that two events occurred in a time sequence. That's all.

Q. Now, another of Dr. Aviram's human studies dealt with ACE, as you called it, and I think that's serum angiotensin converting enzyme; is that right?

A. Correct.

Q. And ACE contributes to the oxidation of LDL; isn't that right?

A. Is that true? No, I don't know.

Q. You don't know.

A. No.

Q. Well, if you don't know, I certainly don't know.

A. I mean, ACE contributes -- I mean, the classic understanding of ACE is that it converts angiotensinogen to angiotensin.

Q. Well, the --

A. Actually the active form of that. I mean, it generates the active form of angiotensin.

Q. Yeah.

It -- the study showed that pomegranate juice significantly reduced ACA -- ACE -- I'm sorry -- in the pomegranate juice; isn't that correct?

A. Again, I just would have to see what you're talking -- if it's one of those before-after uncontrolled studies, then I just -- I don't -- I don't think it shows that pomegranate did anything.

Q. Well, putting aside that it wasn't controlled, wasn't the result that there was a significantly reduced ACE in the pomegranate -- in the people who drank pomegranate juice?

A. Well, I mean, they could have been doing jumping jacks the whole time. I mean, we have absolutely no -- when you're asking me to make those assumptions, you know, I -- I have nothing -- I have nothing in -- decent in scientific -- in the scientific research to work from

in a study like that.

Q. Because it isn't --

A. There's no control.

Q. -- a controlled study.

JUDGE CHAPPELL: Hold on. You guys are talking over each other a little bit.

THE WITNESS: I'm sorry.

JUDGE CHAPPELL: We don't want to descend into last Wednesday afternoon, so just try to let each other finish first.

MR. FIELDS: Okay.

JUDGE CHAPPELL: I don't know if everybody was here last Wednesday afternoon. Some days in here are worse than a year of hard time.

BY MR. FIELDS:

Q. Now, did you also claim that ACE was not a valid surrogate for a healthy heart?

A. Yes. Well, for -- it's not an adequate surrogate marker for -- you know, for evaluation of cardiac health or cardiac disease.

Q. Well, if it does in fact affect the oxidation of LDL cholesterol, wouldn't that have an impact on heart disease?

A. Not necessarily because of a multitude of mechanisms we've discussed. No one has ever proved the

LDL oxidizability theory. In fact it's more or less come up null in tests of antioxidant vitamins.

In other words, antioxidant vitamins prevent the oxidation of LDL, but they sure don't prevent cardiovascular disease, so that's why I say this LDL oxidizability theory is becoming rather passe and supplanted by a lot of new types of investigation.

Q. Now, Dr. Aviram also did a CIMT imaging study that you talked about; correct?

A. Correct.

Q. And that was also at Technion; right?

A. Correct.

Q. And this was a human study, and as you've defined it this morning, it was a controlled study; isn't that right?

A. Well, a poorly controlled study.

Q. A poorly controlled study.

A. Correct.

Q. And it was poorly controlled because the people didn't drink pomegranate juice in the control group? Is that why?

A. It was -- the control group was constructed poorly and also wasn't -- it was -- it was described in several different ways in several different places --

Q. Well, aside --

A. -- in the documents.

Q. I'm sorry.

Aside from a misdescription or what you claim is a misdescription, there was a control group, and what was poorly designed about it was that it didn't drink pomegranate juice; is that it?

A. Well, I don't think one would want the control group to drink pomegranate juice. I'm not sure what you're driving at.

Q. Well, I'm trying to figure out what was so poorly designed about it other than what you've said before.

A. I'll be happy to tell you. It was not a randomized control group.

So the control group -- you know, Dr. Aviram said he just sort of selected individuals to be put in a group that would not get any treatment, so A, the problem is it's not a randomized control group, and secondly, the control group did not receive anything. I mean, there was no placebo or a control substance or control agent given.

Q. Didn't you testify this morning that there is a control group where somebody takes a placebo or where somebody takes nothing?

A. Well, nothing can be used in a control group,

but it's not -- I mean, it's not a good design to use nothing. That's why in the better studies like Dr. Davidson's study they use a control, a control beverage. That's the way it should be.

JUDGE CHAPPELL: Can you explain how that would affect the result of the study if it's not a randomized control group?

THE WITNESS: Sure. It's that -- I mean, the reason we use, you know, a placebo or a control substance is it's really to reduce the bias in the study.

If the control group is given something and the control group is told that they're in group -- they're -- the study is comparing two things, like juice A or juice B, then the control group does not know they're being given a substance that's thought to have no effect, a placebo, and the active group, the group getting pomegranate juice, doesn't know it's getting this great new stuff that's going to help them.

So it prevents bias from getting into, from affecting the results. And also it allows the researchers to be blinded to the measurements also, and that's great insurance against biases creeping into the measurement side.

BY MR. FIELDS:

Q. But as you've told us, in your well-known sodium study, the people knew what they were getting, they were not blinded in any meaningful sense; isn't that right?

A. Well, we told them we were testing the different sodium levels.

Q. But I think you testified they knew from the taste what they were getting, so it wasn't really blinded, was it?

A. It wasn't blinded, but -- but -- no, no, of course it wasn't blinded by -- it was -- the conditions set up -- there was blinding set up, but because the taste was different, many of the participants could -- would know what sodium level they were eating. Correct.

Q. And you knew that.

A. Of course.

Q. And nonetheless you answered -- pardon me -- you told the public that this diet based upon that study would prevent I think you said cardiovascular disease, stroke and kidney disease, you announced to the public; right?

A. Yes.

Q. Based upon something that realistically was not blinded.

A. Well, that is correct.

Q. All right. Now --

JUDGE CHAPPELL: Hold on a second.

But if the participants could taste the salt, then you're talking about participant bias more than the bias of the person conducting the study; correct?

THE WITNESS: Correct.

JUDGE CHAPPELL: And is one any worse than the other?

THE WITNESS: Oh, yes. Let me -- the bias on the part of the researchers is far worse than participants knowing or having some idea of what they're eating. Because the researchers will induce a bias. Their own biases, they communicate them, whether they are trying to or not, communicate them to the participants, and their own biases unconsciously can actually affect the measurement-taking process, so that's why we're extremely careful that the measurers, the researchers, are blinded.

So that in fact in the DASH sodium study, the researchers, the measurers, the analytic team never knew what the participants were actually eating. We built a firewall in that study.

JUDGE CHAPPELL: So if I understand you right, if you are faced with only doing a single-blind study,

you want the blinder to be on the researcher rather than the participant in the study.

THE WITNESS: Absolutely.

JUDGE CHAPPELL: If that's your choice.

THE WITNESS: Absolutely.

BY MR. FIELDS:

Q. Would you say that the medical community would in many instances disagree with you on that and would think it's much less important to blind the researchers and to make sure that the people in the study themselves don't know what they're getting?

A. I disagree with that statement.

Q. Okay. Now, I think you called Dr. Aviram's CIMT study a worthy test; is that correct?

A. I said the C -- well, I said CIMT is a worthy test, that the CIMT test is a worthy test, yes.

Q. I thought you said Dr. Aviram's CIMT test was a worthy test.

Are you making a distinction between the two?

A. Well, but I meant anybody's CIMT test should be good, it should be a worthy test if it's measured with high standards.

Q. And you don't disagree with Dr. Aviram's numbers, do you?

A. Disagree with him? I have no basis to disagree

in the numbers that are reported.

Q. And what he measured is usually relevant to cardiovascular health, isn't it?

A. Correct.

Q. CIMT improvement is an indicator that the treatment may be beneficial; isn't that right?

A. Correct.

Q. And the treatment here was pomegranate juice; right?

A. Correct.

Q. All right. Now, let's turn to Dr. Ornish's study, which you testified about at some length.

That was a randomized, double-blind, placebo-controlled trial; correct?

A. Well, by intent it was.

Q. What did you say?

A. By intent it was.

Q. You think it was not a randomized, double-blind, placebo-controlled trial?

A. Well, as I have described, there are multiple -- there were, well, multiple violations of that trial design as the trial progressed.

Q. But it was in fact what we call an RCT trial despite your criticisms of the way it was done; isn't that correct?

A. Well, we could call it a double-blind, placebo-controlled RCT that had problems in execution that undercut that very fine design.

Q. All right. And you're not a cardiologist; right?

A. Right.

Q. And you're not an expert on the technique that Dr. Ornish used; correct?

A. Excuse me. Which technique are you referring to --

Q. Myocardial perfusion.

A. Correct.

Q. And what Dr. Ornish got as a result was a 35 percent positive difference between the pomegranate juice and the placebo group; isn't that correct?

A. Well, I would have to check, but 35 percent in exactly what?

Q. Wasn't there a 17 percent improvement in the pomegranate juice group and an 18 percent worsening in the placebo group?

A. I think I'll have to look at those numbers.

Q. Yeah. It's on page 13 of the study -- 813.

A. 813?

Q. Yes.

A. Is this the -- are we talking about the Sumner

paper, Sumner, et al.?

Is there a CX number for that?

Q. My associate will give you that.

1198.

A. Okay. I have it.

All right. And I assume that if -- we are talking then about the myocardial perfusion results.

Q. Yes.

A. Okay. So I see them on table 2.

Q. And that's a rather significant improvement; correct?

A. Well, I mean, based -- the question -- I would like to know exactly what you're referring to -- there are a lot of different comparisons here in this table 2 -- when you say there's a 17 or 18 percent change.

Q. Well, whatever additional information you want, it is correct, is it not, that the published result was a 35 percent positive difference between the pomegranate juice group and the placebo group? Right?

A. I'm just reading the results section.

Q. Yes.

A. And I don't see those numbers in the results section. And I do see all the numbers in the table. I see the actual data in the table. I don't see those

percentages that you just quoted to me.

Q. We'll find for them for you at the recess. Let's move on.

Proper blood flow to the coronary artery and to the heart is fundamental to lowering a risk of coronary vascular disease and other heart diseases; is that right?

A. Correct.

Q. As we said, if you don't get blood flow to the heart, you die; right?

A. Correct.

Q. Okay. Now, you'll agree that while you may consider SSS a better surrogate that in fact SDS is a valid surrogate for lowering the risk of coronary vascular disease; isn't that right?

A. I don't -- I can't answer that. I can't agree with that. SSS contains more information, and according to the textbook, it's more -- it's -- it is the measurement that is most validated.

Q. Now, you're referring to Dr. Bromfeld's textbook, sir?

A. Braunwald.

Q. Braunwald.

And doesn't he say that both SSS and SDS are surrogates for the disease, but he thinks SSS is more

important?

A. Well, yes, he assume -- he says that SSS is more important.

Q. But he does make SDS a surrogate for heart disease; right?

A. Well, I really wouldn't characterize it in that way.

Q. Well, isn't that what he says? He says of the two -- the two are surrogates, but SSS is more important. I think --

A. Well, I'd have to look -- well, let's take a look at the quotation exactly.

I mean, I won't answer that until I actually see what he -- what the explicit wording is because I --

Q. I see -- go ahead. Finish your answer. I don't mean to interrupt you.

A. Well, I mean, my memory tells me that he said that the SSS score was the score most closely linked to prognosis in cardiac disease.

Yeah, I'm sure I'm not quoting it perfectly either, so I don't see why we can't just take a look at it if you wish to make a point about it.

Q. I'm looking for it and I'll ask...

(Pause in the proceedings.)

Do you have your report in front of you, Doctor?

A. Okay. I have my report.

Q. You quote it, so I'm sure you quoted it accurately.

A. Well, I found it. If you're looking for it, I've got it. It's page 21 of my report at the very bottom of the page and the sentence -- the final sentence, beginning, "In the leading textbook of cardiology..."

Are you with me?

Q. Yes.

A. Okay.

Q. It says "... a substantial literature has validated these summed scores, particularly the SSS"; isn't that correct? Doesn't Dr. Bromfeld (sic) say that the most validated surrogate between SDS and SSS is SSS?

A. Well, there's the quote, "... a substantial literature has validated these summed scores, particularly the SSS as predictors of natural history outcomes."

Q. Well, that doesn't tell us that SDS is not validated. On the contrary, it indicates they're both validated, but he particularly likes SSS; isn't that

true?

A. Well, maybe, maybe not. I don't know the source documentation for that. When I read a sentence like that, I'm interested in the SSS.

Q. Well, but Dr. Ornish in his study was not interested in SSS; isn't that correct? He was writing on SDS.

A. Well, I disagree with that as a -- as the valid -- as the, you know, most important outcome of the perfusion studies.

JUDGE CHAPPELL: Hold on.

You disagree that he was writing on SDS or you disagree with his method?

THE WITNESS: Oh, I disagree that he -- that he goes with SDS rather than SSS.

BY MR. FIELDS:

Q. You mean you disagree with his choice; you don't disagree with the fact that he did go after SDS?

A. You are correct.

Q. Okay. Now, did you say that you just don't argue with what he was interested in in this experiment?

A. Well, SSS includes dead tissue. If somebody has a heart attack while they're on pomegranate treatment, I think that -- and it causes cardiac muscle

to die, that needs to be included in the evaluation of the effect of pomegranate juice. It shouldn't be just disregarded. And it's the SSS that has both the dead tissue and the functional dead tissue, perfusion of dead tissue and perfusion that's related to function.

Q. But I refer you -- you have your deposition there -- to page 189 of your deposition where you say, and I quote, "I mean I don't argue with what he says he is interested in, but I don't think that priority the SDS is any more valid probably less valid than the SSS in assessing whether pomegranate juice is good for blood flow."

A. Correct, I said that.

JUDGE CHAPPELL: I heard both "I don't agree" and "I don't argue." Which is it? "I don't agree with what he said" or is it --

MR. FIELDS: Also I don't agree -- no. Wait a minute. Now I lost it.

JUDGE CHAPPELL: I just want to make sure that what you read, is it supposed to be "I don't agree with what he says" or "I don't argue with what he says"?

MR. FIELDS: It's "I don't argue with what he says."

JUDGE CHAPPELL: Same answer?

THE WITNESS: Your Honor, I'm not sure what the

question is.

JUDGE CHAPPELL: Why don't we go back, restate the question again.

MR. FIELDS: Sure. I've got to find it again.

JUDGE CHAPPELL: Page 189 you said.

BY MR. FIELDS:

Q. Page 189 line 1 through 5.

And the question is, is this still your testimony: I mean I don't argue with what he says he is interested in, but I don't think that priority, the SDS, is any more valid, probably less valid, than the SSS in assessing whether the pomegranate juice is good for blood flow?

Is that still your opinion?

A. Yes, it is my opinion.

Q. So he gets to choose what he wants to write about even though you think it's less important than a different kind of study; right?

A. Correct.

Q. Okay. And you'll agree then I think that the test of SDS, even though perhaps less valuable, is a surrogate for the likelihood of heart disease; isn't that correct?

A. I'm not -- I'm not offering an independent opinion on the merits of SDS.

Q. Okay. So you're not telling us whether it is or is not a valid surrogate; correct?

A. That is correct.

Q. Okay. Now, another criticism that you had of Dr. Ornish's study was that he wasn't clear in writing up his primary endpoint; is that correct?

A. Correct.

Q. Well, and he -- he said he was studying reversible myocardial ischemia; isn't that right?

A. Correct.

Q. Doesn't that tell you what he's looking for?

A. Well, he has to state what he's looking for in terms of the measurement.

Q. I see. All right.

Now, wasn't his test, his study, approved by the institutional review board at UCLA hospital?

A. Well, I certainly hope it was.

Q. Yes. Well, I -- it indicates that it was, and I don't know anything that suggests that indication here in the report is wrong.

A. Okay.

Q. But if it was approved by the review board, apparently they thought that it was stated with sufficient clarity; isn't that correct?

A. You can't assume that at all, that an

institutional review board, you know, would have necessarily that kind of detail-oriented evaluation of a protocol.

Q. You mean that an institutional review board wouldn't say if it thought so, Well, Dr. Ornish, you haven't sufficiently specified your endpoint here.

A. They might or they might not.

Q. Well, in this case apparently they didn't; isn't that correct? They approved it as it was.

A. Well, you know, if you want me to opine on the institutional review board's opinions, then why don't we see what the institutional review board -- let's look at their actions and what they told Dr. Ornish to do. I think we're just in an entirely hypothetical realm at the moment.

Q. Well, assume for the moment that the institutional review board did in fact approve Dr. Ornish going forward with this study.

A. I'll buy that.

Q. Okay. And isn't that an indication that they at least thought it was not lacking in clarity?

A. Incorrect.

Q. So you think that's no indication at all of that.

A. Different IRBs will put emphases on different

things.

Q. And --

A. I think that -- okay. You can ask your question.

Q. You don't know one way or the other then, is what you're telling me?

A. I don't know one way other about that point.

JUDGE CHAPPELL: How much more time do you think you need?

MR. FIELDS: I'm getting pretty close, Your Honor.

JUDGE CHAPPELL: Okay. Go ahead.

MR. FIELDS: It's shorter than I thought.

JUDGE CHAPPELL: All right.

BY MR. FIELDS:

Q. Your other criticism of Dr. Ornish's study was that there was a difference at baseline in SRS and SSS; isn't that correct?

A. Correct.

Q. And you think that difference at baseline might have affected somehow the SRS and the SSS ultimate results; right?

A. I think it could well have.

Q. It could very well be that people who were sicker at the beginning showed a greater percentage of

improvement than the people who had no problem at the beginning; isn't that correct? We just don't know?

A. Well, it's possible. What you said is possible.

Q. Well, I believe you said that your other objections to the Ornish-Sumner trial were not fatal; is that correct?

I'll go through them if you'd like.

A. Please.

Q. Some patients got blinded -- unblinded at the end of the study. You call that a demerit.

A. Yes, I remember that.

Q. That's a demerit, but it's not a fatal flaw. You're not throwing out the study.

A. Correct.

Q. The same would be true of a change in duration. You said there was a change in duration.

Again, you said it was a demerit but not a fatal effect?

A. Correct.

Q. And with regard to the intention to treat as opposed to the per-protocol measure, I think you also said that was a demerit but not fatal; correct?

A. I don't remember that one, but that's maybe a little more serious than the other two.

Q. Well, let's look and see. That's page 196 of your deposition.

A. Yeah, I call it a demerit.

Q. Yeah, it's a demerit.

A. Okay. I'll go along with that.

Q. All right. Okay.

Now, you then went on to the Bev 2 study, and you said that it was designed -- well-designed and well-conducted study -- the study was well-designed and well-conducted; isn't that true?

A. Correct.

Q. And the concept and study aim were fine; correct?

A. I'm sorry? The what?

Q. The concept and study aim were fine.

A. Correct.

Q. The measurements were read by a good institution.

A. Yes.

Q. Okay. Dr. Ornish wanted to enroll 200 patients, but he only got 50 because of a lack of funding; is that right?

A. Correct.

Didn't he get 70-something?

Q. It was up to 73. He got 50 and upped it to 73.

Okay.

And in fact it showed an improving trend, although it did not reach statistical significance; is that correct?

A. No. That's an incorrect.

Q. Is it?

A. Incorrect.

Q. It didn't show any improvement in the study.

A. Well, a trend has a statistical definition, and this did not meet the definition for trend.

Q. What's the definition of a trend?

A. A p-value of between .05 and .10.

Q. So you're saying if it doesn't have statistical significance, it's not a trend; is that it?

A. A trend is not statistically significant. A trend is a trend, and I defined it just the way I defined it. That's how it's defined in statistical textbooks.

Q. You're not an expert in statistics, though.

A. I happen to know what a trend is defined as in the statistical textbooks, such as Rosner's Fundamentals of Biostatistics.

Q. Well, was there an improvement shown even though it didn't reach statistical significance?

A. Such a thing doesn't exist.

Q. What do you mean, such a thing -- strike that.

Are you telling me that any improvement that doesn't reach statistical significance is not an improvement?

A. Correct.

Q. Well, there's some people who disagree with that; isn't that right?

A. I don't know why they should and still be decent scientists.

Q. Okay. I just wanted that answer plainly on the record.

Now, you said that Dr. Ornish was unreasonable when he said that the study was underpowered and that that's why it didn't reach statistical significance; isn't that correct?

A. Well, it's not a correct statement. Dr. Ornish did not make a correct statement when he said that the difference -- the -- that the -- that the difference in the CIMT measurement, you know, was real. I mean real meaning that it's real rather than just something that occurred by chance, that would have occurred if pomegranate juice was never given.

I mean, his assumption just is absolutely incorrect.

Q. Well, the assumption that it was underpowered;

is that what you mean?

A. Well, we don't know if it's underpowered.

Q. Well, didn't you say it was underpowered?

A. It could have been; it couldn't have been.

Q. Didn't you say it was underpowered sir?

A. It could have been underpowered -- well, if I said it in the deposition, that's a possibility. It could have been or it couldn't have been.

Q. Well, I understand you to say that Dr. Ornish was unreasonable in saying that it was underpowered, and I'm asking you if you said the same thing.

A. Okay. Well, let's go -- then I'd like to see what I said.

JUDGE CHAPPELL: What about what you believe? First of all, was it underpowered?

THE WITNESS: Oh, thank you, Your Honor.

JUDGE CHAPPELL: And then let's worry about what you said.

THE WITNESS: Okay. What I believe is I -- I don't know if the study is underpowered because, I mean, it -- because I don't know what the potential -- what the potential effect the researchers would expect to find.

I mean, for example, some CIMT studies can show significant effects with sample sizes in the seventies

and some require sample sizes in the hundreds. If it -- so I'm just not sure whether his study was truly underpowered.

BY MR. FIELDS:

Q. Well, let me read you from line 20 of page 208 of your deposition:

"Dr. Sacks, if you want to finish." That's the question.

And your answer is (as read): "No. So unfortunately he ended up with a study that was underpowered. That's just unfortunate."

A. Okay. Fair enough.

I mean, my feeling is that at the time -- at the time I -- I mean, my feeling at the moment is that it, as I've gone through this case over and over again since the deposition, is that it may have been underpowered, it may not have been underpowered, depending on the potential of the pomegranate juice to cause the change.

If pomegranate juice is inert, then it wouldn't matter how many subjects were studied. A negative is a negative. If the pomegranate juice is capable of producing a very small effect, then possibly this study was underpowered.

JUDGE CHAPPELL: This might not be a wise

question, but what do you mean by "underpowered"?

THE WITNESS: Well, "underpowered" means that the study has -- does not have you might say the ability or the -- the ability to detect an important effect. And the ability to detect an important effect is governed by first the number of subjects in the study, secondly is the precision in which the measurement is made, and third is what is the important -- an important difference.

So number of subjects is one component of a power estimate.

JUDGE CHAPPELL: Just one component.

THE WITNESS: One of three components.

JUDGE CHAPPELL: All right.

BY MR. FIELDS:

Q. And you agree that it is possible that statistically significant differences could have been there if the sample size was larger?

A. Oh, it is possible, yes.

Q. Now, a moment ago I thought you said it had a negative result, and you said something like that this morning in your testimony I thought. But isn't it true that a lack of statistical significance or a positive result is not proof of the negative?

A. Well, that is correct.

Q. So it doesn't mean, for example, that pomegranate juice doesn't work; it just means we didn't prove that it worked in this experiment.

A. Correct.

Q. Let's go to Dr. Davidson's study.

This was another RCT trial; right?

A. Correct.

Q. And it is correct, is it not, that at 12 months that the composite artery measurement showed improvement?

A. Incorrect.

Q. It didn't show improvement?

A. Incorrect.

Q. You're sure.

A. I am sure of that. I explained it this morning on direct.

Q. Didn't the composite rate for all measured carotid artery walls show a smaller value at 12 months?

A. That is correct.

Q. Isn't that an improvement?

A. No.

Q. You mean smaller artery walls are not better than thick artery walls where they're occluding the carotid artery?

A. Well, Mr. Fields, I explained this in exquisite

detail this morning on direct, and I'd be happy to repeat that now if you'd like me to explain the basis for my short answers.

Q. Well, what I'd like to know is, if a person in a test of the artery walls shows that his artery walls are thicker than they previously were, that is not an improvement, that's bad; isn't that right?

A. Yes.

Q. Okay. And if they are thinner than they were, that is an improvement, it's good, isn't it?

A. It's good.

Q. Okay. And when I ask you if there is an improvement, I refer to the fact that the composite rate for all measured carotid artery walls show a smaller value at 12 months than they did at baseline.

A. Incorrect. You said "rate," and that's where you are wrong.

Q. I said "rate"?

A. Composite rate. And that's where you're wrong. Dr. Davidson did not publish the composite rate at 12 months. But he did state that at any time point the rate was no different. It was no different in the pomegranate compared to placebo.

Q. What -- were the walls thinner at 12 months, Doctor?

The composite walls, were they thinner at 12 months?

A. They were thinner at 12 -- you mean -- well, the composite -- the composite -- what was it? -- the composite value at 12 months was lower, less, in the pomegranate group than in the placebo group. But the change, which is the proper thing to evaluate when you have an intervention study, the change from baseline to 12 months was not different in the pomegranate group than in the placebo group, according to Dr. Davidson.

Q. I'm sorry.

What I asked you was, didn't the composite rate for all measured carotid artery walls show a significantly smaller value at 12 months in the pomegranate juice group?

A. Not shown.

Q. Well, let me read you from paragraph 52 page 28 of your report, and I quote, "The 'composite rate' for all measured carotid artery walls had shown a significantly smaller value at 12 months in the pomegranate juice group."

A. I know, I know that's there. I missed it.

Q. Well, you missed it. You just told us under oath that that was wrong and it wasn't so, and it was so.

A. Well, my apologies to everybody involved. This is a subtle point, and I picked up on it later.

JUDGE CHAPPELL: When you say you missed it, do you mean your answers some moments ago were incorrect or --

THE WITNESS: No. I'm sorry, Your Honor.

JUDGE CHAPPELL: What did you miss?

THE WITNESS: I mean, in the report I missed the fact that this -- I missed the fact that the rate at 12 months was never -- was not reported in that table.

And I picked up on it -- as I reviewed this over and over again, I picked up -- I said, Oh, my God, this is not what -- this is after I read Dr. Ornish's comments, and I said, My God, I've got to go back and look at this, and I said, No, no, no.

The value at 12 months doesn't say anything about the effect of treatment. It's the change from baseline to 12 months or the rate that shows the effect of treatment. And then Dr. Davidson said at no point was the rate different in the placebo -- in the pomegranate and the placebo group.

So I was wrong in the report. Actually I didn't use precise -- I did not use the precise, correct word in the report.

BY MR. FIELDS:

Q. While we're on the subject of change, if I have a -- something that -- let's take cholesterol. That's a surrogate, and I call it a surrogate for, let's say, illness at death. Doesn't it follow that the increases or decreases in that surrogate increase or decrease the likelihood of illness or death?

A. Well, they may if it's -- so they may if that surrogate has been connected to mortality, but not all surrogates are connected to mortality.

Q. Well, let's assume you have a surrogate for mortality, and somebody says this is a surrogate for mortality or a surrogate for a particular illness. It follows, doesn't it, that the increases or decreases, the changes in that surrogate are what predict the likelihood of that illness or death for which it's a surrogate; isn't that correct?

A. Correct.

Q. Okay. Thank you.

Now, let's turn -- we're getting toward the end, Your Honor -- to the post hoc analysis. There's a subgroup that got a benefit of the high-risk people in Dr. Davidson's study.

That could be in the United States alone many millions of people; isn't that correct?

A. Yes.

Q. And you say this is a subgroup analysis that would require further study, but you've done a number of subgroup analyses; isn't that correct?

A. Yes, I have.

Q. You've even published them publicly, the subgroup analyses?

A. I do.

Q. So we don't just disregard subgroup analyses, and if we have one that could bring a major benefit to millions of people throughout the United States, don't we want to get that out to the public?

A. Not unless it's validated by a proper study.

Q. And if those proper studies will take three, four, five, ten more years, you say we just -- we have to wait because it's a post hoc analysis; right?

A. Well, we have to wait until a second study validates the finding in the first study.

Q. So if I have a study that is designed to test blood pressure and it turns out that after three, four years that it doesn't do anything for blood pressure, but it sure as heck reduces cancer, cancerous lesions, I can't get that out. I've got to do another study.

A. Well, I mean, we're dealing with CI- -- we're dealing with CIMT here, so that's -- I mean, that's what

I'm going to opine on. I'm not going to opine on a study that has shown that -- that looks at heart disease and finds something with cancer. That's a whole -- that has happened to me in research, and that's a whole other different thing.

Q. Well, my point is, isn't it correct that when the public health is at stake, you want to get information out, even if it's based on a post hoc study, if it can help millions of people.

A. The results were in the public domain. Dr. Davidson did publish the subgroup analysis. The key here is its interpretation.

Q. But you're saying that we can't inform the public, that my clients, for example, can't tell the public about this result which could help millions of people because it's a post hoc analysis. Right?

A. Well, I'm saying that the analysis is probably not going to pan out to be true because most subgroup analyses don't turn out to be true, and that's why they have to be -- that's why they have to be confirmed.

So, you know, Dr. Davidson wrote about it in a very honest way, and I agree with his opinion completely.

Q. Well, it might turn out to be true; isn't that right?

A. It might, yes.

Q. These figures are in his -- you said he's a very reputable, excellent scientist, that he turned up these figures for this very large subgroup and millions of people, and it certainly could help them if he's right, and you say he's got to wait until he does another study before my clients can put that information out there; right?

A. Correct.

MR. FIELDS: Okay. That's all I have, Your Honor.

JUDGE CHAPPELL: Is there any redirect based on the cross?

MS. EVANS: Yes, sir.

- - - - -

REDIRECT EXAMINATION

BY MS. EVANS:

Q. Dr. Sacks, we won't keep you much longer.

Now, what years was the DASH study data collected?

A. Let's see. Wasn't it -- in the mid-'90s.

Q. And if Mrs. Resnick testified that in 2001 American consumers had never heard of the pomegranate, is there any reason to believe that there was widespread consumption of pomegranates in the DASH

study?

A. No. I don't think we used pomegranates in the DASH study.

Q. Have there been any observational studies on the pomegranates or pomegranate juice, to your knowledge?

A. To my knowledge, no.

Q. Doctor, could you --

JUDGE CHAPPELL: Hold on a second.

Do you want to retrieve your realtime notebook?

MR. GRAUBERT: I'd love to. Thank you.

Excuse me.

MS. EVANS: Sure.

JUDGE CHAPPELL: I thought he was rising to object and I realized he was manipulating equipment over there.

MR. GRAUBERT: Proceed.

MS. EVANS: Sure.

BY MS. EVANS:

Q. Mr. Fields used the term "Aviram's observational study" --

JUDGE CHAPPELL: Can you hold on until we're ready.

(Pause in the proceedings.)

Go ahead.

BY MS. EVANS:

Q. Now, Mr. Fields used the term "Dr. Aviram's observational study," but he, Dr. Aviram, did not conduct observational studies?

A. Correct.

Q. You were talking about some of the omega-6 and sodium trials, and you said that there weren't -- that some of them had flaws. But you also said that they had major strengths.

A. Correct.

Q. Were -- did any of the studies by respondents have major strengths?

A. Oh, well, yes, I mean, certainly.

Q. And those would be the Davidson --

A. Especially the Davidson study.

Q. IMT study?

A. The Bev 2, the Ornish IMT study, yes, that had major strengths.

Q. And how about the Davidson BART study?

A. That had -- yes, that was a strong study.

Q. Now, we were talking -- you were talking with counsel earlier about foods used in cooking.

Have foods used in cooking for many, many years now been shown to increase the risk of cardiovascular disease?

For example, saturated fats?

A. Oh, certainly. Yes.

Q. In fact foods are a major cause of cardiovascular disease?

A. Correct.

Q. Could you turn to CX 716 at page 41.

A. I'm sorry. Which document?

Q. CX 716.

A. CX 716.

Q. At page 41.

A. Okay. I have 716.

Q. And does this show the level of sugars in pomegranate juice?

A. Yes.

Q. Would you characterize these as being meaningful levels of sugars?

A. Yeah, those are -- that's a meaningful level of sugars.

Q. Are changes in microphage -- macrophage --

JUDGE CHAPPELL: Hold on. We have an objection.

MR. FIELDS: An objection and motion to strike. I'm sorry. This witness testified he was giving no opinion as to the contents of pomegranate juice, and now we're getting that very opinion.

JUDGE CHAPPELL: I believe I heard him say that.

MS. EVANS: Excuse me?

JUDGE CHAPPELL: I believe I heard him say that he's not here to talk about pomegranate juice.

MS. EVANS: But he --

JUDGE CHAPPELL: I'll tell you what I'm going to do based on the objection. I'm going to disregard the answer, and I'm going to allow you to ask that question if you lay a foundation and connect it to the cross.

MS. EVANS: Yes, sir.

JUDGE CHAPPELL: Otherwise, I'm going to consider it outside the scope of what he told us he's here to talk about and what he testified to on cross.

BY MS. EVANS:

Q. Sir, did you testify that there were -- when you were discussing with Mr. Fields and he was talking about the safety of foods, do you recall that?

A. Yes.

Q. And when you're considering the safety of foods, is one of the things you consider the level of sugars in them?

A. Yes.

Q. Okay. And did you -- in the course of preparing

your expert report, did you see information regarding the level of sugars in pomegranate juice?

A. Yes.

Q. And is that information shown on CX 716 at page 41?

A. Yes.

Q. Thank you.

You were also asked --

JUDGE CHAPPELL: Hold on.

MR. FIELDS: I thought that complaint counsel was finished, and she apparently is not finished, so I will hold my fire until she's finished.

JUDGE CHAPPELL: Correct.

Are you still on the sugar or are you moving on?

MS. EVANS: I was moving on.

JUDGE CHAPPELL: And am I correct that this exhibit is in evidence?

MS. EVANS: Yes, it is.

JUDGE CHAPPELL: So it's a document in evidence, and I don't see it as an opinion. I'll allow it.

MR. FIELDS: If it's in evidence, we'll argue it later then, Your Honor.

JUDGE CHAPPELL: All right.

BY MS. EVANS:

Q. Sir, during cross-examination, Mr. Fields asked you about macrophage levels?

A. Yes.

Q. Are macrophage -- are changes in macrophage levels shown to be a reliable surrogate marker of heart health?

A. No.

Q. Mr. Fields also asked you whether in vitro evidence can provide competent, reliable evidence; correct?

A. Correct.

Q. And you said that, yes, they can.

A. Correct.

Q. Now, can in vitro evidence provide competent, reliable evidence of a result in humans?

A. They cannot.

Q. If you could turn to Dr. Ornish's myocardial perfusion study, which I believe is CX 10 -- excuse me, Your Honor.

Do you have Dr. Ornish's myocardial perfusion study before you?

1198, CX 1198.

A. Okay.

Q. Okay. Turning to the section that discusses the

results of that study under -- it's on page 4.

And the first sentence says that the results demonstrate an improvement in myocardial perfusion in patients who have ischemic CHD as measured by the SDS.

And then he says, in the sentence below that, the clinical significance of this finding is further illustrated by an average improvement of 17 percent in myocardial perfusion in the experimental group and an average worsening of 18 percent in the control group, i.e., a relative between group -- 35 percent relative between-group difference after three months; correct?

A. Correct.

Q. Now, if that 35 percent improvement were calculated off of the myocardial perfusion SDS rates, would that 35 percent result reflect only one-third of the data?

A. I'm sorry. I don't quite follow that. I don't quite follow --

Q. Okay. If he was using -- if that 35 percent were calculated off of the SDS results --

A. Okay. That's in table 2.

Q. Correct.

A. In table 2.

Q. -- would that mean that it ignores the summed rest score and the summed stress score data?

A. Yes. That only pertains to the SDS.

Q. Now, if you could turn to CX 664.

You were testifying about the relative importance of SSS, SRS and SDS; correct?

A. Okay. I see that.

Q. Okay. Now, when you're looking at CX 664, if I could refer you to page 2.

And let me know when you get there.

A. Okay.

Q. On page 2, under -- there's a chart or there's a couple of lists of data, and under Experimental there's data for patient 555051.

A. Okay.

Q. And is this the patient with the suspected silent heart attack?

A. Correct.

Q. Okay. And in that patient, the change in his SSS data was significant; correct? It went down -- well, I won't characterize it as significant.

It went down by ten points; correct?

A. Correct.

Q. And his SRS data after the heart attack went down by ten points; correct?

A. Correct.

Q. Is there any change in his SDS score?

A. No.

Q. And did the protocol identify any one of these scores, SSS, SDS or SRS, as being the endpoint that he was going to measure?

A. No.

Q. And you were talking to Mr. Fields, and he was talking about the demerits in Dr. Ornish's study, and he asked you about a passage from your deposition, and it was on TR 196.

A. Of the deposition?

Q. Of the deposition. TR 196.

A. Pages 19 -- yes, 196.

Q. And Mr. Fields was asking you if you would -- if you characterized each of the individual problems with -- Dr. Ornish's problems as being demerits; correct?

A. Correct.

Q. But did you say in conclusion (as read), "So accumulatively they have a very adverse impact on the validity of the results. So that's why I really don't think these results really support a statement that there was any benefit to the cardiovascular system or to perfusion, cardiovascular health"?

A. Correct.

MS. EVANS: Thank you. No further questions.

JUDGE CHAPPELL: Any recross based on the redirect?

MR. FIELDS: No questions, Your Honor.

JUDGE CHAPPELL: Thank you, sir. You're excused.

And who's your next witness?

MS. HIPPSLEY: Your Honor, we're going to call Mr. Resnick.

Do you want to take an afternoon break before we start?

JUDGE CHAPPELL: We're going to take a break, and while we're on the break I'd like both sides to think about how much total time you're going to need with this witness so I can plan our schedule for Wednesday. And it looks like we indeed won't be going beyond Wednesday before complaint counsel rests?

MS. HIPPSLEY: I think so, unless we can work out whether or not we can stay a little late this evening to finish Mr. Resnick. We have no other witnesses.

JUDGE CHAPPELL: Oh, you may be able to finish this evening.

MS. HIPPSLEY: Perhaps if -- I'm estimating about two hours, and so if we could stay until 6:30, then we might not have to come back on Wednesday. I

would have a better sense when I get about a half hour into it.

JUDGE CHAPPELL: Well, under the general rule in this ripples in the pond effect, if we went to 6:30 and we didn't finish, we would start very late on Wednesday, like noon.

MS. HIPPSLEY: Okay. Well, let me talk with opposing counsel during the break and see what their preference is.

JUDGE CHAPPELL: Let's do that. And we'll take a shorter break. Why don't we -- we'll reconvene at 4:25.

(Recess)

JUDGE CHAPPELL: Back on the record.

What's the update on time?

MS. HIPPSLEY: Your Honor, I talked with opposing counsel, and I think their preference would be to end at a normal time tonight at 5:30 and finish on Wednesday.

JUDGE CHAPPELL: Okay. At 5:30 let's determine how much time we're going to need. It doesn't sound like we're going to need a full day Wednesday.

MS. HIPPSLEY: No. Absolutely. Well, I can tell you at 5:30 better, but I think we'd be an hour or hour and a half on Wednesday.

JUDGE CHAPPELL: So you're convinced you can finish before 6:30?

MS. HIPPSLEY: I'll have a better sense of it at about a half hour or 45 minutes in.

MR. GRAUBERT: Your Honor, as Heather says, our preference is to try to finish rather than drag on for a long time, and we don't expect it to take much time on Wednesday, but we're perfectly happy if we get to 5:30 or a quarter after 5:00, we can reassess where we are.

JUDGE CHAPPELL: Why don't we do that. Let's do that.

MS. HIPPSLEY: All right.

JUDGE CHAPPELL: All right. Call your next witness.

MS. HIPPSLEY: I'd like to call Mr. Stewart Resnick to the stand, please.

- - - - -

Whereupon --

STEWART RESNICK

a witness, called for examination, having been first duly sworn, was examined and testified as follows:

DIRECT EXAMINATION

Q. Mr. Resnick, I'm going to have counsel give you a binder of the documents that we'll be using today.

And they are in the order of the exhibit numbers.

Good afternoon, Mr. Resnick.

Could you please state your name and spell it for the record.

A. Stewart Resnick, S-T-E-W-A-R-T, R-E-S-N-I-C-K.

Q. Thank you.

And Mr. Resnick, you are chairman and president of Roll Global; is that right?

A. Yes.

Q. And you and Mrs. Resnick are the owners of Roll Global and its affiliated companies; is that correct?

A. Yes.

Q. And one of the affiliated companies is POM Wonderful LLC; correct?

A. Yes.

Q. Now, until this year Roll Global was known as Roll International; is that right?

A. Yes.

Q. And it was reorganized at the end of the year; is that right?

A. Yes.

Q. So for simplicity sake, when I refer to Roll, it will mean Roll International or Roll Global, depending on the time that we're talking about.

Is that all right?

A. Fine.

Q. Okay. And Roll with all its associated businesses is an approximately $2 billion corporation; is that correct?

A. Yes.

Q. And on its Web site Roll refers to itself as the largest privately owned company that you've never heard of; is that right?

A. I've not seen the Web site.

Q. Okay. But if we haven't heard of it, it's because we know the company by the various brands; right, such as Fiji Water, Teleflora, Wonderful Pistachios and POM Wonderful, among others; is that right, that we recognize the brands? Those are your brands?

A. Yes.

Q. And POM Wonderful is a for-profit business; isn't that correct?

A. Not yet.

Q. It's not organized as a nonprofit.

A. No. It's an organized as a profit business, but we haven't made a profit yet.

Q. And it's in the business of selling pomegranates and related products; is that right?

A. Yes.

Q. And in all your businesses you get involved at some level according to what you feel is necessary; is that correct?

A. Correct.

Q. And in part, you run a rather informal organization, as you told me in your deposition; is that right?

A. Yes.

Q. And in the POM business you make the ultimate decisions about what the company invests in and how you're going to expand, as an example of your involvement.

A. Yes.

Q. Thank you.

And you set the budgets for POM Wonderful; is that correct?

A. I would say certainly the macro budget.

Q. Okay. And does that include the budget for marketing and advertising?

Does your involvement include setting the budget for POM Wonderful for marketing and advertising?

A. Yes. I'm not sure I have as much power in that area as the other areas as my wife is quite involved.

Q. Yes, she's very involved.

But you handle the budgeting for what can be spent on advertising and marketing; is that right?

A. If I win the argument.

Q. I'm sorry?

A. If I win the argument.

Q. And you also are involved in the budgeting for POM Wonderful for medical research; is that right?

A. Yes.

Q. And Matt Tupper as the president of POM, he tries to meet with you weekly when you're in town; is that correct?

A. Correct.

Q. And you probably talk three or four times a week by phone; is that also correct?

A. Yes.

Q. Now, Mr. Resnick, I'd like to just get a little of your educational background.

Do you have a college degree?

A. Yes.

Q. And what is that degree in?

A. My undergraduate was in accounting.

Q. Okay.

A. And I have a juris doctorate from UCLA law school.

Q. That was my next question.

And have you ever been licensed to practice law?

A. No.

Q. Now, given the prior testimony and cross exam, I thought maybe we could try and clear up something.

One glass of POM juice is not equal to one pomegranate, to your understanding; is that right?

A. Correct.

Q. Okay. And one glass of POM juice, to your understanding, does not contain any vitamin C; is that right?

A. I don't know. I can't comment on that.

Q. That's fine if you don't know.

Do you know whether or not POM juice has any fiber?

Only if you know.

A. I doubt it, but I don't know.

Q. All right.

A. I'll just say I don't know.

Q. Okay. And is it true that one glass of POM juice equals roughly two and a half pomegranates?

A. I would say roughly.

Q. Okay. And so it would have roughly the amount of sugar that's contained in two and a half pomegranates; is that right?

A. Right.

Q. Okay. Now, I'd like to go over some of the folks who have worked with you on POM's medical research and just figure out their roles.

What is Dr. Harley Liker's role vis-à-vis POM Wonderful?

A. He was our medical adviser.

Q. And you were the one that hired Dr. Liker; is that correct?

A. Correct.

Q. And in fact you renewed his contract in 2005, and I would like to show that. It's CX 706 page 1.

And you can either look at it in the book or look at it on the screen, Mr. Resnick, whatever is better.

A. So where do I find the CX?

Q. 706. They're in numerical order.

A. Okay.

Q. All right. And this is the letter agreement that you signed with Dr. Liker in 2005; is that right?

A. Yes.

Q. And you did this in your position as president and CEO of Roll International; is that correct?

A. Yes.

Q. And this was, as the document states, renewing,

if you look to the second sentence, talking about when you and Mr. Liker met, about his role as medical director of POM in 2002, so this was basically renewing his contract to be the medical director of POM Wonderful; is that right?

A. I'm not sure. This -- he's also a consultant for wellness to our company. I think this may be his total compensation for both.

Q. For both? Okay.

A. Right. A major part of what he plays is a role as sort of the overall medical resource for all our people, to all our employees in case they have a serious problem, and he directs them to that which he thinks is the best available treatment.

Q. All right. And if you look down in the paragraph about midway, he discusses -- let's see.

About in the tenth row he's got a sentence there, "... I am finding that I am consistently spending in excess of 25 percent of my time on POM Wonderful related matters."

Now, POM Wonderful related matters would be in his role as medical director for POM; is that correct?

A. Correct.

Q. Okay. And then this document indicates that he's asking, as of February 1, 2005, to have his salary

increased from 175,000 to 250,000; right?

A. Yes.

Q. Do you know how much Dr. Liker is paid today for his involvement as medical director for POM Wonderful?

A. I -- again, I don't know if this was just for the medical or for POM Wonderful or all of his services.

Q. Uh-huh.

A. But I don't know, but I sort of have a memory that we reduced it some since we involved other professionals along with him.

Q. Okay. And today, though, he is still considered the medical director of POM Wonderful?

A. Yes.

Q. And as we saw here, you made the -- worked out the deal with Dr. Liker instead of POM Wonderful, and I believe, as you told me in your deposition, this in part is because Dr. Liker was your personal doctor; is that right?

A. Yes.

Q. And so it was just something you were able to work out with him; is that correct?

A. Also I worked out the original arrangement with him, and since his services didn't just involve this but

involved other services for the -- for all of Roll, I was the most likely to work it out. I didn't want to do it in a split way.

Q. All right. And now I'd like to turn to Dr. Heber.

To your knowledge, does Dr. David Heber run a center for nutrition at UCLA? Is that right?

A. Yes.

Q. And he's done research for POM Wonderful; is that correct?

A. Correct.

Q. And he is also a consultant for POM Wonderful; is that right?

A. Yes.

Q. And --

A. I'm not sure if it's him or his center.

Q. But Dr. Heber himself, I believe you told me in our deposition, you use him personally to vet ideas for POM Wonderful, such as what medical research proposals to entertain, that sort of thing?

A. Well, he's sort of part of the group that we use to discuss where we're going in the medical area and where we might go, and I mean, he's just a very well-rounded doctor.

Q. Okay. Does he participate in the -- in budget

reviews that you would hold with POM Wonderful to, for example, decide what medical research to fund in the coming year?

A. No. Not that I'm aware.

Q. Okay. But you do meet with him regularly; is that correct?

A. Yes.

Q. Okay. And how long has he served in this role as an adviser, let's say, to POM Wonderful?

A. You know, it's hard -- time goes so fast, it is hard for me to -- but certainly for a period of time. I guess five years.

Q. Okay. Now, I'd like to show you some testimony from Dr. Heber's deposition in this matter just to lay a foundation.

If we could look at CX 1352, and we have the excerpts that I'm going to be looking at from Dr. Heber's deposition in your book, Mr. Resnick, so it's 1352.

And I'd like to turn to the deposition page 424. The pagination at the top of the page.

A. All right. Oh, okay. I see it. I got it. Okay.

Q. Thank you. Page 424.

And to direct your line -- I'm sorry.

To direct your attention to line 12 through 16, and Dr. Heber was asked that he gave prior testimony that his center received several millions over a period of several years, and then the follow-up at the bottom of the page at line 22 (as read):

QUESTION: Okay. And some of these funds were paid by the Stewart and Lynda trust and other funds by POM Wonderful?

And his answer is: "Correct."

And I want to ask you, does that sound about right, in your view, that you've paid Dr. Heber several million dollars over the last several years, he and his center?

A. Yes.

Q. Okay. And then turning again in his deposition to page 417, which was a prior page in his deposition, and if we look there at line 11 through line 16, this states again (as read):

What portion of the money comes from the Resnick related organizations?

ANSWER: This year, less than 50 percent.

QUESTION: And other years?

ANSWER: There have been years, like with the 800,000 where maybe as much as 70 percent was from the Resnicks.

And is it true that --

JUDGE CHAPPELL: Do you have an objection?

MS. DIAZ: Objection, Your Honor. I believe that this portion of the transcript was corrected. I don't know if Ms. Hippsley has the corrected version.

MS. HIPPSLEY: I don't have it in front of me, but I believe the correction goes to the 50 percent being somewhat lower.

Is that correct?

MS. DIAZ: I would have to pull the exact one, but I don't think that reading from here is accurate.

MS. HIPPSLEY: But in some years it's been as high as 70 percent. That was not corrected I believe.

MS. DIAZ: I believe it was corrected, but I'd have to pull the --

JUDGE CHAPPELL: Hold on a second.

If you're going to be using a deposition, it needs to be the corrected version.

MS. HIPPSLEY: Right. I'm sorry, Your Honor. I wasn't aware that it had been corrected, the 70 percent. I think, now that she reminds me, the 50 percent had been corrected down. But we'll take the numbers as wherever they stand on the corrected.

But the point I was trying to make was that -- that Dr. Heber has named a laboratory in his center

after you and Mrs. Resnick; is that correct?

THE WITNESS: Correct.

BY MS. HIPPSLEY:

Q. Okay.

Okay. Now, we've heard a lot today about Dr. Aviram's study in the heart disease area.

And as well as his specific research that we've heard, Dr. Aviram is also considered to be -- I think as you put it in one of your previous depositions with the Ocean Spray counsel, he's considered to be on retainer for POM Wonderful again as a consulting role; is that right?

A. Yes.

Q. And over the course of the years would it be a fair statement to say that Dr. Aviram has been paid roughly $4 million by the Resnick affiliated organization for his research and services?

A. I know we paid him -- he was our original researcher, so I know he's been involved a long time. I don't know formally -- I don't have any reason to believe it's not the right number, and certainly if someone gave you our records and told you that, I would say that's correct. But I can't independently validate that.

Q. All right. Well, let's just double-check.

We were given a spreadsheet, which I think we looked at before, and the spreadsheet that we were provided is CX 1276. And if you could turn to page 3 of this exhibit. And we'll blow up the top quarter. Hopefully it will be legible, or the one you're looking at is probably legible.

And page 3 is the amount of money paid to various medical vendors by the trust.

And if you go down about ten lines, can you see the vendor Dr. Michael Aviram?

A. Yes.

Q. And the total that the trust has paid him from 1999 through 2005, the total amount is $1,744,037; is that right?

A. Yes.

Q. And then if you turn to page 4 of that same exhibit, which is the amount that POM has paid to various vendors, POM corporation, and if we can blow up the bottom of that page, so if you go to the bottom and come up about ten lines, there's an entry for Michael Aviram?

A. Yes.

Q. Okay. And POM has paid him an additional amount from 2006 through 2010 of 2.3 million; is that right?

A. Yes.

Q. Okay. Thank you.

Now, I'd like to show you what's been marked and it's in your book as CX 1241, and this is another chart that was produced by your counsel to the Federal Trade Commission in the summer of 2010.

And Mr. Fields has recounted during some of his examinations about the number of studies that have been conducted by POM Wonderful with the various institutions, and I just wanted to focus here, if you look -- I'm sorry. Do you have the document?

A. Yes.

Q. Okay. Thank you.

If you look to the entry for UCLA and the number of studies that it has conducted is 29; is that right?

A. Yes.

Q. And then it lists the various areas, and it appears that UCLA has conducted research in the areas of cardiovascular, prostate cancer, cognitive function and the chemistry and antioxidant, I would assume of pomegranates. Is that right?

A. Yes.

Q. Okay. And then if you drop down to the bottom of the chart under International, there's a listing for

Rappaport Technion Faculty of Medicine, and that is the medical facility that's related to Dr. Aviram; is that right?

A. Yes.

Q. And there you can see that the number of studies that he has conducted is 20; is that right?

A. Correct.

Q. Okay. And his are listed as being in the area of cardiovascular and again the chemistry of antioxidants.

And the 29 by UCLA and the 20 by Dr. Aviram far exceed any that any of the other institutions have conducted, according to the chart; is that right?

A. Correct.

Q. I believe the next highest number would be five that were conducted at Tufts University.

So do you have any concern that large portions of the research being done are being done by two institutions, UCLA and Dr. Aviram?

A. No.

Q. Okay.

A. We wouldn't have chosen them unless we thought they were totally honest and intellectually moral.

Q. Okay. And did you state in your deposition, though, that one of the reasons that you have branched

out to using Johns Hopkins, for example, for prostate research is to reduce the potential criticism that you sponsored all the research on prostate at one university, that being UCLA?

A. Yes.

Q. Okay.

A. I don't think it's valid criticism. It just happens to be criticism.

Q. Right. Thank you.

Is it true, Mr. Resnick, that patents related to the methods of use for pomegranate extract have been awarded by the U.S. Patent and Trademark Office?

A. I know that we were working on them. I'm not aware of -- if you tell me they were awarded, they were awarded. I know we've been working on them.

Q. But it has been -- to your knowledge, POM Wonderful has applied for such patents for the pomegranate extract?

A. Yes.

Q. All right. And to shift gears a little bit, now, Mr. Resnick, you've decided to take some of the medical research you've been doing and look into drug claims for some of your products; is that correct?

A. Well, we're looking for drug approvals.

Q. Okay. And I believe --

A. We're thinking of looking at drug approvals. Let me say that. It's always been something that we've thought about.

Q. Uh-huh.

A. And the further along we get, we're trying focus on it a little more.

Q. All right. And that's in part why Dr. Dreher was let go and Dr. Gillespie was hired, because Dr. Gillespie has more experience in the drug approval process?

A. Correct.

Q. And I believe you've stated that in fact you're seeking to get FDA approval for a drug claim related to prostate cancer; is that correct?

A. I don't know what seeking -- we're thinking about it. We haven't applied for it yet, but we're waiting for some research that we have in motion at the moment, and then I think we are thinking should we have a discussion with them or not.

Q. Okay.

A. And certainly I hope to do that.

Q. Okay. So -- right.

So you would like to try to get a drug claim in that area of prostate cancer; is that correct?

A. Again, I don't know what a drug claim is. I

just know a drug approval. I mean, we'd like to be able to actually have a drug which would be recommended by doctors and may be prescription, may be over the counter. We haven't really thought that through.

Q. Okay. Well, I just wanted to make sure we are right on the word choice here.

And in your deposition in this matter that was given to me in April, on page 85, we started an area:

QUESTION: (as read) Okay. And now, when you refer to focusing more, which areas would you be focusing on currently?

"ANSWER: Well, prostate is a big one."

And then it goes on to page 86:

"ANSWER: And there again, we're focusing -- you know, I think we'd like to try to get a drug claim in that area --"

And so I'm using the words that you used in the deposition.

A. Whatever I said, let me say this. Since that point in time, I'm a little more confused about what "drug claim" means, so I want -- what I mean is drug approval and I don't want misconceptions of what "claim" is because it seems to me that in this whole procedure so far words have such a big importance even though the meaning isn't any different, so that's why I want to be

careful here because I don't know how you interpret "claim" and how I interpret "claim" may be different, but an approval is clearer to me.

Q. All right. And is that what you meant when you used "drug claim" in the deposition, that you were seeking drug approval?

A. Yes.

Q. Okay. And in fact you're also seeking or would like to try to get FDA approval for a drug related to erectile dysfunction; is that also right?

A. Correct.

Q. And are you interested in trying to get FDA approval for a drug claim related to cardiovascular disease?

A. I'm not aware of that.

Q. Do you know whether or not you're trying to do that?

A. Well, eventually we are looking into further research in that area.

Q. Uh-huh.

A. But it's all -- as I've learned -- I mean, when we started this, I was very naive about all these different areas, and now we're getting more sophisticated. It has to do with practicality, what the FDA would accept as endpoints, and so we have to really

have a conversation with them and see if it's actually practical.

Q. Okay.

A. And I'd like to do these things in my lifetime, and some of these tests they ask for, if they're 25 years, I doubt if I'm going to make it.

Q. And --

A. I'd like to, but I'm not sure I will.

Q. And is that as to --

A. I'd like to make the 25 years is what I'm saying.

Q. I was going to say, or is that as to cardiovascular health?

Would you like to get an approval from the FDA for cardiovascular disease as well?

A. Yes.

Q. Okay.

A. But I'd rather make the 25 years, to tell you the truth.

Q. Okay. And I believe you stated in previous testimony again in one of the other matters, the Ocean Spray matter, that you think that your product has as good a chance as any that it's helpful for prostate as most any other drug that's out there and is accepted by the FDA.

Is that your view?

A. Absolutely.

Q. And is it also your view that if your ads communicate to consumers that POM products can prevent or delay the onset of prostate cancer that you're comfortable with that claim?

A. I believe that.

Q. And would that be the same for heart disease as well?

A. I also believe it for heart disease.

Q. And you're comfortable that if your ads communicate that message about POM products to consumers, you're comfortable with that claim.

A. Yes. We're not making any claims that I'm not comfortable with.

Q. Okay. Now, is it your belief that the kinds of health benefits your research has revealed is the primary reason people buy pomegranate juice?

A. Would you repeat that question.

Q. Yes.

Is it your belief that the kinds of health benefits your research has revealed is the primary reason people buy pomegranate juice?

A. I wouldn't say that. I mean, I think -- I wouldn't say that.

Q. Okay. Well, when you were asked that question -- first of all, do you recall your deposition being taken in the POM versus Tropicana matter, and this was in September of 2010?

A. Yes.

Q. Okay.

A. I don't recall the deposition, but I recall having it taken.

Q. All right. And there on page 31 of the deposition, the question was: "Is it your belief that the kinds of health benefits your research, you believe, revealed is the primary reason people buy pomegranate juice?"

And your answer was: "Yes."

And so do you still agree with that statement today?

A. Yes. But let me explain.

I mean, basically what I think I was saying there and I'm certainly saying now is that people buy pomegranate juice because it's had a mystique for thousands of years to be a very healthy product or an extremely healthy and it's been in every culture. I think the -- I think one of the big London -- English schools of medicine or somebody has a pomegranate on its coat of arms.

And so I think in general people believe that pomegranate juice is very healthy, so the research we're doing is just proving that which has been mystique for coming now up to 6,000 years.

So I think in total people buy pomegranate juice because some people like the taste, some people believe that it's a healthy product, particularly people in cultures where pomegranate juice has been available for years.

Q. But here in the U.S., that was the context of the question; right, that --

A. Yeah. But there's -- there's a lot of those same people in the U.S. that are in these other countries, and when we first started selling pomegranate juice before we had very little of the research done, it started off extremely strong.

Q. Uh-huh.

But in answer to the question that it's the types of health benefits you've researched revealed is the primary reason people buy pomegranate juice, your answer was yes to that question at the deposition with Tropicana; is that correct?

A. Right. But again, you know, I'd have to look at the whole context of the deposition.

Q. Okay. And the next question actually was:

"QUESTION: And is it fair to say that a primary part of POM's messaging about its product is health benefits?

"ANSWER: Yes."

And you would still agree with that today; right?

A. Yes.

Q. And I believe you stated again when you were -- had your deposition in Ocean Spray that you believe that consumers seek out POM Wonderful juice to delay or prevent the onset of prostate cancer. Is that correct?

A. I think that the consumers who are sophisticated about it and particularly where their urologists have recommended it, which I think many urologists do, they certainly seek it out, yes.

Q. Okay. And your view is that people are buying POM products for these very specific reasons; is that right?

A. Some certainly, yes.

Q. And you also believe that consumers seek out POM Wonderful juice to delay or prevent heart disease; is that correct?

A. I wouldn't be as specific about that.

Q. Okay. Well, let's try it this way.

In the Ocean Spray deposition, I believe, if you

recall, you were concerned that the competitors were selling death, as you stated in that deposition. Do you recall that colloquy?

A. Yes.

Q. And in that context, at page 218, the question was: "And the same is true for heart disease" -- the question is: "We're selling death in the form of less heart disease compared to POM Wonderful?"

And the answer was: "Yes. If they," consumers, "believe in it and if what we're saying is correct."

So in that context, your concern is that the competitors are playing off a halo effect of your benefit for heart disease; is that right?

A. Again, the way you read it, I'm not sure that that's what it says, but it could be.

I mean, if people buy it for that reason, just, you know, for general health, which also has to do with cardiovascular, certainly that's correct. I think that the context was that other competitors are selling pomegranate juice with no pomegranate juice or 1 percent, and if people are buying it particularly for prostate health, which I am absolutely convinced without question is helpful, and they think they're getting some benefit from it and they're not, then I think that's

very dangerous, and unfortunately the FTC has done nothing about that.

Q. And do you believe the same way about heart disease?

A. Yes.

Q. And have you also stated that if you, your companies, not you personally but your companies, do not have adequate scientific substantiation for any of POM Wonderful's health claims that that would be fraud?

Isn't that you stated in the Ocean Spray deposition?

A. If I stated that, that's what I felt at the time, yes.

Q. Okay. And have you also stated in prior testimony that you don't refer to any standards promulgated by the FDA or FTC in considering how much evidence is enough to make a claim? Is that right?

A. Well, I haven't seen any standard that we can adhere to for what we're doing, so I can't say that we're hitting your standard or not. We're hitting my standard, and my standard I think is a very, very critical one. And I don't -- we don't make any claims unless we're very comfortable that we've done adequate work and the results are adequate enough to make those claims.

Q. And that would be basically your standard, that the science is adequate enough?

A. My -- yes, my standard. I guess it's my standard, but I think it's an adequate standard. Or more than adequate.

Q. And it's true then, Mr. Resnick, that you spend time reviewing the results of your research when it comes in; is that correct?

A. Yes.

Q. And you've basically seen all of the results as they come in; is that also correct?

A. Most of them. I mean, there's a -- we do a lot of work which tends to -- we look at something to make sure that what we did was correct the first time. We do a lot of mechanistic work, if we get a result, why does it work that way.

So I would say certainly I see all the results of the important tests and -- but there may be some other ones that people build additional research on that I may not have seen.

Q. Okay. And in fact you've seen a lot of the draft manuscripts before they're published; is that also correct?

A. I've seen some. I certainly haven't seen them all because there's a lot more published work than I

realized.

Q. But you have seen some.

A. Yeah. I've seen the bigger ones. Yes.

Q. And now, the funding for the studies that POM conducts, it's come from a variety of the Resnick organizations; is that right?

A. Yes.

Q. Okay. And I believe you've also testified in prior depositions that it doesn't really matter because ultimately it all comes out of your pocket; is that right?

A. Correct.

Q. And you've even corrected it to say yours and Mrs. Resnick's.

A. That's right. 50 percent mine, 50 percent hers.

Q. Okay.

Excuse me, Your Honor.

(Pause in the proceedings.)

Okay. If we can show CX Exhibit 1029, and yes, you can -- it might be easier actually to look in the book. And this is the medical research review summary. It's dated January 13, 2009.

Okay. And you've seen this document before; correct?

A. Yes.

Q. And is one of the purposes for this document to review the medical research that POM has been doing and set a budget for future research?

A. Yes.

Q. And now, if you could turn to page 3, which is the -- of CX 1029, which is the heart disease summary page.

A. Yes.

Q. Okay. And first I wanted to direct your attention to the information in the top about blood pressure and the blood pressure studies, human studies that have been conducted.

And if you look across that chart, would you agree that the company does not have enough evidence to make a blood pressure benefit claim?

A. I don't know. I mean, I know that there's most -- there's nothing inconsistent with any of our research that says it doesn't lower blood pressure. However, from my knowledge, we're not making that as a major claim at all. And if we made those claims, they were probably fairly early on, although I do believe that it does reduce blood pressure, but not to the -- not to a large enough extent for me to make the claim on a continuous basis.

Q. But you agree that looking at this chart and

what you heard today, many of the studies that studied the endpoint of blood pressure did not get results where the blood pressure had a positive result as an endpoint that was being studied; is that right?

A. Correct.

Q. Okay. And you've seen the "Decompress" ad that has the picture of the bottle of POM juice in a blood pressure cuff; correct?

A. Correct.

Q. And Mr. Tupper has testified in the hearing last week that this ad -- and we can actually show that, to keep me honest.

A. That would be good.

Q. Okay. This was on June 8, page 28 of the rough, and Mr. Tupper testified that the "Decompress" ad he believe ran in '07, '08 and '09.

A. Okay.

Q. And you've also heard testimony I believe when Mrs. Resnick was on the stand that your consumer research showed that 21 percent of the consumers thought there was a -- who thought there was a health benefit after seeing the "Decompress" ad thought that it reduced blood pressure; right?

A. I don't remember.

Q. If that is the case, though, what -- is it your

view that if the consumers misinterpreted the claim, that that's not your problem?

A. We certainly didn't do that ad with the idea, again, to tell people that it substantially reduces blood pressure.

Q. But if that was their understanding, have you testified previously that that's their problem if they misinterpret it and --

A. I would say if we didn't -- you know, you -- there's always unintended consequences, and in my view, if somebody misinterprets something, I'm not sure that's our fault.

Q. And if you have that information and the ad is still running and you know that some of the consumers misinterpret the ad, do you feel that you have a responsibility to change the advertising?

A. I would say that I would change the advertising. I'm not sure we have a responsibility to change the advertising.

Q. Okay.

All right. Let's go to Dr. Aviram's study, which is CX 611.

And looking at page 1 of this study, do you --

A. CX 611?

Q. I'm sorry. CX 0611.

A. Is that in the back or the front?

Q. It should be by the --

A. Oh, okay.

Q. -- 611 maybe. Okay.

A. Okay.

Q. All right. And to your knowledge, how much did this study cost, like in a range? It was not more than a couple hundred thousand dollars; correct?

A. I don't remember.

Q. Okay.

A. But again, we're happy to give you that information.

Q. Why don't we finish with the study and then we'll go to the spreadsheet.

So first, if you can turn to page 4 of this study under the Results section.

And I think we heard some of this today, but I just want to make sure you and I are on the same page.

So under the results, the first paragraph there, the sentence that sort of ends that first paragraph under Results says: In contrast, mean IMT in CAS patients that consumed POM juice for up to one year was reduced after 3, 6, 9 and 12 months of POM juice consumption by 13 percent, 22 percent, 26 percent and 35 percent, respectively, in comparison to baseline

values.

And do you understand what that means when it's in comparison to baseline values?

A. No. I mean, I think I do.

Look, I've learned more about the medical research since we've been involved in this just sitting here in this lawsuit than I have in terms of specifics.

Q. Okay.

A. My view is I depended on people who were experts and had no reason to tell me anything but the truth.

Q. Okay. But you would agree then, listening to things that we've heard and looking at these results, that this is not a comparison -- the 35 percent is comparing people who drank the POM juice to their original baseline number; is that right?

A. No. It's not compared to their original baseline. Is that what it --

Q. It says "in comparison to baseline," the 35 percent.

So it's studying people in relation to their own entry number.

A. I don't know -- are you saying that he's saying here that the people who took the pomegranate juice reduced their baseline by 35 percent?

Q. Reduced the measure of cardiac plaque 35 percent from where they started when they entered the study at their baseline measure.

A. Just looking at this quickly, I don't know that that's what it says. It could either say that or it could say that they're talking about both baselines.

Q. Meaning?

A. Meaning compared to the control group.

Q. Right. And that was my point.

Do you know whether or not all these years you've had an understanding that this study actually compared across to a control group rather than measuring against baseline?

A. No. All I know is that and everybody asks me that, you know, very unusually, result that was very important in terms of people who have a high level of plaque in their arteries.

Q. Okay. And did you understand --

A. I also understood -- again, I understood it had a very strong p-value which gave it a lot of credibility.

Q. Uh-huh.

But did you over these years have any understanding of whether that was measuring people against their own baseline or against the control

group?

A. No. I never thought about it.

Q. Okay. And then if you look at page 5 of the results, at the top, this is the measurements again of the blood pressure and the sort of -- in lay terms I'll say the ultimate result was 12 percent at 12 months for the POM juice consumption again compared to values obtained before treatment.

And now I want to go back to our heart chart if we can.

So if you look at the top, Mr. Resnick, where we have a list of the studies --

A. What was that again?

Q. On the blood pressure on the heart disease summary. Oh, I'm sorry. It's CX 1029.

And it's page 3 of that exhibit. It's also on the screen --

A. Unfortunately, the screen is right between my bifocals.

Q. Okay. That's fine.

A. If I sit further back, you won't be able to hear me, so I'm stuck.

Q. That's okay.

If you look at the blood pressure study results, 21 percent is listed for Aviram 2004, but as

we just saw, the actual number was 12 percent; isn't that right?

MS. DIAZ: Objection, Your Honor. Lack of foundation.

THE WITNESS: Yeah. Again, I'm looking at these --

JUDGE CHAPPELL: Hold on. We have an objection.

What's your response?

MS. HIPPSLEY: Well, this is listing the Aviram 2004 study that we just looked at. The publication date was 2004, the 19 patients. And I'm pointing out that the blood pressure number in the chart states that there's a 21 percent reduction, but we just went through that the study itself lists a 12 percent reduction.

MS. DIAZ: Your Honor, I can clarify if you like.

JUDGE CHAPPELL: Please do.

MS. DIAZ: There's no foundation that -- at the outset on whether he understands the numbers in the research that was cited -- okay? -- in comparison to this chart and certainly no foundation that -- in connection with his understanding of the numbers in this chart. On both documents there's no foundation, let

alone a comparison between the two.

JUDGE CHAPPELL: Are the charts in evidence?

MS. HIPPSLEY: Yes. And so is the study.

JUDGE CHAPPELL: But you're asking him to read a number from a document that's in evidence?

MS. HIPPSLEY: I was asking him to observe and affirm whether the number on the chart is erroneous because the study that's being referred to is actually a 12 percent number.

JUDGE CHAPPELL: And the objection is correct. There's been no foundation to tell us that he's competent to give that information.

Sustained.

BY MS. HIPPSLEY:

Q. Now, let's go back to the issue of cost for the Aviram study.

And if we look again at that spreadsheet, which is CX 1276.

And if we go to the third page, which is the amount that again the trust was paying to various vendors, and we look at the amount of -- so it's page 3.

And again we're looking at the numbers for Dr. Michael Aviram?

A. Yes.

Q. Okay.

A. Yes.

Q. All right. And his study was received for publication in June 2003, according to the publication we just looked at, which is CX 611.

So if we look at the amount of money that he had received, you know, at most from '99 to halfway to -- through 2003, it would be in the six or seven hundred thousand dollar range; is that right?

A. Through 3,000 -- through 2003?

Q. Through half of 2003 when the study was submitted for publication.

A. Well, it's more than that.

From what dates are you talking about?

Q. Well --

A. From the beginning or --

Q. Yeah. From 1999, that's a hundred --

A. I don't know how you -- 530, it's like 800. It's over $900,000.

Q. Well, there's 105,000 in 1999; right?

A. Yeah.

Q. And then 40,000.

A. That's 146, 263 is 400, and then 350 is 750, and half is 180, 930.

Q. Okay. And would all of that research have been

for this one study?

We've heard he's done other studies; correct?

A. No, It wasn't that one study. No.

Q. So at most, this study would have cost the 900,000 if all that money had gone to this study; right?

A. Yes.

Q. Okay. But in fact he was doing a lot of other research at that time for --

A. Correct.

Q. Okay.

JUDGE CHAPPELL: Okay. We're at 5:25. What's the reassessment?

MS. HIPPSLEY: In fairness, I'd say an hour and a half.

MR. GRAUBERT: I'd prefer we stop at 5:30, Your Honor, and resume Wednesday morning, given the time estimate.

JUDGE CHAPPELL: This is the only witness Wednesday?

MS. HIPPSLEY: Correct.

JUDGE CHAPPELL: How much is the anticipated cross?

MS. DIAZ: Very little, Your Honor.

JUDGE CHAPPELL: All right. We will reconvene

on Wednesday at 10:30.

We're in recess.

(Whereupon, the foregoing hearing was adjourned at 5:26 p.m.)

C E R T I F I C A T I O N O F R E P O R T E R

DOCKET/FILE NUMBER: 9344

CASE TITLE: In Re POM Wonderful LLC, et al.

HEARING DATE: June 13, 2011

I HEREBY CERTIFY that the transcript contained herein is a full and accurate transcript of the notes taken by me at the hearing on the above cause before the FEDERAL TRADE COMMISSION to the best of my knowledge and belief.

DATED: JUNE 19, 2011

JOSETT F. WHALEN, RMR

C E R T I F I C A T I O N O F P R O O F R E A D E R

I HEREBY CERTIFY that I proofread the transcript for accuracy in spelling, hyphenation, punctuation and format.

ELIZABETH M. FARRELL