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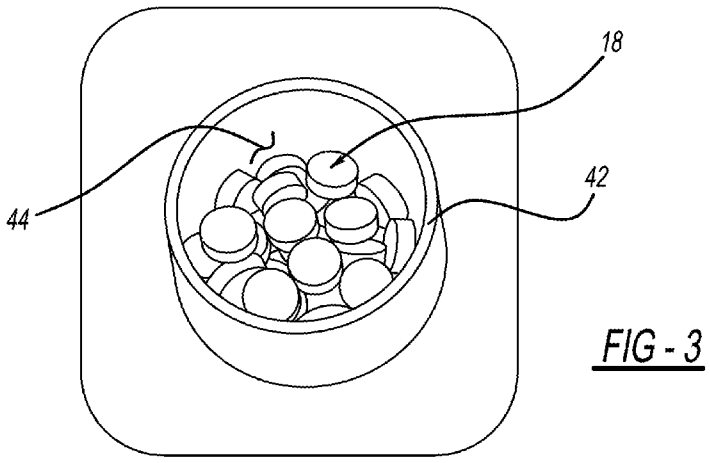

FIG - 3

(57) Abstract: A system and method for determining the presence and amount of one or more elements in a plurality of sample pills include a sample holder, X-ray source, detector and a data acquisition device. The plurality of sample pills is placed in a sample holder where they are irradiated with x-rays from an x-ray source. X-rays fluoresced from the plurality of sample pills in the sample holder are received by a detector which outputs a signal based on the received x-rays fluoresced from the plurality of sample pills in the sample holder. The data acquisition device determines the presence and amount of one or more elements in the plurality of sample pills based on the signal and at least one predetermined calibration curve.

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SYSTEM AND METHOD FOR DETERMINING THE COMPOSITION OF A PLURALITY OF PILLS USING X-RAY FLUORESCENCE

CROSS REFERENCE TO RELATED APPLICATION

[0001] This application claims the benefit of U.S. Provisional Application No. 62/319,506 filed on April 7, 2016, which is herein incorporated by reference in its entirety.

BACKGROUND

1. Field of the Invention

[0002] The present invention generally relates to systems and methods for determining the presence and amount of one or more elements in a plurality of pills.

2. Description of Related Art

[0003] Currently, x-ray fluorescence ("XRF") systems can be utilized to determine the composition of a sample. When a sample is exposed to short-wavelength X-rays or gamma rays, ionization of their component atoms may take place. Ionization consists of the ejection of one or more electrons from the atom and may occur if the atom is exposed to radiation with energy greater than its ionization potential. X-rays and gamma rays can be energetic enough to expel tightly held electrons from the inner orbitals of the atom. The removal of an electron in this way makes the electronic structure of the atom unstable, and electrons in higher orbitals "fall" into the lower orbital to fill the hole left behind. In falling, energy is released in the form of a photon, the energy of which is equal to the energy difference of the two orbitals involved. Thus, the sample emits radiation, which has energy characteristic of the atoms present. The term fluorescence is applied to phenomena in which the

absorption of radiation of a specific energy results in the re-emission of radiation of a different energy.

[0004] XRF systems can be utilized to determine the composition of pharmaceutical pills. While an accurate composition analysis can be performed, current implementations are laborious and destructive to the sample, making the use of XRF systems to determine pill composition impractical. More specifically, current implementations require first constructing a pressed pellet, sometimes referred to as a puck that is composed of a matrix material and has been spiked with known amounts of heavy metals or other elements to be detected. The large pressed pellet is constructed and placed in a sample holder of an XRF system. This pressed pellet is analyzed by the XRF system, and one or more reference curves are developed. These reference curves are developed based on the fact that the pressed pellet has a known amount of heavy metals to be detected.

[0005] Next, the pills or tablets to be analyzed, such as pharmaceutical pills that are ingested by an end user, are crushed and stamped into another pressed pellet similar in size shape to the earlier pressed pellet that was used to generate reference curves. Because of this process, the pills to be analyzed are destroyed and cannot be sold for pharmaceutical purposes. The pressed pellet cannot be resold, as it may contain more than one pill and are very large preventing any ingestion. After the pressed pellet has been constructed, the pressed pellet is placed in the sample holder of the XRF system where it is analyzed. Using the reference curves previously developed by utilizing the pressed pellet having a known amount of heavy metals, the information outputted by the detector of the XRF system is then compared to the reference curves to determine the presence and

amount of any heavy metals. This has a drawback in that such a methodology requires destruction of the original pills and takes more time and equipment to complete, thus making the use of XRF systems to determine pill composition impractical.

SUMMARY

[0006] A system for determining the presence and amount of one or more elements in a plurality of sample pills includes an X-ray source, a sample holder, an x-ray detector, and a data acquisition device. The sample holder is configured to retain the plurality of sample pills and allow the plurality of sample pills in the sample holder to be irradiated with x-rays from the X-ray source. The x-ray detector receives the x-rays fluoresced from the plurality of sample pills in the sample holder and outputs a signal based on the detected x-rays fluoresced from the plurality of sample pills in the sample holder.

[0007] The data acquisition device is configured to receive the signal from the x-ray detector and determine the presence and amount of the one of more elements in the plurality of sample pills based on the signal from the detector and at least one calibration curve. The calibration curve is pre-determined and is based on a reference signal generated by the x-ray detector by a set of a plurality of reference pills having a known amount of the one or more elements to be detected.

[0008] The method for determining the presence and amount of one or more elements in a plurality of sample pills begins with placing the plurality of sample pills in a sample holder. The pills are then irradiated with x-rays from the X-ray source. A detector then receives x-rays fluoresced from the plurality of sample pills in the

sample holder and outputs a signal based on the received x-rays fluoresced from the plurality of sample pills in the sample holder. A determination is then made regarding the presence and amount of the one of more elements in the plurality of sample pills based on the signal and at least one calibration curve, which was pre-determined based on a reference signal generated by the x-ray detector of by a set of a plurality of reference pills having a known amount of the one or more elements to be detected.

[0009] Further objects, features, and advantages of this invention will become readily apparent to persons skilled in the art after a review of the following description, with reference to the drawings and claims that are appended to and form a part of this specification.

BRIEF DESCRIPTION OF THE DRAWINGS

[0010] Figure 1 illustrates a system for determining the presence and amount of one or more elements in a plurality of pills;

[0011] Figure 2 illustrates a block diagram of a data acquisition device used in the system of Figure 1;

[0012] Figures 3 and 4 illustrate a more detailed view of a sample holder of Figure 1;

[0013] Figures 5A and 5B illustrate reference curves of several elements;

[0014] Figure 6 illustrates a method to determine the presence and amount of elements in a plurality of pills; and

[0015] Figure 7 illustrates a method for generating at least one calibration curve.

DETAILED DESCRIPTION

[0016] Figure 1 illustrates a system 10 for determining the presence and amount of one or more elements in a plurality of pills. A pill may be a mass of medicine that may be swallowed whole. The terms "pill," "capsule" and/or "tablet" and their plurals could be used interchangeable throughout this description. For uniformity, the term “pill” will be used throughout this description. As its primary components, the system 10 includes an X-ray source 12 for generating x-rays 14, a sample holder 16 for retaining a plurality of pills 18, an X-ray detector 20, and a data acquisition device 22.

[0017] The X-ray source 12 may be any one of a number of different types of X-ray sources. For example, the X-ray source 12 may be found in a wavelength dispersive X-ray fluorescence spectrometer. An example of a wavelength dispersive X-ray fluorescence spectrometer is the ZSX Primus and/or ZSX Primus II, available from Rigaku Americas, 9009 New Trails Drive, The Woodlands, TX 77381.

[0018] The x-rays 14 are directed to the sample holder 16 by the X-ray source 12 which may include any one of a number of additional optics so as to correctly direct the x-rays 14 to the sample holder 16. The sample holder 16 is configured to retain the pills 18 in the sample holder 16. The x-rays 14, when coming into contact with the pills 18, are fluoresced, creating fluorescent x-rays 24 that are received by the detector 20 which may include any one of a number of different optics. While the x-ray source 12 is shown as being below the pills 18, it should be understood that the x-ray source 12 and/or the detector 20 may be located above the pills 18.

[0019] The analysis of major and trace elements in the pills 18 by x-ray fluorescence is made possible by the behavior of atoms when they interact with radiation. When pills 18 are excited with high-energy, short wavelength radiation (e.g., X-rays), they can become ionized. If the energy of the radiation is sufficient to dislodge a tightly-held inner electron, the atom becomes unstable, and an outer electron replaces the missing inner electron. When this happens, energy is released due to the decreased binding energy of the inner electron orbital compared with an outer one. The fluorescent x-rays 24 are of lower energy than the primary incident X-rays 14 and is termed fluorescent radiation. Because the energy of the emitted photon is characteristic of a transition between specific electron orbitals in a particular element, the resulting fluorescent x-rays 24 can be used to detect the abundances of elements that are present in the pills 18.

[0020] To these ends, the detector 20 is configured to output a signal 26 based on the fluorescent x-rays 24 received by the detector 20. This signal 26 is then provided to a data acquisition device 22. The data acquisition device 22 is configured to receive the signal 26 from the X-ray detector 20 and is configured to determine the presence and amount of one or more elements in the pills 18 based on the signal 26 from the detector 20. This is accomplished by utilizing at least one calibration curve being predetermined based on a reference signal generated by the detector 20 by a plurality of reference tablets having a known amount of one or more the elements detected.

[0021] As will be described later in this description, a set of a plurality of reference pills having known elements are purposely constructed and then utilized by the system 10. Based on the output of any signal 26 generated by the detector

20, calibration curves can be created because the signal 26 generated can be interpolated or extrapolated to a known element and amount of the known element. As the plurality of reference pills was purposely created with a specific known element and amount, any signal generated by the detector 20 from the plurality of reference pills can be used to create a calibration curve. Each element to be detected generally has a separate calibration curve. As such, by taking the output of the signal 26 and comparing it to the calibration curve by the data acquisition device 22, a determination of the presence and amount of an element can be made by the data acquisition device 22.

[0022] The data acquisition device 22 may be connected to the detector 20 by a cable 28 sufficient to transmit the signal 26 from the detector 20 to the data acquisition device 22. Of course, instead of a cable 28, any other methodology capable of transmitting data from one point to another may be utilized, such as wireless communication.

[0023] Referring to Figure 2, a more detailed view of the data acquisition device 22 is shown. The data acquisition device 22 may include a housing 30 containing a processor 32. The processor 32 may be in communication with a memory 34 and a network access device 36. The memory 34 may be able to store signals 26 received by the detector 20 and may further contain executable code for executing any the methods disclosed in this description including those methods related to determining the presence and amount of elements in the pills 18. Of course, it should be understood that the processor 32 may be a single processor or may be multiple processors working in concert. Further, the memory 34 may be any type of memory capable of storing information, such as magnetic media, optical

media, solid-state devices, holographic memories, and the like. Further, the memory 34 may be integrated within the processor 32 or may be separate as shown.

[0024] The data acquisition device 22 may also include an output device 38 that is in communication with the processor 32. The output device 38 may be a display capable of displaying information, a printer, a storage device such as a hard drive, magnetic media, optical media, solid-state media, and the like. The data acquisition device 22 may also include one or more input devices 40 that are in communication with the processor 32. The input devices 40 may be a keyboard, mouse, touchscreen, and the like. Further, in the case of a touchscreen, the output device 38 and the input device 40 may be housed within the same housing and appear to be a single device.

[0025] The network access device 36 allows the data acquisition device 22 to communicate with the detector 20. The network access device 36 may be as simple as a data access point, such as a serial or parallel communication protocol that utilizes a physical cable. However, the network access device 36 may also be a wireless or wired network access device capable of either direct communication with the detector 20 or indirect communication with the detector 20 via a network.

[0026] Referring to Figures 3 and 4, a more detailed view of the sample holder 16 is shown. The sample holder 16 includes a sample cup 42 having a cavity 44 for receiving the pills 18. The pills 18 do not need to be arranged in any particular orientation. As shown in Figures 3 and 4, the pills 18 can be arranged in a completely random orientation that may vary from tablet to tablet. After loading the sample cup 42 with pills 18, the sample cup 42 is then placed within a retaining ring

46 that is capable of being placed in a fixed position relative to the detector 20 and the X-ray source 12 of Figure 1.

[0027] Referring to Figure 5A, reference curves 48, 50, and 52 are shown for cadmium, lead, and arsenic, respectively. Of course, it should be understood that reference curves could be generated for any element and not just those listed above. For example, in the pharmaceutical industry, in addition to those listed above, reference curves may be generated for mercury so as to allow the detection of mercury. In Figure 5B, reference curves 54, 56, and 58 are shown for cobalt, vanadium, and nickel, respectively. The reference curves 48, 50, 52, 54, 56, and 58 essentially plot intensity versus amount. By using the set of the plurality of reference pills that have known amounts of these elements, the signals 26 (intensity) generated can be plotted to the amount of each known element. These generated curves can then be used when examining tablets of an unknown composition, wherein the signal 26 (intensity) is known and therefore using these reference curves the amount can be determined.

[0028] As stated in the background section, the prior art would utilize sets of single pressed pellets that were spiked with appropriate elements to generate reference curves for these elements. Because these pressed pellets essentially acted as a reference, the pills to be examined would need to be crushed and formed into an equally sized pressed pellet. The system and method described in the specification have a significant advantage in that the actual pills intended to be ingested by an end user will be subject to the examination without any need to create a pressed pellet, which essentially destroys the pills. Additionally, in order to generate the reference curves, the set of the plurality of reference pills may

generally have the same size and shape as the pills to be examined. However, the size and shape of the set of the plurality of reference pills may differ from that of the sample pills. More specifically, the size and shape of the set of the plurality of reference pills may take the form in the universal size and shape that may differ from the size and shape of the sample pills.

[0029] Further, the number of pills to be examined and the number of reference pills in the set utilized to generate the reference curves should be generally equal. However, equality may be based not only on the number of pills but by weight as well. As such, the number of pills under examination may not be exactly equal to the number of pills forming the set of the plurality of reference pills; however, the larger the variance between the pills under examination and the set of the plurality of reference pills, either by weight or number, may affect the accuracy of the examination.

[0030] Referring to Figure 6, a method 60 for determining the presence and amount of elements in a plurality of pills 18 is shown. Reference will also be made to items found in Figure 1. The method 60 begins with step 62, wherein the plurality of sample pills 18 is placed in a sample holder 16. In step 64, the plurality of sample pills 18 are radiated with x-rays 14 from the X-ray source 12.

[0031] In step 66, the detector 20 receives x-rays 24 fluoresced from the plurality of sample pills 18 in the sample holder 16. In step 68, the detector 20 outputs a signal based on the received x-rays 24 fluoresced from the plurality of sample pills 18 in the sample holder 16. In step 70, a determination is made regarding the presence and amount of one or more elements in the plurality of sample pills 18 based on the signal 26 and at least one calibration curve. As stated

before, the calibration curve is a predetermined calibration curve that was generated by irradiating a set of a plurality of reference pills containing a known amount of an element.

[0032] Referring to Figure 7, the method 72 for generating at least one calibration curve is shown. Reference will also be made to elements found in Figure 1. The method 72 begins with step 74, wherein the plurality of reference tablets are constructed. The plurality of reference tablets may be constructed such that they mimic both the size and shape of sample pills 18 of an unknown composition. The reference tablets are composed of matrix material or specific formulation(s) and spiked with known amount(s) of element(s). Depending on the number of elements added to the set of the plurality reference pills one reference curve may be generated for each element.

[0033] In step 76, the set of the plurality of reference tablets is placed in the sample holder 16. In step 78, the plurality of reference tablets are irradiated with x-rays 14 from the X-ray source 12. In step 80, the detector 20 then receives x-rays 24 fluoresced from the plurality of reference tablets in the sample holder 16. In step 82, the detector 20 then outputs a reference signal based on the received x-rays 24 fluoresced from the plurality of reference tablets from the sample holder 16.

[0034] In step 84 at least one calibration curve is generated. The calibration curve is predetermined based on a reference signal generated by the x-ray detector 20 by the fluoresced x-rays 24 from the plurality of reference tablets. Because the amount of each element is known, the intensity of the signal can be traced to a certain amount, and a reference curve is then created.

[0035] In practice, the system and methods described in the specification have the advantage in that the sample pills 18 are such that they are ready for commercial distribution to be ingested by an end user. Therefore, the actual pills that will be sold to the end user can be actually tested. As stated before, the prior art required making from the pills a single large pressed pellet for examination making testing of pharmaceuticals impractical and destructive to the pills examined. The system and method described have the advantage in that testing can be accomplished, without destroying the pills under examination and without spending additional time creating the pressed pill. In effect, pills can be examined by the system and method described in this specification in a matter of minutes instead of hours. In an alternative example, dedicated hardware implementations, such as application specific integrated circuits, programmable logic arrays, and other hardware devices, can be constructed to implement one or more of the methods described herein. Applications that may include the apparatus and systems of various embodiments can broadly include a variety of electronic and computer systems. One or more embodiments described herein may implement functions using two or more specific interconnected hardware modules or devices with related control and data signals that can be communicated between and through the modules, or as portions of an application-specific integrated circuit. Accordingly, the present system encompasses software, firmware, and hardware implementations.

[0036] In accordance with various embodiments of the present disclosure, the methods described herein may be implemented by software programs executable by a computer system. Further, in an exemplary, non-limited example, implementations can include distributed processing, component/object distributed processing, and

parallel processing. Alternatively, virtual computer system processing can be constructed to implement one or more of the methods or functionality as described herein.

[0037] Further, the methods described herein may be embodied in a computer-readable medium. The term "computer-readable medium" includes a single medium or multiple media, such as a centralized or distributed database, and/or associated caches and servers that store one or more sets of instructions. The term "computer-readable medium" shall also include any medium that is capable of storing, encoding or carrying a set of instructions for execution by a processor or that cause a computer system to perform any one or more of the methods or operations disclosed herein.

[0038] As a person skilled in the art will readily appreciate, the above description is meant as an illustration of the principles of this invention. This description is not intended to limit the scope or application of this invention in that the invention is susceptible to modification, variation, and change, without departing from the spirit of this invention, as defined in the following claims.

CLAIMS

1. A system for determining a presence and amount of one or more elements in a plurality of sample pills, the system comprising:

an x-ray source for generating x-rays;

a sample holder, the sample holder configured to retain the plurality of sample pills, the sample holder being configured to allow the plurality of sample pills in the sample holder to be irradiated with x-rays from the x-ray source;

an x-ray detector for receiving x-rays fluoresced from the plurality of sample pills in the sample holder, the x-ray detector configured to output a signal based on the received x-rays fluoresced from the plurality of sample pills in the sample holder; and

a data acquisition device configured to receive the signal from the x-ray detector, the data acquisition device configured to determine the presence and amount of the one of more elements in the plurality of sample pills based on the signal from the x-ray detector and at least one calibration curve, the calibration curve being pre-determined based on a reference signal generated by the x-ray detector of by a plurality of reference pills having a known amount of the one or more elements to be detected.

2. The system of claim 1, wherein each element of the one or more elements has a corresponding reference curve.

3. The system of claim 1, wherein the plurality of reference pills and the plurality of sample pills are substantially the same size and shape.

4. The system of claim 1, wherein the plurality of reference pills have a universal size and shape.

5. The system of claim 1, wherein the plurality of sample pills are commercial pills (or a designated subset thereof) intended for digestion by an end user.

6. The system of claim 1, wherein the one or more elements include at least one of cadmium (Cd), lead (Pb), arsenic (As), cobalt (Co), vanadium (V), nickel (Ni), or mercury (Hg).

7. The system of claim 1, wherein the sample holder further comprises a sample cup.

8. The system of claim 1, wherein the weight of the plurality of reference pills is substantially similar to the weight of the sample pills.

9. The system of claim 1, wherein the number of the plurality of reference pills is substantially similar to the number of the sample pills.

10. A method for determining a presence and amount of one or more elements in a plurality of sample pills, the method comprising the steps of:

placing the plurality of sample pills in a sample holder;

irradiating the plurality of sample pills in the sample holder with x-rays from an x-ray source;

receiving by a detector x-rays fluoresced from the plurality of sample pills in the sample holder;

outputting by the detector a signal based on the received x-rays fluoresced from the plurality of sample pills in the sample holder; and

determining the presence and amount of the one of more elements in the plurality of sample pills based on the signal and at least one calibration curve, the calibration curve being pre-determined based on a reference signal generated by the x-ray detector of by a plurality of reference pills having a known amount of the one or more elements to be detected.

11. The method of claim 10, wherein each element of one or more elements has a corresponding reference curve.

12. The method of claim 10, wherein the plurality of reference pills and the plurality of sample pills are substantially the same size and shape.

13. The method of claim 10, wherein the plurality of reference pills have a universal size and shape.

14. The method of claim 10, wherein the plurality of sample pills are commercial pills intended for digestion by an end user.

15. The method of claim 10, wherein the one or more elements include at least one of cadmium (Cd), lead (Pb), arsenic (As), cobalt (Co), vanadium (V), nickel (Ni) or mercury (Hg).

16. The method of claim 10, wherein the weight of the plurality of reference pills is substantially similar to the weight of the sample pills.

17. The method of claim 16, wherein the weight of the plurality of reference pills is substantially similar to the weight of the sample pills.

18. The method of claim 16, wherein the number of the plurality of reference pills is substantially similar to the number of the sample pills.

19. The method of claim 10, wherein the number of the plurality of reference pills is substantially similar to the number of the sample pills.

20. The method of claim 10, further comprising the steps of:

constructing the plurality of reference pills, wherein the plurality of reference pills having the known amount of the one or more elements to be detected;

placing the plurality of reference pills in a sample holder;

irradiating the plurality of reference pills in the sample holder with x-rays from an x-ray source;

receiving by a detector x-rays fluoresced from the plurality of reference pills in the sample holder;

outputting by the detector the reference signal based on the received x-rays fluoresced from the plurality of reference pills in the sample holder; and

generating at least one calibration curve, the calibration curve being pre-determined based on a reference signal generated by the x-ray detector of by a plurality of reference pills.

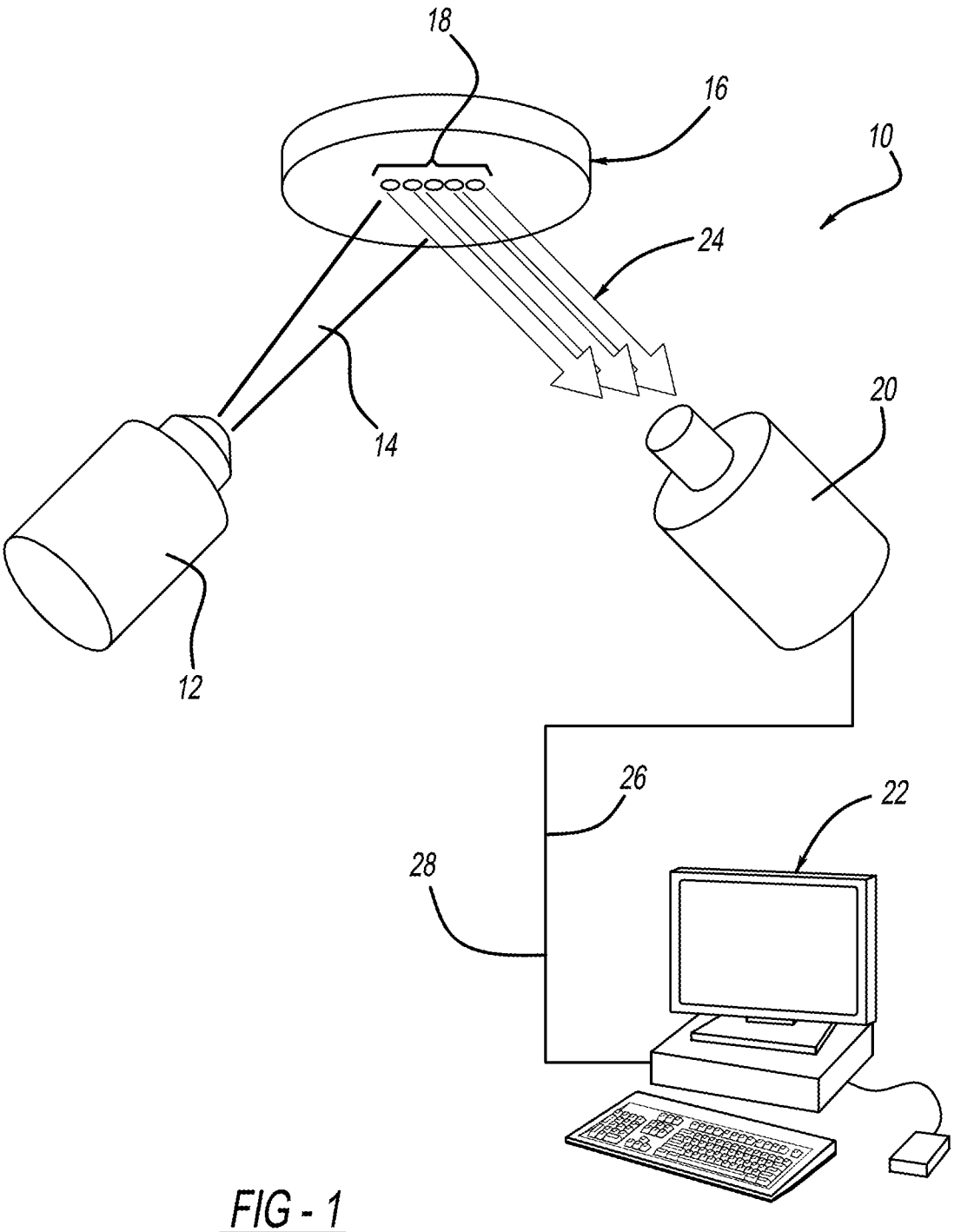


FIG - 1

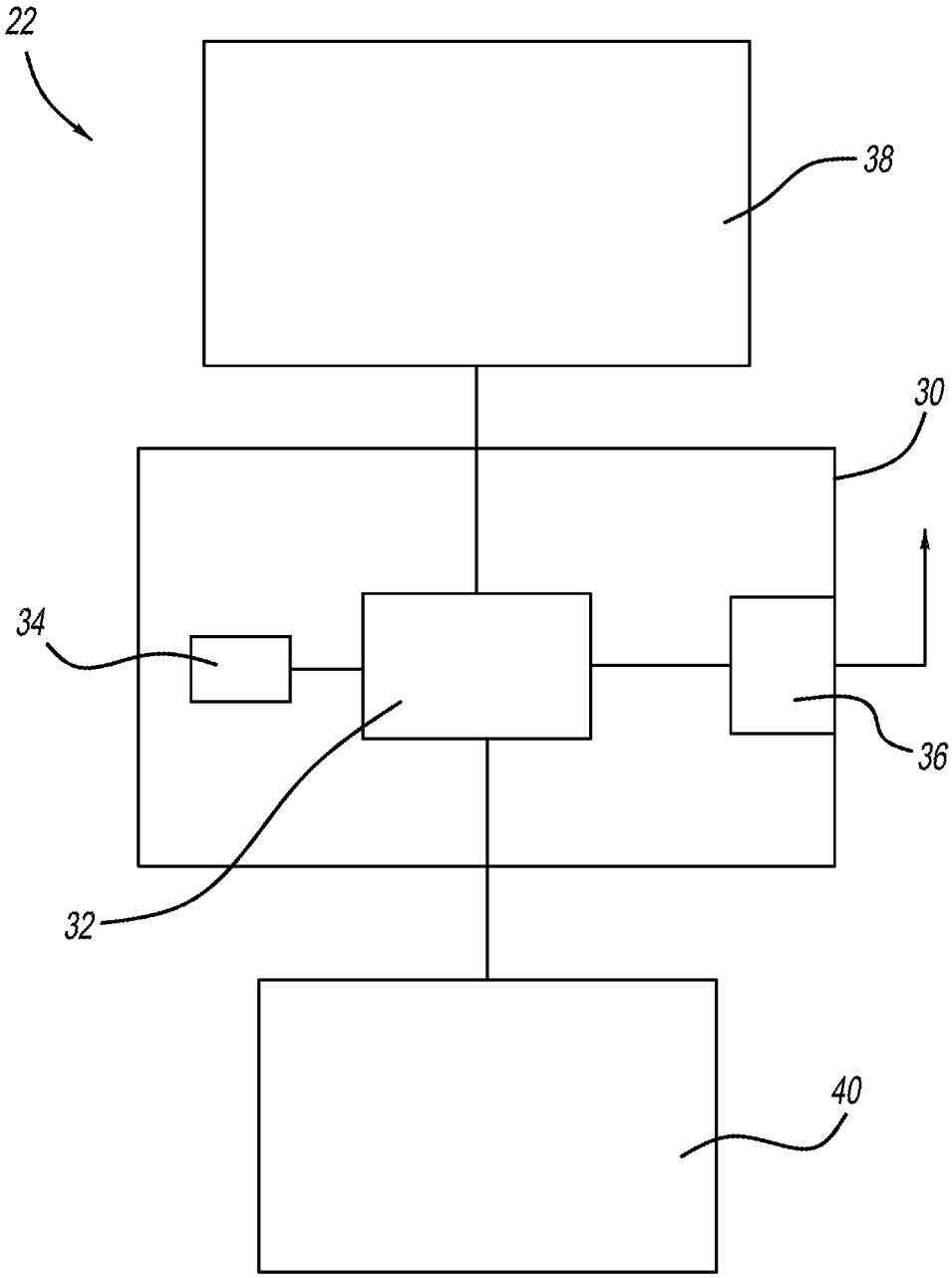


FIG - 2

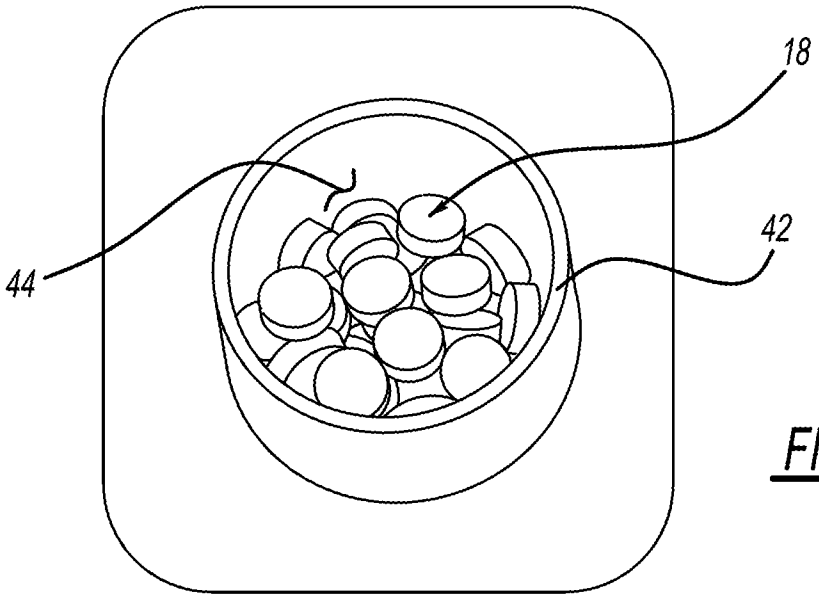


FIG - 3

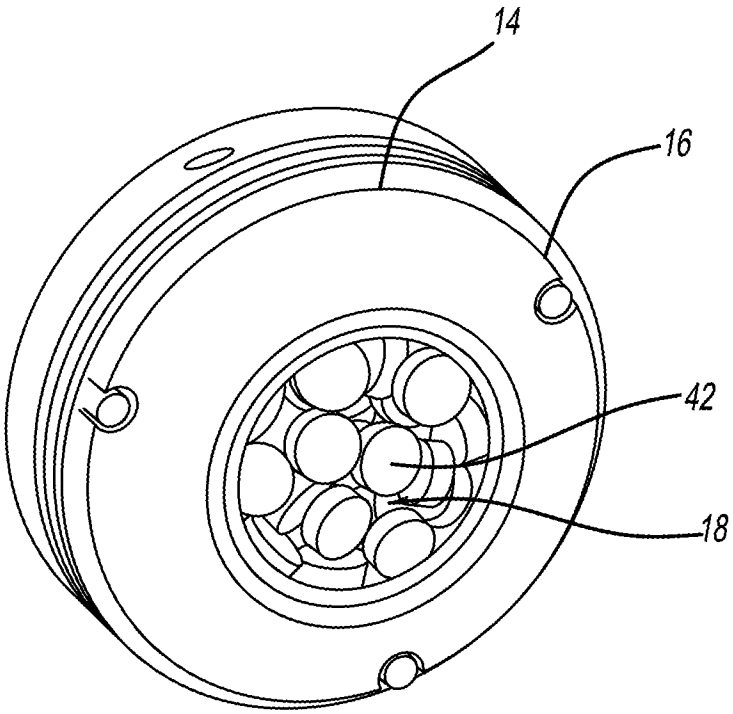
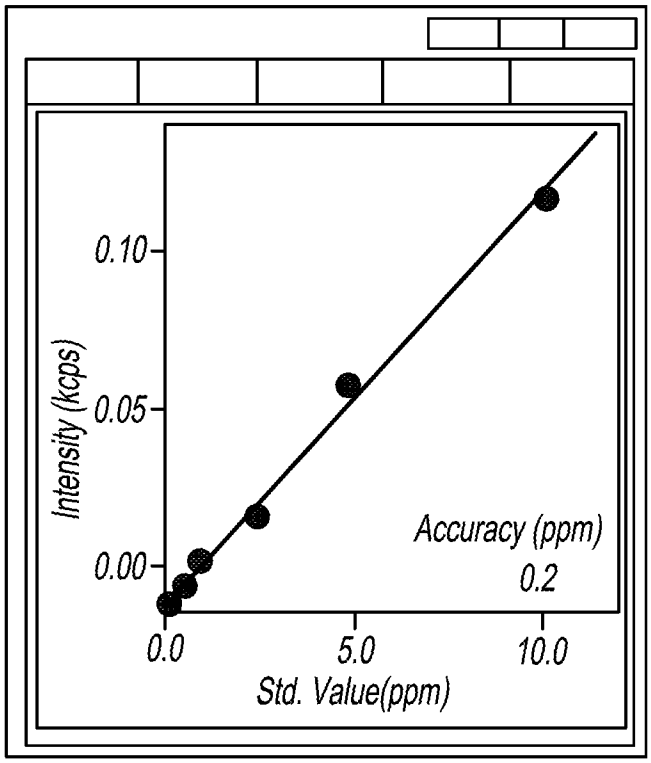


FIG - 4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Accuracy (ppm)
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0.0
5.0
10.0
Std. Value(ppm)
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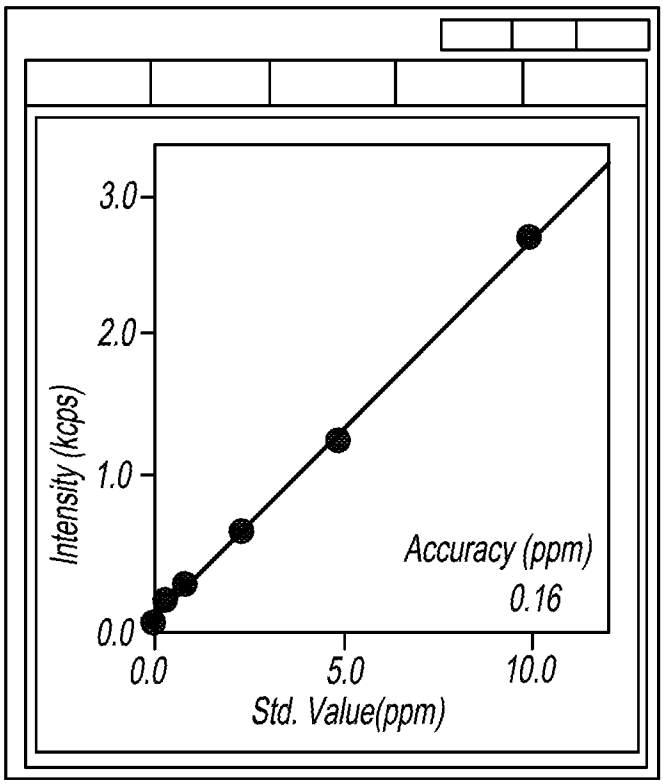
FIG - 5A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0.0
5.0
10.0
Std. Value(ppm)
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FIG - 5B

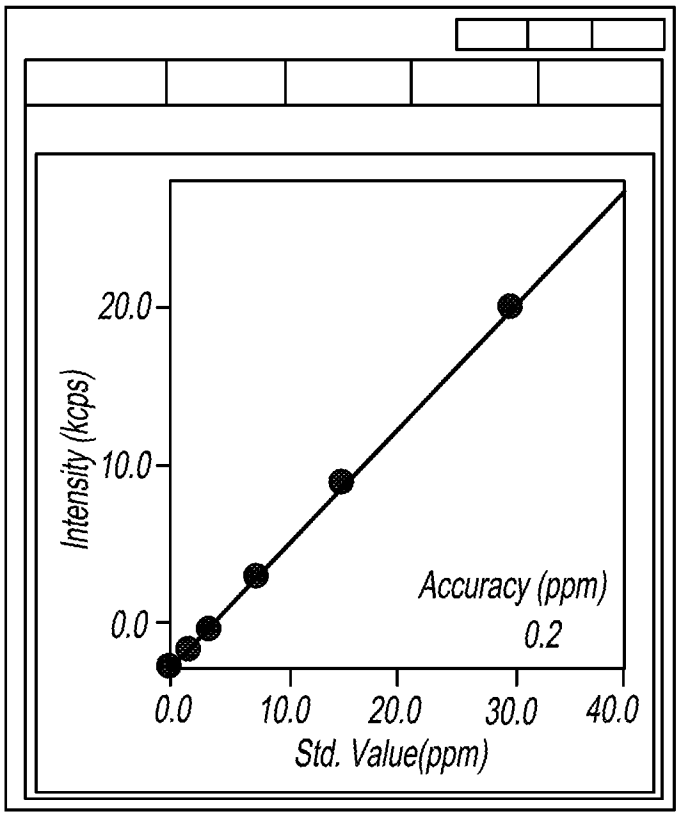

FIG - 5C

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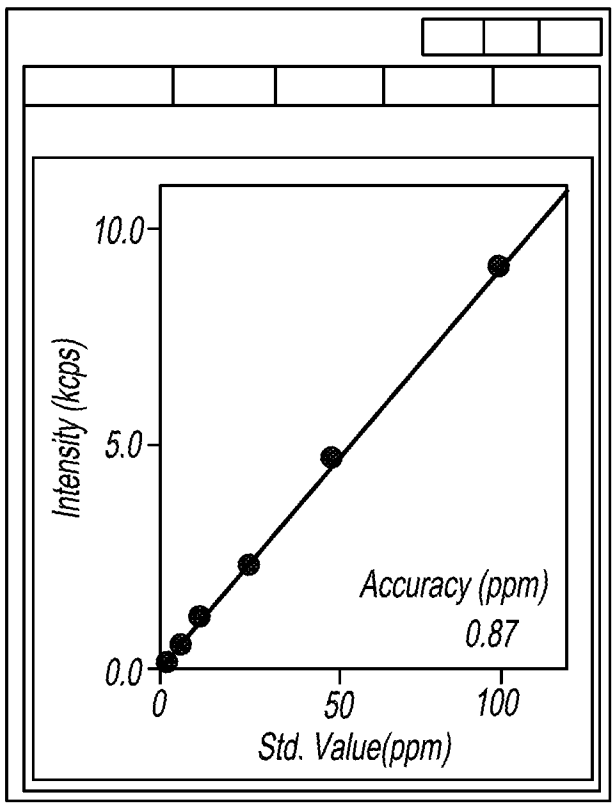

FIG - 5D

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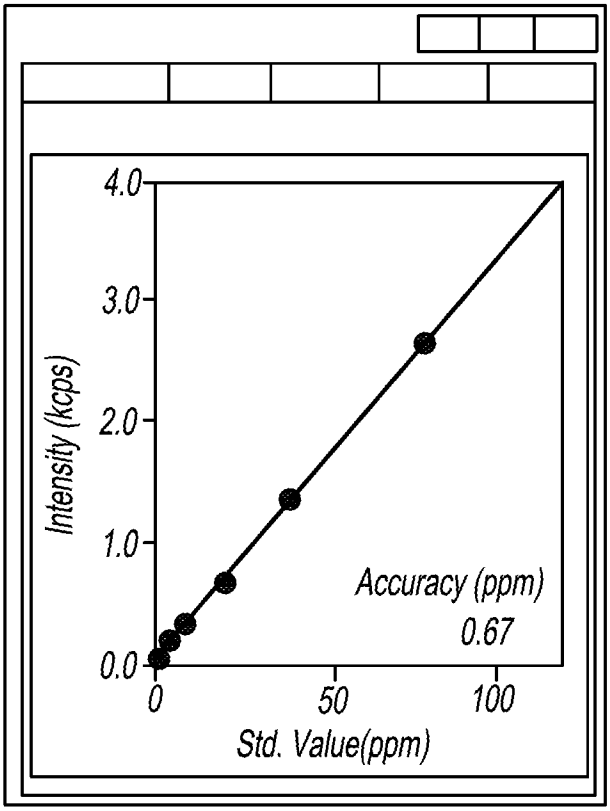

FIG - 5E

56

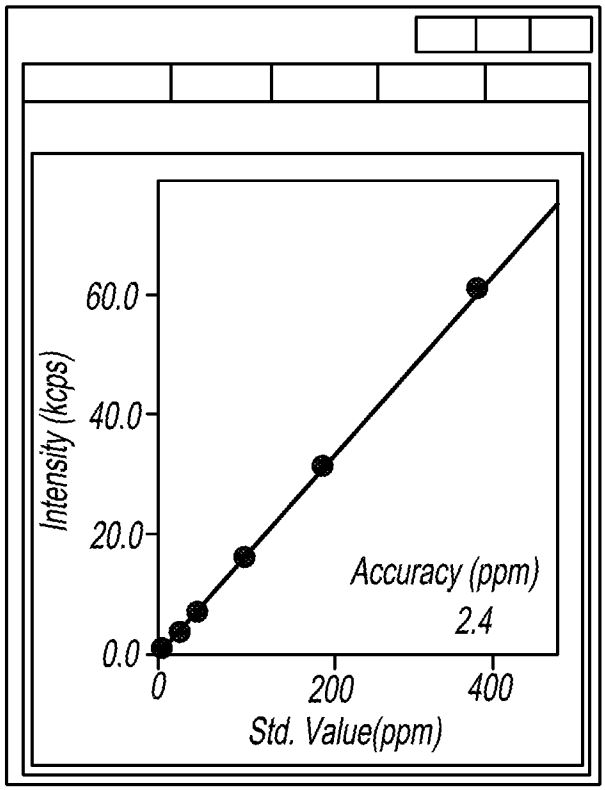

FIG - 5F

58

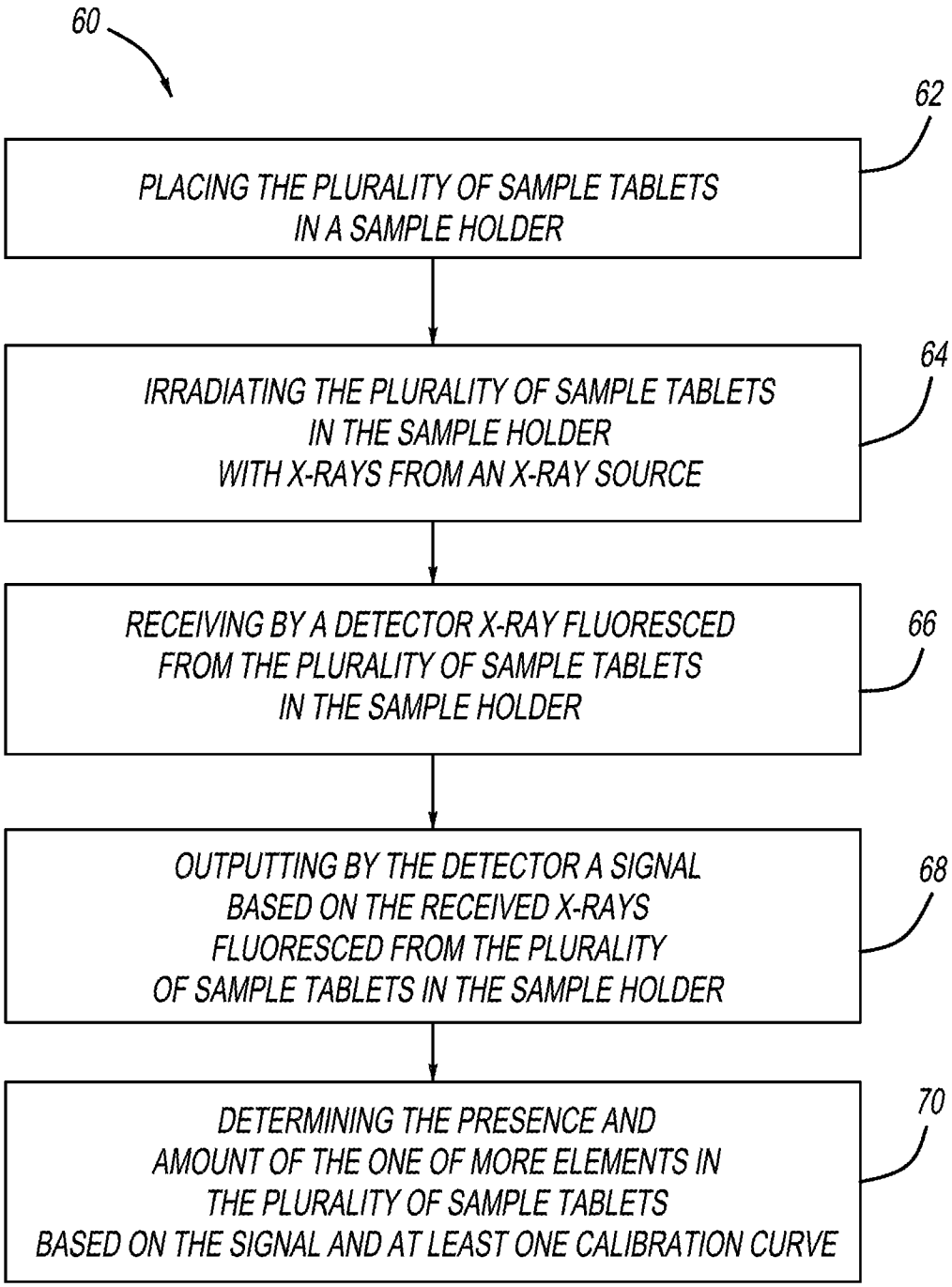
60
62
PLACING THE PLURALITY OF SAMPLE TABLETS IN A SAMPLE HOLDER
64
IRRADIATING THE PLURALITY OF SAMPLE TABLETS IN THE SAMPLE HOLDER WITH X-RAYS FROM AN X-RAY SOURCE
66
RECEIVING BY A DETECTOR X-RAY FLUORESCED FROM THE PLURALITY OF SAMPLE TABLETS IN THE SAMPLE HOLDER
68
OUTPUTTING BY THE DETECTOR A SIGNAL BASED ON THE RECEIVED X-RAYS FLUORESCED FROM THE PLURALITY OF SAMPLE TABLETS IN THE SAMPLE HOLDER
70
DETERMINING THE PRESENCE AND AMOUNT OF THE ONE OF MORE ELEMENTS IN THE PLURALITY OF SAMPLE TABLETS BASED ON THE SIGNAL AND AT LEAST ONE CALIBRATION CURVE

FIG - 6

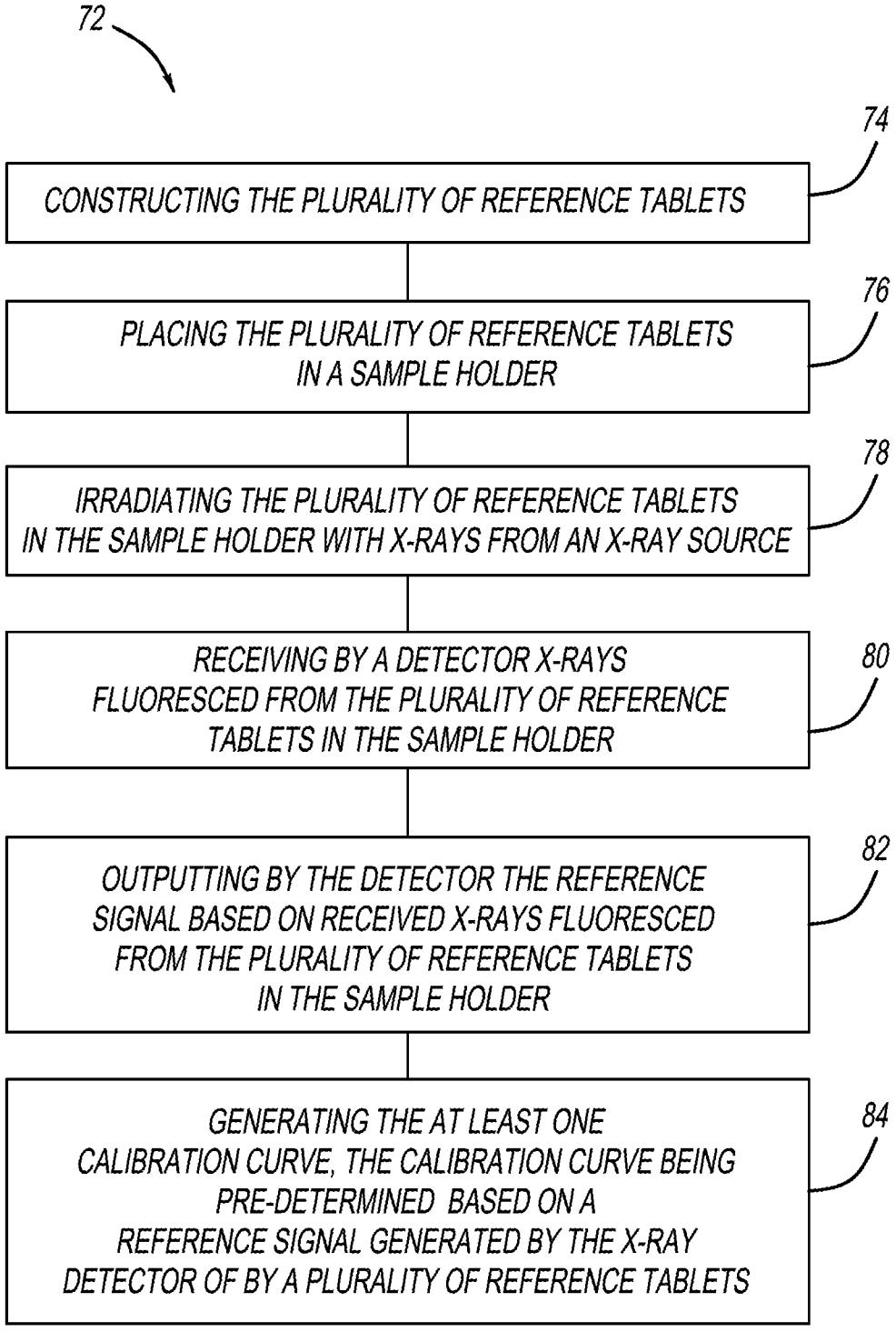
72
74
CONSTRUCTING THE PLURALITY OF REFERENCE TABLETS
76
PLACING THE PLURALITY OF REFERENCE TABLETS IN A SAMPLE HOLDER
78
IRRADIATING THE PLURALITY OF REFERENCE TABLETS IN THE SAMPLE HOLDER WITH X-RAYS FROM AN X-RAY SOURCE
80
RECEIVING BY A DETECTOR X-RAYS FLUORESCED FROM THE PLURALITY OF REFERENCE TABLETS IN THE SAMPLE HOLDER
82
OUTPUTTING BY THE DETECTOR THE REFERENCE SIGNAL BASED ON RECEIVED X-RAYS FLUORESCED FROM THE PLURALITY OF REFERENCE TABLETS IN THE SAMPLE HOLDER
84
GENERATING THE AT LEAST ONE CALIBRATION CURVE, THE CALIBRATION CURVE BEING PRE-DETERMINED BASED ON A REFERENCE SIGNAL GENERATED BY THE X-RAY DETECTOR OF BY A PLURALITY OF REFERENCE TABLETS

FIG - 7

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US17/25710

A. CLASSIFICATION OF SUBJECT MATTER
IPC - G01N 23/223, G01J 3/443; G01T 1/28 (2017.01)
CPC - G01N 23/223, 23/2076

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
See Search History document

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
See Search History document

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
See Search History document

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 2011/0103547 A1 (OHZAWA, S) May 5, 2011; figure 1; paragraphs [0016-0017], [0033], [0034]	1-20
A	CN 104374790 A (SHANGHAI JIAOTONG UNIVERSITY) February 25, 2015; see machine translation; paragraphs [0034], [0035], [0071]; claim 1, 2, 3, 8	1-20
A	US 2014/0050299 A1 (RUNFT, W et al.) February 20, 2014; figures 1, 2; paragraphs [0031-0032], [0037]	1-20
A	US 2012/0330684 A1 (JACOBS, A et al.) December 27, 2012; figures 1, 5A-5D; paragraph [0027], [0059-0060], [0068]; claim 46	1-20
P, Y	US 2017/0038319 A1 (UHV TECHNOLOGIES, INC) February 9, 2017; entire document	1-20

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:
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"O" document referring to an oral disclosure, use, exhibition or other means
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"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
15 July 2017 (15.07.2017)	11 AUG 2017
Name and mailing address of the ISA/ Mail Stop PCT, Attn: ISA/US, Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-8300	Authorized officer Shane Thomas PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774

Form PCT/ISA/210 (second sheet) (January 2015)