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March 27, 2018

VIA HAND DELIVERY

The Honorable Lisa Barton
Secretary
U.S. INTERNATIONAL TRADE COMMISSION
500 E Street, S.W., Room 112
Washington, D.C. 20436

Re: In the Matter of Certain Strontium-Rubidium Radioisotope Infusion Systems, and Components Thereof Including Generators
U.S. ITC Inv. No. 337-TA-

Dear Secretary Barton,

Enclosed for filing on behalf of Complainant Bracco Diagnostics Inc. ("Bracco" or "Complainant") against the proposed Respondents Jubilant DraxImage Inc., Jubilant Pharma Limited, and Jubilant Life Sciences (collectively, the "Proposed Respondents") are documents in support of Bracco's request that the Commission commence an investigation pursuant to Section 337 of the Tariff Act of 1930, as amended. A request for confidential treatment of Confidential Exhibit 22 and the Complaint is included with this letter.

Accordingly, Complainant submits the following documents for filing:

1. An original and eight (8) paper copies of the verified Non-Confidential Complaint and the Public Interest Statement. (19 CFR § § 210.8(a)(1)(i), 210.8(b).)

2. An original and eight (8) paper copies of the verified Confidential Complaint and the Public Interest Statement. (19 CFR § § 210.8(a)(1)(i), 210.8(b).)

3. One (1) copy, on CD of the accompanying Non-Confidential exhibits 1-21 and 23-28 and public version of Confidential Exhibit 22. (19 CFR §210.8(a)(1)(i).)

4. One (1) copy, on CD with Confidential Exhibit 22. (19 CFR §§ 201.6(c).)

5. One (1) copy, on CD of Physical Exhibit 1. (19 CFR §210.8(a)(1)(i).)

6. Six (6) additional copies of the verified Non-Confidential Complaint and the Public Interest Statement and three (3) CDs of the Non-Confidential exhibits, one (1) of each for service upon each of the Proposed Respondents. (19 CFR §§ 210.8(a)(1)(iii) and 210.11(a).)

7. Three (3) CDs of Confidential Exhibit 22, one (1) of each for service upon each of the Proposed Respondents. (19 CFR §§ 210.8(a)(1)(iii) and 210.11(a).)

8. Three (3) CDs of Physical Exhibit 1, one (1) of each for service upon each of the Proposed Respondents. (19 CFR §§ 210.8(a)(1)(iii) and 210.11(a).)

9. Certified copies of United States Patent Nos. 9,814,826 ("the '826 Patent"); 9,750,869 ("the '869 Patent"); and 9,750,870 ("the '870 Patent), included in the Complaint as Exhibits, 1, 3, and 5. (19 CFR §§ 210.8(a)(1)(iii) and 210.12(a)(9)(i).)

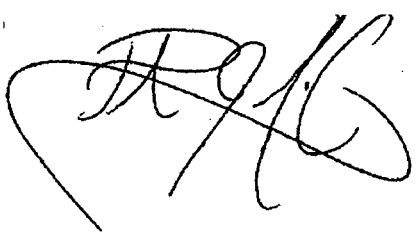
10. Certified copies of the assignments for the '826, '869, and '870 patents included in the Complaint as Exhibits 2, 4, and 6. (19 CFR §§ 210.8(a)(1)(iii) and 210.12(a)(9)(ii).)

11. Certified copies of the prosecution histories of the '826, '869, and '870 patents, included in the Complaint as Appendices 1, 3, and 5, and three (3) additional copies of each on separate CDs. (19 CFR §210.12(c)(1)).

12. Four (4) copies on separate CDs of patent and technical reference documents identified in the each of the prosecution histories of the '826, '869, and '870 patents, included in the Complaint as Appendices 2, 4, and 6. (19 CFR §210.12(c)(2)).

Thank you for your attention to this matter. Please contact me if you have any questions.

Respectfully submitted,



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Re: In the Matter of Certain Strontium-Rubidium Radioisotope Infusion Systems, and Components Thereof Including Generators
U.S. ITC Inv. No. 337-TA-

Dear Secretary Barton,

In accordance with Commission Rules 201.6 and 210.5, Complainant Bracco Diagnostics Inc. ("Bracco") requests confidential treatment of the business information contained in the Complaint and Confidential Exhibit 22.

The information for which confidential treatment is sought is proprietary commercial information not otherwise publicly available. Specifically, these exhibits contain proprietary commercial information concerning Bracco's business records, trade secrets, processes, sales, licenses, expenditures and/or other information of commercial value.

The information described above qualifies as confidential business information pursuant to Commission Rule 201.6(a) because:

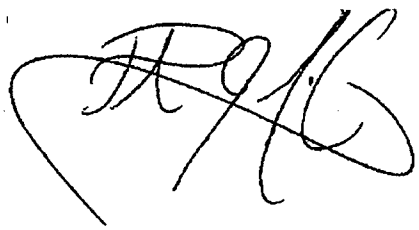
1. It is not available to the public;

2. unauthorized disclosure of such information could cause substantial harm to the competitive position of Bracco and/or a third party;

3. Its disclosure could impair the Commission's ability to obtain information necessary to perform its statutory function.

If you have any questions, please do not hesitate to contact me at (202) 533-2386.

Sincerely,



Patrick J. McCarthy

UNITED STATES INTERNATIONAL TRADE COMMISSION
WASHINGTON, D.C.

In the Matter of	
CERTAIN STRONTIUM-RUBIDIUM RADIOISOTOPE INFUSION SYSTEMS, AND COMPONENTS THEREOF INCLUDING GENERATORS	Investigation No. 337-TA-____

STATEMENT REGARDING THE PUBLIC INTEREST

Complainant Bracco Diagnostics Inc. ("Bracco" or "Complainant") submits this public-interest statement pursuant to Commission Rule 210.8(b), 19 C.F.R. § 210.8(b). As discussed below, the remedies sought against Jubilant DraxImage Inc., Jubilant Pharma Limited, and Jubilant Life Sciences (collectively, the "Proposed Respondents" or "Jubilant") will not have an adverse effect on public health and welfare in the United States, competitive conditions in the United States economy, the production of competitive articles in the United States, or U.S. consumers.

The products at issue in this Investigation are strontium-rubidium radioisotope infusion systems and component thereof that infringe one or more claims of the Asserted Patents: U.S. Patent No. 9,814,826 ("the '826 patent"); U.S. Patent No. 9,750,869 ("the '869 patent"); and U.S. Patent No. 9,750,870 ("the '870 patent"). Bracco seeks a limited exclusion order barring from entry into the United States all infringing strontium-rubidium radioisotope infusion systems and components thereof sold for importation, imported, or sold within the United States after importation by the Proposed Respondents. Bracco also seeks a cease and desist order prohibiting the Proposed Respondents from engaging in the unlawful sale for importation into the United

States, importation into the United States, and/or the sale within the United States after importation of infringing strontium-rubidium radioisotope infusion systems and components thereof. These requested remedies do not and will not adversely affect the public interest.

I. HOW THE ARTICLES SUBJECT TO THE PROPOSED REMEDIAL ORDERS ARE USED IN THE UNITED STATES

The Accused Product is a strontium-rubidium radioisotope infusion system, including rubidium generator, sold under the tradename Ruby-Fill®. Ruby-Fill® and/or components thereof are imported into the United States and/or sold in the United States after importation, at least, by the Proposed Respondents. The Ruby-Fill® system is used in the medical field to produce rubidium Rb 82 chloride injection for intravenous administration. Rubidium Rb 82 chloride injection is indicated by the U.S. Food and Drug Administration ("FDA") for Positron Emission Tomography ("PET") imaging of the myocardium under rest or pharmacologic stress conditions to evaluate regional myocardial perfusion in adult patients with suspected or existing coronary artery disease. The resulting images allow a physician to evaluate the blood flow (perfusion) through the coronary arteries to the heart muscle, and thus diagnose whether any heart disease exists.

II. IDENTIFY AND PUBLIC HEALTH, SAFETY, OR WELFARE CONCERNS RELATING TO THE REQUESTED REMEDIAL ORDERS

The ITC has made clear that the public interest rests in the protection of intellectual property rights.[1] The question with respect to public interest, then, is not whether a "balancing" of factors merely favors a remedy, but rather whether competing interests exist of so great a significance with regard to only the Accused Products that the strong public policy of protecting

[1] *See, e.g., Certain Digital Television Prods. & Certain Prods. Containing Same & Methods of Using Same*, Inv. No. 337-TA-617, Comm'n Op., at 9 (Aug. 23, 2009) ("*Digital TV Products*").

intellectual property rights must give way. As shown below, any public interest concerns invoked by this Investigation pales in comparison to this countervailing interest.

Issuance of the requested relief, a limited exclusion order and/or a cease and desist order will have no adverse effect on the public health, safety or welfare in the United States. Bracco's CardioGen-82® is the first FDA-approved radioimaging agent dedicated to cardiac PET, and is available today for patients in need of cardiac PET exams, including patients in the United States. Proposed Respondents submitted an abbreviated new drug application ("ANDA") to the U.S. Food and Drug Administration on June 18, 2010 to market a system Proposed Respondents described as the ***equivalent*** of Bracco's CardioGen-82®. Due to variations in administration rates, the FDA reclassified the ANDA application as a 505(b)(2) NDA application. However, Proposed Respondents still stated that since "both generators are systems for the production of rubidium 82, ***equal utility is expected*** from Ruby-Fill." Thus, an alternative system, which Proposed Respondents represented to the FDA is ***equivalent*** to the Ruby-Fill® system, is readily available to the public.

III. IDENTIFY LIKE OR DIRECTLY COMPETITIVE ARTICLES THAT COMPLAINANTS, THEIR LICENSEES, OR THIRD PARTIES MAKE WHICH COULD REPLACE THE SUBJECT ARTICLE IF THEY WERE TO BE EXCLUDED

As set out in the Complaint, Bracco manufactures CardioGen-82® which is like or directly competitive with the Ruby-Fill® system and could seamlessly replace it. Thus, any U.S. consumer with a desire to purchase or use a strontium-rubidium radioisotope infusion system can purchase or use the existing CardioGen-82® immediately. Proposed Respondents have a relatively small portion of the U.S. market for strontium-rubidium radioisotope infusion systems. Accordingly, Bracco would easily be able to fill the demand gap, if any, felt by the requested remedies.

IV. IDENTIFY WHETHER COMPLAINANTS, COMPLAINANTS' LICENSEES, AND/OR THIRD PARTY SUPPLIERS HAVE THE CAPACITY TO REPLACE THE VOLUME OF ARTICLES SUBJECT TO THE REQUESTED REMEDIAL ORDERS IN A COMMERCIALLY REASONABLE TIME

There is no question that Bracco has the capacity to replace the volume of Accused Products subject to the requested remedial orders within a commercially reasonable time. As stated above, Proposed Respondents have a relatively low market share. Thus, there is no indication that excluding the Accused Products will harm the public interest via unmet demand.

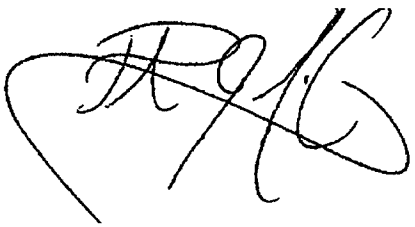
V. STATE HOW THE REQUESTED REMEDIAL ORDER WOULD IMPACT CONSUMERS

As discussed above, even after the requested remedy is issued, customers may purchase and consumers will have access to strontium-rubidium radioisotope infusion systems, namely CardioGen-82®. Proposed Respondents represented to the FDA that the Accused Product (Ruby-Fill®) is ***equivalent*** to CardioGen-82®. Accordingly, the issuance of such relief will have no relevant public interest impact on U.S. consumers.

For the foregoing reasons, no public-interest concerns preclude the issuance of the proposed remedies against the Proposed Respondents in this matter.

Dated: March 27, 2018

By:



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Attorneys for Complainant

UNITED STATES INTERNATIONAL TRADE COMMISSION
WASHINGTON, D.C.

In the Matter of	
CERTAIN STRONTIUM-RUBIDIUM RADIOISOTOPE INFUSION SYSTEMS, AND COMPONENTS THEREOF INCLUDING GENERATORS	Investigation No. 337-TA-____

COMPLAINT UNDER SECTION 337 OF THE TARRIF ACT OF 1930, AS AMENDED

COMPLAINANT:
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PROPOSED RESPONDENTS:
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Kirkland, Québec, Canada
H9H 4J4

Jubilant Pharma Limited
6 Temasek Boulevard, #20-06 Suntec City
Tower Four,
Singapore 038986

Jubilant Life Sciences
Plot 1-A Sector 16-A Institutional Area
Noida, Uttar Pradesh, 201301 India

TABLE OF CONTENTS

EXHIBIT LIST

Exhibit Number	Description
Exhibit No. 1	Certified Copy of U.S. Patent No. 9,814,826
Exhibit No. 2	Certified Copy of the assignment for U.S. Patent No. 9,814,826
Exhibit No. 3	Certified Copy of U.S. Patent No. 9,750,869
Exhibit No. 4	Certified Copy of the assignment for U.S. Patent No. 9,750,869
Exhibit No. 5	Certified Copy of U.S. Patent No. 9,750,870
Exhibit No. 6	Certified Copy of the assignment for U.S. Patent No. 9,750,870
Exhibit No. 7	Westlaw Company Investigator Report for Jubilant DraxImage Inc.
Exhibit No. 8	Westlaw Company Investigator Report for Jubilant Pharma Limited
Exhibit No. 9	Jubilant DraxImage website
Exhibit No. 10	Jubilant DraxImage Oct. 3, 2016 press release
Exhibit No. 11	May 28, 2005 Bracco Press Release
Exhibit No. 12	Prescribing Information for Ruby-Fill®
Exhibit No. 13	January 18, 2018 Earnings Call summary by Prabhudas Lilladher
Exhibit No. 14	ASNC 2017 Final Program
Exhibit No. 15	List of Foreign Counterparts to the Asserted Patents
Exhibit No. 16	Mo-99 2017 Technical Program, Sept. 10-13, 2017
Exhibit No. 17	Claim Chart showing infringement of U.S. Patent No. 9,814,826
Exhibit No. 18	Claim Chart showing infringement of U.S. Patent No. 9,750,869
Exhibit No. 19	Claim Chart showing infringement of U.S. Patent No. 9,750,870
Exhibit No. 20	FDA Approval Package for Application No. 202153
Exhibit No. 21	Ruby-Fill® User Manual
Exhibit No. 22	Declaration of Ken Troger (**Confidential**)
Exhibit No. 23	Domestic Industry chart regarding U.S. Patent No. 9,814,826
Exhibit No. 24	Domestic Industry chart regarding U.S. Patent No. 9,750,869
Exhibit No. 25	Domestic Industry chart regarding U.S. Patent No. 9,750,870
Exhibit No. 26	INTENTIONALLY LEFT BLANK
Exhibit No. 27	INTENTIONALLY LEFT BLANK
Exhibit No. 28	Westlaw Company Investigator Report for Jubilant Life Sciences

PHYSICAL EXHIBIT LIST

Physical Exhibit Number	Description
Physical Exhibit No. 1	Ruby-Fill® video file, previously available at http://www.draximage.com/

APPENDICES

Appendix Number	Description
Appendix No. 1	Certified copy of Prosecution History of U.S. Patent No. 9,814,826
Appendix No. 2	Cited references for Prosecution History of U.S. Patent No. 9,814,826
Appendix No. 3	Certified copy of Prosecution History of U.S. Patent No. 9,750,869
Appendix No. 4	Cited references for Prosecution History of U.S. Patent No. 9,750,869
Appendix No. 5	Certified copy of Prosecution History of U.S. Patent No. 9,750,870
Appendix No. 6	Cited references for Prosecution History of U.S. Patent No. 9,750,870

I. Introduction

1. This Complaint is filed by Bracco Diagnostics Inc. ("Bracco" or "Complainant"), pursuant to Section 337 of the Tariff Act of 1930, as amended, 19 U.S.C. § 1337 ("Section 1337"), against the proposed Respondents Jubilant DraxImage Inc., Jubilant Pharma Limited, and Jubilant Life Sciences (collectively, the "Proposed Respondents" or "Jubilant"). Bracco respectfully requests that the United States International Trade Commission (the "Commission") institute an investigation relating to the unlawful sale for importation into the United States, importation into the United States, and/or the sale within the United States after importation of certain strontium-rubidium radioisotope infusion systems and/or components thereof, including but not limited to rubidium-82 generators.

2. The Proposed Respondents have engaged in unfair acts in violation of Section 337(a)(1)(B) through and in connection with the unlicensed importation into the United States, sale for importation, and/or sale within the United States after importation of the Proposed Respondent's strontium-rubidium radioisotope infusion systems and components thereof, that infringe one or more of the following U.S. patents owned by Bracco (collectively, "the Asserted Patents"): 9,814,826 ("the '826 patent") (**Exhibit No. 1**).; 9,750,869 ("the '869 patent") (**Exhibit No. 3**); and 9,750,870 ("the '870 patent") (**Exhibit No. 5**). The non-exclusive list of claims that the Proposed Respondents infringe, and/or induce or contribute to the infringement of is as follows:

Infringing Product	Asserted Claims of the '826 Patent	Asserted Claims of the '869 Patent	Asserted Claims of the '870 Patents
Ruby-Fill®	1, 2, 3, 5, 9, 10, 11, 12, 13, 14, 17, 18, 19, 26, and 28	1, 2, 3, 4, 5, 8, 14, 24, 27, 28, 29, and 30	1, 2, 8, 9, 10, 11, 12, 13, 16, 17, 22, and 27

3. The Proposed Respondents have violated and continue to violate Section 337 to the detriment of the domestic industry of Bracco that exists or is in the process of being established in the United States relating to the Asserted Patents.

4. To remedy the Proposed Respondents' continuing and unlawful violation of Section 337, Bracco hereby states pursuant to Commission Rule 210.12(a)(11) that it seeks, as permanent relief, a limited exclusion order, pursuant to 19 U.S.C. § 1337(d), barring from entry into the United States all infringing strontium-rubidium radioisotope infusion systems and components thereof sold for importation, imported, or sold within the United States after importation by the Proposed Respondents. Bracco also seeks cease and desist orders, pursuant to 19 U.S.C. § 1337(f), prohibiting the Proposed Respondents from engaging in the unlawful sale for importation into the United States, importation into the United States, and/or the sale within the United States after importation of infringing strontium-rubidium radioisotope infusion systems and components thereof that infringe, induce or contribute to the infringement of one or more claims of the Asserted Patents. Further, Bracco requests that the Commission impose a bond upon Proposed Respondents' importation of infringing strontium-rubidium radioisotope infusion systems and components thereof during the 60-day Presidential review period, pursuant to 19 U.S.C. § 1337(j), to prevent further injury to the domestic industry that exists or is in the process of being established in the United States relating to the Asserted Patents.

A. Complainant

5. Bracco Diagnostics Inc. is a corporation organized and existing under the laws of the State of Delaware, with a principal place of business at 259 Prospect Plains Road, Monroe Township, New Jersey 08831.

6. Bracco Diagnostics Inc., the U.S.-based subsidiary of Bracco Imaging SpA, was established in 1994 and has since become a leader in the U.S. in innovative contrast imaging agents. Bracco Diagnostics Inc., with headquarters and research offices in Monroe Township, New Jersey, offers a product and solution portfolio for all key diagnostic imaging modalities: X-Ray Imaging (including Computed Tomography, Interventional Radiology, and Cardiac Catheterization), Magnetic Resonance Imaging (MRI), Contrast Enhanced Ultrasound (CEUS), and Nuclear Medicine through radioactive tracers.

7. Bracco Diagnostics Inc. is committed to the discovery, development, manufacturing and marketing of imaging agents and solutions aimed at providing quality solutions in terms of diagnostic efficacy, patient safety and cost effectiveness.

8. Bracco's innovative and impressive product portfolio includes Bracco's nuclear medicine and radiopharmaceuticals, such as strontium-rubidium radioisotope infusion systems and rubidium-82 generators that are used with such systems. Bracco's strontium-rubidium radioisotope infusion system is sold under the trade name CardioGen-82®.

9. CardioGen-82® is a closed system used to produce rubidium Rb 82 chloride injection for intravenous administration. Rubidium Rb 82 chloride injection is indicated by the U.S. Food and Drug Administration ("FDA") for Positron Emission Tomography ("PET") imaging of the myocardium under rest or pharmacologic stress conditions to evaluate regional myocardial perfusion in adult patients with suspected or existing coronary artery disease. The resulting images allow a physician to evaluate the blood flow (perfusion) through the coronary arteries to the heart muscle, and thus diagnose whether any heart disease exists.

10. PET is an imaging technique that uses small amounts of a radioactive tracer to help in the diagnosis of heart disease. The tracer is introduced into the body, by IV injection

directly from a small and portable generator (*e.g.*, CardioGen-82®), and a PET scanner is used to produce an image showing the distribution of the tracer in the heart.

11. In 1989, Bracco's CardioGen-82® became the first FDA-approved radioimaging agent dedicated to cardiac PET, and it is available today for patients in need of cardiac PET exams, including patients in the United States.

12. As a pioneer in the field of cardiac PET imaging, Bracco has enjoyed tremendous success based on its innovative strontium-rubidium radioisotope infusion system. Bracco's initial and continued success is based on extensive domestic research and development efforts.

B. Proposed Respondents

13. Jubilant DraxImage Inc. is a corporation organized and existing under the laws of Canada with its principal place of business at 16751 TransCanada Highway Kirkland, Québec, Canada H9H 4J4.[1] ***See*** **Exhibit No. 7.**

14. Jubilant DraxImage Inc. received FDA approval for Ruby-Fill® rubidium-82 generator and elution system on September 30, 2016. ***See*** **Exhibit No. 20.**

15. Jubilant Pharma Limited is a corporation organized and existing under the laws of Singapore with its principal of place of business at 6 Temasek Boulevard, #20-06 Suntec City Tower Four, Singapore 038986. ***See*** **Exhibit No. 8.**

16. Jubilant Life Sciences is a corporation existing under the laws of India with its principal place of business at Plot 1-A Sector 16-A Institutional Area Noida, Uttar Pradesh, 201301 India. ***See*** **Exhibit No. 28.**

17. Jubilant DraxImage Inc. is a subsidiary of Jubilant Pharma Limited. *See* **Exhibit No. 9.**

[1] http://www.draximage.com/

18. Jubilant Pharma Limited is a subsidiary of Jubilant Life Sciences.

19. Jubilant DraxImage Inc. is the manufacturer of the infringing strontium-rubidium radioisotope infusion system, which it sells under the tradename Ruby-Fill®. ***See, e.g.,*** **Exhibit Nos. 12 and 21**. Jubilant DraxImage Inc. also filed 505(b)(2) New Drug Application (NDA or 505(b)(2) NDA) to market and sell the infringing strontium-rubidium radioisotope infusion system (Ruby-Fill®) in the United States. **Exhibit No. 20**.

20. At least Jubilant Pharma Limited and Jubilant DraxImage Inc. actively participated in the development and regulatory approval process for the infringing strontium-rubidium radioisotope infusion system (Ruby-Fill®). **Exhibit No. 20** at 436-38, 449-50, 461-62, 473-74 (identifying employees from each company that participated in meetings with the FDA to discuss NDA No. 202153).

21. On October 3, 2016, after the 505(b)(2) NDA was approved by the FDA, Jubilant Pharma Limited's CEO (GP Singh) commented "***we*** are proud to bring to the US market" the Ruby-Fill® system. **Exhibit No. 10** (emphasis added).

22. In recent earnings calls, Jubilant Life Sciences stated that it had completed installation of Ruby-Fill® systems in the United States. **Exhibit No. 13**.

23. Thus, upon information and belief, Jubilant Pharma Limited, Jubilant Life Sciences, and Jubilant DraxImage Inc. direct the manufacture and development of the Ruby-Fill® system that is the subject of NDA No. 202153, and directly or indirectly, derive substantial revenue from the sale of the Ruby-Fill® system and its components thereof.

24. Furthermore, upon information and belief, Jubilant Pharma Limited, Jubilant Life Sciences, and Jubilant DraxImage Inc. are agents of each other and/or work in concert with each other with respect to the development, regulatory approval, marketing, sale, importation, and

distribution of the infringing strontium-rubidium radioisotope infusion system (Ruby-Fill®) and/or components thereof throughout the United States.

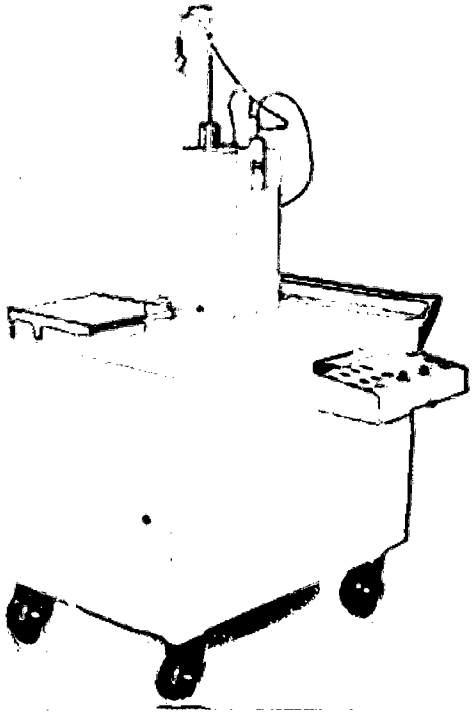
II. Technology and Products-At-Issue

A. Bracco's Products

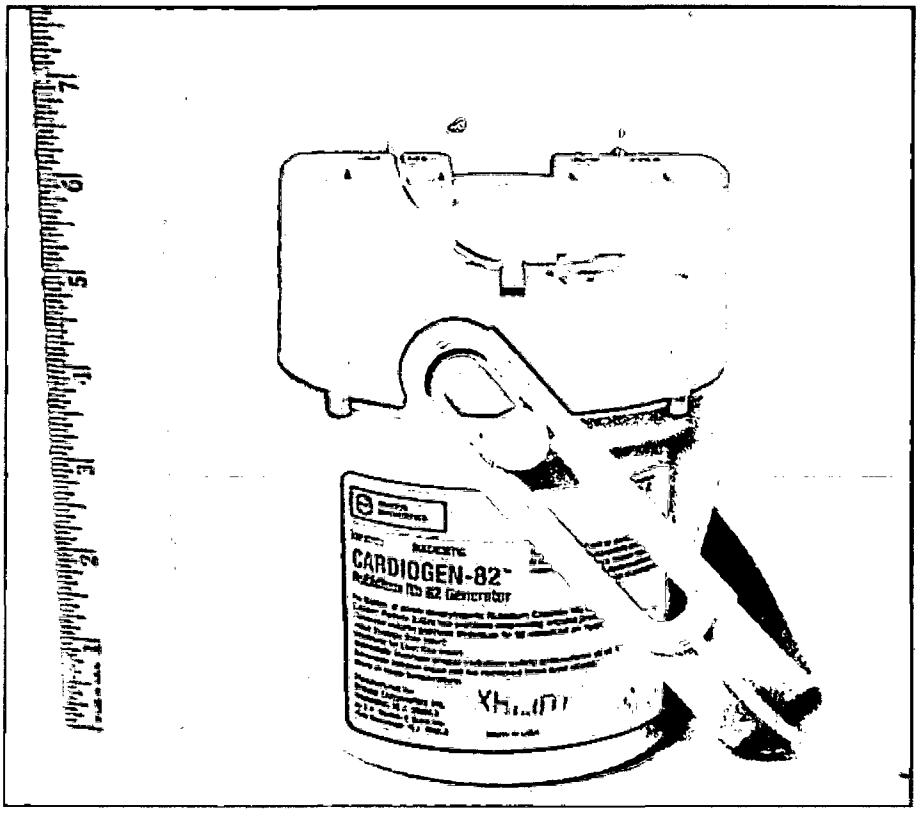
25. Heart disease is the number one killer of American men and women. Approximately 650,000 Americans die each year from heart disease related illness. Early detection is critical to effectively treat the disease. Tools for evaluating heart disease include treadmill evaluation, stress echocardiogram, perfusion imaging, coronary calcium screening, and coronary angiography.

26. As a pioneer in the strontium-rubidium radioisotope infusion systems market, Bracco is an industry leader for such devices. The existing CardioGen-82® system was the first FDA approved generator-based PET perfusion agent reimbursed for the evaluation of coronary artery disease. ***See*** **Exhibit No. 11.**

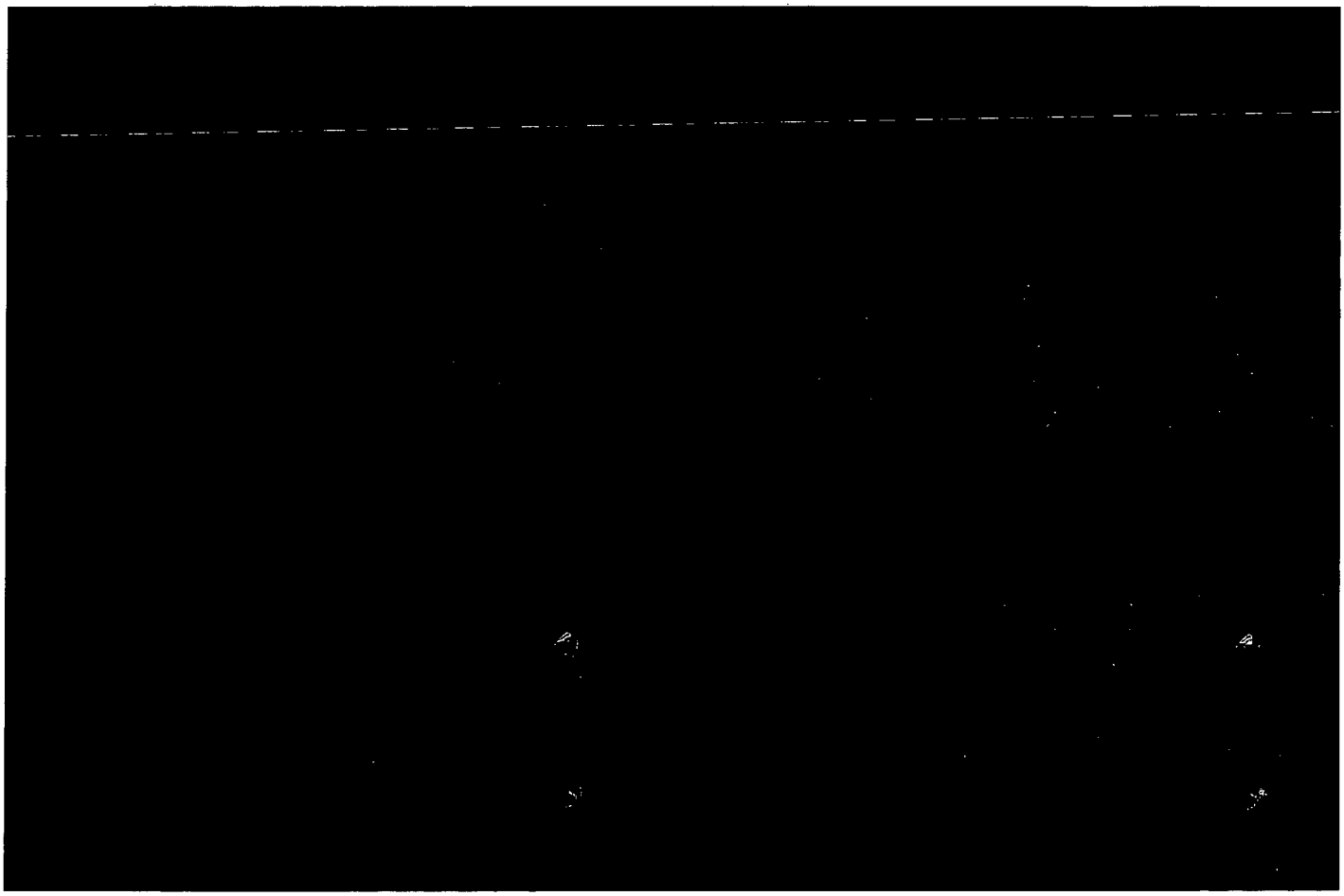
27. The existing CardioGen-82® system infuses a radioactive nuclear medicine agent, rubidium-82 which is produced from its precursor strontium-82, for the purpose of imaging the heart to determine if the heart's blood supply is normal or not. By way of example, the existing CardioGen-82® system can be seen below (the actual generator is housed underneath in lead shielding):



28. Contained inside this cart is the rubidium generator:



29. Continuing with its strong tradition of providing strontium-rubidium radioisotope infusion systems for the U.S. Market, Bracco has developed the next generation CardioGen-82® Infusion System, Model 1700 (hereinafter "Model 1700") for the U.S. Market.



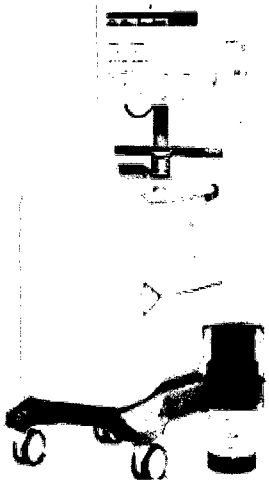
30. The development of the Model 1700 system [redacted] ***See*** **Confidential Exhibit No. 22.**

31. The Model 1700 system is and will be manufactured using Bracco's proprietary processes and equipment, and practices one or more claims of the Asserted Patents. Likewise,

the Model 1700 system and the use thereof also practices one or more of the Asserted Patents, as explained below.

B. Jubilant's Ruby-Fill Is Manufactured And/Or Imported by Jubilant.

32. Jubilant DraxImage Inc. manufactures and/or imports strontium-rubidium radioisotope infusion systems and/or components thereof, including but not limited to rubidium-82 generators, under the tradename Ruby-Fill®, which are sold in the United States. ***See* Exhibit No. 12** (stating Ruby-Fill® system is manufactured by Jubilant DraxImage Inc. with an address in Canada). The Ruby-Fill® system is pictured below:



See http://www.draximage.com/products/us/ruby-fill/.

33. The 2017 Mo-99 Topical Meeting presented by Argonne National Laboratory in Montreal included a "technical tour" of the Jubilant DraxImage Inc. facilities. **Exhibit No. 16.** On September 14, 2017 the participants took a "technical tour of Jubilant DraxImage Inc. I-131 solutions/capsules, I-131 mIBG and ***Rb-82 generator manufacturing at its site in Montreal.***" *Id.* (emphasis added).

34. It has been reported that Jubilant "soft launched" a purported equivalent to the CardioGen-82® system (branded as Ruby-Fill®) and "completed its installation at three sites is (sic) USA." ***See*** **Exhibit No. 13.** Jubilant further reported that they expect the Ruby-Fill® system to reach $250 million in sales and achieve "at least 30-40% market share" over 5 years. *Id.*

35. The Ruby-Fill® system utilizes a rubidium (Rb 82) generator. ***See*** **Exhibit No. 21.** The Ruby-Fill® system pumps saline through the generator to elute rudibium-82 for injection into the patient. *Id.* Jubilant's rubidium (Rb 82) generator is a critical component to the overall Ruby-Fill® system, because it is the source of the rubidium-82. There is no use for Jubilant's rubidium (Rb 82) generator other than with the Ruby-Fill® system. Jubilant's rubidium (Rb 82) generator is manufactured outside of the United States. ***See*** **Exhibit No. 20.** The following is a picture of Jubilant's rubidium (Rb 82) generator:

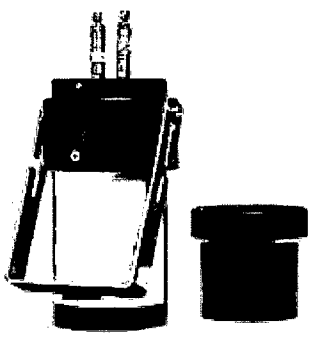


Figure 3, Generator, Generator Handle & Lead Cover

See **Exhibit No. 21.**

36. Jubilant provided a "live demo" of the Ruby-Fill® system at the 22nd Annual Scientific Session of the American Society of Nuclear Cardiology on September 14-17, 2017 in Kansas City Missouri. ***See*** **Exhibit No. 14.** As explained below in further detail, Ruby-Fill®, its use, and the processes of manufacturing Ruby-Fill® infringe upon Bracco's patented technology.

III. The Asserted Patents and Non-Technical Description[2]

37. The Asserted Patents teach novel and nonobvious technology related to strontium-rubidium radioisotope infusion systems and methods for making and using such infusion systems. As explained below, Bracco owns by assignment the entire right, title, and interest in each of the Asserted Patents. Also explained below, Bracco's Model 1700 system, as well as manufacturing and the use thereof, practices the Asserted Patents. Bracco's relevant domestic operations include significant investment in plant and equipment, significant employment of labor and capital, and substantial investment in engineering, research and development.

A. The '826 Patent

38. The '826 patent is entitled "Integrated strontium-rubidium radioisotope infusion systems," and names Stephen E. Hidem, Aaron M. Fontaine, Janet L. Gelbach, Patrick M. McDonald, Kathryn M. Hunter, Rolf E. Swenson, and Julius P. Zodda as inventors. The '826 patent was filed on June 12, 2017 as a continuation of U.S. Patent Application No. 15/389,200, filed Dec. 22, 2016, which is a continuation of U.S. Patent Application No. 12/808,467, filed Jun. 16, 2010 (now U.S. Pat. No. 9,607,722), which is a National Stage of Int'l Application No. PCT/US09/47031, filed Jun. 11, 2009, which in turn is a continuation of the following four patent applications: U.S. Patent Application No. 12/137,356, filed Jun. 11, 2008 (now U.S. Pat. No. 8,317,674); U.S. Patent Application No. 12/137,363, filed Jun. 11, 2008 (now U.S. Pat. No. 7,862,534); U.S. Patent Application No. 12/137,364, filed Jun. 11, 2008 (now U.S. Pat. No. 9,597,053); and U.S. Patent Application No. 12/137,377, filed Jun. 11, 2008 (now U.S. Pat. No.

[2] This Complaint and the included non-technical descriptions are not intended to and do not construe either the specification or the claims of the Asserted Patents.

8,708,352). The '826 patent has twenty-nine claims – one independent and twenty-eight dependent. A certified copy of the '826 patent is attached to the Complaint as **Exhibit No. 1**.

39. The '826 patent was legally and duly issued on November 14, 2017.

40. Bracco owns by assignment the entire right, title, and interest in the '826 patent. A certified copy of the assignment is attached as **Exhibit No. 2**.

41. Together with this Complaint, Bracco has filed a copy and three (3) additional copies of the prosecution history of the '826 patent as **Appendix No. 1**. Bracco has also filed four (4) copies of each patent and technical reference identified in the prosecution history of the application leading to the issuance of the '826 Patent as **Appendix No. 2**.

B. The '869 Patent

42. The '869 patent is entitled "Integrated strontium-rubidium radioisotope infusion systems," and names Stephen E. Hidem, Aaron M. Fontaine, Janet L. Gelbach, Patrick M. McDonald, Kathryn M. Hunter, Rolf E. Swenson, and Julius P. Zodda as inventors. The '869 patent was filed on December 22, 2016 as a continuation of U.S. Patent Application No. 12/808,467, filed Jun. 16, 2010 (now U.S. Pat. No. 9,607,722), which is a National Stage of Int'l Application No. PCT/US09/47031, filed Jun. 11, 2009, which in turn is a continuation of the following four patent applications: U.S. Patent Application No. 12/137,356, filed Jun. 11, 2008 (now U.S. Pat. No. 8,317,674); U.S. Patent Application No. 12/137,363, filed Jun. 11, 2008 (now U.S. Pat. No. 7,862,534); U.S. Patent Application No. 12/137,364, filed Jun. 11, 2008 (now U.S. Pat. No. 9,597,053); and U.S. Patent Application No. 12/137,377, filed Jun. 11, 2008 (now U.S. Pat. No. 8,708,352). The '869 patent has thirty claims – one independent and twenty-nine dependent. A certified copy of the '869 patent is attached to the Complaint as **Exhibit No. 3**.

43. The '869 patent was legally and duly issued on September 5, 2017.

44. Bracco owns by assignment the entire right, title, and interest in the '869 patent. A certified copy of the assignment is attached as **Exhibit No. 4**.

45. Together with this Complaint, Bracco has filed a copy and three (3) additional copies of the prosecution history of the '869 patent as **Appendix No. 3**. Bracco has also filed four (4) copies of each patent and technical reference identified in the prosecution history of the application leading to the issuance of the '869 Patent as **Appendix No. 4**.

C. The '870 Patent

46. The '870 patent is entitled "Integrated strontium-rubidium radioisotope infusion systems," and names Stephen E. Hidem, Aaron M. Fontaine, Janet L. Gelbach, Patrick M. McDonald, Kathryn M. Hunter, Rolf E. Swenson, and Julius P. Zodda as inventors. The '870 patent was filed on April 18, 2017 as a continuation of U.S. Patent Application No. 15/389,200, filed Dec. 22, 2016, which is a continuation of U.S. Patent Application No. 12/808,467, filed Jun. 16, 2010 (now U.S. Pat. No. 9,607,722), which is a National Stage of Int'l Application No. PCT/US09/47031, filed Jun. 11, 2009, which in turn is a continuation of the following four patent applications: U.S. Patent Application No. 12/137,356, filed Jun. 11, 2008 (now U.S. Pat. No. 8,317,674); U.S. Patent Application No. 12/137,363, filed Jun. 11, 2008 (now U.S. Pat. No. 7,862,534); U.S. Patent Application No. 12/137,364, filed Jun. 11, 2008 (now U.S. Pat. No. 9,597,053); and U.S. Patent Application No. 12/137,377, filed Jun. 11, 2008 (now U.S. Pat. No. 8,708,352). The '870 patent has thirty claims – one independent and twenty-nine dependent. A certified copy of the '870 patent is attached to the Complaint as **Exhibit No. 5**.

47. The '870 patent was legally and duly issued on September 5, 2017.

48. Bracco owns by assignment the entire right, title, and interest in the '870 patent. A certified copy of the assignment is attached as **Exhibit No. 6**.

49. Together with this Complaint, Bracco has filed a copy and three (3) additional copies of the prosecution history of the '870 patent as **Appendix No. 5**. Bracco has also filed four (4) copies of each patent and technical reference identified in the prosecution history of the application leading to the issuance of the '870 Patent as **Appendix No. 6**.

D. Foreign Patents and Applications Corresponding to the Asserted Patents

50. A listing of all foreign patents and foreign patent applications corresponding to the respective Asserted Patents can be found as **Exhibit No. 15.**

E. Licensees to the Asserted Patents

51. There are no licensees to the Asserted Patents.

IV. Unlawful and Unfair Acts of the Proposed Respondents

52. Proposed Respondents submitted an abbreviated new drug application ("ANDA") to the U.S. Food and Drug Administration on June 18, 2010 to market a system Proposed Respondents described as the ***equivalent*** of CardioGen-82®. **Exhibit No. 20**. Due to variations in administration rates, the FDA reclassified the ANDA application as a 505(b)(2) application. *Id.* However, Proposed Respondents still relied on clinical studies that Bracco performed in submitting its proposed equivalent version of Bracco's product. *Id.* Proposed Respondents stated that since "both generators are systems for the production of rubidium 82, equal utility is expected from Ruby-Fill." *Id.*

53. Proposed Respondents represented to the FDA that the Ruby-Fill® system is a "pharmaceutical equivalent" to Bracco's CardioGen-82®. *Id.* Pharmaceutical equivalents are drug products in identical dosage forms intended for the same route of administration that: (1) contain identical amounts of the identical active drug ingredient, i.e., the same salt or ester of the same therapeutic moiety, or, in the case of modified release dosage forms that require a reservoir

or overage or such forms as prefilled syringes where residual volume may vary, that deliver identical amounts of the active drug ingredient over the identical dosing period; (2) do not necessarily contain the same inactive ingredients; and (3) meet the identical compendial or other applicable standard of identity, strength, quality, and purity, including potency and, where applicable, content uniformity, disintegration times, and/or dissolution rates. *See* 21 C.F.R. § 320.1(c).

54. Proposed Respondents received FDA approval for the Ruby-Fill® rubidium-82 generator and elution system on September 30, 2016 (***See* Exhibit No. 20)** and began selling such units in the United States immediately thereafter.

55. The Proposed Respondents unlawfully sell for importation, import, and/or sell after importation into the United States strontium-rubidium radioisotope infusion systems and components thereof that infringe the Asserted Patents. **Exhibits 17, 18, and 19** contain claim charts that detail examples of how the asserted independent claims of the Asserted Patents read on the Proposed Respondents' Ruby-Fill® product, based on information discovered through Bracco's investigation to date.

56. The infringement at issue in this Complaint includes infringement (either literally or under the doctrine of equivalents) under 35 U.S.C. § 271, including without limitation, sections (a)-(c) and (g).

57. Contemporaneously with the filing of this Complaint, Bracco has provided the Proposed Respondents with a copy of the Complaint and the non-confidential exhibits to the Complaint. As a result, the Proposed Respondents received notice of the Asserted Patents and the infringement at issue no later than the filing of this Complaint.

V. Specific Acts of Unfair Importation and Sale

58. Proposed Respondents sell for importation into the United States, import into the United States, and/or sell after importation into the United States at least non-staple components of the Accused Product, including for example the rubidium-82 generator that is used specifically and exclusively with the Ruby-Fill® system, which infringes the Asserted Patents in violation of Section 337.

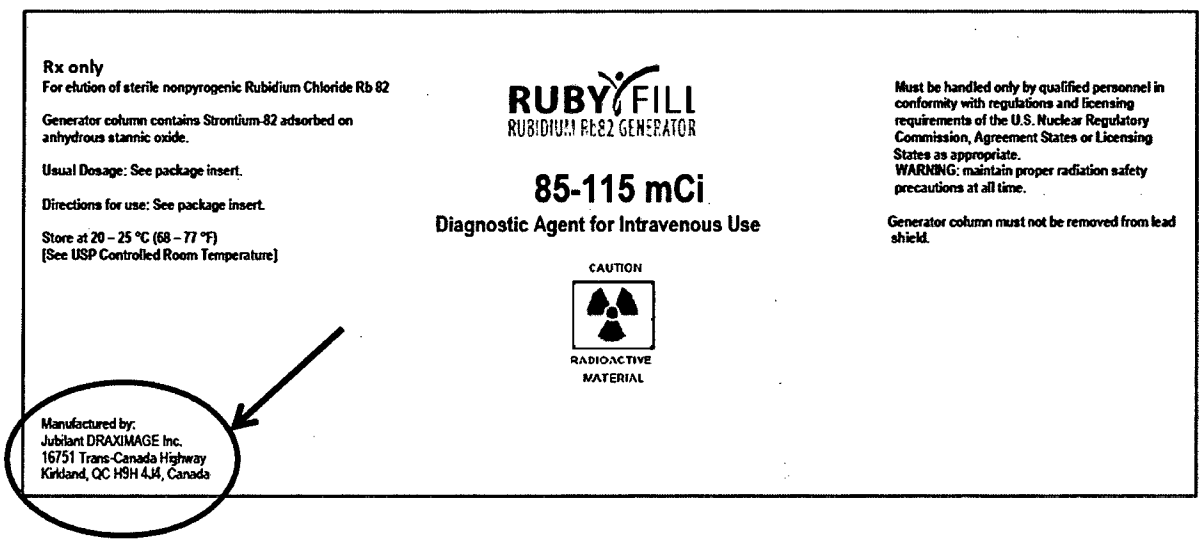
59. Bracco has obtained in the United States a user manual of the Proposed Respondents' Accused Product that infringes the Asserted Patents. **Exhibit No. 21.**

60. Proposed Respondents' Accused Product and/or non-staple components of the Accused Product, including for example the rubidium-82 generator, are manufactured in Canada, sold for importation into the United States, imported into the United States, and/or sold after importation into the United States by Proposed Respondents and/or its authorized agents. **Exhibit Nos. 12, 16, 20, and 21.**

61. As discussed above, Proposed Respondents manufacture the rubidium-82 generator outside of the United States. This generator is an essential component of the Ruby-Fill® system as it is the source of the rubidium-82 that is used in the rubidium-82 chloride for injection into patients. The FDA approved labeling for Ruby-Fill® states that this generator may be used "only with an appropriate, properly calibrated Elution System (RUBY Rubidium Elution System) labeled for use with the generator." **Exhibit No. 20.** Proposed Respondents understands and intends that the rubidium-82 generator that it imports into the United States from Canada has no other approved use except as part of the infringing Ruby-Fill® system. Thus, Proposed Respondents encourages, recommends, and promotes the use of its rubidium-82 generators as part of the infringing Ruby-Fill® system.

62. The Accused Product bearing the brand name Ruby-Fill®, as identified in the claim charts, infringes one or more of the Asserted Patents and is imported and/or sold after importation from Canada within the United States by the Proposed Respondents who manufacture and supply this system for use in the United States to, for example, the radiopharmacy, hospital and/or imaging center.

63. On information and belief, the Ruby-Fill® system and/or rubidium-82 generators are manufactured by Proposed Respondents and/or its authorized agents in Canada. For example, the FDA approved labeling clearly identifies Proposed Respondents' address in Canada as the manufacturer:



***See* Exhibit No. 20.**

64. Proposed Respondents' 505(b)(2) NDA No. 202153, which was submitted to the FDA, also clearly identifies the location of manufacturing as Canada:

Product Quality Microbiology Data Sheet

A. 1. **TYPE OF SUBMISSION** NDA Resubmission

2. **SUBMISSION PROVIDES FOR:** Response to CMC deficiencies in Agency's Complete Response letter

3. **MANUFACTURING SITE:**
Jubilant DraxImage Inc.
16751 TransCanada Highway
Kirkland, QC
Canada H9H4J4

***

4. **MANUFACTURING FACILITY OF FINISHED DOSAGE FORM**
DRAXIMAGE, (a division of DRAXIS Specialty Pharmaceuticals Inc.)
16751 TransCanada Highway
Kirkland, Quebec
Canada H9H 4J4

***See* Exhibit No. 20.**

65. Moreover, as part of a recent technical conference in Canada hosted by Argonne National Laboratory, Jubilant DraxImage provided a "technical tour" of its manufacturing facilities "in Montreal" for its "Rb-82 generator." ***See* Exhibit No. 16.**

66. The Ruby-Fill® system has been imported, sold and installed in the United States at a minimum of "three sites." ***See* Exhibit No. 13.** The Ruby-Fill® system has been offered for importation into the United States after September -November, 2017 (*i.e.*, after the patents-in-suit issued). Proposed Respondents induce and contribute to the infringement of the patents-in-suit by importing into the United States replacement rubidium 82 generators for use in infringing Ruby-Fill® system, including after November 2017. **Exhibit Nos. 21.** As shown in Exhibit 12, rubidium 82 generators must be replaced at least every 60 days. Accordingly, such generators

must have been imported to each location using the Ruby-Fill® system after November 14, 2017 (*i.e.*, the issue date of the latest Asserted Patent).

VI. Harmonized Tariff Schedule Information

67. On information and belief, the articles subject to this Complaint are classifiable under at least the following headings and subheadings of the Harmonized Tariff Schedule ("HTS") of the United States: 9022.14.00.00; 9022.21.00.00; and 9022.90.05.00.

68. These classifications are intended for illustration only and are not intended to restrict the scope of this investigation.

VII. Related Litigation

69. Bracco is not aware of any court or agency actions previously filed involving the Asserted Patents or in any way related to the proposed investigation.

70. Concurrently with the filing of this complaint, Bracco will file a complaint in the U.S. District Court for the District of New Jersey alleging infringement of at least the Asserted Patents against Jubilant DraxImage Inc., Jubilant Pharma Limited, and Jubilant Life Sciences.

VIII. Domestic Industry

71. A domestic industry, as required and defined by 19 U.S.C. § 1337(a)(2)-(3), exists or is in the process of being established by virtue of significant investment in plant and equipment, significant employment of labor or capital, and substantial investment in engineering, research, and development, all related to the Asserted Patents.

A. The Economic Prong

72. An industry, as defined in Section 337(a)(3), exists in the United States by virtue of Bracco's significant and substantial investments directed to Bracco's strontium-rubidium radioisotope infusion systems and manufacturing equipment and processes therefore, each of

which is protected by one or more of the Asserted Patents. Bracco has [redacted] More information showing Bracco has an existing domestic industry can be found in **Confidential Exhibit No. 22.**

73. Bracco conducts significant, substantial, and extensive activities in the United States related to its strontium-rubidium radioisotope infusion system domestic industry. These activities include, but are not limited to significant domestic investment in employees and labor related to the engineering, research, and development and manufacturing of strontium-rubidium radioisotope infusion systems. Further included are Bracco's significant domestic investment in plant and equipment related to Bracco's engineering, research, and development and manufacturing of strontium-rubidium radioisotope infusion systems. Additionally, Bracco's domestic investment in engineering and research and development for strontium-rubidium radioisotope infusion systems is substantial.

74. In addition to the domestic industry that exists because of the numerous Model 1700 systems that have already been produced, a domestic industry is in the process of being established [redacted]. Bracco is taking the necessary and tangible steps to establish such an industry, to the extent it does not already exist, in the United States, and there is a significant likelihood that the Model 1700 system will be available in the United States in the near future. For example, [redacted] From this work, [redacted]

[redacted] The Model 1700 system will be manufactured in the United States [redacted] Bracco's Model 1700 system and the use thereof, practices the Asserted Patents (as shown in the attached claim charts related to the technical prong of the domestic industry requirement). Moreover, Bracco has a substantial research and development presence in the United States related to its systems that practice the Asserted Patents. More information showing Bracco has a domestic industry that is in the process of being established can be found in **Confidential Exhibit No. 22.**

B. The Technical Prong

75. Bracco practices the Asserted Patents in the United States through at least the Model 1700 system. [redacted] The Model 1700 system is an infusion system as recited in the claims of the '869 patent. In addition, the Model 1700 system is used in a manner recited in the claims of the '870 patent, and the Model 1700 system is made using the methods recited in the claims of the '826 patent.

76. The Model 1700 system practices at least claim 1 of the '826 patent, claim 1 of the '869 patent, and claim 1 of the '870 patent.

77. A chart applying the claims of the '869 patent to the Model 1700 system is attached as **Exhibit No. 23**.

78. A chart applying the claims of the '870 patent to the use of the Model 1700 system is attached as **Exhibit No. 24**.

79. A chart applying the claims of the '869 patent to the manufacture of the Model 1700 system is attached as **Exhibit No. 25.**

IX. Request for Relief

WHEREFORE, Bracco respectfully requests that the United States International Trade Commission:

80. Institute an immediate investigation pursuant to Section 337(b)(1) of the Tariff Act of 1930, as amended, 19 U.S.C. § 1337, into the violation by Proposed Respondents of Section 337 arising from the importation into the United States and/or sale within the United States after the importation of Proposed Respondents' products and/or components that infringe or induce or contribute to the infringement of one or more claims of the Asserted Patents;

81. Schedule and conduct a hearing pursuant to Section 337(c), for purposes of receiving evidence and hearing argument concerning whether there has been a violation of Section 337 and, following the hearing, determine that there has been a violation of Section 337;

82. Issue a permanent limited exclusion order pursuant to 19 U.S.C. § 1337 (d) forbidding entry into the United States of Proposed Respondents' products or components that infringe or induce or contribute to the infringement of one or more claims of the Asserted Patents;

83. Issue a permanent cease and desist order, pursuant to 19 U.S.C. § 1337(f), directing Proposed Respondents to cease and desist from the importation, sale, offer for sale, advertising, packaging or solicitation of any sale by Proposed Respondents of products or components that infringe or induce or contribute to the infringement of one or more claims of the Asserted Patents;

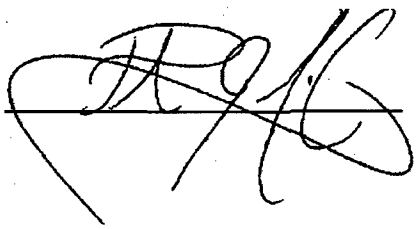
84. Issue a permanent cease and desist order, pursuant to 19 U.S.C. § 1337(f), directing Proposed Respondents to cease and desist from inducing or contributing to infringement of the Asserted Patents by providing maintenance, service, direction, training, or instruction of any kind to the existing users of the Proposed Respondents products or components that infringe or induce or contribute to the infringement of one or more claims of the Asserted Patents.

85. Impose a bond upon Proposed Respondents who continue to import infringing articles during the 60-day Presidential review period per 19 U.S.C. § 1337(j); and

86. Grant all such other and further relief as it deems appropriate under the law, based upon the facts complained of herein and as determined by the investigation.

Dated: March 27, 2018

By:



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Attorneys for Complainant

VERIFICATION OF COMPLAINT

I, Vito DeBari, declare, in accordance with 19 CFR §§ 210.4 and 210.12(a), under penalty of perjury that the following statements are true:

1. I am Vice President and General Counsel at Bracco Diagnostics Inc., and am duly authorized to sign this complaint on behalf of the Complainants.

2. I have read the Complaint and am aware of its contents;

3. The Complaint is not being presented for any improper purpose, such as to harass or to cause unnecessary delay or needless increase in the cost of litigation;

4. To the best of my knowledge founded upon reasonable inquiry, the claims and legal contentions of this Complaint are warranted by existing law or a good faith argument for the extension, modification, or reversal of existing law;

5. The allegations and other factual contentions in the Complaint have evidentiary support or are likely to have evidentiary support after a reasonable opportunity for further investigation or discovery.

Executed on March 27, 2018

EXHIBIT 1

U 7667315

THE UNITED STATES OF AMERICA

TO ALL TO WHOM THESE PRESENTS SHALL COME:

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office

February 12, 2018

THIS IS TO CERTIFY THAT ANNEXED HERETO IS A TRUE COPY FROM THE RECORDS OF THIS OFFICE OF:

U.S. PATENT: ***9,814,826***
ISSUE DATE: ***November 14, 2017***

By Authority of the
Under Secretary of Commerce for Intellectual Property
and Director of the United States Patent and Trademark Office

P. R. GRANT
Certifying Officer

US009814826B2

(12) **United States Patent**
Hidem et al.

(10) **Patent No.: US 9,814,826 B2**
(45) **Date of Patent: *Nov. 14, 2017**

(54) **INTEGRATED STRONTIUM-RUBIDIUM RADIOISOTOPE INFUSION SYSTEMS**

(71) Applicant: **Bracco Diagnostics Inc.**, Monroe Township, NJ (US)

(72) Inventors: **Stephen E. Hidem**, Edina, MN (US); **Aaron M. Fontaine**, Minneapolis, MN (US); **Janet L. Gelbach**, Schaumburg, IL (US); **Patrick M. McDonald**, Omaha, NE (US); **Kathryn M. Hunter**, Knoxville, TN (US); **Rolf E. Swenson**, Silver Spring, MD (US); **Julius P. Zodda**, Mercerville, NJ (US)

(73) Assignee: **Bracco Diagnostics Inc.**, Monroe Township, NJ (US)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

This patent is subject to a terminal disclaimer.

(21) Appl. No.: **15/620,320**

(22) Filed: **Jun. 12, 2017**

(65) **Prior Publication Data**

US 2017/0274138 A1 Sep. 28, 2017

Related U.S. Application Data

(63) Continuation of application No. 15/389,200, filed on Dec. 22, 2016, now Pat. No. 9,750,869, which is a (Continued)

(51) **Int. Cl.**
A61M 5/00 (2006.01)
A61M 5/14 (2006.01)
(Continued)

(52) **U.S. Cl.**
CPC ***A61M 5/007*** (2013.01); ***A61B 6/037*** (2013.01); ***A61B 6/107*** (2013.01); ***A61B 6/481*** (2013.01);
(Continued)

(58) **Field of Classification Search**
CPC .. A61M 5/007; A61M 5/1001; A61M 5/1002; A61M 5/1007;
(Continued)

(56) **References Cited**

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3,535,085 A 10/1970 Shumate
(Continued)

FOREIGN PATENT DOCUMENTS

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CN 1968653 A 5/2007
(Continued)

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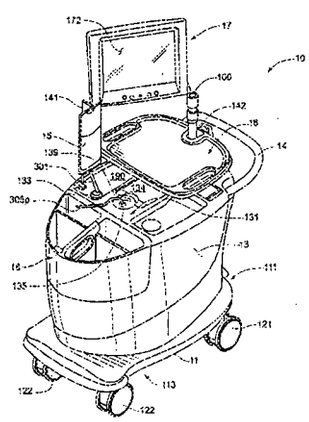
Alvarez-Diez et al. "Manufacture of strontium-82/rubidium-82 generators and quality control of rubidium-82 chloride for myocardial perfusion imaging in patients using positron emission tomography," Applied Radiation and Isotopes, 1999, pp. 1015-1023.
(Continued)

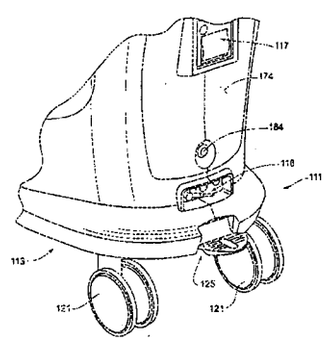
Primary Examiner — Charles A Marmor, II
Assistant Examiner — Carrie R Dorna
(74) *Attorney, Agent, or Firm* — Fredrikson & Byron, P.A.

(57) **ABSTRACT**

Methods for setting up, maintaining and operating a radiopharmaceutical infusion system, that includes a radioisotope generator, are facilitated by a computer of the system. The computer may include pre-programmed instructions and a computer interface, for interaction with a user of the system, for example, in order to track contained volumes of eluant and/or eluate, and/or to track time from completion of an elution performed by the system, and/or to calculate one or more system and/or injection parameters for quality control, and/or to perform purges of the system, and/or to facilitate diagnostic imaging.

30 Claims, 27 Drawing Sheets





Related U.S. Application Data

continuation of application No. 12/808,467, filed as application No. PCT/US2009/047031 on Jun. 11, 2009, now Pat. No. 9,607,722, which is a continuation of application No. 12/137,377, filed on Jun. 11, 2008, now Pat. No. 8,708,352, and a continuation of application No. 12/137,363, filed on Jun. 11, 2008, now Pat. No. 7,862,534, and a continuation of application No. 12/137,356, filed on Jun. 11, 2008, now Pat. No. 8,317,674, and a continuation of application No. 12/137,364, filed on Jun. 11, 2008, now Pat. No. 9,597,053.

(51) **Int. Cl.**

A61B 90/00	(2016.01)
A61M 5/145	(2006.01)
G21F 3/00	(2006.01)
A61M 5/158	(2006.01)
G21F 7/00	(2006.01)
A61M 5/168	(2006.01)
G21G 1/00	(2006.01)
A61B 6/00	(2006.01)
A61B 6/03	(2006.01)
G21G 4/08	(2006.01)
A61B 50/13	(2016.01)
A61M 5/142	(2006.01)
A61K 51/00	(2006.01)
G06F 21/31	(2013.01)
A61B 6/10	(2006.01)
A61B 50/10	(2016.01)
A61N 5/10	(2006.01)
B62B 3/00	(2006.01)

(52) **U.S. Cl.**

CPC ***A61B 6/507*** (2013.01); ***A61B 50/13*** (2016.02); ***A61B 90/39*** (2016.02); ***A61K 51/00*** (2013.01); ***A61M 5/14*** (2013.01); ***A61M 5/142*** (2013.01); ***A61M 5/1409*** (2013.01); ***A61M 5/1452*** (2013.01); ***A61M 5/158*** (2013.01); ***A61M 5/16854*** (2013.01); ***A61M 5/16881*** (2013.01); ***A61N 5/1001*** (2013.01); ***A61N 5/1007*** (2013.01); ***A61N 5/1075*** (2013.01); ***G06F 21/31*** (2013.01); ***G21F 3/00*** (2013.01); ***G21F 7/00*** (2013.01); ***G21G 1/001*** (2013.01); ***G21G 1/0005*** (2013.01); ***G21G 4/08*** (2013.01); *A61B 2050/105* (2016.02); *A61B 2090/392* (2016.02); *A61M 2005/1403* (2013.01); *A61M 2205/18* (2013.01); *A61M 2205/276* (2013.01); *A61M 2205/50* (2013.01); *A61M 2205/505* (2013.01); *A61M 2205/52* (2013.01); *A61M 2209/084* (2013.01); *A61N 2005/1021* (2013.01); *A61N 2005/1022* (2013.01); *A61N 2005/1074* (2013.01); *A61N 2005/1094* (2013.01); *B62B 3/005* (2013.01); *G21G 2001/0031* (2013.01)

(58) **Field of Classification Search**

CPC A61M 5/1014–5/1017; A61M 5/1027; A61M 5/1028; A61M 5/1071; A61M 5/14; A61M 5/142; A61M 2005/1021; G21G 4/08; G21G 1/0005; G06F 19/3468; A61B 2050/105

See application file for complete search history.

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Fig. 1A

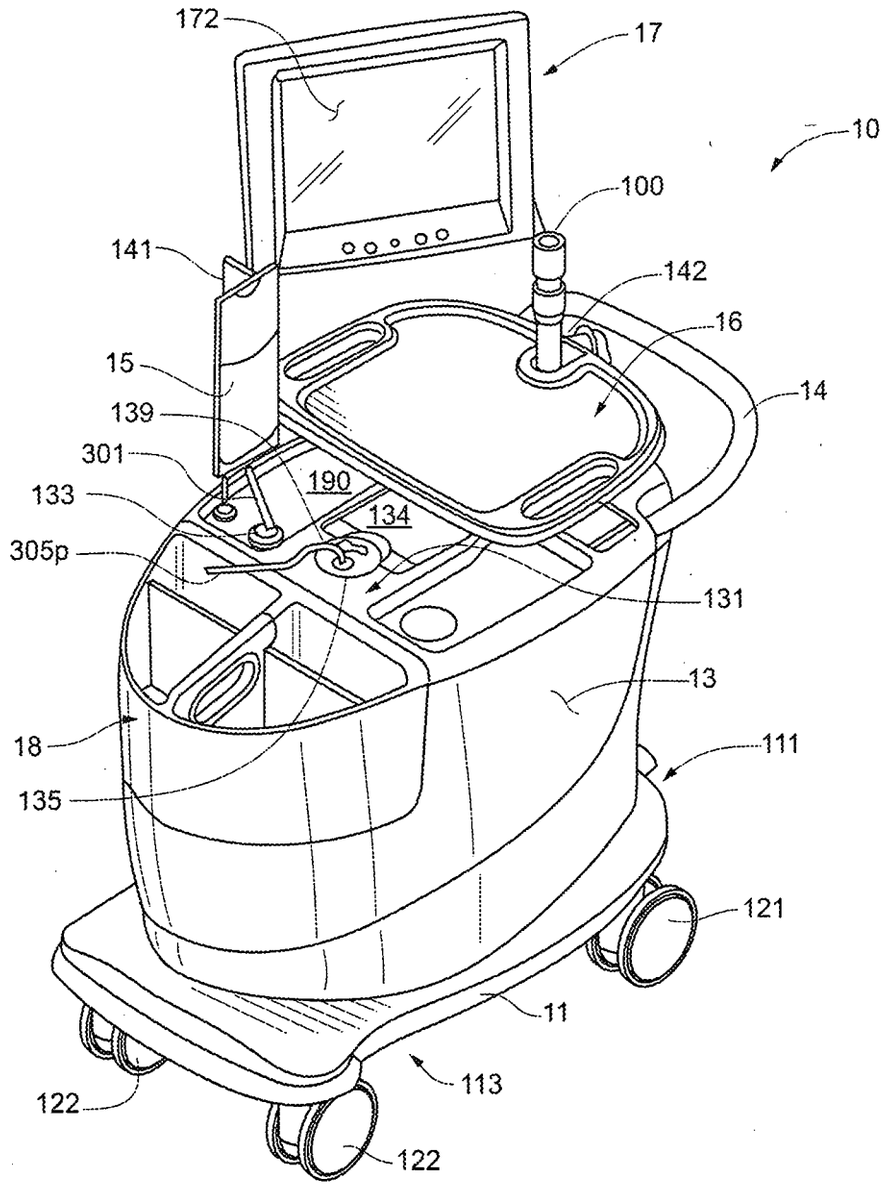
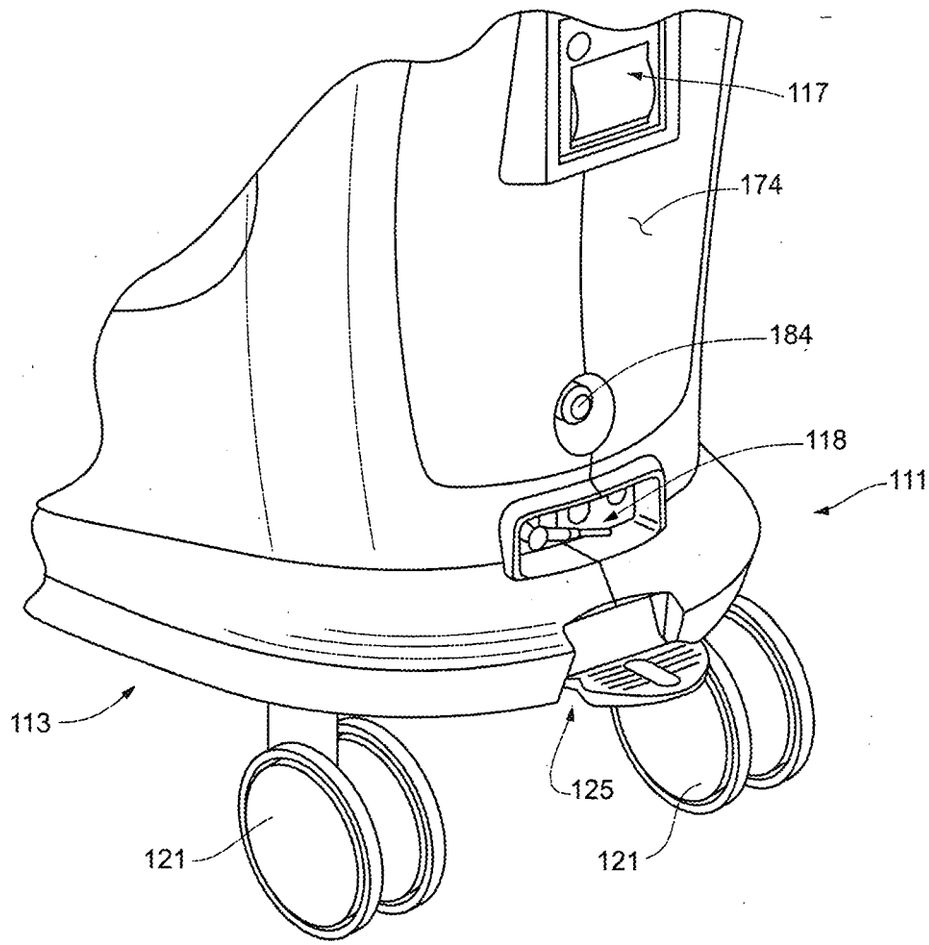


Fig. 1B



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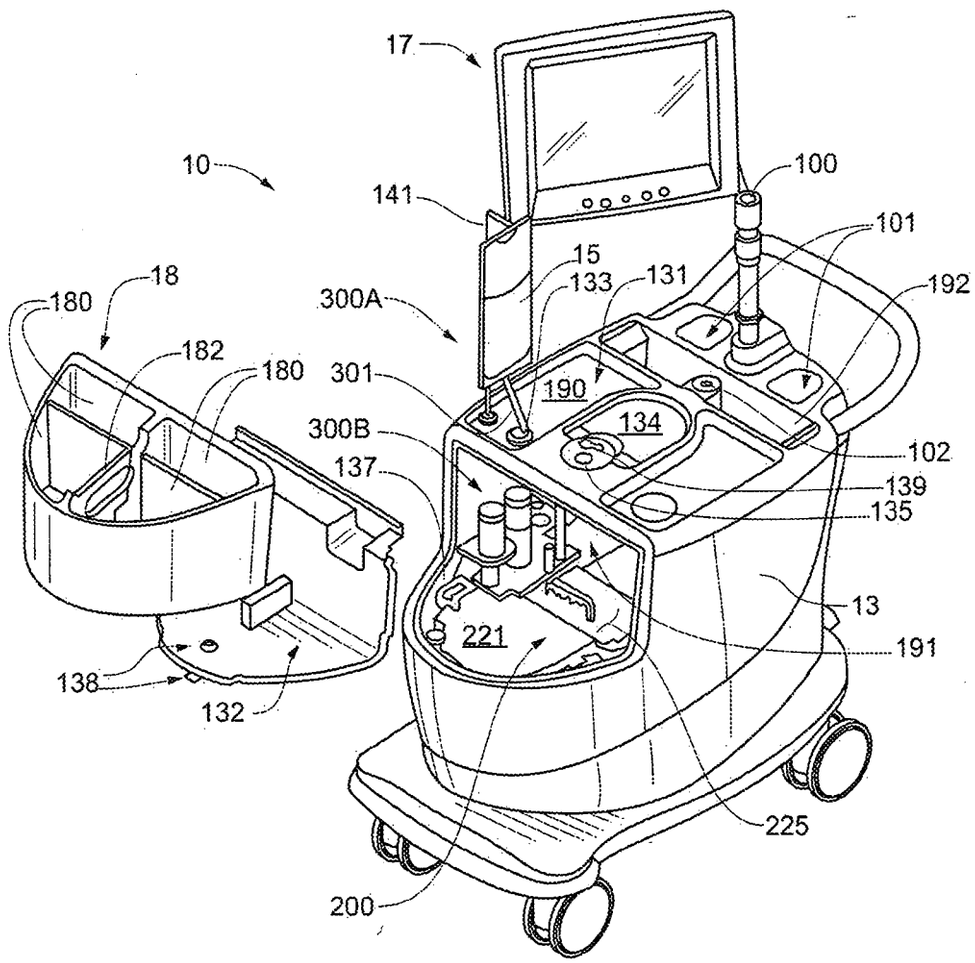


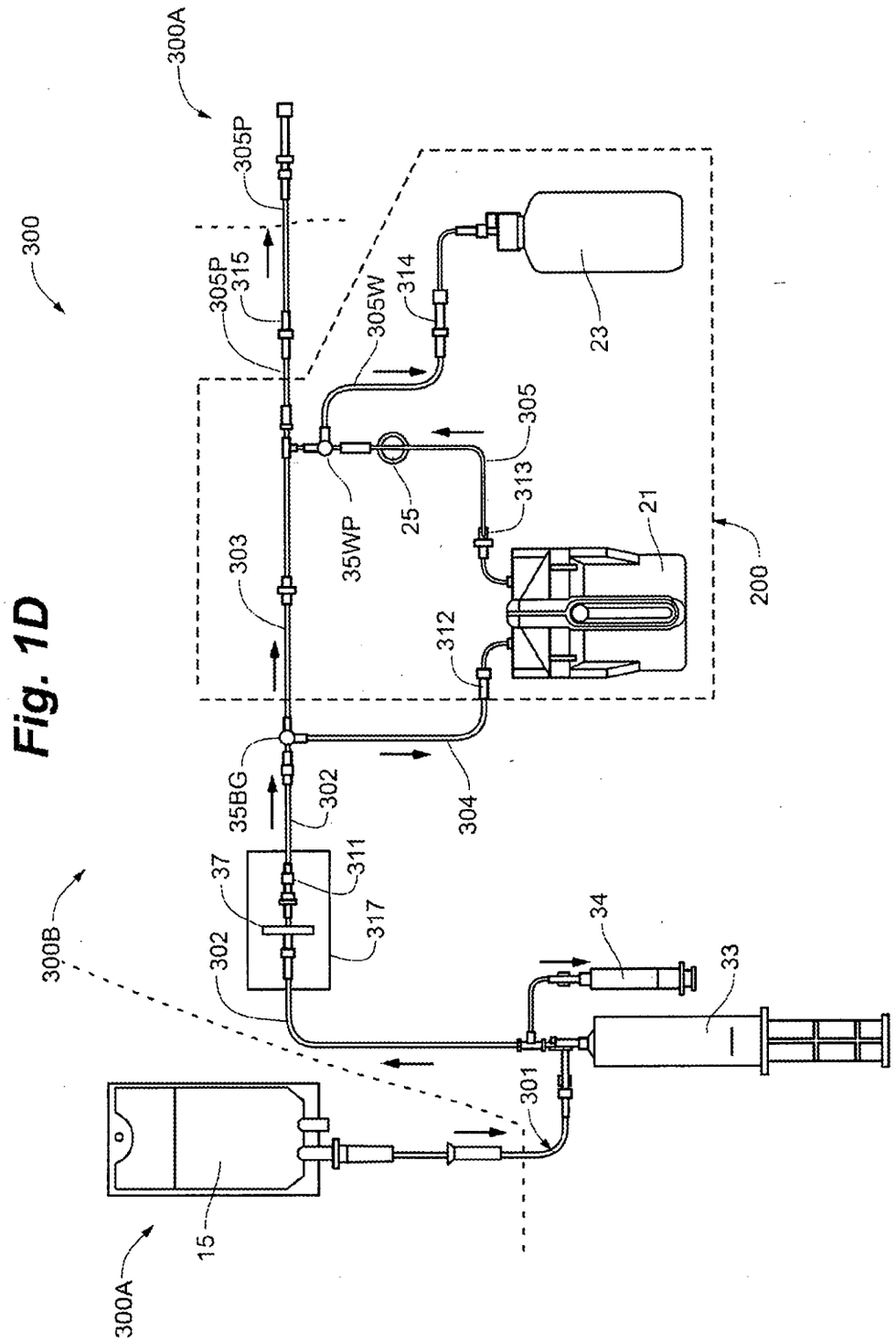


Fig. 1D

Fig. 1E

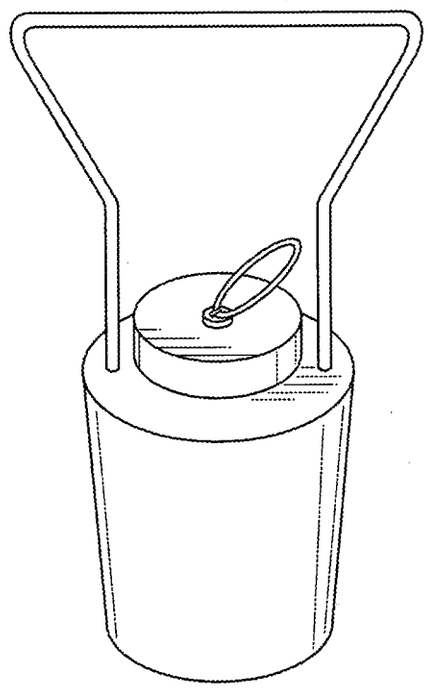


Fig. 2A

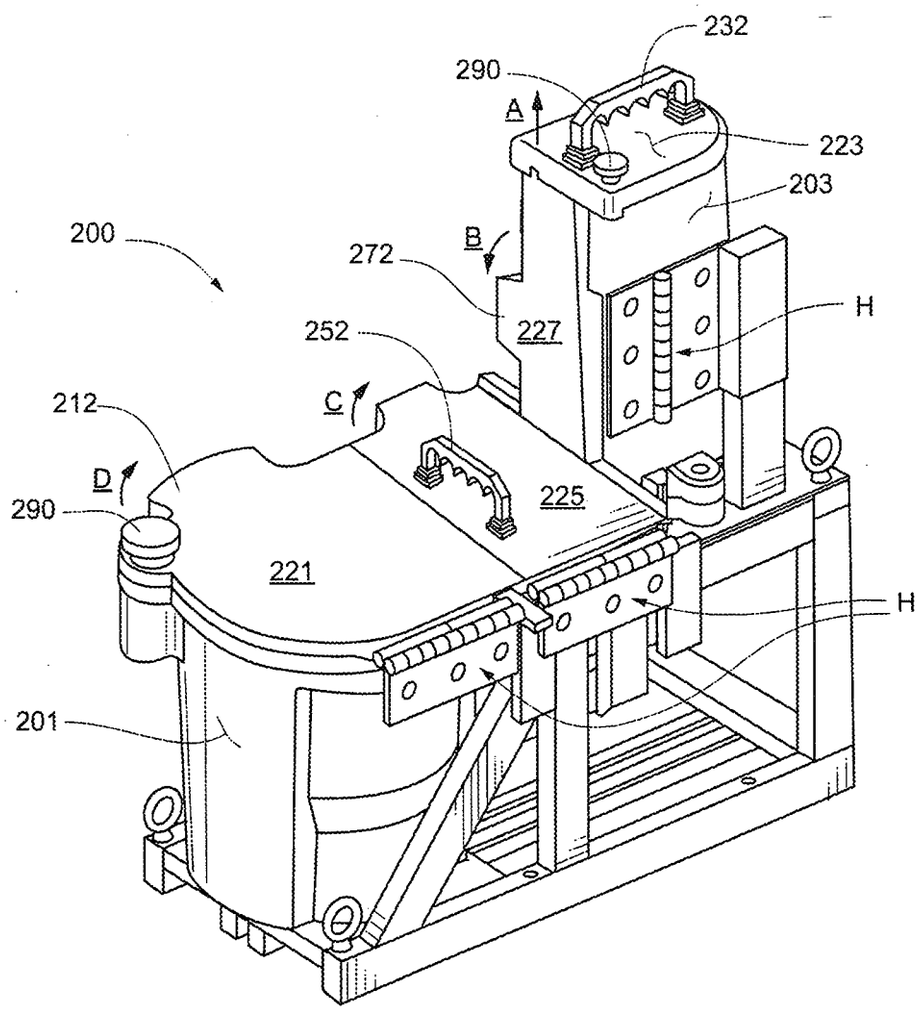


Fig. 2B-1

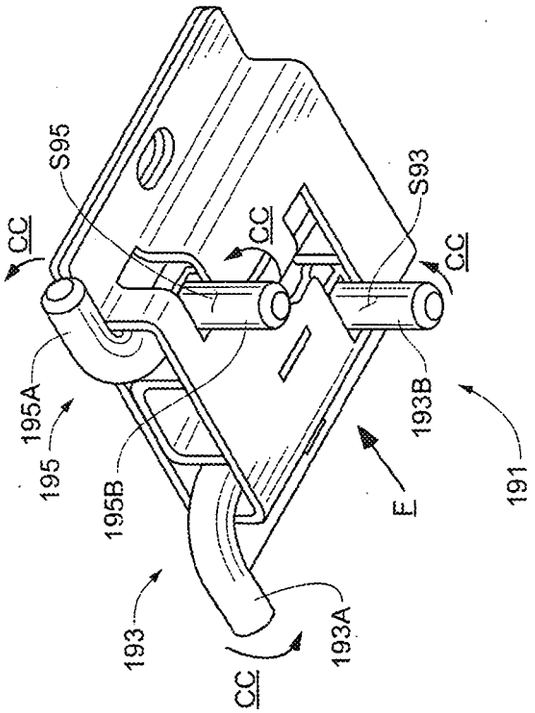


Fig. 2B

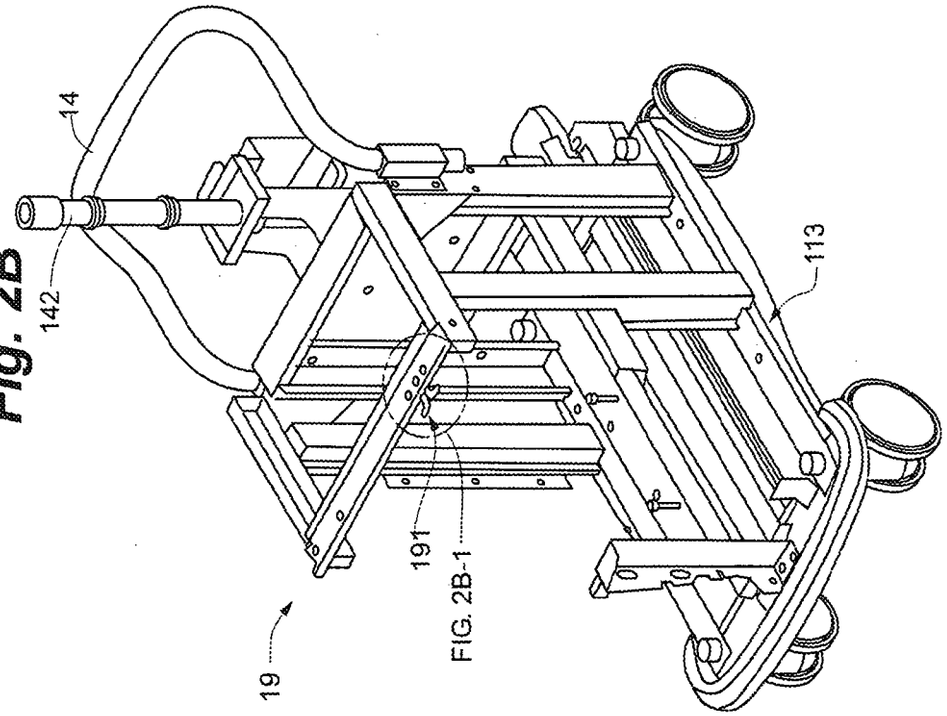
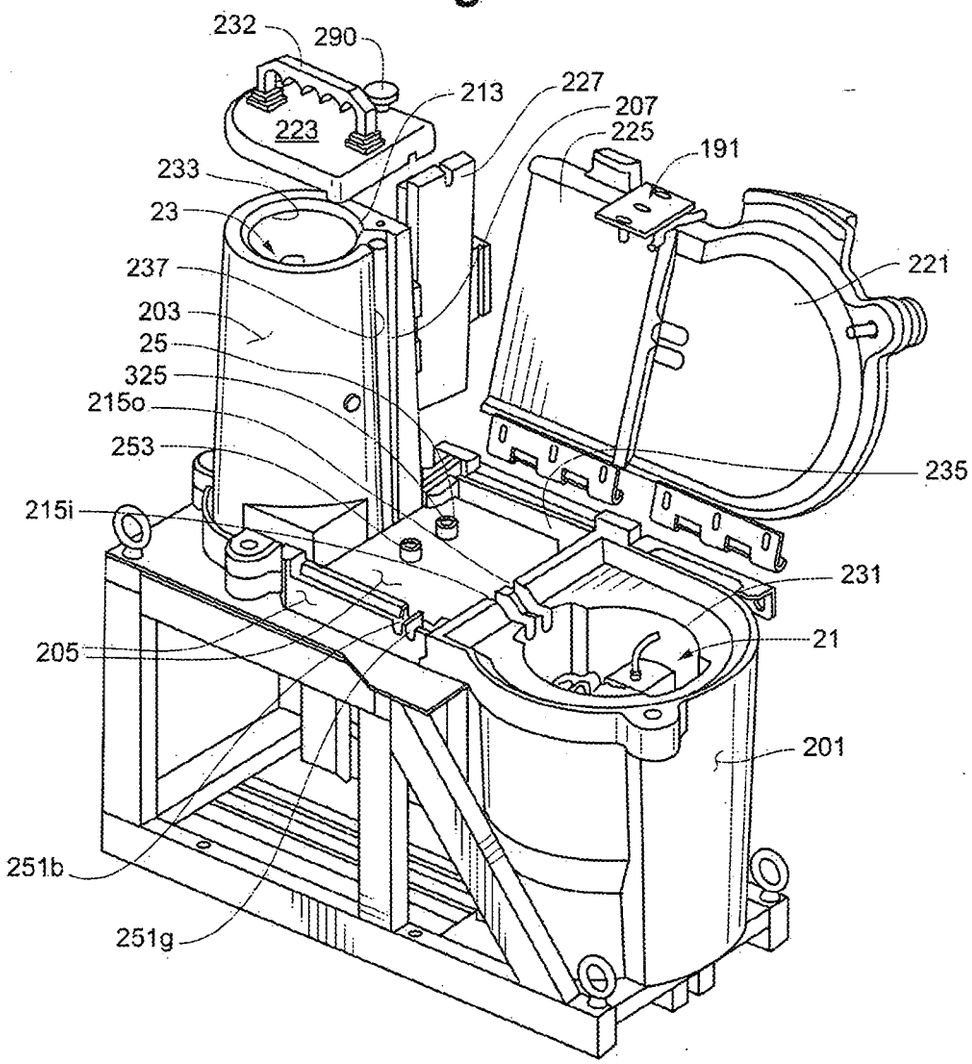
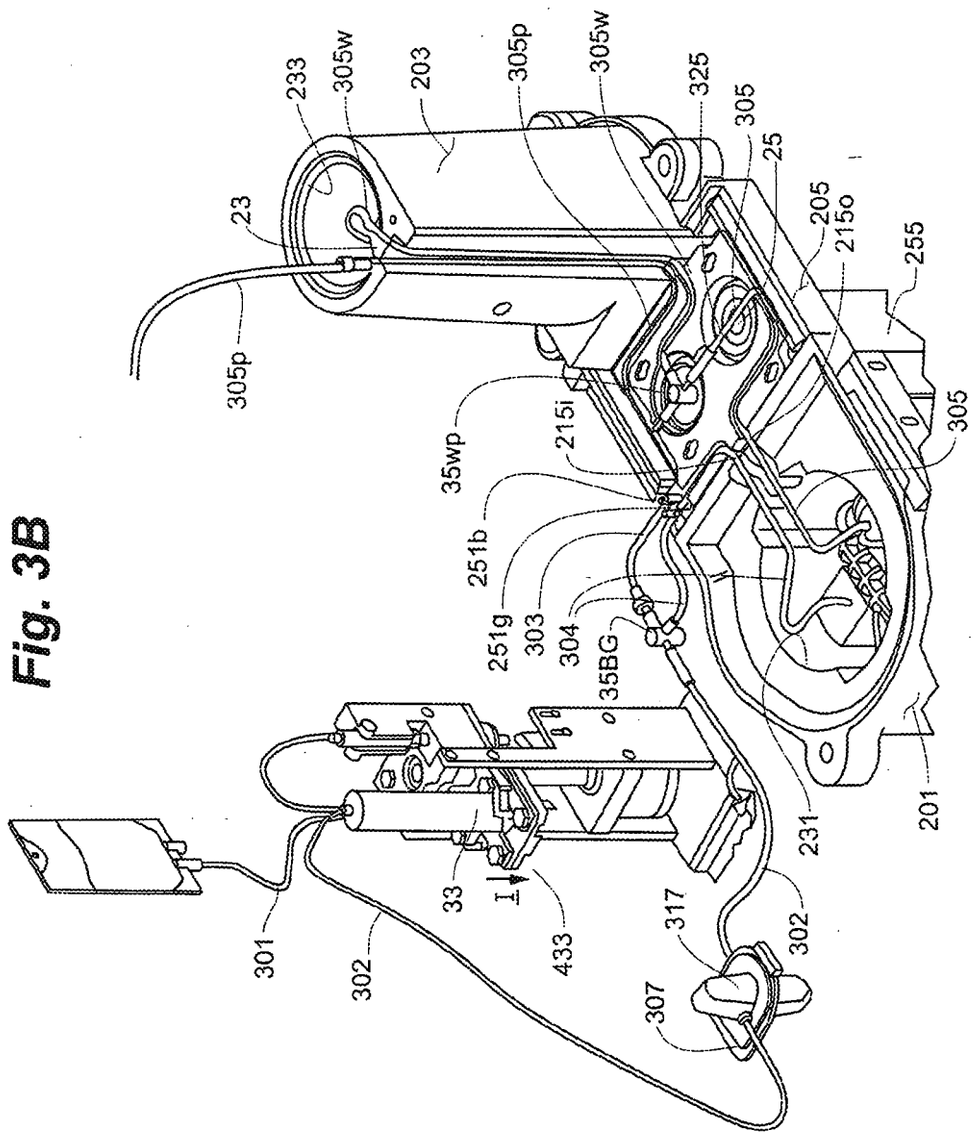


Fig. 3A





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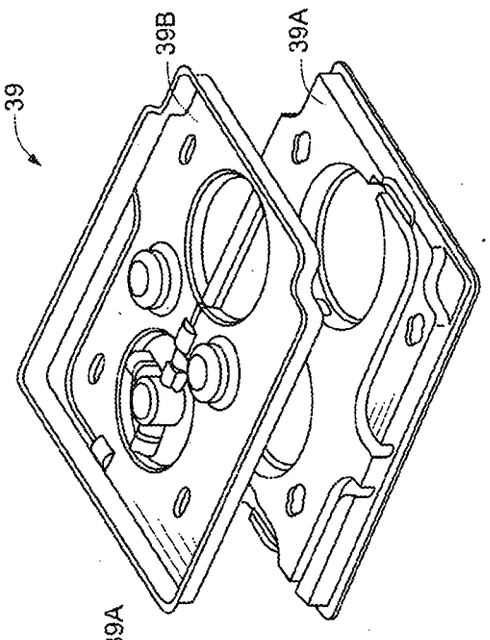


Fig. 3D

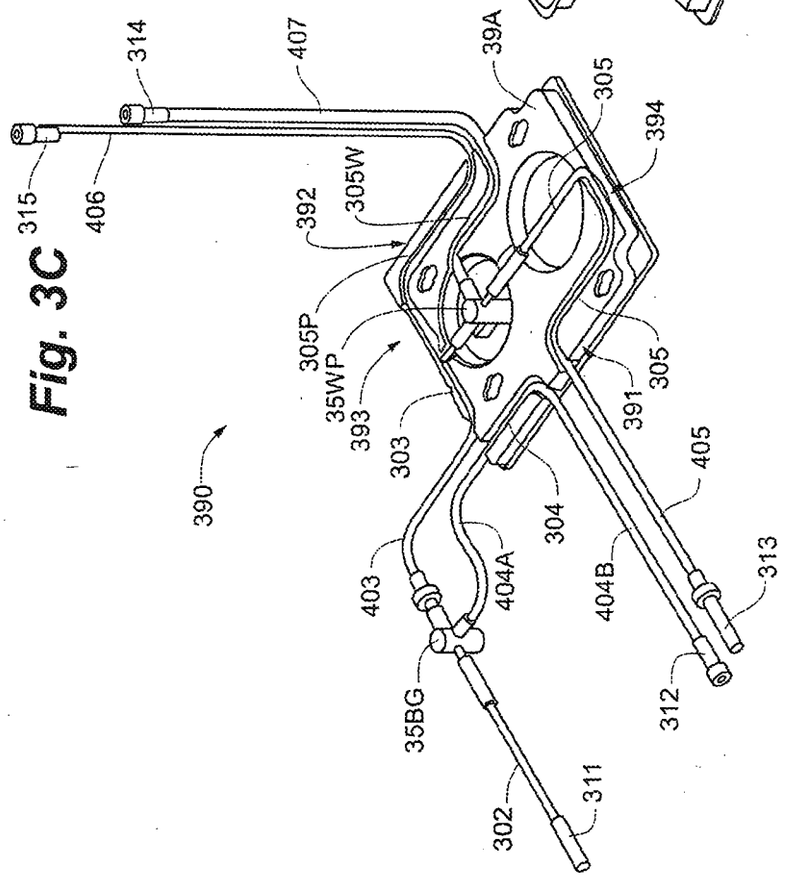


Fig. 3C

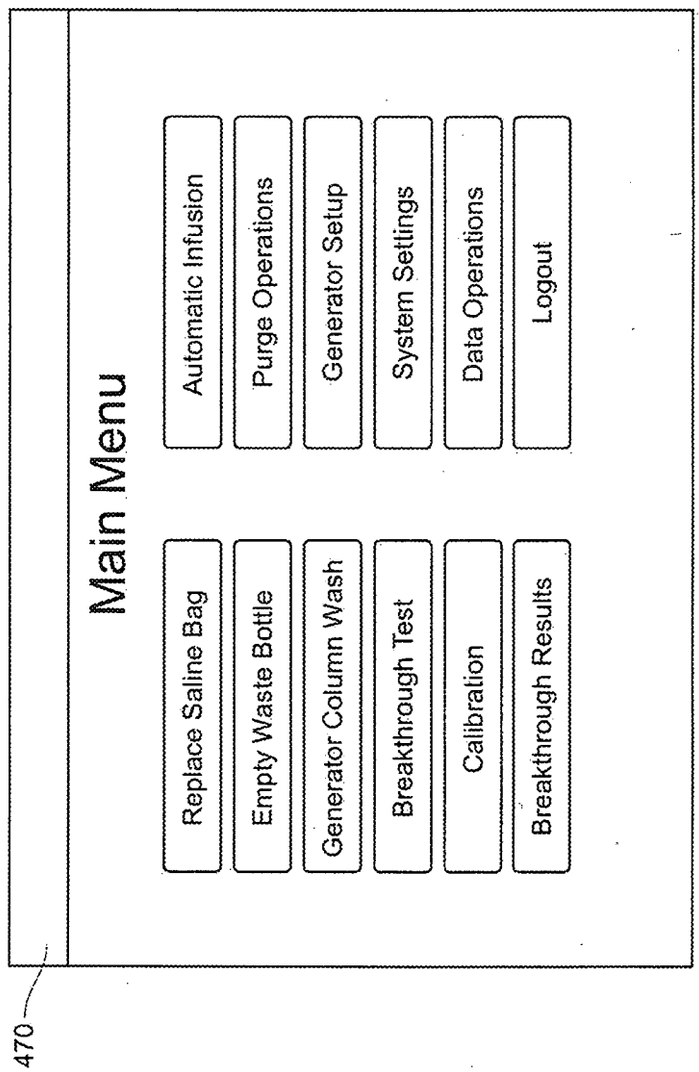


Fig. 4

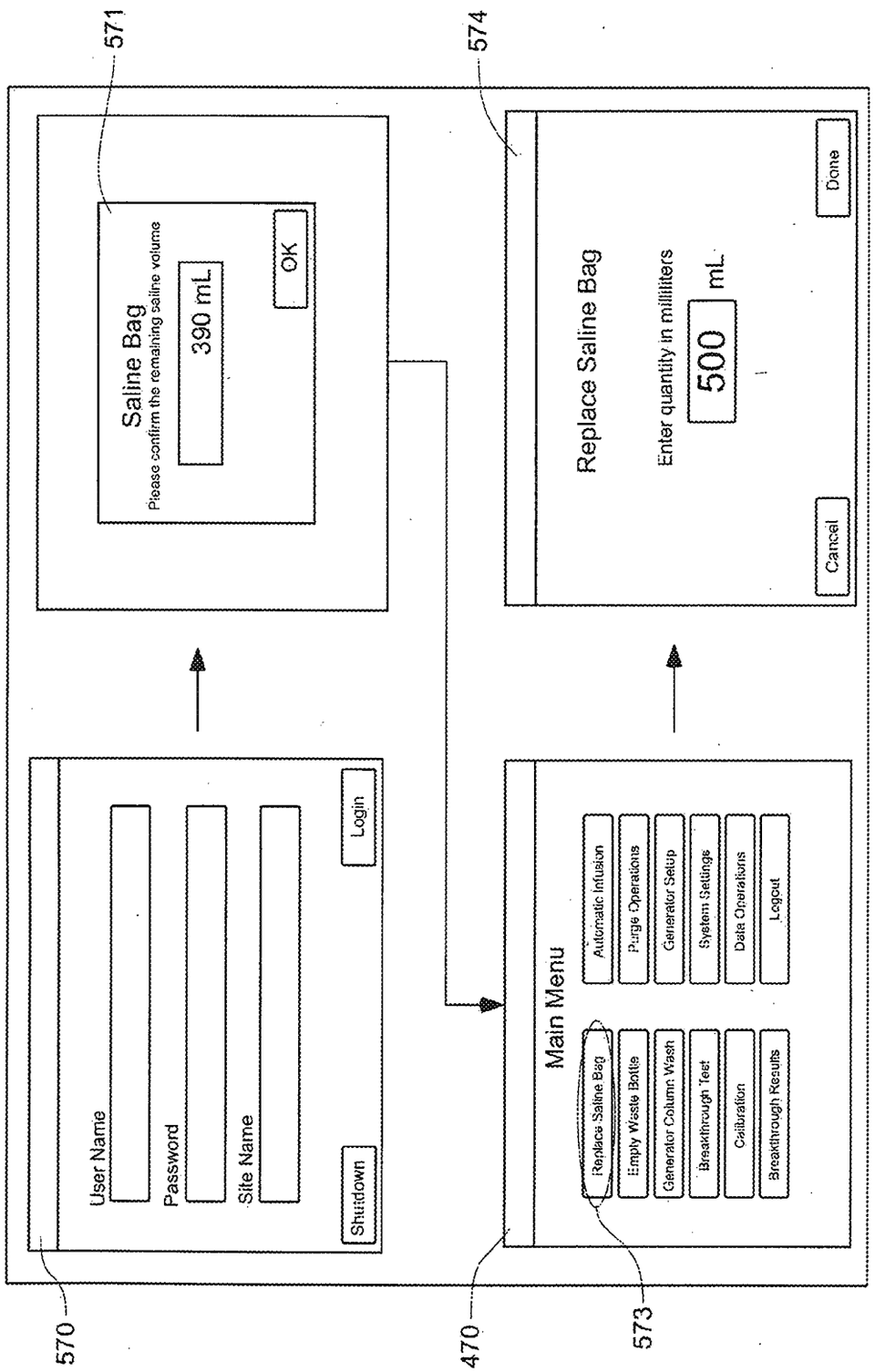


Fig. 5A

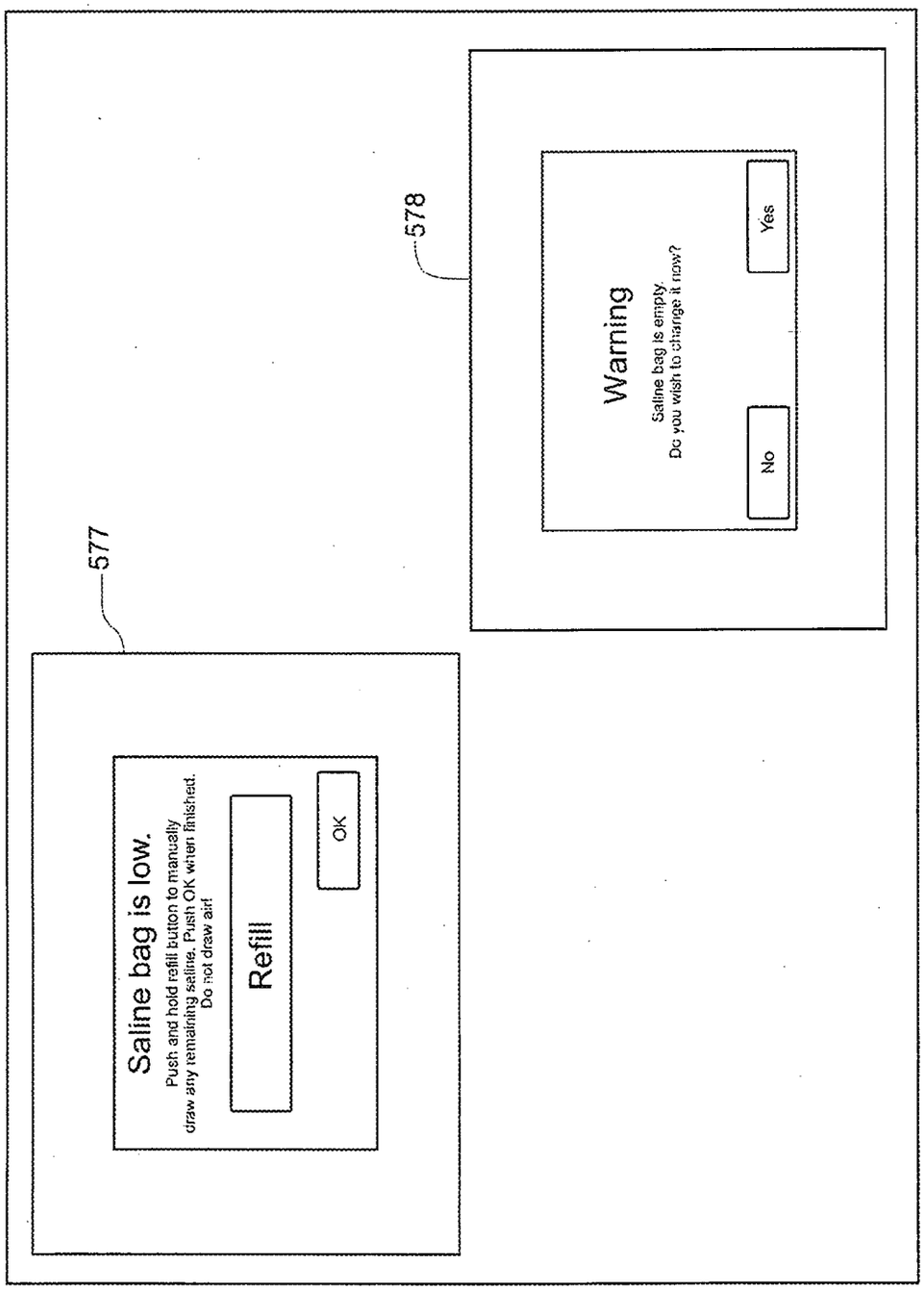
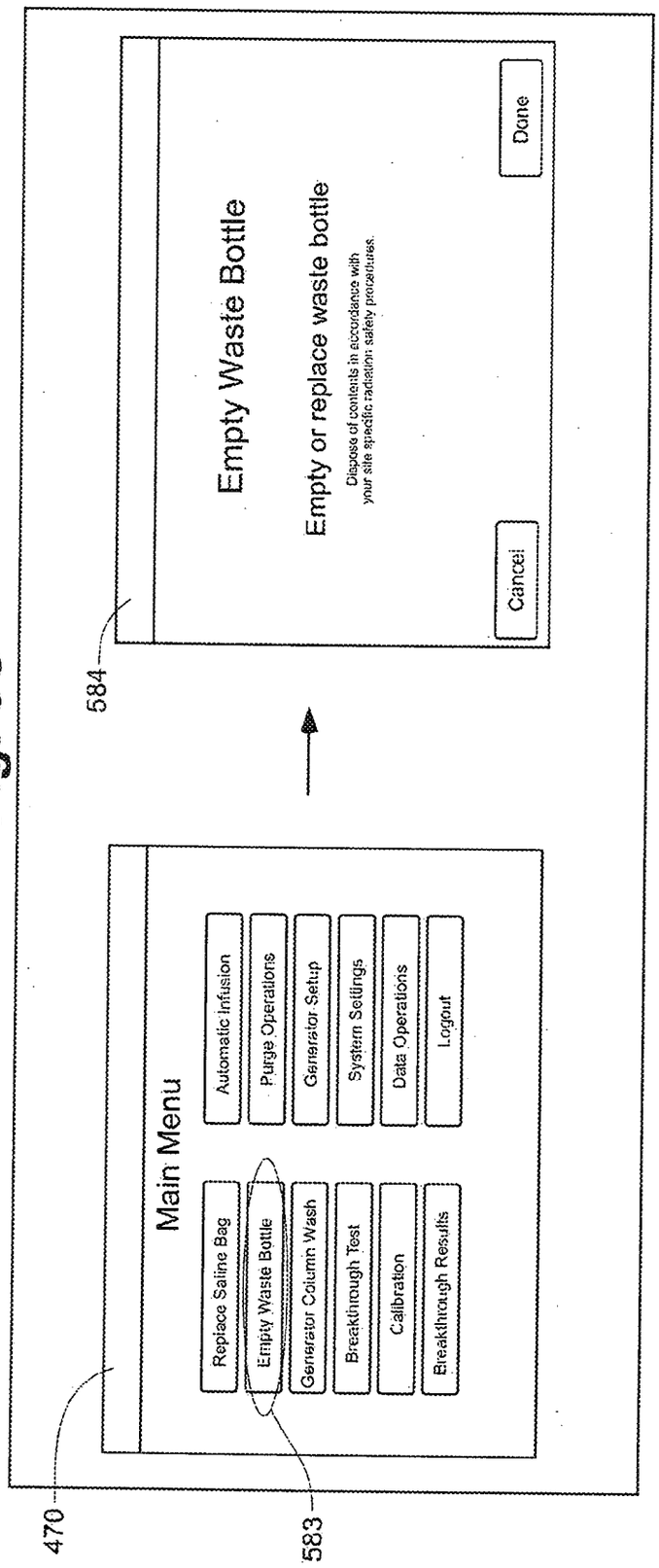


Fig. 5B



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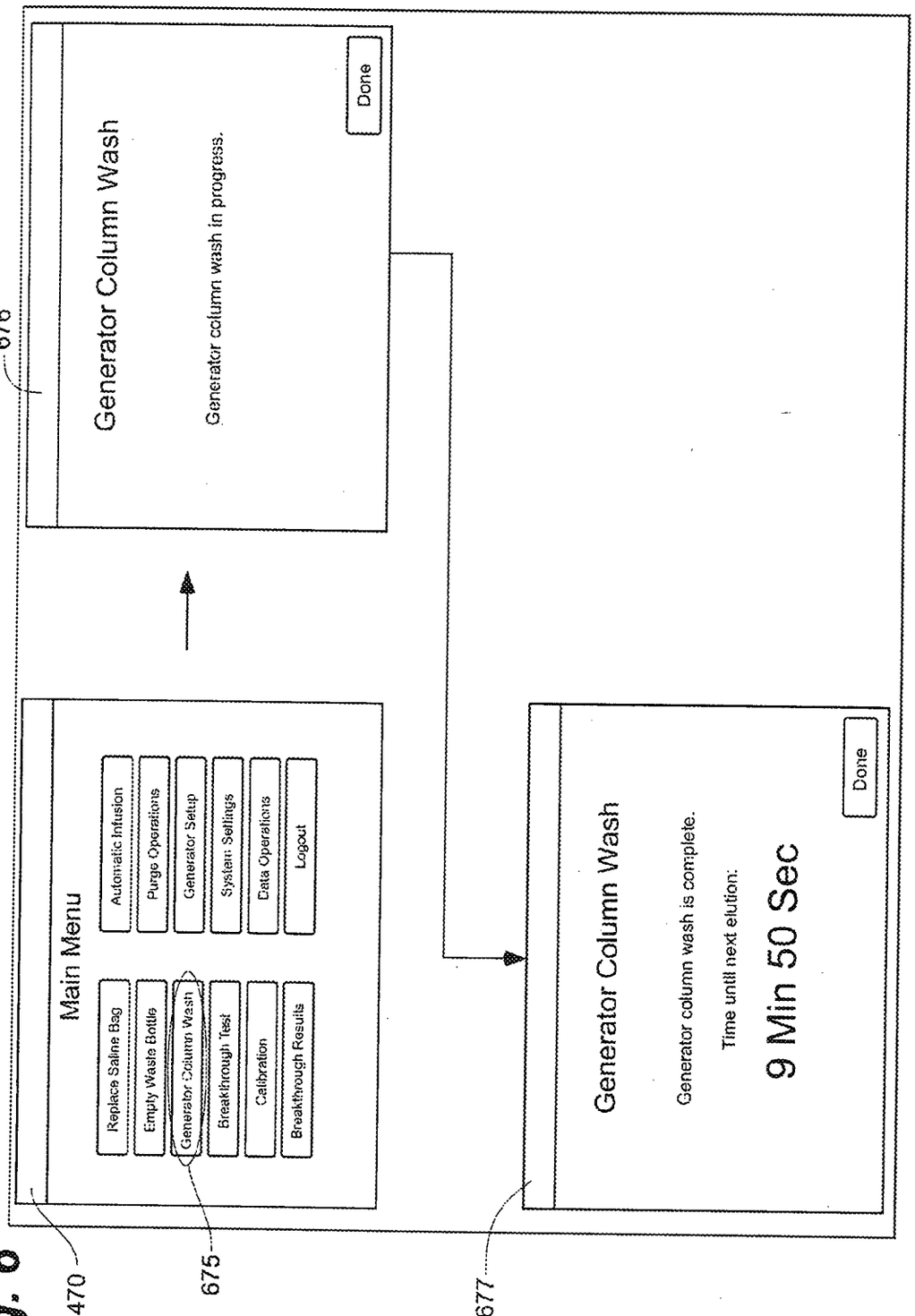
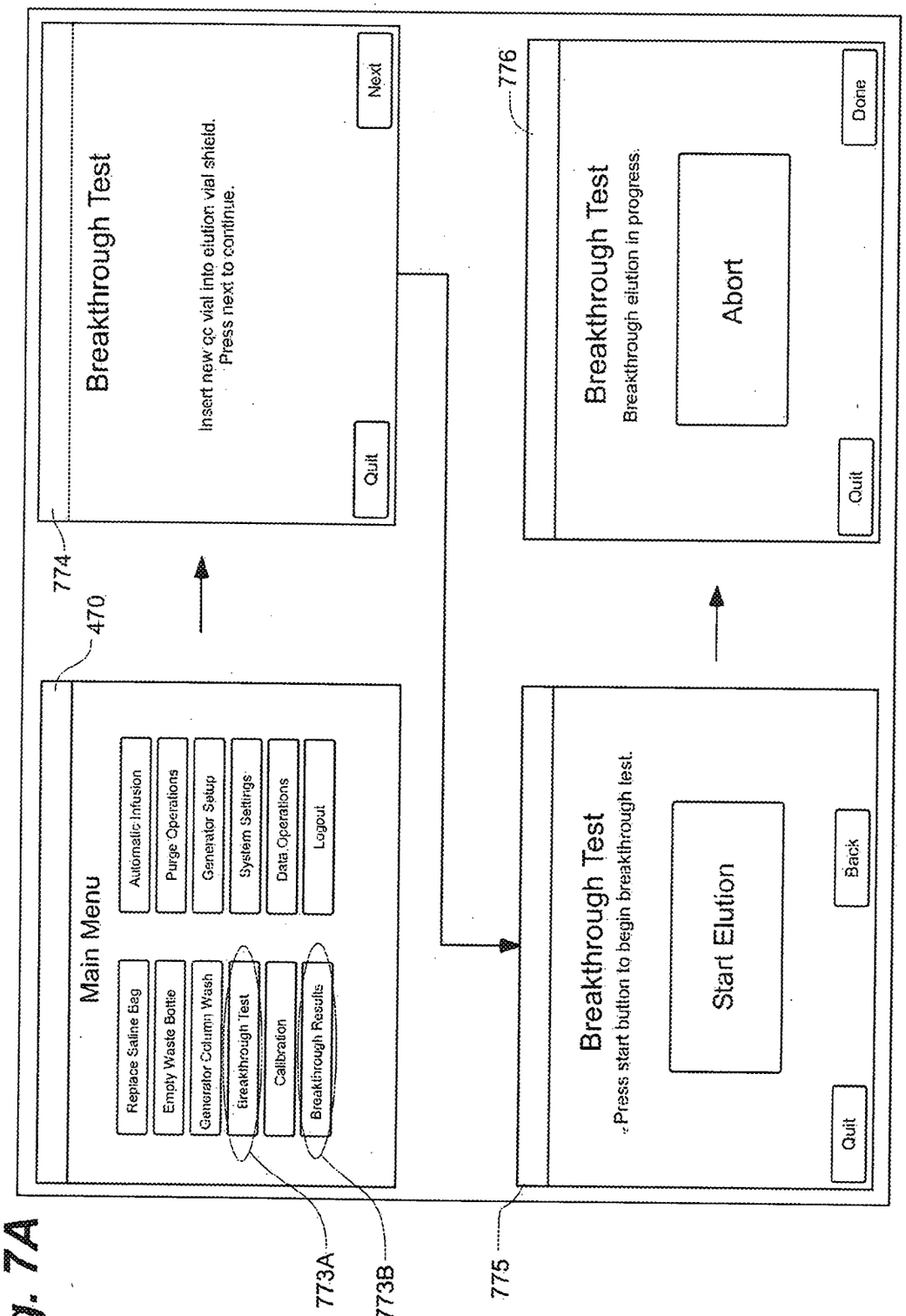


Fig. 6



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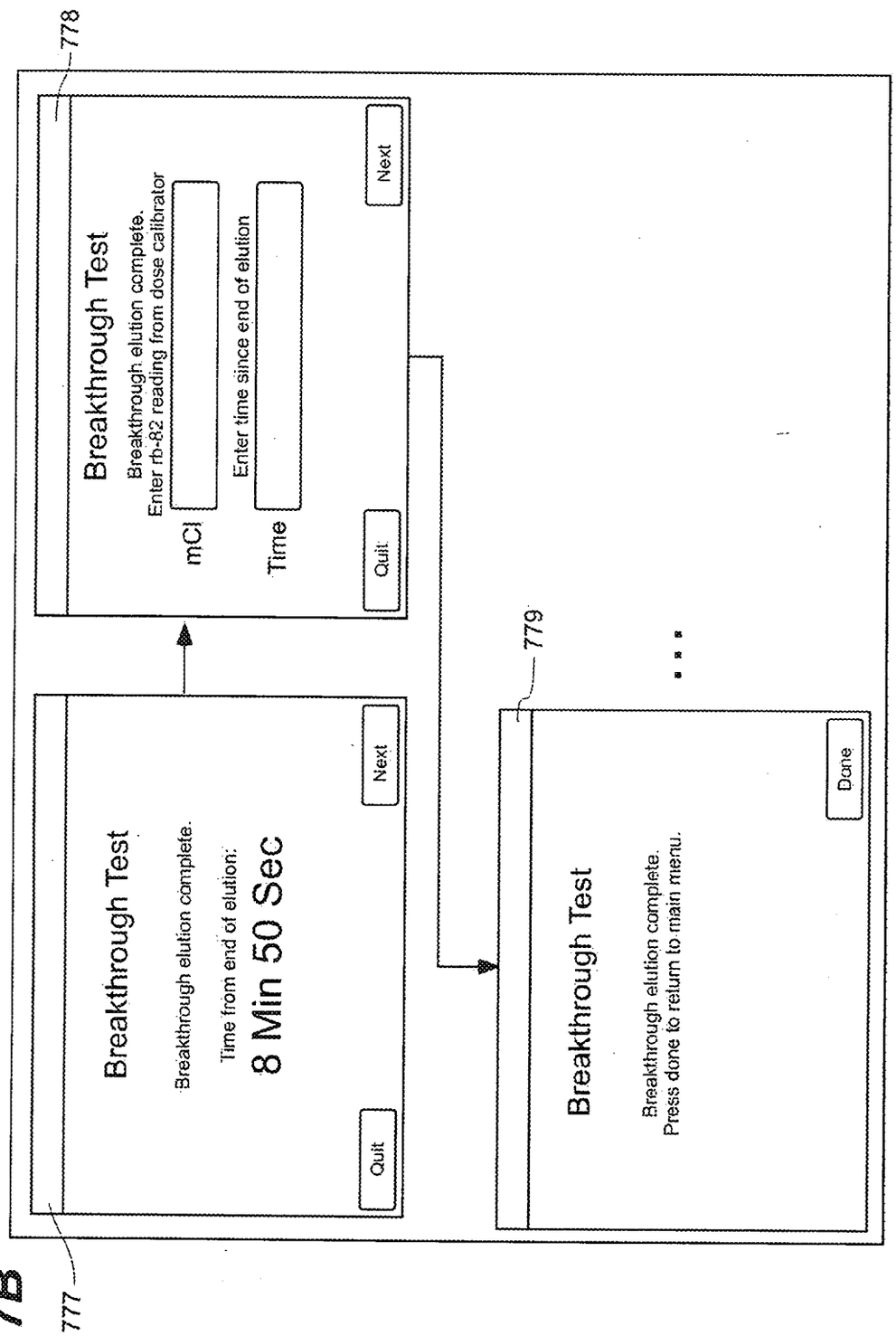


Fig. 7B

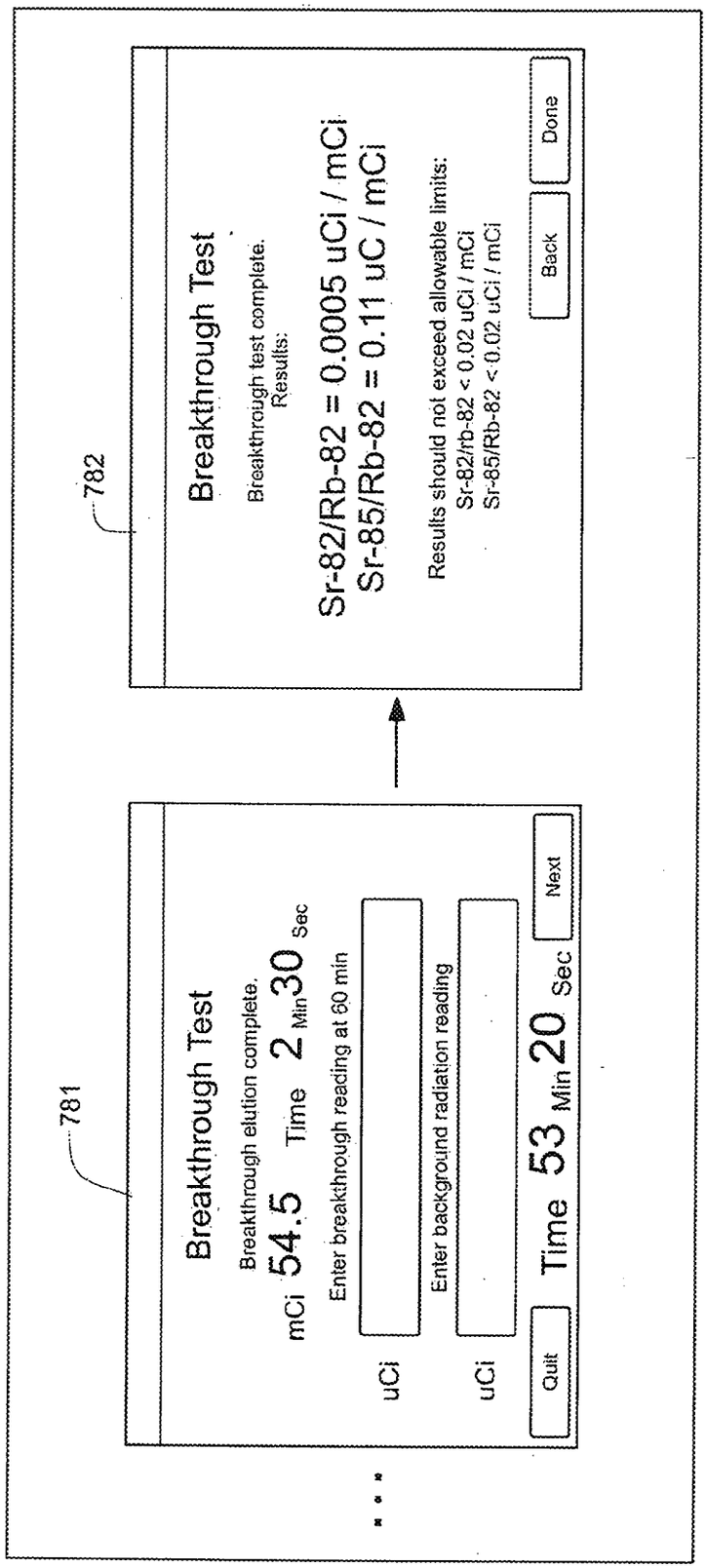


Fig. 7C

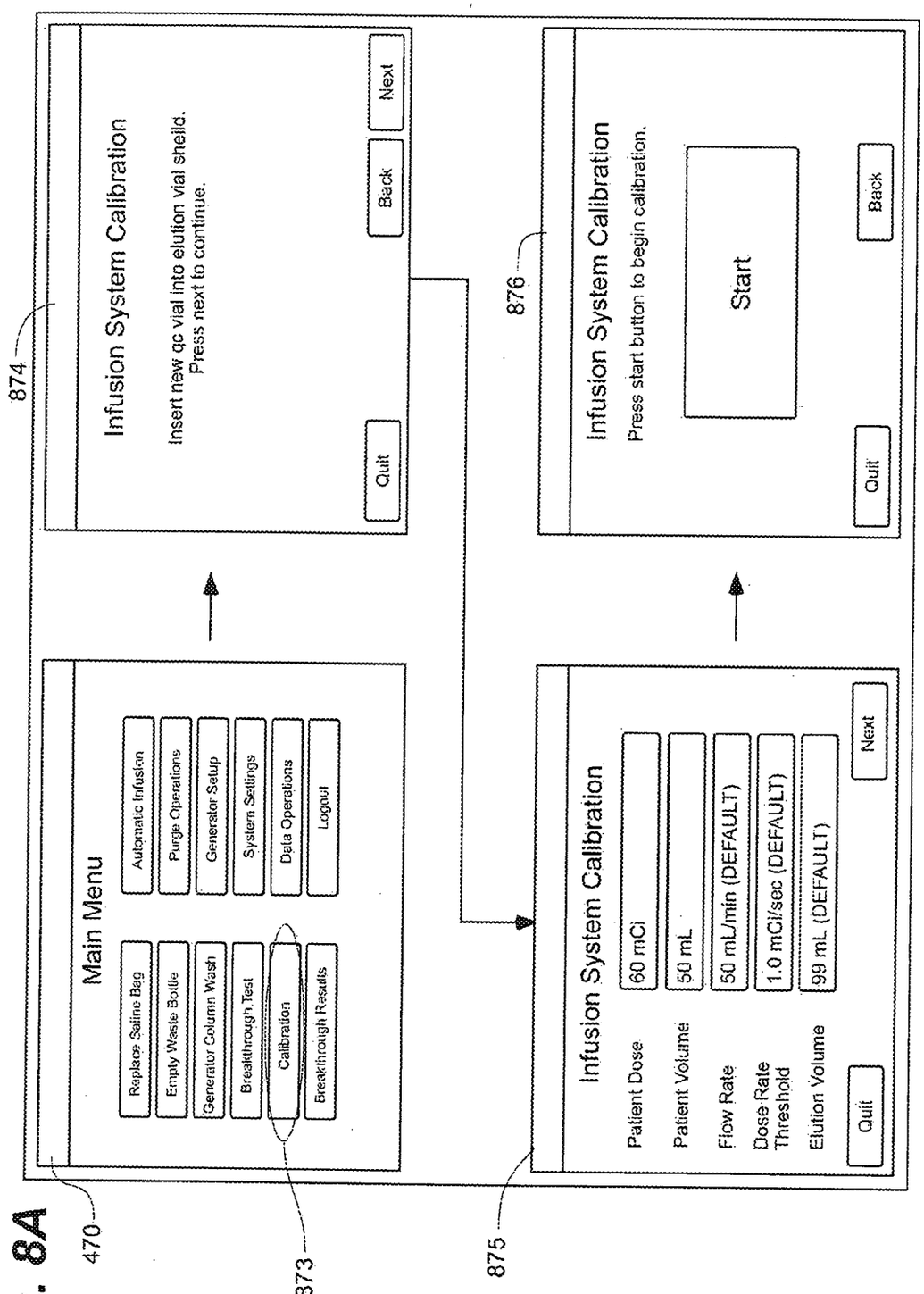


Fig. 8A

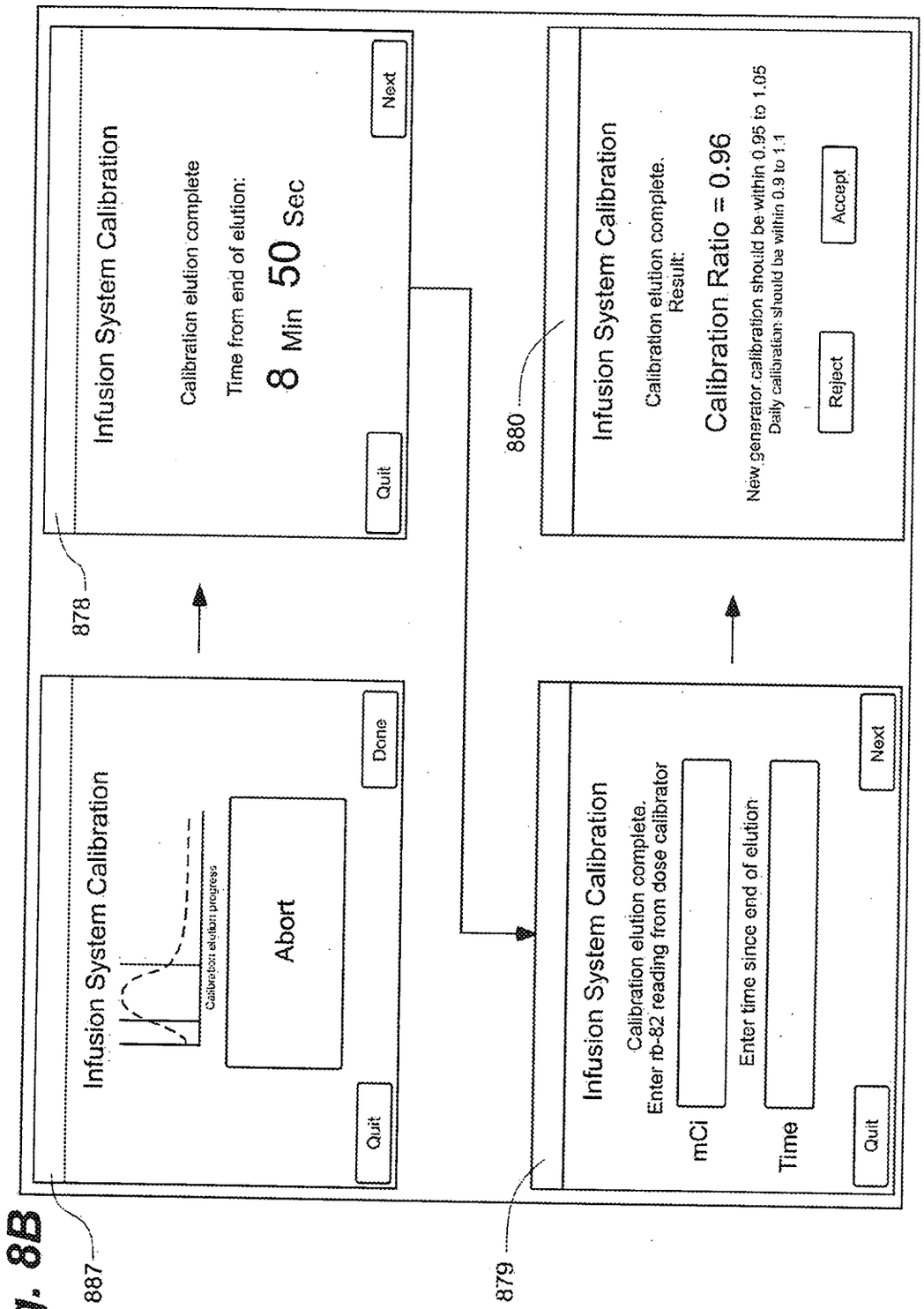


Fig. 8B

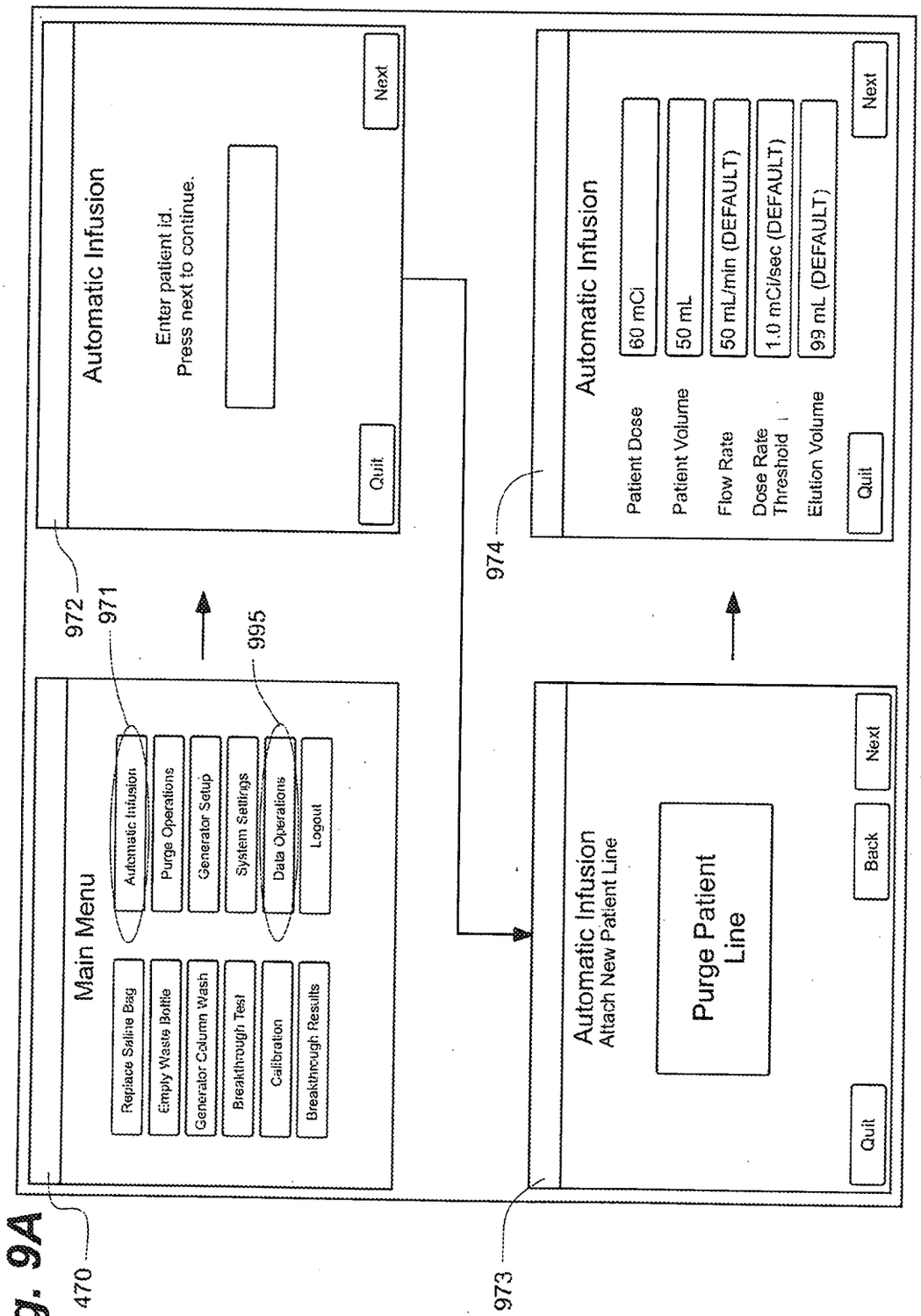


Fig. 9A

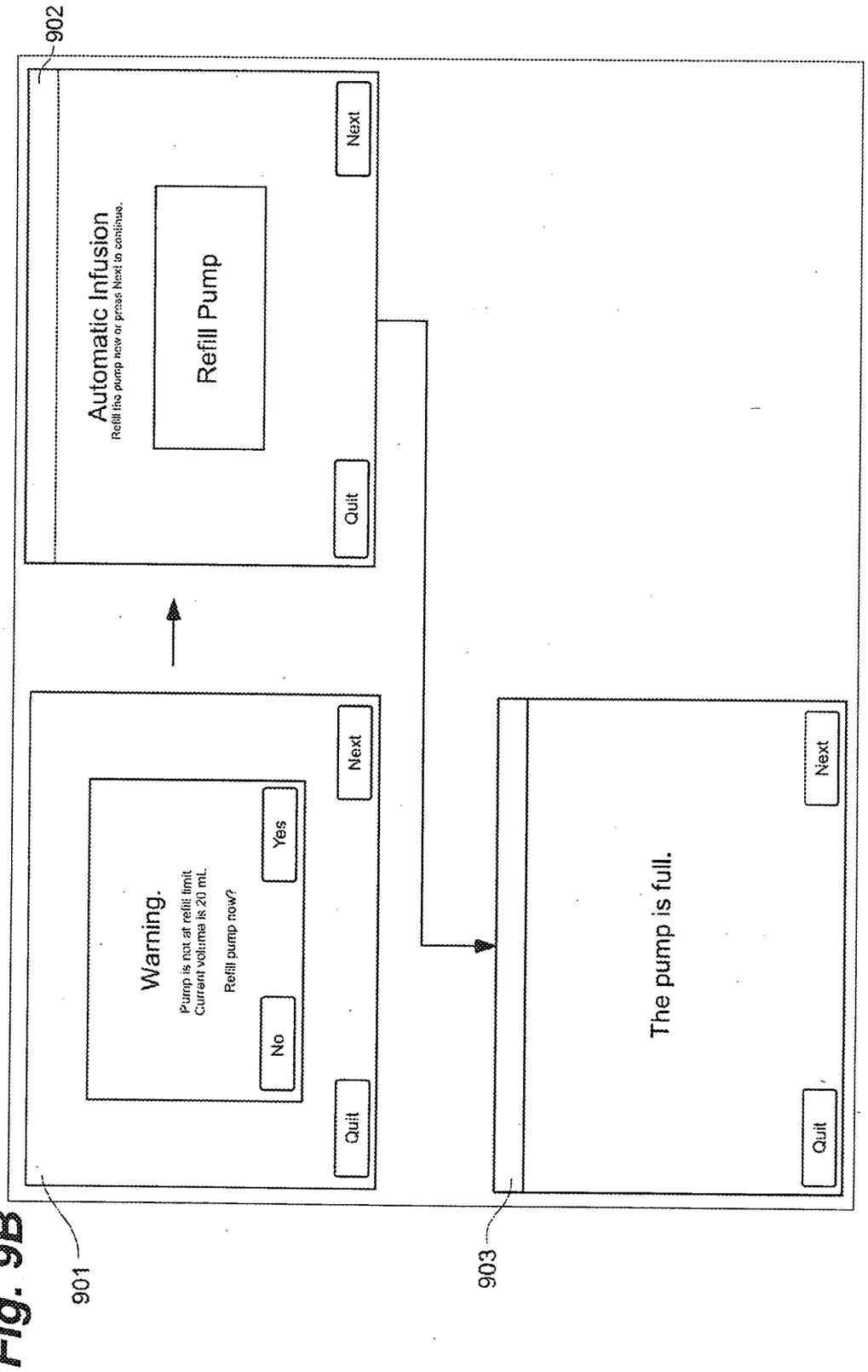


Fig. 9B

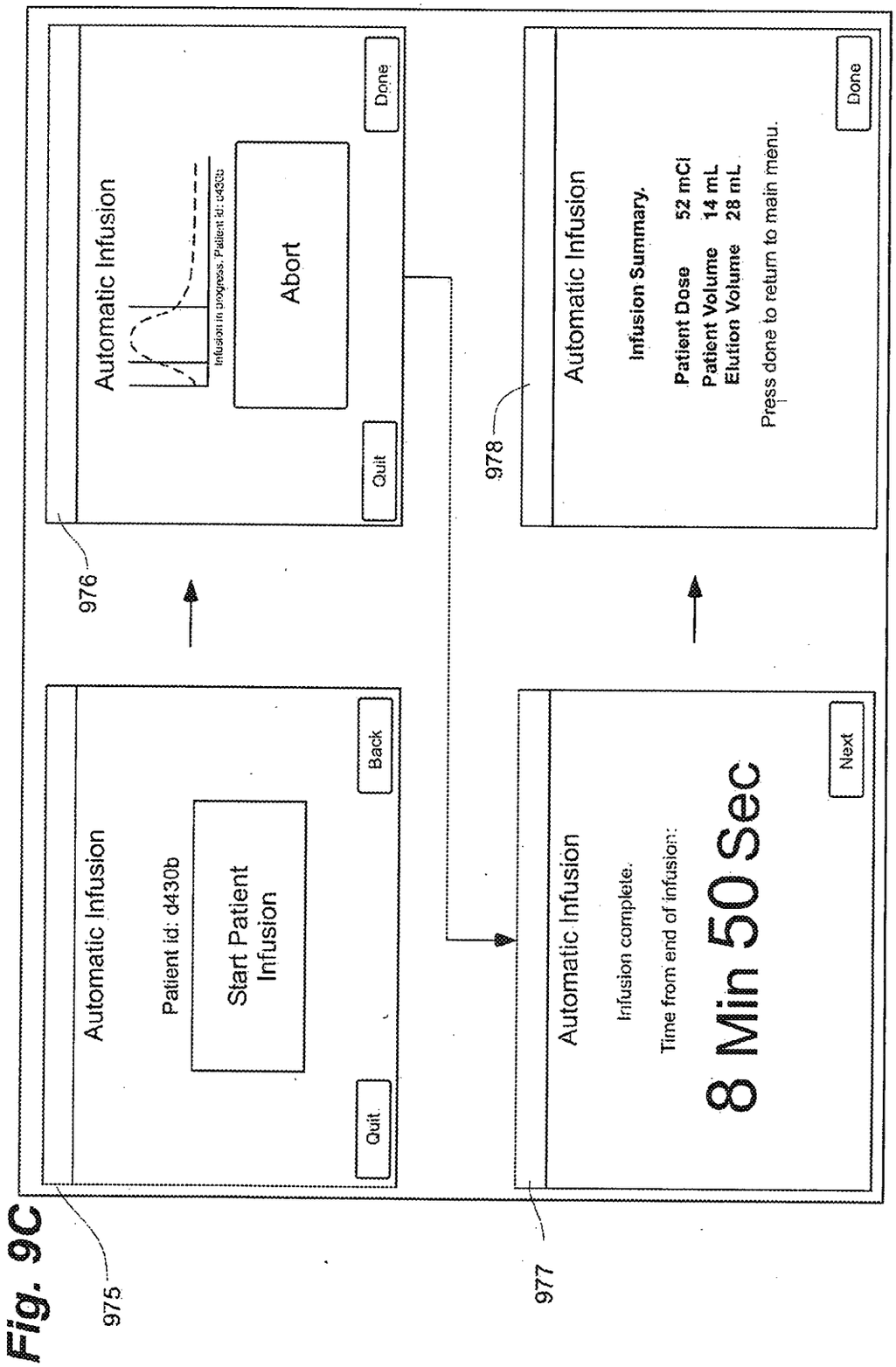


Fig. 9C

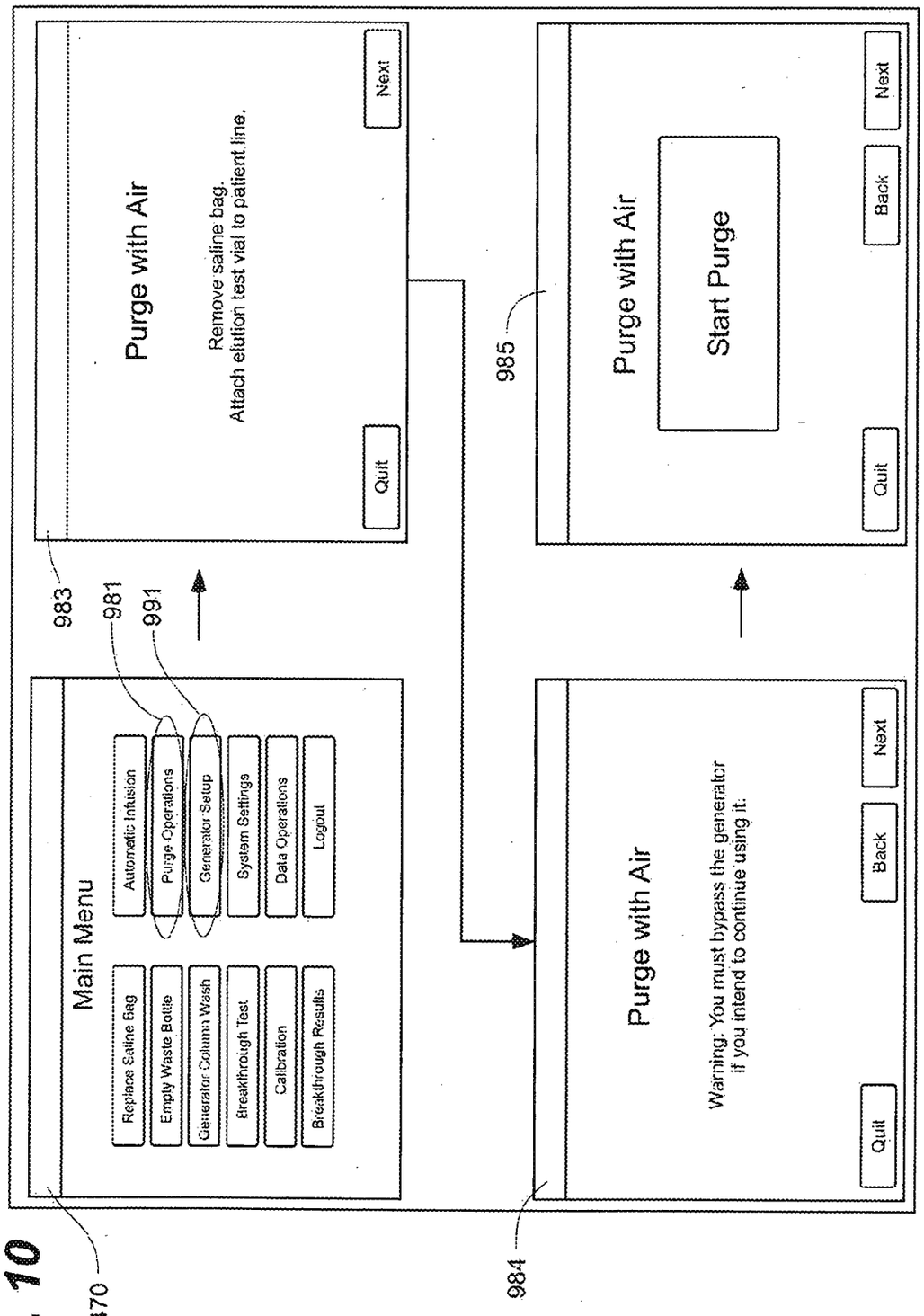
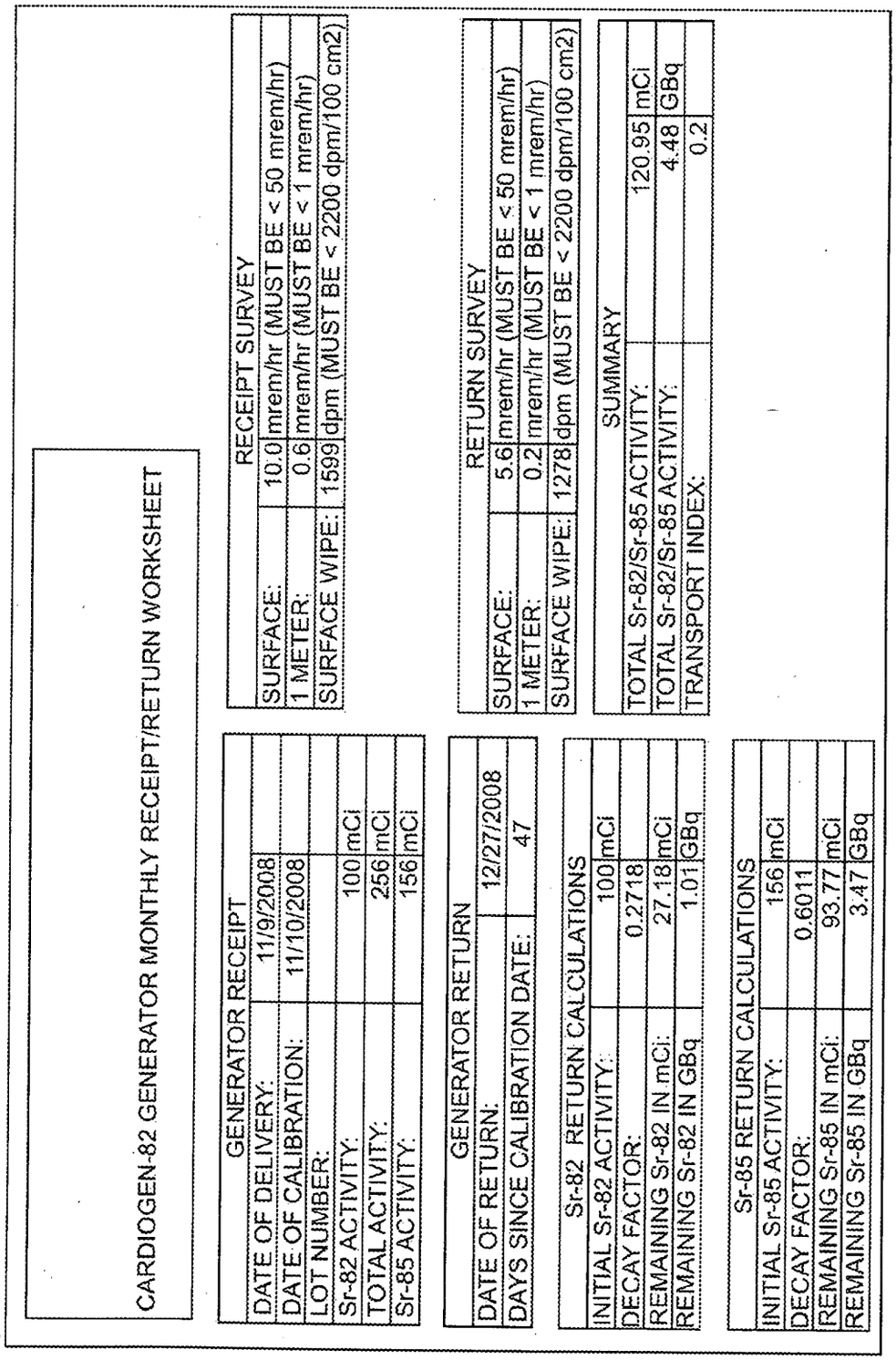


Fig. 10

Fig. 11



CARDIOGEN-82 GENERATOR MONTHLY RECEIPT/RETURN WORKSHEET

GENERATOR RECEIPT		
DATE OF DELIVERY:	11/9/2008	
DATE OF CALIBRATION:	11/10/2008	
LOT NUMBER:		
Sr-82 ACTIVITY:	100	mCi
TOTAL ACTIVITY:	256	mCi
Sr-85 ACTIVITY:	156	mCi

RECEIPT SURVEY		
SURFACE:	10.0	mrem/hr (MUST BE < 50 mrem/hr)
1 METER:	0.6	mrem/hr (MUST BE < 1 mrem/hr)
SURFACE WIPE:	1599	dpm (MUST BE < 2200 dpm/100 cm2)

GENERATOR RETURN	
DATE OF RETURN:	12/27/2008
DAYS SINCE CALIBRATION DATE:	47

RETURN SURVEY		
SURFACE:	5.6	mrem/hr (MUST BE < 50 mrem/hr)
1 METER:	0.2	mrem/hr (MUST BE < 1 mrem/hr)
SURFACE WIPE:	1278	dpm (MUST BE < 2200 dpm/100 cm2)

Sr-82 RETURN CALCULATIONS		
INITIAL Sr-82 ACTIVITY:	100	mCi
DECAY FACTOR:	0.2718	
REMAINING Sr-82 IN mCi:	27.18	mCi
REMAINING Sr-82 IN GBq	1.01	GBq

SUMMARY		
TOTAL Sr-82/Sr-85 ACTIVITY:	120.95	mCi
TOTAL Sr-82/Sr-85 ACTIVITY:	4.48	GBq
TRANSPORT INDEX:	0.2	

Sr-85 RETURN CALCULATIONS		
INITIAL Sr-85 ACTIVITY:	156	mCi
DECAY FACTOR:	0.6011	
REMAINING Sr-85 IN mCi:	93.77	mCi
REMAINING Sr-85 IN GBq	3.47	GBq

Fig. 12A

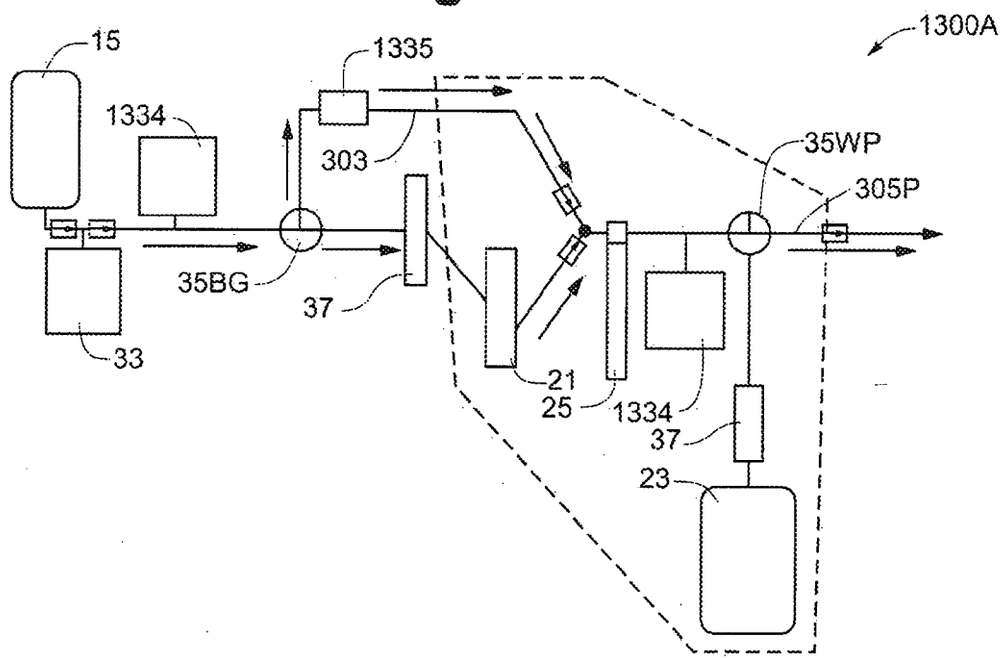


Fig. 12B

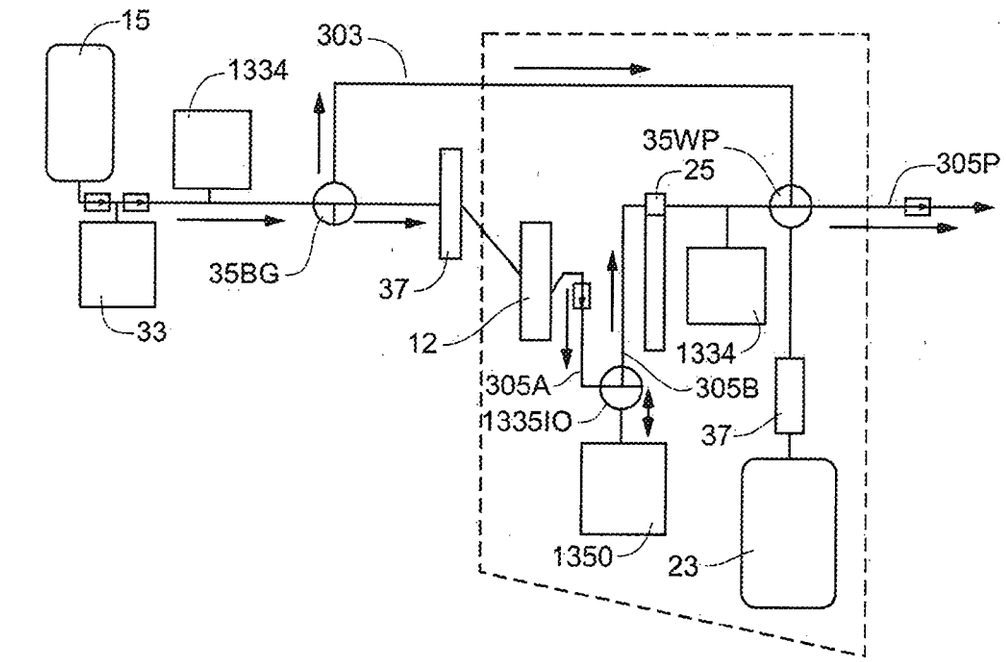
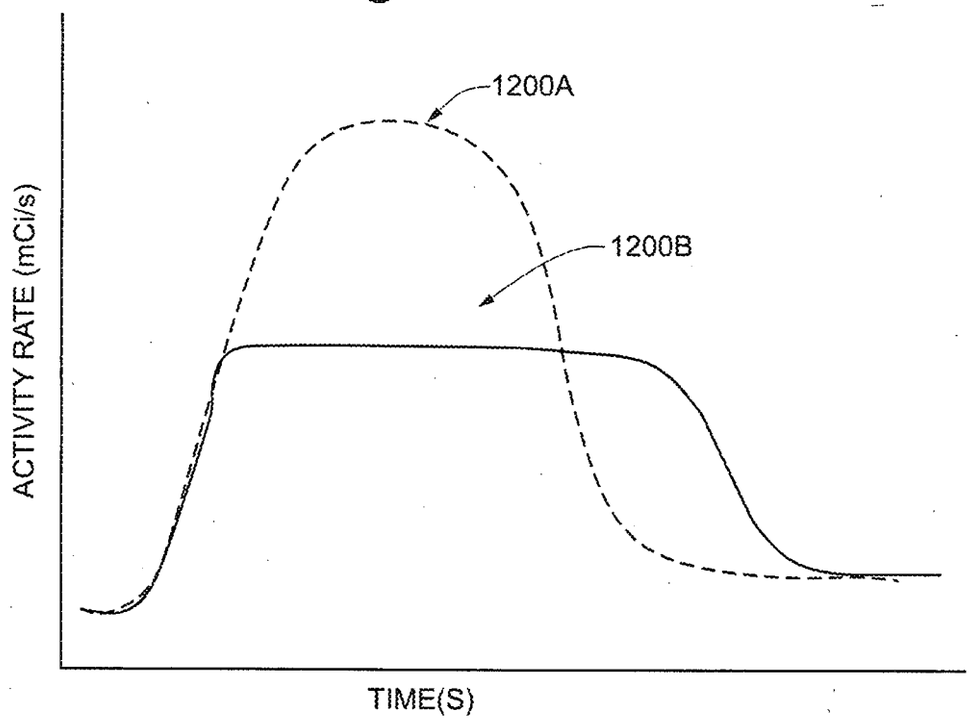


Fig. 12C



INTEGRATED STRONTIUM-RUBIDIUM RADIOISOTOPE INFUSION SYSTEMS

CROSS REFERENCE TO RELATED APPLICATIONS

This application is a continuation of U.S. patent application Ser. No. 15/389,200, filed Dec. 22, 2016, which is a continuation of U.S. patent application Ser. No. 12/808,467, filed Jun. 16, 2010, now U.S. Pat. No. 9,607,722, issued Mar. 28, 2017, which is a 371 National Stage of International Application No. PCT/US09/47031, filed Jun. 11, 2009, which in turn is a continuation of the following four patent applications: U.S. patent application Ser. No. 12/137,356, filed Jun. 11, 2008, now U.S. Pat. No. 8,317,674, issued Nov. 27, 2012; U.S. patent application Ser. No. 12/137,363, filed Jun. 11, 2008, now U.S. Pat. No. 7,862,534, issued Jan. 4, 2011; U.S. patent application Ser. No. 12/137,364, filed Jun. 11, 2008, now U.S. Pat. No. 9,597,053, issued Mar. 21, 2017; and U.S. patent application Ser. No. 12/137,377, filed Jun. 11, 2008, now U.S. Pat. No. 8,708,352, issued Apr. 29, 2014. The entire contents of all of these applications are incorporated herein by reference.

TECHNICAL FIELD

The present invention pertains to systems that generate and infuse radiopharmaceuticals, and, more particularly, to systems including computer-facilitated maintenance and/or operation.

BACKGROUND

Nuclear medicine employs radioactive material for therapy and diagnostic imaging. Positron emission tomography (PET) is one type of diagnostic imaging, which utilizes doses of radiopharmaceuticals, for example, generated by elution within a radioisotope generator, that are injected, or infused into a patient. The infused dose of radiopharmaceutical is absorbed by cells of a target organ, of the patient, and emits radiation, which is detected by a PET scanner, in order to generate an image of the organ. An example of a radioactive isotope, which may be used for PET, is Rubidium-82 (produced by the decay of Strontium-82); and an example of a radioisotope generator, which yields a saline solution of Rubidium-82, via elution, is the CardioGen-82® available from Bracco Diagnostics Inc. (Princeton, N.J.). A PET scanner in combination with infused doses of radiopharmaceuticals may also be employed to quantify blood flow rate, for example, through the coronary arteries of a patient.

Set up, maintenance and operational procedures for infusion systems that both generate and inject doses of radiopharmaceuticals are relatively involved in order to assure the safety and efficacy of each injected dose for the patient. Efficiency in carrying out these procedures is highly desirable for technical personnel, who work with these systems on a routine basis and would like to avoid unnecessarily prolonged exposure to radioactive radiation. Thus there is a need for new system configurations that facilitate more efficient set up, maintenance and operation.

BRIEF DESCRIPTION OF THE DRAWINGS

The following drawings are illustrative of particular embodiments of the present invention and therefore do not limit the scope of the invention. The drawings are not to scale (unless so stated) and are intended for use in conjunction with the explanations in the following detailed description. Embodiments of the present invention will hereinafter be described in conjunction with the appended drawings, wherein like numerals denote like elements.

FIG. **1A** is a first perspective view of an infusion system, according to some embodiments of the present invention.

FIG. **1B** is another perspective view of a portion of a cabinet structure of the system shown in FIG. **1A**, according to some embodiments.

FIG. **1C** is a second perspective view of the system shown in FIG. **1A**, according to some embodiments.

FIG. **1D** is a schematic of an infusion circuit, according to some embodiments of the present invention.

FIG. **1E** is a perspective view of exemplary sample vial shielding that may be employed in conjunction with the infusion system of FIG. **1A**.

FIG. **2A** is a perspective view of a shielding assembly for an infusion system, such as that shown in FIGS. **1A-C**, according to some embodiments of the present invention.

FIG. **2B** is a perspective view of a framework of the system, according to some embodiments, and FIG. **2B-1** is an enlarged detailed view of a component of the system, according to some embodiments.

FIG. **3A** is another perspective view of the shielding assembly shown in FIG. **2A**.

FIG. **3B** is a perspective view of the infusion circuit, shown in FIG. **1C**, configured and routed, according to some embodiments.

FIG. **3C** is a perspective view of a disposable infusion circuit subassembly, according to some embodiments.

FIG. **3D** is a frame for the subassembly shown in FIG. **3C**, according to some embodiments.

FIG. **4** is a main menu screen shot from an interface of a computer, which may be included in systems of the present invention, according to some embodiments.

FIG. **5A** is a schematic showing a first group of successive screen shots from the computer interface, according to some embodiments.

FIG. **5B** is a pair of screen shots from the computer interface, which provide indications related to eluant volume levels in a reservoir of the system, according to some embodiments.

FIG. **5C** is a schematic showing a second group of successive screen shots from the computer interface, according to some embodiments.

FIG. **6** is a schematic showing a third group of successive screen shots from the computer interface, according to some embodiments.

FIGS. **7A-C** are schematics showing a fourth group of successive screen shots from the computer interface, according to some embodiments.

FIGS. **8A-B** are schematics showing a fifth group of successive screen shots from the computer interface, according to some embodiments.

FIGS. **9A-C** are schematics showing a sixth group of successive screen shots from the computer interface, according to some embodiments.

FIG. **10** is a schematic showing a seventh group of successive screen shots from the computer interface, according to some embodiments.

FIG. **11** is an exemplary report which may be generated by the computer included in infusion systems, according to some embodiments.

FIGS. **12A-B** are schematics of alternative infusion circuits that may be employed by embodiments of the present invention.

FIG. 12C is a schematic illustrating exemplary activity profiles of injected doses of a radiopharmaceutical.

DETAILED DESCRIPTION

The following detailed description is exemplary in nature and is not intended to limit the scope, applicability, or configuration of the invention in any way. Rather, the following description provides practical illustrations for implementing exemplary embodiments. Utilizing the teaching provided herein, those skilled in the art will recognize that many of the examples have suitable alternatives that can be utilized.

FIG. **1A** is a first perspective view of an infusion system **10**, according to some embodiments of the present invention, wherein system **10** is shown supported by a cabinet structure, which includes a platform **113** (seen better in FIG. **2B**) and a shell **13**; shell **13** extends upward from a skirt **11**, that surrounds platform **113**, to surround an interior space in which a portion of infusion system **10** is contained (seen in FIG. **1C**). Shell **13** may be formed from panels of injection-molded polyurethane fitted together according to methods known to those skilled in the art. FIG. **1A** illustrates the cabinet structure of system **10** including a grip or handle **14**, which extends laterally from shell **13**, in proximity to an upper surface **131** thereof, and a post **142**, which extends upward from shell **13**, and to which a work surface, or tray **16** and a computer **17** are, preferably, attached, via an ergonomic, positionable mount. According to some embodiments, computer **17** is coupled to a controller of system **10**, which is mounted within the interior space surrounded by shell **13**; and, a monitor **172** of computer **17** not only displays indications of system operation for a user of system **10**, but also serves as a device for user input (e.g. touch screen input). However, according to alternate embodiments, another type of user input device, known to those skilled in the art, may be employed by computer **17**. Other types of user input devices may be included, for example, a keyboard, a series of control buttons or levers, a bar code reader (or other reader of encoded information), a scanner, a computer readable medium containing pertinent data, etc. The user input device may be mounted on the cabinet structure of system **10**, as shown, or may be tethered thereto; alternatively the user input device may be remote from system **10**, for example, located in a separate control room. According to some additional embodiments, another user input device, for example, in addition to a touch screen of computer **17**, may be remote from system **10** and used to start and stop infusions, as well as to monitor system operation both during quality control infusions and during patient infusions. Operation of system **10**, which is facilitated by computer **17**, will be described below, in conjunction with FIGS. **4-9C**.

FIG. **1A** further illustrates two pairs of wheels **121**, **122**, mounted to an underside of platform **113**, to make system **10** mobile; handle **14** is shown located at an elevation suitable for a person to grasp in order to maneuver system **10**, from one location to another, upon pairs of wheels **121**, **122**. According to some preferred embodiments, one or both pairs of wheels **121**, **122**, are casters, allowing for rotation in a horizontal plane (swivel), in order to provide additional flexibility for maneuvering system **10** in relatively tight spaces.

FIG. **1B** is a perspective view of a portion of system **10**, on a side **111** of the cabinet structure, which is in proximity to wheels **121**, **122**. FIG. **1B** illustrates a lever or pedal **125**, which is located for activation by a foot of the person, who grasps handle **14** to maneuver system **10**. In a neutral position, pedal **125** allows wheels **121**, **122** to rotate, and, if embodied as casters, to swivel freely. Pedal **125** may be depressed to a first position which prevents a swiveling of wheels **121**, **122**, according to those embodiments in which wheels **121**, **122** are casters, and may be further depressed to brake wheels **121**, **122** from rolling and swiveling, upon reaching a desired location. According to some embodiments, braking may be designed to slow system **10**, for example, when rolling down an incline, and, according to yet further embodiments, system **10** may include a motor to power movement thereof.

FIG. **1B** further illustrates: a rear access panel **174** of shell **13**, for example, providing access to circuit boards of the aforementioned controller contained within the interior space that is surrounded by shell **13**; an optional lock **184**, to secure panel **174**; a power jack **118**, for connecting system **10** to a power source; and a printer **117** for providing documentation of each patient infusion carried out by system **10**, and of system quality control test results. In some embodiments, system **10** may further include a power strip by which auxiliary equipment may be powered, and one or more additional electrical connectors, or ports (not shown), which are supported by platform **113** and may be integrated into shell **13**, for example, in proximity to jack **118** or printer **117**; these electrical connectors/ports allow system **10** to communicate with, other devices used for nuclear imaging procedures, for example, a PET scanner/camera, and/or for coupling to an intranet network, and/or to the internet, for example, to link up with software programs for various types of data analysis, and/or to link to computers of consulting clinicians/physicians, and/or to link into service providers and/or component suppliers data bases for enhanced maintenance and inventory management.

FIG. **1A** further illustrates upper surface **131** of shell **13** including several openings **133**, **135**, **139** formed therein. FIG. **1C** is a partially exploded perspective view of system **10**, wherein a removable access panel **132** is shown as a contoured portion of upper surface **131**, which, when exposed, by lifting away a bin **18**, that mates therewith, may be removed from another opening **137** formed in upper surface **131**. FIG. **1C** also provides a better view of another panel **134** which may be lifted away from opening **139**. According to the illustrated embodiment, openings **139** and **137** provide a user of system **10** with independent access to separate portions of infusion system **10**, which are contained within shell **13**, for example, to set up and maintain system **10**; and openings **133** and **135** provide passageways for tubing lines to pass through shell **13**. FIG. **1C** further illustrates an optional switch **102**, which in case of an emergency, may be activated to abort function of system **10**. With reference to FIGS. **1A** and **1C**, it may be appreciated that an arrangement of features formed in upper surface **131** of shell **13**, in conjunction with bin **18**, tray **16** and computer **17**, provide a relatively ergonomic and organized work area for technical personnel who operate system **10**.

Turning now to FIG. **1D**, a schematic of an infusion circuit **300**, which may be incorporated by system **10**, is shown. FIG. **1D** illustrates circuit **300** generally divided into a first part **300A**, which includes components mounted outside shell **13**, and a second part **300B**, which includes components mounted within the interior space surrounded by shell **13**. (Parts **300A** and **300B** are delineated by dotted lines in FIG. **1D**.) FIG. **1D** further illustrates second part **300B** of circuit **300** including a portion contained within a shielding assembly **200**, which is designated schematically as a dashed line. Some embodiments of shielding assembly

200 will be described in greater detail, in conjunction with FIGS. 2A-B and 3A-B, below.

According to the illustrated embodiment, circuit **300** includes: an eluant reservoir **15**, for example, a bag, bottle or other container, containing saline as the eluant, which is shown hanging from a post, or hanger **141** above upper surface **131** of shell **13** in FIG. 1A; a syringe pump **33**, for pumping the eluant from reservoir **15**, and a pressure syringe **34** (or other device or sensor), for monitoring pumping pressure; a filter **37**, which may also serve as a bubble trap, for the pumped eluant; a radioisotope generator **21**, through which the filtered eluant is pumped to create a radioactive eluate, for example an eluate carrying Rubidium-82 that is generated by the decay of Strontium-82, via elution, within a column of generator **21**; and an activity detector **25**, for measuring the activity of the eluate discharged from generator **21**, in order to provide feedback for directing the flow of the eluate, via a divergence valve **35**WP, either to a waste bottle **23** or through a patient line **305***p*, for example, to inject a dose of the radiopharmaceutical eluate into a patient. With reference back to FIG. 1A, patient line **305***p* is shown extending out from shell **13**, through opening **135**, to a distal end thereof, which, according to some embodiments, includes a filter. Patient line **305***p* may be coupled to another line that includes a patient injection needle (not shown). Alternatively, patient line **305***p* may be coupled to another line (not shown), which extends from a source of another active substance, for example, a stress agent; the other line is coupled to the line that includes the patient injection needle, in order to permit injection of the additional active substance.

FIG. 1D illustrates an eluant tubing line **301** coupled to reservoir **15** and to pump **33**, and, with reference to FIGS. 1A-B, it may be appreciated that opening **133** provides the passageway for tubing line **301** to enter the interior space surrounded by shell **13**. According to some preferred embodiments, opening **133** includes a grommet-type seal that prevents leakage of eluant, which may spill from reservoir **15**, into the interior space through opening **133**, while allowing a user to assemble tubing line **301** through opening **133**. Likewise opening **135**, which provides a passageway for patient line **305***p*, may include a grommet-type seal. According to some embodiments, shell **13** further supports holders to safely hold, for example, during transport of system **10**, portions of tubing lines that extend outward therefrom, for example, line **301** and/or line **305***p*.

FIG. 1D further illustrates another eluant tubing line **302** coupled to pump **33** and a divergence valve **35**BG, which may either direct pumped eluant through a tubing line **304**, to generator **21**, or direct the pumped eluant through a by-pass tubing line **303**, directly to patient line **305***p*. Divergence valve **35**BG, as well as divergence valve **35**WP, which directs eluate from an eluate tubing line **305** either to a waste line **305***w* or to patient line **305***p*, may each be automatically operated by a corresponding servomotor (not shown), coupled to the controller (not shown) of system **10**, which controller receives feedback from activity detector **25**. When system **10** is operating for automatic infusion, to deliver a dose of radiopharmaceutical to a patient, for example, Rubidium-82 for diagnostic imaging, divergence valve **35**BG is initially set to direct eluant to generator **21** and divergence valve **35**WP is set to direct eluate from the generator into waste bottle **23**, until activity detector **25** detects the desired activity of the eluate, at which time the feedback from activity detector **25** causes the controller to direct the corresponding servo-motor to re-set valve **35**WP for diverting the flow of eluate into patient line **305***p*.

According to some embodiments, once a prescribed volume of the eluate has passed through patient line **305***p*, the controller directs the corresponding servomotor to re-set divergence valve **35**BG for diverting the flow of eluant through by-pass line **303** and into patient line **305***p* in order to flush, or push any eluate remaining in patient line **305***p* into the patient. According to some embodiments, the controller may also direct the corresponding servomotor to re-set divergence valve **35**WP back toward waste bottle **23**, prior to the flush through by-pass line **303**, in order to prevent back flow of eluant, through line **305**, toward generator **21**. According to some preferred methods of operation, in certain situations, which will be described in greater detail below, eluant is pumped through by-pass line **303** immediately following the flow of the prescribed volume of eluate into patient line **305***p*, at a higher speed, in order to push the eluate in patient line **305**, thereby increasing a flow rate of the injection of eluate out from patient line **305***p* and into the patient. For example, once the prescribed volume of eluate has flowed into patient line **305***p*, and once divergence valve **35**BG is set to divert flow through by-pass line **303**, the speed of pump **33** may be adjusted to increase the flow rate of eluant to between approximately 70 mL/min and approximately 100 mL/min. This method for increasing the injection flow rate, is desirable, if a relatively high flow rate is desired for patient injection and a flow rate through generator **21** is limited, for example, to below approximately 70 mL/min, maximum (typical flow rate may be approximately 50 mL/min), in order to avoid an excessive back pressure created by the column of generator **21** in upstream portions of tubing circuit **300**; the excessive back pressure could damage filter **37** or otherwise impede flow through eluant tubing line **302**.

Although not shown in FIG. 1D, a number of sensors, for example, to measure pressure and/or flow velocity, may be incorporated into circuit **300**, according to some alternate embodiments, in order to monitor for flow anomalies, for example, related to occlusions/plugs in circuit **300** and/or leaks, and/or to provide feedback for control of an activity level of infused doses of radiopharmaceutical. Suitable sensors for any of the above purposes are known to those skilled in the art. Examples of flow meters that may be incorporated into circuit **300**, include the Innova-Sonic® Model 205 Transit-Time Ultrasonic Liquid Flow Meter that employs digital signal processing (available from Sierra Instruments, Inc.) and the Flocat LA10-C differential pressure flow meter. One example of a pressure sensor that may be employed to detect infusion circuit occlusions is the PRO/Pressure-Occlusion Detector (available from INTROTEK® of Edgewood, N.Y., a subsidiary of Magnetrol of Downers Grove, Ill.), which employs pulse-type ultrasound; this sensor detects subtle changes in positive and negative air pressure and produces a corresponding passive resistive output signal, which may be routed to the system controller and/or computer **17**. One or more of this type of sensor may be incorporated into infusion circuit **300** by simply fitting the sensor around any of the tubing lines of infusion circuit **300**; in fact, the PRO/Pressure-Occlusion Detector may be a suitable alternative to pressure syringe **34** of circuit **300**. Other types of pressure sensors, for example, similar to those known in the art for blood pressure monitoring, may be employed in infusion circuit **300**.

System **10** may further include sensors to detect fluid levels in eluant reservoir **15** and waste bottle **23**. Some examples of such sensors, which also employ the aforementioned pulse-type ultrasound, are the Drip Chamber Liquid Level Sensor and the CLD/Continuous Level Detector (both

available from INTROTEK®); alternatively, for example, an HPQ-T pipe mounted, self-contained liquid sensor (available from Yamatake Sensing Control, Ltd.), or an SL-630 Non-Invasive Disposable/Reusable Level Switch (available from Cosense, Inc. of Hauppauge, N.Y.) may be employed to detect the fluid levels. Alternately or in addition, system **10** can include additional radiation and/or moisture detection sensors, which can detect leaks. With reference to FIG. **1**D, such sensors are preferably located in proximity to fittings **311**, **312**, **313**, **314** and **315** that join portions of circuit **300** to one another. Some examples of leak detection sensors include, without limitation, those in the HPQ-D leak detection sensor family, and the HPF-D040 fiberoptic leak detector (all available from Yamatake Sensing Control, Ltd.). System **10** may further include additional sensors to detect contaminants and/or air bubbles within the tubing lines of circuit; examples of such sensors include the Point-air Detection (PAD) Sensor, that employs pulse-type ultrasound for air bubble detection, and the Blood Component Detector that employs optical sensing technology to perform Colorimetry-based fluid detection of unwanted elements in the tubing lines (both available from INTROTEK®).

According to those embodiments that include any of the above sensors, the sensors are linked into the controller of system **10** and/or computer **17**, either of which may provide a signal to a user of system **10**, when a flow anomaly is detected, and/or information to the user, via monitor **172**, concerning fluid levels, pressure and/or flow through circuit **300**. Computer **17** may be pre-programmed to display, for example, on monitor **172**, a graphic of infusion circuit **300** wherein each zone of the circuit, where an anomaly has been detected, is highlighted, and/or to provide guidance, to the system user, for correcting the anomaly. It should be noted that the alternative infusion circuits illustrated in FIGS. **12**A-B, which will be described below, may also include any or all of these types of sensors.

With further reference to FIG. **1**D, it may be appreciated that shielding assembly **200** encloses those portions of circuit **300** from which radioactive radiation may emanate, with the exception of that portion of patient line **305***p*, which must extend out from shielding assembly **200** in order to be coupled to the patient for injection, or in order to be coupled to shielded sample vials, as will be described below. Thus, technical personnel, who operate system **10**, are protected from radiation by shielding assembly **200**, except at those times when an infusion is taking place, or when quality control tests require collection of eluate into sample vials. During infusions and quality control test sample collection, all technical personnel are typically in another room, or otherwise distanced from system **10**, in order to avoid exposure to radiation during the infusion, and, according to some preferred embodiments of the present invention, system **10** includes at least one means for informing technical personnel that an infusion is about to take place or is taking place. With reference back to FIGS. **1**A and **1**C, system **10** is shown including a light projector **100**, mounted on post **142**. According to the illustrated embodiment, projector **100**, projects a light signal upward, for maximum visibility, when pump **33** is pumping eluant and elution is taking place within generator **21**, or at all times when pump **33** is pumping eluant. According to some embodiments, the light signal flashes on and off when the eluate is being diverted from generator **21** into waste bottle **23**, and the light signal shines steadily when the eluate is being diverted through patient line **305***p*, or visa versa. According to other embodiments, a projector **100** shines a light having a first color, to indicate that eluate is being diverted to waste bottle **23**, and then shines a light having a second, different color, to indicate that eluate is being directed to patient line **305***p* for infusion. Light projector **100** may further project a more rapidly flashing light, for example, for approximately five seconds, once a peak bolus of radioactivity is detected in the eluate, to provide further information to technical personnel. Alternative means of informing technical personnel that an infusion is taking place may also be incorporated by system **10**, for example, including audible alarms or other types of visible or readable signals that are apparent at a distance from system **10**, including in the control room.

It should be noted that, according to alternate embodiments, system **10** includes an 'on board' dose calibrator for quality control tests, and circuit **300** is expanded to include elements for an automated collection of eluate samples for activity measurements, via the on board dose calibrator. According to a first set of these alternate embodiments, a sample collection reservoir is integrated into circuit **300**, downstream of divergence valve **35**WP and in communication with tubing line **305**P, in order to receive quality control test samples of eluate, via tubing line **305**P, and both the reservoir and the dose calibrator are located in a separate shielded well. According to a second set of these alternate embodiments, waste bottle **23** is configured to receive the quality control test samples of eluate, via tubing line **305**W, and a dose calibrator is integrated into shielding assembly **200**. Quality control procedures will be described in greater detail below, in conjunction with FIGS. **6**-**8**B.

When maintenance of system **10** requires the emptying waste bottle **23**, relatively easy access to waste bottle **23** is provided through opening **139** in top surface **131** of shell **13**. It should be noted that technical personnel are preferably trained to empty waste bottle **23** at times when the eluate, contained in waste bottle **23**, has decayed sufficiently to ensure that the radioactivity thereof has fallen below a threshold to be safe. Opening **139** is preferably located at an elevation of between approximately 2 feet and approximately 3 feet; for example, opening **139** may be at an elevation of approximately 24 inches, with respect to a lower surface of platform **113**, or at an elevation of approximately 32 inches, with respect to a ground surface upon which wheels **121**, **122** rest. According to the illustrated embodiment, opening **139** is accessed by lifting panel **134**; just within opening **139**, a shielded lid or door **223** (FIG. **2**A) may be lifted away from a compartment of shielding assembly **200** that contains waste bottle **23**. With further reference to FIG. **1**C, it may be appreciated that opening **137** provides access to other portions of circuit **300** for additional maintenance procedures, such as changing out generator **21** and/or other components of circuit **300**, as will be described below.

For those embodiments of system **10** in which automated quality control tests are performed and/or when system **10** is employed for relatively high volume operation, management of waste may become burdensome, even though access to waste bottle **23** is greatly facilitated, as described above. Thus, in order to facilitate waste management, some embodiments of system **10** may employ a separation system to separate salts, including radioactive elements, from water, for example, via evaporation or reverse osmosis. In an evaporation type system, the water component of the waste is evaporated, while in a reverse osmosis type system the water is separated from the salts, and, then, once confirmed to be non-radioactive, via a radiation detector, is piped to a drain. According to some other embodiments, circuit **300** may be configured so that the waste may be used to purge air from the tubing lines thereof and/or to perform the bypass

flush that was described above, preferably after the radioactivity of the waste drops below a critical threshold.

FIGS. **1**A and **1**C further illustrate a pair of relatively shallow external recesses **190**, which are formed in upper surface **131** of shell **13**, for example, in order to catch any spills from the infusion system; one of recesses **190** is shown located in proximity to post, or hanger **141**, which holds reservoir **15**, and in proximity to opening **133**, through which tubing line **301** passes. Another recess **192** is shown formed in upper surface **131**; a width and depth of recess **192** may accommodate storage of technical documentation associated with infusion system **10**, for example, a technical manual and/or maintenance records, or printouts from printer **117** (FIG. **1**B). With reference to FIG. **1**C, upper surface **131** of shell **13** is shown to also include additional recesses **101**, which are each sized to hold a shielded test vial, which contains samples from infusion system **10**, for example, for breakthrough testing and/or calibration, which will be described in greater detail, below. An exemplary test vial shield is shown in FIG. **1**E. The test vial shield of FIG. **1**E is preferably formed from Tungsten rather than lead, for example, to reduce exposure to lead, for improved shielding, and to reduce the weight of the shield. FIG. **1**E illustrates the test vial shield including a handle to simplify manipulation thereof, but alternative configurations of test vial shields have no handle—for these a sling, or strap, may be employed for handling.

Additional receptacles **180** are shown formed in bin **18**, on either side of a handle **182**, which facilitates removal of bin **18** away from shell **13**. Technical personnel may, thus, conveniently transport bin **18** to a storage area for a collection of supplies, for example, sharps, gloves, tubing lines, etc. . . . , into one or more receptacles **180** thereof, and/or to a waste container where separate receptacles **180** of bin **18** may be emptied of waste, such as packaging for the aforementioned supplies, for example, deposited therein during infusion procedures. According to some embodiments, one or more additional receptacles are formed in one or more disposal containers, for example, to contain sharps and/or radioactive waste (other than that contained in waste bottle **23**), which may be integrated into bin **18**, or otherwise fitted into, or attached to shell **13**, separate from bin **18**.

FIG. **2**A is a perspective view of shielding assembly **200**, according to some embodiments of the present invention. With reference to FIGS. **1**C and **2**A, together, it may be appreciated that opening **137**, in upper surface **131** of shell **13**, provides access to a lid or door **221** of a sidewall **201** of shielding assembly **200**, which sidewall **201** encloses a compartment sized to contain a radioisotope generator of system **10**, for example, generator **21**, previously introduced. It should be noted that, according to alternate embodiments, the compartment enclosed by sidewall **201** is large enough to hold more than one generator, for example, to increase system operating efficiency for relatively high volume operation. In some of these alternate embodiments, tubing lines **304** and **305** are each branched for parallel flow through the multiple generators, in which case divergence valves may be employed to alternate the flow through the generators, one at a time. In others of these alternate embodiments, the multiple generators are connected in series between tubing line **304** and tubing line **305**. In addition, a reservoir for accumulating eluate may be included in circuit **300**, downstream of the generators and upstream of divergence valve **35** WP, in conjunction with a second pump, in some cases. Embodiments including multiple generators and/or an eluate reservoir and second pump can be employed to better manage an activity level of each dose, or patient injection, for example, as described below, in conjunction with FIGS. **12**A-B.

According to the embodiment illustrated in FIG. **2**A, opening **137** and door **221** are located at a lower elevation, for example, with respect to platform **113**, than are opening **139** and lid **223**, which provide access to the compartment being formed by a sidewall **203** of shielding assembly **200** to contain waste bottle **23**, as previously described. When panel **132** is separated from shell **13**, and door **221** opened, generator **21** may be lifted out from an opening **231** (FIG. **3**A) which mates with door **221** of sidewall **201**. A weight of generator **21**, which includes its own shielding, may be between approximately 23 and approximately 25 pounds, thus, according to some preferred embodiments of the present invention, the elevation of each of openings **137** and **231**, with respect to the lowermost portion of the cabinet structure, is between approximately 1 foot and approximately 2 feet, in order to facilitate an ergonomic stance for technical personnel to lift generator **21** out from the compartment. According to an exemplary embodiment, when shielding assembly **200** is contained in the cabinet structure of FIG. **1**A, openings **137** and **231** are located at an elevation of approximately 12 inches, with respect to the lower surface of platform **113**, or at an elevation of approximately 19 inches, with respect to the ground surface upon which wheels **121**, **122** rest. FIG. **1**C further illustrates access panel **132** including a security lock **138**, which mates with a framework **19** of system **10**, shown in FIG. **2**B, in order to limit access to generator **21**.

FIGS. **1**C and **2**A further illustrate a lid or a door **225** of another sidewall **205** (FIG. **3**A) of shielding assembly **200**, which encloses another compartment that is accessible through opening **137** of shell **13**, and which is located adjacent the compartment enclosed by sidewall **201**. Each of doors **221**, **225** are shown being attached by a corresponding hinge H, and another door **227** is shown attached to sidewall **203** by another hinge H. FIG. **2**A illustrates each of lid **223** and doors **221**, **225**, **227** including a handle **232**, **212**, **252** and **272**, respectively, for moving lid **223** and doors **221**, **225**, **227**, in order to provide access to the corresponding compartments, which can be seen in FIGS. **3**A-B. FIG. **2**A further illustrates optional thumb screws **290**, one securing lid **223** to sidewall **203** and another securing door **221** to sidewall **201**, or other means for securing the doors, which are known to those skilled in the art, may be incorporated. Each sidewall **201**, **203**, **205** and the corresponding lid/door **223**, **221**, **225**, **227** thereof may be individually cast from 3% antimony lead, or from other known shielding materials, and then assembled together according to methods known to those skilled in the art.

According to the illustrated embodiment, doors **221**, **225** are hinged to open in an upward direction, per arrows D and C, and, with reference back to FIG. **1**C, a latch component **191** is provided to hold each of doors **221**, **225** in an opened position, thereby, preventing doors **221**, **225** from falling closed, which could pinch/crush fingers of technical personnel and/or tubing lines of circuit **300**, when in the midst of a maintenance procedure. FIG. **2**B is a perspective view of framework **19** of the cabinet structure of system **10**, according to some embodiments, to which latch component **191** is mounted; FIG. **2**B-**1** is an enlarged detailed view of latch component **191**, according to some embodiments. FIG. **2**B illustrates latch component **191** including a first pin **193**, corresponding to door **225**, and a second pin **195**, corresponding to door **221**; each pin **193**, **195** includes a lever end **193**A, **193**B, respectively, and a holding end **193**B, **195**B, respectively. An edge of each door **221**, **225**, upon opening

of doors **221**, **225**, may push past the holding end **195**B, **193**B of the corresponding pin **195**, **193**, in a first direction, per arrow F, and then may rest against a respective side **S95** and **S93** of each end **195**B, **193**B, until the corresponding lever end **195**A, **193**A is rotated in a counter-clockwise direction, per arrow cc, thereby moving the corresponding holding end **193**B, **195**B to make way for the closing of doors **221**, **225**. Doors **221**, **225** being held by latch component **191** in an open position may be seen in FIG. **3**A.

With further reference to FIG. **2**A, according to some preferred embodiments of the present invention, an edge of door **225** overlaps door **221** to prevent door **221** from being opened, per arrow D, if door **225** is not opened, per arrow C; and an edge of door **227** overlaps an edge of door **225** to prevent door **225** from being opened if door **227** is not opened, per arrow B; and an edge of lid **223** overlaps door **227** to prevent door **227** from being opened if lid **223** is not opened, per arrow A. Thus, access to the compartment enclosed by sidewall **201** and containing generator **21** is only systematically allowed through a sequential opening of lid **223** and doors **227**, **225**, **221**, since, when generator **21** is replaced it is typically desirable to also replace those portions of circuit **300** which are shielded behind lid **223** and doors **227**, **225**. The routing of these portions of circuit **300** will be described in conjunction with FIGS. **3**A-C.

FIG. **3**A is another perspective view of shielding assembly **200**, according to some embodiments of the present invention. In FIG. **3**A, lid **223** and doors **221**, **225**, and **227** are opened to provide a view into openings **233**, **235** and **231** of sidewalls **203**, **205** and **201**, respectively, and into a passageway **207**, which is formed in sidewall **203**, opposite the compartment, which contains waste bottle **23**. Passageway **207** is shown extending vertically along sidewall **203** and having a grooved extension **213** formed in a perimeter surface of opening **233**. An optional retaining member **237**, for example, formed from an elongate strip of resilient plastic having a generally c-shape cross-section, is shown being mounted along a length of passageway **207** to hold lines **305***w* and **305***p* in place within passageway **207**. FIG. **3**A further illustrates a pair of passageways **251***b* and **251***g*, which are formed as grooves in a portion of sidewall **205**, and another pair of passageways **215***i* and **215***o*, which are formed as grooves in a portion of sidewall **201**. A routing of portions of tubing circuit **300** (FIG. **1**D) through passageways **207**, **251***b*, **251***c*, **215***i* and **215***o* is shown in FIG. **3**B.

FIG. **3**B illustrates tubing line **304** being routed through passageways **251***g* and **215***i*, eluate tubing line **305** being routed through passageway **215***o*, and both waste line **305***w* and patient line **305***p* being routed along passageway **207**. Waste line **305***w* further extends through grooved extension **213** to waste bottle **23**, and patient line **305***p* further extends outward from shielding assembly **200**, for example, to extend out through opening **135** in upper surface **131** of shell **13** (FIG. **1**A). According to the illustrated embodiment, each passageway formed in shielding assembly **200**, by being accessible along a length thereof, can facilitate a relatively easy routing of the corresponding tubing line therethrough, when the corresponding lid/door is open, and a depth of each passageway prevents pinching and/or crushing of the corresponding tubing line routed therethrough, when the corresponding lid/door is closed down thereover. With further reference to FIGS. **3**A-B, it may be appreciated that the compartment formed by sidewall **201** may have a shape matching an exterior contour of generator **21**, such that generator **21** is 'keyed' to the compartment, for example, to prevent installation of an improper generator into system **10**, and/or to facilitate the proper orientation of generator **21** within the compartment for the proper routing of tubing lines. Alternately, or in addition, according to alternate embodiments, if system **10** includes a reader of encoded information in communication with computer **17**, a unique identification and/or data associated with each generator may be provided, for example, in a bar code label or a radiofrequency identification (RFID) tag that is attached to each generator, so that the reader may transfer the information to computer **17**, when a generator is installed, in order to either enable system operation or to provide an indication to the user that an incorrect generator has been installed. Of course a user of system **10** may, alternately, manually enter information, that is provided on a generator label or marking, into computer **17**, in order to either enable system **10**, or to receive feedback from computer **17** that the incorrect generator is installed.

FIG. **3**A further illustrates sidewall **205** including a valve actuator receptacle **253**, into which divergence valve **35**WP is mounted, to be controlled by one of the servomotors (not shown) of system **10**, and an opening **325** for activity detector **25**. Activity detector **25** is mounted in a shielded well **255** that extends downward from opening **325** (shown in FIG. **3**B), and, with reference to FIG. **3**B, tubing line **305** passes over opening **325** so that detector **25** can detect an activity of the eluate, which passes therethrough. According to some embodiments, the positioning, within the compartment enclosed by sidewall **205**, of the components of the portion of infusion circuit **300** which are shown routed therein, is facilitated by providing the components mounted in a frame **39** as a disposable subassembly **390**, an embodiment of which is illustrated by FIGS. **3**C-D.

FIG. **3**C is a perspective view of subassembly **390**, and FIG. **3**D is a perspective view of frame **39**. According to the embodiment illustrated by FIG. **3**D, frame **39** is formed from mating trays **39**A, **39**B, for example, formed from a thermoformed plastic, which fit together to capture, therebetween, and hold, in fixed relation to a perimeter edge of frame **39**, divergence valve **35**WP and portions of eluant tubing line **304**, by-pass tubing line **303**, eluate tubing line **305**, waste line **305***w* and patient line **305***p*. FIG. **3**C illustrates the perimeter edge divided into a first side **391**, a second side **392**, opposite first side **391**, a third side **393**, extending between first and second sides **391**, **392**, and a fourth side **394**, opposite third side **393**. Although FIG. **3**D shows trays **39**A, **39**B individually formed for fitting together, according to alternate embodiments, mating trays of frame **39** may be parts of a continuous sheet of plastic folded over on itself.

According to the illustrated embodiment, an end **404**A, of eluant line **304**, and an end **403**, of by-pass line **303** extend from third side **393** of frame **39** to couple with divergence valve **35**BG and an upstream section of eluant tubing line **302**. FIG. **3**C further illustrates an opposite end **404**B of eluant line extending from first side **391** of frame **39**, alongside a similarly extending end **405** of eluate line **305**, and ends **406** and **407** of patient line **305***p* and waste line **305***w*, respectively, extending from second side **392** of frame **39**. Although ends **406**, **407** are shown extending upward from tray **39***a*, as they would within shielding assembly **200**, it should be appreciated that the tubing lines of circuit **300** are preferably flexible and would drop down under their own weight rather than extending upward, as shown, if not supported. Referring back to FIG. **1**D, in conjunction with FIG. **3**C, it can be seen that the aforementioned fittings are provided for coupling subassembly **390** into circuit **300**: first fitting **311** couples the section of eluant line **302** to filter **37**; second fitting **312** couples eluant line **304** to an inlet port of

generator **21**; third fitting **313**, which may incorporate a check valve, couples eluate line **305** to an outlet port of generator **21**; fourth fitting **314** couples waste line **305***w* to waste bottle **23**; and fifth fitting **315** couples patient line **305***p* to an extension thereof, which extends outside shell **13** (designated by the dotted line). Each of the fittings **311**, **312**, **313**, **314**, **315** may be of the Luer type, may be a type suitable for relatively high pressure applications, or may be any other suitable type that is known to those skilled in the art.

As previously mentioned, when generator **21** is replaced, it is typically desirable to also replace those portions of circuit **300** which are shielded behind lid **223** and doors **227**, **225**, and, in those instances wherein system **10** is moved to a new site each day, these portions may be replaced daily. Thus, according to the illustrated embodiment, these portions are conveniently held together by frame **39**, as subassembly **390**, in order to facilitate relatively speedy removal and replacement, while assuring a proper assembly orientation, via registration with features formed in sidewall **205** (FIG. **3**A), for example: registration of divergence valve **35**WP with valve actuator receptacle **253**, registration of tubing line ends **403** and **404**A with passageways **251***b* and **251***g*, respectively, registration of tubing line ends **404**B and **405** with passageways **215***i* and **215***o*, respectively, and registration of tubing line ends **406** and **407** with passageway **207**.

With further reference to FIG. **3**B, other portions of tubing circuit **300** are shown. FIG. **3**B illustrates eluant tubing line **301** extending from reservoir **15**, outside of shell **13** (FIG. **1**A), to syringe pump **33**, which is mounted to an actuating platform **433**. According to the illustrated embodiment, platform **433** is actuated by another servomotor (not shown) of system **10**, which is controlled by the controller and computer **17** of system **10**, to cause a plunger of pump **33** to move, per arrow I, so as to draw in eluant, from reservoir **15**, through tubing line **301**, and then to cause the plunger to move in the opposite direction so as to pump the eluant, through tubing line **302**, to either generator **21** or to by-pass line **303**. Although the illustrated embodiment includes syringe pump **33**, other suitable pumps, known to those skilled in the art, may be substituted for pump **33**, in order to draw eluant from reservoir **15** and to pump the eluant throughout circuit **300**. Although not shown, it should be appreciated that divergence valve **35**BG is fitted into another valve actuating receptacle mounted within shell **13** and coupled to yet another servomotor (not shown) of system **10**.

FIG. **3**B further illustrates a filter holder **317** that is mounted alongside an interior surface of shell **13** to hold filter **37** (FIG. **1**D) of tubing line **302**. Filter holder **317**, like frame **39** for subassembly **390**, may be formed from a thermoformed plastic sheet; holder **317** may have a clam-shell structure to enclose filter **37** in an interior space, yet allow tubing line **302**, on either side of filter **37**, to extend out from the interior space, in between opposing sides of the clam-shell structure. Holder **317** is shown including an appendage **307** for hanging holder **317** from a structure (not shown) inside shell **13**.

Turning now to FIGS. **4**-**9**C details concerning computer-facilitated operation of system **10** will be described, according to some embodiments of the present invention. As previously mentioned, and with reference back to FIG. **1**A, computer **17** of system **10** includes monitor **172**, which, preferably, not only displays indications of system operation to inform a user of system **10**, but is also configured as a touch screen to receive input from the user. It should be understood that computer **17** is coupled to the controller of system **10**, which may be mounted within the interior space surrounded by shell **13**. Although FIG. **1**A shows computer **17** mounted to post **142** of system **10**, for direct hardwiring to the controller of system **10**, according to some alternate embodiments, computer **17** is coupled to the controller via a flexible lead that allows computer **17** to be positioned somewhat remotely from those portions of system **10**, from which radioactive radiation may emanate; or, according to some other embodiments, computer **17** is wirelessly coupled, for example, via two-way telemetry, to the controller of system **10**, for even greater flexibility in positioning computer **17**, so that the operation of system **10** may be monitored and controlled remotely, away from radioactive radiation.

According to some preferred embodiments, computer **17** is pre-programmed to guide the user, via monitor **172**, through procedures necessary to maintain system **10**, to perform quality control tests on system **10**, and to operate system **10** for patient infusions, as well as to interact with the user, via the touch-screen capability of monitor **172**, according to preferred embodiments, in order to track volumes of eluant and eluate contained within system **10**, to track a time from completion of each elution performed by system **10**, to calculate one or more system parameters for the quality control tests, and to perform various data operations. Computer **17** may also be pre-programmed to interact with the controller of system **10** in order to keep a running tally or count of elutions per unit time, for a given generator employed by the system, and may further categorize each of the counted elutions, for example, as being generated either as a sample, for quality control testing, or as a dose, for patient injection. The elution count and categorization, along with measurements made on each sample or dose, for example, activity level, volume, flow rate, etc. . . . , may be maintained in a stored record on computer **17**. All or a portion of this stored information can be compiled in a report, to be printed locally, and/or to be electronically transferred to a remote location, for example, via an internet connection to technical support personnel, suppliers, service providers, etc. . . . , as previously described. Computer **17** may further interact with the user and/or a reader of encoded information, for example, a bar code reader or a radiofrequency identification (RFID) tag reader, to store and organize product information collected from product labels/tags, thereby facilitating inventory control, and/or confirming that the proper components, for example, of the tubing circuit, and/or accessories, and/or solutions are being used in the system.

It should be understood that screen shots shown in FIGS. **4**-**9**C are exemplary in nature and are presented to provide an outline of some methods of the present invention in which computer **17** facilitates the aforementioned procedures, without limiting the scope of the invention to any particular computer interface format. Computer **17** may also include a pre-programmed user manual, which may be viewed on monitor **172**, either independent of system operation or in conjunction with system operation, for example, via pop-up help screens. Although the English language is employed in the screen shots of FIGS. **4**-**9**C, it should be understood that, according to some embodiments, computer **17** is pre-programmed to provide guidance in multiple languages.

FIG. **4** is a screen shot of a main menu **470**, which is presented by computer **17** on monitor **172**, according to some embodiments. Main menu **470** includes a listing of each computer-facilitated operation that may be selected by the user, once the user has logged on. According to some

multi-lingual embodiments, computer **17** presents a list of languages from which the user may select, prior to presenting main menu **470**.

FIG. **5**A is a schematic showing a series of screen shots which includes a log in screen **570**. According to some embodiments, when the user touch-selects the data entry fields of screen **570** or **571**, or of any of the other screens presented herein, below, a virtual keyboard is displayed for touch-select data entry into the selected data entry field; alternately, computer **17** may be augmented with another type of device for user data entry, examples of which include, without limitation, a peripheral keyboard device, a storage medium (i.e. disk) reader, a scanner, a bar code reader (or other reader of encoded information), a hand control (i.e. mouse, joy stick, etc. . . .). Although not shown, according to some embodiments, screen **570** may further include another data entry field in which the user is required to enter a license key related to the generator employed by system **10** in order to enable operation of system **10**; the key may be time sensitive, related to generator contract terms. Of course any number of log in requirements may be employed, according to various embodiments, and may be presented on multiple sequentially appearing screens rather than on a single log in screen.

After the user enters the appropriate information into data entry fields of log in screen **570**, computer **17** presents a request for the user to confirm the volume of eluant that is within reservoir **15** (e.g. saline in saline bag), via a screen **571**, and then brings up main menu **470**. If the user determines that the volume of eluant/saline is insufficient, the user selects a menu item **573**, to replace the saline bag. If system **10** includes an encoded information reader, such as a bar code or RFID tag reader, confirmation that the selected reservoir is proper, i.e., contains the proper saline solution, may be carried out by computer **17**, prior to connecting the reservoir into circuit **300**, by processing information read from a label/tag attached to the reservoir. Alternatively, or in addition, tubing line **301** of circuit **300** may be provided with a connector which only mates with the proper type of reservoir **15**. According to some embodiments, system **10** may further include an osmolarity or charge detector, which is located just downstream of reservoir **15** and is linked to computer **17**, so that an error message may be presented on monitor **172** stating that the wrong osmolarity or charge is detected in the eluant supplied by reservoir, indicating an improper solution. One example of a charge detector that may be employed by system **10** is the SciCon™ Conductivity Sensor (available from SciLog, Inc. of Middleton, Wis.).

Once the reservoir/saline bag is successfully replaced, computer **17** prompts the user to enter a quantity of saline contained by the new saline bag, via a screen **574**. Alternately, if system **10** includes the aforementioned reader, and the saline bag includes a tag by which volume information is provided, the reader may automatically transfer the quantity information to computer **17**. Thus, computer **17** uses either the confirmed eluant/saline volume, via screen **571**, or the newly entered eluant/saline volume as a baseline from which to track depletion of reservoir volume, via activations of pump **33**, in the operation of system **10**. With reference to FIG. **5**B, during the operation of system **10**, when computer **17** detects that the eluant reservoir/saline bag has been depleted to a predetermined volume threshold, computer **17** warns the user, via a screen **577**. If the user has disregarded screen **577** and continues to deplete the saline bag, computer **17** detects when the saline bag is empty and provides indication of the same to the user, via a screen **578**. To replenish the reservoir/saline bag, the user may either refill the reservoir/bag or replace the empty reservoir/bag with a full reservoir/bag. According to some embodiments, system **10** automatically precludes any further operation of the system until the reservoir is replenished. It should be noted that, as previously mentioned, system **10** can include a fluid level sensor coupled to the eluant reservoir in order to detect when the level of saline drops below a certain level.

In addition to tracking the volume of eluant in reservoir **15**, computer **17** also tracks a volume of the eluate which is discharged from generator **21** into waste bottle **23**. With reference to FIG. **5**C, an item **583** is provided in main menu **470**, to be selected by the user when the user empties waste bottle **23**. When the user selects item **583**, computer **17** presents a screen **584**, by which the user may effectively command computer **17** to set a waste bottle level indicator to zero, once the user has emptied waste bottle **23**. Typically, the user, when powering up system **10** for operation, each day, will either empty waste bottle **23**, or confirm that waste bottle **23** was emptied at the end of operation the previous day, and utilize screen **584** to set the waste bottle level indicator to zero. Thus, computer **17**, can track the filling of waste bottle **23** via monitoring of the operation of pump **33** and divergence valve **35**WP, and provide an indication to the user when waste bottle **23** needs to be emptied, for example, via presentation of screen **584**, in order to warn the user that, unless emptied, the waste bottle will overflow. According to some embodiments, system **10** automatically precludes any further operation of the system until the waste bottle is emptied. According to some alternative embodiments, a fluid level sensor may be coupled to waste bottle **23**, for example, as mentioned above in conjunction with FIG. **1**D, in order to automatically detect when waste bottle **23** is filled to a predetermined level and to provide, via computer **17**, an indication to the user that waste bottle **23** needs to be emptied and/or to automatically preclude operation of system **10** until the waste bottle is emptied.

In addition to the above maintenance steps related to eluant and eluate volumes of system **10**, the user of system **10** will typically perform quality control tests each day, prior to any patient infusions. With reference to FIG. **6**, according to preferred methods, prior to performing the quality control tests (outlined in conjunction with FIGS. **7**A-C and **8**A-B), the user may select an item **675** from main menu **470**, in order to direct system **10** to wash the column of generator **21**. During the generator column wash, which is performed by pumping a predetermined volume of eluant, for example, approximately 50 milliliters, through generator **21** and into waste bottle **23**, computer **17** provides an indication, via a screen **676**, that the wash is in progress. Also, during the generator column wash, the system may provide a signal to indicate that eluate it being diverted to waste bottle **23**, for example, light projector **100** (FIG. **1**C) may project a flashing light signal, as previously described.

FIG. **6** further illustrates a screen **677**, which is presented by computer **17** upon completion of the column wash, and which provides an indication of a time lapse since the completion of the wash, in terms of a time countdown, until a subsequent elution process may be effectively carried out. While screen **677** is displayed, system **10** may be refilling, from reservoir **15**, pump **33**, which has a capacity of approximately 55 milliliters, according to some embodiments. According to some preferred embodiments of the present invention, computer **17** starts a timer once any elution process is completed and informs the user of the time lapse, either in terms of the time countdown (screen **677**), or in terms of a time from completion of the elution, for

example, as will be described in conjunction with FIG. 7B. According to an exemplary embodiment, wherein generator **21** is the CardioGen-82® that yields a saline solution of Rubidium-82, produced by the decay of Strontium-82, via the elution, a time required between two effective elution processes is approximately 10 minutes.

Once the appropriate amount of time has lapsed, after the elution process of generator column wash, a first quality control test may be performed. With reference to FIG. 7A, the user may select, from main menu **470**, an item **773**A, which directs computer **17** to begin a sequence for breakthrough testing. According to some embodiments, in conjunction with the selection of item **773**A, the user attaches a needle to an end of patient line **305***p* and inserts the needle into to a test vial, for the collection of an eluate sample therefrom, and, according to FIG. 7A, computer **17** presents a screen **774**, which instructs the user to insert the test vial into a vial shield, which may be held in recess **101** of shell **13** (FIG. 1C).

FIG. 7A further illustrates a subsequent screen **775**, by which computer **17** receives input, from the user, for system **10** to start the breakthrough elution, followed by a screen **776**, which provides both an indication that the elution is in progress and an option for the user to abort the elution. As previously described, the system may provide a signal to indicate that elution is in progress, for example, light projector **100** (FIG. 1C) may project a flashing light signal during that portion of the elution process when eluate is diverted from generator **21** through waste line **305***w* and into waste bottle **23**, and then a steady light signal during that portion of the elution process when the eluate is diverted from generator **21** through patient line **305***p* and into the test vial, for example, once activity detector **25** detects a dose rate of approximately 1.0 mCi/sec in the eluate discharged from generator **21**. Another type of light signal, for example, the more rapidly flashing light, as previously described, may be projected when a peak bolus of radioactivity is detected in the eluate.

Upon completion of the elution process for breakthrough testing, computer **17** presents a screen **777**, shown in FIG. 7B, which, like screen **677**, provides an indication of a time lapse since the completion of the elution, but now in terms of a time since completion of the breakthrough elution process. When the user transfers the vial containing the sample of eluate into a dose calibrator, to measure the activity of the sample, the user may make a note of the time lapse indicated on screen **777**. With further reference to FIG. 7B, once the user has received the activity measure from the dose calibrator, the user proceeds to a screen **778**, which includes data entry fields for the activity measure and the time between that at which the dose calibrator measured the activity of the sample and that at which the elution was completed. The user may enter the data via the touch-screen interface of monitor **172**, or via any of the other aforementioned devices for user data entry. According to some alternate embodiments, computer **17** may receive the data, electronically, from the dose calibrator, either via wireless communication or a cable connection.

After the data is entered by the user, computer **17** presents screen **779**, from which the user moves back to main menu **470** to perform a system calibration, for example, as will be described in conjunction with FIGS. **8**A-B, although the breakthrough testing is not completed. With reference back to FIG. 7A, an item **773**B is shown in main menu **470**; item **773**B may only be effectively selected following the completion of steps for item **773**A, so as to perform a second stage of breakthrough testing. In the second stage, the breakthrough of the sample of eluate collected in the test vial for the breakthrough testing is measured, at a time of approximately 60 minutes from the completion of the elution that produced the sample. With reference to FIG. 7C, after the user has selected item **773**B from main menu **470**, in order to direct computer **17** to provide breakthrough test results, a screen **781** is displayed. Screen **781** includes, for reference, the values previously entered by the user in screen **778**, along with another pair of data entry fields into which the user is instructed to enter the breakthrough reading of the sample at 60 minutes and the background radiation reading, respectively. After the user enters this remaining information, as described above, computer **17** may calculate and then display, on a screen **782**, the breakthrough test results. According to the illustrated embodiment, computer **17** also displays on screen **782** pre-programmed allowable limits for the results, so that the user may verify that the breakthrough test results are in compliance with acceptable limits, before moving on to a patient infusion. According to some embodiments, system **10** will not allow an infusion if the results exceed the acceptable limits, and may present a screen explaining that the results are outside the acceptable limits; the screen may further direct the user to contact the generator supplier, for example, to order a replacement generator.

With reference to FIG. **8**A, during the aforementioned 60 minute time period, while waiting to complete the breakthrough testing, the user may perform calibration by selecting item **873** from main menu **470**. Upon selection of item **873**, computer **17** presents a screen **874**, which instructs the user to insert a new test vial into an elution vial shield. In addition to placing the vial in the shield, the user, preferably, replaces patient line **305***p* with a new patient line, and then attaches a needle to the end of the new patient line for insertion into the test vial, in order to collect an eluate sample therefrom. After performing these steps, the user may move to screen **875**, wherein a plurality of data entry fields are presented; all or some of the fields may be filled in with pre-programmed default parameters, which the user has an option to change, if necessary. Once the user confirms entry of desired parameters for the calibration, the user may enter a command, via interaction with a subsequent screen **876**, to start the calibration elution.

With reference to FIG. **8**B, after computer **17** starts the elution process, a screen **87** informs the user that the calibration elution is in progress and provides an option to abort the elution. As previously described, the system may provide an indication that elution is in progress, for example, light projector **100** (FIG. 1C) may project a flashing light signal during that portion of the elution process when eluate is diverted from generator **21** through waste line **305***w* and into waste bottle **23**, and then a steady light signal during that portion of the elution process when activity detector **25** has detected that a prescribed dose rate threshold is reached, for example, 1.0 mCi/sec, and the eluate is being diverted from generator **21**, through the new patient line, and into the test vial. Another type of light signal, for example, the more rapidly flashing light, as previously described, may be projected when a peak bolus of radioactivity is detected in the eluate. Upon completion of the elution process for calibration, computer **17** presents a screen **878**, which provides an indication of a time lapse since the completion of the elution, in terms of a time since completion of the calibration elution process. When the user transfers the vial containing the sample of eluate into the dose calibrator, to measure the activity of the sample, the user may make a note of the time lapse indicated on screen **878**. With further reference to FIG. **8**B, once the user has received the activity

measure from the dose calibrator, the user proceeds to a screen **879**, which includes data entry fields for the activity measure and the time, with respect to the completion of elution, at which the dose calibrator measured the activity of the sample. Once the data is input by the user, as described above, the computer calculates a calibration coefficient, or ratio, and presents the ratio on a screen **880**. According to FIG. **8**B, screen **880** further provides an indication of a desirable range for the calibration ratio and presents an option for the user to reject the calculated ratio, in which case, the user may instruct computer **17** to recalculate the ratio.

As previously mentioned, some alternate embodiments of the present invention include an on board dose calibrator so that the entire sequence of sample collection and calculation steps, which are described above, in conjunction with FIGS. **6**-**8**B, for the quality control procedures, may be automated. This automated alternative preferably includes screen shots, similar to some of those described above, which provide a user of the system with information at various stages over the course of the automated procedure and that provide the user with opportunities to modify, override and/or abort one or more steps in the procedure. Regardless of the embodiment (i.e. whether system **10** employs an on board dose calibrator or not), computer **17** may further collect all quality control test parameters and results into a stored record and/or compile a report including all or some of the parameters and results for local print out and/or electronic transfer to a remote location.

With reference to FIG. **9**A, upon completion of the above-described quality control tests, the user may select an item **971**, from main menu **470**, in order to direct system **10** to begin a procedure for the generation and automatic infusion of a radiopharmaceutical into a patient. As previously described, system **10** infuses the patient with the radiopharmaceutical so that nuclear diagnostic imaging equipment, for example, a PET scanner, can create images of an organ of the patient, which absorbs the radiopharmaceutical, via detection of radioactive radiation therefrom. According to FIG. **9**A, upon selection of item **971**, computer **17** presents a screen **972** which includes a data entry field for a patient identification number. This identification number that is entered by the user is retained by computer **17**, in conjunction with the pertinent system parameters associated with the patient's infusion. After the user enters the patient identification number, computer **17** directs, per a screen **973**, the user to attach a new patient line and to purge the patient line of air. A subsequent screen **974** presented by computer **17** includes data entry fields by which the user may establish parameters for the automatic infusion; all or some of the fields may be filled in with pre-programmed default parameters, which the user has an option to change, if necessary.

With reference to FIG. **9**B, if pump **33** does not contain enough eluant/saline for the patient infusion, computer **17** will present a warning, via a screen **901**, which includes an option for the user to direct the refilling of pump **33**, via a subsequent screen **902**. Once pump **33** has been filled, computer **17** presents an indication to the user, via a screen **903**. According to some embodiments, if the user does not re-fill pump **33**, yet attempts to proceed with an infusion, system **10** will preclude the infusion and present another screen, that communicates to the user that no infusion is possible, if the pump is not refilled, and asking the user to refill the pump, as in screen **901**. When pump **33** contains a sufficient volume of eluant for the patient infusion, computer **17** presents a screen **975**, which is shown in FIG. **9**C, and allows the user to enter a command for system **10** to start the patient infusion. During the infusion, computer **17** provides the user with an indication that the infusion is in process and with an option for the user to abort the infusion, via a screen **976**. As previously described, the system may provide an indication that an elution is in progress, for example, light projector **100** (FIG. **1**C) may project a flashing light signal during that portion of the elution process when eluate is diverted from generator **21** through waste line **305***w* and into waste bottle **23**, and then a steady light signal during that portion of the elution process when activity detector **25** has detected that a prescribed dose rate threshold is reached, for example, 1.0 mCi/sec, and the eluate is being diverted from generator **21**, through the new patient line for infusion into the patient. Another type of light signal, for example, the more rapidly flashing light, previously described, may be projected when a peak bolus of radioactivity is detected in the eluate. At the completion of the infusion, a screen **977** is displayed by computer **17** to inform the user of the completion of the infusion and a time since the completion. Computer **17** also displays a summary of the infusion, per screen **978**.

With further reference to FIG. **9**C, screen **976** shows an exemplary activity profile (activity—mCi/sec, on y-axis, versus time—sec, on x-axis) for the infusion/injected dose (designated between the two vertical lines). Those skilled in the art will appreciate that the shape of this profile depends upon the infusion flow rate, for a given volume of the dose, which flow rate is controlled, for example, by the speed at which pump **33** drives flow through the patient line, and upon the amount of Strontium-82 remaining in the generator. In the absence of flow rate control, activity profiles may change over the life of the generator. Furthermore, the peak bolus of radioactivity, particularly for injected doses from a relatively new generator, may exceed a saturation level of the imaging equipment, i.e. PET scanner. According to some preferred methods of the present invention, in order to maintain relatively consistent, and desirable/effective, activity profiles for patient injections, over the life of the generator, the operating speed of pump **33** may be varied (both over the course of a single injection and from injection to injection), according to feedback from activity detector **25**. Such a method may be implemented via incorporation of another quality control test in which pump **33** is operated to drive flow through the generator at a constant rate, in order to collect, into computer, a plurality of activity measurements from activity detector **25**; the plurality of measurements comprise a characteristic, or baseline activity profile from which the computer **17** may calculate an appropriate flow rate profile to control a speed of pump **33**, in order to achieve the desirable/effective activity profile. In general, at the start of generator life, when Strontium-82 is plentiful, the pump is controlled to drive infusion flow at relatively lower rates, and, then, toward the end of generator life, when much of the Strontium-82 has been depleted, the pump is controlled to drive infusion flow at relatively higher rates. As was described above, in conjunction with FIG. **1**D, if a desired infusion/injection flow rate is relatively high, that is, high enough to create too much back pressure, via flow through the column of generator **21**, by-pass line **303** may be employed by adjusting divergence valve **35**BG to divert a flow of eluant therethrough after a sufficient volume has been pumped through generator at a lower flow rate. According to this method, once a dose of eluate, from generator **21**, has flowed into patient line **305***p*, divergence valve **35**BG is set to divert the flow of eluant through by-pass line **303**, and then pump speed is increased to pump eluant at a higher flow

rate in order to push the dose out from patient line **305***p*, for injection at the higher flow rate.

Consistency of activity profiles among injected doses can greatly facilitate the use of PET scanning for the quantification of flow, for example, in coronary perfusion studies. Alternative infusion circuit configurations, operable according to alternative methods, to achieve consistency of activity profiles among injected doses, as well as a more uniform level of radioactivity across each individual dose, will be described below, in conjunction with FIGS. **12**A-C.

Printer **117** (FIG. **1**B) may be activated to print out a hard copy of the infusion summary, on which the patient identification number and pertinent infusion and system parameters are also printed, for reference. Alternatively, or in addition, according to some embodiments, the summary may be downloaded onto a computer readable storage device to be electronically transferred to one or more remote computers and/or the summary may be automatically transferred to the one or more remote computers, via wireless communication or a cable connection, for example, over an intranet network and/or the internet. In order to protect private patient information, the files may be encrypted for transmission over the internet. The one or more remote computers may be included, for example, in a hospital information system, and/or a billing system, and/or in a medical imaging system. Infusion parameters, for example, corresponding to the activity profile, may also be collected and electronically transferred for analysis in conjunction with captured images, for example, in order to quantify coronary flow, via a software package that is loaded into a system that includes the PET scanner.

With reference back to FIG. **9**A the user may select an item **995**, from main menu **470**, in order have system **10** perform data operations, such as, archiving a data base of patient infusion information and quality control test results, transmitting patient infusion summary records to USB mass storage devices, and various types of data filtering, for example, according to date ranges and/or patient identification numbers, for example, to search for a particular set of data and/or to compile a summary report of related sets of data. Additionally, certain information, which is collected by computer **17** over the course of system operation, and which defines system operation, may be transmitted to a local or remote computerized inventory system and/or to computers of technical support personnel, maintenance/service providers and/or suppliers of infusion circuit elements/components, thereby facilitating more efficient system operation and maintenance.

Turning now to FIG. **10**, an item **981** for computer-facilitated purging of the tubing lines of system **10** is shown included in main menu **470**. When a user selects item **981**, computer **17** guides the user to select either an air purge or a saline purge. The direction provided by computer **17** is not explicitly laid out herein, for a saline purge, as procedures for saline purging should be readily apparent to those skilled in the art, with reference to the schematic of infusion circuit **300** shown in FIG. **1**D. A saline purge of circuit **300** is desired to assure that all the air is removed from circuit **300** when a new generator and/or a new complete or partial tubing set is installed. An air purge of the tubing lines of circuit **300** may be performed after removing reservoir **15**, by-passing generator **21**, by connecting tubing line **304** to tubing line **305**, and coupling patient line **305***p* to a vial, for example, as is directed by the computer interface, in screens **983** and **984** shown in FIG. **10**. The air purge is desirable for blowing out the tubing lines, thereby removing all remaining eluant and eluate, prior to installing a new generator and/or prior to transporting system **10** from one site to another. If generator **21** is not depleted and will be used in system **10** at the new site, it is important to by-pass the generator prior to purging the tubing lines of circuit **300** with air, so that air is not blown across the generator, since air through generator **21** may compromise both the function and the aseptic nature of generator **21**.

According to preferred embodiments, once the user has followed the instructions presented in screens **983** and **984** and selects to start the air purge, for example, via screen **985**, computer **17** directs the controller of system **10** to carry out a complete air purge, in which pump **33** and divergence valves **35**BG and **35**WP are automatically controlled. The automated air purge preferably includes the following steps, which may be best understood with reference to tubing circuit **300** in FIG. **1**D: pumping any remaining volume of eluant left in pump **33**, through lines **302**, **304**, **305** and **305***w*, to waste bottle **23**; refilling pump **33** with air and pumping the air through lines **302**, **304**, **305** and **305***w*, into waste bottle **23** (lines **304** and **305** have been previously connected directly to one another, in order to by-pass generator **21**; if generator **21** is depleted and will be replaced with a new generator, pumping air through generator **21** may be acceptable); refilling pump **33** with air and then pumping a portion of the air through lines **302**, **304**, **305** and **305***p*, into the vial, and then a remaining portion of the air through lines **302**, **304**, **303** and **305***p*, into the vial. With reference to FIG. **1**D and the previous description of divergence valves **35**BG, **35**WP, it should be understood how divergence valves **35**BG, **35**WP are automatically controlled to carry out the above steps.

The purge operations, which are facilitated by selecting item **981** from main menu **470**, may also be accessed via the selection of an item **991** for generator setup. When the user selects item **991**, computer **17** may present an option for guidance in removing an old, depleted, generator and a set of tubing lines, prior to installing the new generator, or an option to just be guided in the installation of the new generator.

According to some embodiments, computer **17** is pre-programmed to calculate an amount of activity left in a depleted generator, for example, by tracking activity of eluate over a life of the generator. At an end of the life of the generator, computer **17** may further compile this information, along with other pertinent generator information, into a report that may accompany a declaration of dangerous goods for shipping the depleted generator out for disposal or, in some cases, back to the manufacturer for investigation. An example of such a report is shown in FIG. **11**. According to those embodiments of system **10** that include an encoded information reader, computer **17** may confirm that the new generator is proper by processing information that is read from an encoded label/tag attached thereto.

FIGS. **12**A-B are schematics of alternative infusion circuits **1300**A, **1300**B that may be employed by system **10**, in place of circuit **300** (FIG. **1**D), according to some additional embodiments of the present invention. Circuits **1300**A, **1300**B are configured to allow for alternative methods of operation, to that previously described for circuit **300**, when a relatively even, or uniform level of activity over each injected dose, along with the relatively consistent level of activity from injection to injection is desired, for example, in order to facilitate a quantification of coronary artery blood flow via PET scanning. FIG. **12**C is a schematic illustrating activity profiles **1200**A, **1200**B for two injected doses, wherein profile **1200**B has a more uniform level of activity

than profile **1200**A; profile **1200**B may be achieved via the operation of circuits **1300**A, **1300**B as described below.

Similar to circuit **300** (FIG. 1D), dashed lines are shown in each of FIGS. **12**A-B to indicate a general boundary of a shielding assembly for portions of each circuit **1300**A, **1300**B. The shielding assembly for each of circuits **1300**A, **1300**B may be very similar, in most respects, to shielding assembly **200**, which is described above for system **10**, and the elements of each of circuits **1300**A, **1300**B may be arranged with respect to their respective shielding and with respect to shell **13** of system **10** in a similar manner to that described above for circuit **300**.

FIG. **12**A illustrates circuit **1300**A including, like the previously described circuit **300**, eluant reservoir **15**, pump **33**, radioisotope generator **21**, through which the filtered eluant is pumped to create the radioactive eluate, activity detector **25**, and waste bottle **23**. FIG. **12**A further illustrates two filters **37** and two pressure transducers **1334** included in circuit **1300**A. Circuit **1300**A further includes by-pass tubing line **303**, which is located downstream of divergence valve **35**BG, like in circuit **300**, and which accommodates the previously described eluant/saline flush. However, in contrast to circuit **300**, circuit **1300**A further includes a linear/proportional valve **1335** integrated into by-pass/flush line **303** so that circuit **1300**A may be operated, for example, according to pre-programmed parameters of computer **17**, in conjunction with feedback of information from activity detector **25**, for a controlled by-pass of generator **21** in order to mix eluant with eluate and, thereby, achieve a relatively uniform level of activity over each patient injection, for example, according to profile **1200**B of FIG. **12**C. It should be noted that, in addition to the controlled mixing, a flow rate of each injection may be varied, if necessary, in order to maintain a consistent activity level.

FIG. **12**B illustrates circuit **1300**B including, like the previously described circuit **300**, eluant reservoir **15**, pump **33**, radioisotope generator **21**, activity detector **25**, and waste bottle **23**, as well as the two filters **37** and two pressure transducers **1334**, as in circuit **1300**A. In contrast to circuits **300** and **1300**A, circuit **1300**B further includes an eluate reservoir **1350**, which is shown located downstream of generator **21**, in between first and second segments **305**A, **305**B of the eluate tubing line. It should be noted that a pump is combined with reservoir **1350**, for example, similar to syringe pump **33**, such that, when a divergence valve **1335**IO is set to allow fluid communication between reservoir **1350** and tubing line segment **305**A, the associated pump may be operated to draw in a volume of eluate, and, then, when divergence valve **1335**IO is set to allow fluid communication between reservoir **1350** and tubing line segment **305**B, the pump may be operated to push the volume of eluate out through tubing line segment **305**B for a patient injection, when divergence valve **35**WP is set to direct flow into patient line **305***p*. With reference back to FIGS. **3**A-B, sidewall **205** of shielding assembly **200** may be enlarged to further enclose eluate reservoir **1350**. For example, another shielded well, to house the eluate reservoir, may extend alongside well **255**, in which activity detector **25** is described as being mounted. Furthermore, sidewall **205** may include another valve actuator receptacle for divergence valve **1335**IO, similar to receptacle **253**, shown in FIG. **3**A for divergence valve **35**WP.

Collection of discrete volumes of eluate, in reservoir **1350**, may help to achieve a more uniform activity level over each injection, for example, like that of profile **1200**B in FIG. **12**C, and, according to preferred methods, feedback from activity detector **25** may be used to control the pump associated with reservoir **1350**, in order to vary injection flow rate and, thereby, maintain a relatively consistent activity level across multiple injections, and, when necessary, to vary injection flow rate over an individual injection to maintain the uniform activity level. Feedback from the pressure transducer **1334**, that is downstream from detector **25**, and/or from a flow meter (not shown) of circuit **1300**B may also be used to control the varying of injection flow rate.

With further reference to FIGS. **12**A-B, it should be noted that alternative circuits may be configured to employ a combination of the methods described for circuits **1300**A and **1300**B. Furthermore, some infusion circuits of the present invention may employ multiple generators **21**, as mentioned above, in conjunction with FIG. **2**A, to help maintain the relatively uniform level of activity over each injection and the relatively consistent level of activity from injection to injection.

In the foregoing detailed description, the invention has been described with reference to specific embodiments. However, it may be appreciated that various modifications and changes can be made without departing from the scope of the invention as set forth in the appended claims.

The invention claimed is:

1. A method of building an infusion system to deliver a rubidium radioactive eluate comprising:

installing a first shielding compartment, a second shielding compartment, and a shielded well on a platform of a cart, wherein:

the first shielding compartment has a first opening facing vertically upwardly,

the first opening is configured for a strontium-rubidium radioisotope generator to be inserted into and removed from the first shielding compartment,

the second shielding compartment has a second opening facing vertically upwardly,

the second opening is configured for a waste bottle to be inserted into and removed from the second shielding compartment,

the first opening is located at a lower elevation than the second opening, and

the shielded well is configured to receive an eluate reservoir that is configured to receive a sample of the rubidium radioactive eluate;

configuring a computer with a touch screen display for the infusion system to:

fill the eluate reservoir in the shielded well on-board the cart with the sample of the rubidium radioactive eluate by pumping saline from a saline reservoir into the strontium-rubidium radioisotope generator via a saline tubing line thereby generating the rubidium radioactive eluate that is discharged through an eluate tubing line,

determine a strontium breakthrough test result on the sample of the rubidium radioactive eluate filled into the eluate reservoir in the shielded well on-board the cart while the eluate reservoir remains in the shielded well on-board the cart, and

not allow a patient infusion if the strontium breakthrough test result is greater than or equal to an allowed limit.

2. The method of claim **1**, further comprising configuring the computer to:

measure a radioactivity of the sample of the rubidium radioactive eluate while the sample is flowing through the eluate tubing line to the eluate reservoir;

measure a calibration radioactivity of the sample while the sample remains in the eluate reservoir in the shielded well on-board the cart; and

compare the radioactivity of the sample measured while flowing through the eluate tubing line with the calibration radioactivity of the sample measured in the eluate reservoir in the shielded well on-board the cart.

3. The method of claim **2**, further comprising installing a dose calibrator in the shielded well on-board the cart, wherein the dose calibrator is in communication with the computer to measure the strontium breakthrough test result and the calibration radioactivity of the sample pumped into the eluate reservoir.

4. The method of claim **2**, further comprising configuring the computer to allow a user to:

log into the computer by entering a user login credential on the touch screen display, transfer a patient infusion record via a USB port, and

print a document concerning the patient infusion or a quality control test result via a printer.

5. The method of claim **2**, further comprising configuring the computer to allow a user to:

initiate a purging process through the touch screen display to purge a patient tubing line of air, wherein the patient tubing line is in fluid communication with the eluate tubing line.

6. The method of claim **2**, further comprising configuring the computer to present on the touch screen display a screen reminding a user to insert the eluate reservoir in the shielded well on-board the cart.

7. The method of claim **2**, further comprising configuring the computer to present on the touch screen display a screen for starting the patient infusion by touching a button on the touch screen display.

8. The method of claim **2**, further comprising configuring the computer to present on the touch screen display a screen indicating that the patient infusion is in process, wherein the screen indicating that the patient infusion is in process displays a stop button to abort the patient infusion.

9. The method of claim **2**, further comprising configuring the computer to:

present on the touch screen display a screen for starting the patient infusion by touching a button on the touch screen display;

present on the touch screen display a screen reminding a user to insert the eluate reservoir in the shielded well on-board the cart;

present on the touch screen display a screen indicating that the patient infusion is in process, wherein the screen indicating that the patient infusion is in process displays a stop button to abort the patient infusion; and

present on the touch screen display the strontium breakthrough test result.

10. The method of claim **9**, further comprising configuring the computer to allow the user to:

log into the computer by entering a user login credential on the touch screen display,

enter a patient ID on the touch screen display,

enter a patient dose on the touch screen display, and

enter a flow rate on the touch screen display.

11. The method of claim **10**, further comprising configuring the computer to:

track time passed from completion of pumping the sample of the rubidium radioactive eluate into the eluate reservoir to measuring the strontium breakthrough test result,

track a volume of saline remaining in the saline reservoir,

provide an alert via the touch screen display when the volume of saline remaining in the saline reservoir is below a predetermined volume threshold,

track a volume of the rubidium radioactive eluate discharged from the strontium-rubidium radioisotope generator to the waste bottle, and

present on the touch screen display a screen reminding the user to empty the waste bottle.

12. The method of claim **11**, further comprising configuring the computer to allow the user to:

initiate a generator column wash through the touch screen display, wherein a predetermined amount of saline is pumped through the strontium-rubidium radioisotope generator and directed to the waste bottle during the generator column wash, and

initiate a purging process through the touch screen display to purge a patient tubing line of air, wherein the patient tubing line is in fluid communication with the eluate tubing line.

13. The method of claim **12**, wherein the infusion system is configured for the saline tubing line and the eluate tubing line to be routed through two tubing passageways formed in a perimeter surface of the first opening, wherein each of the two tubing passageways has a depth configured to prevent pinching or crushing of a corresponding tubing line routed therethrough when a first door is closed over the first opening.

14. The method of claim **13**, wherein the infusion system further comprises:

an exterior shell extending upwardly above the platform, wherein the platform and the exterior shell collectively define an interior space of a cabinet structure,

a handle configured for the user to grasp in order to move the infusion system, and

four wheels mounted to an underside of the platform of the cabinet structure.

15. The method of claim **14**, further comprising configuring the computer to:

project a first light signal from a light projector mounted on a top end of a vertical post extending above the cabinet structure to indicate that an elution is taking place, and

project a second light signal from the light projector to indicate that a peak bolus of radioactivity is detected.

16. The method of claim **15**, wherein

the cabinet structure has a lowermost portion and the platform has a lower surface,

the first opening is at a first elevation,

the second opening is at a second elevation,

the first elevation is between approximately 1 foot and approximately 2 feet, with respect to the lowermost portion of the cabinet structure, and

the second elevation is between approximately 2 feet and approximately 3 feet, with respect to the lower surface of the platform.

17. The method of claim **14**, wherein the infusion system further comprises a dose calibrator in the shielded well on-board the cart and wherein the dose calibrator is in communication with the computer to measure the strontium breakthrough test result.

18. The method of claim **17**, wherein

the cabinet structure has a lowermost portion and the platform has a lower surface,

the first opening is at a first elevation,

the second opening is at a second elevation,

the first elevation is between approximately 1 foot and approximately 2 feet, with respect to the lowermost portion of the cabinet structure, and

the second elevation is between approximately 2 feet and approximately 3 feet, with respect to the lower surface of the platform.

19. The method of claim **1**, further comprising configuring the computer to:

control a fluid communication between the strontium-rubidium radioisotope generator and the saline reservoir,

control a fluid communication between the eluate tubing line and the eluate reservoir,

control a fluid communication between the eluate tubing line and the waste bottle,

place the eluate tubing line in fluid communication with a patient,

pump a dose of the rubidium radioactive eluate to the patient; and

flush the rubidium radioactive eluate remaining in at least a portion of the eluate tubing line into the patient by pumping saline from the saline reservoir to the eluate tubing line through a by-pass line that by-passes the strontium-rubidium radioisotope generator.

20. The method of claim **1**, further comprising installing an exterior shell extending upwardly above the platform, wherein:

the exterior shell comprises a front side; a rear side; two sidewalls; and a top surface,

the platform and the exterior shell collectively define an interior space of a cabinet structure,

the cabinet structure has a lowermost portion and the platform has a lower surface,

the first opening is at a first elevation,

the second opening is at a second elevation,

the first elevation is between approximately 1 foot and approximately 2 feet, with respect to the lowermost portion of the cabinet structure, and

the second elevation is between approximately 2 feet and approximately 3 feet, with respect to the lower surface of the platform.

21. The method of claim **20**, further comprising installing a light projector on a top end of a vertical post extending above the cabinet structure to:

project a first light signal from the light projector to indicate that an elution is taking place, and

project a second light signal from the light projector to indicate that a peak bolus of radioactivity is detected.

22. The method of claim **20**, wherein the saline reservoir is located outside of the interior space of the cabinet structure.

23. The method of claim **20**, wherein the infusion system further comprises:

a handle configured for a user to grasp in order to move the infusion system, and

four wheels mounted to an underside of the platform of the cabinet structure.

24. The method of claim **1**, wherein the infusion system is configured for the saline tubing line and the eluate tubing line to be routed through two tubing passageways formed in a perimeter surface of the first opening, wherein each of the two tubing passageways has a depth configured to prevent pinching or crushing of a corresponding tubing line routed therethrough when a first door is closed over the first opening.

25. The method of claim **1**, further comprising configuring the computer to:

track a volume of saline remaining in the saline reservoir, and

provide an alert via the touch screen display when the volume of saline remaining in the saline reservoir is below a predetermined volume threshold.

26. The method of claim **1**, further comprising configuring the computer to:

track a volume of the rubidium radioactive eluate discharged from the strontium-rubidium radioisotope generator to the waste bottle, and

present on the touch screen display a screen reminding a user to empty the waste bottle.

27. The method of claim **1**, wherein the infusion system is configured to pump saline through the strontium-rubidium radioisotope generator at a rate less than approximately 70 ml/min.

28. The method of claim **1**, further comprising configuring the computer to allow a user to:

initiate a generator column wash through the touch screen display, wherein a predetermined amount of saline is pumped through the strontium-rubidium radioisotope generator and directed to the waste bottle during the generator column wash.

29. The method of claim **1**, further comprising configuring the computer to track time passed from completion of pumping the sample of the rubidium radioactive eluate into the eluate reservoir to measuring the strontium breakthrough test result.

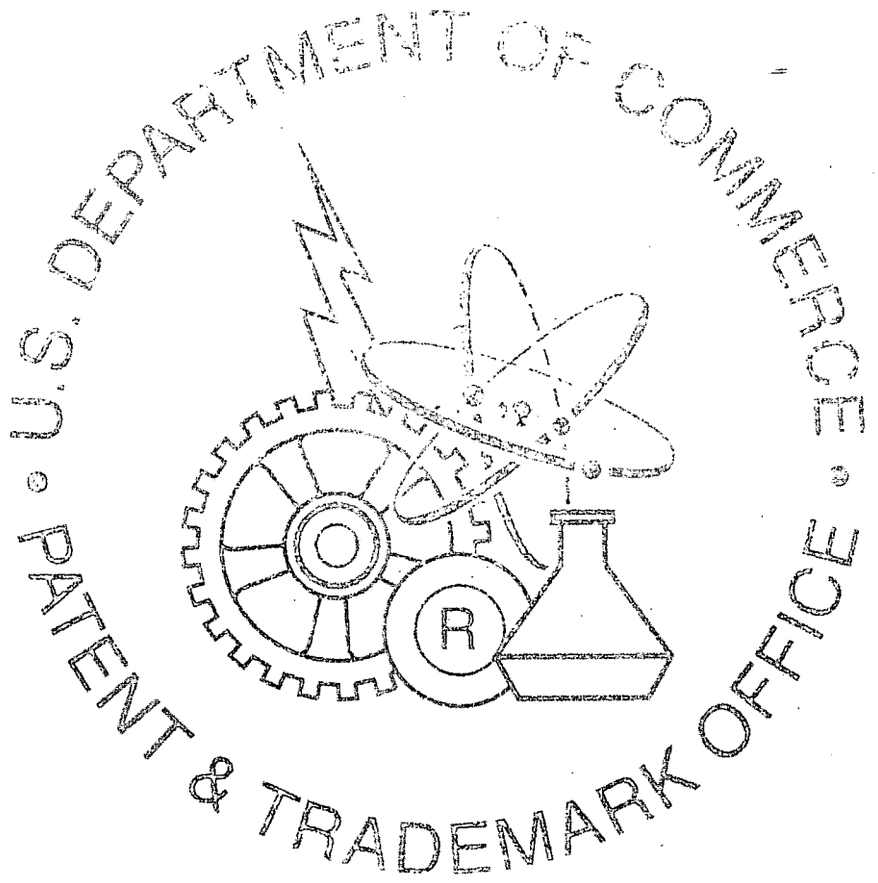
30. The method of claim **1**, further comprising configuring the computer to allow a user to:

enter a patient ID on the touch screen display,

enter a patient dose on the touch screen display, and

enter a flow rate on the touch screen display.

* * * * *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PATENT & TRADEMARK OFFICE
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EXHIBIT 2

A 7667315

THE UNITED STATES OF AMERICA

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United States Patent and Trademark Office

February 08, 2018

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By Authority of the
Under Secretary of Commerce for Intellectual Property
and Director of the United States Patent and Trademark Office

UNITED STATES PATENT AND TRADEMARK OFFICE
DEPARTMENT OF COMMERCE

R GLOVER
Certifying Officer

PATENT ASSIGNMENT COVER SHEET

Electronic Version v1.1
Stylesheet Version v1.2

EPAS ID: PAT4461109

SUBMISSION TYPE:	NEW ASSIGNMENT
NATURE OF CONVEYANCE:	ASSIGNMENT

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Property Type	Number
Application Number:	15620320

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NAME OF SUBMITTER:	PAUL J. LAVANWAY, JR.
SIGNATURE:	/Paul J. LaVanway, Jr./
DATE SIGNED:	06/15/2017

Total Attachments: 7
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ASSIGNMENT

We, Stephen E. Hidem, residing at 4710 Juneau Lane North, Plymouth, Minnesota 55446, Aaron M. Fontaine, residing at 5663 West Bavarian Pass, Fridley, Minnesota 55432, Janet L. Gelbach, residing at 4204 Shetland Court, New Albany, Indiana 47150, Patrick M. McDonald, residing at 15395 Nicholas Street, Omaha, Nebraska 68154, Kathryn M. Hunter, residing at 1312 Judy Reagan Lane, Knoxville, Tennessee 37931, Rolf E. Swenson, residing at 35 Fieldston Road, Princeton, New Jersey 08540 and Julius P. Zodda, residing at 3 Tigers Court, Mercerville, New Jersey 08619 ("Assignor"), have made invention(s) for which United States and foreign patents and patent applications have been filed and are identified on the attached Schedule 1;

Whereas, Bracco Diagnostics Inc., a Delaware corporation having a place of business at 107 College Road East, Princeton, NJ 08540 ("Assignee"), desires to acquire the entire right, title and interest in and to the United States and foreign patents and patent applications identified on the attached Schedule 1 and in and to the inventions described and claimed therein (the "Patents"); and

NOW, THEREFORE, in exchange for good and valuable consideration, the receipt of which is hereby acknowledged, Assignor hereby assigns to Assignee, and its successors and assigns the following:

(1) The entire right, title and interest to the Patents including the inventions described or claimed therein, and to each U.S. and foreign patent application and patent from which the Patents claim priority to, in whole or in part, and to which the Patents claim priority; and

(2) The entire right, title and interest to any United States or foreign patents that may issue with respect to the inventions described or claimed in the Patents;

(3) The entire right, title and interest to any renewals, reissues, extensions, substitutions, continuations, continuations-in-part, or divisions of the Patents, and all foreign applications based thereon;

(4) The right to apply for patents in foreign countries in its own name and to claim any priority rights to which such foreign applications are entitled under international conventions, treaties or otherwise; and

(5) The right to enforce patent rights to such Patents as fully and entirely as the same would have been held and enjoyed by the Assignors if this assignment had not been made; together with all claims by Assignors for damages by reason of past infringement or for provisional rights and including the right to sue for, and collect the same for its own use and benefit, and for the use and benefit of its successors, assigns, and other legal representatives.

Assignor further agrees for himself and for his successors and assigns to execute and deliver without further consideration any further applications, assignments or other documents and to perform such other lawful acts as Assignee its successors and assigns may deem necessary to fully secure, maintain and enforce its rights, title or interest as outlined herein.

Assignor hereby authorizes and requests the Commissioner of Patents to issue to Assignee any patents that may be granted in accordance with this Assignment.

We hereby authorize attorneys associated with Customer No. 22859, of 200 South Sixth Street, Suite 4000, Minneapolis, Minnesota, 55402-1425, to insert the Application Nos. and Filing Dates of said application when known.

This Agreement may be executed in one or more counterparts, all of which shall be considered one and the same agreement. The signatures from each counterpart may be combined with a copy of the Agreement to constitute the entire Agreement.

Date: 4/28/2010

Stephen E. Hidem

Subscribed to and sworn to before me this 28 day of APRIL, 2010.

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Notary Seal

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MINNESOTA
My Commission Expires Jan. 31, 2015

Date: 4/28/2010

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SCHEDULE 1

US Patent Applications

Patent App. No.	Date Filed	Title	Attorney Docket No.
12/137,356	6/11/2008	SHIELDING ASSEMBLIES FOR INFUSION SYSTEMS	56782.1.5
12/137,363	6/11/2008	INFUSION SYSTEM CONFIGURATIONS	56782.1.6
12/137,364	6/11/2008	INFUSION SYSTEMS INCLUDING COMPUTER-FACILITATED MAINTENANCE AND/OR OPERATION AND METHODS OF USE	56782.1.7
12/137,377	6/11/2008	CABINET STRUCTURE CONFIGURATIONS FOR INFUSION SYSTEMS	56782.1.8
12/808,467	6/16/2010	INFUSION SYSTEMS INCLUDING COMPUTER-FACILITATED MAINTENANCE AND/OR OPERATION AND METHODS OF USE	56782.1.7.2
15/389,200	12/22/2016	INTEGRATED STRONTIUM-RUBIDIUM RADIOISOTOPE INFUSION SYSTEMS	56782.4.1
15/620,320	6/12/2017	INTEGRATED STRONTIUM-RUBIDIUM RADIOISOTOPE INFUSION SYSTEMS	56782.4.3

US Patents

Patent No.	Date Issued	Title

Foreign and International Patent Applications

Country	Patent App. No.	Date Filed	Title	Attorney Docket No.
WO	PCT/US09/47031	6/11/2009	INFUSION SYSTEMS INCLUDING COMPUTER-FACILITATED MAINTENANCE AND/OR OPERATION AND METHODS OF USE	56782.1.7.1

Foreign Patents

Country	Patent No.	Date of Issue	Title

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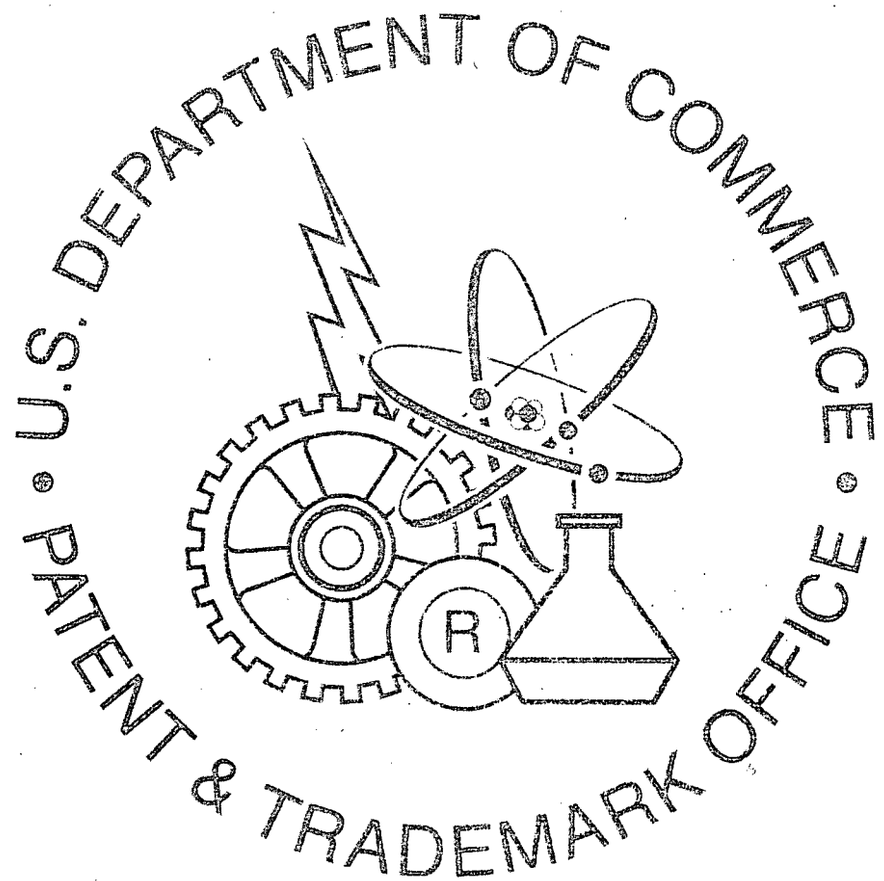
U.S. DEPARTMENT OF COMMERCE
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PTO-1683
(Rev. 7-96)

EXHIBIT 3

U 7667315

THE UNITED STATES OF AMERICA

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UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office

February 12, 2018

THIS IS TO CERTIFY THAT ANNEXED HERETO IS A TRUE COPY FROM THE RECORDS OF THIS OFFICE OF:

U.S. PATENT: ***9,750,869***
ISSUE DATE: ***September 05, 2017***

By Authority of the
Under Secretary of Commerce for Intellectual Property
and Director of the United States Patent and Trademark Office

P. R. GRANT
Certifying Officer

US009750869B2

(12) **United States Patent**
Hidem et al.

(10) **Patent No.: US 9,750,869 B2**
(45) **Date of Patent: *Sep. 5, 2017**

(54) **INTEGRATED STRONTIUM-RUBIDIUM RADIOISOTOPE INFUSION SYSTEMS**

(71) Applicant: **Bracco Diagnostics Inc.**, Monroe Township, NJ (US)

(72) Inventors: **Stephen E. Hidem**, Edina, MN (US); **Aaron M. Fontaine**, Minneapolis, MN (US); **Janet L. Gelbach**, Rolling Meadows, IL (US); **Patrick M. McDonald**, Omaha, NE (US); **Kathryn M. Hunter**, Knoxville, TN (US); **Rolf E. Swenson**, Silver Spring, MD (US); **Julius P. Zodda**, Mercerville, NJ (US)

(73) Assignee: **Bracco Diagnostics, Inc.**, Monroe Township, NJ (US)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

This patent is subject to a terminal disclaimer.

(21) Appl. No.: **15/389,200**

(22) Filed: **Dec. 22, 2016**

(65) **Prior Publication Data**

US 2017/0100535 A1 Apr. 13, 2017

Related U.S. Application Data

(63) Continuation of application No. 12/808,467, filed as application No. PCT/US2009/047031 on Jun. 11, (Continued)

(51) **Int. Cl.**
A61M 5/00 (2006.01)
A61N 5/10 (2006.01)
(Continued)

(52) **U.S. Cl.**
CPC ***A61M 5/007*** (2013.01); ***A61B 6/037*** (2013.01); ***A61B 6/107*** (2013.01); ***A61B 6/481*** (2013.01);
(Continued)

(58) **Field of Classification Search**
CPC .. A61N 5/1001; A61N 5/1002; A61N 5/1007; A61N 5/1014–5/1017;
(Continued)

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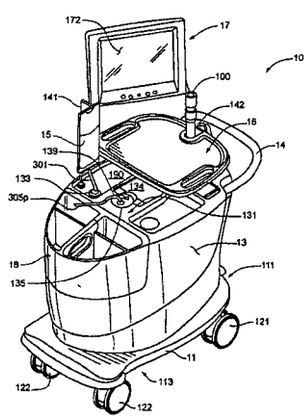
(Continued)

Primary Examiner — Charles A Marmor, II
Assistant Examiner — Carrie R Dorna
(74) *Attorney, Agent, or Firm* — Fredrikson & Byron, P.A.

(57) **ABSTRACT**

Methods for setting up, maintaining and operating a radiopharmaceutical infusion system, that includes a radioisotope generator, are facilitated by a computer of the system. The computer may include pre-programmed instructions and a computer interface, for interaction with a user of the system, for example, in order to track contained volumes of eluant and/or eluate, and/or to track time from completion of an elution performed by the system, and/or to calculate one or more system and/or injection parameters for quality control, and/or to perform purges of the system, and/or to facilitate diagnostic imaging.

30 Claims, 27 Drawing Sheets



Related U.S. Application Data

2009, now Pat. No. 9,607,722, which is a continuation of application No. 12/137,356, filed on Jun. 11, 2008, now Pat. No. 8,317,674, and a continuation of application No. 12/137,363, filed on Jun. 11, 2008, now Pat. No. 7,862,534, and a continuation of application No. 12/137,377, filed on Jun. 11, 2008, now Pat. No. 8,708,352, and a continuation of application No. 12/137,364, filed on Jun. 11, 2008, now Pat. No. 9,597,053.

(51) **Int. Cl.**

A61B 90/00	(2016.01)
A61M 5/14	(2006.01)
G21F 7/00	(2006.01)
G21G 1/00	(2006.01)
A61B 6/00	(2006.01)
A61B 6/10	(2006.01)
A61M 5/142	(2006.01)
G21F 3/00	(2006.01)
A61K 51/00	(2006.01)
G21G 4/08	(2006.01)
A61B 6/03	(2006.01)
A61M 5/168	(2006.01)
A61B 50/13	(2016.01)
A61M 5/145	(2006.01)
A61M 5/158	(2006.01)
G06F 21/31	(2013.01)
A61B 50/10	(2016.01)
B62B 3/00	(2006.01)

(52) **U.S. Cl.**

CPC ***A61B 6/507*** (2013.01); ***A61B 50/13*** (2016.02); ***A61B 90/39*** (2016.02); ***A61K 51/00*** (2013.01); ***A61M 5/14*** (2013.01); ***A61M 5/142*** (2013.01); ***A61M 5/1409*** (2013.01); ***A61M 5/1452*** (2013.01); ***A61M 5/158*** (2013.01); ***A61M 5/16854*** (2013.01); ***A61M 5/16881*** (2013.01); ***A61N 5/1001*** (2013.01); ***A61N 5/1007*** (2013.01); ***A61N 5/1075*** (2013.01); ***G06F 21/31*** (2013.01); ***G21F 3/00*** (2013.01); ***G21F 7/00*** (2013.01); ***G21G 1/001*** (2013.01); ***G21G 1/0005*** (2013.01); ***G21G 4/08*** (2013.01); *A61B 2050/105* (2016.02); *A61B 2090/392* (2016.02); *A61M 2005/1403* (2013.01); *A61M 2205/18* (2013.01); *A61M 2205/276* (2013.01); *A61M 2205/50* (2013.01); *A61M 2205/505* (2013.01); *A61M 2205/52* (2013.01); *A61M 2209/084* (2013.01); *A61N 2005/1021* (2013.01); *A61N 2005/1022* (2013.01); *A61N 2005/1074* (2013.01); *A61N 2005/1094* (2013.01); *B62B 3/005* (2013.01); *G21G 2001/0031* (2013.01)

(58) **Field of Classification Search**

CPC .. A61N 5/1027; A61N 5/1028; A61N 5/1071; A61N 2005/1021; A61M 5/007; A61M 5/14; A61M 5/142; G06F 19/3468; G21G 4/08; A61B 2050/105

See application file for complete search history.

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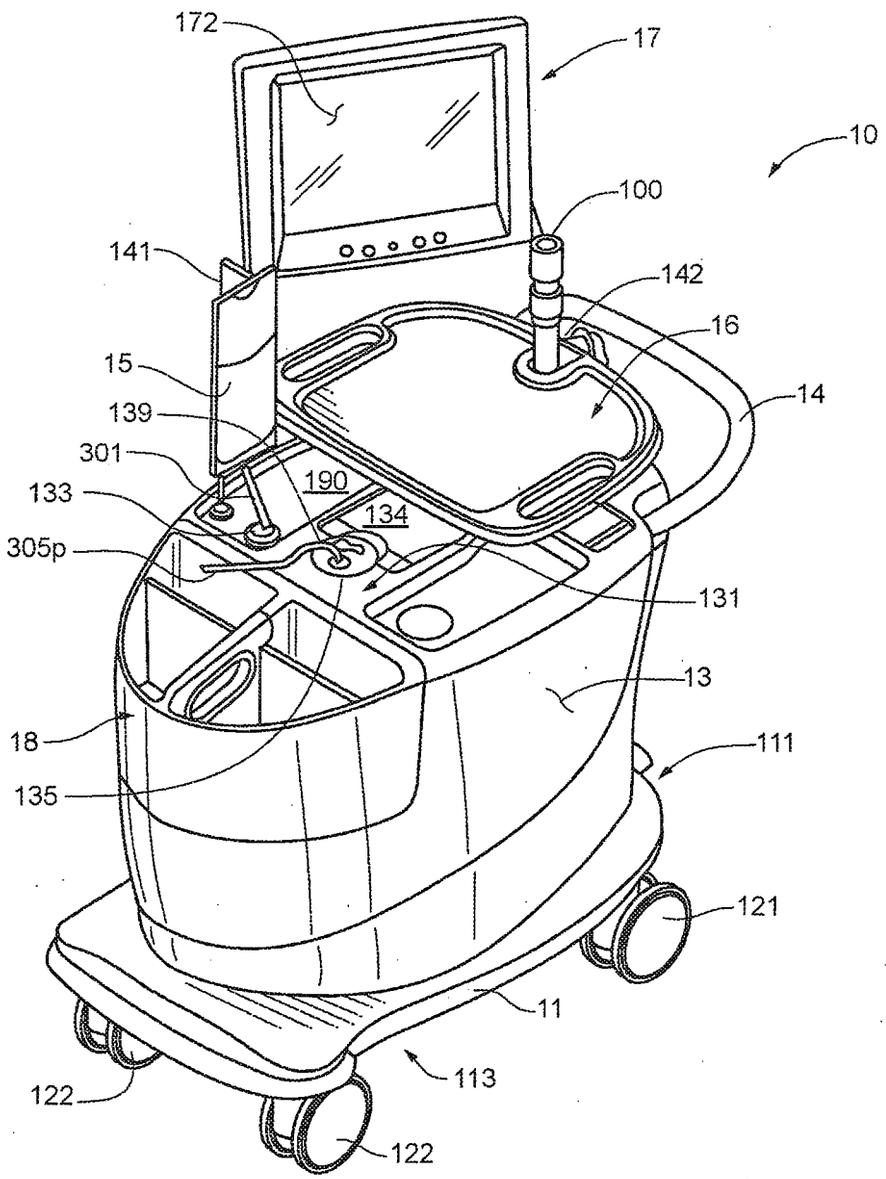
Fig. 1A



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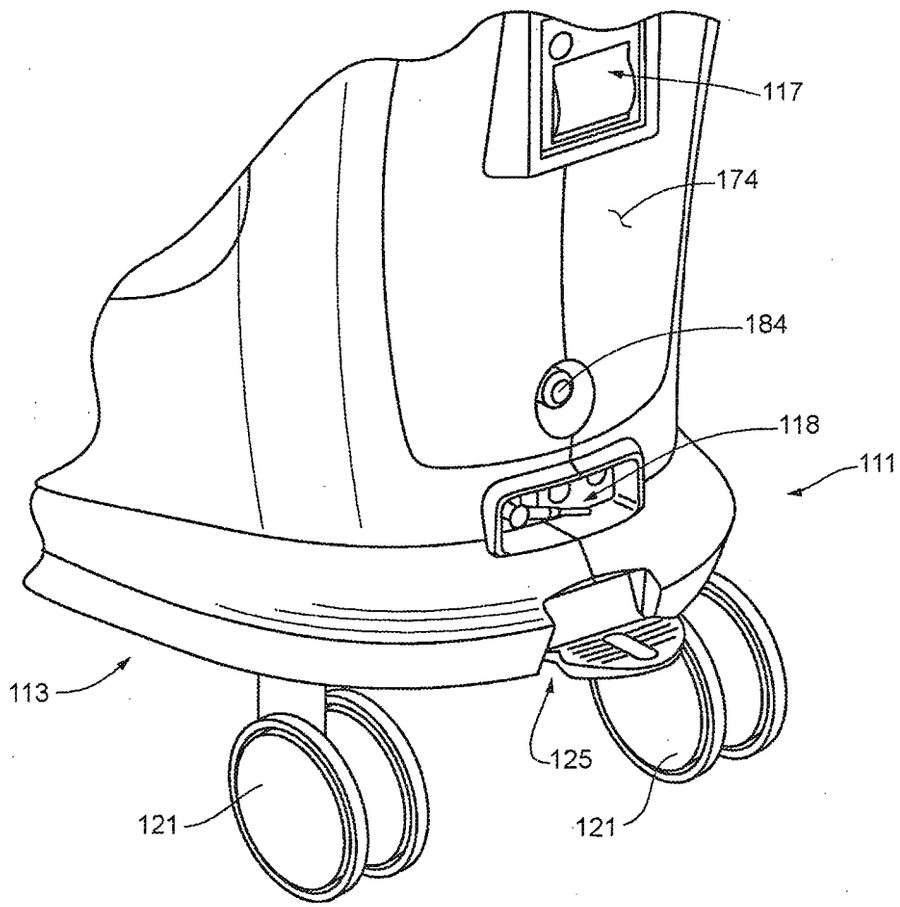

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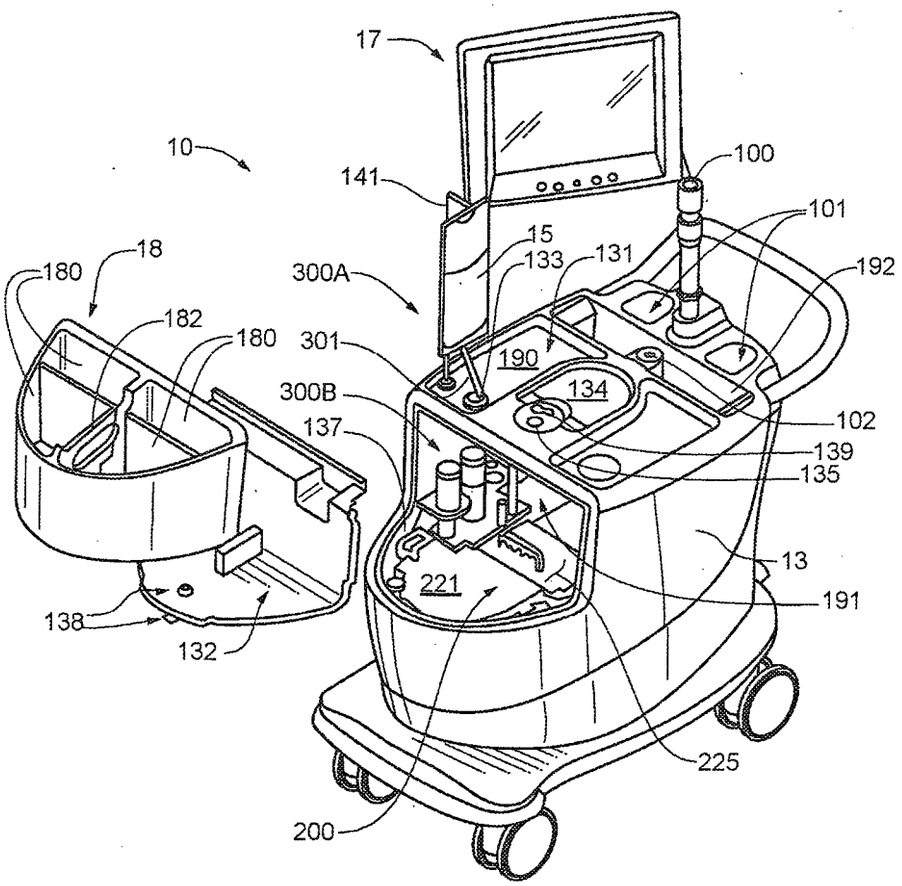


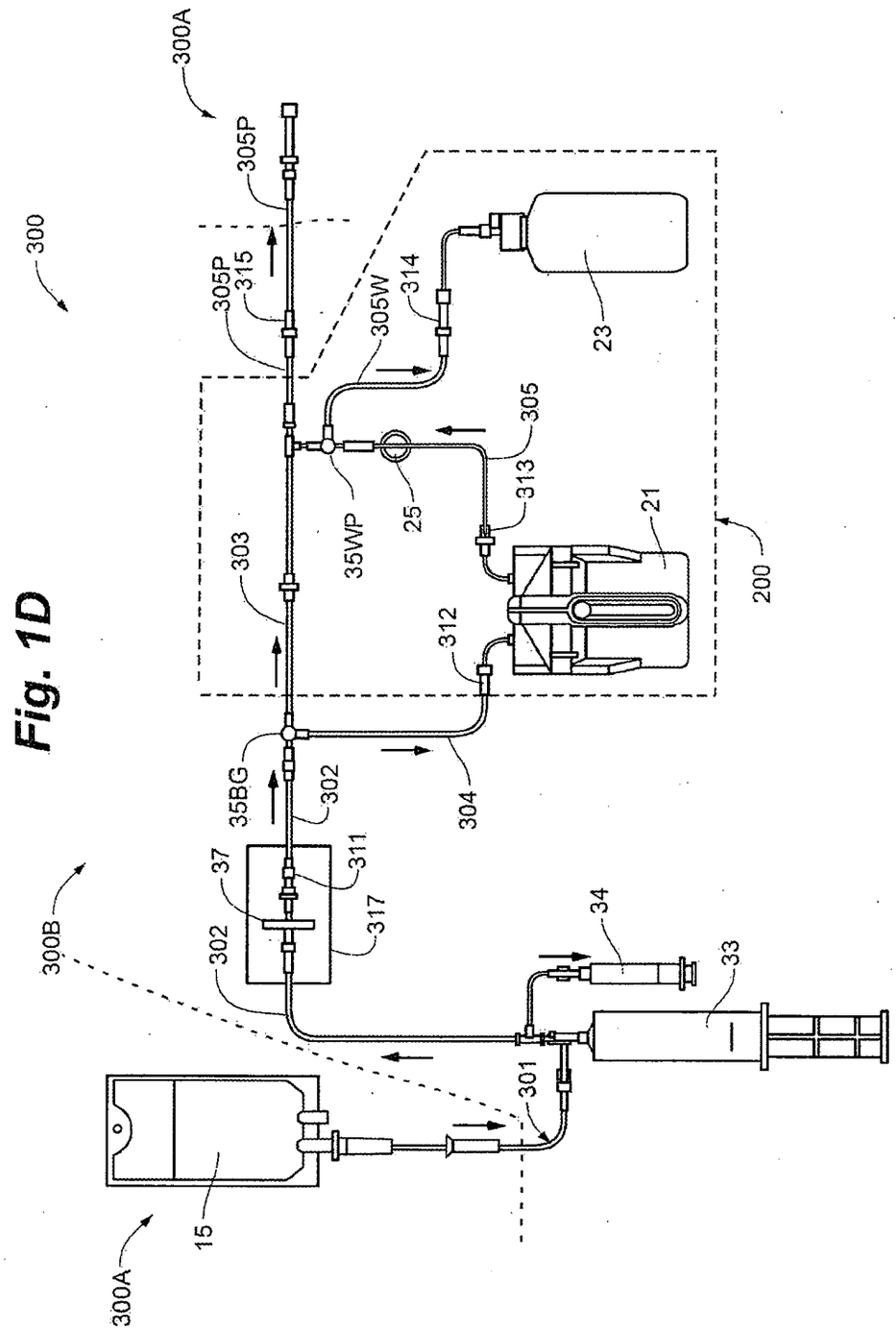
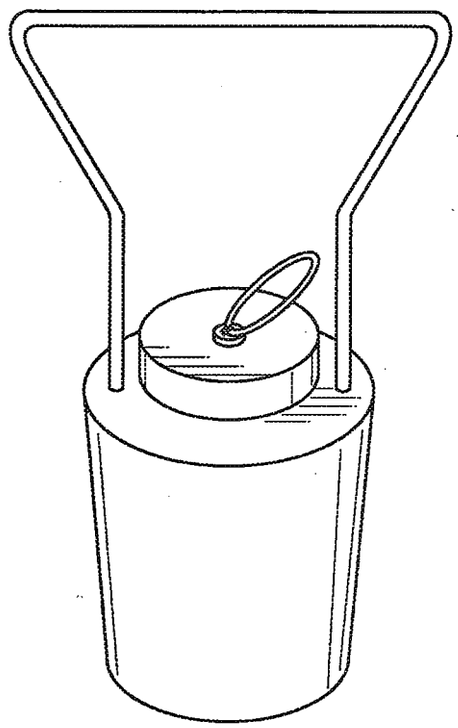


Fig. 1D

Fig. 1E



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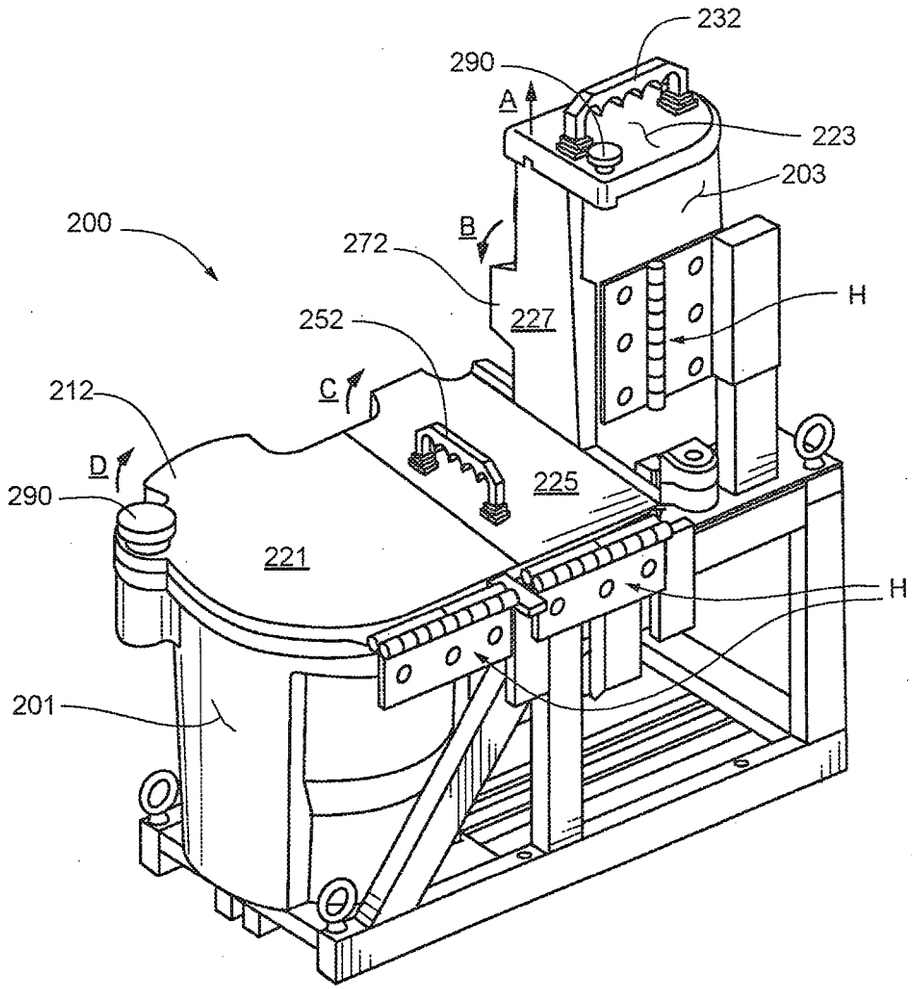
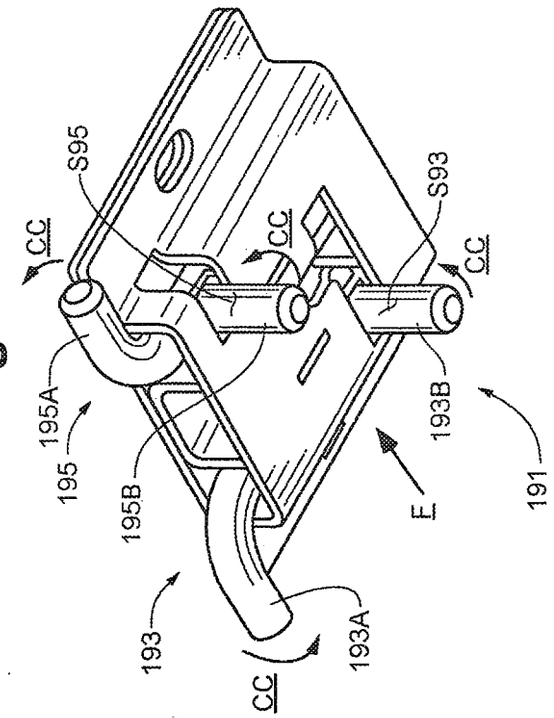


Fig. 2B-1



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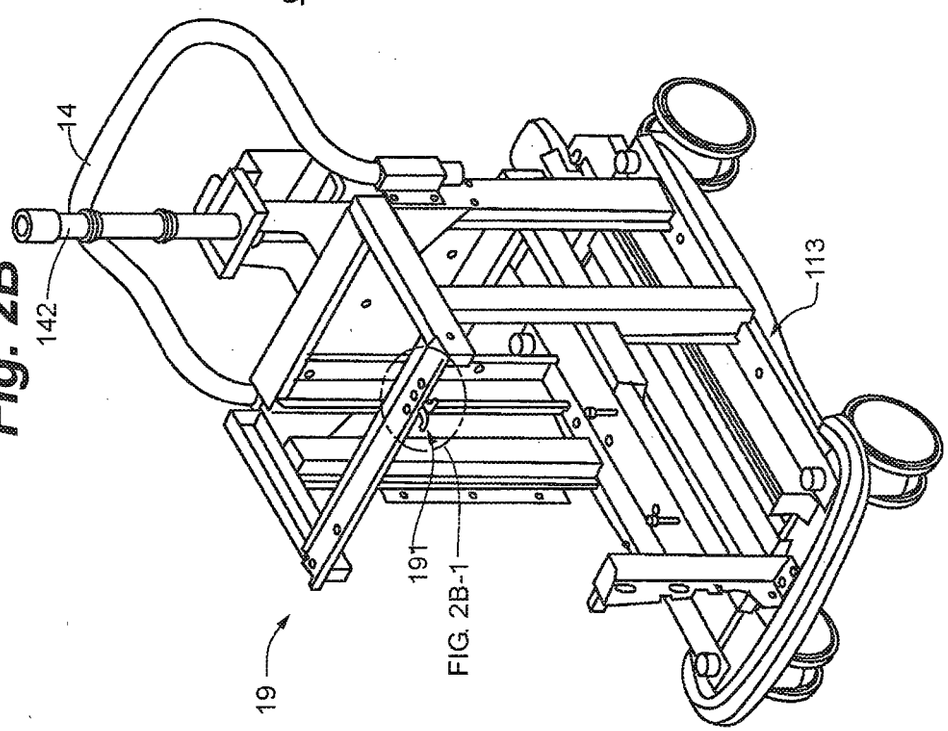

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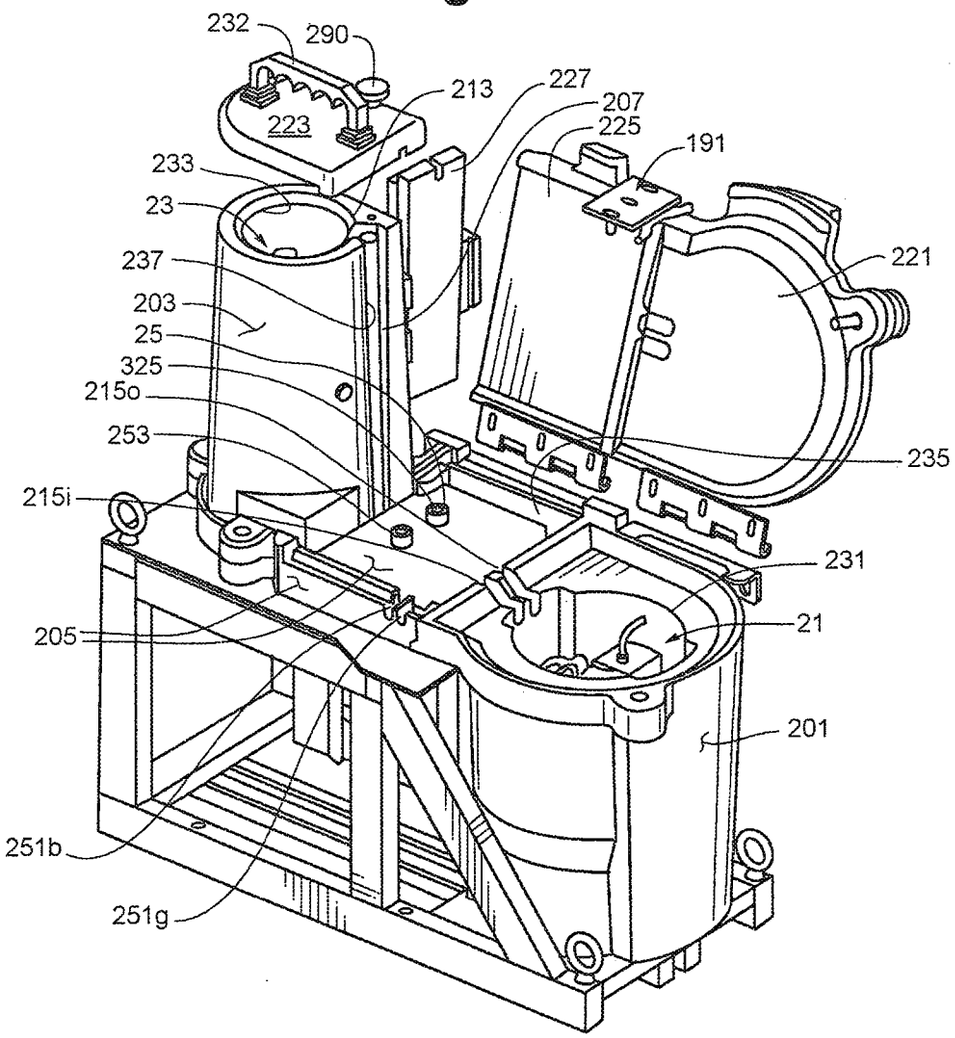

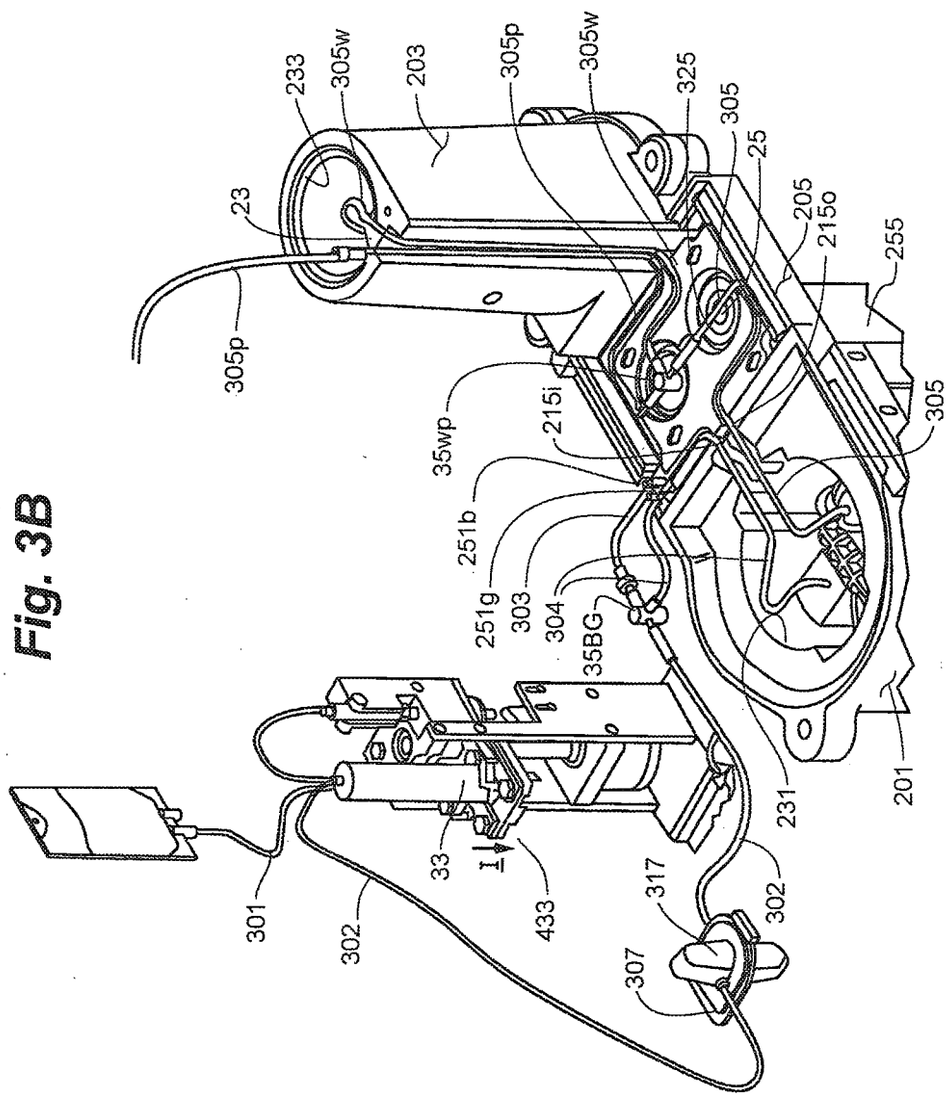

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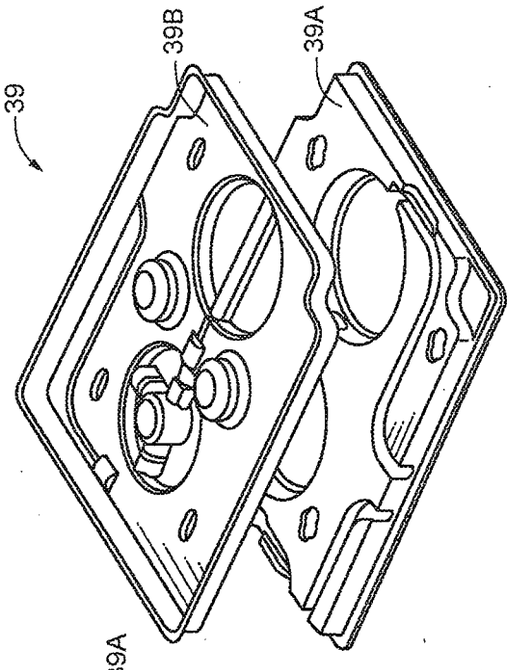

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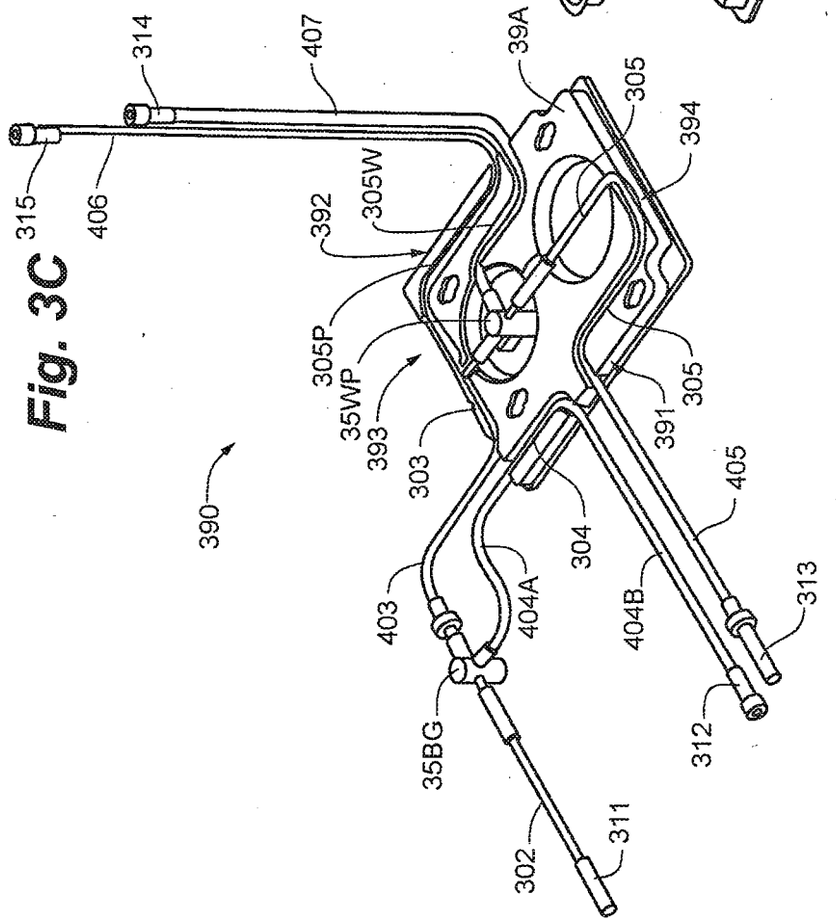
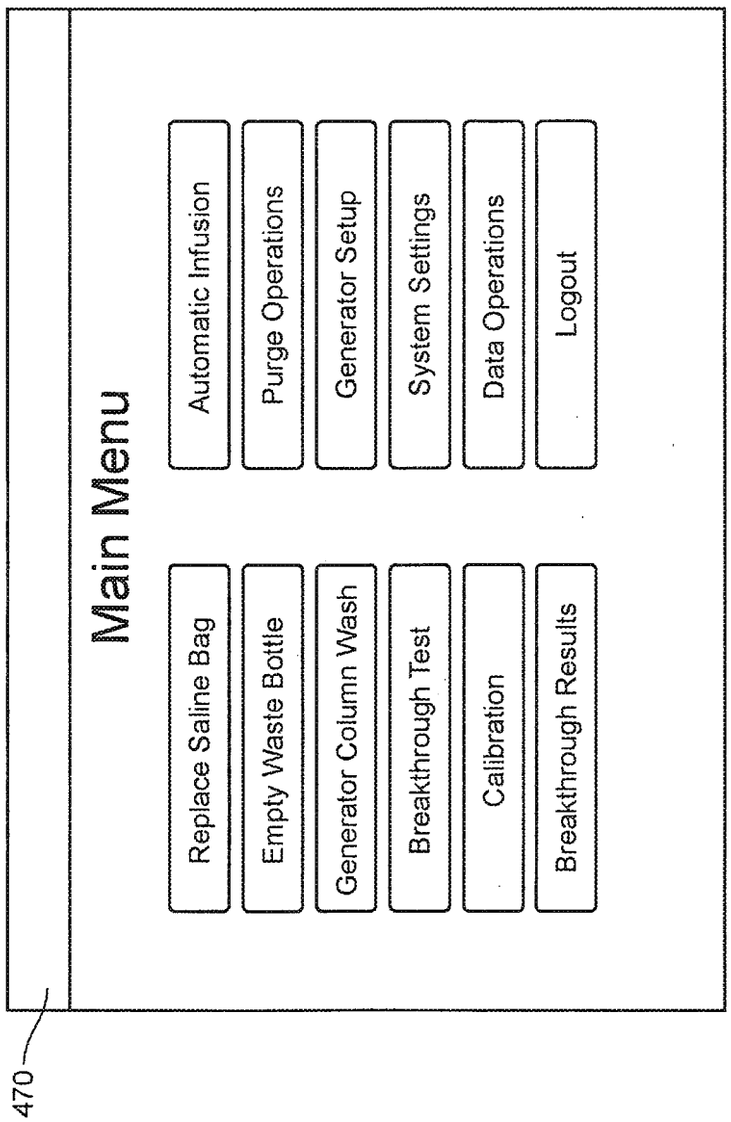


Fig. 3C



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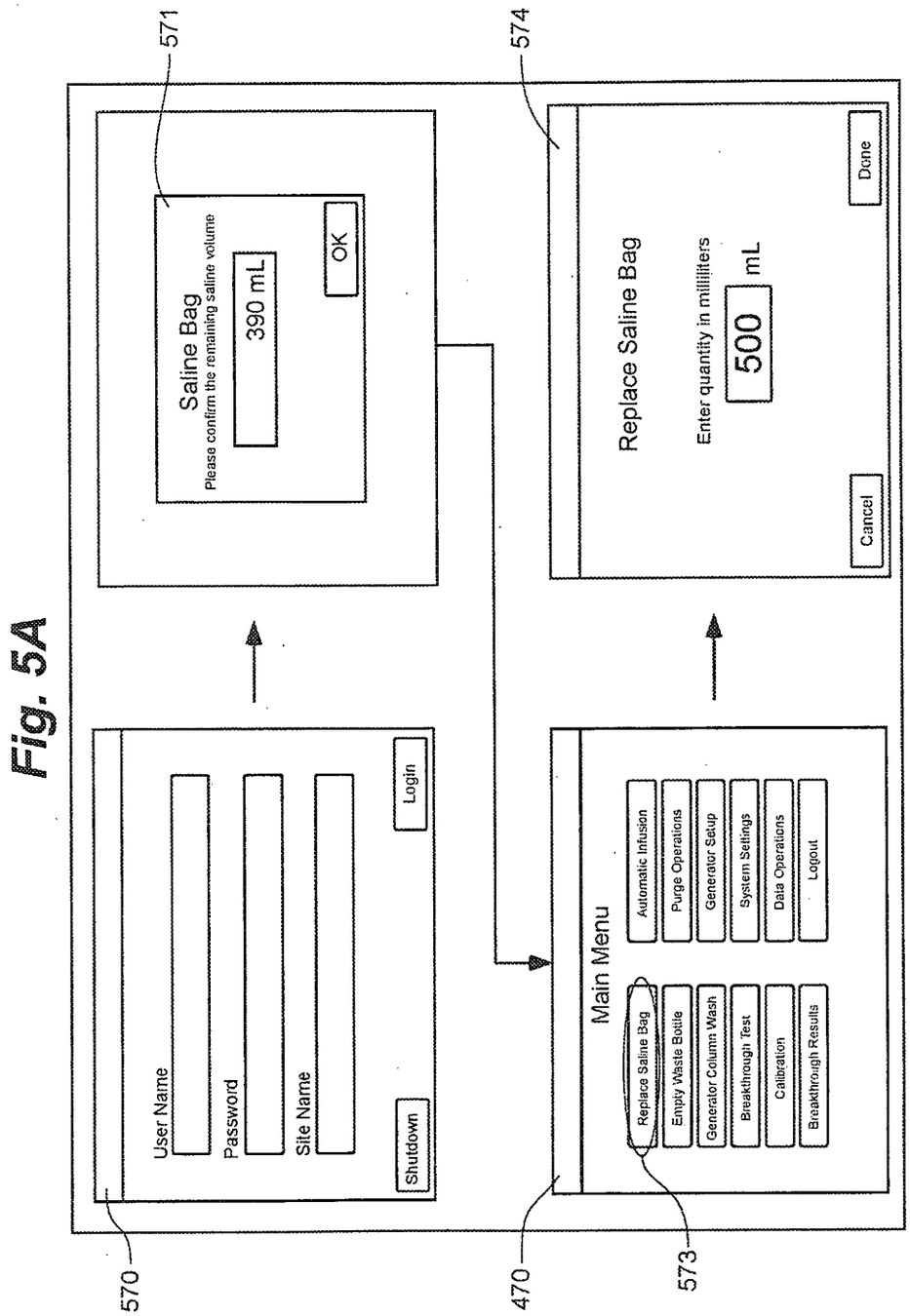

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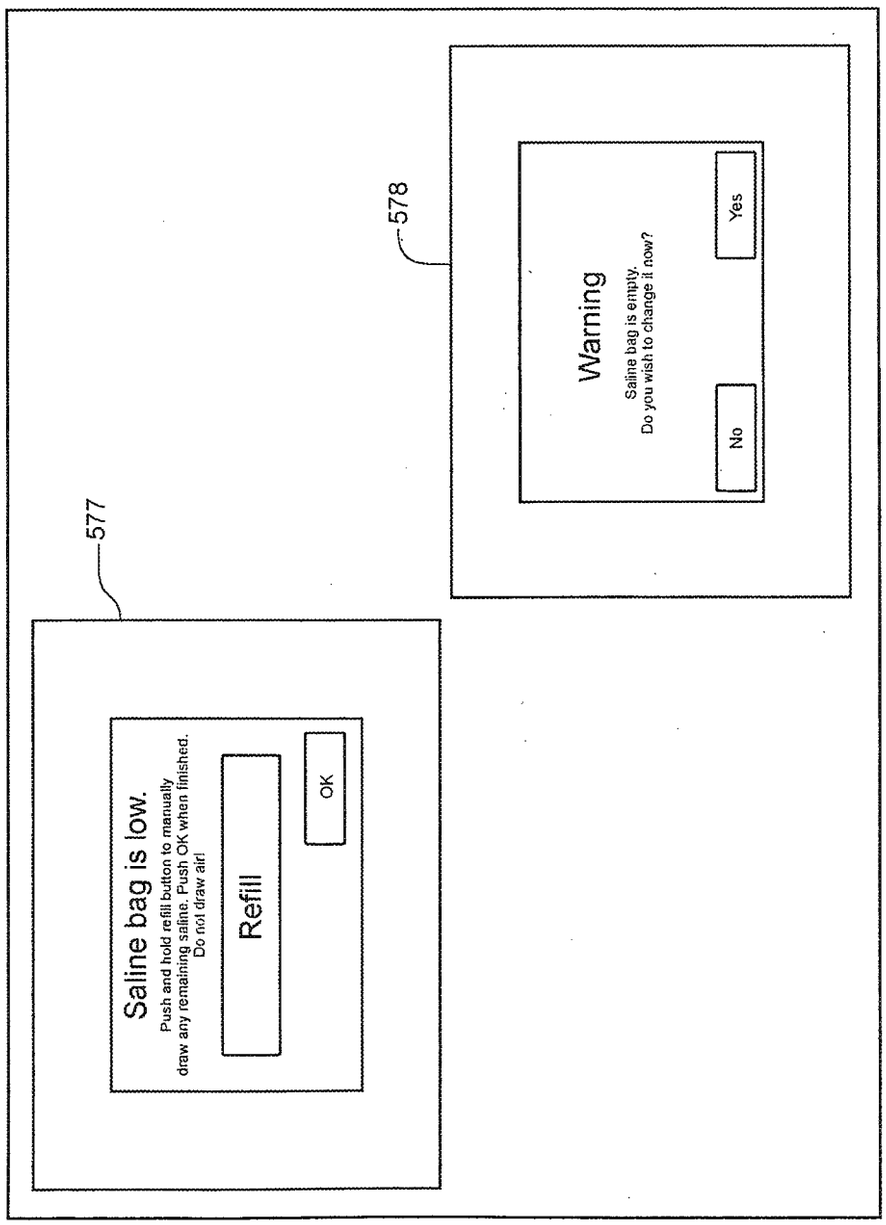

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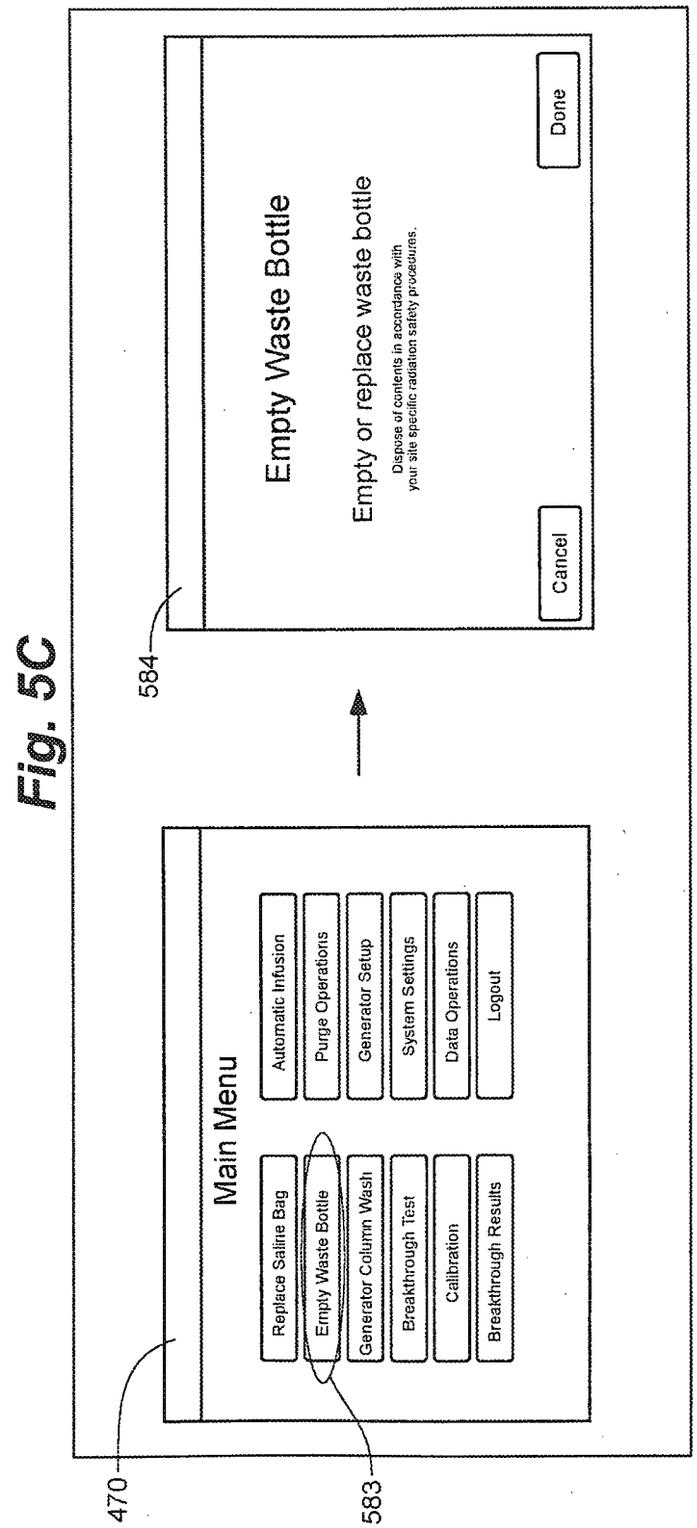

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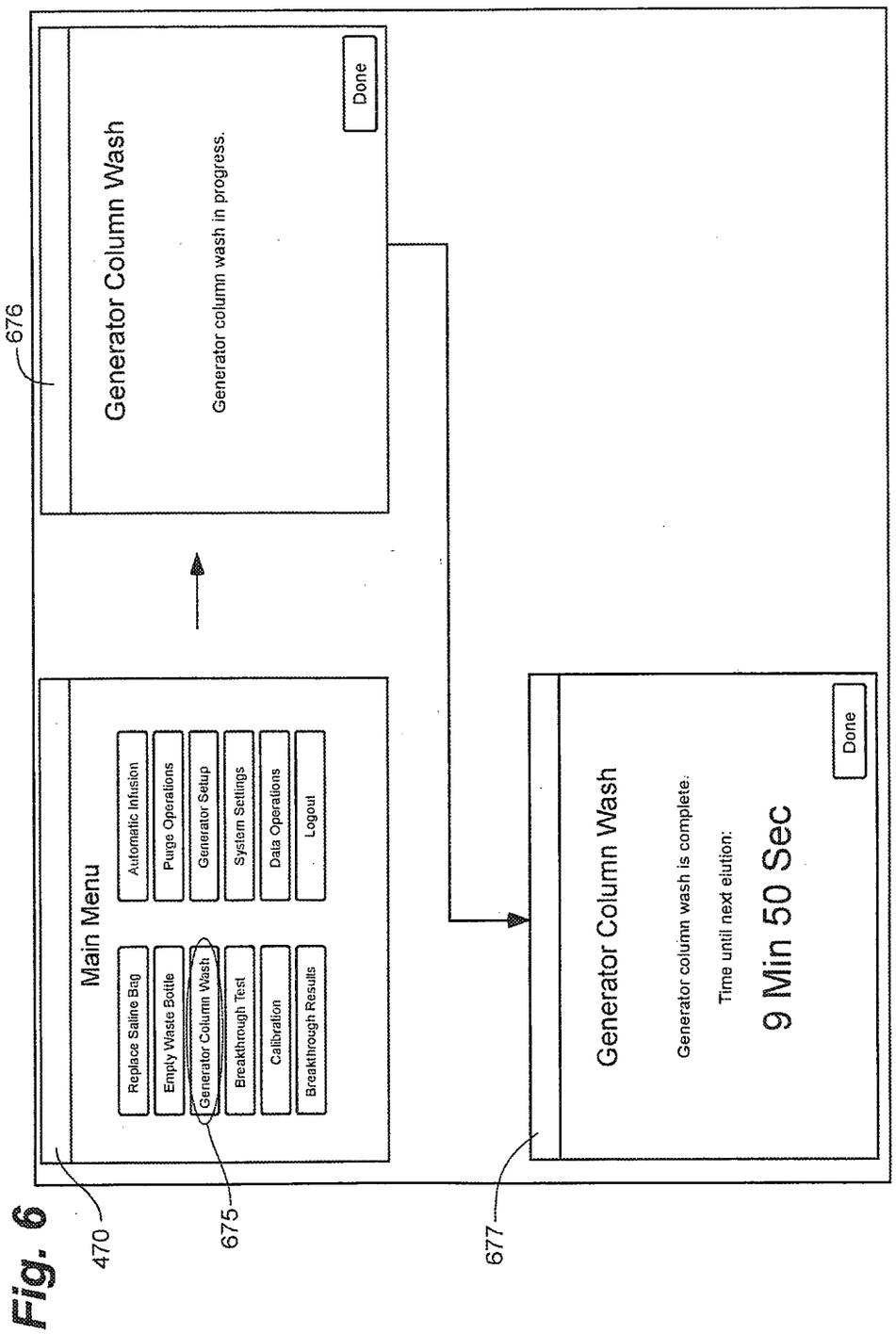

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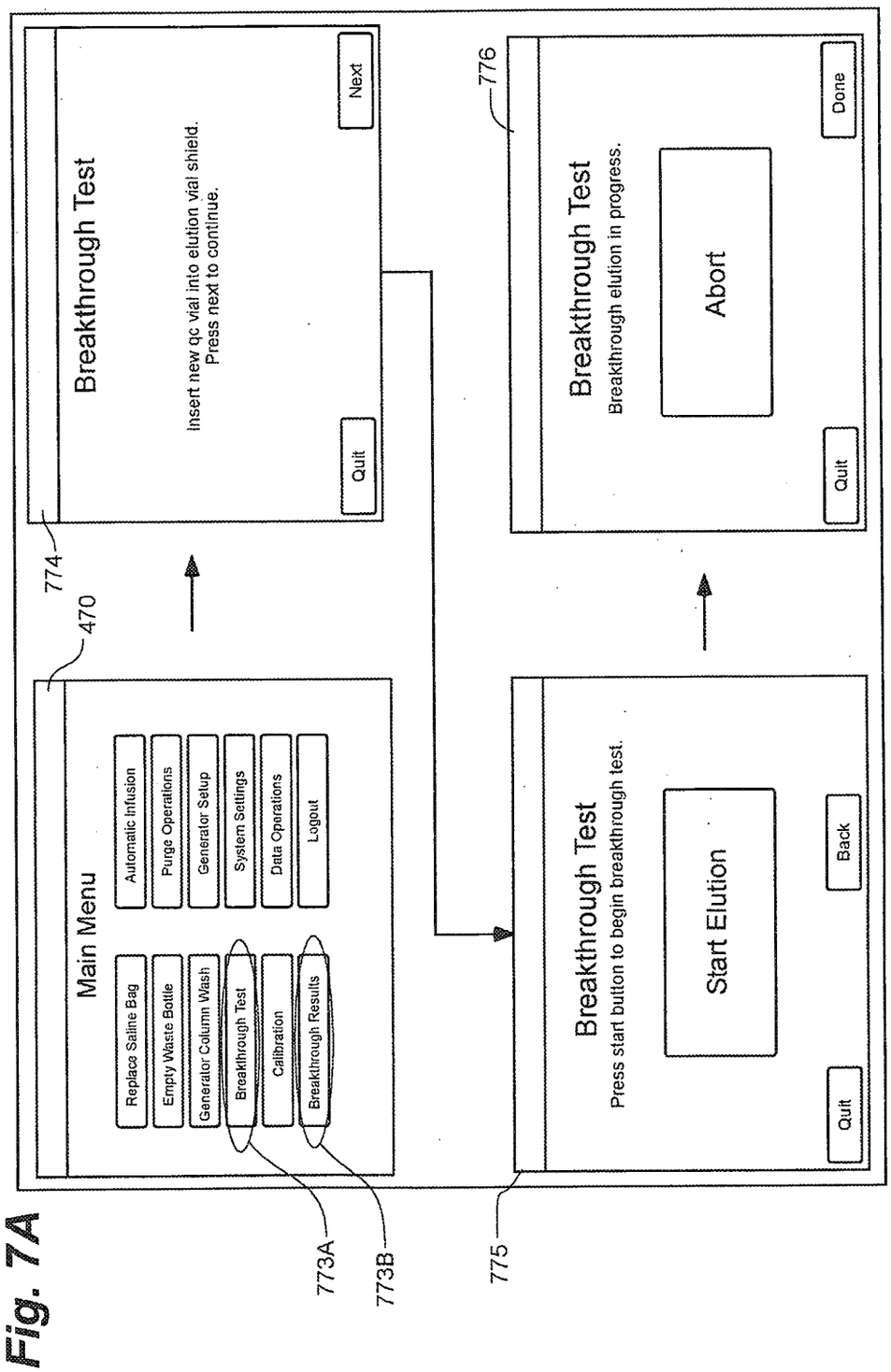

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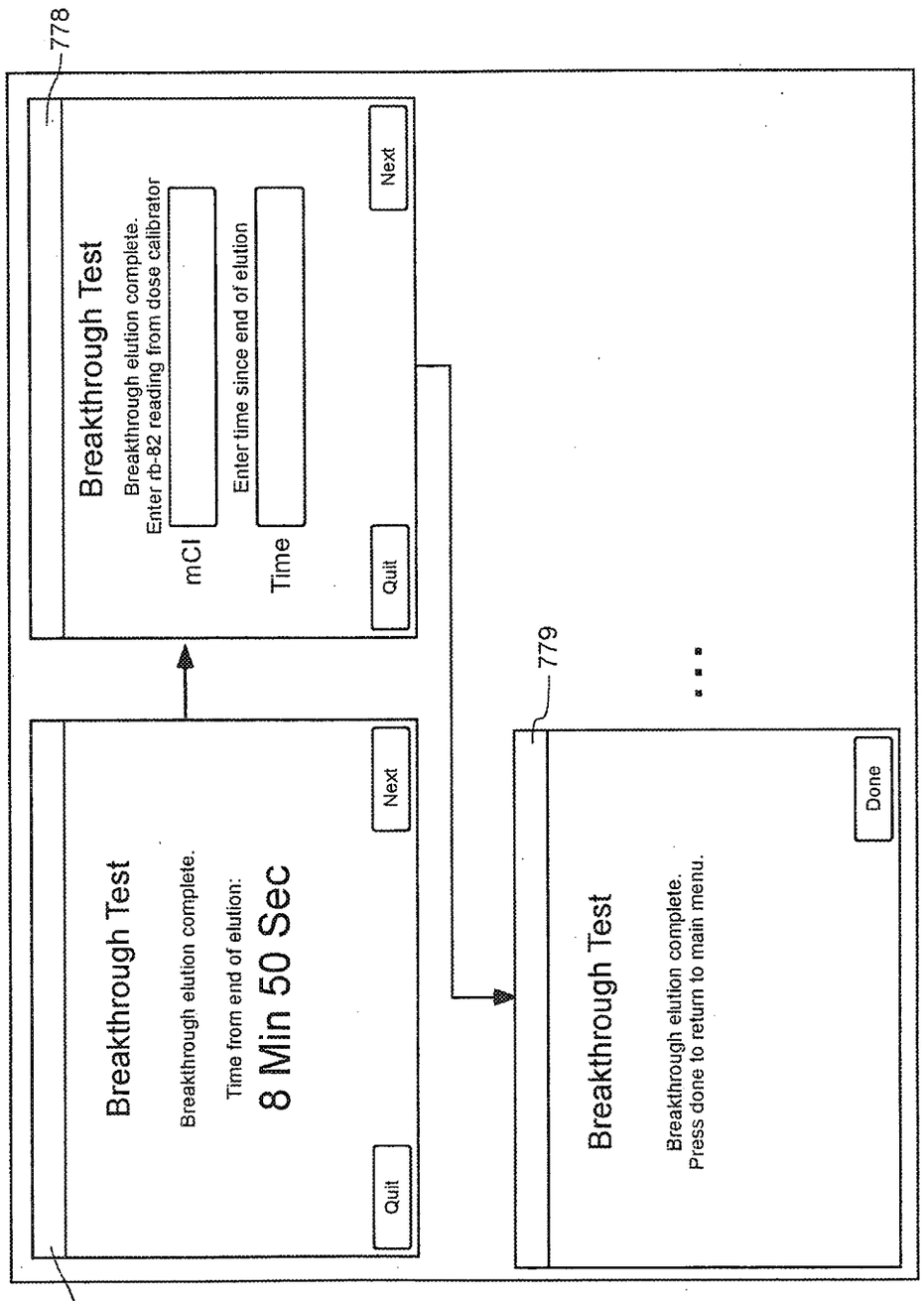

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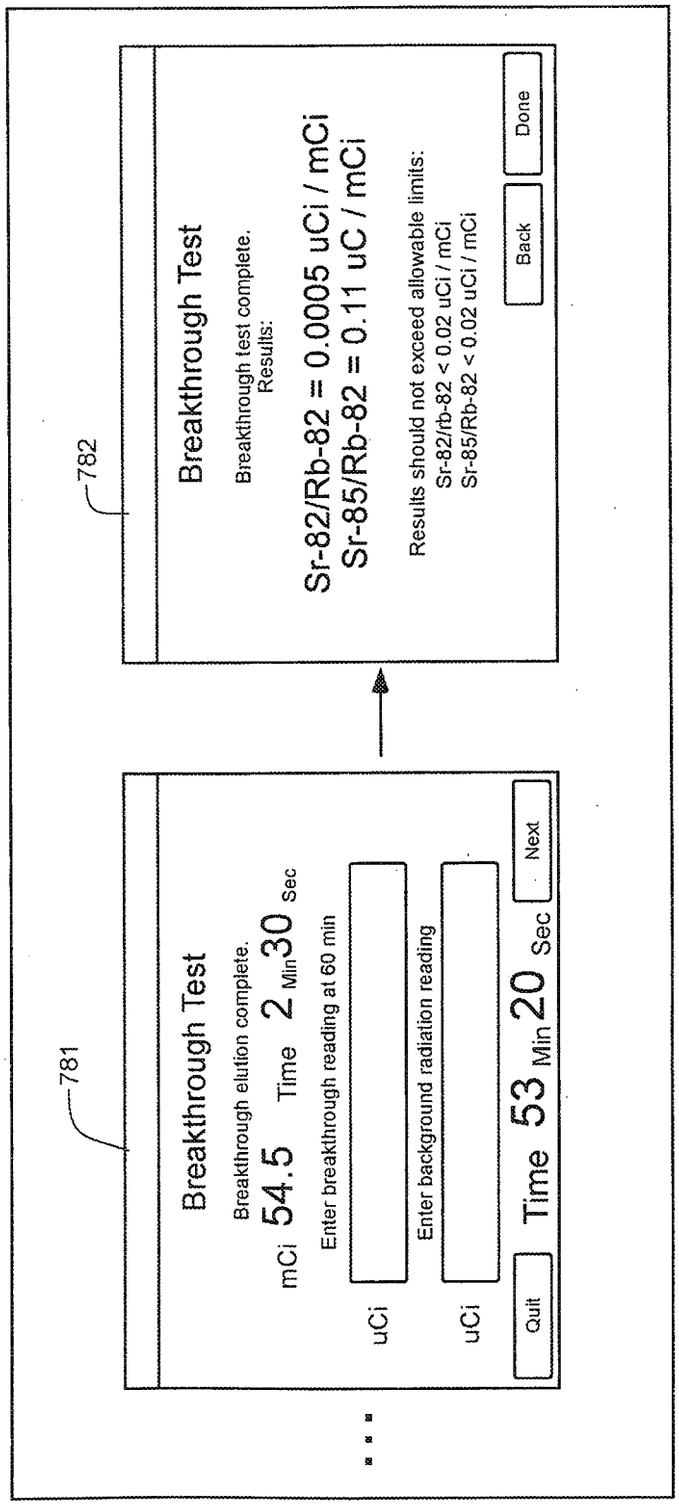

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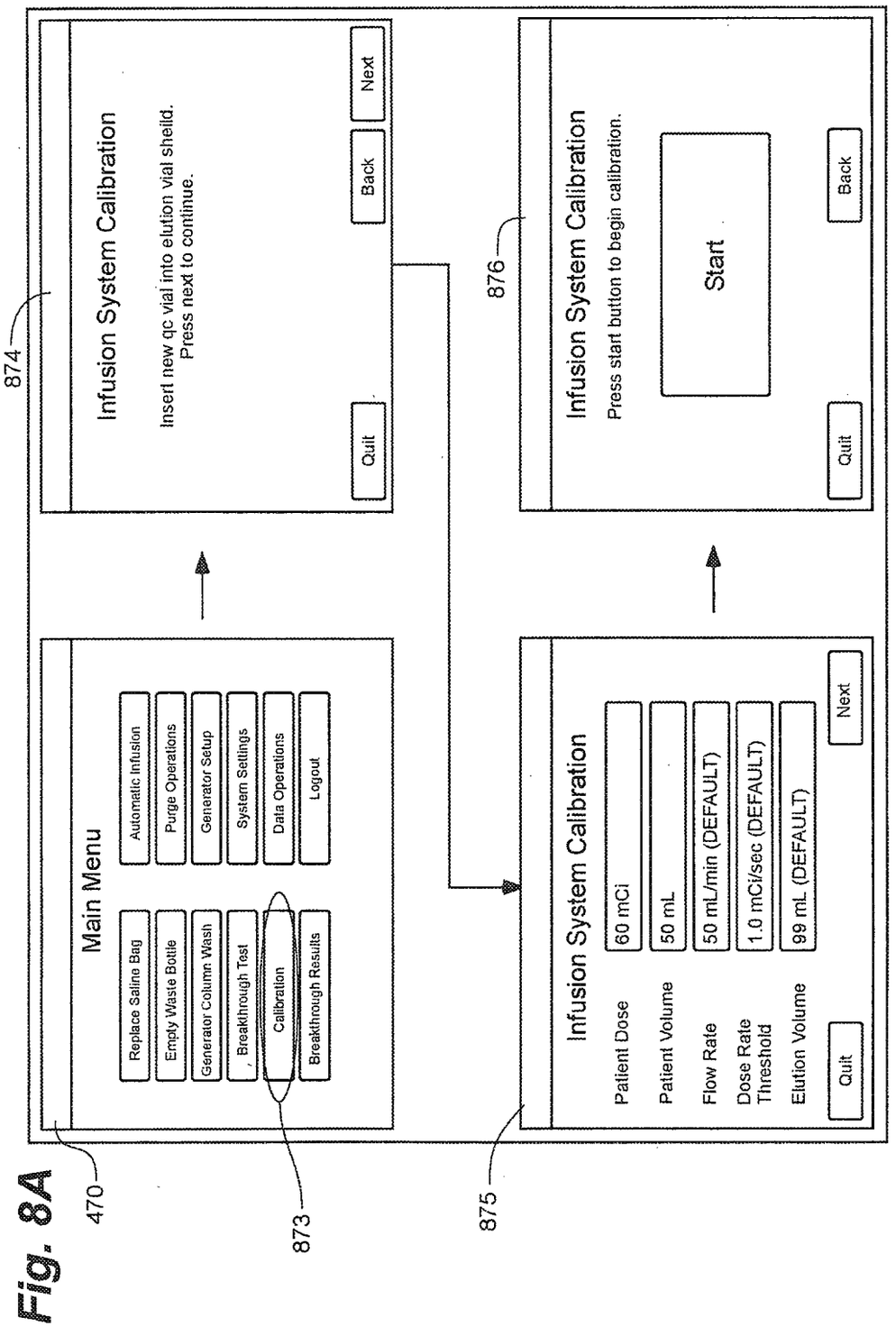

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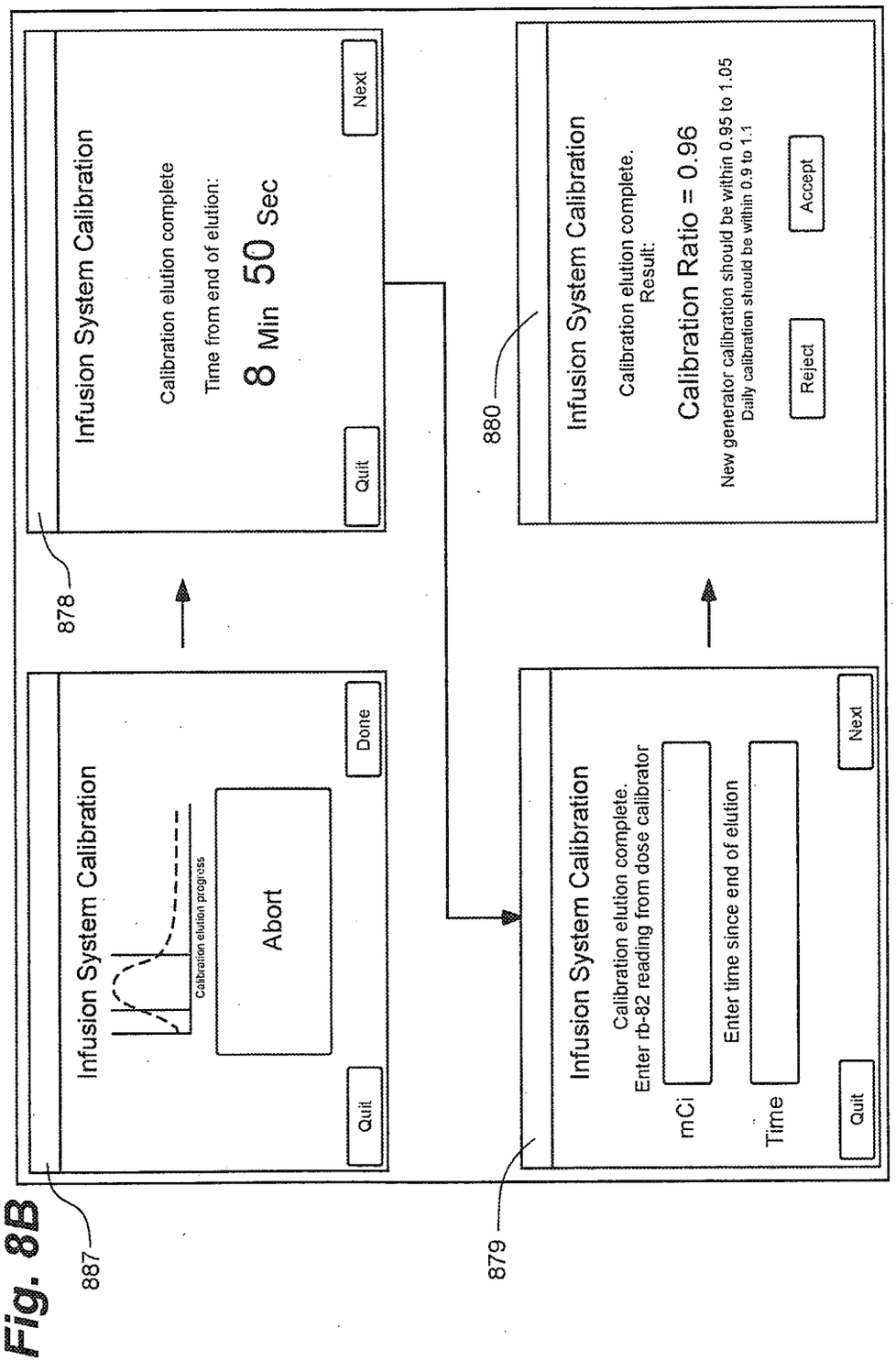

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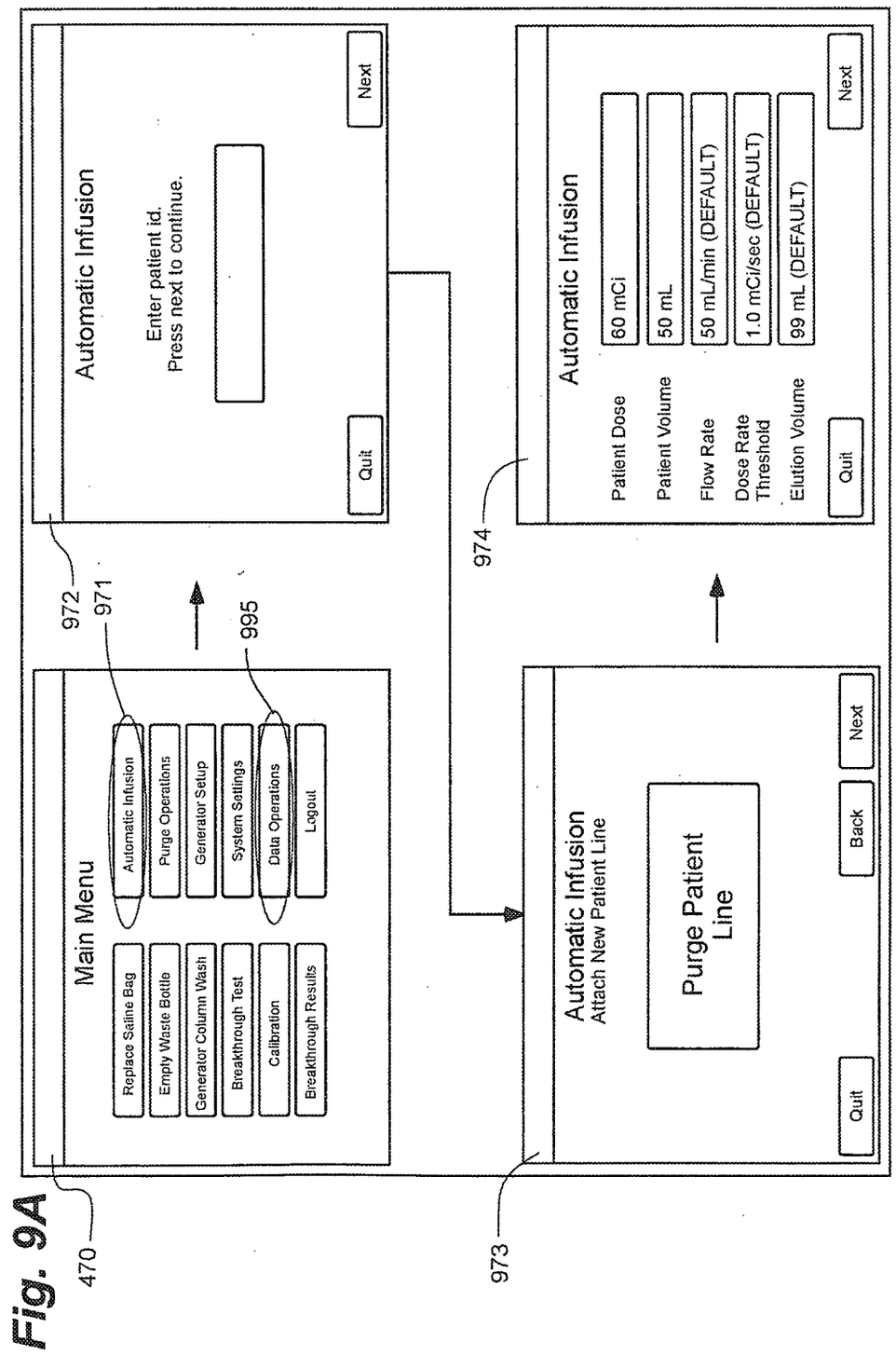

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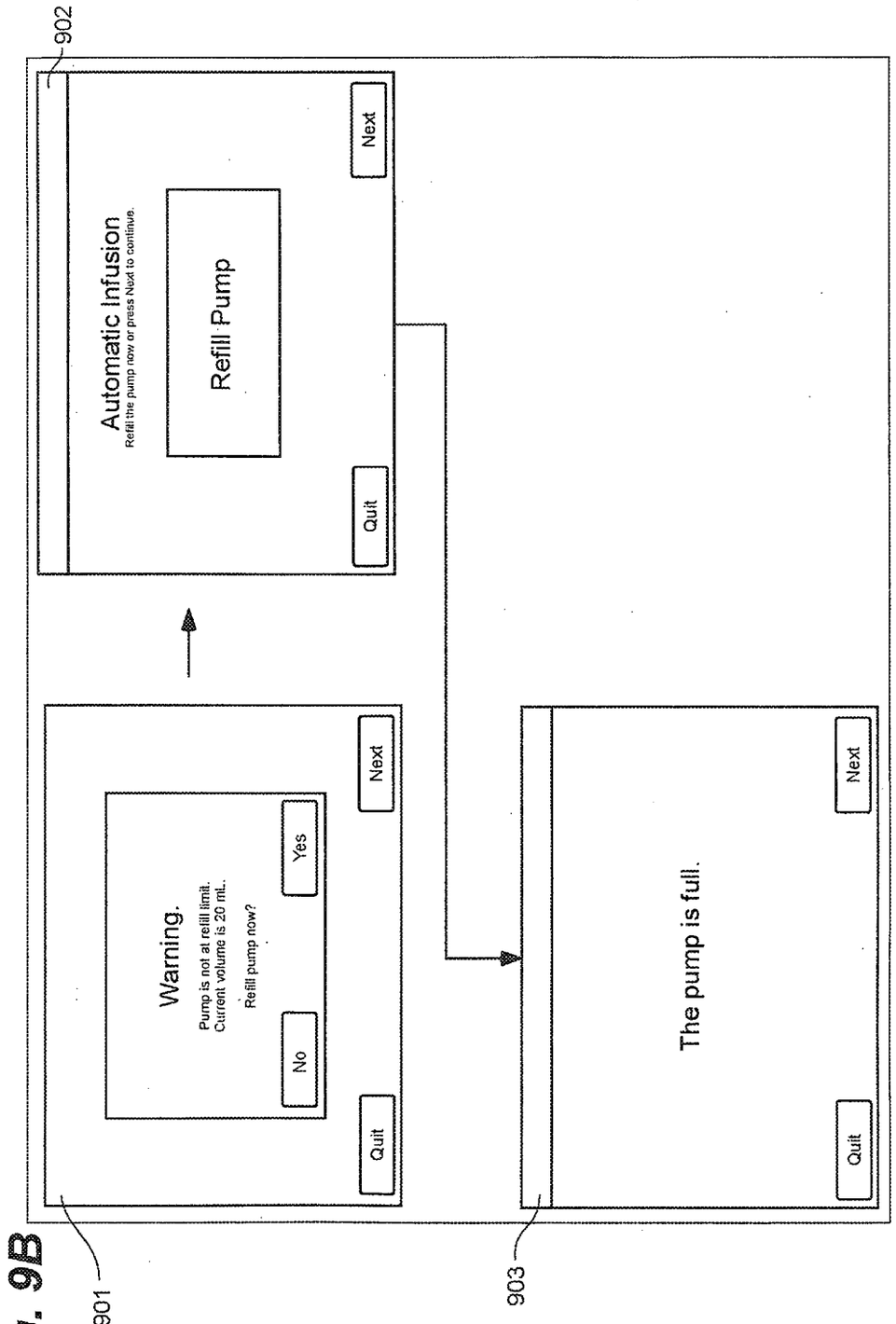


Fig. 9B

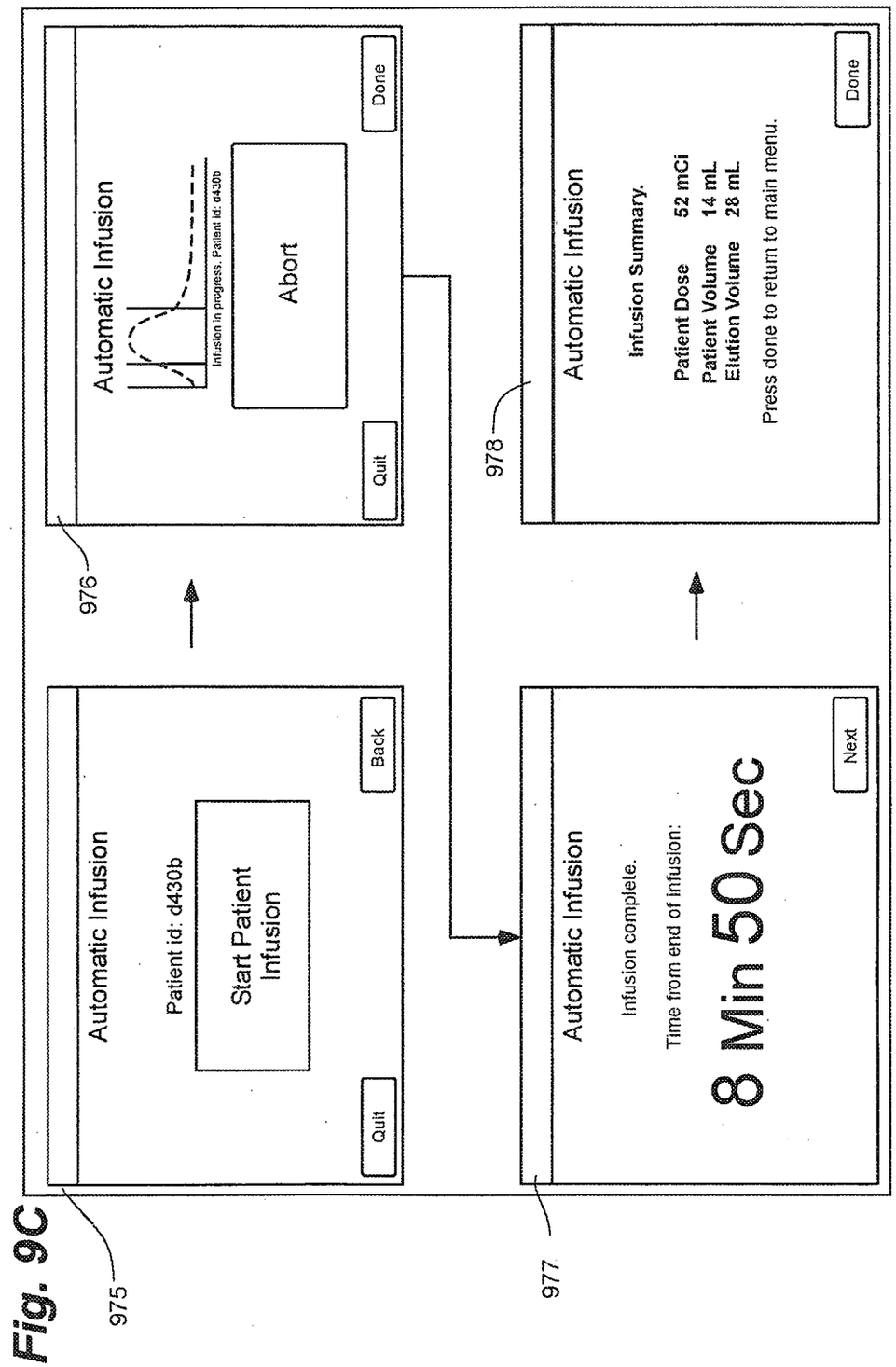


Fig. 9C

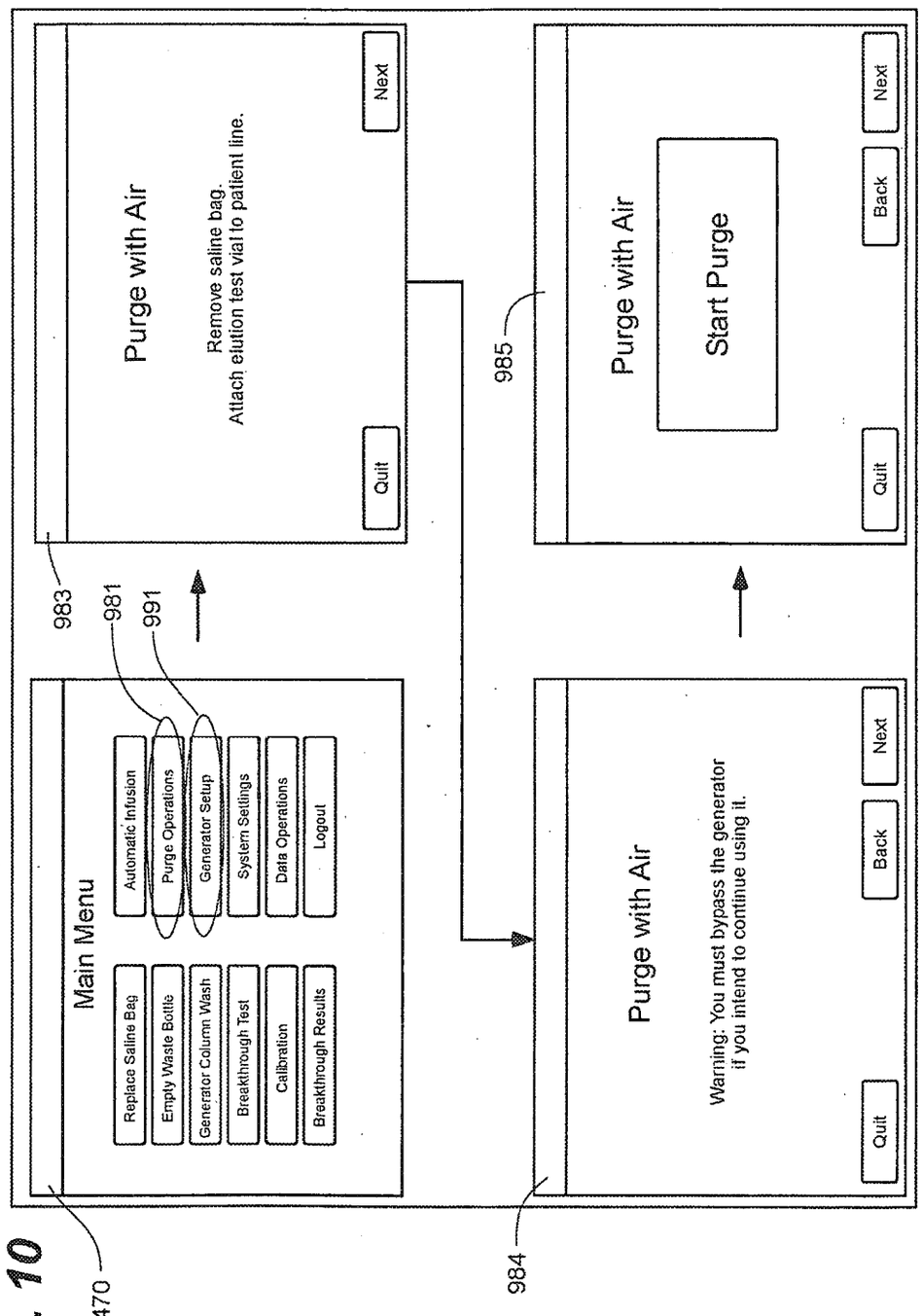
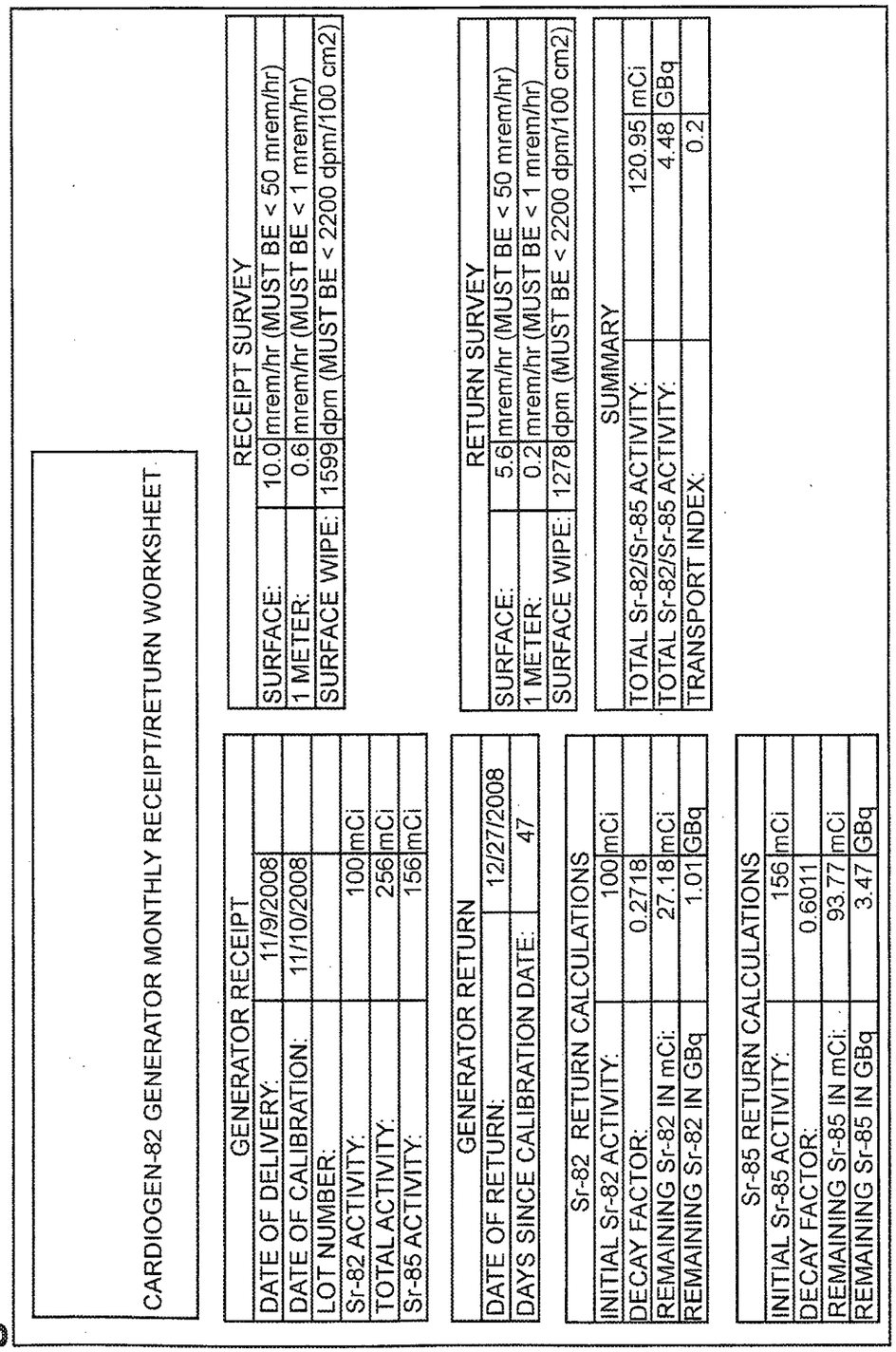


Fig. 10

Fig. 11



CARDIOGEN-82 GENERATOR MONTHLY RECEIPT/RETURN WORKSHEET

GENERATOR RECEIPT		
DATE OF DELIVERY:	11/9/2008	
DATE OF CALIBRATION:	11/10/2008	
LOT NUMBER:		
Sr-82 ACTIVITY:	100	mCi
TOTAL ACTIVITY:	256	mCi
Sr-85 ACTIVITY:	156	mCi

RECEIPT SURVEY		
SURFACE:	10.0	mrem/hr (MUST BE < 50 mrem/hr)
1 METER:	0.6	mrem/hr (MUST BE < 1 mrem/hr)
SURFACE WIPE:	1599	dpm (MUST BE < 2200 dpm/100 cm2)

GENERATOR RETURN	
DATE OF RETURN:	12/27/2008
DAYS SINCE CALIBRATION DATE:	47

RETURN SURVEY		
SURFACE:	5.6	mrem/hr (MUST BE < 50 mrem/hr)
1 METER:	0.2	mrem/hr (MUST BE < 1 mrem/hr)
SURFACE WIPE:	1278	dpm (MUST BE < 2200 dpm/100 cm2)

Sr-82 RETURN CALCULATIONS		
INITIAL Sr-82 ACTIVITY:	100	mCi
DECAY FACTOR:	0.2718	
REMAINING Sr-82 IN mCi:	27.18	mCi
REMAINING Sr-82 IN GBq	1.01	GBq

SUMMARY		
TOTAL Sr-82/Sr-85 ACTIVITY:	120.95	mCi
TOTAL Sr-82/Sr-85 ACTIVITY:	4.48	GBq
TRANSPORT INDEX:	0.2	

Sr-85 RETURN CALCULATIONS		
INITIAL Sr-85 ACTIVITY:	156	mCi
DECAY FACTOR:	0.6011	
REMAINING Sr-85 IN mCi:	93.77	mCi
REMAINING Sr-85 IN GBq	3.47	GBq

Fig. 12A

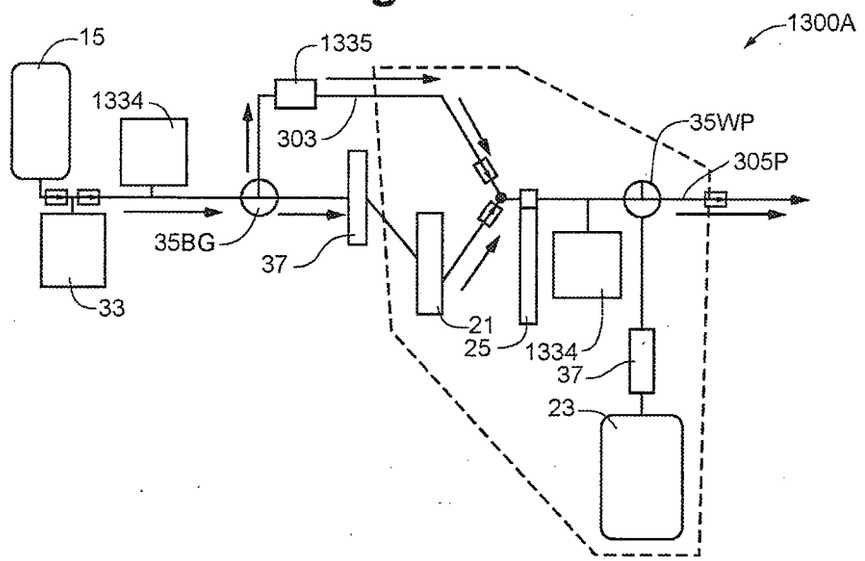


Fig. 12B

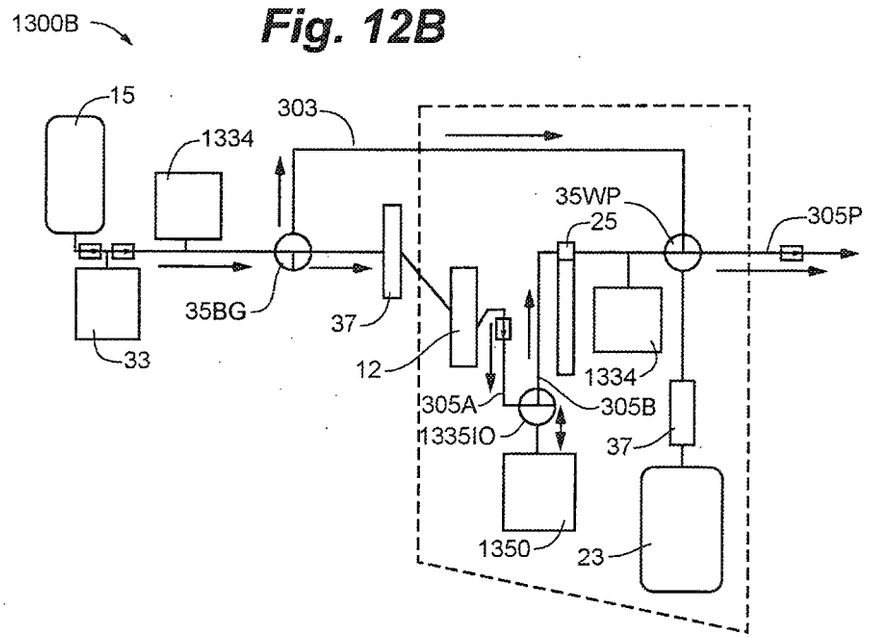
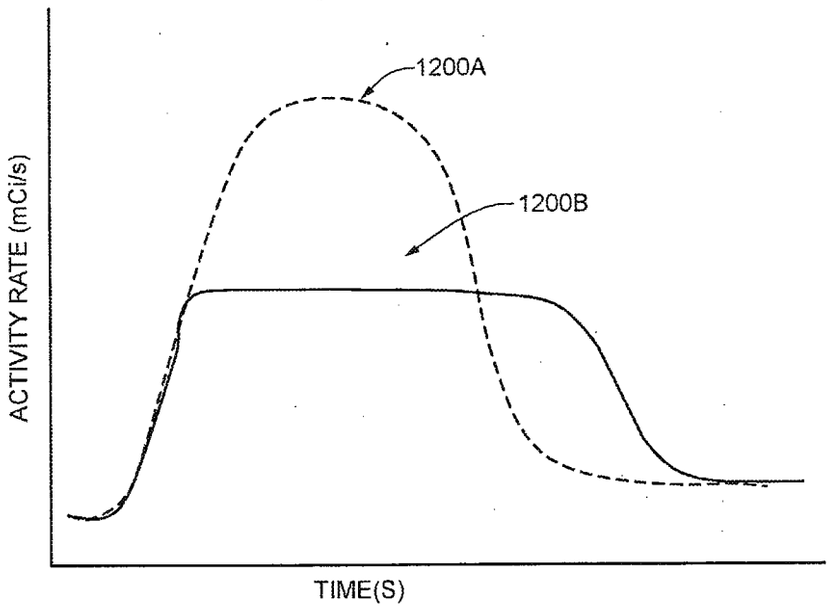


Fig. 12C



INTEGRATED STRONTIUM-RUBIDIUM RADIOISOTOPE INFUSION SYSTEMS

CROSS REFERENCE TO RELATED APPLICATIONS

This application is a continuation of U.S. patent application Ser. No. 12/808,467, filed Jun. 16, 2010, which is a 371 National Stage of International Application No. PCT/US09/47031, filed Jun. 11, 2009, which in turn is a continuation of the following four patent applications: U.S. patent application Ser. No. 12/137,356, filed Jun. 11, 2008, now U.S. Pat. No. 8,317,674, issued Nov. 27, 2012; U.S. patent application Ser. No. 12/137,363, filed Jun. 11, 2008, now U.S. Pat. No. 7,862,534, issued Jan. 4, 2011; U.S. patent application Ser. No. 12/137,364, filed Jun. 11, 2008; and U.S. patent application Ser. No. 12/137,377, filed Jun. 11, 2008, now U.S. Pat. No. 8,708,352, issued Apr. 29, 2014. The entire contents of all of these applications are incorporated herein by reference.

TECHNICAL FIELD

The present invention pertains to systems that generate and infuse radiopharmaceuticals, and, more particularly, to systems including computer-facilitated maintenance and/or operation.

BACKGROUND

Nuclear medicine employs radioactive material for therapy and diagnostic imaging. Positron emission tomography (PET) is one type of diagnostic imaging, which utilizes doses of radiopharmaceuticals, for example, generated by elution within a radioisotope generator, that are injected, or infused into a patient. The infused dose of radiopharmaceutical is absorbed by cells of a target organ, of the patient, and emits radiation, which is detected by a PET scanner, in order to generate an image of the organ. An example of a radioactive isotope, which may be used for PET, is Rubidium-82 (produced by the decay of Strontium-82); and an example of a radioisotope generator, which yields a saline solution of Rubidium-82, via elution, is the CardioGen-82® available from Bracco Diagnostics Inc. (Princeton, N.J.). A PET scanner in combination with infused doses of radiopharmaceuticals may also be employed to quantify blood flow rate, for example, through the coronary arteries of a patient.

Set up, maintenance and operational procedures for infusion systems that both generate and inject doses of radiopharmaceuticals are relatively involved in order to assure the safety and efficacy of each injected dose for the patient. Efficiency in carrying out these procedures is highly desirable for technical personnel, who work with these systems on a routine basis and would like to avoid unnecessarily prolonged exposure to radioactive radiation. Thus there is a need for new system configurations that facilitate more efficient set up, maintenance and operation.

BRIEF DESCRIPTION OF THE DRAWINGS

The following drawings are illustrative of particular embodiments of the present invention and therefore do not limit the scope of the invention. The drawings are not to scale (unless so stated) and are intended for use in conjunction with the explanations in the following detailed description. Embodiments of the present invention will hereinafter

be described in conjunction with the appended drawings, wherein like numerals denote like elements.

FIG. **1A** is a first perspective view of an infusion system, according to some embodiments of the present invention.

FIG. **1B** is another perspective view of a portion of a cabinet structure of the system shown in FIG. **1A**, according to some embodiments.

FIG. **1C** is a second perspective view of the system shown in FIG. **1A**, according to some embodiments.

FIG. **1D** is a schematic of an infusion circuit, according to some embodiments of the present invention.

FIG. **1E** is a perspective view of exemplary sample vial shielding that may be employed in conjunction with the infusion system of FIG. **1A**.

FIG. **2A** is a perspective view of a shielding assembly for an infusion system, such as that shown in FIGS. **1A-C**, according to some embodiments of the present invention.

FIG. **2B** is a perspective view of a framework of the system, according to some embodiments, and FIG. **2B-1** is an enlarged detailed view of a component of the system, according to some embodiments.

FIG. **3A** is another perspective view of the shielding assembly shown in FIG. **2A**.

FIG. **3B** is a perspective view of the infusion circuit, shown in FIG. **1C**, configured and routed, according to some embodiments.

FIG. **3C** is a perspective view of a disposable infusion circuit subassembly, according to some embodiments.

FIG. **3D** is a frame for the subassembly shown in FIG. **3C**, according to some embodiments.

FIG. **4** is a main menu screen shot from an interface of a computer, which may be included in systems of the present invention, according to some embodiments.

FIG. **5A** is a schematic showing a first group of successive screen shots from the computer interface, according to some embodiments.

FIG. **5B** is a pair of screen shots from the computer interface, which provide indications related to eluant volume levels in a reservoir of the system, according to some embodiments.

FIG. **5C** is a schematic showing a second group of successive screen shots from the computer interface, according to some embodiments.

FIG. **6** is a schematic showing a third group of successive screen shots from the computer interface, according to some embodiments.

FIGS. **7A-C** are schematics showing a fourth group of successive screen shots from the computer interface, according to some embodiments.

FIGS. **8A-B** are schematics showing a fifth group of successive screen shots from the computer interface, according to some embodiments.

FIGS. **9A-C** are schematics showing a sixth group of successive screen shots from the computer interface, according to some embodiments.

FIG. **10** is a schematic showing a seventh group of successive screen shots from the computer interface, according to some embodiments.

FIG. **11** is an exemplary report which may be generated by the computer included in infusion systems, according to some embodiments.

FIGS. **12A-B** are schematics of alternative infusion circuits that may be employed by embodiments of the present invention.

FIG. 12C is a schematic illustrating exemplary activity profiles of injected doses of a radiopharmaceutical.

DETAILED DESCRIPTION

The following detailed description is exemplary in nature and is not intended to limit the scope, applicability, or configuration of the invention in any way. Rather, the following description provides practical illustrations for implementing exemplary embodiments. Utilizing the teaching provided herein, those skilled in the art will recognize that many of the examples have suitable alternatives that can be utilized.

FIG. 1A is a first perspective view of an infusion system **10**, according to some embodiments of the present invention, wherein system **10** is shown supported by a cabinet structure, which includes a platform **113** (seen better in FIG. 2B) and a shell **13**; shell **13** extends upward from a skirt **11**, that surrounds platform **113**, to surround an interior space in which a portion of infusion system **10** is contained (seen in FIG. 1C). Shell **13** may be formed from panels of injection-molded polyurethane fitted together according to methods known to those skilled in the art. FIG. 1A illustrates the cabinet structure of system **10** including a grip or handle **14**, which extends laterally from shell **13**, in proximity to an upper surface **131** thereof, and a post **142**, which extends upward from shell **13**, and to which a work surface, or tray **16** and a computer **17** are, preferably, attached, via an ergonomic, positionable mount. According to some embodiments, computer **17** is coupled to a controller of system **10**, which is mounted within the interior space surrounded by shell **13**; and, a monitor **172** of computer **17** not only displays indications of system operation for a user of system **10**, but also serves as a device for user input (e.g. touch screen input). However, according to alternate embodiments, another type of user input device, known to those skilled in the art, may be employed by computer **17**. Other types of user input devices may be included, for example, a keyboard, a series of control buttons or levers, a bar code reader (or other reader of encoded information), a scanner, a computer readable medium containing pertinent data, etc. The user input device may be mounted on the cabinet structure of system **10**, as shown, or may be tethered thereto; alternatively the user input device may be remote from system **10**, for example, located in a separate control room. According to some additional embodiments, another user input device, for example, in addition to a touch screen of computer **17**, may be remote from system **10** and used to start and stop infusions, as well as to monitor system operation both during quality control infusions and during patient infusions. Operation of system **10**, which is facilitated by computer **17**, will be described below, in conjunction with FIGS. **4-9C**.

FIG. 1A further illustrates two pairs of wheels **121**, **122**, mounted to an underside of platform **113**, to make system **10** mobile; handle **14** is shown located at an elevation suitable for a person to grasp in order to maneuver system **10**, from one location to another, upon pairs of wheels **121**, **122**. According to some preferred embodiments, one or both pairs of wheels **121**, **122**, are casters, allowing for rotation in a horizontal plane (swivel), in order to provide additional flexibility for maneuvering system **10** in relatively tight spaces.

FIG. 1B is a perspective view of a portion of system **10**, on a side **111** of the cabinet structure, which is in proximity to wheels **121**, **122**. FIG. 1B illustrates a lever or pedal **125**, which is located for activation by a foot of the person, who grasps handle **14** to maneuver system **10**. In a neutral position, pedal **125** allows wheels **121**, **122** to rotate, and, if embodied as casters, to swivel freely. Pedal **125** may be depressed to a first position which prevents a swiveling of wheels **121**, **122**, according to those embodiments in which wheels **121**, **122** are casters, and may be further depressed to brake wheels **121**, **122** from rolling and swiveling, upon reaching a desired location. According to some embodiments, braking may be designed to slow system **10**, for example, when rolling down an incline, and, according to yet further embodiments, system **10** may include a motor to power movement thereof.

FIG. 1B further illustrates: a rear access panel **174** of shell **13**, for example, providing access to circuit boards of the aforementioned controller contained within the interior space that is surrounded by shell **13**; an optional lock **184**, to secure panel **174**; a power jack **118**, for connecting system **10** to a power source; and a printer **117** for providing documentation of each patient infusion carried out by system **10**, and of system quality control test results. In some embodiments, system **10** may further include a power strip by which auxiliary equipment may be powered, and one or more additional electrical connectors, or ports (not shown), which are supported by platform **113** and may be integrated into shell **13**, for example, in proximity to jack **118** or printer **117**; these electrical connectors/ports allow system **10** to communicate with, other devices used for nuclear imaging procedures, for example, a PET scanner/camera, and/or for coupling to an intranet network, and/or to the internet, for example, to link up with software programs for various types of data analysis, and/or to link to computers of consulting clinicians/physicians, and/or to link into service providers and/or component suppliers data bases for enhanced maintenance and inventory management.

FIG. 1A further illustrates upper surface **131** of shell **13** including several openings **133**, **135**, **139** formed therein. FIG. 1C is a partially exploded perspective view of system **10**, wherein a removable access panel **132** is shown as a contoured portion of upper surface **131**, which, when exposed, by lifting away a bin **18**, that mates therewith, may be removed from another opening **137** formed in upper surface **131**. FIG. 1C also provides a better view of another panel **134** which may be lifted away from opening **139**. According to the illustrated embodiment, openings **139** and **137** provide a user of system **10** with independent access to separate portions of infusion system **10**, which are contained within shell **13**, for example, to set up and maintain system **10**; and openings **133** and **135** provide passageways for tubing lines to pass through shell **13**. FIG. 1C further illustrates an optional switch **102**, which in case of an emergency, may be activated to abort function of system **10**. With reference to FIGS. 1A and 1C, it may be appreciated that an arrangement of features formed in upper surface **131** of shell **13**, in conjunction with bin **18**, tray **16** and computer **17**, provide a relatively ergonomic and organized work area for technical personnel who operate system **10**.

Turning now to FIG. 1D, a schematic of an infusion circuit **300**, which may be incorporated by system **10**, is shown. FIG. 1D illustrates circuit **300** generally divided into a first part **300A**, which includes components mounted outside shell **13**, and a second part **300B**, which includes components mounted within the interior space surrounded by shell **13**. (Parts **300A** and **300B** are delineated by dotted lines in FIG. 1D.) FIG. 1D further illustrates second part **300B** of circuit **300** including a portion contained within a shielding assembly **200**, which is designated schematically as a dashed line. Some embodiments of shielding assembly

200 will be described in greater detail, in conjunction with FIGS. 2A-B and 3A-B, below.

According to the illustrated embodiment, circuit **300** includes: an eluant reservoir **15**, for example, a bag, bottle or other container, containing saline as the eluant, which is shown hanging from a post, or hanger **141** above upper surface **131** of shell **13** in FIG. 1A; a syringe pump **33**, for pumping the eluant from reservoir **15**, and a pressure syringe **34** (or other device or sensor), for monitoring pumping pressure; a filter **37**, which may also serve as a bubble trap, for the pumped eluant; a radioisotope generator **21**, through which the filtered eluant is pumped to create a radioactive eluate, for example an eluate carrying Rubidium-82 that is generated by the decay of Strontium-82, via elution, within a column of generator **21**; and an activity detector **25**, for measuring the activity of the eluate discharged from generator **21**, in order to provide feedback for directing the flow of the eluate, via a divergence valve **35**WP, either to a waste bottle **23** or through a patient line **305***p*, for example, to inject a dose of the radiopharmaceutical eluate into a patient. With reference back to FIG. **1**A, patient line **305***p* is shown extending out from shell **13**, through opening **135**, to a distal end thereof, which, according to some embodiments, includes a filter. Patient line **305***p* may be coupled to another line that includes a patient injection needle (not shown). Alternatively, patient line **305***p* may be coupled to another line (not shown), which extends from a source of another active substance, for example, a stress agent; the other line is coupled to the line that includes the patient injection needle, in order to permit injection of the additional active substance.

FIG. **1**D illustrates an eluant tubing line **301** coupled to reservoir **15** and to pump **33**, and, with reference to FIGS. **1**A-B, it may be appreciated that opening **133** provides the passageway for tubing line **301** to enter the interior space surrounded by shell **13**. According to some preferred embodiments, opening **133** includes a grommet-type seal that prevents leakage of eluant, which may spill from reservoir **15**, into the interior space through opening **133**, while allowing a user to assemble tubing line **301** through opening **133**. Likewise opening **135**, which provides a passageway for patient line **305***p*, may include a grommet-type seal. According to some embodiments, shell **13** further supports holders to safely hold, for example, during transport of system **10**, portions of tubing lines that extend outward therefrom, for example, line **301** and/or line **305***p*.

FIG. **1**D further illustrates another eluant tubing line **302** coupled to pump **33** and a divergence valve **35**BG, which may either direct pumped eluant through a tubing line **304**, to generator **21**, or direct the pumped eluant through a by-pass tubing line **303**, directly to patient line **305***p*. Divergence valve **35**BG, as well as divergence valve **35**WP, which directs eluate from an eluate tubing line **305** either to a waste line **305***w* or to patient line **305***p*, may each be automatically operated by a corresponding servomotor (not shown), coupled to the controller (not shown) of system **10**, which controller receives feedback from activity detector **25**. When system **10** is operating for automatic infusion, to deliver a dose of radiopharmaceutical to a patient, for example, Rubidium-82 for diagnostic imaging, divergence valve **35**BG is initially set to direct eluant to generator **21** and divergence valve **35**WP is set to direct eluate from the generator into waste bottle **23**, until activity detector **25** detects the desired activity of the eluate, at which time the feedback from activity detector **25** causes the controller to direct the corresponding servo-motor to re-set valve **35**WP for diverting the flow of eluate into patient line **305***p*. According to some embodiments, once a prescribed volume of the eluate has passed through patient line **305***p*, the controller directs the corresponding servomotor to re-set divergence valve **35**BG for diverting the flow of eluant through by-pass line **303** and into patient line **305***p* in order to flush, or push any eluate remaining in patient line **305***p* into the patient. According to some embodiments, the controller may also direct the corresponding servomotor to re-set divergence valve **35**WP back toward waste bottle **23**, prior to the flush through by-pass line **303**, in order to prevent back flow of eluant, through line **305**, toward generator **21**. According to some preferred methods of operation, in certain situations, which will be described in greater detail below, eluant is pumped through by-pass line **303** immediately following the flow of the prescribed volume of eluate into patient line **305***p*, at a higher speed, in order to push the eluate in patient line **305**, thereby increasing a flow rate of the injection of eluate out from patient line **305***p* and into the patient. For example, once the prescribed volume of eluate has flowed into patient line **305***p*, and once divergence valve **35**BG is set to divert flow through by-pass line **303**, the speed of pump **33** may be adjusted to increase the flow rate of eluant to between approximately 70 mL/min and approximately 100 mL/min. This method for increasing the injection flow rate, is desirable, if a relatively high flow rate is desired for patient injection and a flow rate through generator **21** is limited, for example, to below approximately 70 mL/min, maximum (typical flow rate may be approximately 50 mL/min), in order to avoid an excessive back pressure created by the column of generator **21** in upstream portions of tubing circuit **300**; the excessive back pressure could damage filter **37** or otherwise impede flow through eluant tubing line **302**.

Although not shown in FIG. **1**D, a number of sensors, for example, to measure pressure and/or flow velocity, may be incorporated into circuit **300**, according to some alternate embodiments, in order to monitor for flow anomalies, for example, related to occlusions/plugs in circuit **300** and/or leaks, and/or to provide feedback for control of an activity level of infused doses of radiopharmaceutical. Suitable sensors for any of the above purposes are known to those skilled in the art. Examples of flow meters that may be incorporated into circuit **300**, include the Innova-Sonic® Model 205 Transit-Time Ultrasonic Liquid Flow Meter that employs digital signal processing (available from Sierra Instruments, Inc.) and the Flocat LA10-C differential pressure flow meter. One example of a pressure sensor that may be employed to detect infusion circuit occlusions is the PRO/Pressure-Occlusion Detector (available from INTROTEK® of Edgewood, N.Y., a subsidiary of Magnetrol of Downers Grove, Ill.), which employs pulse-type ultrasound; this sensor detects subtle changes in positive and negative air pressure and produces a corresponding passive resistive output signal, which may be routed to the system controller and/or computer **17**. One or more of this type of sensor may be incorporated into infusion circuit **300** by simply fitting the sensor around any of the tubing lines of infusion circuit **300**; in fact, the PRO/Pressure-Occlusion Detector may be a suitable alternative to pressure syringe **34** of circuit **300**. Other types of pressure sensors, for example, similar to those known in the art for blood pressure monitoring, may be employed in infusion circuit **300**.

System **10** may further include sensors to detect fluid levels in eluant reservoir **15** and waste bottle **23**. Some examples of such sensors, which also employ the aforementioned pulse-type ultrasound, are the Drip Chamber Liquid Level Sensor and the CLD/Continuous Level Detector (both

available from INTROTEK®); alternatively, for example, an HPQ-T pipe mounted, self-contained liquid sensor (available from Yamatake Sensing Control, Ltd.), or an SL-630 Non-Invasive Disposable/Reusable Level Switch (available from Cosense, Inc. of Hauppauge, N.Y.) may be employed to detect the fluid levels. Alternately or in addition, system **10** can include additional radiation and/or moisture detection sensors, which can detect leaks. With reference to FIG. **1**D, such sensors are preferably located in proximity to fittings **311**, **312**, **313**, **314** and **315** that join portions of circuit **300** to one another. Some examples of leak detection sensors include, without limitation, those in the HPQ-D leak detection sensor family, and the HPF-D040 fiberoptic leak detector (all available from Yamatake Sensing Control, Ltd.). System **10** may further include additional sensors to detect contaminants and/or air bubbles within the tubing lines of circuit; examples of such sensors include the Point-air Detection (PAD) Sensor, that employs pulse-type ultrasound for air bubble detection, and the Blood Component Detector that employs optical sensing technology to perform Colorimetry-based fluid detection of unwanted elements in the tubing lines (both available from INTROTEK®).

According to those embodiments that include any of the above sensors, the sensors are linked into the controller of system **10** and/or computer **17**, either of which may provide a signal to a user of system **10**, when a flow anomaly is detected, and/or information to the user, via monitor **172**, concerning fluid levels, pressure and/or flow through circuit **300**. Computer **17** may be pre-programmed to display, for example, on monitor **172**, a graphic of infusion circuit **300** wherein each zone of the circuit, where an anomaly has been detected, is highlighted, and/or to provide guidance, to the system user, for correcting the anomaly. It should be noted that the alternative infusion circuits illustrated in FIGS. **12**A-B, which will be described below, may also include any or all of these types of sensors.

With further reference to FIG. **1**D, it may be appreciated that shielding assembly **200** encloses those portions of circuit **300** from which radioactive radiation may emanate, with the exception of that portion of patient line **305***p*, which must extend out from shielding assembly **200** in order to be coupled to the patient for injection, or in order to be coupled to shielded sample vials, as will be described below. Thus, technical personnel, who operate system **10**, are protected from radiation by shielding assembly **200**, except at those times when an infusion is taking place, or when quality control tests require collection of eluate into sample vials. During infusions and quality control test sample collection, all technical personnel are typically in another room, or otherwise distanced from system **10**, in order to avoid exposure to radiation during the infusion, and, according to some preferred embodiments of the present invention, system **10** includes at least one means for informing technical personnel that an infusion is about to take place or is taking place. With reference back to FIGS. **1**A and **1**C, system **10** is shown including a light projector **100**, mounted on post **142**. According to the illustrated embodiment, projector **100**, projects a light signal upward, for maximum visibility, when pump **33** is pumping eluant and elution is taking place within generator **21**, or at all times when pump **33** is pumping eluant. According to some embodiments, the light signal flashes on and off when the eluate is being diverted from generator **21** into waste bottle **23**, and the light signal shines steadily when the eluate is being diverted through patient line **305***p*, or visa versa. According to other embodiments, a projector **100** shines a light having a first color, to indicate that eluate is being diverted to waste bottle **23**, and then shines a light having a second, different color, to indicate that eluate is being directed to patient line **305***p* for infusion. Light projector **100** may further project a more rapidly flashing light, for example, for approximately five seconds, once a peak bolus of radioactivity is detected in the eluate, to provide further information to technical personnel. Alternative means of informing technical personnel that an infusion is taking place may also be incorporated by system **10**, for example, including audible alarms or other types of visible or readable signals that are apparent at a distance from system **10**, including in the control room.

It should be noted that, according to alternate embodiments, system **10** includes an 'on board' dose calibrator for quality control tests, and circuit **300** is expanded to include elements for an automated collection of eluate samples for activity measurements, via the on board dose calibrator. According to a first set of these alternate embodiments, a sample collection reservoir is integrated into circuit **300**, downstream of divergence valve **35**WP and in communication with tubing line **305**P, in order to receive quality control test samples of eluate, via tubing line **305**P, and both the reservoir and the dose calibrator are located in a separate shielded well. According to a second set of these alternate embodiments, waste bottle **23** is configured to receive the quality control test samples of eluate, via tubing line **305**W, and a dose calibrator is integrated into shielding assembly **200**. Quality control procedures will be described in greater detail below, in conjunction with FIGS. **6**-**8**B.

When maintenance of system **10** requires the emptying waste bottle **23**, relatively easy access to waste bottle **23** is provided through opening **139** in top surface **131** of shell **13**. It should be noted that technical personnel are preferably trained to empty waste bottle **23** at times when the eluate, contained in waste bottle **23**, has decayed sufficiently to ensure that the radioactivity thereof has fallen below a threshold to be safe. Opening **139** is preferably located at an elevation of between approximately 2 feet and approximately 3 feet; for example, opening **139** may be at an elevation of approximately 24 inches, with respect to a lower surface of platform **113**, or at an elevation of approximately 32 inches, with respect to a ground surface upon which wheels **121**, **122** rest. According to the illustrated embodiment, opening **139** is accessed by lifting panel **134**; just within opening **139**, a shielded lid or door **223** (FIG. **2**A) may be lifted away from a compartment of shielding assembly **200** that contains waste bottle **23**. With further reference to FIG. **1**C, it may be appreciated that opening **137** provides access to other portions of circuit **300** for additional maintenance procedures, such as changing out generator **21** and/or other components of circuit **300**, as will be described below.

For those embodiments of system **10** in which automated quality control tests are performed and/or when system **10** is employed for relatively high volume operation, management of waste may become burdensome, even though access to waste bottle **23** is greatly facilitated, as described above. Thus, in order to facilitate waste management, some embodiments of system **10** may employ a separation system to separate salts, including radioactive elements, from water, for example, via evaporation or reverse osmosis. In an evaporation type system, the water component of the waste is evaporated, while in a reverse osmosis type system the water is separated from the salts, and, then, once confirmed to be non-radioactive, via a radiation detector, is piped to a drain. According to some other embodiments, circuit **300** may be configured so that the waste may be used to purge air from the tubing lines thereof and/or to perform the bypass

flush that was described above, preferably after the radioactivity of the waste drops below a critical threshold.

FIGS. **1A** and **1C** further illustrate a pair of relatively shallow external recesses **190**, which are formed in upper surface **131** of shell **13**, for example, in order to catch any spills from the infusion system; one of recesses **190** is shown located in proximity to post, or hanger **141**, which holds reservoir **15**, and in proximity to opening **133**, through which tubing line **301** passes. Another recess **192** is shown formed in upper surface **131**; a width and depth of recess **192** may accommodate storage of technical documentation associated with infusion system **10**, for example, a technical manual and/or maintenance records, or printouts from printer **117** (FIG. **1B**). With reference to FIG. **1C**, upper surface **131** of shell **13** is shown to also include additional recesses **101**, which are each sized to hold a shielded test vial, which contains samples from infusion system **10**, for example, for breakthrough testing and/or calibration, which will be described in greater detail, below. An exemplary test vial shield is shown in FIG. **1E**. The test vial shield of FIG. **1E** is preferably formed from Tungsten rather than lead, for example, to reduce exposure to lead, for improved shielding, and to reduce the weight of the shield. FIG. **1E** illustrates the test vial shield including a handle to simplify manipulation thereof, but alternative configurations of test vial shields have no handle—for these a sling, or strap, may be employed for handling.

Additional receptacles **180** are shown formed in bin **18**, on either side of a handle **182**, which facilitates removal of bin **18** away from shell **13**. Technical personnel may, thus, conveniently transport bin **18** to a storage area for a collection of supplies, for example, sharps, gloves, tubing lines, etc . . . , into one or more receptacles **180** thereof, and/or to a waste container where separate receptacles **180** of bin **18** may be emptied of waste, such as packaging for the aforementioned supplies, for example, deposited therein during infusion procedures. According to some embodiments, one or more additional receptacles are formed in one or more disposal containers, for example, to contain sharps and/or radioactive waste (other than that contained in waste bottle **23**), which may be integrated into bin **18**, or otherwise fitted into, or attached to shell **13**, separate from bin **18**.

FIG. **2A** is a perspective view of shielding assembly **200**, according to some embodiments of the present invention. With reference to FIGS. **1C** and **2A**, together, it may be appreciated that opening **137**, in upper surface **131** of shell **13**, provides access to a lid or door **221** of a sidewall **201** of shielding assembly **200**, which sidewall **201** encloses a compartment sized to contain a radioisotope generator of system **10**, for example, generator **21**, previously introduced. It should be noted that, according to alternate embodiments, the compartment enclosed by sidewall **201** is large enough to hold more than one generator, for example, to increase system operating efficiency for relatively high volume operation. In some of these alternate embodiments, tubing lines **304** and **305** are each branched for parallel flow through the multiple generators, in which case divergence valves may be employed to alternate the flow through the generators, one at a time. In others of these alternate embodiments, the multiple generators are connected in series between tubing line **304** and tubing line **305**. In addition, a reservoir for accumulating eluate may be included in circuit **300**, downstream of the generators and upstream of divergence valve **35** WP, in conjunction with a second pump, in some cases. Embodiments including multiple generators and/or an eluate reservoir and second pump can be employed to better manage an activity level of each dose, or patient injection, for example, as described below, in conjunction with FIGS. **12A-B**.

According to the embodiment illustrated in FIG. **2A**, opening **137** and door **221** are located at a lower elevation, for example, with respect to platform **113**, than are opening **139** and lid **223**, which provide access to the compartment being formed by a sidewall **203** of shielding assembly **200** to contain waste bottle **23**, as previously described. When panel **132** is separated from shell **13**, and door **221** opened, generator **21** may be lifted out from an opening **231** (FIG. **3A**) which mates with door **221** of sidewall **201**. A weight of generator **21**, which includes its own shielding, may be between approximately 23 and approximately 25 pounds, thus, according to some preferred embodiments of the present invention, the elevation of each of openings **137** and **231**, with respect to the lowermost portion of the cabinet structure, is between approximately 1 foot and approximately 2 feet, in order to facilitate an ergonomic stance for technical personnel to lift generator **21** out from the compartment. According to an exemplary embodiment, when shielding assembly **200** is contained in the cabinet structure of FIG. **1A**, openings **137** and **231** are located at an elevation of approximately 12 inches, with respect to the lower surface of platform **113**, or at an elevation of approximately 19 inches, with respect to the ground surface upon which wheels **121**, **122** rest. FIG. **1C** further illustrates access panel **132** including a security lock **138**, which mates with a framework **19** of system **10**, shown in FIG. **2B**, in order to limit access to generator **21**.

FIGS. **1C** and **2A** further illustrate a lid or a door **225** of another sidewall **205** (FIG. **3A**) of shielding assembly **200**, which encloses another compartment that is accessible through opening **137** of shell **13**, and which is located adjacent the compartment enclosed by sidewall **201**. Each of doors **221**, **225** are shown being attached by a corresponding hinge H, and another door **227** is shown attached to sidewall **203** by another hinge H. FIG. **2A** illustrates each of lid **223** and doors **221**, **225**, **227** including a handle **232**, **212**, **252** and **272**, respectively, for moving lid **223** and doors **221**, **225**, **227**, in order to provide access to the corresponding compartments, which can be seen in FIGS. **3A-B**. FIG. **2A** further illustrates optional thumb screws **290**, one securing lid **223** to sidewall **203** and another securing door **221** to sidewall **201**, or other means for securing the doors, which are known to those skilled in the art, may be incorporated. Each sidewall **201**, **203**, **205** and the corresponding lid/door **223**, **221**, **225**, **227** thereof may be individually cast from 3% antimony lead, or from other known shielding materials, and then assembled together according to methods known to those skilled in the art.

According to the illustrated embodiment, doors **221**, **225** are hinged to open in an upward direction, per arrows D and C, and, with reference back to FIG. **1C**, a latch component **191** is provided to hold each of doors **221**, **225** in an opened position, thereby, preventing doors **221**, **225** from falling closed, which could pinch/crush fingers of technical personnel and/or tubing lines of circuit **300**, when in the midst of a maintenance procedure. FIG. **2B** is a perspective view of framework **19** of the cabinet structure of system **10**, according to some embodiments, to which latch component **191** is mounted; FIG. **2B-1** is an enlarged detailed view of latch component **191**, according to some embodiments. FIG. **2B** illustrates latch component **191** including a first pin **193**, corresponding to door **225**, and a second pin **195**, corresponding to door **221**; each pin **193**, **195** includes a lever end **193A**, **193B**, respectively, and a holding end **193B**, **195B**, respectively. An edge of each door **221**, **225**, upon opening

of doors **221**, **225**, may push past the holding end **195**B, **193**B of the corresponding pin **195**, **193**, in a first direction, per arrow F, and then may rest against a respective side S**95** and S**93** of each end **195**B, **193**B, until the corresponding lever end **195**A, **193**A is rotated in a counter-clockwise direction, per arrow cc, thereby moving the corresponding holding end **193**B, **195**B to make way for the closing of doors **221**, **225**. Doors **221**, **225** being held by latch component **191** in an open position may be seen in FIG. **3**A.

With further reference to FIG. **2**A, according to some preferred embodiments of the present invention, an edge of door **225** overlaps door **221** to prevent door **221** from being opened, per arrow D, if door **225** is not opened, per arrow C; and an edge of door **227** overlaps an edge of door **225** to prevent door **225** from being opened if door **227** is not opened, per arrow B; and an edge of lid **223** overlaps door **227** to prevent door **227** from being opened if lid **223** is not opened, per arrow A. Thus, access to the compartment enclosed by sidewall **201** and containing generator **21** is only systematically allowed through a sequential opening of lid **223** and doors **227**, **225**, **221**, since, when generator **21** is replaced it is typically desirable to also replace those portions of circuit **300** which are shielded behind lid **223** and doors **227**, **225**. The routing of these portions of circuit **300** will be described in conjunction with FIGS. **3**A-C.

FIG. **3**A is another perspective view of shielding assembly **200**, according to some embodiments of the present invention. In FIG. **3**A, lid **223** and doors **221**, **225**, and **227** are opened to provide a view into openings **233**, **235** and **231** of sidewalls **203**, **205** and **201**, respectively, and into a passageway **207**, which is formed in sidewall **203**, opposite the compartment, which contains waste bottle **23**. Passageway **207** is shown extending vertically along sidewall **203** and having a grooved extension **213** formed in a perimeter surface of opening **233**. An optional retaining member **237**, for example, formed from an elongate strip of resilient plastic having a generally c-shape cross-section, is shown being mounted along a length of passageway **207** to hold lines **305***w* and **305***p* in place within passageway **207**. FIG. **3**A further illustrates a pair of passageways **251***b* and **251***g*, which are formed as grooves in a portion of sidewall **205**, and another pair of passageways **215***i* and **215***o*, which are formed as grooves in a portion of sidewall **201**. A routing of portions of tubing circuit **300** (FIG. **1**D) through passageways **207**, **251***b*, **251***c*, **215***i* and **215***o* is shown in FIG. **3**B.

FIG. **3**B illustrates tubing line **304** being routed through passageways **251***g* and **215***i*, eluate tubing line **305** being routed through passageway **215***o*, and both waste line **305***w* and patient line **305***p* being routed along passageway **207**. Waste line **305***w* further extends through grooved extension **213** to waste bottle **23**, and patient line **305***p* further extends outward from shielding assembly **200**, for example, to extend out through opening **135** in upper surface **131** of shell **13** (FIG. **1**A). According to the illustrated embodiment, each passageway formed in shielding assembly **200**, by being accessible along a length thereof, can facilitate a relatively easy routing of the corresponding tubing line therethrough, when the corresponding lid/door is open, and a depth of each passageway prevents pinching and/or crushing of the corresponding tubing line routed therethrough, when the corresponding lid/door is closed down thereover. With further reference to FIGS. **3**A-B, it may be appreciated that the compartment formed by sidewall **201** may have a shape matching an exterior contour of generator **21**, such that generator **21** is 'keyed' to the compartment, for example, to prevent installation of an improper generator into system **10**, and/or to facilitate the proper orientation of generator **21** within the compartment for the proper routing of tubing lines. Alternately, or in addition, according to alternate embodiments, if system **10** includes a reader of encoded information in communication with computer **17**, a unique identification and/or data associated with each generator may be provided, for example, in a bar code label or a radiofrequency identification (RFID) tag that is attached to each generator, so that the reader may transfer the information to computer **17**, when a generator is installed, in order to either enable system operation or to provide an indication to the user that an incorrect generator has been installed. Of course a user of system **10** may, alternately, manually enter information, that is provided on a generator label or marking, into computer **17**, in order to either enable system **10**, or to receive feedback from computer **17** that the incorrect generator is installed.

FIG. **3**A further illustrates sidewall **205** including a valve actuator receptacle **253**, into which divergence valve **35**WP is mounted, to be controlled by one of the servomotors (not shown) of system **10**, and an opening **325** for activity detector **25**. Activity detector **25** is mounted in a shielded well **255** that extends downward from opening **325** (shown in FIG. **3**B), and, with reference to FIG. **3**B, tubing line **305** passes over opening **325** so that detector **25** can detect an activity of the eluate, which passes therethrough. According to some embodiments, the positioning, within the compartment enclosed by sidewall **205**, of the components of the portion of infusion circuit **300** which are shown routed therein, is facilitated by providing the components mounted in a frame **39** as a disposable subassembly **390**, an embodiment of which is illustrated by FIGS. **3**C-D.

FIG. **3**C is a perspective view of subassembly **390**, and FIG. **3**D is a perspective view of frame **39**. According to the embodiment illustrated by FIG. **3**D, frame **39** is formed from mating trays **39**A, **39**B, for example, formed from a thermoformed plastic, which fit together to capture, therebetween, and hold, in fixed relation to a perimeter edge of frame **39**, divergence valve **35**WP and portions of eluant tubing line **304**, by-pass tubing line **303**, eluate tubing line **305**, waste line **305***w* and patient line **305***p*. FIG. **3**C illustrates the perimeter edge divided into a first side **391**, a second side **392**, opposite first side **391**, a third side **393**, extending between first and second sides **391**, **392**, and a fourth side **394**, opposite third side **393**. Although FIG. **3**D shows trays **39**A, **39**B individually formed for fitting together, according to alternate embodiments, mating trays of frame **39** may be parts of a continuous sheet of plastic folded over on itself.

According to the illustrated embodiment, an end **404**A, of eluant line **304**, and an end **403**, of by-pass line **303** extend from third side **393** of frame **39** to couple with divergence valve **35**BG and an upstream section of eluant tubing line **302**. FIG. **3**C further illustrates an opposite end **404**B of eluant line extending from first side **391** of frame **39**, alongside a similarly extending end **405** of eluate line **305**, and ends **406** and **407** of patient line **305***p* and waste line **305***w*, respectively, extending from second side **392** of frame **39**. Although ends **406**, **407** are shown extending upward from tray **39***a*, as they would within shielding assembly **200**, it should be appreciated that the tubing lines of circuit **300** are preferably flexible and would drop down under their own weight rather than extending upward, as shown, if not supported. Referring back to FIG. **1**D, in conjunction with FIG. **3**C, it can be seen that the aforementioned fittings are provided for coupling subassembly **390** into circuit **300**: first fitting **311** couples the section of eluant line **302** to filter **37**; second fitting **312** couples eluant line **304** to an inlet port of

generator **21**; third fitting **313**, which may incorporate a check valve, couples eluate line **305** to an outlet port of generator **21**; fourth fitting **314** couples waste line **305***w* to waste bottle **23**; and fifth fitting **315** couples patient line **305***p* to an extension thereof, which extends outside shell **13** (designated by the dotted line). Each of the fittings **311**, **312**, **313**, **314**, **315** may be of the Luer type, may be a type suitable for relatively high pressure applications, or may be any other suitable type that is known to those skilled in the art.

As previously mentioned, when generator **21** is replaced, it is typically desirable to also replace those portions of circuit **300** which are shielded behind lid **223** and doors **227**, **225**, and, in those instances wherein system **10** is moved to a new site each day, these portions may be replaced daily. Thus, according to the illustrated embodiment, these portions are conveniently held together by frame **39**, as subassembly **390**, in order to facilitate relatively speedy removal and replacement, while assuring a proper assembly orientation, via registration with features formed in sidewall **205** (FIG. **3**A), for example: registration of divergence valve **35**WP with valve actuator receptacle **253**, registration of tubing line ends **403** and **404**A with passageways **251***b* and **251***g*, respectively, registration of tubing line ends **404**B and **405** with passageways **215***i* and **215***o*, respectively, and registration of tubing line ends **406** and **407** with passageway **207**.

With further reference to FIG. **3**B, other portions of tubing circuit **300** are shown. FIG. **3**B illustrates eluant tubing line **301** extending from reservoir **15**, outside of shell **13** (FIG. **1**A), to syringe pump **33**, which is mounted to an actuating platform **433**. According to the illustrated embodiment, platform **433** is actuated by another servomotor (not shown) of system **10**, which is controlled by the controller and computer **17** of system **10**, to cause a plunger of pump **33** to move, per arrow I, so as to draw in eluant, from reservoir **15**, through tubing line **301**, and then to cause the plunger to move in the opposite direction so as to pump the eluant, through tubing line **302**, to either generator **21** or to by-pass line **303**. Although the illustrated embodiment includes syringe pump **33**, other suitable pumps, known to those skilled in the art, may be substituted for pump **33**, in order to draw eluant from reservoir **15** and to pump the eluant throughout circuit **300**. Although not shown, it should be appreciated that divergence valve **35**BG is fitted into another valve actuating receptacle mounted within shell **13** and coupled to yet another servomotor (not shown) of system **10**.

FIG. **3**B further illustrates a filter holder **317** that is mounted alongside an interior surface of shell **13** to hold filter **37** (FIG. **1**D) of tubing line **302**. Filter holder **317**, like frame **39** for subassembly **390**, may be formed from a thermoformed plastic sheet; holder **317** may have a clam-shell structure to enclose filter **37** in an interior space, yet allow tubing line **302**, on either side of filter **37**, to extend out from the interior space, in between opposing sides of the clam-shell structure. Holder **317** is shown including an appendage **307** for hanging holder **317** from a structure (not shown) inside shell **13**.

Turning now to FIGS. **4**-**9**C details concerning computer-facilitated operation of system **10** will be described, according to some embodiments of the present invention. As previously mentioned, and with reference back to FIG. **1**A, computer **17** of system **10** includes monitor **172**, which, preferably, not only displays indications of system operation to inform a user of system **10**, but is also configured as a touch screen to receive input from the user. It should be understood that computer **17** is coupled to the controller of system **10**, which may be mounted within the interior space surrounded by shell **13**. Although FIG. **1**A shows computer **17** mounted to post **142** of system **10**, for direct hardwiring to the controller of system **10**, according to some alternate embodiments, computer **17** is coupled to the controller via a flexible lead that allows computer **17** to be positioned somewhat remotely from those portions of system **10**, from which radioactive radiation may emanate; or, according to some other embodiments, computer **17** is wirelessly coupled, for example, via two-way telemetry, to the controller of system **10**, for even greater flexibility in positioning computer **17**, so that the operation of system **10** may be monitored and controlled remotely, away from radioactive radiation.

According to some preferred embodiments, computer **17** is pre-programmed to guide the user, via monitor **172**, through procedures necessary to maintain system **10**, to perform quality control tests on system **10**, and to operate system **10** for patient infusions, as well as to interact with the user, via the touch-screen capability of monitor **172**, according to preferred embodiments, in order to track volumes of eluant and eluate contained within system **10**, to track a time from completion of each elution performed by system **10**, to calculate one or more system parameters for the quality control tests, and to perform various data operations. Computer **17** may also be pre-programmed to interact with the controller of system **10** in order to keep a running tally or count of elutions per unit time, for a given generator employed by the system, and may further categorize each of the counted elutions, for example, as being generated either as a sample, for quality control testing, or as a dose, for patient injection. The elution count and categorization, along with measurements made on each sample or dose, for example, activity level, volume, flow rate, etc. . . . , may be maintained in a stored record on computer **17**. All or a portion of this stored information can be compiled in a report, to be printed locally, and/or to be electronically transferred to a remote location, for example, via an internet connection to technical support personnel, suppliers, service providers, etc. . . . , as previously described. Computer **17** may further interact with the user and/or a reader of encoded information, for example, a bar code reader or a radiofrequency identification (RFID) tag reader, to store and organize product information collected from product labels/tags, thereby facilitating inventory control, and/or confirming that the proper components, for example, of the tubing circuit, and/or accessories, and/or solutions are being used in the system.

It should be understood that screen shots shown in FIGS. **4**-**9**C are exemplary in nature and are presented to provide an outline of some methods of the present invention in which computer **17** facilitates the aforementioned procedures, without limiting the scope of the invention to any particular computer interface format. Computer **17** may also include a pre-programmed user manual, which may be viewed on monitor **172**, either independent of system operation or in conjunction with system operation, for example, via pop-up help screens. Although the English language is employed in the screen shots of FIGS. **4**-**9**C, it should be understood that, according to some embodiments, computer **17** is pre-programmed to provide guidance in multiple languages.

FIG. **4** is a screen shot of a main menu **470**, which is presented by computer **17** on monitor **172**, according to some embodiments. Main menu **470** includes a listing of each computer-facilitated operation that may be selected by the user, once the user has logged on. According to some

multi-lingual embodiments, computer **17** presents a list of languages from which the user may select, prior to presenting main menu **470**.

FIG. **5**A is a schematic showing a series of screen shots which includes a log in screen **570**. According to some embodiments, when the user touch-selects the data entry fields of screen **570** or **571**, or of any of the other screens presented herein, below, a virtual keyboard is displayed for touch-select data entry into the selected data entry field; alternately, computer **17** may be augmented with another type of device for user data entry, examples of which include, without limitation, a peripheral keyboard device, a storage medium (i.e. disk) reader, a scanner, a bar code reader (or other reader of encoded information), a hand control (i.e. mouse, joy stick, etc . . .). Although not shown, according to some embodiments, screen **570** may further include another data entry field in which the user is required to enter a license key related to the generator employed by system **10** in order to enable operation of system **10**; the key may be time sensitive, related to generator contract terms. Of course any number of log in requirements may be employed, according to various embodiments, and may be presented on multiple sequentially appearing screens rather than on a single log in screen.

After the user enters the appropriate information into data entry fields of log in screen **570**, computer **17** presents a request for the user to confirm the volume of eluant that is within reservoir **15** (e.g. saline in saline bag), via a screen **571**, and then brings up main menu **470**. If the user determines that the volume of eluant/saline is insufficient, the user selects a menu item **573**, to replace the saline bag. If system **10** includes an encoded information reader, such as a bar code or RFID tag reader, confirmation that the selected reservoir is proper, i.e., contains the proper saline solution, may be carried out by computer **17**, prior to connecting the reservoir into circuit **300**, by processing information read from a label/tag attached to the reservoir. Alternatively, or in addition, tubing line **301** of circuit **300** may be provided with a connector which only mates with the proper type of reservoir **15**. According to some embodiments, system **10** may further include an osmolarity or charge detector, which is located just downstream of reservoir **15** and is linked to computer **17**, so that an error message may be presented on monitor **172** stating that the wrong osmolarity or charge is detected in the eluant supplied by reservoir, indicating an improper solution. One example of a charge detector that may be employed by system **10** is the SciCon™ Conductivity Sensor (available from SciLog, Inc. of Middleton, Wis.).

Once the reservoir/saline bag is successfully replaced, computer **17** prompts the user to enter a quantity of saline contained by the new saline bag, via a screen **574**. Alternately, if system **10** includes the aforementioned reader, and the saline bag includes a tag by which volume information is provided, the reader may automatically transfer the quantity information to computer **17**. Thus, computer **17** uses either the confirmed eluant/saline volume, via screen **571**, or the newly entered eluant/saline volume as a baseline from which to track depletion of reservoir volume, via activations of pump **33**, in the operation of system **10**. With reference to FIG. **5**B, during the operation of system **10**, when computer **17** detects that the eluant reservoir/saline bag has been depleted to a predetermined volume threshold, computer **17** warns the user, via a screen **577**. If the user has disregarded screen **577** and continues to deplete the saline bag, computer **17** detects when the saline bag is empty and provides indication of the same to the user, via a screen **578**. To replenish the reservoir/saline bag, the user may either refill the reservoir/bag or replace the empty reservoir/bag with a full reservoir/bag. According to some embodiments, system **10** automatically precludes any further operation of the system until the reservoir is replenished. It should be noted that, as previously mentioned, system **10** can include a fluid level sensor coupled to the eluant reservoir in order to detect when the level of saline drops below a certain level.

In addition to tracking the volume of eluant in reservoir **15**, computer **17** also tracks a volume of the eluate which is discharged from generator **21** into waste bottle **23**. With reference to FIG. **5**C, an item **583** is provided in main menu **470**, to be selected by the user when the user empties waste bottle **23**. When the user selects item **583**, computer **17** presents a screen **584**, by which the user may effectively command computer **17** to set a waste bottle level indicator to zero, once the user has emptied waste bottle **23**. Typically, the user, when powering up system **10** for operation, each day, will either empty waste bottle **23**, or confirm that waste bottle **23** was emptied at the end of operation the previous day, and utilize screen **584** to set the waste bottle level indicator to zero. Thus, computer **17**, can track the filling of waste bottle **23** via monitoring of the operation of pump **33** and divergence valve **35**WP, and provide an indication to the user when waste bottle **23** needs to be emptied, for example, via presentation of screen **584**, in order to warn the user that, unless emptied, the waste bottle will overflow. According to some embodiments, system **10** automatically precludes any further operation of the system until the waste bottle is emptied. According to some alternative embodiments, a fluid level sensor may be coupled to waste bottle **23**, for example, as mentioned above in conjunction with FIG. **1**D, in order to automatically detect when waste bottle **23** is filled to a predetermined level and to provide, via computer **17**, an indication to the user that waste bottle **23** needs to be emptied and/or to automatically preclude operation of system **10** until the waste bottle is emptied.

In addition to the above maintenance steps related to eluant and eluate volumes of system **10**, the user of system **10** will typically perform quality control tests each day, prior to any patient infusions. With reference to FIG. **6**, according to preferred methods, prior to performing the quality control tests (outlined in conjunction with FIGS. **7**A-C and **8**A-B), the user may select an item **675** from main menu **470**, in order to direct system **10** to wash the column of generator **21**. During the generator column wash, which is performed by pumping a predetermined volume of eluant, for example, approximately 50 milliliters, through generator **21** and into waste bottle **23**, computer **17** provides an indication, via a screen **676**, that the wash is in progress. Also, during the generator column wash, the system may provide a signal to indicate that eluate it being diverted to waste bottle **23**, for example, light projector **100** (FIG. **1**C) may project a flashing light signal, as previously described.

FIG. **6** further illustrates a screen **677**, which is presented by computer **17** upon completion of the column wash, and which provides an indication of a time lapse since the completion of the wash, in terms of a time countdown, until a subsequent elution process may be effectively carried out. While screen **677** is displayed, system **10** may be refilling, from reservoir **15**, pump **33**, which has a capacity of approximately 55 milliliters, according to some embodiments. According to some preferred embodiments of the present invention, computer **17** starts a timer once any elution process is completed and informs the user of the time lapse, either in terms of the time countdown (screen **677**), or in terms of a time from completion of the elution, for

example, as will be described in conjunction with FIG. 7B. According to an exemplary embodiment, wherein generator **21** is the CardioGen-82® that yields a saline solution of Rubidium-82, produced by the decay of Strontium-82, via the elution, a time required between two effective elution processes is approximately 10 minutes.

Once the appropriate amount of time has lapsed, after the elution process of generator column wash, a first quality control test may be performed. With reference to FIG. 7A, the user may select, from main menu **470**, an item **773**A, which directs computer **17** to begin a sequence for breakthrough testing. According to some embodiments, in conjunction with the selection of item **773**A, the user attaches a needle to an end of patient line **305***p* and inserts the needle into to a test vial, for the collection of an eluate sample therefrom, and, according to FIG. 7A, computer **17** presents a screen **774**, which instructs the user to insert the test vial into a vial shield, which may be held in recess **101** of shell **13** (FIG. 1C).

FIG. 7A further illustrates a subsequent screen **775**, by which computer **17** receives input, from the user, for system **10** to start the breakthrough elution, followed by a screen **776**, which provides both an indication that the elution is in progress and an option for the user to abort the elution. As previously described, the system may provide a signal to indicate that elution is in progress, for example, light projector **100** (FIG. 1C) may project a flashing light signal during that portion of the elution process when eluate is diverted from generator **21** through waste line **305***w* and into waste bottle **23**, and then a steady light signal during that portion of the elution process when the eluate is diverted from generator **21** through patient line **305***p* and into the test vial, for example, once activity detector **25** detects a dose rate of approximately 1.0 mCi/sec in the eluate discharged from generator **21**. Another type of light signal, for example, the more rapidly flashing light, as previously described, may be projected when a peak bolus of radioactivity is detected in the eluate.

Upon completion of the elution process for breakthrough testing, computer **17** presents a screen **777**, shown in FIG. 7B, which, like screen **677**, provides an indication of a time lapse since the completion of the elution, but now in terms of a time since completion of the breakthrough elution process. When the user transfers the vial containing the sample of eluate into a dose calibrator, to measure the activity of the sample, the user may make a note of the time lapse indicated on screen **777**. With further reference to FIG. 7B, once the user has received the activity measure from the dose calibrator, the user proceeds to a screen **778**, which includes data entry fields for the activity measure and the time between that at which the dose calibrator measured the activity of the sample and that at which the elution was completed. The user may enter the data via the touch-screen interface of monitor **172**, or via any of the other aforementioned devices for user data entry. According to some alternate embodiments, computer **17** may receive the data, electronically, from the dose calibrator, either via wireless communication or a cable connection.

After the data is entered by the user, computer **17** presents screen **779**, from which the user moves back to main menu **470** to perform a system calibration, for example, as will be described in conjunction with FIGS. **8**A-B, although the breakthrough testing is not completed. With reference back to FIG. 7A, an item **773**B is shown in main menu **470**; item **773**B may only be effectively selected following the completion of steps for item **773**A, so as to perform a second stage of breakthrough testing. In the second stage, the breakthrough of the sample of eluate collected in the test vial for the breakthrough testing is measured, at a time of approximately 60 minutes from the completion of the elution that produced the sample. With reference to FIG. 7C, after the user has selected item **773**B from main menu **470**, in order to direct computer **17** to provide breakthrough test results, a screen **781** is displayed. Screen **781** includes, for reference, the values previously entered by the user in screen **778**, along with another pair of data entry fields into which the user is instructed to enter the breakthrough reading of the sample at 60 minutes and the background radiation reading, respectively. After the user enters this remaining information, as described above, computer **17** may calculate and then display, on a screen **782**, the breakthrough test results. According to the illustrated embodiment, computer **17** also displays on screen **782** pre-programmed allowable limits for the results, so that the user may verify that the breakthrough test results are in compliance with acceptable limits, before moving on to a patient infusion. According to some embodiments, system **10** will not allow an infusion if the results exceed the acceptable limits, and may present a screen explaining that the results are outside the acceptable limits; the screen may further direct the user to contact the generator supplier, for example, to order a replacement generator.

With reference to FIG. **8**A, during the aforementioned 60 minute time period, while waiting to complete the breakthrough testing, the user may perform calibration by selecting item **873** from main menu **470**. Upon selection of item **873**, computer **17** presents a screen **874**, which instruets the user to insert a new test vial into an elution vial shield. In addition to placing the vial in the shield, the user, preferably, replaces patient line **305***p* with a new patient line, and then attaches a needle to the end of the new patient line for insertion into the test vial, in order to collect an eluate sample therefrom. After performing these steps, the user may move to screen **875**, wherein a plurality of data entry fields are presented; all or some of the fields may be filled in with pre-programmed default parameters, which the user has an option to change, if necessary. Once the user confirms entry of desired parameters for the calibration, the user may enter a command, via interaction with a subsequent screen **876**, to start the calibration elution.

With reference to FIG. **8**B, after computer **17** starts the elution process, a screen **87** informs the user that the calibration elution is in progress and provides an option to abort the elution. As previously described, the system may provide an indication that elution is in progress, for example, light projector **100** (FIG. 1C) may project a flashing light signal during that portion of the elution process when eluate is diverted from generator **21** through waste line **305***w* and into waste bottle **23**, and then a steady light signal during that portion of the elution process when activity detector **25** has detected that a prescribed dose rate threshold is reached, for example, 1.0 mCi/sec, and the eluate is being diverted from generator **21**, through the new patient line, and into the test vial. Another type of light signal, for example, the more rapidly flashing light, as previously described, may be projected when a peak bolus of radioactivity is detected in the eluate. Upon completion of the elution process for calibration, computer **17** presents a screen **878**, which provides an indication of a time lapse since the completion of the elution, in terms of a time since completion of the calibration elution process. When the user transfers the vial containing the sample of eluate into the dose calibrator, to measure the activity of the sample, the user may make a note of the time lapse indicated on screen **878**. With further reference to FIG. **8**B, once the user has received the activity

measure from the dose calibrator, the user proceeds to a screen **879**, which includes data entry fields for the activity measure and the time, with respect to the completion of elution, at which the dose calibrator measured the activity of the sample. Once the data is input by the user, as described above, the computer calculates a calibration coefficient, or ratio, and presents the ratio on a screen **880**. According to FIG. 8B, screen **880** further provides an indication of a desirable range for the calibration ratio and presents an option for the user to reject the calculated ratio, in which case, the user may instruct computer **17** to recalculate the ratio.

As previously mentioned, some alternate embodiments of the present invention include an on board dose calibrator so that the entire sequence of sample collection and calculation steps, which are described above, in conjunction with FIGS. **6**-8B, for the quality control procedures, may be automated. This automated alternative preferably includes screen shots, similar to some of those described above, which provide a user of the system with information at various stages over the course of the automated procedure and that provide the user with opportunities to modify, override and/or abort one or more steps in the procedure. Regardless of the embodiment (i.e. whether system **10** employs an on board dose calibrator or not), computer **17** may further collect all quality control test parameters and results into a stored record and/or compile a report including all or some of the parameters and results for local print out and/or electronic transfer to a remote location.

With reference to FIG. **9**A, upon completion of the above-described quality control tests, the user may select an item **971**, from main menu **470**, in order to direct system **10** to begin a procedure for the generation and automatic infusion of a radiopharmaceutical into a patient. As previously described, system **10** infuses the patient with the radiopharmaceutical so that nuclear diagnostic imaging equipment, for example, a PET scanner, can create images of an organ of the patient, which absorbs the radiopharmaceutical, via detection of radioactive radiation therefrom. According to FIG. **9**A, upon selection of item **971**, computer **17** presents a screen **972** which includes a data entry field for a patient identification number. This identification number that is entered by the user is retained by computer **17**, in conjunction with the pertinent system parameters associated with the patient's infusion. After the user enters the patient identification number, computer **17** directs, per a screen **973**, the user to attach a new patient line and to purge the patient line of air. A subsequent screen **974** presented by computer **17** includes data entry fields by which the user may establish parameters for the automatic infusion; all or some of the fields may be filled in with pre-programmed default parameters, which the user has an option to change, if necessary.

With reference to FIG. **9**B, if pump **33** does not contain enough eluant/saline for the patient infusion, computer **17** will present a warning, via a screen **901**, which includes an option for the user to direct the refilling of pump **33**, via a subsequent screen **902**. Once pump **33** has been filled, computer **17** presents an indication to the user, via a screen **903**. According to some embodiments, if the user does not re-fill pump **33**, yet attempts to proceed with an infusion, system **10** will preclude the infusion and present another screen, that communicates to the user that no infusion is possible, if the pump is not refilled, and asking the user to refill the pump, as in screen **901**. When pump **33** contains a sufficient volume of eluant for the patient infusion, computer **17** presents a screen **975**, which is shown in FIG. **9**C, and allows the user to enter a command for system **10** to start the patient infusion. During the infusion, computer **17** provides the user with an indication that the infusion is in process and with an option for the user to abort the infusion, via a screen **976**. As previously described, the system may provide an indication that an elution is in progress, for example, light projector **100** (FIG. 1C) may project a flashing light signal during that portion of the elution process when eluate is diverted from generator **21** through waste line **305***w* and into waste bottle **23**, and then a steady light signal during that portion of the elution process when activity detector **25** has detected that a prescribed dose rate threshold is reached, for example, 1.0 mCi/sec, and the eluate is being diverted from generator **21**, through the new patient line for infusion into the patient. Another type of light signal, for example, the more rapidly flashing light, previously described, may be projected when a peak bolus of radioactivity is detected in the eluate. At the completion of the infusion, a screen **977** is displayed by computer **17** to inform the user of the completion of the infusion and a time since the completion. Computer **17** also displays a summary of the infusion, per screen **978**.

With further reference to FIG. **9**C, screen **976** shows an exemplary activity profile (activity—mCi/sec, on y-axis, versus time—sec, on x-axis) for the infusion/injected dose (designated between the two vertical lines). Those skilled in the art will appreciate that the shape of this profile depends upon the infusion flow rate, for a given volume of the dose, which flow rate is controlled, for example, by the speed at which pump **33** drives flow through the patient line, and upon the amount of Strontium-82 remaining in the generator. In the absence of flow rate control, activity profiles may change over the life of the generator. Furthermore, the peak bolus of radioactivity, particularly for injected doses from a relatively new generator, may exceed a saturation level of the imaging equipment, i.e. PET scanner. According to some preferred methods of the present invention, in order to maintain relatively consistent, and desirable/effective, activity profiles for patient injections, over the life of the generator, the operating speed of pump **33** may be varied (both over the course of a single injection and from injection to injection), according to feedback from activity detector **25**. Such a method may be implemented via incorporation of another quality control test in which pump **33** is operated to drive flow through the generator at a constant rate, in order to collect, into computer, a plurality of activity measurements from activity detector **25**; the plurality of measurements comprise a characteristic, or baseline activity profile from which the computer **17** may calculate an appropriate flow rate profile to control a speed of pump **33**, in order to achieve the desirable/effective activity profile. In general, at the start of generator life, when Strontium-82 is plentiful, the pump is controlled to drive infusion flow at relatively lower rates, and, then, toward the end of generator life, when much of the Strontium-82 has been depleted, the pump is controlled to drive infusion flow at relatively higher rates. As was described above, in conjunction with FIG. 1D, if a desired infusion/injection flow rate is relatively high, that is, high enough to create too much back pressure, via flow through the column of generator **21**, by-pass line **303** may be employed by adjusting divergence valve **35**BG to divert a flow of eluant therethrough after a sufficient volume has been pumped through generator at a lower flow rate. According to this method, once a dose of eluate, from generator **21**, has flowed into patient line **305***p*, divergence valve **35**BG is set to divert the flow of eluant through by-pass line **303**, and then pump speed is increased to pump eluant at a higher flow

rate in order to push the dose out from patient line **305***p*, for injection at the higher flow rate.

Consistency of activity profiles among injected doses can greatly facilitate the use of PET scanning for the quantification of flow, for example, in coronary perfusion studies. Alternative infusion circuit configurations, operable according to alternative methods, to achieve consistency of activity profiles among injected doses, as well as a more uniform level of radioactivity across each individual dose, will be described below, in conjunction with FIGS. **12**A-C.

Printer **117** (FIG. 1B) may be activated to print out a hard copy of the infusion summary, on which the patient identification number and pertinent infusion and system parameters are also printed, for reference. Alternatively, or in addition, according to some embodiments, the summary may be downloaded onto a computer readable storage device to be electronically transferred to one or more remote computers and/or the summary may be automatically transferred to the one or more remote computers, via wireless communication or a cable connection, for example, over an intranet network and/or the internet. In order to protect private patient information, the files may be encrypted for transmission over the internet. The one or more remote computers may be included, for example, in a hospital information system, and/or a billing system, and/or in a medical imaging system. Infusion parameters, for example, corresponding to the activity profile, may also be collected and electronically transferred for analysis in conjunction with captured images, for example, in order to quantify coronary flow, via a software package that is loaded into a system that includes the PET scanner.

With reference back to FIG. **9**A the user may select an item **995**, from main menu **470**, in order have system **10** perform data operations, such as, archiving a data base of patient infusion information and quality control test results, transmitting patient infusion summary records to USB mass storage devices, and various types of data filtering, for example, according to date ranges and/or patient identification numbers, for example, to search for a particular set of data and/or to compile a summary report of related sets of data. Additionally, certain information, which is collected by computer **17** over the course of system operation, and which defines system operation, may be transmitted to a local or remote computerized inventory system and/or to computers of technical support personnel, maintenance/service providers and/or suppliers of infusion circuit elements/components, thereby facilitating more efficient system operation and maintenance.

Turning now to FIG. **10**, an item **981** for computer-facilitated purging of the tubing lines of system **10** is shown included in main menu **470**. When a user selects item **981**, computer **17** guides the user to select either an air purge or a saline purge. The direction provided by computer **17** is not explicitly laid out herein, for a saline purge, as procedures for saline purging should be readily apparent to those skilled in the art, with reference to the schematic of infusion circuit **300** shown in FIG. 1D. A saline purge of circuit **300** is desired to assure that all the air is removed from circuit **300** when a new generator and/or a new complete or partial tubing set is installed. An air purge of the tubing lines of circuit **300** may be performed after removing reservoir **15**, by-passing generator **21**, by connecting tubing line **304** to tubing line **305**, and coupling patient line **305***p* to a vial, for example, as is directed by the computer interface, in screens **983** and **984** shown in FIG. **10**. The air purge is desirable for blowing out the tubing lines, thereby removing all remaining eluant and eluate, prior to installing a new generator and/or prior to transporting system **10** from one site to another. If generator **21** is not depleted and will be used in system **10** at the new site, it is important to by-pass the generator prior to purging the tubing lines of circuit **300** with air, so that air is not blown across the generator, since air through generator **21** may compromise both the function and the aseptic nature of generator **21**.

According to preferred embodiments, once the user has followed the instructions presented in screens **983** and **984** and selects to start the air purge, for example, via screen **985**, computer **17** directs the controller of system **10** to carry out a complete air purge, in which pump **33** and divergence valves **35**BG and **35**WP are automatically controlled. The automated air purge preferably includes the following steps, which may be best understood with reference to tubing circuit **300** in FIG. 1D: pumping any remaining volume of eluant left in pump **33**, through lines **302**, **304**, **305** and **305***w*, to waste bottle **23**; refilling pump **33** with air and pumping the air through lines **302**, **304**, **305** and **305***w*, into waste bottle **23** (lines **304** and **305** have been previously connected directly to one another, in order to by-pass generator **21**; if generator **21** is depleted and will be replaced with a new generator, pumping air through generator **21** may be acceptable); refilling pump **33** with air and then pumping a portion of the air through lines **302**, **304**, **305** and **305***p*, into the vial, and then a remaining portion of the air through lines **302**, **304**, **303** and **305***p*, into the vial. With reference to FIG. 1D and the previous description of divergence valves **35**BG, **35**WP, it should be understood how divergence valves **35**BG, **35**WP are automatically controlled to carry out the above steps.

The purge operations, which are facilitated by selecting item **981** from main menu **470**, may also be accessed via the selection of an item **991** for generator setup. When the user selects item **991**, computer **17** may present an option for guidance in removing an old, depleted, generator and a set of tubing lines, prior to installing the new generator, or an option to just be guided in the installation of the new generator. According to some embodiments, computer **17** is pre-programmed to calculate an amount of activity left in a depleted generator, for example, by tracking activity of eluate over a life of the generator. At an end of the life of the generator, computer **17** may further compile this information, along with other pertinent generator information, into a report that may accompany a declaration of dangerous goods for shipping the depleted generator out for disposal or, in some cases, back to the manufacturer for investigation. An example of such a report is shown in FIG. **11**. According to those embodiments of system **10** that include an encoded information reader, computer **17** may confirm that the new generator is proper by processing information that is read from an encoded label/tag attached thereto.

FIGS. **12**A-B are schematics of alternative infusion circuits **1300**A, **1300**B that may be employed by system **10**, in place of circuit **300** (FIG. 1D), according to some additional embodiments of the present invention. Circuits **1300**A, **1300**B are configured to allow for alternative methods of operation, to that previously described for circuit **300**, when a relatively even, or uniform level of activity over each injected dose, along with the relatively consistent level of activity from injection to injection is desired, for example, in order to facilitate a quantification of coronary artery blood flow via PET scanning FIG. **12**C is a schematic illustrating activity profiles **1200**A, **1200**B for two injected doses, wherein profile **1200**B has a more uniform level of activity than profile **1200**A; profile **1200**B may be achieved via the operation of circuits **1300**A, **1300**B as described below.

Similar to circuit **300** (FIG. **1**D), dashed lines are shown in each of FIGS. **12**A-B to indicate a general boundary of a shielding assembly for portions of each circuit **1300**A, **1300**B. The shielding assembly for each of circuits **1300**A, **1300**B may be very similar, in most respects, to shielding assembly **200**, which is described above for system **10**, and the elements of each of circuits **1300**A, **1300**B may be arranged with respect to their respective shielding and with respect to shell **13** of system **10** in a similar manner to that described above for circuit **300**.

FIG. **12**A illustrates circuit **1300**A including, like the previously described circuit **300**, eluant reservoir **15**, pump **33**, radioisotope generator **21**, through which the filtered eluant is pumped to create the radioactive eluate, activity detector **25**, and waste bottle **23**. FIG. **12**A further illustrates two filters **37** and two pressure transducers **1334** included in circuit **1300**A. Circuit **1300**A further includes by-pass tubing line **303**, which is located downstream of divergence valve **35**BG, like in circuit **300**, and which accommodates the previously described eluant/saline flush. However, in contrast to circuit **300**, circuit **1300**A further includes a linear/proportional valve **1335** integrated into by-pass/flush line **303** so that circuit **1300**A may be operated, for example, according to pre-programmed parameters of computer **17**, in conjunction with feedback of information from activity detector **25**, for a controlled by-pass of generator **21** in order to mix eluant with eluate and, thereby, achieve a relatively uniform level of activity over each patient injection, for example, according to profile **1200**B of FIG. **12**C. It should be noted that, in addition to the controlled mixing, a flow rate of each injection may be varied, if necessary, in order to maintain a consistent activity level.

FIG. **12**B illustrates circuit **1300**B including, like the previously described circuit **300**, eluant reservoir **15**, pump **33**, radioisotope generator **21**, activity detector **25**, and waste bottle **23**, as well as the two filters **37** and two pressure transducers **1334**, as in circuit **1300**A. In contrast to circuits **300** and **1300**A, circuit **1300**B further includes an eluate reservoir **1350**, which is shown located downstream of generator **21**, in between first and second segments **305**A, **305**B of the eluate tubing line. It should be noted that a pump is combined with reservoir **1350**, for example, similar to syringe pump **33**, such that, when a divergence valve **1335**IO is set to allow fluid communication between reservoir **1350** and tubing line segment **305**A, the associated pump may be operated to draw in a volume of eluate, and, then, when divergence valve **1335**IO is set to allow fluid communication between reservoir **1350** and tubing line segment **305**B, the pump may be operated to push the volume of eluate out through tubing line segment **305**B for a patient injection, when divergence valve **35**WP is set to direct flow into patient line **305***p*. With reference back to FIGS. **3**A-B, sidewall **205** of shielding assembly **200** may be enlarged to further enclose eluate reservoir **1350**. For example, another shielded well, to house the eluate reservoir, may extend alongside well **255**, in which activity detector **25** is described as being mounted. Furthermore, sidewall **205** may include another valve actuator receptacle for divergence valve **1335**IO, similar to receptacle **253**, shown in FIG. **3**A for divergence valve **35**WP.

Collection of discrete volumes of eluate, in reservoir **1350**, may help to achieve a more uniform activity level over each injection, for example, like that of profile **1200**B in FIG. **12**C, and, according to preferred methods, feedback from activity detector **25** may be used to control the pump associated with reservoir **1350**, in order to vary injection flow rate and, thereby, maintain a relatively consistent activity level across multiple injections, and, when necessary, to vary injection flow rate over an individual injection to maintain the uniform activity level. Feedback from the pressure transducer **1334**, that is downstream from detector **25**, and/or from a flow meter (not shown) of circuit **1300**B may also be used to control the varying of injection flow rate.

With further reference to FIGS. **12**A-B, it should be noted that alternative circuits may be configured to employ a combination of the methods described for circuits **1300**A and **1300**B. Furthermore, some infusion circuits of the present invention may employ multiple generators **21**, as mentioned above, in conjunction with FIG. **2**A, to help maintain the relatively uniform level of activity over each injection and the relatively consistent level of activity from injection to injection.

In the foregoing detailed description, the invention has been described with reference to specific embodiments. However, it may be appreciated that various modifications and changes can be made without departing from the scope of the invention as set forth in the appended claims.

The invention claimed is:

1. An infusion system on-board a cart comprising:

a cabinet structure that comprises:

a platform,

an exterior shell that extends upwardly above the platform and has a front side; a rear side; two sidewalls connecting the front side to the rear side; and a top surface; wherein the platform and the exterior shell collectively define an interior space of the cabinet structure and wherein the interior space of the cabinet structure is configured to receive a strontium-rubidium radioisotope generator having an inlet tubing port configured to receive saline and an outlet tubing port configured to discharge a rubidium radioactive eluate,

an opening through the exterior shell configured to provide access to the strontium-rubidium radioisotope generator within the interior space of the cabinet structure, and

an opening through the top surface of the exterior shell configured to provide access for inserting a waste bottle into or removing the waste bottle from the interior space of the cabinet structure;

a computer with a touch screen display configured to receive an input from a user for controlling operation of the infusion system, wherein the touch screen display is mounted on a vertical post having a top end extending above the cabinet structure;

a first shielding compartment in the interior space of the cabinet structure having a first opening facing vertically upwardly through which the strontium-rubidium radioisotope generator can be inserted into and removed from the first shielding compartment;

a first door accessible via the opening through the exterior shell, the first door being configured to provide access to the first shielding compartment and to close over the first opening;

a second shielding compartment having a second opening facing vertically upwardly through which the waste bottle can be inserted into and removed from the second shielding compartment;

a second door accessible via the opening through the top surface of the exterior shell, the second door being configured to provide access to the second shielding compartment and to close over the second opening;

wherein the first opening is located at a lower elevation than the second opening;

a radioactivity detector positioned to measure radioactivity of the rubidium radioactive eluate flowing through an eluate tubing line in fluid communication with the outlet tubing port of the strontium-rubidium radioisotope generator;

a shielded well on-board the cart configured to receive an eluate reservoir, wherein the eluate reservoir is configured to receive a test sample; and

wherein the computer of the infusion system is configured to:

provide a stop button on the touch screen display to abort a function of the infusion system in response to a user input activating the stop button,

pump saline from a saline reservoir positioned outside of the interior space of the cabinet structure into the strontium-rubidium radioisotope generator through the inlet tubing port of the strontium-rubidium radioisotope generator thereby generating the rubidium radioactive eluate that is discharged through the outlet tubing port,

fill the eluate reservoir in the shielded well on-board the cart with the test sample of the rubidium radioactive eluate,

determine a strontium breakthrough test result on the test sample filled into the eluate reservoir in the shielded well on-board the cart while the eluate reservoir remains in the shielded well on-board the cart, and

not allow a patient infusion if the strontium breakthrough test result is greater than or equal to an allowed limit.

2. The infusion system of claim **1**, further comprising:

the strontium-rubidium radioisotope generator in the first shielding compartment in the interior space of the cabinet structure, and

the eluate reservoir located in the shielded well on-board the cart and in fluid communication with the eluate tubing line.

3. The infusion system of claim **2**, wherein

the cabinet structure has a lowermost portion and the platform has a lower surface,

the first opening is at a first elevation,

the second opening is at a second elevation,

the first elevation is between approximately 1 foot and approximately 2 feet, with respect to the lowermost portion of the cabinet structure, and

the second elevation is between approximately 2 feet and approximately 3 feet, with respect to the lower surface of the platform.

4. The infusion system of claim **1**, wherein the first shielding compartment comprises two tubing passageways formed in a perimeter surface of the first opening, and each of the two tubing passageways has a depth configured to prevent pinching or crushing of a corresponding tubing line routed therethrough when the first door is closed thereover.

5. The infusion system of claim **1**, wherein the opening through the exterior shell configured to provide access to the strontium-rubidium radioisotope generator within the interior space of the cabinet structure is through the front side of the exterior shell.

6. The infusion system of claim **1**, further comprising:

a handle configured for the user to grasp in order to move the infusion system, and

four wheels mounted to an underside of the platform of the cabinet structure.

7. The infusion system of claim **1**, wherein access to an operation of the computer is regulated through a user login credential.

8. The infusion system of claim **1**, wherein the infusion system is configured to determine the strontium breakthrough test result on the test sample at least once a day.

9. The infusion system of claim **1**, wherein the function of the infusion system aborted in response to the user input activating the stop button is a patient infusion procedure.

10. The infusion system of claim **1**, further comprising a waste tubing line and a valve, wherein the waste tubing line is in fluid communication with the eluate tubing line and the waste bottle, and the valve is configured to control fluid flow between the eluate tubing line and the waste bottle via the waste tubing line.

11. The infusion system of claim **1**, further comprising a hanger configured to hold the saline reservoir at an elevation above the top surface of the exterior shell.

12. The infusion system of claim **1**, wherein

the cabinet structure has a lowermost portion and the platform has a lower surface,

the first opening is at a first elevation,

the second opening is at a second elevation,

the first elevation is between approximately 1 foot and approximately 2 feet, with respect to the lowermost portion of the cabinet structure, and

the second elevation is between approximately 2 feet and approximately 3 feet, with respect to the lower surface of the platform.

13. The infusion system of claim **1**, further comprising a dose calibrator in the shielded well on-board the cart and in communication with the computer to determine the strontium breakthrough test result.

14. The infusion system of claim **1**, wherein the computer of the infusion system is further configured to track a volume of the saline remaining in the saline reservoir and to alert the user via the touch screen display when the volume of the saline remaining in the saline reservoir is below a predetermined volume threshold.

15. The infusion system of claim **1**, wherein the strontium breakthrough test result is for at least one of strontium-82 and strontium-85.

16. The infusion system of claim **1**, wherein the computer of the infusion system is further configured to track a volume of the rubidium radioactive eluate discharged from the strontium-rubidium radioisotope generator to the waste bottle and to control the touch screen display to display a user screen guiding the user to empty the waste bottle.

17. The infusion system of claim **1**, wherein the first door is mounted via a hinge and configured to open in an upward direction.

18. The infusion system of claim **1**, further comprising:

a USB port to transfer data and a power inlet port for connecting the infusion system to a power source, and

a printer configured to print a document concerning a patient infusion or a quality control test result generated by the infusion system.

19. The infusion system of claim **1**, further comprising a light projector mounted on the top end of the vertical post extending above the cabinet structure, wherein the light projector is configured to:

project a first light signal to indicate that an elution is taking place, and

project a second light signal to indicate that a peak bolus of radioactivity is detected.

20. The infusion system of claim **1**, wherein the exterior shell further includes a saline tubing opening configured for

a saline tubing line to pass from the saline reservoir outside of the exterior shell to the interior space of the cabinet structure.

21. The infusion system of claim **1**, wherein the computer of the infusion system is further configured to pump saline through the strontium-rubidium radioisotope generator at a rate less than approximately 70 ml/min.

22. The infusion system of claim **1**, further comprising an electrical connector port accessible through an electrical connector port opening on the exterior shell and configured to place the infusion system in communication with at least one of an intranet network, an internet network, and a device used for a nuclear imaging procedure.

23. The infusion system of claim **1**, further comprising:

a front cover that is movable relative to the exterior shell to close the opening through the exterior shell configured to provide access to the strontium-rubidium radioisotope generator, and

a top cover that is movable relative to the exterior shell to close the opening through the top surface of the exterior shell.

24. The infusion system of claim **1**, further comprising:

a hanger configured to hold the saline reservoir at an elevation above the top surface of the exterior shell,

a handle configured for the user to grasp in order to move the infusion system,

four wheels mounted to an underside of the platform,

a power inlet port for connecting the infusion system to a power source, and

a printer configured to print a document concerning a patient infusion or a quality control test result generated by the infusion system;

wherein:

the first shielding compartment comprises two tubing passageways formed in a perimeter surface of the first opening,

each of the two tubing passageways has a depth configured to prevent pinching or crushing of a corresponding tubing line routed therethrough when the first door is closed thereover,

the first door is mounted via a hinge,

access to an operation of the computer is regulated through a user login credential,

the strontium breakthrough test result is for at least one of strontium-82 and strontium-85, and

the exterior shell further includes a saline tubing opening configured for a saline tubing line to pass from the saline reservoir outside of the exterior shell to the interior space of the cabinet structure; and

wherein the computer of the infusion system is further configured to:

determine the strontium breakthrough test result on the test sample at least once a day,

pump saline through the strontium-rubidium radioisotope generator at a rate less than approximately 70 ml/min,

track a volume of the rubidium radioactive eluate discharged from the strontium-rubidium radioisotope generator to the waste bottle and to control the touch screen display to display a user screen guiding the user to empty the waste bottle, and

track a volume of the saline remaining in the saline reservoir and to alert the user via the touch screen display when the volume of the saline remaining in the saline reservoir is below a predetermined volume threshold.

25. The infusion system of claim **24**, wherein the infusion system further comprises:

the strontium-rubidium radioisotope generator with the inlet tubing port configured to receive saline and the outlet tubing port configured to discharge the rubidium radioactive eluate;

a light projector mounted on the top end of the vertical post extending above the cabinet structure, wherein the light projector is configured to:

project a first light signal to indicate that an elution is taking place, and

project a second light signal to indicate that a peak bolus of radioactivity is detected;

the eluate reservoir located inside the shielded well on-board the cart and in fluid communication with the eluate tubing line;

a waste tubing line in fluid communication with the eluate tubing line and the waste bottle;

a valve configured to control fluid flow between the eluate tubing line and the waste bottle via the waste tubing line; and

a pedal configured to brake at least one of the four wheels when the pedal is depressed.

26. The infusion system of claim **25**, wherein

the cabinet structure has a lowermost portion and the platform has a lower surface,

the first opening is at a first elevation,

the second opening is at a second elevation,

the first elevation is between approximately 1 foot and approximately 2 feet, with respect to the lowermost portion of the cabinet structure, and

the second elevation is between approximately 2 feet and approximately 3 feet, with respect to the lower surface of the platform.

27. The infusion system of claim **24**, further comprising a dose calibrator located in the shielded well on-board the cart and in communication with the computer, wherein the dose calibrator is configured to determine the strontium breakthrough test result; and

wherein the opening through the exterior shell configured to provide access to the strontium-rubidium radioisotope generator within the interior space of the cabinet structure is through the front side of the exterior shell.

28. The infusion system of claim **27**, further comprising:

the strontium-rubidium radioisotope generator with the inlet tubing port configured to receive saline and the outlet tubing port configured to discharge the rubidium radioactive eluate,

the eluate reservoir located inside the shielded well on-board the cart and in fluid communication with the eluate tubing line,

a waste tubing line in fluid communication with the eluate tubing line and the waste bottle, and

a valve configured to control fluid flow between the eluate tubing line and the waste bottle via the waste tubing line.

29. The infusion system of claim **28**, wherein the computer of the infusion system is configured to:

measure an activity of the test sample filled into the eluate reservoir in the shielded well on-board the cart while the eluate reservoir remains in the shielded well on-board the cart, wherein the activity is measured with the dose calibrator in the shielded well on-board the cart, and

calibrate the infusion system based on the activity measured by the dose calibrator.

30. The infusion system of claim 29, wherein

the cabinet structure has a lowermost portion and the platform has a lower surface,

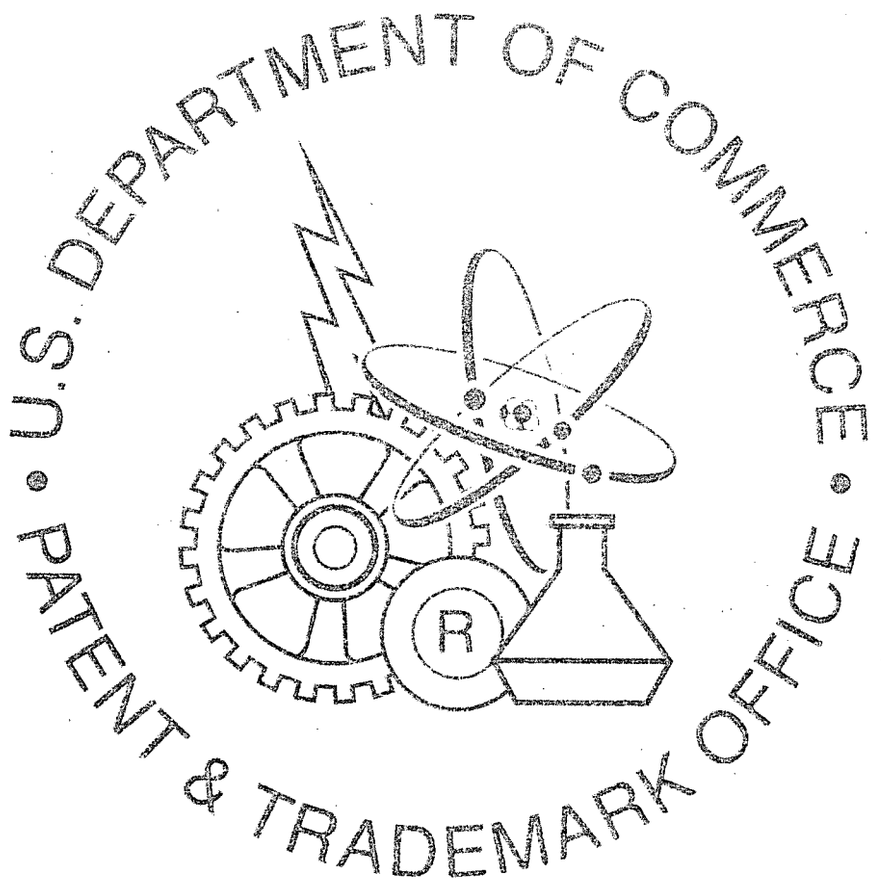
the first opening is at a first elevation,

the second opening is at a second elevation,

the first elevation is between approximately 1 foot and approximately 2 feet, with respect to the lowermost portion of the cabinet structure, and

the second elevation is between approximately 2 feet and approximately 3 feet, with respect to the lower surface of the platform.

* * * * *


U.S. DEPARTMENT OF COMMERCE
PATENT & TRADEMARK OFFICE

PTO-1683
(Rev. 7-96)

EXHIBIT 4

A 7667315

THE UNITED STATES OF AMERICA

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UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office

February 08, 2018

THIS IS TO CERTIFY THAT ANNEXED IS A TRUE COPY FROM THE RECORDS OF THIS OFFICE OF A DOCUMENT RECORDED ON MARCH 13, 2017.

By Authority of the
Under Secretary of Commerce for Intellectual Property
and Director of the United States Patent and Trademark Office

R GLOVER
Certifying Officer

PATENT ASSIGNMENT COVER SHEET

Electronic Version v1.1
Stylesheet Version v1.2

EPAS ID: PAT4315106

SUBMISSION TYPE:	NEW ASSIGNMENT
NATURE OF CONVEYANCE:	ASSIGNMENT

CONVEYING PARTY DATA

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JANET L. GELBACH	04/20/2010
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PROPERTY NUMBERS Total: 1

Property Type	Number
Application Number:	15389200

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NAME OF SUBMITTER:	PAUL J. LAVANWAY, JR.
SIGNATURE:	/Paul J. LaVanway, Jr./
DATE SIGNED:	03/13/2017

Total Attachments: 7
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ASSIGNMENT

We, Stephen E. Hidem, residing at 4710 Juneau Lane North, Plymouth, Minnesota 55446, Aaron M. Fontaine, residing at 5663 West Bavarian Pass, Fridley, Minnesota 55432, Janet L. Gelbach, residing at 4204 Shetland Court, New Albany, Indiana 47150, Patrick M. McDonald, residing at 15395 Nicholas Street, Omaha, Nebraska 68154, Kathryn M. Hunter, residing at 1312 Judy Reagan Lane, Knoxville, Tennessee 37931, Rolf E. Swenson, residing at 35 Fieldston Road, Princeton, New Jersey 08540 and Julius P. Zodda, residing at 3 Tigers Court, Mercerville, New Jersey 08619 ("Assignor"), have made invention(s) for which United States and foreign patents and patent applications have been filed and are identified on the attached Schedule 1;

Whereas, Bracco Diagnostics Inc., a Delaware corporation having a place of business at 107 College Road East, Princeton, NJ 08540 ("Assignee"), desires to acquire the entire right, title and interest in and to the United States and foreign patents and patent applications identified on the attached Schedule 1 and in and to the inventions described and claimed therein (the "Patents"); and

NOW, THEREFORE, in exchange for good and valuable consideration, the receipt of which is hereby acknowledged, Assignor hereby assigns to Assignee, and its successors and assigns the following:

(1) The entire right, title and interest to the Patents including the inventions described or claimed therein, and to each U.S. and foreign patent application and patent from which the Patents claim priority to, in whole or in part, and to which the Patents claim priority; and

(2) The entire right, title and interest to any United States or foreign patents that may issue with respect to the inventions described or claimed in the Patents;

(3) The entire right, title and interest to any renewals, reissues, extensions, substitutions, continuations, continuations-in-part, or divisions of the Patents, and all foreign applications based thereon;

(4) The right to apply for patents in foreign countries in its own name and to claim any priority rights to which such foreign applications are entitled under international conventions, treaties or otherwise; and

(5) The right to enforce patent rights to such Patents as fully and entirely as the same would have been held and enjoyed by the Assignors if this assignment had not been made; together with all claims by Assignors for damages by reason of past infringement or for provisional rights and including the right to sue for, and collect the same for its own use and benefit, and for the use and benefit of its successors, assigns, and other legal representatives.

Assignor further agrees for himself and for his successors and assigns to execute and deliver without further consideration any further applications, assignments or other documents and to perform such other lawful acts as Assignee its successors and assigns may deem necessary to fully secure, maintain and enforce its rights, title or interest as outlined herein.

Assignor hereby authorizes and requests the Commissioner of Patents to issue to Assignee any patents that may be granted in accordance with this Assignment.

We hereby authorize attorneys associated with Customer No. 22859, of 200 South Sixth Street, Suite 4000, Minneapolis, Minnesota, 55402-1425, to insert the Application Nos. and Filing Dates of said application when known.

This Agreement may be executed in one or more counterparts, all of which shall be considered one and the same agreement. The signatures from each counterpart may be combined with a copy of the Agreement to constitute the entire Agreement.

Date: 4/28/2010

Stephen E. Hidem

Subscribed to and sworn to before me this 28 day of APRIL, 2010.

Notary Public

Notary Seal

CHARLES N THOMPSON
NOTARY PUBLIC
MINNESOTA
My Commission Expires Jan. 31, 2015

Date: 4/28/2010

Aaron M. Fontaine

Subscribed to and sworn to before me this 28 day of APRIL, 2010.

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SCHEDULE 1

US Patent Applications

Patent App. No.	Date Filed	Title	Attorney Docket No.
12/137,356	6/11/2008	SHIELDING ASSEMBLIES FOR INFUSION SYSTEMS	56782.1.5
12/137,363	6/11/2008	INFUSION SYSTEM CONFIGURATIONS	56782.1.6
12/137,364	6/11/2008	INFUSION SYSTEMS INCLUDING COMPUTER-FACILITATED MAINTENANCE AND/OR OPERATION AND METHODS OF USE	56782.1.7
12/137,377	6/11/2008	CABINET STRUCTURE CONFIGURATIONS FOR INFUSION SYSTEMS	56782.1.8
12/808,467	6/16/2010	INFUSION SYSTEMS INCLUDING COMPUTER-FACILITATED MAINTENANCE AND/OR OPERATION AND METHODS OF USE	56782.1.7.2
15/389,200	12/22/2016	INTEGRATED STRONTIUM-RUBIDIUM RADIOISOTOPE INFUSION SYSTEMS	56782.4.1

US Patents

Patent No.	Date Issued	Title

Foreign and International Patent Applications

Country	Patent App. No.	Date Filed	Title	Attorney Docket No.
WO	PCT/US09/47031	6/11/2009	INFUSION SYSTEMS INCLUDING COMPUTER-FACILITATED MAINTENANCE AND/OR OPERATION AND METHODS OF USE	56782.1.7.1

Foreign Patents

Country	Patent No.	Date of Issue	Title

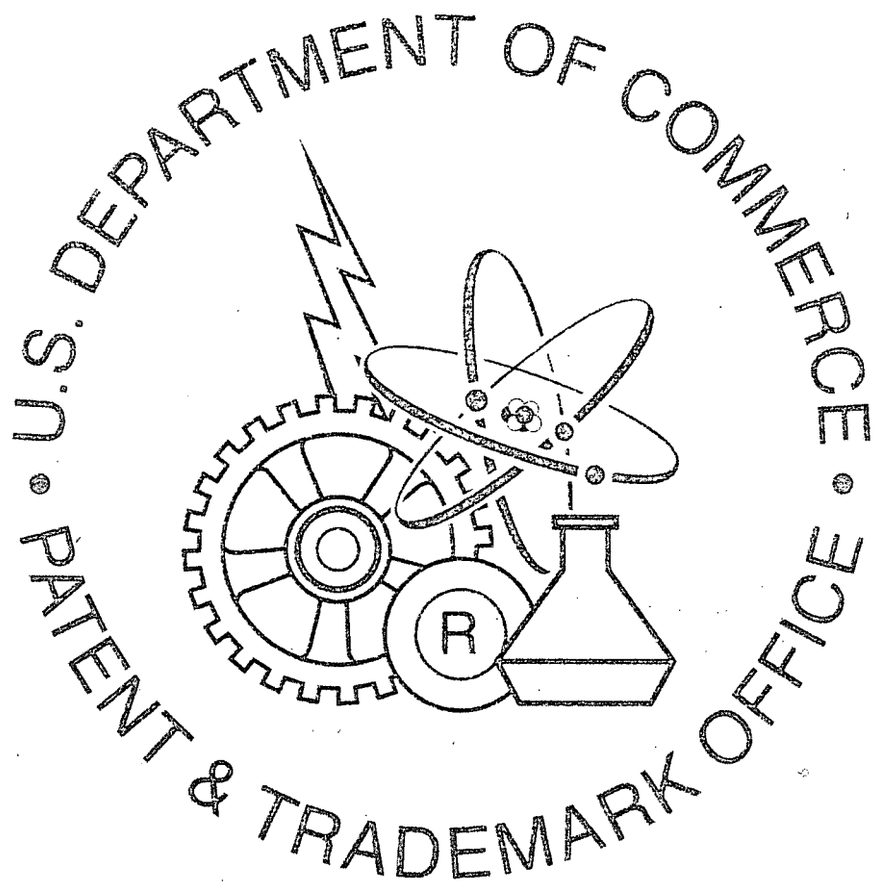
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EXHIBIT 5

U 7667315

THE UNITED STATES OF AMERICA

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UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office

February 12, 2018

THIS IS TO CERTIFY THAT ANNEXED HERETO IS A TRUE COPY FROM THE RECORDS OF THIS OFFICE OF:

U.S. PATENT: *9,750,870*
ISSUE DATE: *September 05, 2017*

By Authority of the
Under Secretary of Commerce for Intellectual Property
and Director of the United States Patent and Trademark Office

UNITED STATES PATENT AND TRADEMARK OFFICE
DEPARTMENT OF COMMERCE

P. R. GRANT
Certifying Officer

US009750870B2

(12) **United States Patent**
Hidem et al.

(10) **Patent No.: US 9,750,870 B2**
(45) **Date of Patent: *Sep. 5, 2017**

(54) **INTEGRATED STRONTIUM-RUBIDIUM RADIOISOTOPE INFUSION SYSTEMS**

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(72) Inventors: **Stephen E. Hidem**, Edina, MN (US); **Aaron M. Fontaine**, Minneapolis, MN (US); **Janet L. Gelbach**, Rolling Meadows, IL (US); **Patrick M. McDonald**, Omaha, NE (US); **Kathryn M. Hunter**, Knoxville, TN (US); **Rolf E. Swenson**, Silver Spring, MD (US); **Julius P. Zodda**, Mercerville, NJ (US)

(73) Assignee: **Bracco Diagnostics, Inc.**, Monroe Township, NJ (US)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

This patent is subject to a terminal disclaimer.

(21) Appl. No.: **15/490,484**

(22) Filed: **Apr. 18, 2017**

(65) **Prior Publication Data**

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(51) **Int. Cl.**
A61M 5/00 (2006.01)
A61B 50/13 (2016.01)
(Continued)

(52) **U.S. Cl.**
CPC ***A61M 5/007*** (2013.01); ***A61B 50/13*** (2016.02); ***A61M 5/1409*** (2013.01);
(Continued)

(58) **Field of Classification Search**
CPC A61M 5/007; A61M 5/14; A61M 5/142; A61N 5/1001; A61N 5/1002;
(Continued)

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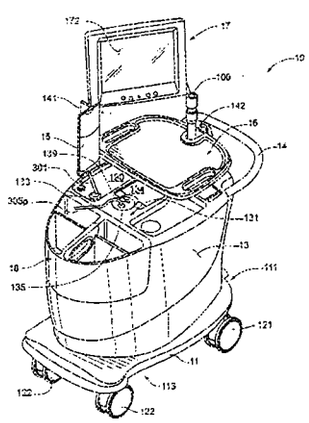
Primary Examiner — Charles A Marmor, II
Assistant Examiner — Carrie R Dorna
(74) *Attorney, Agent, or Firm* — Fredrikson & Byron, P.A.

(57) **ABSTRACT**

Methods for setting up, maintaining and operating a radiopharmaceutical infusion system, that includes a radioisotope generator, are facilitated by a computer of the system. The computer may include pre-programmed instructions and a computer interface, for interaction with a user of the system, for example, in order to track contained volumes of eluant and/or eluate, and/or to track time from completion of an elution performed by the system, and/or to calculate one or more system and/or injection parameters for quality control, and/or to perform purges of the system, and/or to facilitate diagnostic imaging.

30 Claims, 27 Drawing Sheets



Related U.S. Application Data

No. 12/808,467, filed as application No. PCT/US2009/047031 on Jun. 11, 2009, now Pat. No. 9,607,722, which is a continuation of application No. 12/137,377, filed on Jun. 11, 2008, now Pat. No. 8,708,352, and a continuation of application No. 12/137,363, filed on Jun. 11, 2008, now Pat. No. 7,862,534, and a continuation of application No. 12/137,356, filed on Jun. 11, 2008, now Pat. No. 8,317,674, and a continuation of application No. 12/137,364, filed on Jun. 11, 2008, now Pat. No. 9,597,053.

(51) **Int. Cl.**

A61M 5/14	(2006.01)
A61M 5/145	(2006.01)
A61M 5/168	(2006.01)
A61M 5/36	(2006.01)
G21F 7/00	(2006.01)
G21G 1/00	(2006.01)
G21G 4/08	(2006.01)
G06F 19/00	(2011.01)
A61B 50/10	(2016.01)

(52) **U.S. Cl.**

CPC ***A61M 5/1452*** (2013.01); ***A61M 5/16854*** (2013.01); ***A61M 5/16881*** (2013.01); ***A61M 5/365*** (2013.01); ***G06F 19/3468*** (2013.01); ***G21F 7/00*** (2013.01); ***G21G 1/001*** (2013.01); ***G21G 1/0005*** (2013.01); ***G21G 4/08*** (2013.01); *A61B 2050/105* (2016.02); *A61M 2005/1403* (2013.01); *A61M 2205/18* (2013.01); *A61M 2205/3375* (2013.01); *A61M 2205/50* (2013.01); *A61M 2205/505* (2013.01); *A61M 2205/52* (2013.01); *A61M 2205/584* (2013.01); *A61M 2205/587* (2013.01); *A61M 2205/6009* (2013.01); *A61M 2205/6054* (2013.01); *A61M 2205/6072* (2013.01); *A61M 2205/70* (2013.01); *A61M 2205/75* (2013.01); *G21G 2001/0031* (2013.01)

(58) **Field of Classification Search**

CPC .. A61N 5/1007; A61N 5/1014–5/1017; A61N 5/1027; A61N 5/1028; A61N 5/1071; A61N 2005/1021; G21G 1/0005; G21G 4/08

See application file for complete search history.

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Fig. 1A

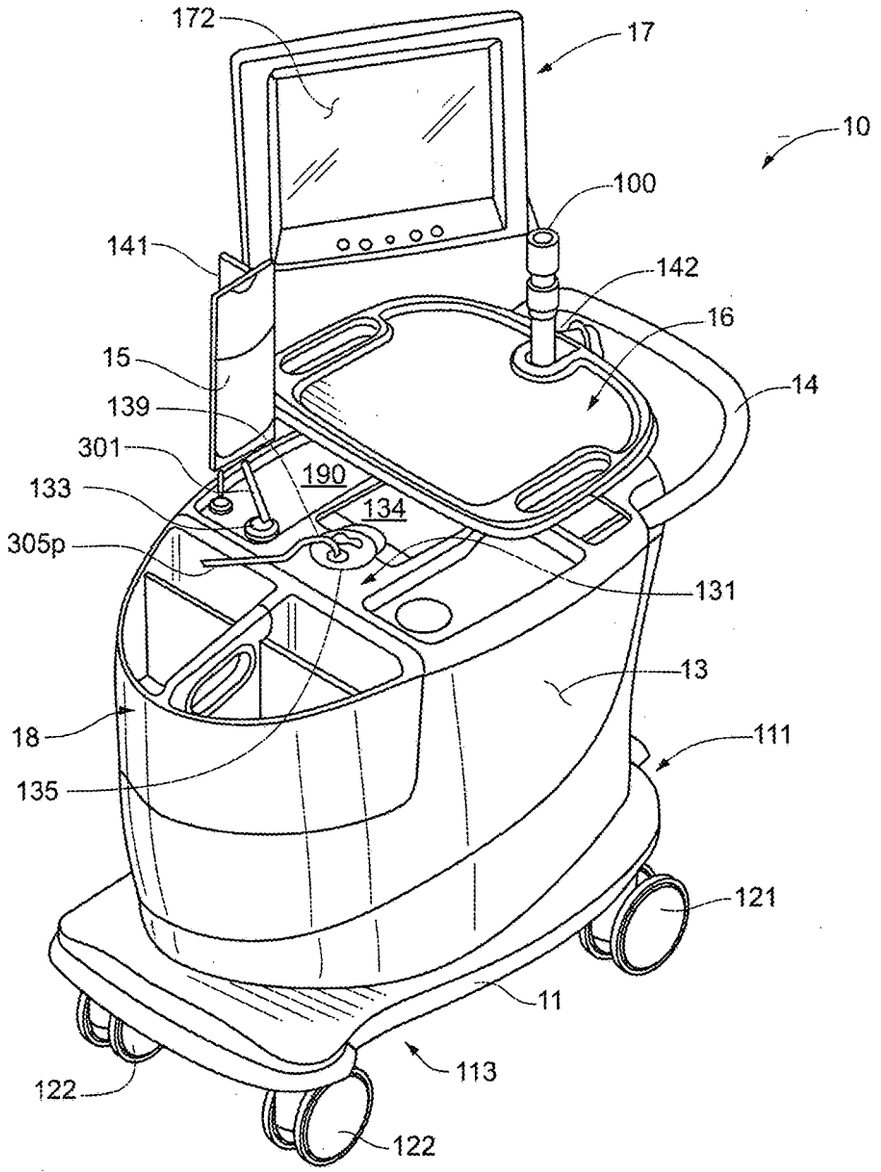


Fig. 1B

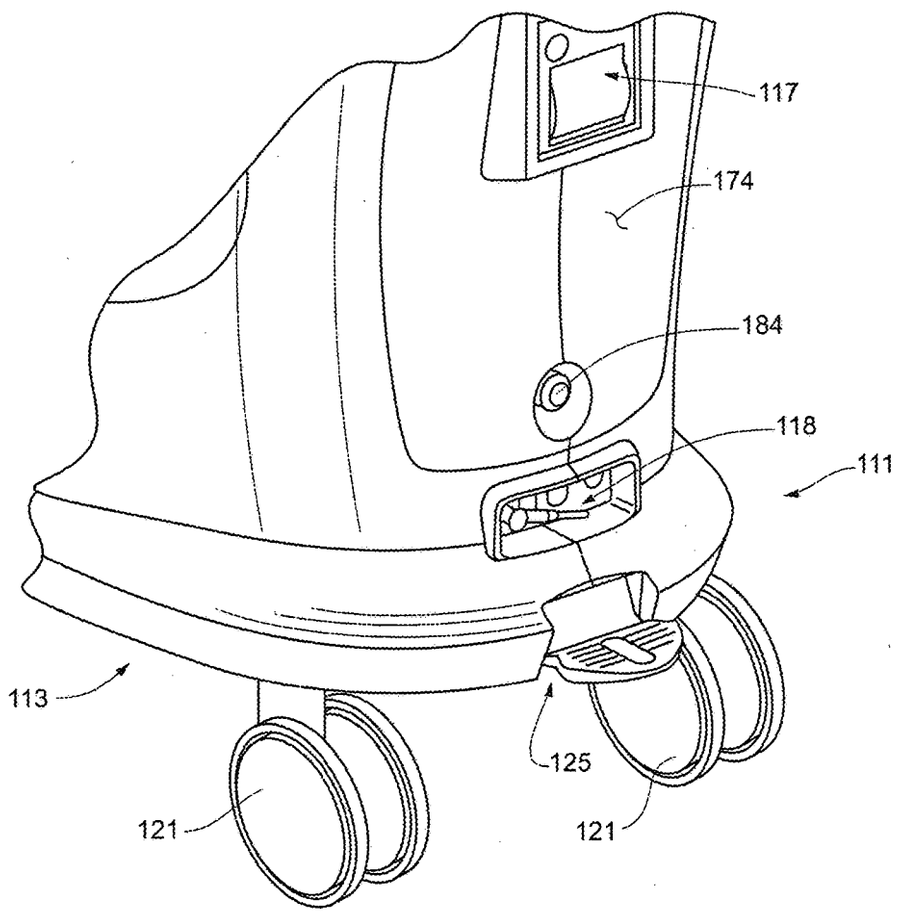
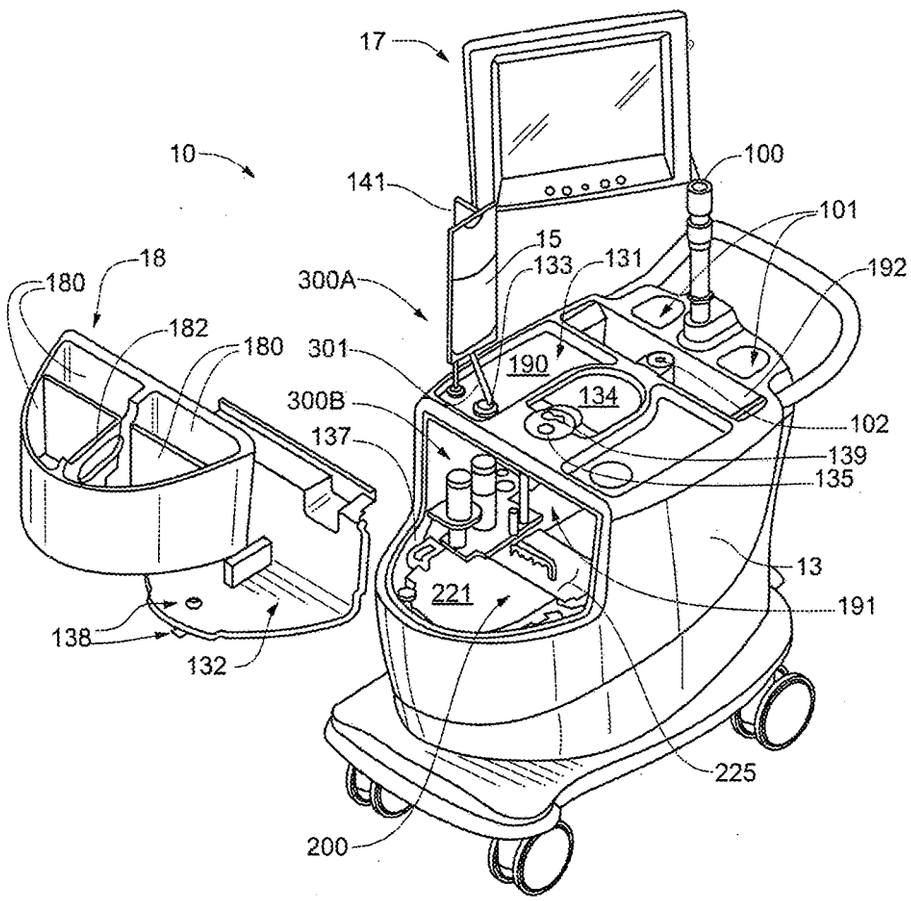


Fig. 1C



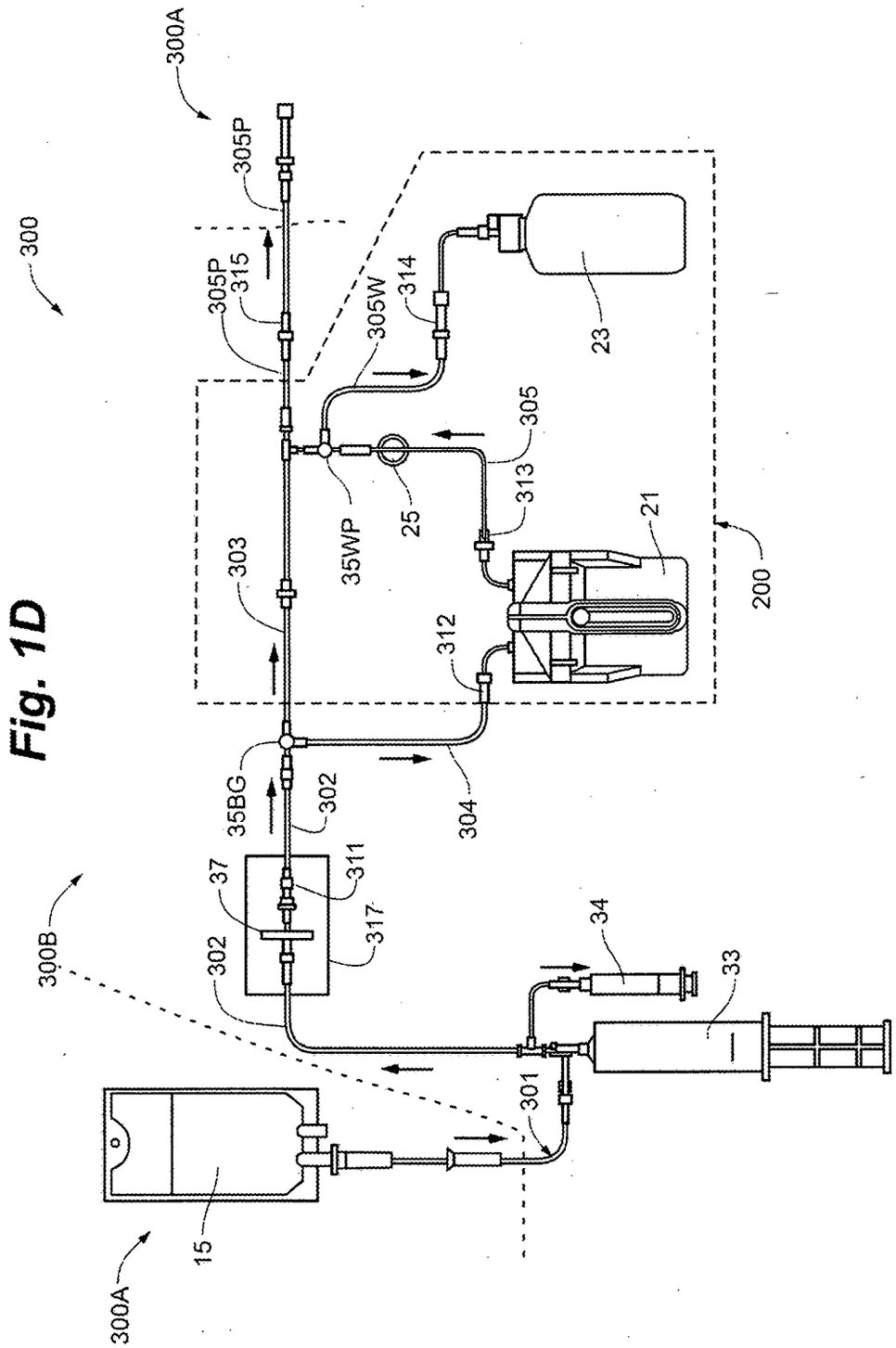


Fig. 1D

Fig. 1E

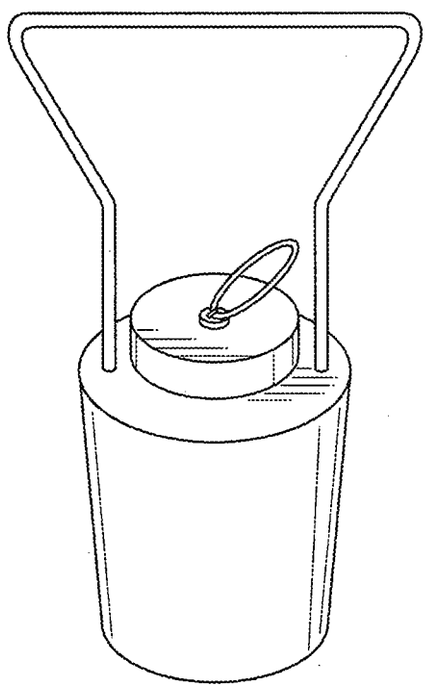


Fig. 2A

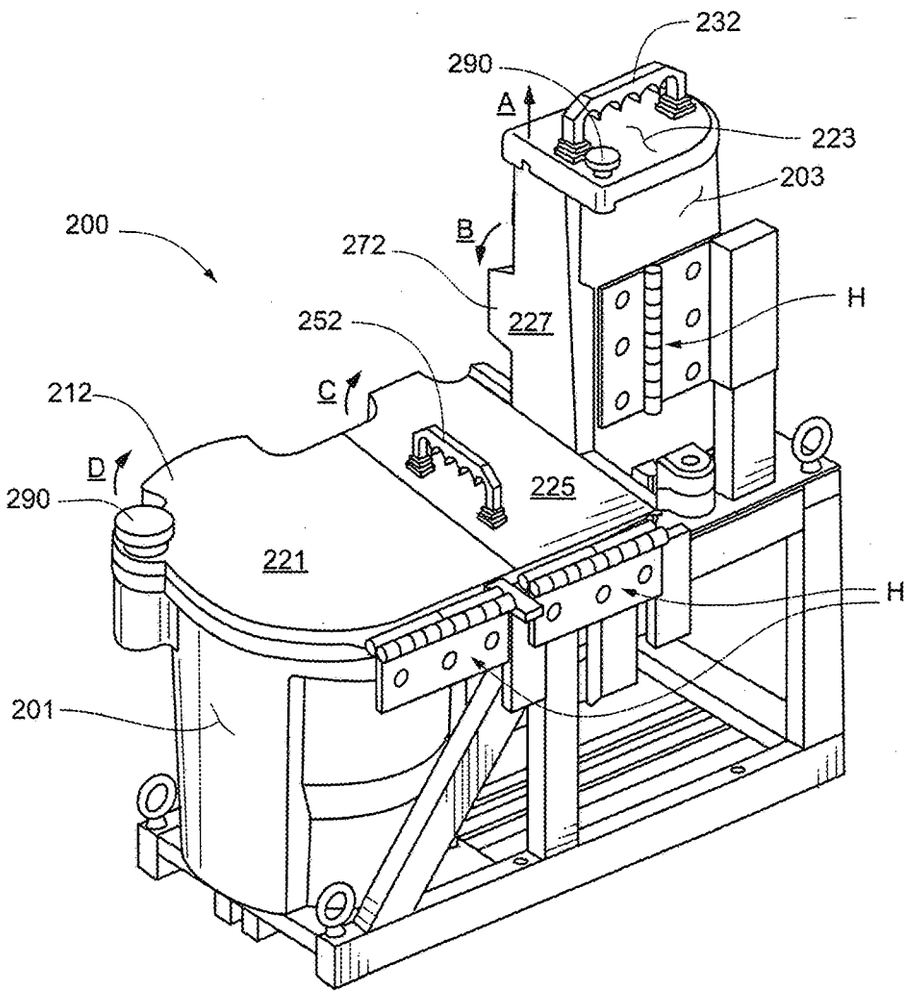


Fig. 2B-1

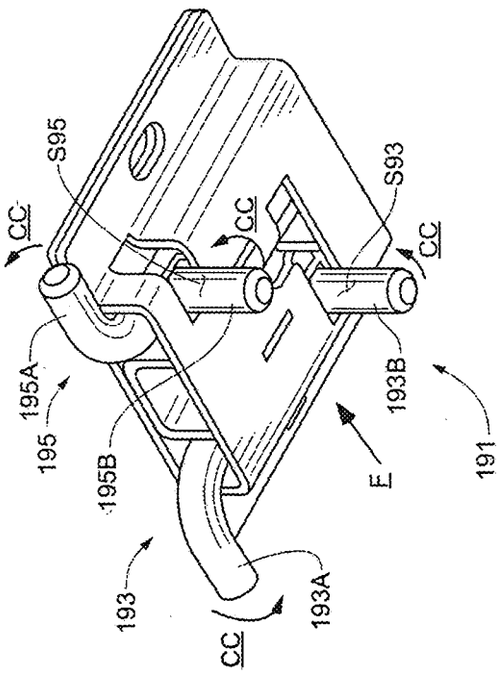


Fig. 2B

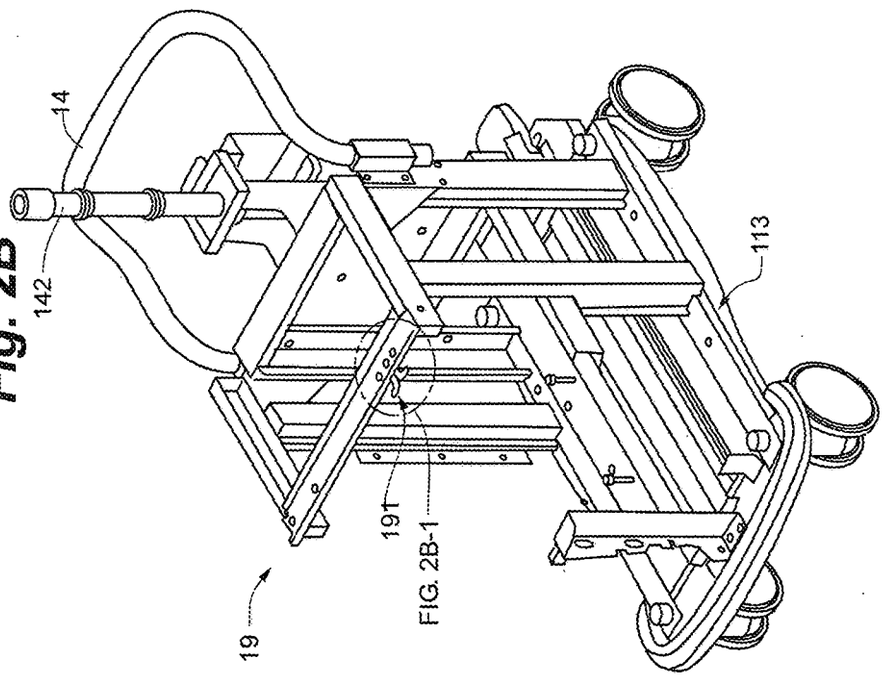
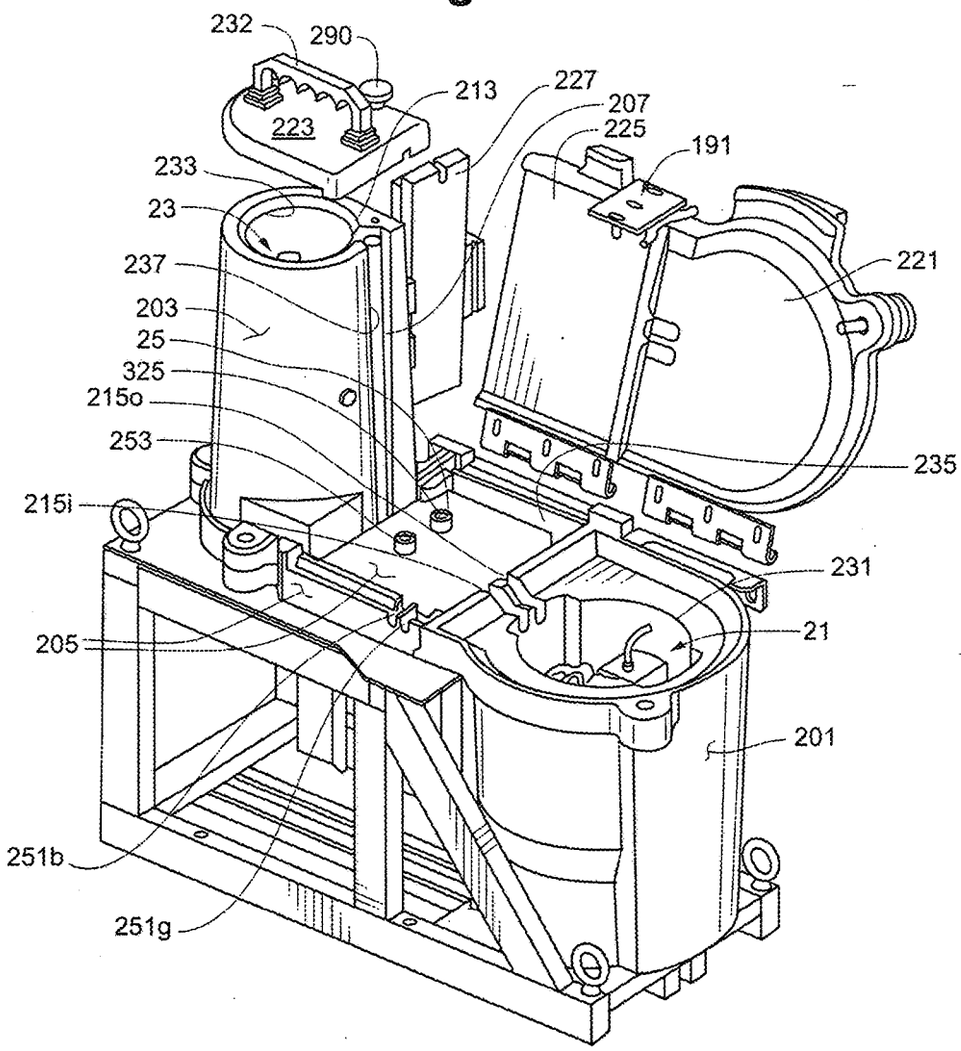


Fig. 3A



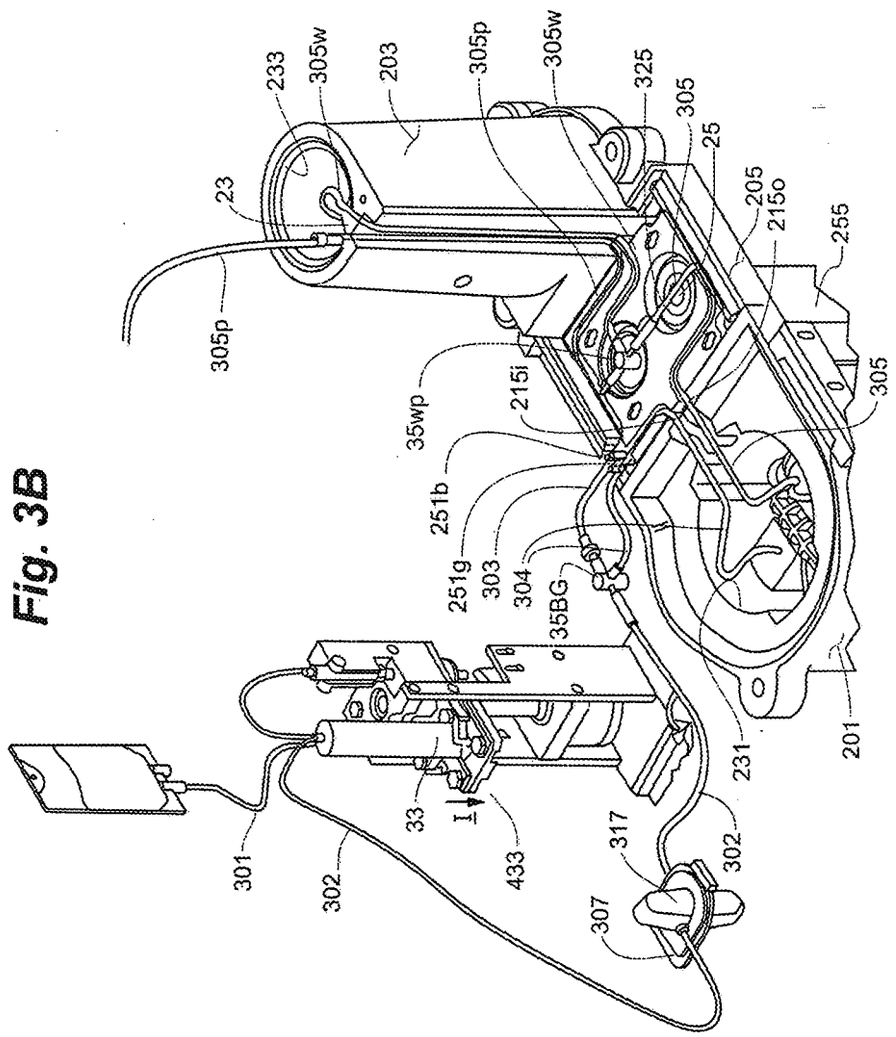


Fig. 3B

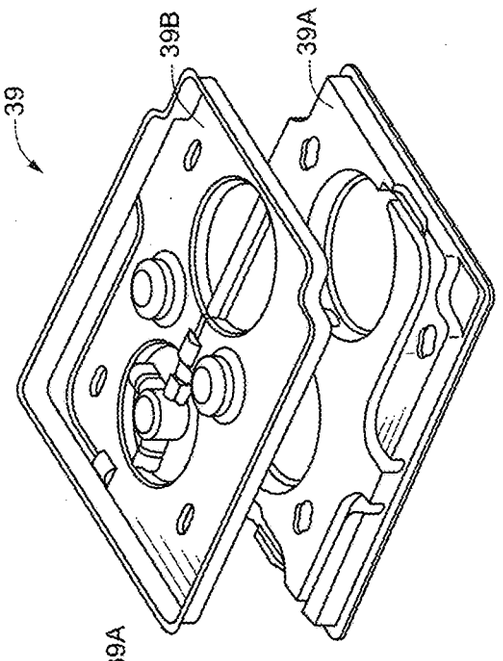


Fig. 3D

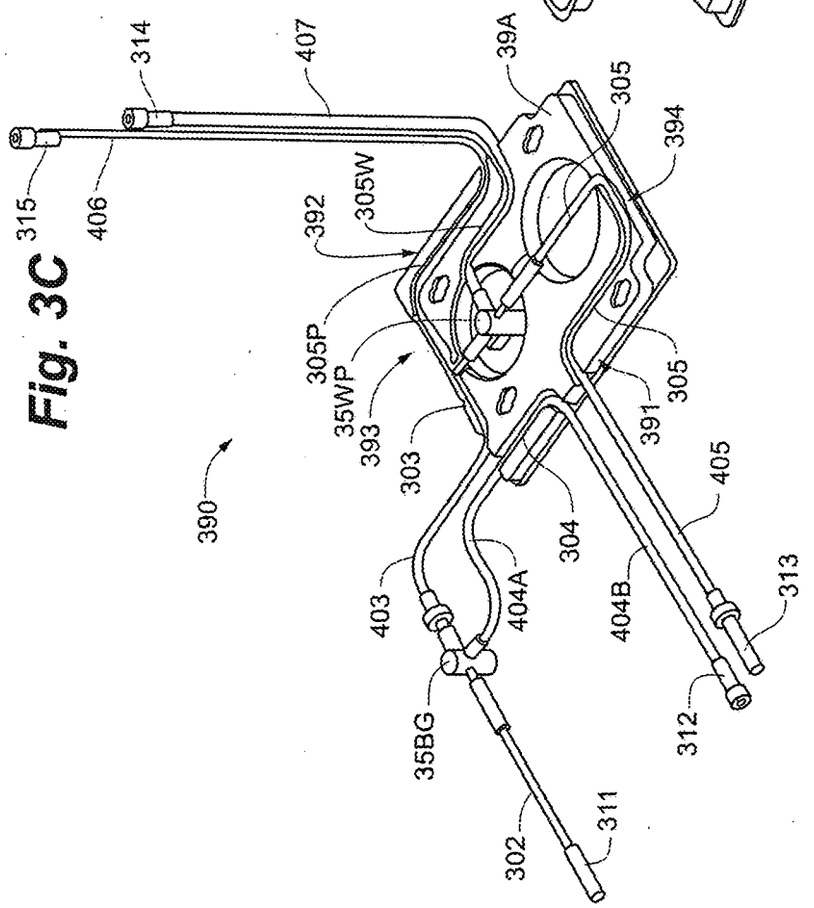


Fig. 3C

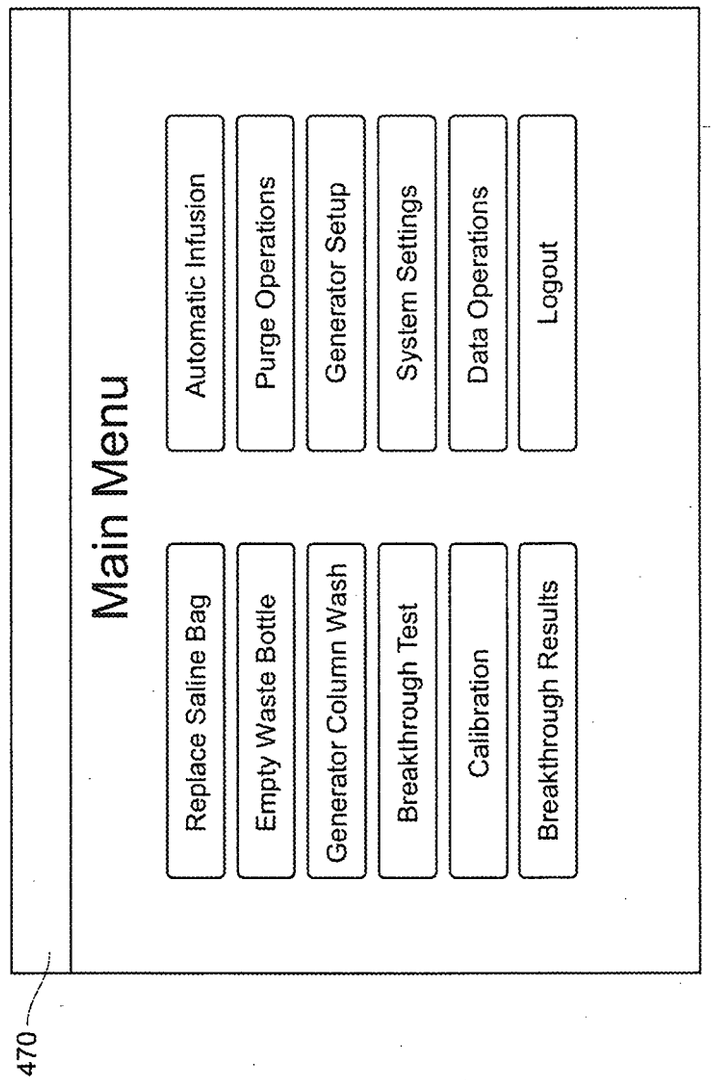


Fig. 4

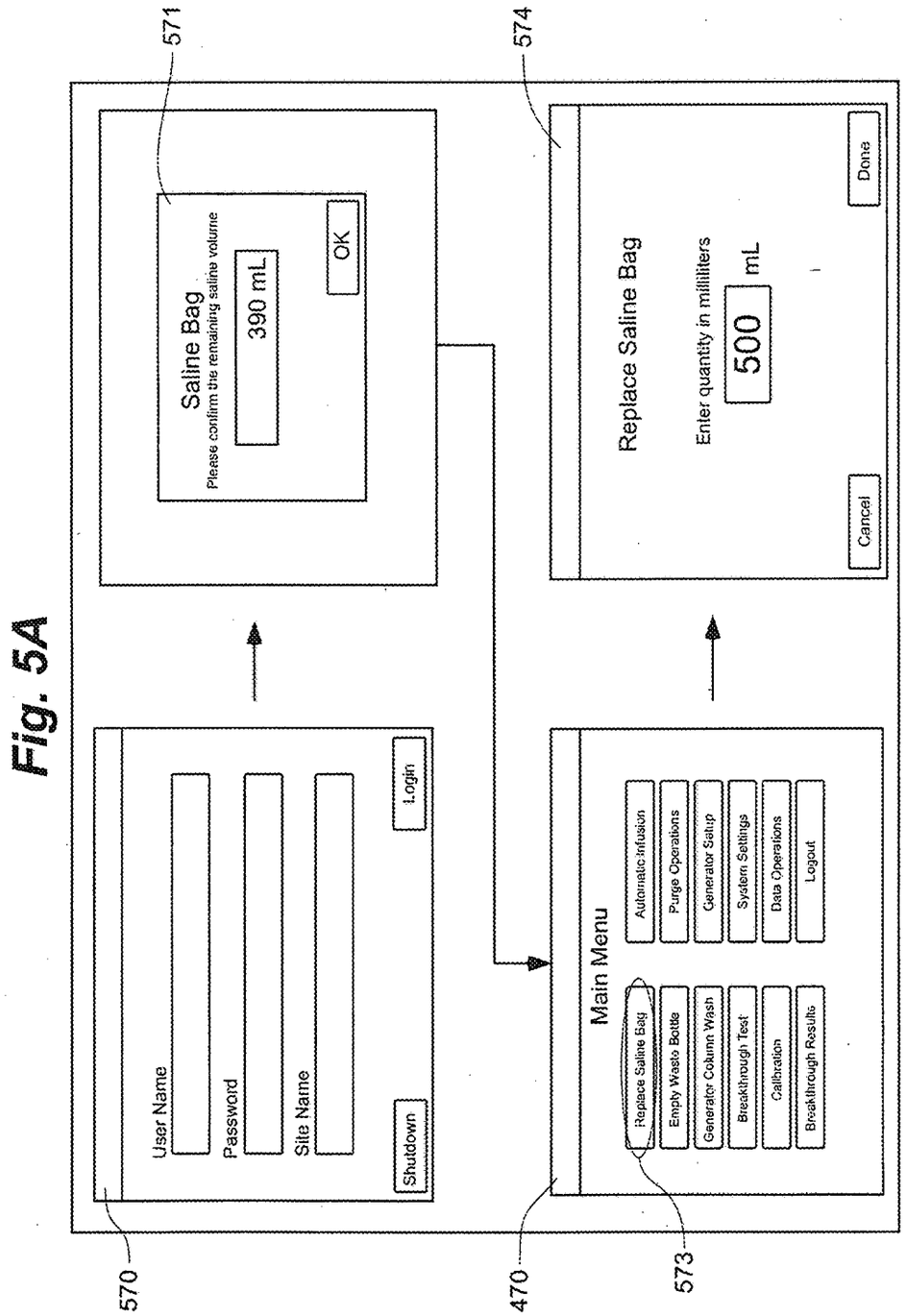
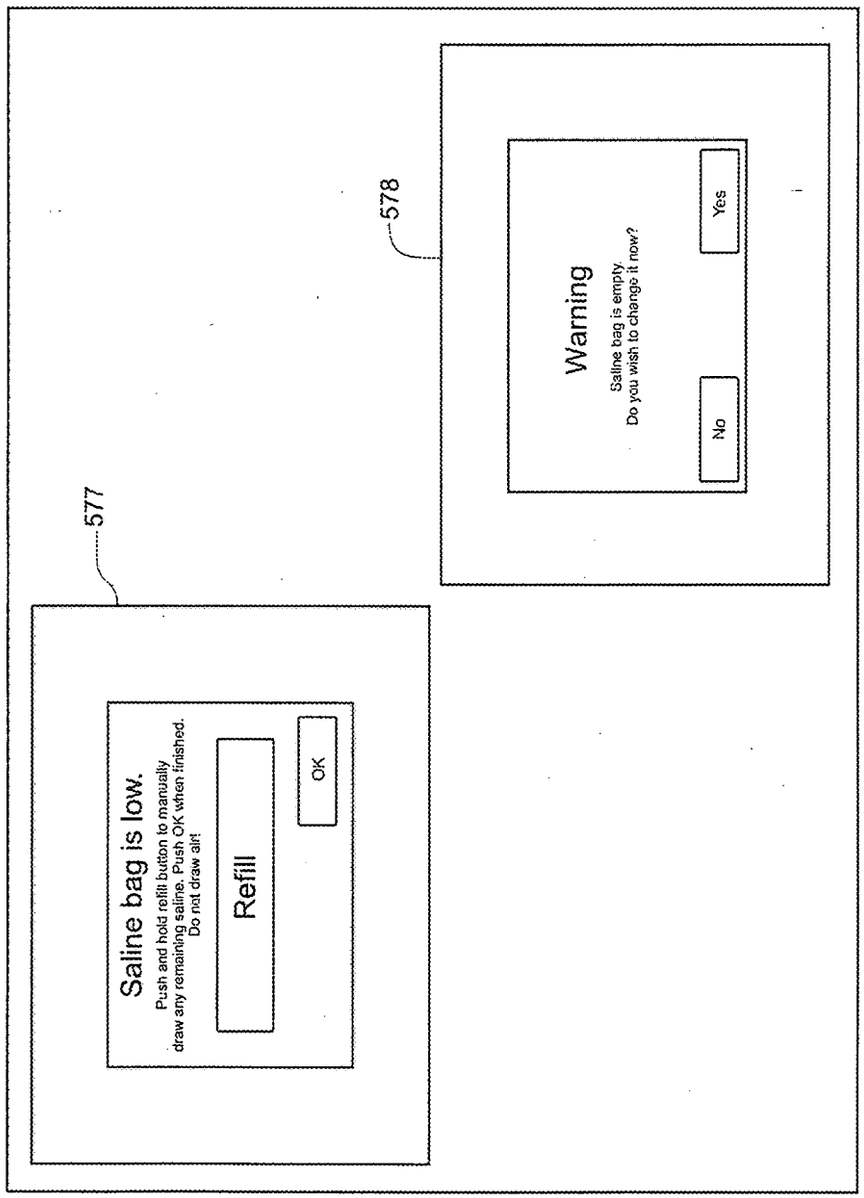


Fig. 5A

Fig. 5B



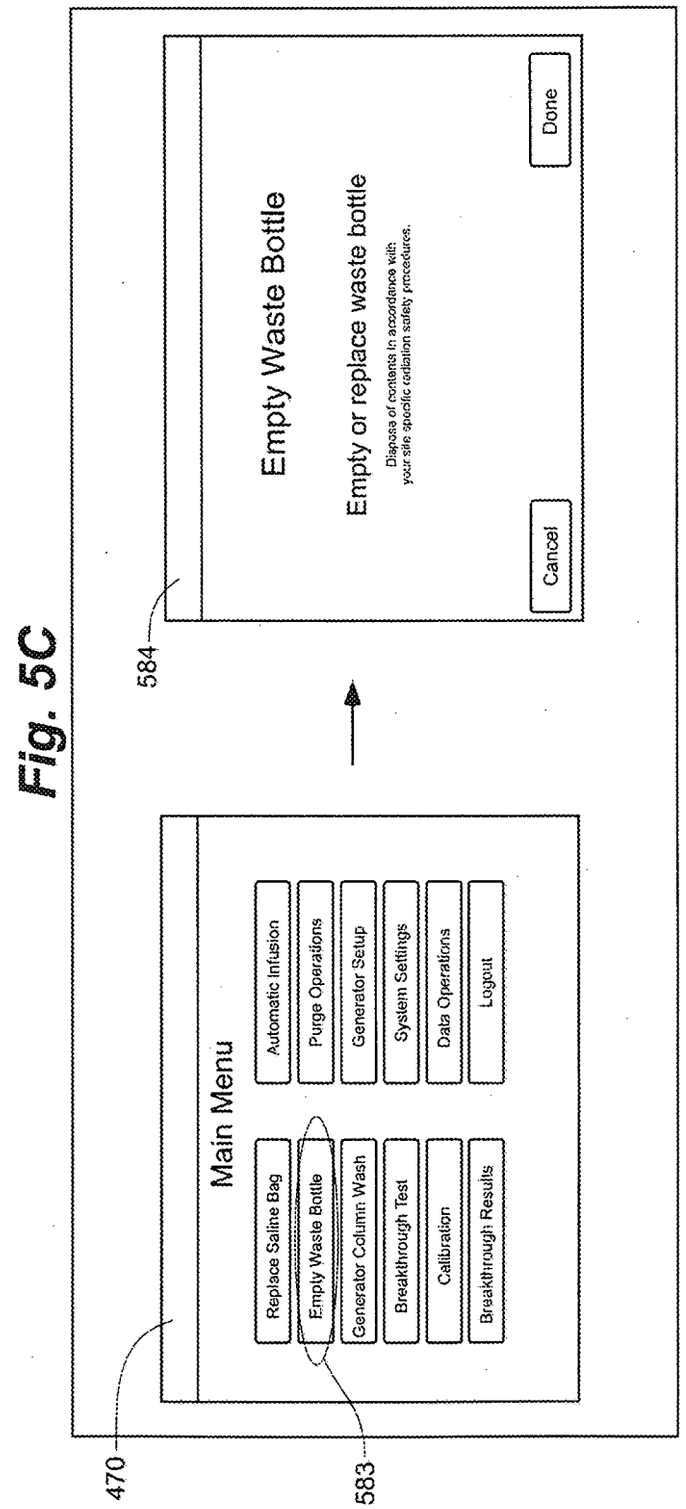


Fig. 5C

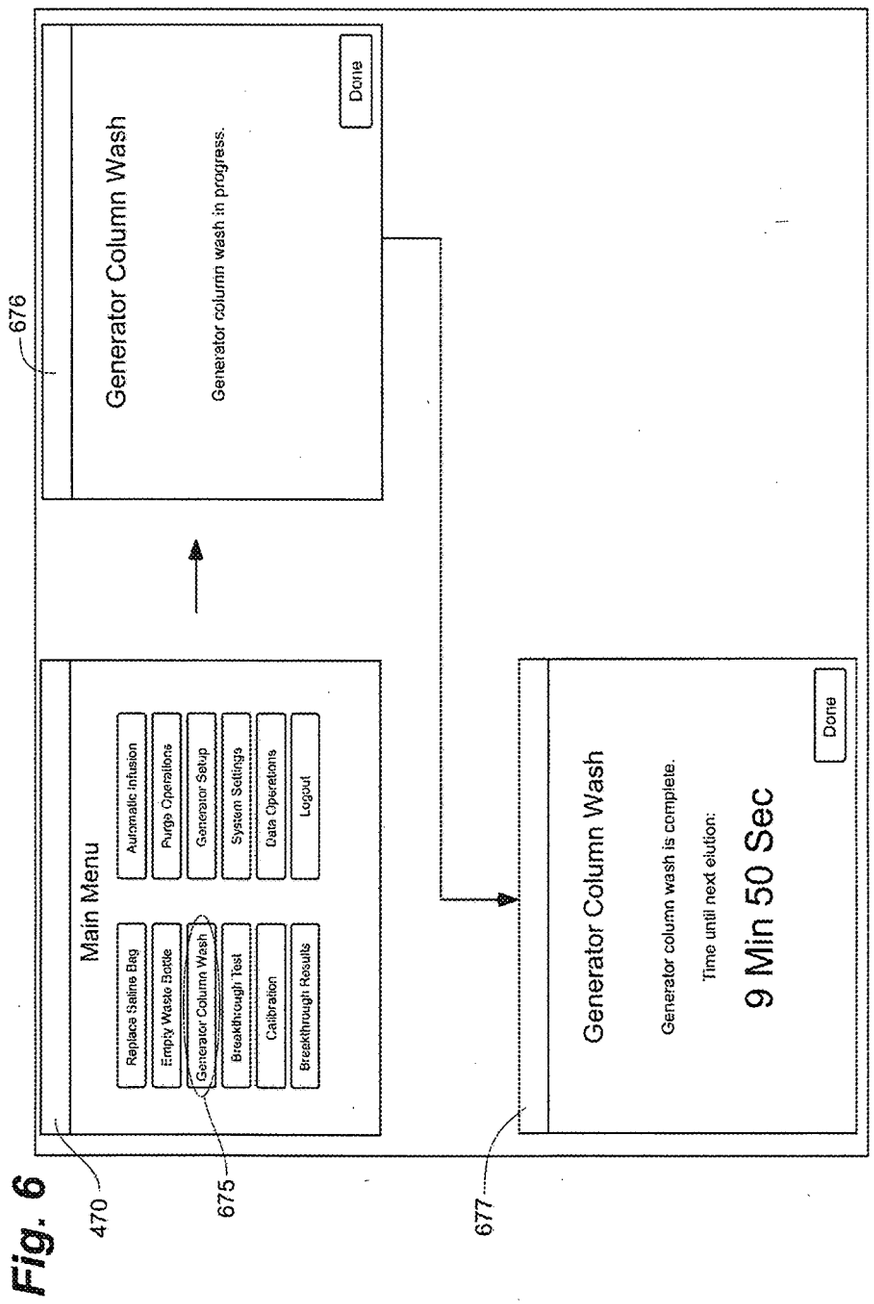


Fig. 6

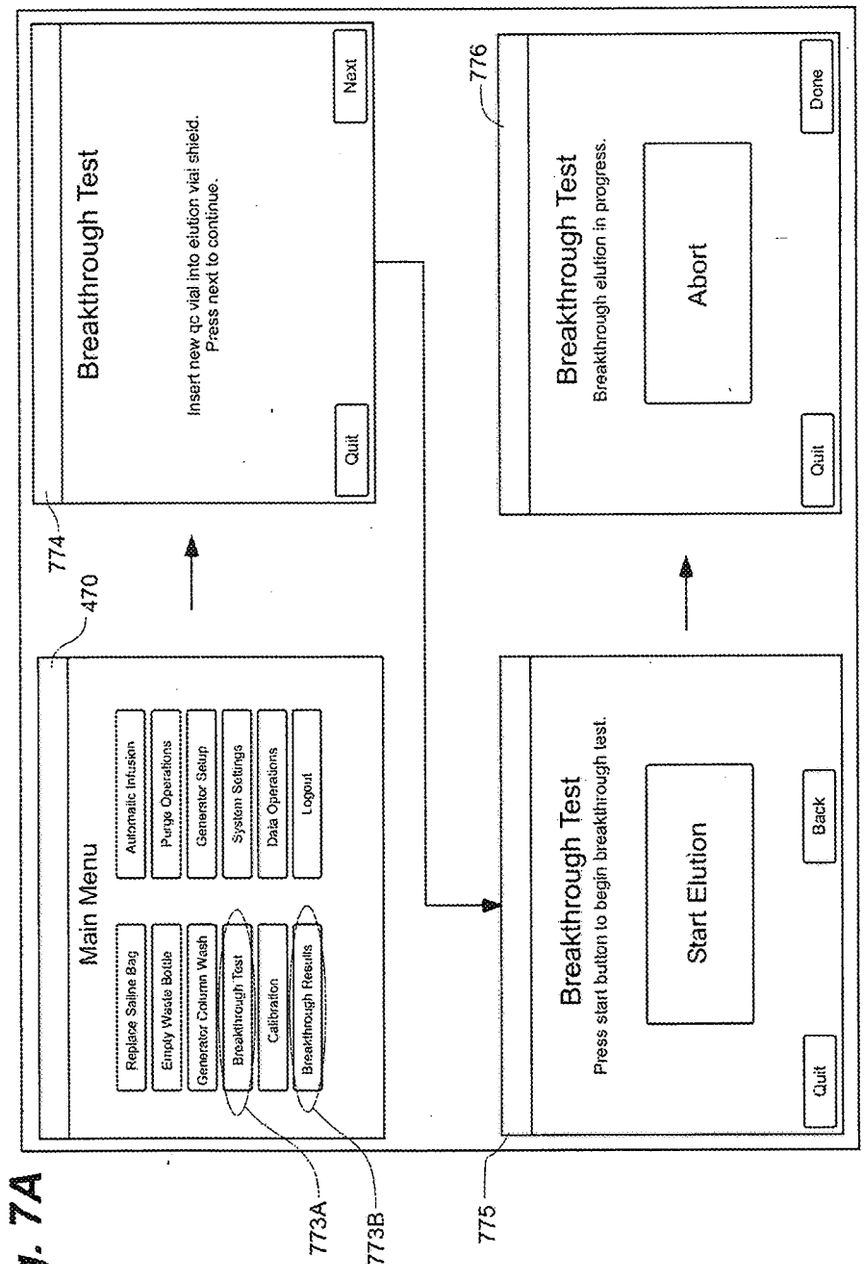


Fig. 7A

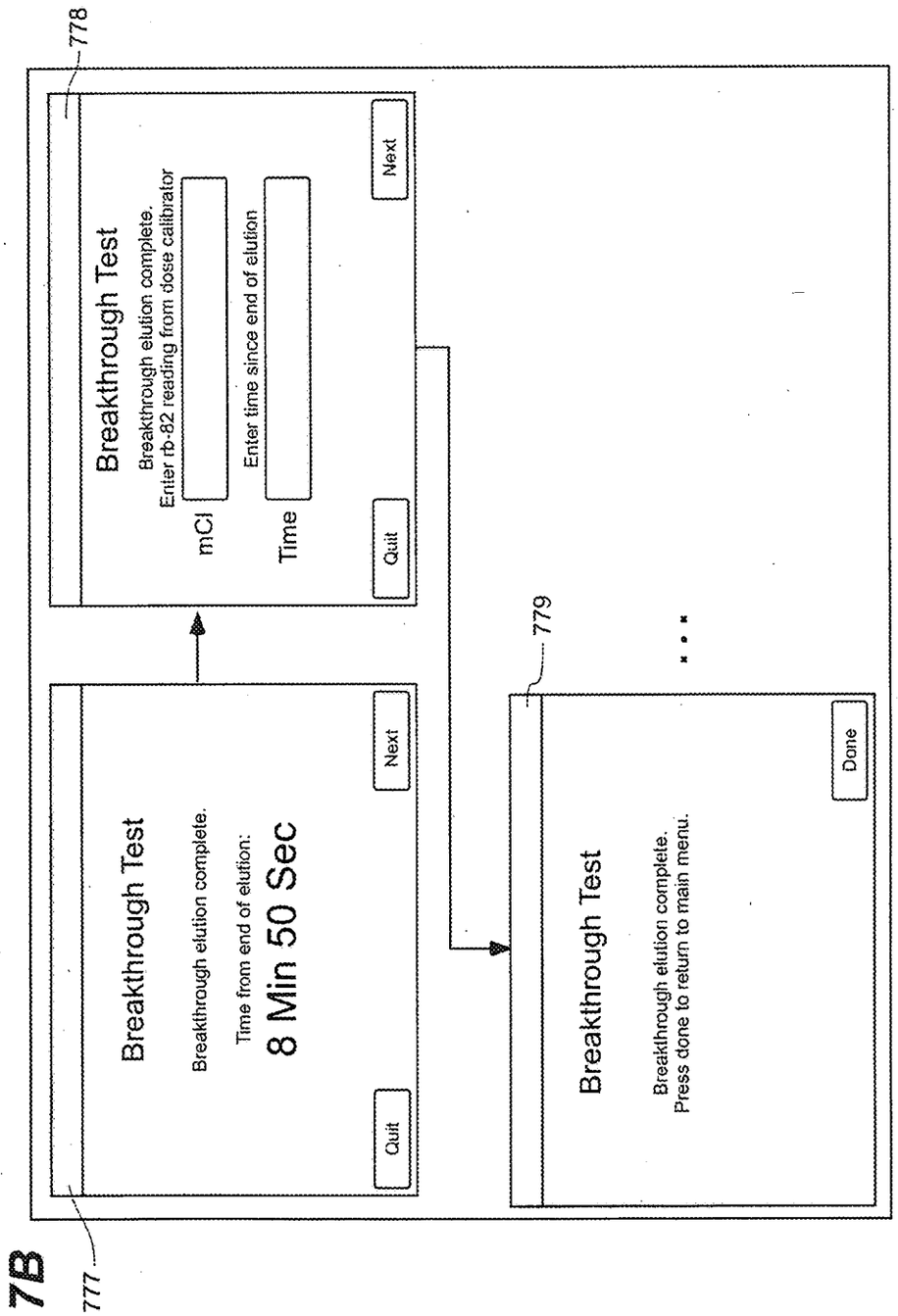


Fig. 7B

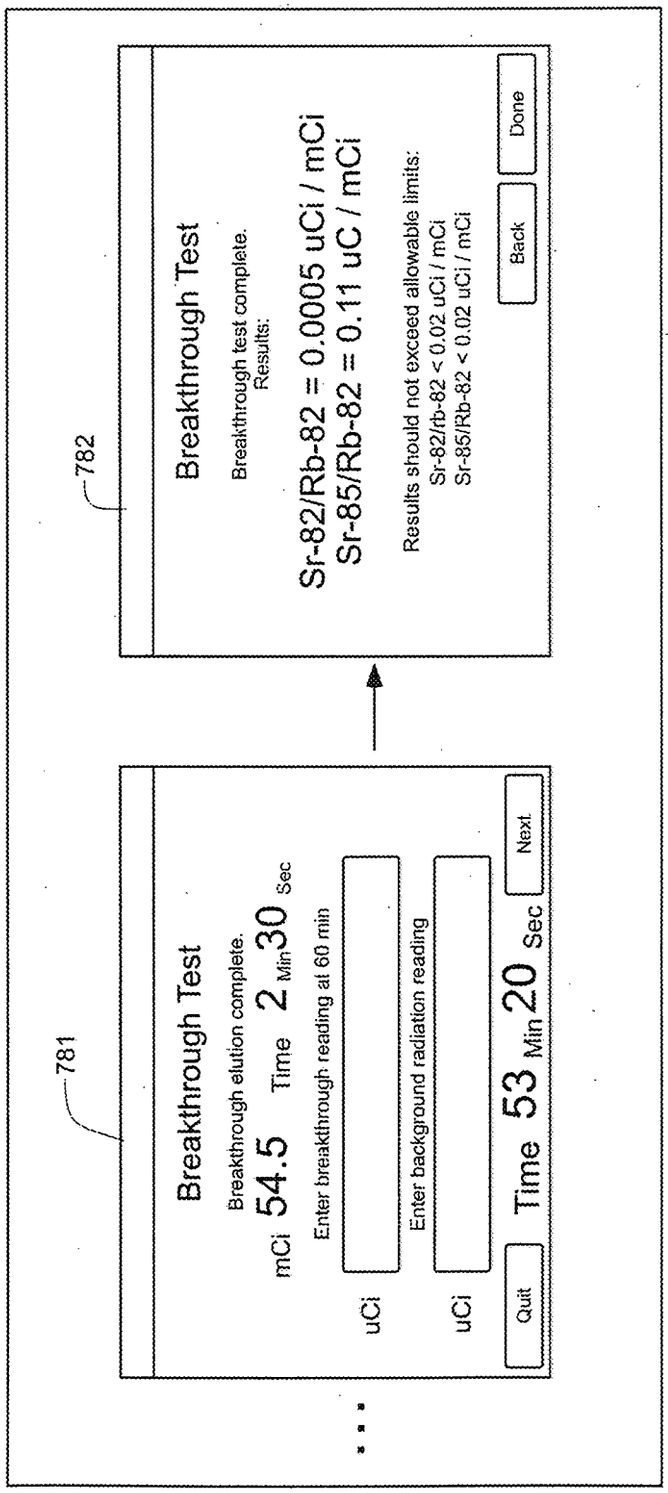


Fig. 7C

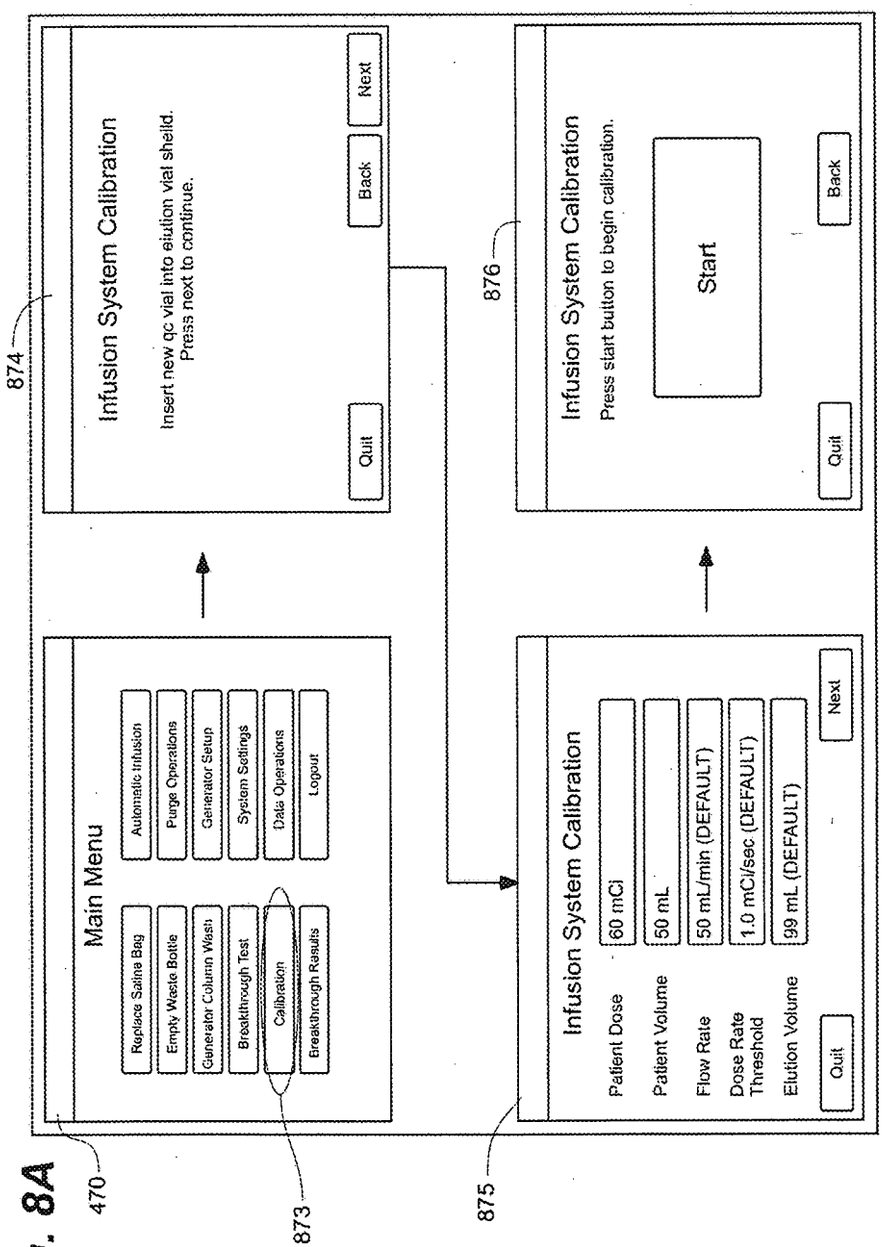


Fig. 8A

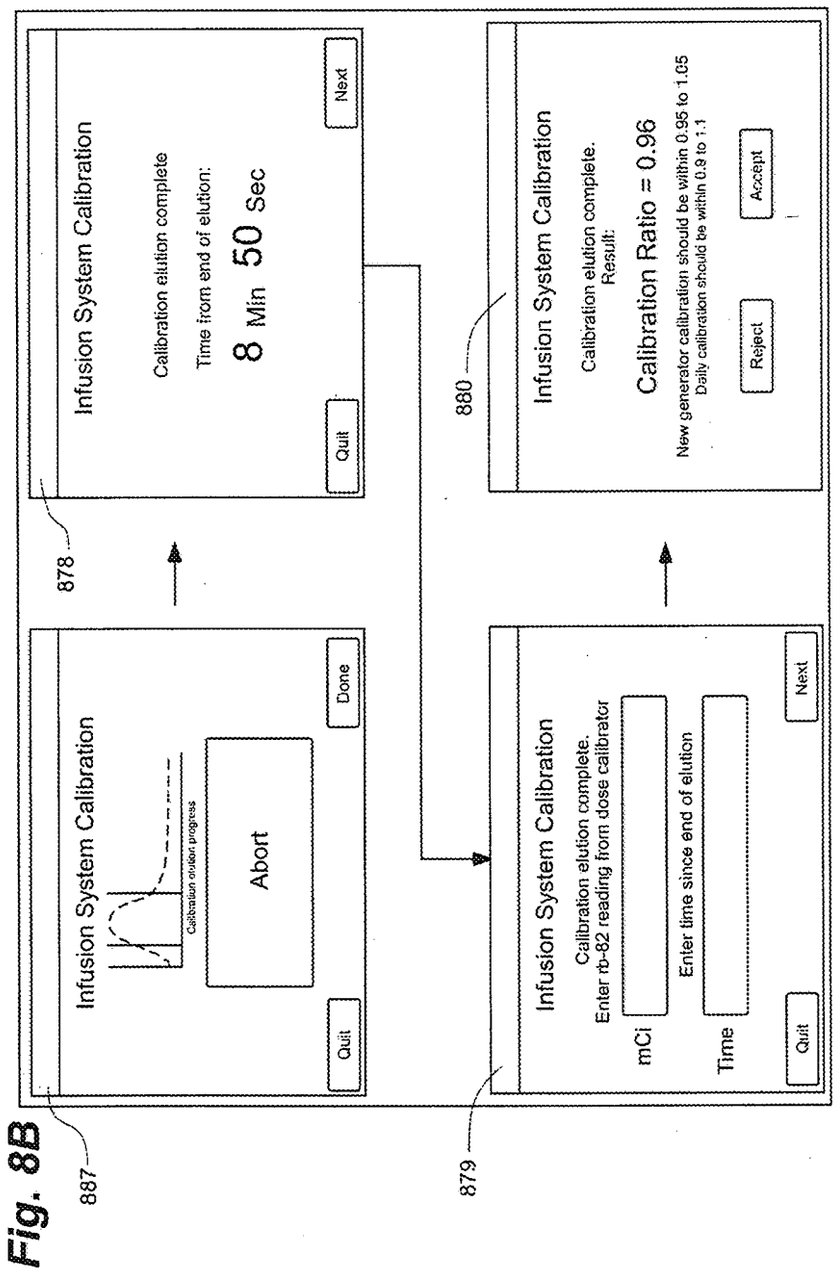


Fig. 8B

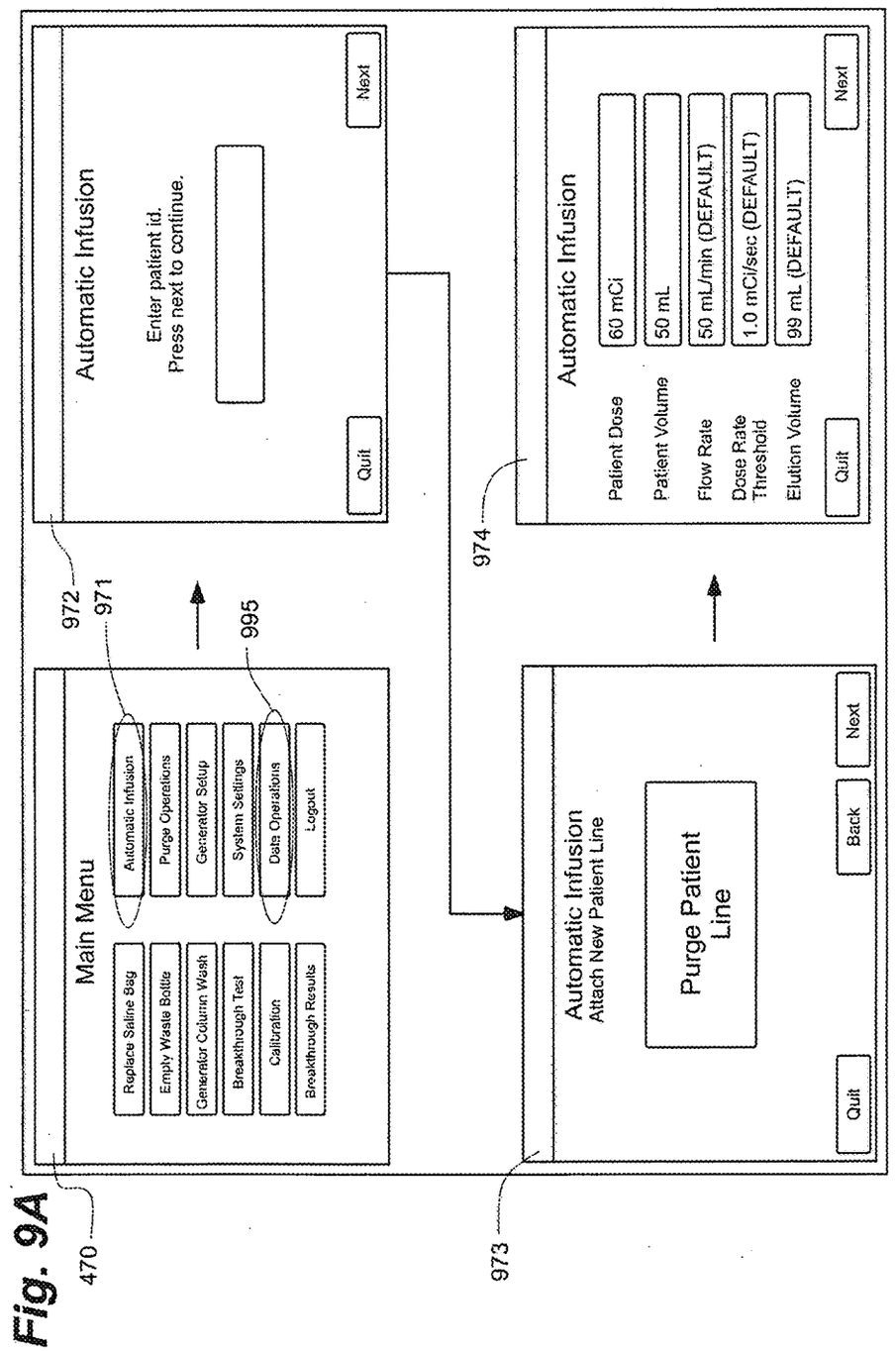


Fig. 9A

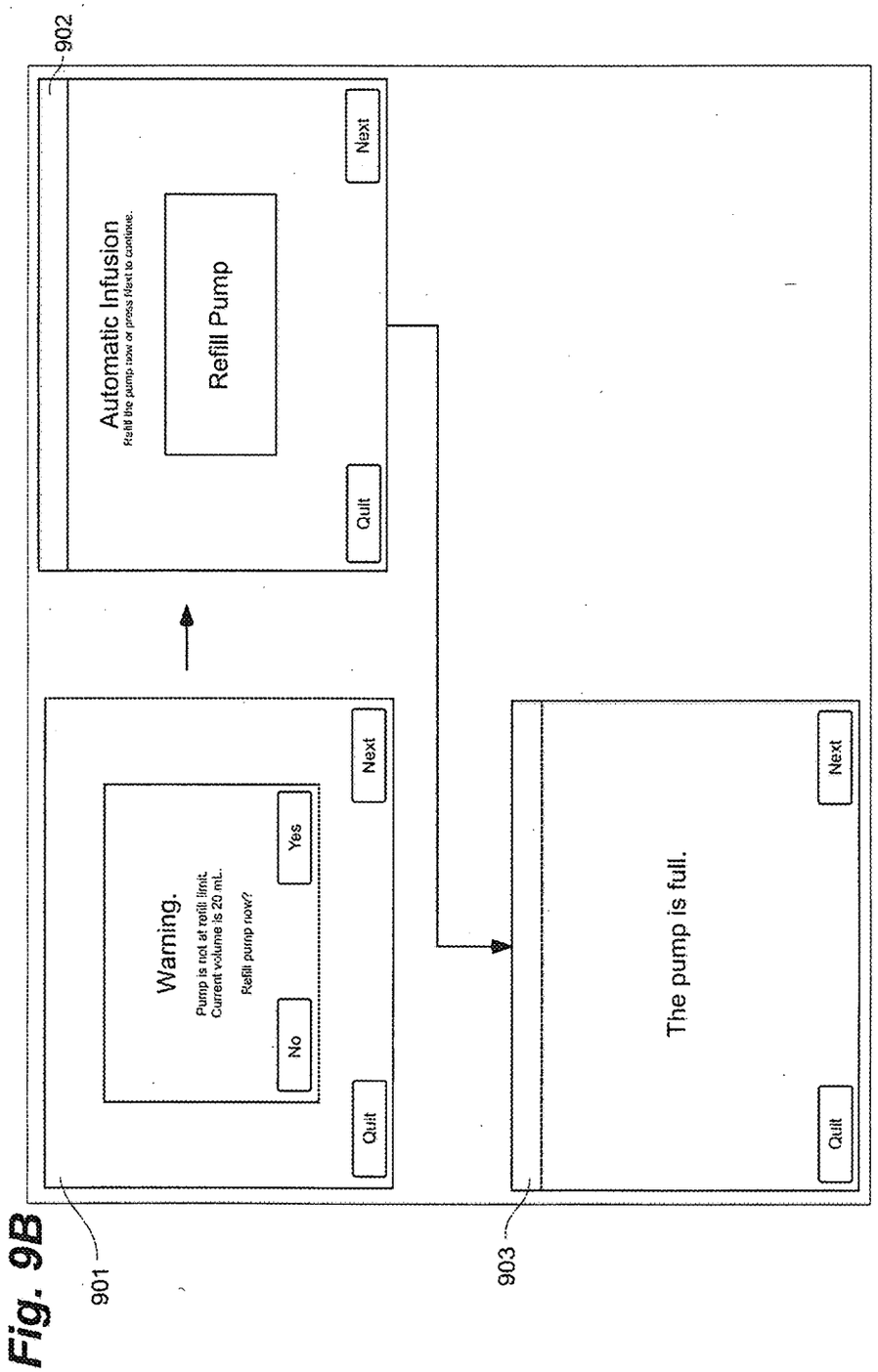


Fig. 9B

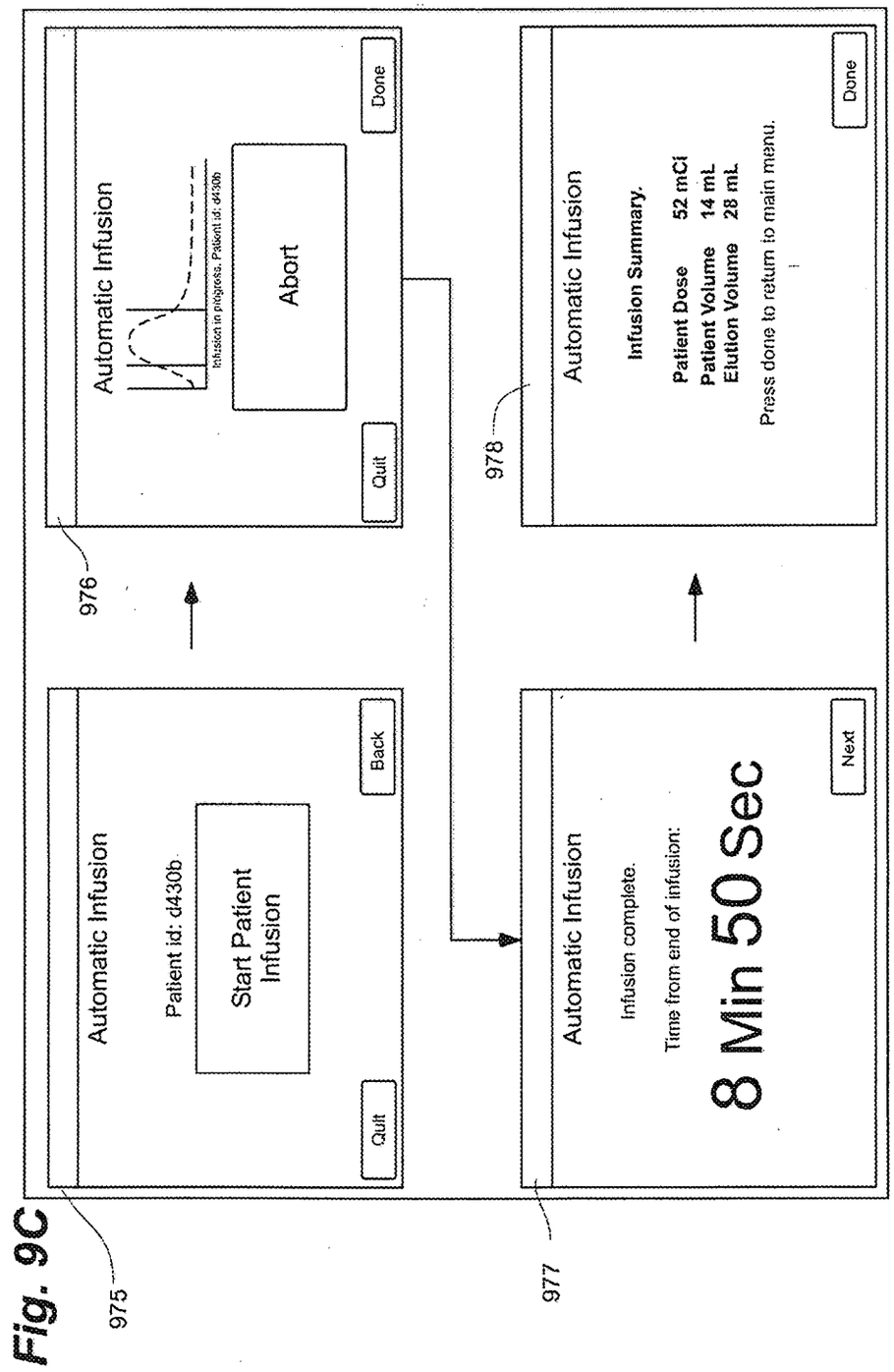


Fig. 9C

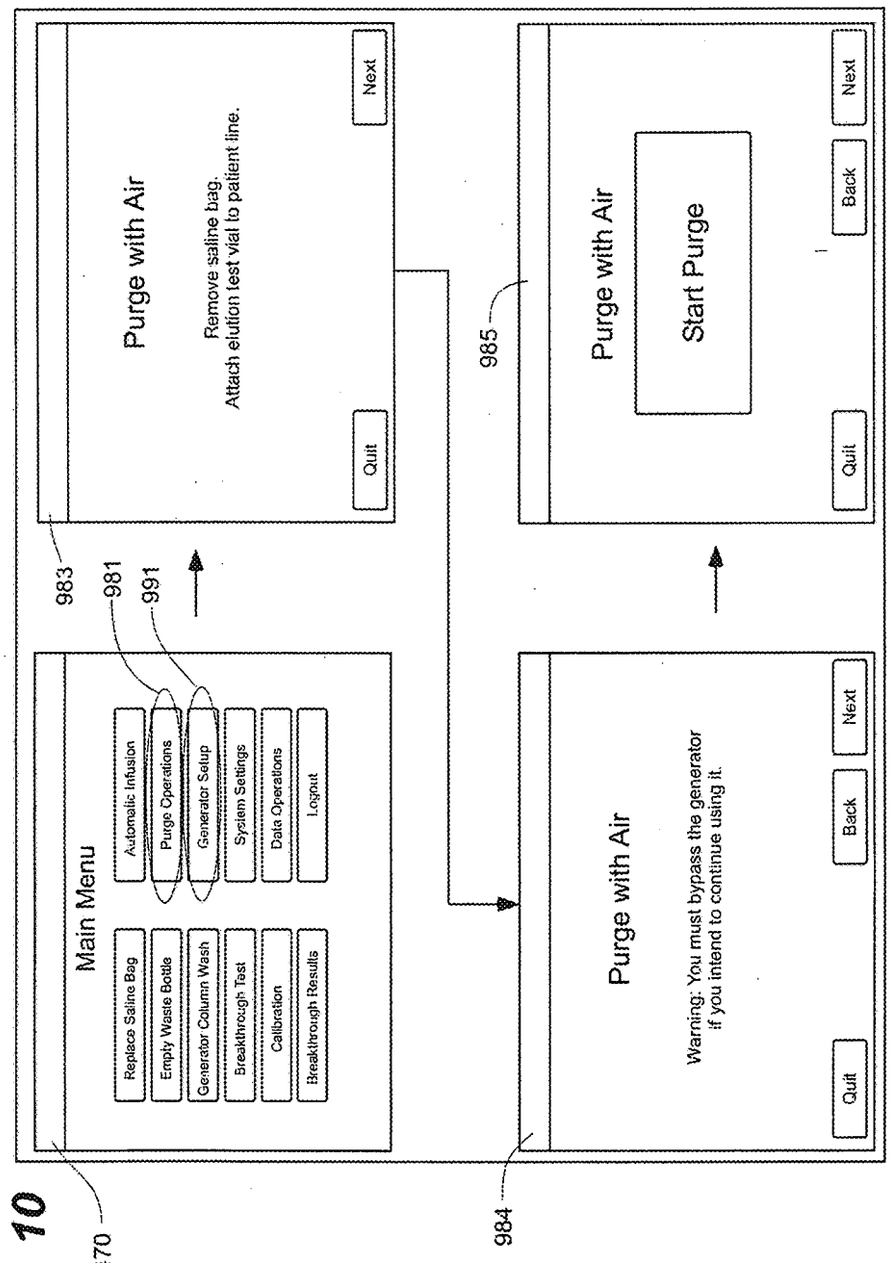


Fig. 10

Fig. 11

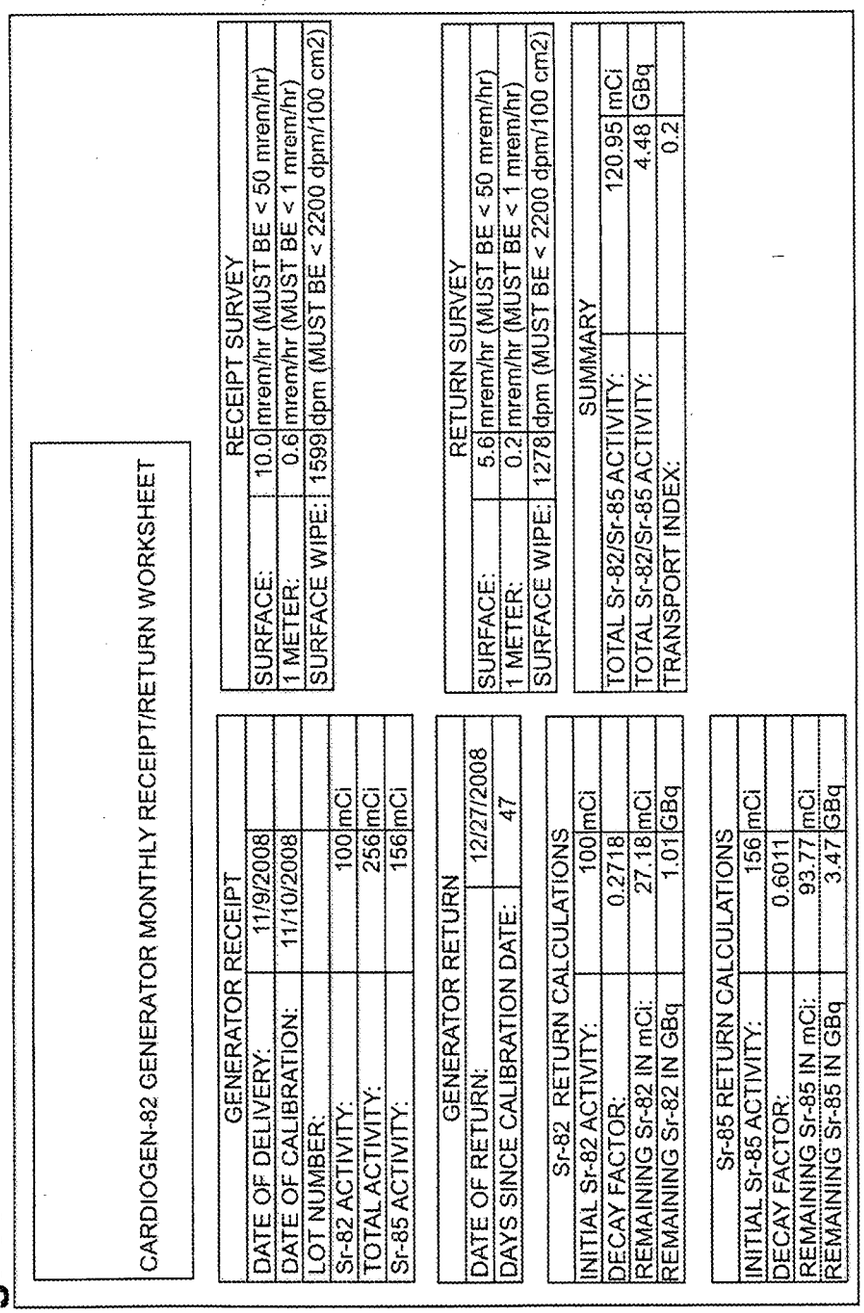
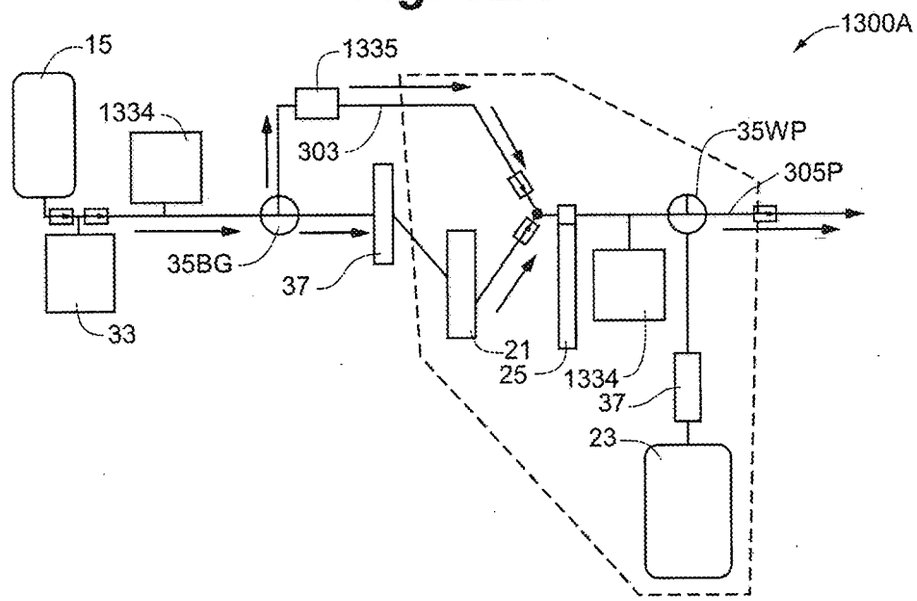


Fig. 12A



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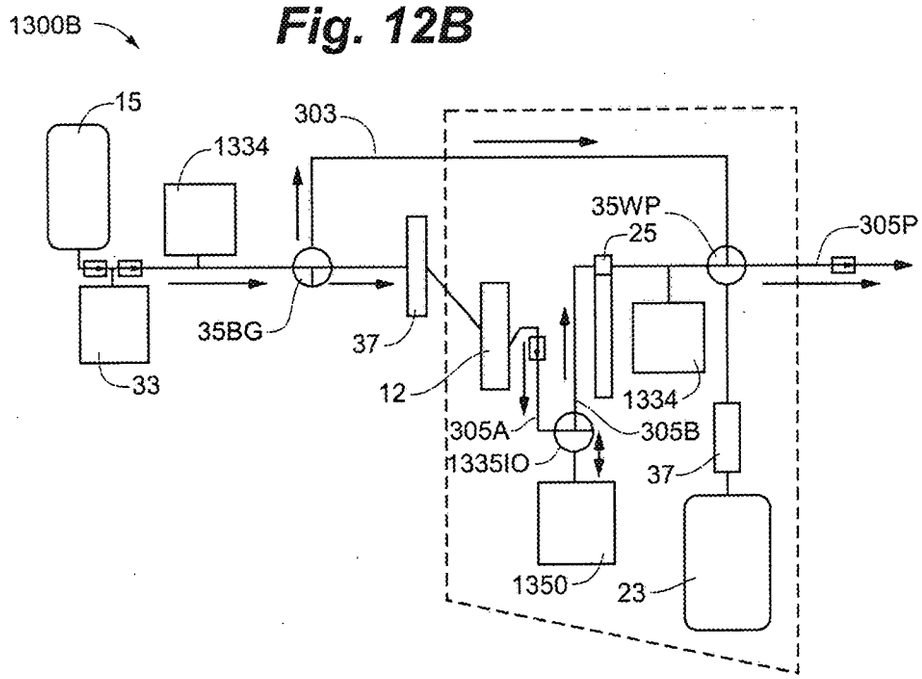
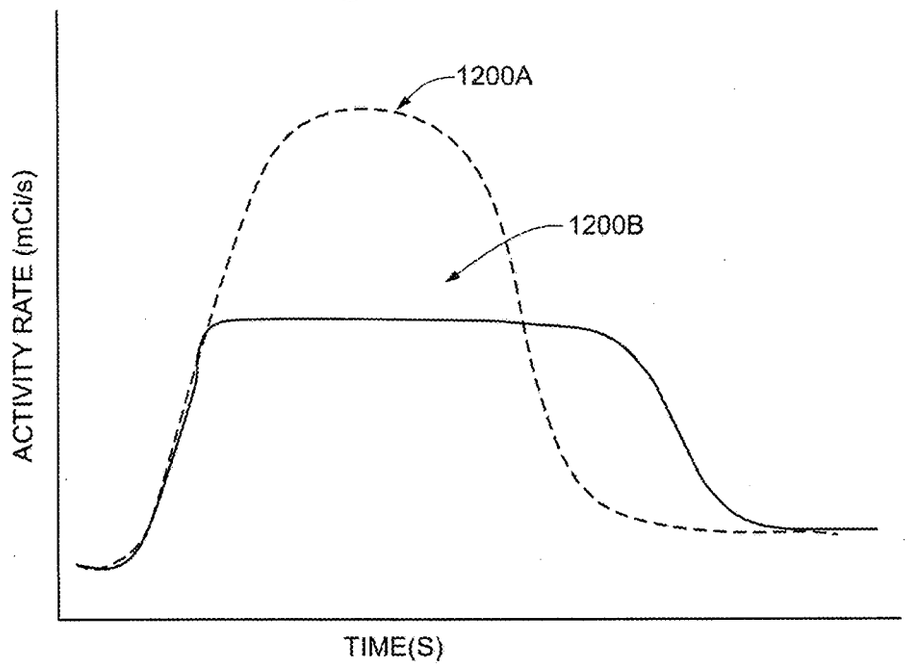


Fig. 12C



INTEGRATED STRONTIUM-RUBIDIUM RADIOISOTOPE INFUSION SYSTEMS

CROSS REFERENCE TO RELATED APPLICATIONS

This application is a continuation of U.S. patent application Ser. No. 15/389,200, filed Dec. 22, 2016, which is a continuation of U.S. patent application Ser. No. 12/808,467, filed Jun. 16, 2010, now U.S. Pat. No. 9,607,722, issued Mar. 28, 2017, which is a 371 National Stage of International Application No. PCT/US09/47031, filed Jun. 11, 2009, which in turn is a continuation of the following four patent applications: U.S. patent application Ser. No. 12/137,356, filed Jun. 11, 2008, now U.S. Pat. No. 8,317,674, issued Nov. 27, 2012; U.S. patent application Ser. No. 12/137,363, filed Jun. 11, 2008, now U.S. Pat. No. 7,862,534, issued Jan. 4, 2011; U.S. patent application Ser. No. 12/137,364, filed Jun. 11, 2008, now U.S. Pat. No. 9,597,053, issued Mar. 21, 2017; and U.S. patent application Ser. No. 12/137,377, filed Jun. 11, 2008, now U.S. Pat. No. 8,708,352, issued Apr. 29, 2014. The entire contents of all of these applications are incorporated herein by reference.

TECHNICAL FIELD

The present invention pertains to systems that generate and infuse radiopharmaceuticals, and, more particularly, to systems including computer-facilitated maintenance and/or operation.

BACKGROUND

Nuclear medicine employs radioactive material for therapy and diagnostic imaging. Positron emission tomography (PET) is one type of diagnostic imaging, which utilizes doses of radiopharmaceuticals, for example, generated by elution within a radioisotope generator, that are injected, or infused into a patient. The infused dose of radiopharmaceutical is absorbed by cells of a target organ, of the patient, and emits radiation, which is detected by a PET scanner, in order to generate an image of the organ. An example of a radioactive isotope, which may be used for PET, is Rubidium-82 (produced by the decay of Strontium-82); and an example of a radioisotope generator, which yields a saline solution of Rubidium-82, via elution, is the CardioGen-82® available from Bracco Diagnostics Inc. (Princeton, N.J.). A PET scanner in combination with infused doses of radiopharmaceuticals may also be employed to quantify blood flow rate, for example, through the coronary arteries of a patient.

Set up, maintenance and operational procedures for infusion systems that both generate and inject doses of radiopharmaceuticals are relatively involved in order to assure the safety and efficacy of each injected dose for the patient. Efficiency in carrying out these procedures is highly desirable for technical personnel, who work with these systems on a routine basis and would like to avoid unnecessarily prolonged exposure to radioactive radiation. Thus there is a need for new system configurations that facilitate more efficient set up, maintenance and operation.

BRIEF DESCRIPTION OF THE DRAWINGS

The following drawings are illustrative of particular embodiments of the present invention and therefore do not limit the scope of the invention. The drawings are not to scale (unless so stated) and are intended for use in conjunction with the explanations in the following detailed description. Embodiments of the present invention will hereinafter be described in conjunction with the appended drawings, wherein like numerals denote like elements.

FIG. **1**A is a first perspective view of an infusion system, according to some embodiments of the present invention.

FIG. **1**B is another perspective view of a portion of a cabinet structure of the system shown in FIG. **1**A, according to some embodiments.

FIG. **1**C is a second perspective view of the system shown in FIG. **1**A, according to some embodiments.

FIG. **1**D is a schematic of an infusion circuit, according to some embodiments of the present invention.

FIG. **1**E is a perspective view of exemplary sample vial shielding that may be employed in conjunction with the infusion system of FIG. **1**A.

FIG. **2**A is a perspective view of a shielding assembly for an infusion system, such as that shown in FIGS. **1**A-C, according to some embodiments of the present invention.

FIG. **2**B is a perspective view of a framework of the system, according to some embodiments, and FIG. **2**B-**1** is an enlarged detailed view of a component of the system, according to some embodiments.

FIG. **3**A is another perspective view of the shielding assembly shown in FIG. **2**A.

FIG. **3**B is a perspective view of the infusion circuit, shown in FIG. **1**C, configured and routed, according to some embodiments.

FIG. **3**C is a perspective view of a disposable infusion circuit subassembly, according to some embodiments.

FIG. **3**D is a frame for the subassembly shown in FIG. **3**C, according to some embodiments.

FIG. **4** is a main menu screen shot from an interface of a computer, which may be included in systems of the present invention, according to some embodiments.

FIG. **5**A is a schematic showing a first group of successive screen shots from the computer interface, according to some embodiments.

FIG. **5**B is a pair of screen shots from the computer interface, which provide indications related to eluant volume levels in a reservoir of the system, according to some embodiments.

FIG. **5**C is a schematic showing a second group of successive screen shots from the computer interface, according to some embodiments.

FIG. **6** is a schematic showing a third group of successive screen shots from the computer interface, according to some embodiments.

FIGS. **7**A-C are schematics showing a fourth group of successive screen shots from the computer interface, according to some embodiments.

FIGS. **8**A-B are schematics showing a fifth group of successive screen shots from the computer interface, according to some embodiments.

FIGS. **9**A-C are schematics showing a sixth group of successive screen shots from the computer interface, according to some embodiments.

FIG. **10** is a schematic showing a seventh group of successive screen shots from the computer interface, according to some embodiments.

FIG. **11** is an exemplary report which may be generated by the computer included in infusion systems, according to some embodiments.

FIGS. **12**A-B are schematics of alternative infusion circuits that may be employed by embodiments of the present invention.

FIG. 12C is a schematic illustrating exemplary activity profiles of injected doses of a radiopharmaceutical.

DETAILED DESCRIPTION

The following detailed description is exemplary in nature and is not intended to limit the scope, applicability, or configuration of the invention in any way. Rather, the following description provides practical illustrations for implementing exemplary embodiments. Utilizing the teaching provided herein, those skilled in the art will recognize that many of the examples have suitable alternatives that can be utilized.

FIG. **1A** is a first perspective view of an infusion system **10**, according to some embodiments of the present invention, wherein system **10** is shown supported by a cabinet structure, which includes a platform **113** (seen better in FIG. **2B**) and a shell **13**; shell **13** extends upward from a skirt **11**, that surrounds platform **113**, to surround an interior space in which a portion of infusion system **10** is contained (seen in FIG. **1C**). Shell **13** may be formed from panels of injection-molded polyurethane fitted together according to methods known to those skilled in the art. FIG. **1A** illustrates the cabinet structure of system **10** including a grip or handle **14**, which extends laterally from shell **13**, in proximity to an upper surface **131** thereof, and a post **142**, which extends upward from shell **13**, and to which a work surface, or tray **16** and a computer **17** are, preferably, attached, via an ergonomic, positionable mount. According to some embodiments, computer **17** is coupled to a controller of system **10**, which is mounted within the interior space surrounded by shell **13**; and, a monitor **172** of computer **17** not only displays indications of system operation for a user of system **10**, but also serves as a device for user input (e.g. touch screen input). However, according to alternate embodiments, another type of user input device, known to those skilled in the art, may be employed by computer **17**. Other types of user input devices may be included, for example, a keyboard, a series of control buttons or levers, a bar code reader (or other reader of encoded information), a scanner, a computer readable medium containing pertinent data, etc. The user input device may be mounted on the cabinet structure of system **10**, as shown, or may be tethered thereto; alternatively the user input device may be remote from system **10**, for example, located in a separate control room. According to some additional embodiments, another user input device, for example, in addition to a touch screen of computer **17**, may be remote from system **10** and used to start and stop infusions, as well as to monitor system operation both during quality control infusions and during patient infusions. Operation of system **10**, which is facilitated by computer **17**, will be described below, in conjunction with FIGS. **4-9C**.

FIG. **1A** further illustrates two pairs of wheels **121**, **122**, mounted to an underside of platform **113**, to make system **10** mobile; handle **14** is shown located at an elevation suitable for a person to grasp in order to maneuver system **10**, from one location to another, upon pairs of wheels **121**, **122**. According to some preferred embodiments, one or both pairs of wheels **121**, **122**, are casters, allowing for rotation in a horizontal plane (swivel), in order to provide additional flexibility for maneuvering system **10** in relatively tight spaces.

FIG. **1B** is a perspective view of a portion of system **10**, on a side **111** of the cabinet structure, which is in proximity to wheels **121**, **122**. FIG. **1B** illustrates a lever or pedal **125**, which is located for activation by a foot of the person, who grasps handle **14** to maneuver system **10**. In a neutral position, pedal **125** allows wheels **121**, **122** to rotate, and, if embodied as casters, to swivel freely. Pedal **125** may be depressed to a first position which prevents a swiveling of wheels **121**, **122**, according to those embodiments in which wheels **121**, **122** are casters, and may be further depressed to brake wheels **121**, **122** from rolling and swiveling, upon reaching a desired location. According to some embodiments, braking may be designed to slow system **10**, for example, when rolling down an incline, and, according to yet further embodiments, system **10** may include a motor to power movement thereof.

FIG. **1B** further illustrates: a rear access panel **174** of shell **13**, for example, providing access to circuit boards of the aforementioned controller contained within the interior space that is surrounded by shell **13**; an optional lock **184**, to secure panel **174**; a power jack **118**, for connecting system **10** to a power source; and a printer **117** for providing documentation of each patient infusion carried out by system **10**, and of system quality control test results. In some embodiments, system **10** may further include a power strip by which auxiliary equipment may be powered, and one or more additional electrical connectors, or ports (not shown), which are supported by platform **113** and may be integrated into shell **13**, for example, in proximity to jack **118** or printer **117**; these electrical connectors/ports allow system **10** to communicate with, other devices used for nuclear imaging procedures, for example, a PET scanner/camera, and/or for coupling to an intranet network, and/or to the internet, for example, to link up with software programs for various types of data analysis, and/or to link to computers of consulting clinicians/physicians, and/or to link into service providers and/or component suppliers data bases for enhanced maintenance and inventory management.

FIG. **1A** further illustrates upper surface **131** of shell **13** including several openings **133**, **135**, **139** formed therein. FIG. **1C** is a partially exploded perspective view of system **10**, wherein a removable access panel **132** is shown as a contoured portion of upper surface **131**, which, when exposed, by lifting away a bin **18**, that mates therewith, may be removed from another opening **137** formed in upper surface **131**. FIG. **1C** also provides a better view of another panel **134** which may be lifted away from opening **139**. According to the illustrated embodiment, openings **139** and **137** provide a user of system **10** with independent access to separate portions of infusion system **10**, which are contained within shell **13**, for example, to set up and maintain system **10**; and openings **133** and **135** provide passageways for tubing lines to pass through shell **13**. FIG. **1C** further illustrates an optional switch **102**, which in case of an emergency, may be activated to abort function of system **10**. With reference to FIGS. **1A** and **1C**, it may be appreciated that an arrangement of features formed in upper surface **131** of shell **13**, in conjunction with bin **18**, tray **16** and computer **17**, provide a relatively ergonomic and organized work area for technical personnel who operate system **10**.

Turning now to FIG. **1D**, a schematic of an infusion circuit **300**, which may be incorporated by system **10**, is shown. FIG. **1D** illustrates circuit **300** generally divided into a first part **300A**, which includes components mounted outside shell **13**, and a second part **300B**, which includes components mounted within the interior space surrounded by shell **13**. (Parts **300A** and **300B** are delineated by dotted lines in FIG. **1D**.) FIG. **1D** further illustrates second part **300B** of circuit **300** including a portion contained within a shielding assembly **200**, which is designated schematically as a dashed line. Some embodiments of shielding assembly

200 will be described in greater detail, in conjunction with FIGS. 2A-B and 3A-B, below.

According to the illustrated embodiment, circuit **300** includes: an eluant reservoir **15**, for example, a bag, bottle or other container, containing saline as the eluant, which is shown hanging from a post, or hanger **141** above upper surface **131** of shell **13** in FIG. **1**A; a syringe pump **33**, for pumping the eluant from reservoir **15**, and a pressure syringe **34** (or other device or sensor), for monitoring pumping pressure; a filter **37**, which may also serve as a bubble trap, for the pumped eluant; a radioisotope generator **21**, through which the filtered eluant is pumped to create a radioactive eluate, for example an eluate carrying Rubidium-82 that is generated by the decay of Strontium-82, via elution, within a column of generator **21**; and an activity detector **25**, for measuring the activity of the eluate discharged from generator **21**, in order to provide feedback for directing the flow of the eluate, via a divergence valve **35**WP, either to a waste bottle **23** or through a patient line **305***p*, for example, to inject a dose of the radiopharmaceutical eluate into a patient. With reference back to FIG. **1**A, patient line **305***p* is shown extending out from shell **13**, through opening **135**, to a distal end thereof, which, according to some embodiments, includes a filter. Patient line **305***p* may be coupled to another line that includes a patient injection needle (not shown). Alternatively, patient line **305***p* may be coupled to another line (not shown), which extends from a source of another active substance, for example, a stress agent; the other line is coupled to the line that includes the patient injection needle, in order to permit injection of the additional active substance.

FIG. **1**D illustrates an eluant tubing line **301** coupled to reservoir **15** and to pump **33**, and, with reference to FIGS. **1**A-B, it may be appreciated that opening **133** provides the passageway for tubing line **301** to enter the interior space surrounded by shell **13**. According to some preferred embodiments, opening **133** includes a grommet-type seal that prevents leakage of eluant, which may spill from reservoir **15**, into the interior space through opening **133**, while allowing a user to assemble tubing line **301** through opening **133**. Likewise opening **135**, which provides a passageway for patient line **305***p*, may include a grommet-type seal. According to some embodiments, shell **13** further supports holders to safely hold, for example, during transport of system **10**, portions of tubing lines that extend outward therefrom, for example, line **301** and/or line **305***p*.

FIG. **1**D further illustrates another eluant tubing line **302** coupled to pump **33** and a divergence valve **35**BG, which may either direct pumped eluant through a tubing line **304**, to generator **21**, or direct the pumped eluant through a by-pass tubing line **303**, directly to patient line **305***p*. Divergence valve **35**BG, as well as divergence valve **35**WP, which directs eluate from an eluate tubing line **305** either to a waste line **305***w* or to patient line **305***p*, may each be automatically operated by a corresponding servomotor (not shown), coupled to the controller (not shown) of system **10**, which controller receives feedback from activity detector **25**. When system **10** is operating for automatic infusion, to deliver a dose of radiopharmaceutical to a patient, for example, Rubidium-82 for diagnostic imaging, divergence valve **35**BG is initially set to direct eluant to generator **21** and divergence valve **35**WP is set to direct eluate from the generator into waste bottle **23**, until activity detector **25** detects the desired activity of the eluate, at which time the feedback from activity detector **25** causes the controller to direct the corresponding servo-motor to re-set valve **35**WP for diverting the flow of eluate into patient line **305***p*. According to some embodiments, once a prescribed volume of the eluate has passed through patient line **305***p*, the controller directs the corresponding servomotor to re-set divergence valve **35**BG for diverting the flow of eluant through by-pass line **303** and into patient line **305***p* in order to flush, or push any eluate remaining in patient line **305***p* into the patient. According to some embodiments, the controller may also direct the corresponding servomotor to re-set divergence valve **35**WP back toward waste bottle **23**, prior to the flush through by-pass line **303**, in order to prevent back flow of eluant, through line **305**, toward generator **21**. According to some preferred methods of operation, in certain situations, which will be described in greater detail below, eluant is pumped through by-pass line **303** immediately following the flow of the prescribed volume of eluate into patient line **305***p*, at a higher speed, in order to push the eluate in patient line **305**, thereby increasing a flow rate of the injection of eluate out from patient line **305***p* and into the patient. For example, once the prescribed volume of eluate has flowed into patient line **305***p*, and once divergence valve **35**BG is set to divert flow through by-pass line **303**, the speed of pump **33** may be adjusted to increase the flow rate of eluant to between approximately 70 mL/min and approximately 100 mL/min. This method for increasing the injection flow rate, is desirable, if a relatively high flow rate is desired for patient injection and a flow rate through generator **21** is limited, for example, to below approximately 70 mL/min, maximum (typical flow rate may be approximately 50 mL/min), in order to avoid an excessive back pressure created by the column of generator **21** in upstream portions of tubing circuit **300**; the excessive back pressure could damage filter **37** or otherwise impede flow through eluant tubing line **302**.

Although not shown in FIG. **1**D, a number of sensors, for example, to measure pressure and/or flow velocity, may be incorporated into circuit **300**, according to some alternate embodiments, in order to monitor for flow anomalies, for example, related to occlusions/plugs in circuit **300** and/or leaks, and/or to provide feedback for control of an activity level of infused doses of radiopharmaceutical. Suitable sensors for any of the above purposes are known to those skilled in the art. Examples of flow meters that may be incorporated into circuit **300**, include the Innova-Sonic® Model 205 Transit-Time Ultrasonic Liquid Flow Meter that employs digital signal processing (available from Sierra Instruments, Inc.) and the Flocat LA10-C differential pressure flow meter. One example of a pressure sensor that may be employed to detect infusion circuit occlusions is the PRO/Pressure-Occlusion Detector (available from INTROTEK® of Edgewood, N.Y., a subsidiary of Magnetrol of Downers Grove, Ill.), which employs pulse-type ultrasound; this sensor detects subtle changes in positive and negative air pressure and produces a corresponding passive resistive output signal, which may be routed to the system controller and/or computer **17**. One or more of this type of sensor may be incorporated into infusion circuit **300** by simply fitting the sensor around any of the tubing lines of infusion circuit **300**; in fact, the PRO/Pressure-Occlusion Detector may be a suitable alternative to pressure syringe **34** of circuit **300**. Other types of pressure sensors, for example, similar to those known in the art for blood pressure monitoring, may be employed in infusion circuit **300**.

System **10** may further include sensors to detect fluid levels in eluant reservoir **15** and waste bottle **23**. Some examples of such sensors, which also employ the aforementioned pulse-type ultrasound, are the Drip Chamber Liquid Level Sensor and the CLD/Continuous Level Detector (both

available from INTROTEK®); alternatively, for example, an HPQ-T pipe mounted, self-contained liquid sensor (available from Yamatake Sensing Control, Ltd.), or an SL-630 Non-Invasive Disposable/Reusable Level Switch (available from Cosense, Inc. of Hauppauge, N.Y.) may be employed to detect the fluid levels. Alternately or in addition, system **10** can include additional radiation and/or moisture detection sensors, which can detect leaks. With reference to FIG. **1**D, such sensors are preferably located in proximity to fittings **311**, **312**, **313**, **314** and **315** that join portions of circuit **300** to one another. Some examples of leak detection sensors include, without limitation, those in the HPQ-D leak detection sensor family, and the HPF-D040 fiberoptic leak detector (all available from Yamatake Sensing Control, Ltd.). System **10** may further include additional sensors to detect contaminants and/or air bubbles within the tubing lines of circuit; examples of such sensors include the Point-air Detection (PAD) Sensor, that employs pulse-type ultrasound for air bubble detection, and the Blood Component Detector that employs optical sensing technology to perform Colorimetry-based fluid detection of unwanted elements in the tubing lines (both available from INTROTEK®).

According to those embodiments that include any of the above sensors, the sensors are linked into the controller of system **10** and/or computer **17**, either of which may provide a signal to a user of system **10**, when a flow anomaly is detected, and/or information to the user, via monitor **172**, concerning fluid levels, pressure and/or flow through circuit **300**. Computer **17** may be pre-programmed to display, for example, on monitor **172**, a graphic of infusion circuit **300** wherein each zone of the circuit, where an anomaly has been detected, is highlighted, and/or to provide guidance, to the system user, for correcting the anomaly. It should be noted that the alternative infusion circuits illustrated in FIGS. **12**A-B, which will be described below, may also include any or all of these types of sensors.

With further reference to FIG. **1**D, it may be appreciated that shielding assembly **200** encloses those portions of circuit **300** from which radioactive radiation may emanate, with the exception of that portion of patient line **305***p*, which must extend out from shielding assembly **200** in order to be coupled to the patient for injection, or in order to be coupled to shielded sample vials, as will be described below. Thus, technical personnel, who operate system **10**, are protected from radiation by shielding assembly **200**, except at those times when an infusion is taking place, or when quality control tests require collection of eluate into sample vials. During infusions and quality control test sample collection, all technical personnel are typically in another room, or otherwise distanced from system **10**, in order to avoid exposure to radiation during the infusion, and, according to some preferred embodiments of the present invention, system **10** includes at least one means for informing technical personnel that an infusion is about to take place or is taking place. With reference back to FIGS. **1**A and **1**C, system **10** is shown including a light projector **100**, mounted on post **142**. According to the illustrated embodiment, projector **100**, projects a light signal upward, for maximum visibility, when pump **33** is pumping eluant and elution is taking place within generator **21**, or at all times when pump **33** is pumping eluant. According to some embodiments, the light signal flashes on and off when the eluate is being diverted from generator **21** into waste bottle **23**, and the light signal shines steadily when the eluate is being diverted through patient line **305***p*, or visa versa. According to other embodiments, a projector **100** shines a light having a first color, to indicate that eluate is being diverted to waste bottle **23**, and then shines a light having a second, different color, to indicate that eluate is being directed to patient line **305***p* for infusion. Light projector **100** may further project a more rapidly flashing light, for example, for approximately five seconds, once a peak bolus of radioactivity is detected in the eluate, to provide further information to technical personnel. Alternative means of informing technical personnel that an infusion is taking place may also be incorporated by system **10**, for example, including audible alarms or other types of visible or readable signals that are apparent at a distance from system **10**, including in the control room.

It should be noted that, according to alternate embodiments, system **10** includes an 'on board' dose calibrator for quality control tests, and circuit **300** is expanded to include elements for an automated collection of eluate samples for activity measurements, via the on board dose calibrator. According to a first set of these alternate embodiments, a sample collection reservoir is integrated into circuit **300**, downstream of divergence valve **35**WP and in communication with tubing line **305**P, in order to receive quality control test samples of eluate, via tubing line **305**P, and both the reservoir and the dose calibrator are located in a separate shielded well. According to a second set of these alternate embodiments, waste bottle **23** is configured to receive the quality control test samples of eluate, via tubing line **305**W, and a dose calibrator is integrated into shielding assembly **200**. Quality control procedures will be described in greater detail below, in conjunction with FIGS. **6**-**8**B.

When maintenance of system **10** requires the emptying waste bottle **23**, relatively easy access to waste bottle **23** is provided through opening **139** in top surface **131** of shell **13**. It should be noted that technical personnel are preferably trained to empty waste bottle **23** at times when the eluate, contained in waste bottle **23**, has decayed sufficiently to ensure that the radioactivity thereof has fallen below a threshold to be safe. Opening **139** is preferably located at an elevation of between approximately 2 feet and approximately 3 feet; for example, opening **139** may be at an elevation of approximately 24 inches, with respect to a lower surface of platform **113**, or at an elevation of approximately 32 inches, with respect to a ground surface upon which wheels **121**, **122** rest. According to the illustrated embodiment, opening **139** is accessed by lifting panel **134**; just within opening **139**, a shielded lid or door **223** (FIG. **2**A) may be lifted away from a compartment of shielding assembly **200** that contains waste bottle **23**. With further reference to FIG. **1**C, it may be appreciated that opening **137** provides access to other portions of circuit **300** for additional maintenance procedures, such as changing out generator **21** and/or other components of circuit **300**, as will be described below.

For those embodiments of system **10** in which automated quality control tests are performed and/or when system **10** is employed for relatively high volume operation, management of waste may become burdensome, even though access to waste bottle **23** is greatly facilitated, as described above. Thus, in order to facilitate waste management, some embodiments of system **10** may employ a separation system to separate salts, including radioactive elements, from water, for example, via evaporation or reverse osmosis. In an evaporation type system, the water component of the waste is evaporated, while in a reverse osmosis type system the water is separated from the salts, and, then, once confirmed to be non-radioactive, via a radiation detector, is piped to a drain. According to some other embodiments, circuit **300** may be configured so that the waste may be used to purge air from the tubing lines thereof and/or to perform the bypass

flush that was described above, preferably after the radioactivity of the waste drops below a critical threshold.

FIGS. 1A and 1C further illustrate a pair of relatively shallow external recesses **190**, which are formed in upper surface **131** of shell **13**, for example, in order to catch any spills from the infusion system; one of recesses **190** is shown located in proximity to post, or hanger **141**, which holds reservoir **15**, and in proximity to opening **133**, through which tubing line **301** passes. Another recess **192** is shown formed in upper surface **131**; a width and depth of recess **192** may accommodate storage of technical documentation associated with infusion system **10**, for example, a technical manual and/or maintenance records, or printouts from printer **117** (FIG. **1**B). With reference to FIG. 1C, upper surface **131** of shell **13** is shown to also include additional recesses **101**, which are each sized to hold a shielded test vial, which contains samples from infusion system **10**, for example, for breakthrough testing and/or calibration, which will be described in greater detail, below. An exemplary test vial shield is shown in FIG. **1**E. The test vial shield of FIG. 1E is preferably formed from Tungsten rather than lead, for example, to reduce exposure to lead, for improved shielding, and to reduce the weight of the shield. FIG. **1**E illustrates the test vial shield including a handle to simplify manipulation thereof, but alternative configurations of test vial shields have no handle—for these a sling, or strap, may be employed for handling.

Additional receptacles **180** are shown formed in bin **18**, on either side of a handle **182**, which facilitates removal of bin **18** away from shell **13**. Technical personnel may, thus, conveniently transport bin **18** to a storage area for a collection of supplies, for example, sharps, gloves, tubing lines, etc. . . . , into one or more receptacles **180** thereof, and/or to a waste container where separate receptacles **180** of bin **18** may be emptied of waste, such as packaging for the aforementioned supplies, for example, deposited therein during infusion procedures. According to some embodiments, one or more additional receptacles are formed in one or more disposal containers, for example, to contain sharps and/or radioactive waste (other than that contained in waste bottle **23**), which may be integrated into bin **18**, or otherwise fitted into, or attached to shell **13**, separate from bin **18**.

FIG. **2**A is a perspective view of shielding assembly **200**, according to some embodiments of the present invention. With reference to FIGS. 1C and **2**A, together, it may be appreciated that opening **137**, in upper surface **131** of shell **13**, provides access to a lid or door **221** of a sidewall **201** of shielding assembly **200**, which sidewall **201** encloses a compartment sized to contain a radioisotope generator of system **10**, for example, generator **21**, previously introduced. It should be noted that, according to alternate embodiments, the compartment enclosed by sidewall **201** is large enough to hold more than one generator, for example, to increase system operating efficiency for relatively high volume operation. In some of these alternate embodiments, tubing lines **304** and **305** are each branched for parallel flow through the multiple generators, in which case divergence valves may be employed to alternate the flow through the generators, one at a time. In others of these alternate embodiments, the multiple generators are connected in series between tubing line **304** and tubing line **305**. In addition, a reservoir for accumulating eluate may be included in circuit **300**, downstream of the generators and upstream of divergence valve **35**WP, in conjunction with a second pump, in some cases. Embodiments including multiple generators and/or an eluate reservoir and second pump can be employed to better manage an activity level of each dose, or patient injection, for example, as described below, in conjunction with FIGS. **12**A-B.

According to the embodiment illustrated in FIG. **2**A, opening **137** and door **221** are located at a lower elevation, for example, with respect to platform **113**, than are opening **139** and lid **223**, which provide access to the compartment being formed by a sidewall **203** of shielding assembly **200** to contain waste bottle **23**, as previously described. When panel **132** is separated from shell **13**, and door **221** opened, generator **21** may be lifted out from an opening **231** (FIG. **3**A) which mates with door **221** of sidewall **201**. A weight of generator **21**, which includes its own shielding, may be between approximately 23 and approximately 25 pounds, thus, according to some preferred embodiments of the present invention, the elevation of each of openings **137** and **231**, with respect to the lowermost portion of the cabinet structure, is between approximately 1 foot and approximately 2 feet, in order to facilitate an ergonomic stance for technical personnel to lift generator **21** out from the compartment. According to an exemplary embodiment, when shielding assembly **200** is contained in the cabinet structure of FIG. **1**A, openings **137** and **231** are located at an elevation of approximately 12 inches, with respect to the lower surface of platform **113**, or at an elevation of approximately 19 inches, with respect to the ground surface upon which wheels **121**, **122** rest. FIG. 1C further illustrates access panel **132** including a security lock **138**, which mates with a framework **19** of system **10**, shown in FIG. **2**B, in order to limit access to generator **21**.

FIGS. 1C and **2**A further illustrate a lid or a door **225** of another sidewall **205** (FIG. **3**A) of shielding assembly **200**, which encloses another compartment that is accessible through opening **137** of shell **13**, and which is located adjacent the compartment enclosed by sidewall **201**. Each of doors **221**, **225** are shown being attached by a corresponding hinge H, and another door **227** is shown attached to sidewall **203** by another hinge H. FIG. **2**A illustrates each of lid **223** and doors **221**, **225**, **227** including a handle **232**, **212**, **252** and **272**, respectively, for moving lid **223** and doors **221**, **225**, **227**, in order to provide access to the corresponding compartments, which can be seen in FIGS. **3**A-B. FIG. **2**A further illustrates optional thumb screws **290**, one securing lid **223** to sidewall **203** and another securing door **221** to sidewall **201**, or other means for securing the doors, which are known to those skilled in the art, may be incorporated. Each sidewall **201**, **203**, **205** and the corresponding lid/door **223**, **221**, **225**, **227** thereof may be individually cast from 3% antimony lead, or from other known shielding materials, and then assembled together according to methods known to those skilled in the art.

According to the illustrated embodiment, doors **221**, **225** are hinged to open in an upward direction, per arrows D and C, and, with reference back to FIG. 1C, a latch component **191** is provided to hold each of doors **221**, **225** in an opened position, thereby, preventing doors **221**, **225** from falling closed, which could pinch/crush fingers of technical personnel and/or tubing lines of circuit **300**, when in the midst of a maintenance procedure. FIG. **2**B is a perspective view of framework **19** of the cabinet structure of system **10**, according to some embodiments, to which latch component **191** is mounted; FIG. **2**B-1 is an enlarged detailed view of latch component **191**, according to some embodiments. FIG. **2**B illustrates latch component **191** including a first pin **193**, corresponding to door **225**, and a second pin **195**, corresponding to door **221**; each pin **193**, **195** includes a lever end **193**A, **193**B, respectively, and a holding end **193**B, **195**B, respectively. An edge of each door **221**, **225**, upon opening

of doors **221**, **225**, may push past the holding end **195**B, **193**B of the corresponding pin **195**, **193**, in a first direction, per arrow F, and then may rest against a respective side S**95** and S**93** of each end **195**B, **193**B, until the corresponding lever end **195**A, **193**A is rotated in a counter-clockwise direction, per arrow cc, thereby moving the corresponding holding end **193**B, **195**B to make way for the closing of doors **221**, **225**. Doors **221**, **225** being held by latch component **191** in an open position may be seen in FIG. **3**A.

With further reference to FIG. **2**A, according to some preferred embodiments of the present invention, an edge of door **225** overlaps door **221** to prevent door **221** from being opened, per arrow D, if door **225** is not opened, per arrow C; and an edge of door **227** overlaps an edge of door **225** to prevent door **225** from being opened if door **227** is not opened, per arrow B; and an edge of lid **223** overlaps door **227** to prevent door **227** from being opened if lid **223** is not opened, per arrow A. Thus, access to the compartment enclosed by sidewall **201** and containing generator **21** is only systematically allowed through a sequential opening of lid **223** and doors **227**, **225**, **221**, since, when generator **21** is replaced it is typically desirable to also replace those portions of circuit **300** which are shielded behind lid **223** and doors **227**, **225**. The routing of these portions of circuit **300** will be described in conjunction with FIGS. **3**A-C.

FIG. **3**A is another perspective view of shielding assembly **200**, according to some embodiments of the present invention. In FIG. **3**A, lid **223** and doors **221**, **225**, and **227** are opened to provide a view into openings **233**, **235** and **231** of sidewalls **203**, **205** and **201**, respectively, and into a passageway **207**, which is formed in sidewall **203**, opposite the compartment, which contains waste bottle **23**. Passageway **207** is shown extending vertically along sidewall **203** and having a grooved extension **213** formed in a perimeter surface of opening **233**. An optional retaining member **237**, for example, formed from an elongate strip of resilient plastic having a generally c-shape cross-section, is shown being mounted along a length of passageway **207** to hold lines **305***w* and **305***p* in place within passageway **207**. FIG. **3**A further illustrates a pair of passageways **251***b* and **251***g*, which are formed as grooves in a portion of sidewall **205**, and another pair of passageways **215***i* and **215***o*, which are formed as grooves in a portion of sidewall **201**. A routing of portions of tubing circuit **300** (FIG. **1**D) through passageways **207**, **251***b*, **251***c*, **215***i* and **215***o* is shown in FIG. **3**B.

FIG. **3**B illustrates tubing line **304** being routed through passageways **251***g* and **215***i*, eluate tubing line **305** being routed through passageway **215***o*, and both waste line **305***w* and patient line **305***p* being routed along passageway **207**. Waste line **305***w* further extends through grooved extension **213** to waste bottle **23**, and patient line **305***p* further extends outward from shielding assembly **200**, for example, to extend out through opening **135** in upper surface **131** of shell **13** (FIG. **1**A). According to the illustrated embodiment, each passageway formed in shielding assembly **200**, by being accessible along a length thereof, can facilitate a relatively easy routing of the corresponding tubing line therethrough, when the corresponding lid/door is open, and a depth of each passageway prevents pinching and/or crushing of the corresponding tubing line routed therethrough, when the corresponding lid/door is closed down thereover. With further reference to FIGS. **3**A-B, it may be appreciated that the compartment formed by sidewall **201** may have a shape matching an exterior contour of generator **21**, such that generator **21** is 'keyed' to the compartment, for example, to prevent installation of an improper generator into system **10**, and/or to facilitate the proper orientation of generator **21** within the compartment for the proper routing of tubing lines. Alternately, or in addition, according to alternate embodiments, if system **10** includes a reader of encoded information in communication with computer **17**, a unique identification and/or data associated with each generator may be provided, for example, in a bar code label or a radiofrequency identification (RFID) tag that is attached to each generator, so that the reader may transfer the information to computer **17**, when a generator is installed, in order to either enable system operation or to provide an indication to the user that an incorrect generator has been installed. Of course a user of system **10** may, alternately, manually enter information, that is provided on a generator label or marking, into computer **17**, in order to either enable system **10**, or to receive feedback from computer **17** that the incorrect generator is installed.

FIG. **3**A further illustrates sidewall **205** including a valve actuator receptacle **253**, into which divergence valve **35**WP is mounted, to be controlled by one of the servomotors (not shown) of system **10**, and an opening **325** for activity detector **25**. Activity detector **25** is mounted in a shielded well **255** that extends downward from opening **325** (shown in FIG. **3**B), and, with reference to FIG. **3**B, tubing line **305** passes over opening **325** so that detector **25** can detect an activity of the eluate, which passes therethrough. According to some embodiments, the positioning, within the compartment enclosed by sidewall **205**, of the components of the portion of infusion circuit **300** which are shown routed therein, is facilitated by providing the components mounted in a frame **39** as a disposable subassembly **390**, an embodiment of which is illustrated by FIGS. **3**C-D.

FIG. **3**C is a perspective view of subassembly **390**, and FIG. **3**D is a perspective view of frame **39**. According to the embodiment illustrated by FIG. **3**D, frame **39** is formed from mating trays **39**A, **39**B, for example, formed from a thermoformed plastic, which fit together to capture, therebetween, and hold, in fixed relation to a perimeter edge of frame **39**, divergence valve **35**WP and portions of eluant tubing line **304**, by-pass tubing line **303**, eluate tubing line **305**, waste line **305***w* and patient line **305***p*. FIG. **3**C illustrates the perimeter edge divided into a first side **391**, a second side **392**, opposite first side **391**, a third side **393**, extending between first and second sides **391**, **392**, and a fourth side **394**, opposite third side **393**. Although FIG. **3**D shows trays **39**A, **39**B individually formed for fitting together, according to alternate embodiments, mating trays of frame **39** may be parts of a continuous sheet of plastic folded over on itself.

According to the illustrated embodiment, an end **404**A, of eluant line **304**, and an end **403**, of by-pass line **303** extend from third side **393** of frame **39** to couple with divergence valve **35**BG and an upstream section of eluant tubing line **302**. FIG. **3**C further illustrates an opposite end **404**B of eluant line extending from first side **391** of frame **39**, alongside a similarly extending end **405** of eluate line **305**, and ends **406** and **407** of patient line **305***p* and waste line **305***w*, respectively, extending from second side **392** of frame **39**. Although ends **406**, **407** are shown extending upward from tray **39***a*, as they would within shielding assembly **200**, it should be appreciated that the tubing lines of circuit **300** are preferably flexible and would drop down under their own weight rather than extending upward, as shown, if not supported. Referring back to FIG. **1**D, in conjunction with FIG. **3**C, it can be seen that the aforementioned fittings are provided for coupling subassembly **390** into circuit **300**: first fitting **311** couples the section of eluant line **302** to filter **37**; second fitting **312** couples eluant line **304** to an inlet port of

generator **21**; third fitting **313**, which may incorporate a check valve, couples eluate line **305** to an outlet port of generator **21**; fourth fitting **314** couples waste line **305***w* to waste bottle **23**; and fifth fitting **315** couples patient line **305***p* to an extension thereof, which extends outside shell **13** (designated by the dotted line). Each of the fittings **311**, **312**, **313**, **314**, **315** may be of the Luer type, may be a type suitable for relatively high pressure applications, or may be any other suitable type that is known to those skilled in the art.

As previously mentioned, when generator **21** is replaced, it is typically desirable to also replace those portions of circuit **300** which are shielded behind lid **223** and doors **227**, **225**, and, in those instances wherein system **10** is moved to a new site each day, these portions may be replaced daily. Thus, according to the illustrated embodiment, these portions are conveniently held together by frame **39**, as subassembly **390**, in order to facilitate relatively speedy removal and replacement, while assuring a proper assembly orientation, via registration with features formed in sidewall **205** (FIG. **3**A), for example: registration of divergence valve **35**WP with valve actuator receptacle **253**, registration of tubing line ends **403** and **404**A with passageways **251***b* and **251***g*, respectively, registration of tubing line ends **404**B and **405** with passageways **215***i* and **215***o*, respectively, and registration of tubing line ends **406** and **407** with passageway **207**.

With further reference to FIG. **3**B, other portions of tubing circuit **300** are shown. FIG. **3**B illustrates eluant tubing line **301** extending from reservoir **15**, outside of shell **13** (FIG. **1**A), to syringe pump **33**, which is mounted to an actuating platform **433**. According to the illustrated embodiment, platform **433** is actuated by another servomotor (not shown) of system **10**, which is controlled by the controller and computer **17** of system **10**, to cause a plunger of pump **33** to move, per arrow I, so as to draw in eluant, from reservoir **15**, through tubing line **301**, and then to cause the plunger to move in the opposite direction so as to pump the eluant, through tubing line **302**, to either generator **21** or to by-pass line **303**. Although the illustrated embodiment includes syringe pump **33**, other suitable pumps, known to those skilled in the art, may be substituted for pump **33**, in order to draw eluant from reservoir **15** and to pump the eluant throughout circuit **300**. Although not shown, it should be appreciated that divergence valve **35**BG is fitted into another valve actuating receptacle mounted within shell **13** and coupled to yet another servomotor (not shown) of system **10**.

FIG. **3**B further illustrates a filter holder **317** that is mounted alongside an interior surface of shell **13** to hold filter **37** (FIG. **1**D) of tubing line **302**. Filter holder **317**, like frame **39** for subassembly **390**, may be formed from a thermoformed plastic sheet; holder **317** may have a clam-shell structure to enclose filter **37** in an interior space, yet allow tubing line **302**, on either side of filter **37**, to extend out from the interior space, in between opposing sides of the clam-shell structure. Holder **317** is shown including an appendage **307** for hanging holder **317** from a structure (not shown) inside shell **13**.

Turning now to FIGS. **4**-**9**C details concerning computer-facilitated operation of system **10** will be described, according to some embodiments of the present invention. As previously mentioned, and with reference back to FIG. **1**A, computer **17** of system **10** includes monitor **172**, which, preferably, not only displays indications of system operation to inform a user of system **10**, but is also configured as a touch screen to receive input from the user. It should be understood that computer **17** is coupled to the controller of system **10**, which may be mounted within the interior space surrounded by shell **13**. Although FIG. **1**A shows computer **17** mounted to post **142** of system **10**, for direct hardwiring to the controller of system **10**, according to some alternate embodiments, computer **17** is coupled to the controller via a flexible lead that allows computer **17** to be positioned somewhat remotely from those portions of system **10**, from which radioactive radiation may emanate; or, according to some other embodiments, computer **17** is wirelessly coupled, for example, via two-way telemetry, to the controller of system **10**, for even greater flexibility in positioning computer **17**, so that the operation of system **10** may be monitored and controlled remotely, away from radioactive radiation.

According to some preferred embodiments, computer **17** is pre-programmed to guide the user, via monitor **172**, through procedures necessary to maintain system **10**, to perform quality control tests on system **10**, and to operate system **10** for patient infusions, as well as to interact with the user, via the touch-screen capability of monitor **172**, according to preferred embodiments, in order to track volumes of eluant and eluate contained within system **10**, to track a time from completion of each elution performed by system **10**, to calculate one or more system parameters for the quality control tests, and to perform various data operations. Computer **17** may also be pre-programmed to interact with the controller of system **10** in order to keep a running tally or count of elutions per unit time, for a given generator employed by the system, and may further categorize each of the counted elutions, for example, as being generated either as a sample, for quality control testing, or as a dose, for patient injection. The elution count and categorization, along with measurements made on each sample or dose, for example, activity level, volume, flow rate, etc. . . . , may be maintained in a stored record on computer **17**. All or a portion of this stored information can be compiled in a report, to be printed locally, and/or to be electronically transferred to a remote location, for example, via an internet connection to technical support personnel, suppliers, service providers, etc. . . . , as previously described. Computer **17** may further interact with the user and/or a reader of encoded information, for example, a bar code reader or a radiofrequency identification (RFID) tag reader, to store and organize product information collected from product labels/tags, thereby facilitating inventory control, and/or confirming that the proper components, for example, of the tubing circuit, and/or accessories, and/or solutions are being used in the system.

It should be understood that screen shots shown in FIGS. **4**-**9**C are exemplary in nature and are presented to provide an outline of some methods of the present invention in which computer **17** facilitates the aforementioned procedures, without limiting the scope of the invention to any particular computer interface format. Computer **17** may also include a pre-programmed user manual, which may be viewed on monitor **172**, either independent of system operation or in conjunction with system operation, for example, via pop-up help screens. Although the English language is employed in the screen shots of FIGS. **4**-**9**C, it should be understood that, according to some embodiments, computer **17** is pre-programmed to provide guidance in multiple languages.

FIG. **4** is a screen shot of a main menu **470**, which is presented by computer **17** on monitor **172**, according to some embodiments. Main menu **470** includes a listing of each computer-facilitated operation that may be selected by the user, once the user has logged on. According to some

multi-lingual embodiments, computer **17** presents a list of languages from which the user may select, prior to presenting main menu **470**.

FIG. **5**A is a schematic showing a series of screen shots which includes a log in screen **570**. According to some embodiments, when the user touch-selects the data entry fields of screen **570** or **571**, or of any of the other screens presented herein, below, a virtual keyboard is displayed for touch-select data entry into the selected data entry field; alternately, computer **17** may be augmented with another type of device for user data entry, examples of which include, without limitation, a peripheral keyboard device, a storage medium (i.e. disk) reader, a scanner, a bar code reader (or other reader of encoded information), a hand control (i.e. mouse, joy stick, etc. . . .). Although not shown, according to some embodiments, screen **570** may further include another data entry field in which the user is required to enter a license key related to the generator employed by system **10** in order to enable operation of system **10**; the key may be time sensitive, related to generator contract terms. Of course any number of log in requirements may be employed, according to various embodiments, and may be presented on multiple sequentially appearing screens rather than on a single log in screen.

After the user enters the appropriate information into data entry fields of log in screen **570**, computer **17** presents a request for the user to confirm the volume of eluant that is within reservoir **15** (e.g. saline in saline bag), via a screen **571**, and then brings up main menu **470**. If the user determines that the volume of eluant/saline is insufficient, the user selects a menu item **573**, to replace the saline bag. If system **10** includes an encoded information reader, such as a bar code or RFID tag reader, confirmation that the selected reservoir is proper, i.e., contains the proper saline solution, may be carried out by computer **17**, prior to connecting the reservoir into circuit **300**, by processing information read from a label/tag attached to the reservoir. Alternatively, or in addition, tubing line **301** of circuit **300** may be provided with a connector which only mates with the proper type of reservoir **15**. According to some embodiments, system **10** may further include an osmolarity or charge detector, which is located just downstream of reservoir **15** and is linked to computer **17**, so that an error message may be presented on monitor **172** stating that the wrong osmolarity or charge is detected in the eluant supplied by reservoir, indicating an improper solution. One example of a charge detector that may be employed by system **10** is the SciCon™ Conductivity Sensor (available from SciLog, Inc. of Middleton, Wis.).

Once the reservoir/saline bag is successfully replaced, computer **17** prompts the user to enter a quantity of saline contained by the new saline bag, via a screen **574**. Alternately, if system **10** includes the aforementioned reader, and the saline bag includes a tag by which volume information is provided, the reader may automatically transfer the quantity information to computer **17**. Thus, computer **17** uses either the confirmed eluant/saline volume, via screen **571**, or the newly entered eluant/saline volume as a baseline from which to track depletion of reservoir volume, via activations of pump **33**, in the operation of system **10**. With reference to FIG. **5**B, during the operation of system **10**, when computer **17** detects that the eluant reservoir/saline bag has been depleted to a predetermined volume threshold, computer **17** warns the user, via a screen **577**. If the user has disregarded screen **577** and continues to deplete the saline bag, computer **17** detects when the saline bag is empty and provides indication of the same to the user, via a screen **578**. To replenish the reservoir/saline bag, the user may either refill the reservoir/bag or replace the empty reservoir/bag with a full reservoir/bag. According to some embodiments, system **10** automatically precludes any further operation of the system until the reservoir is replenished. It should be noted that, as previously mentioned, system **10** can include a fluid level sensor coupled to the eluant reservoir in order to detect when the level of saline drops below a certain level.

In addition to tracking the volume of eluant in reservoir **15**, computer **17** also tracks a volume of the eluate which is discharged from generator **21** into waste bottle **23**. With reference to FIG. **5**C, an item **583** is provided in main menu **470**, to be selected by the user when the user empties waste bottle **23**. When the user selects item **583**, computer **17** presents a screen **584**, by which the user may effectively command computer **17** to set a waste bottle level indicator to zero, once the user has emptied waste bottle **23**. Typically, the user, when powering up system **10** for operation, each day, will either empty waste bottle **23**, or confirm that waste bottle **23** was emptied at the end of operation the previous day, and utilize screen **584** to set the waste bottle level indicator to zero. Thus, computer **17**, can track the filling of waste bottle **23** via monitoring of the operation of pump **33** and divergence valve **35**WP, and provide an indication to the user when waste bottle **23** needs to be emptied, for example, via presentation of screen **584**, in order to warn the user that, unless emptied, the waste bottle will overflow. According to some embodiments, system **10** automatically precludes any further operation of the system until the waste bottle is emptied. According to some alternative embodiments, a fluid level sensor may be coupled to waste bottle **23**, for example, as mentioned above in conjunction with FIG. **1**D, in order to automatically detect when waste bottle **23** is filled to a predetermined level and to provide, via computer **17**, an indication to the user that waste bottle **23** needs to be emptied and/or to automatically preclude operation of system **10** until the waste bottle is emptied.

In addition to the above maintenance steps related to eluant and eluate volumes of system **10**, the user of system **10** will typically perform quality control tests each day, prior to any patient infusions. With reference to FIG. **6**, according to preferred methods, prior to performing the quality control tests (outlined in conjunction with FIGS. **7**A-C and **8**A-B), the user may select an item **675** from main menu **470**, in order to direct system **10** to wash the column of generator **21**. During the generator column wash, which is performed by pumping a predetermined volume of eluant, for example, approximately 50 milliliters, through generator **21** and into waste bottle **23**, computer **17** provides an indication, via a screen **676**, that the wash is in progress. Also, during the generator column wash, the system may provide a signal to indicate that eluate it being diverted to waste bottle **23**, for example, light projector **100** (FIG. **1**C) may project a flashing light signal, as previously described.

FIG. **6** further illustrates a screen **677**, which is presented by computer **17** upon completion of the column wash, and which provides an indication of a time lapse since the completion of the wash, in terms of a time countdown, until a subsequent elution process may be effectively carried out. While screen **677** is displayed, system **10** may be refilling, from reservoir **15**, pump **33**, which has a capacity of approximately 55 milliliters, according to some embodiments. According to some preferred embodiments of the present invention, computer **17** starts a timer once any elution process is completed and informs the user of the time lapse, either in terms of the time countdown (screen **677**), or in terms of a time from completion of the elution, for

example, as will be described in conjunction with FIG. **7**B. According to an exemplary embodiment, wherein generator **21** is the CardioGen-82® that yields a saline solution of Rubidium-82, produced by the decay of Strontium-82, via the elution, a time required between two effective elution processes is approximately 10 minutes.

Once the appropriate amount of time has lapsed, after the elution process of generator column wash, a first quality control test may be performed. With reference to FIG. **7**A, the user may select, from main menu **470**, an item **773**A, which directs computer **17** to begin a sequence for breakthrough testing. According to some embodiments, in conjunction with the selection of item **773**A, the user attaches a needle to an end of patient line **305***p* and inserts the needle into to a test vial, for the collection of an eluate sample therefrom, and, according to FIG. **7**A, computer **17** presents a screen **774**, which instructs the user to insert the test vial into a vial shield, which may be held in recess **101** of shell **13** (FIG. **1**C).

FIG. **7**A further illustrates a subsequent screen **775**, by which computer **17** receives input, from the user, for system **10** to start the breakthrough elution, followed by a screen **776**, which provides both an indication that the elution is in progress and an option for the user to abort the elution. As previously described, the system may provide a signal to indicate that elution is in progress, for example, light projector **100** (FIG. **1**C) may project a flashing light signal during that portion of the elution process when eluate is diverted from generator **21** through waste line **305***w* and into waste bottle **23**, and then a steady light signal during that portion of the elution process when the eluate is diverted from generator **21** through patient line **305***p* and into the test vial, for example, once activity detector **25** detects a dose rate of approximately 1.0 mCi/sec in the eluate discharged from generator **21**. Another type of light signal, for example, the more rapidly flashing light, as previously described, may be projected when a peak bolus of radioactivity is detected in the eluate.

Upon completion of the elution process for breakthrough testing, computer **17** presents a screen **777**, shown in FIG. **7**B, which, like screen **677**, provides an indication of a time lapse since the completion of the elution, but now in terms of a time since completion of the breakthrough elution process. When the user transfers the vial containing the sample of eluate into a dose calibrator, to measure the activity of the sample, the user may make a note of the time lapse indicated on screen **777**. With further reference to FIG. **7**B, once the user has received the activity measure from the dose calibrator, the user proceeds to a screen **778**, which includes data entry fields for the activity measure and the time between that at which the dose calibrator measured the activity of the sample and that at which the elution was completed. The user may enter the data via the touch-screen interface of monitor **172**, or via any of the other aforementioned devices for user data entry. According to some alternate embodiments, computer **17** may receive the data, electronically, from the dose calibrator, either via wireless communication or a cable connection.

After the data is entered by the user, computer **17** presents screen **779**, from which the user moves back to main menu **470** to perform a system calibration, for example, as will be described in conjunction with FIGS. **8**A-B, although the breakthrough testing is not completed. With reference back to FIG. **7**A, an item **773**B is shown in main menu **470**; item **773**B may only be effectively selected following the completion of steps for item **773**A, so as to perform a second stage of breakthrough testing. In the second stage, the breakthrough of the sample of eluate collected in the test vial for the breakthrough testing is measured, at a time of approximately 60 minutes from the completion of the elution that produced the sample. With reference to FIG. **7**C, after the user has selected item **773**B from main menu **470**, in order to direct computer **17** to provide breakthrough test results, a screen **781** is displayed. Screen **781** includes, for reference, the values previously entered by the user in screen **778**, along with another pair of data entry fields into which the user is instructed to enter the breakthrough reading of the sample at 60 minutes and the background radiation reading, respectively. After the user enters this remaining information, as described above, computer **17** may calculate and then display, on a screen **782**, the breakthrough test results. According to the illustrated embodiment, computer **17** also displays on screen **782** pre-programmed allowable limits for the results, so that the user may verify that the breakthrough test results are in compliance with acceptable limits, before moving on to a patient infusion. According to some embodiments, system **10** will not allow an infusion if the results exceed the acceptable limits, and may present a screen explaining that the results are outside the acceptable limits; the screen may further direct the user to contact the generator supplier, for example, to order a replacement generator.

With reference to FIG. **8**A, during the aforementioned 60 minute time period, while waiting to complete the breakthrough testing, the user may perform calibration by selecting item **873** from main menu **470**. Upon selection of item **873**, computer **17** presents a screen **874**, which instructs the user to insert a new test vial into an elution vial shield. In addition to placing the vial in the shield, the user, preferably, replaces patient line **305***p* with a new patient line, and then attaches a needle to the end of the new patient line for insertion into the test vial, in order to collect an eluate sample therefrom. After performing these steps, the user may move to screen **875**, wherein a plurality of data entry fields are presented; all or some of the fields may be filled in with pre-programmed default parameters, which the user has an option to change, if necessary. Once the user confirms entry of desired parameters for the calibration, the user may enter a command, via interaction with a subsequent screen **876**, to start the calibration elution.

With reference to FIG. **8**B, after computer **17** starts the elution process, a screen **87** informs the user that the calibration elution is in progress and provides an option to abort the elution. As previously described, the system may provide an indication that elution is in progress, for example, light projector **100** (FIG. **1**C) may project a flashing light signal during that portion of the elution process when eluate is diverted from generator **21** through waste line **305***w* and into waste bottle **23**, and then a steady light signal during that portion of the elution process when activity detector **25** has detected that a prescribed dose rate threshold is reached, for example, 1.0 mCi/sec, and the eluate is being diverted from generator **21**, through the new patient line, and into the test vial. Another type of light signal, for example, the more rapidly flashing light, as previously described, may be projected when a peak bolus of radioactivity is detected in the eluate. Upon completion of the elution process for calibration, computer **17** presents a screen **878**, which provides an indication of a time lapse since the completion of the elution, in terms of a time since completion of the calibration elution process. When the user transfers the vial containing the sample of eluate into the dose calibrator, to measure the activity of the sample, the user may make a note of the time lapse indicated on screen **878**. With further reference to FIG. **8**B, once the user has received the activity

measure from the dose calibrator, the user proceeds to a screen **879**, which includes data entry fields for the activity measure and the time, with respect to the completion of elution, at which the dose calibrator measured the activity of the sample. Once the data is input by the user, as described above, the computer calculates a calibration coefficient, or ratio, and presents the ratio on a screen **880**. According to FIG. **8**B, screen **880** further provides an indication of a desirable range for the calibration ratio and presents an option for the user to reject the calculated ratio, in which case, the user may instruct computer **17** to recalculate the ratio.

As previously mentioned, some alternate embodiments of the present invention include an on board dose calibrator so that the entire sequence of sample collection and calculation steps, which are described above, in conjunction with FIGS. **6**-**8**B, for the quality control procedures, may be automated. This automated alternative preferably includes screen shots, similar to some of those described above, which provide a user of the system with information at various stages over the course of the automated procedure and that provide the user with opportunities to modify, override and/or abort one or more steps in the procedure. Regardless of the embodiment (i.e. whether system **10** employs an on board dose calibrator or not), computer **17** may further collect all quality control test parameters and results into a stored record and/or compile a report including all or some of the parameters and results for local print out and/or electronic transfer to a remote location.

With reference to FIG. **9**A, upon completion of the above-described quality control tests, the user may select an item **971**, from main menu **470**, in order to direct system **10** to begin a procedure for the generation and automatic infusion of a radiopharmaceutical into a patient. As previously described, system **10** infuses the patient with the radiopharmaceutical so that nuclear diagnostic imaging equipment, for example, a PET scanner, can create images of an organ of the patient, which absorbs the radiopharmaceutical, via detection of radioactive radiation therefrom. According to FIG. **9**A, upon selection of item **971**, computer **17** presents a screen **972** which includes a data entry field for a patient identification number. This identification number that is entered by the user is retained by computer **17**, in conjunction with the pertinent system parameters associated with the patient's infusion. After the user enters the patient identification number, computer **17** directs, per a screen **973**, the user to attach a new patient line and to purge the patient line of air. A subsequent screen **974** presented by computer **17** includes data entry fields by which the user may establish parameters for the automatic infusion; all or some of the fields may be filled in with pre-programmed default parameters, which the user has an option to change, if necessary.

With reference to FIG. **9**B, if pump **33** does not contain enough eluant/saline for the patient infusion, computer **17** will present a warning, via a screen **901**, which includes an option for the user to direct the refilling of pump **33**, via a subsequent screen **902**. Once pump **33** has been filled, computer **17** presents an indication to the user, via a screen **903**. According to some embodiments, if the user does not re-fill pump **33**, yet attempts to proceed with an infusion, system **10** will preclude the infusion and present another screen, that communicates to the user that no infusion is possible, if the pump is not refilled, and asking the user to refill the pump, as in screen **901**. When pump **33** contains a sufficient volume of eluant for the patient infusion, computer **17** presents a screen **975**, which is shown in FIG. **9**C, and allows the user to enter a command for system **10** to start the patient infusion. During the infusion, computer **17** provides the user with an indication that the infusion is in process and with an option for the user to abort the infusion, via a screen **976**. As previously described, the system may provide an indication that an elution is in progress, for example, light projector **100** (FIG. **1**C) may project a flashing light signal during that portion of the elution process when eluate is diverted from generator **21** through waste line **305***w* and into waste bottle **23**, and then a steady light signal during that portion of the elution process when activity detector **25** has detected that a prescribed dose rate threshold is reached, for example, 1.0 mCi/sec, and the eluate is being diverted from generator **21**, through the new patient line for infusion into the patient. Another type of light signal, for example, the more rapidly flashing light, previously described, may be projected when a peak bolus of radioactivity is detected in the eluate. At the completion of the infusion, a screen **977** is displayed by computer **17** to inform the user of the completion of the infusion and a time since the completion. Computer **17** also displays a summary of the infusion, per screen **978**.

With further reference to FIG. **9**C, screen **976** shows an exemplary activity profile (activity—mCi/sec, on y-axis, versus time—sec, on x-axis) for the infusion/injected dose (designated between the two vertical lines). Those skilled in the art will appreciate that the shape of this profile depends upon the infusion flow rate, for a given volume of the dose, which flow rate is controlled, for example, by the speed at which pump **33** drives flow through the patient line, and upon the amount of Strontium-82 remaining in the generator. In the absence of flow rate control, activity profiles may change over the life of the generator. Furthermore, the peak bolus of radioactivity, particularly for injected doses from a relatively new generator, may exceed a saturation level of the imaging equipment, i.e. PET scanner. According to some preferred methods of the present invention, in order to maintain relatively consistent, and desirable/effective, activity profiles for patient injections, over the life of the generator, the operating speed of pump **33** may be varied (both over the course of a single injection and from injection to injection), according to feedback from activity detector **25**. Such a method may be implemented via incorporation of another quality control test in which pump **33** is operated to drive flow through the generator at a constant rate, in order to collect, into computer, a plurality of activity measurements from activity detector **25**; the plurality of measurements comprise a characteristic, or baseline activity profile from which the computer **17** may calculate an appropriate flow rate profile to control a speed of pump **33**, in order to achieve the desirable/effective activity profile. In general, at the start of generator life, when Strontium-82 is plentiful, the pump is controlled to drive infusion flow at relatively lower rates, and, then, toward the end of generator life, when much of the Strontium-82 has been depleted, the pump is controlled to drive infusion flow at relatively higher rates. As was described above, in conjunction with FIG. **1**D, if a desired infusion/injection flow rate is relatively high, that is, high enough to create too much back pressure, via flow through the column of generator **21**, by-pass line **303** may be employed by adjusting divergence valve **35**BG to divert a flow of eluant therethrough after a sufficient volume has been pumped through generator at a lower flow rate. According to this method, once a dose of eluate, from generator **21**, has flowed into patient line **305***p*, divergence valve **35**BG is set to divert the flow of eluant through by-pass line **303**, and then pump speed is increased to pump eluant at a higher flow

rate in order to push the dose out from patient line **305***p*, for injection at the higher flow rate.

Consistency of activity profiles among injected doses can greatly facilitate the use of PET scanning for the quantification of flow, for example, in coronary perfusion studies. Alternative infusion circuit configurations, operable according to alternative methods, to achieve consistency of activity profiles among injected doses, as well as a more uniform level of radioactivity across each individual dose, will be described below, in conjunction with FIGS. **12**A-C.

Printer **117** (FIG. **1**B) may be activated to print out a hard copy of the infusion summary, on which the patient identification number and pertinent infusion and system parameters are also printed, for reference. Alternatively, or in addition, according to some embodiments, the summary may be downloaded onto a computer readable storage device to be electronically transferred to one or more remote computers and/or the summary may be automatically transferred to the one or more remote computers, via wireless communication or a cable connection, for example, over an intranet network and/or the internet. In order to protect private patient information, the files may be encrypted for transmission over the internet. The one or more remote computers may be included, for example, in a hospital information system, and/or a billing system, and/or in a medical imaging system. Infusion parameters, for example, corresponding to the activity profile, may also be collected and electronically transferred for analysis in conjunction with captured images, for example, in order to quantify coronary flow, via a software package that is loaded into a system that includes the PET scanner.

With reference back to FIG. **9**A the user may select an item **995**, from main menu **470**, in order have system **10** perform data operations, such as, archiving a data base of patient infusion information and quality control test results, transmitting patient infusion summary records to USB mass storage devices, and various types of data filtering, for example, according to date ranges and/or patient identification numbers, for example, to search for a particular set of data and/or to compile a summary report of related sets of data. Additionally, certain information, which is collected by computer **17** over the course of system operation, and which defines system operation, may be transmitted to a local or remote computerized inventory system and/or to computers of technical support personnel, maintenance/service providers and/or suppliers of infusion circuit elements/components, thereby facilitating more efficient system operation and maintenance.

Turning now to FIG. **10**, an item **981** for computer-facilitated purging of the tubing lines of system **10** is shown included in main menu **470**. When a user selects item **981**, computer **17** guides the user to select either an air purge or a saline purge. The direction provided by computer **17** is not explicitly laid out herein, for a saline purge, as procedures for saline purging should be readily apparent to those skilled in the art, with reference to the schematic of infusion circuit **300** shown in FIG. **1**D. A saline purge of circuit **300** is desired to assure that all the air is removed from circuit **300** when a new generator and/or a new complete or partial tubing set is installed. An air purge of the tubing lines of circuit **300** may be performed after removing reservoir **15**, by-passing generator **21**, by connecting tubing line **304** to tubing line **305**, and coupling patient line **305***p* to a vial, for example, as is directed by the computer interface, in screens **983** and **984** shown in FIG. **10**. The air purge is desirable for blowing out the tubing lines, thereby removing all remaining eluant and eluate, prior to installing a new generator and/or prior to transporting system **10** from one site to another. If generator **21** is not depleted and will be used in system **10** at the new site, it is important to by-pass the generator prior to purging the tubing lines of circuit **300** with air, so that air is not blown across the generator, since air through generator **21** may compromise both the function and the aseptic nature of generator **21**.

According to preferred embodiments, once the user has followed the instructions presented in screens **983** and **984** and selects to start the air purge, for example, via screen **985**, computer **17** directs the controller of system **10** to carry out a complete air purge, in which pump **33** and divergence valves **35**BG and **35**WP are automatically controlled. The automated air purge preferably includes the following steps, which may be best understood with reference to tubing circuit **300** in FIG. **1**D: pumping any remaining volume of eluant left in pump **33**, through lines **302**, **304**, **305** and **305***w*, to waste bottle **23**; refilling pump **33** with air and pumping the air through lines **302**, **304**, **305** and **305***w*, into waste bottle **23** (lines **304** and **305** have been previously connected directly to one another, in order to by-pass generator **21**; if generator **21** is depleted and will be replaced with a new generator, pumping air through generator **21** may be acceptable); refilling pump **33** with air and then pumping a portion of the air through lines **302**, **304**, **305** and **305***p*, into the vial, and then a remaining portion of the air through lines **302**, **304**, **303** and **305***p*, into the vial. With reference to FIG. **1**D and the previous description of divergence valves **35**BG, **35**WP, it should be understood how divergence valves **35**BG, **35**WP are automatically controlled to carry out the above steps.

The purge operations, which are facilitated by selecting item **981** from main menu **470**, may also be accessed via the selection of an item **991** for generator setup. When the user selects item **991**, computer **17** may present an option for guidance in removing an old, depleted, generator and a set of tubing lines, prior to installing the new generator, or an option to just be guided in the installation of the new generator. According to some embodiments, computer **17** is pre-programmed to calculate an amount of activity left in a depleted generator, for example, by tracking activity of eluate over a life of the generator. At an end of the life of the generator, computer **17** may further compile this information, along with other pertinent generator information, into a report that may accompany a declaration of dangerous goods for shipping the depleted generator out for disposal or, in some cases, back to the manufacturer for investigation. An example of such a report is shown in FIG. **11**. According to those embodiments of system **10** that include an encoded information reader, computer **17** may confirm that the new generator is proper by processing information that is read from an encoded label/tag attached thereto.

FIGS. **12**A-B are schematics of alternative infusion circuits **1300**A, **1300**B that may be employed by system **10**, in place of circuit **300** (FIG. **1**D), according to some additional embodiments of the present invention. Circuits **1300**A, **1300**B are configured to allow for alternative methods of operation, to that previously described for circuit **300**, when a relatively even, or uniform level of activity over each injected dose, along with the relatively consistent level of activity from injection to injection is desired, for example, in order to facilitate a quantification of coronary artery blood flow via PET scanning. FIG. **12**C is a schematic illustrating activity profiles **1200**A, **1200**B for two injected doses, wherein profile **1200**B has a more uniform level of activity than profile **1200**A; profile **1200**B may be achieved via the operation of circuits **1300**A, **1300**B as described below.

Similar to circuit **300** (FIG. **1**D), dashed lines are shown in each of FIGS. **12**A-B to indicate a general boundary of a shielding assembly for portions of each circuit **1300**A, **1300**B. The shielding assembly for each of circuits **1300**A, **1300**B may be very similar, in most respects, to shielding assembly **200**, which is described above for system **10**, and the elements of each of circuits **1300**A, **1300**B may be arranged with respect to their respective shielding and with respect to shell **13** of system **10** in a similar manner to that described above for circuit **300**.

FIG. **12**A illustrates circuit **1300**A including, like the previously described circuit **300**, eluant reservoir **15**, pump **33**, radioisotope generator **21**, through which the filtered eluant is pumped to create the radioactive eluate, activity detector **25**, and waste bottle **23**. FIG. **12**A further illustrates two filters **37** and two pressure transducers **1334** included in circuit **1300**A. Circuit **1300**A further includes by-pass tubing line **303**, which is located downstream of divergence valve **35**BG, like in circuit **300**, and which accommodates the previously described eluant/saline flush. However, in contrast to circuit **300**, circuit **1300**A further includes a linear/proportional valve **1335** integrated into by-pass/flush line **303** so that circuit **1300**A may be operated, for example, according to pre-programmed parameters of computer **17**, in conjunction with feedback of information from activity detector **25**, for a controlled by-pass of generator **21** in order to mix eluant with eluate and, thereby, achieve a relatively uniform level of activity over each patient injection, for example, according to profile **1200**B of FIG. **12**C. It should be noted that, in addition to the controlled mixing, a flow rate of each injection may be varied, if necessary, in order to maintain a consistent activity level.

FIG. **12**B illustrates circuit **1300**B including, like the previously described circuit **300**, eluant reservoir **15**, pump **33**, radioisotope generator **21**, activity detector **25**, and waste bottle **23**, as well as the two filters **37** and two pressure transducers **1334**, as in circuit **1300**A. In contrast to circuits **300** and **1300**A, circuit **1300**B further includes an eluate reservoir **1350**, which is shown located downstream of generator **21**, in between first and second segments **305**A, **305**B of the eluate tubing line. It should be noted that a pump is combined with reservoir **1350**, for example, similar to syringe pump **33**, such that, when a divergence valve **1335**IO is set to allow fluid communication between reservoir **1350** and tubing line segment **305**A, the associated pump may be operated to draw in a volume of eluate, and, then, when divergence valve **1335**IO is set to allow fluid communication between reservoir **1350** and tubing line segment **305**B, the pump may be operated to push the volume of eluate out through tubing line segment **305**B for a patient injection, when divergence valve **35**WP is set to direct flow into patient line **305***p*. With reference back to FIGS. **3**A-B, sidewall **205** of shielding assembly **200** may be enlarged to further enclose eluate reservoir **1350**. For example, another shielded well, to house the eluate reservoir, may extend alongside well **255**, in which activity detector **25** is described as being mounted. Furthermore, sidewall **205** may include another valve actuator receptacle for divergence valve **1335**IO, similar to receptacle **253**, shown in FIG. **3**A for divergence valve **35**WP.

Collection of discrete volumes of eluate, in reservoir **1350**, may help to achieve a more uniform activity level over each injection, for example, like that of profile **1200**B in FIG. **12**C, and, according to preferred methods, feedback from activity detector **25** may be used to control the pump associated with reservoir **1350**, in order to vary injection flow rate and, thereby, maintain a relatively consistent activity level across multiple injections, and, when necessary, to vary injection flow rate over an individual injection to maintain the uniform activity level. Feedback from the pressure transducer **1334**, that is downstream from detector **25**, and/or from a flow meter (not shown) of circuit **1300**B may also be used to control the varying of injection flow rate.

With further reference to FIGS. **12**A-B, it should be noted that alternative circuits may be configured to employ a combination of the methods described for circuits **1300**A and **1300**B. Furthermore, some infusion circuits of the present invention may employ multiple generators **21**, as mentioned above, in conjunction with FIG. **2**A, to help maintain the relatively uniform level of activity over each injection and the relatively consistent level of activity from injection to injection.

In the foregoing detailed description, the invention has been described with reference to specific embodiments. However, it may be appreciated that various modifications and changes can be made without departing from the scope of the invention as set forth in the appended claims.

The invention claimed is:

1. A method of using an infusion system on-board a cart to deliver a rubidium radioactive eluate comprising:

installing a saline reservoir on the infusion system, wherein the infusion system comprises a platform and an exterior shell extending upwardly above the platform, and wherein the platform and the exterior shell collectively define an interior space of a cabinet structure;

placing the saline reservoir in fluid communication through a saline tubing line with an inlet tubing port of a strontium-rubidium radioisotope generator located in a first shielding compartment in the interior space of the cabinet structure, wherein the strontium-rubidium radioisotope generator further comprises an outlet tubing port configured to discharge the rubidium radioactive eluate, and wherein the first shielding compartment has a first opening facing vertically upwardly;

inserting a waste bottle into a second shielding compartment on-board the cart, wherein the second shielding compartment on-board the cart has a second opening facing vertically upwardly and being at a higher elevation than the first opening;

placing the waste bottle in fluid communication with the outlet tubing port of the strontium-rubidium radioisotope generator through an eluate tubing line, wherein a computer on-board the cart is configured to control the fluid communication between the waste bottle and the outlet tubing port, and wherein the computer has a touch screen display mounted on a vertical post with a top end extending above the cabinet structure;

inserting an eluate reservoir in a shielded well on-board the cart;

placing the eluate reservoir in fluid communication with the eluate tubing line, wherein the computer is further configured to control the fluid communication between the eluate reservoir and the eluate tubing line;

pumping a sample of the rubidium radioactive eluate into the eluate reservoir in the shielded well on-board the cart;

measuring a radioactivity of the sample of the rubidium radioactive eluate flowing through the eluate tubing line with a radioactivity detector on-board the cart while the sample of the rubidium radioactive eluate is flowing through the eluate tubing line;

measuring a calibration radioactivity of the sample pumped into the eluate reservoir in the shielded well on-board the cart while the eluate reservoir remains in the shielded well on-board the cart;

comparing the radioactivity of the sample of the rubidium radioactive eluate flowing through the eluate tubing line measured by the radioactivity detector on-board the cart while the sample of the rubidium radioactive eluate is flowing through the eluate tubing line with the calibration radioactivity of the sample pumped into the eluate reservoir in the shielded well on-board the cart; and

determining a strontium breakthrough test result on the sample pumped into the eluate reservoir in the shielded well on-board the cart while the eluate reservoir remains in the shielded well on-board the cart, wherein the computer of the infusion system is further configured to not allow a patient infusion if the strontium breakthrough test result is greater than or equal to an allowed limit.

2. The method of claim **1**, further comprising:

placing the eluate tubing line in fluid communication with a patient, wherein the computer is further configured to control the fluid communication between the eluate tubing line and the patient;

pumping a dose of the rubidium radioactive eluate to the patient; and

flushing the rubidium radioactive eluate remaining in at least a portion of the eluate tubing line into the patient by pumping saline from the saline reservoir to the eluate tubing line through a by-pass line that by-passes the strontium-rubidium radioisotope generator, wherein the computer is further configured to control fluid communication via the by-pass line.

3. The method of claim **2**, further comprising:

logging into the computer by entering a user login credential on the touch screen display,

transferring a patient infusion record via a USB port, and

printing a document concerning the patient infusion or a quality control test result via a printer.

4. The method of claim **2**, further comprising:

initiating a purging process through the touch screen display to purge a patient tubing line of air, wherein the patient tubing line is in fluid communication with the eluate tubing line.

5. The method of claim **2**, wherein the computer of the infusion system is further configured to present on the touch screen display a screen reminding a user to insert the eluate reservoir in the shielded well on-board the cart.

6. The method of claim **2**, wherein the computer of the infusion system is further configured to present on the touch screen display a screen for starting the patient infusion by touching a button on the touch screen display.

7. The method of claim **2**, wherein the computer of the infusion system is further configured to present on the touch screen display a screen indicating that the patient infusion is in process, wherein the screen indicating that the patient infusion is in process displays a stop button to abort the patient infusion.

8. The method of claim **2**, wherein the computer of the infusion system is further configured to:

present on the touch screen display a screen for starting the patient infusion by touching a button on the touch screen display;

present on the touch screen display a screen reminding a user to insert the eluate reservoir in the shielded well on-board the cart;

present on the touch screen display a screen indicating that the patient infusion is in process, wherein the screen indicating that the patient infusion is in process displays a stop button to abort the patient infusion; and

present on the touch screen display the strontium breakthrough test result.

9. The method of claim **8**, further comprising:

logging into the computer by entering a user login credential on the touch screen display,

entering a patient ID on the touch screen display,

entering a patient dose on the touch screen display, and

entering a flow rate on the touch screen display.

10. The method of claim **9**, wherein the computer of the infusion system is further configured to:

track a volume of saline remaining in the saline reservoir,

provide an alert via the touch screen display when the volume of saline remaining in the saline reservoir is below a predetermined volume threshold,

and

present on the touch screen display a screen reminding the user to empty the waste bottle.

11. The method of claim **10**, further comprising:

initiating a generator column wash through the touch screen display, wherein a predetermined amount of saline is pumped through the strontium-rubidium radioisotope generator and directed to the waste bottle during the generator column wash, and

initiating a purging process through the touch screen display to purge a patient tubing line of air, wherein the patient tubing line is in fluid communication with the eluate tubing line.

12. The method of claim **11**, wherein the saline tubing line and the eluate tubing line are routed through two tubing passageways formed in a perimeter surface of the first opening, wherein each of the two tubing passageways has a depth configured to prevent pinching or crushing of a corresponding tubing line routed therethrough when a first door is closed over the first opening.

13. The method of claim **12**, wherein the infusion system further comprises:

a handle configured for the user to grasp in order to move the infusion system, and

four wheels mounted to an underside of the platform of the cabinet structure.

14. The method of claim **13**, wherein the computer of the infusion system is further configured to:

project a first light signal from a light projector mounted on the top end of the vertical post extending above the cabinet structure to indicate that an elution is taking place, and

project a second light signal from the light projector to indicate that a peak bolus of radioactivity is detected.

15. The method of claim **14**, wherein

the cabinet structure has a lowermost portion and the platform has a lower surface,

the first opening is at a first elevation,

the second opening is at a second elevation,

the first elevation is between approximately 1 foot and approximately 2 feet, with respect to the lowermost portion of the cabinet structure, and

the second elevation is between approximately 2 feet and approximately 3 feet, with respect to the lower surface of the platform.

16. The method of claim **13**, wherein the infusion system further comprises a dose calibrator in the shielded well on-board the cart and in communication with the computer to determine the strontium breakthrough test result.

17. The method of claim 16, wherein
the cabinet structure has a lowermost portion and the platform has a lower surface,
the first opening is at a first elevation,
the second opening is at a second elevation,
the first elevation is between approximately 1 foot and approximately 2 feet, with respect to the lowermost portion of the cabinet structure, and
the second elevation is between approximately 2 feet and approximately 3 feet, with respect to the lower surface of the platform.

18. The method of claim 1, wherein the computer of the infusion system is further configured to present on the touch screen display the strontium breakthrough test result.

19. The method of claim 1, wherein
the cabinet structure has a lowermost portion and the platform has a lower surface,
the first opening is at a first elevation,
the second opening is at a second elevation,
the first elevation is between approximately 1 foot and approximately 2 feet, with respect to the lowermost portion of the cabinet structure, and
the second elevation is between approximately 2 feet and approximately 3 feet, with respect to the lower surface of the platform.

20. The method of claim 1, wherein the saline tubing line and the eluate tubing line are routed through two tubing passageways formed in a perimeter surface of the first opening, wherein each of the two tubing passageways has a depth configured to prevent pinching or crushing of a corresponding tubing line routed therethrough when a first door is closed over the first opening.

21. The method of claim 1, wherein the infusion system further comprises a dose calibrator in the shielded well on-board the cart, wherein the dose calibrator is in communication with the computer to determine the strontium breakthrough test result.

22. The method of claim 1, wherein the computer of the infusion system is further configured to:
track a volume of saline remaining in the saline reservoir, and
provide an alert via the touch screen display when the volume of saline remaining in the saline reservoir is below a predetermined volume threshold.

23. The method of claim 1, wherein the computer of the infusion system is further configured to:
track a volume of the rubidium radioactive eluate discharged from the strontium-rubidium radioisotope generator to the waste bottle, and
present on the touch screen display a screen reminding a user to empty the waste bottle.

24. The method of claim 1, wherein the computer of the infusion system is further configured to:
project a first light signal from a light projector mounted on the top end of the vertical post extending above the cabinet structure to indicate that an elution is taking place, and
project a second light signal from the light projector to indicate that a peak bolus of radioactivity is detected.

25. The method of claim 1, wherein the computer of the infusion system is further configured to pump saline through the strontium-rubidium radioisotope generator at a rate less than approximately 70 ml/min.

26. The method of claim 1, further comprising:
initiating a generator column wash through the touch screen display, wherein a predetermined amount of saline is pumped through the strontium-rubidium radioisotope generator and directed to the waste bottle during the generator column wash.

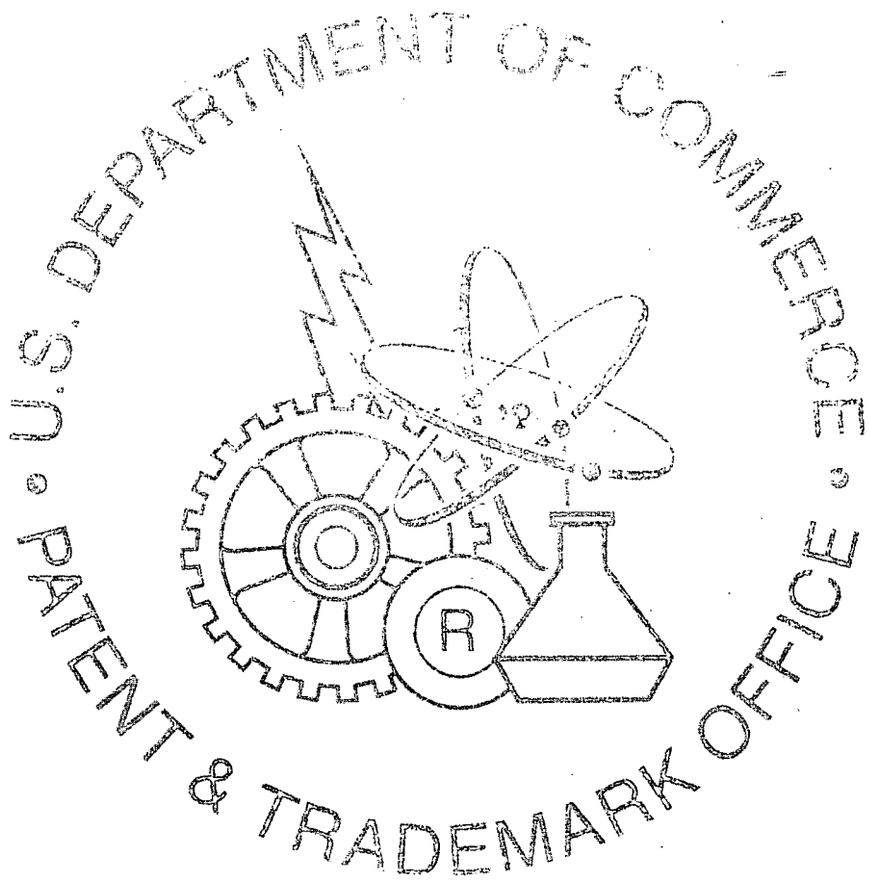
27. The method of claim 1, wherein the computer of the infusion system is further configured to track time passed from completion of pumping the sample of the rubidium radioactive eluate into the eluate reservoir to determining the strontium breakthrough test result.

28. The method of claim 1, further comprising:
entering a patient ID on the touch screen display,
entering a patient dose on the touch screen display, and
entering a flow rate on the touch screen display.

29. The method of claim 1, wherein the saline reservoir is located outside of the interior space of the cabinet structure.

30. The method of claim 1, wherein the infusion system further comprises:
a handle configured for a user to grasp in order to move the infusion system, and
four wheels mounted to an underside of the platform of the cabinet structure.

* * * * *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R GLOVER
Certifying Officer

PATENT ASSIGNMENT COVER SHEET

Electronic Version v1.1
Stylesheet Version v1.2

EPAS ID: PAT4375013

SUBMISSION TYPE:	NEW ASSIGNMENT
NATURE OF CONVEYANCE:	ASSIGNMENT

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Property Type	Number
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Total Attachments: 7
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source=56782.4.2_Executed Assignment#page7.tif

ASSIGNMENT

We, Stephen E. Hidem, residing at 4710 Juneau Lane North, Plymouth, Minnesota 55446, Aaron M. Fontaine, residing at 5663 West Bavarian Pass, Fridley, Minnesota 55432, Janet L. Gelbach, residing at 4204 Shetland Court, New Albany, Indiana 47150, Patrick M. McDonald, residing at 15395 Nicholas Street, Omaha, Nebraska 68154, Kathryn M. Hunter, residing at 1312 Judy Reagan Lane, Knoxville, Tennessee 37931, Rolf E. Swenson, residing at 35 Fieldston Road, Princeton, New Jersey 08540 and Julius P. Zodda, residing at 3 Tigers Court, Mercerville, New Jersey 08619 ("Assignor"), have made invention(s) for which United States and foreign patents and patent applications have been filed and are identified on the attached Schedule 1;

Whereas, Bracco Diagnostics Inc., a Delaware corporation having a place of business at 107 College Road East, Princeton, NJ 08540 ("Assignee"), desires to acquire the entire right, title and interest in and to the United States and foreign patents and patent applications identified on the attached Schedule 1 and in and to the inventions described and claimed therein (the "Patents"); and

NOW, THEREFORE, in exchange for good and valuable consideration, the receipt of which is hereby acknowledged, Assignor hereby assigns to Assignee, and its successors and assigns the following:

(1) The entire right, title and interest to the Patents including the inventions described or claimed therein, and to each U.S. and foreign patent application and patent from which the Patents claim priority to, in whole or in part, and to which the Patents claim priority; and

(2) The entire right, title and interest to any United States or foreign patents that may issue with respect to the inventions described or claimed in the Patents;

(3) The entire right, title and interest to any renewals, reissues, extensions, substitutions, continuations, continuations-in-part, or divisions of the Patents, and all foreign applications based thereon;

(4) The right to apply for patents in foreign countries in its own name and to claim any priority rights to which such foreign applications are entitled under international conventions, treaties or otherwise; and

(5) The right to enforce patent rights to such Patents as fully and entirely as the same would have been held and enjoyed by the Assignors if this assignment had not been made; together with all claims by Assignors for damages by reason of past infringement or for provisional rights and including the right to sue for, and collect the same for its own use and benefit, and for the use and benefit of its successors, assigns, and other legal representatives.

Assignor further agrees for himself and for his successors and assigns to execute and deliver without further consideration any further applications, assignments or other documents and to perform such other lawful acts as Assignee its successors and assigns may deem necessary to fully secure, maintain and enforce its rights, title or interest as outlined herein.

Assignor hereby authorizes and requests the Commissioner of Patents to issue to Assignee any patents that may be granted in accordance with this Assignment.

We hereby authorize attorneys associated with Customer No. 22859, of 200 South Sixth Street, Suite 4000, Minneapolis, Minnesota, 55402-1425, to insert the Application Nos. and Filing Dates of said application when known.

This Agreement may be executed in one or more counterparts, all of which shall be considered one and the same agreement. The signatures from each counterpart may be combined with a copy of the Agreement to constitute the entire Agreement.

Date: 4/28/2010

Stephen E. Hidem

Subscribed to and sworn to before me this 28 day of APRIL, 2010.

Notary Public

Notary Seal

CHARLES N THOMPSON
NOTARY PUBLIC
MINNESOTA
My Commission Expires Jan. 31, 2015

Date: 4/28/2010

Aaron M. Fontaine

Subscribed to and sworn to before me this 28 day of APRIL, 2010.

Notary Public

Notary Seal

CHARLES N THOMPSON
NOTARY PUBLIC
MINNESOTA
My Commission Expires Jan. 31, 2015

Date: 4-20-2010

Janet L. Gelbach

Witnessed by: Esther B. Paris on 4-20-10
(Signature) (Date)

Esther B. Paris
(Name)

4204 Shetland Ct. New Albany, IN 47150
(Address)

Date: _____

Patrick M. McDonald

Witnessed by: _____ on _____
(Signature) (Date)

_____
(Name)

_____
(Address)

Date: _____

Kathryn M. Hunter

Witnessed by: _____ on _____
(Signature) (Date)

_____
(Name)

_____
(Address)

Date:_____ _____
Janet L. Gelbach

Witnessed by: _____ on _____
(Signature) (Date)

_____
(Name)

_____
(Address)

Date: 16-APR-2010 Patrick M McDonald
Patrick M. McDonald

Witnessed by: Renee McDonald on 4/16/10
(Signature) (Date)

Renee McDonald
(Name)

15395 NICHOLAS ST. OMAHA, NE 68154
(Address)

Date:_____ _____
Kathryn M. Hunter

Witnessed by: _____ on _____
(Signature) (Date)

_____
(Name)

_____
(Address)

Date:_____

_____
Janet L. Gelbach

Witnessed by: _____ on _____
(Signature) (Date)

_____
(Name)

_____
(Address)

Date:_____

_____
Patrick M. McDonald

Witnessed by: _____ on _____
(Signature) (Date)

_____
(Name)

_____
(Address)

Date: April 12, 2010

Kathryn M. Hunter
Kathryn M. Hunter

Witnessed by: _____ on April 12, 2010
(Signature) (Date)

Jim Clare
(Name)

1312 Judy Reagan Lane Knoxville, TN 37931
(Address)

Date: 4/13/10

Rolf E. Swenson

Rolf E. Swenson

Witnessed by: Patricia Bussiere (Signature) on 4/13/2010 (Date)

Patricia Bussiere (Name)

10 Garfield Court, Dayton, NJ 08810 (Address)

Date: Apr. 13, 2010

Julius P. Zodda

Julius P. Zodda

Witnessed by: Patricia Bussiere (Signature) on April 13, 2010 (Date)

Patricia Bussiere (Name)

10 Garfield Court, Dayton NJ 08810 (Address)

SCHEDULE 1

US Patent Applications

Patent App. No.	Date Filed	Title	Attorney Docket No.
12/137,356	6/11/2008	SHIELDING ASSEMBLIES FOR INFUSION SYSTEMS	56782.1.5
12/137,363	6/11/2008	INFUSION SYSTEM CONFIGURATIONS	56782.1.6
12/137,364	6/11/2008	INFUSION SYSTEMS INCLUDING COMPUTER-FACILITATED MAINTENANCE AND/OR OPERATION AND METHODS OF USE	56782.1.7
12/137,377	6/11/2008	CABINET STRUCTURE CONFIGURATIONS FOR INFUSION SYSTEMS	56782.1.8
12/808,467	6/16/2010	INFUSION SYSTEMS INCLUDING COMPUTER-FACILITATED MAINTENANCE AND/OR OPERATION AND METHODS OF USE	56782.1.7.2
15/389,200	12/22/2016	INTEGRATED STRONTIUM-RUBIDIUM RADIOISOTOPE INFUSION SYSTEMS	56782.4.1
15/490,484	4/18/2017	INTEGRATED STRONTIUM-RUBIDIUM RADIOISOTOPE INFUSION SYSTEMS	56782.4.2

US Patents

Patent No.	Date Issued	Title

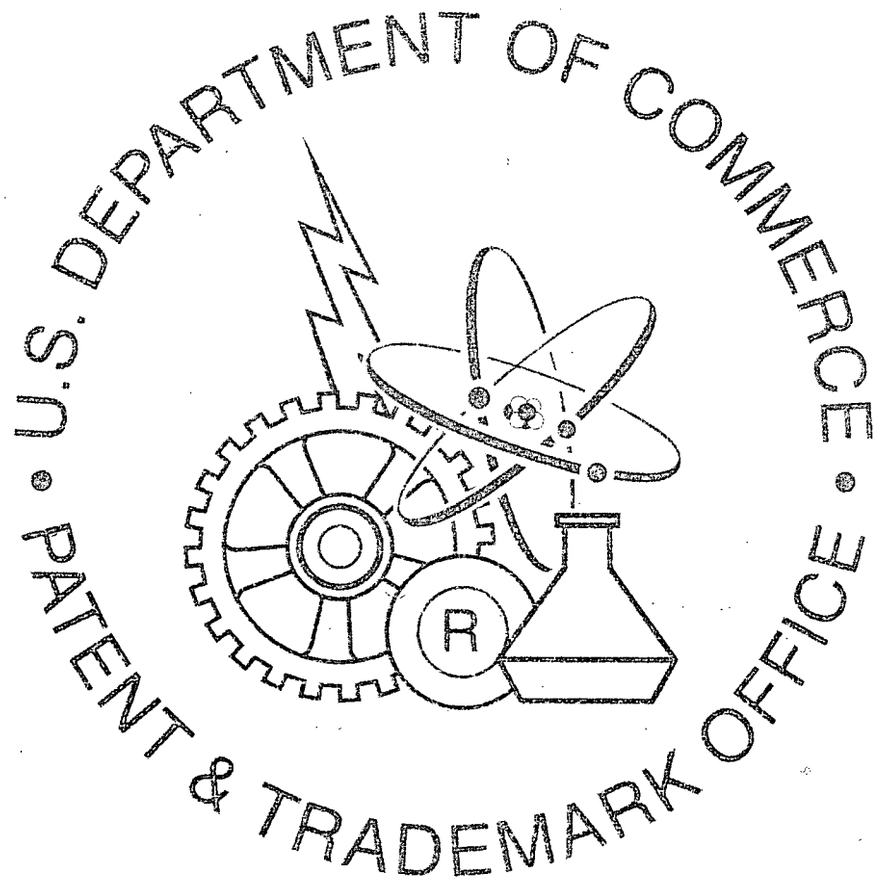
Foreign and International Patent Applications

Country	Patent App. No.	Date Filed	Title	Attorney Docket No.
WO	PCT/US09/47031	6/11/2009	INFUSION SYSTEMS INCLUDING COMPUTER-FACILITATED MAINTENANCE AND/OR OPERATION AND METHODS OF USE	56782.1.7.1

Foreign Patents

Country	Patent No.	Date of Issue	Title

4661175_1.DOC


U.S. DEPARTMENT OF COMMERCE
PATENT & TRADEMARK OFFICE
R

PTO-1683
(Rev. 7-96)

EXHIBIT 7

WESTLAW

JUBILANT DRAXIMAGE INC.

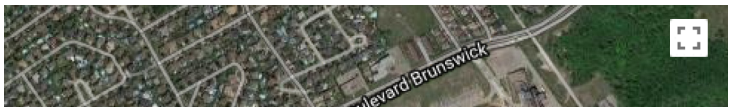
16751 RTE TRANS-CANADA
KIRKLAND, QUEBEC H9H 4J4

JUBILANT DRAXIMAGE INC.

Location Of Incorporation:	CA, Canada
Incorporation Date:	05/28/2008
Primary SIC Code:	2834
Website Address:	www.draximage.com
Officers/Directors/Contacts:	MICHAEL ROSSI, PRESIDENT & BOARD MEMBER MARCELO MORALES, PRESIDENT ARPITA CHATTERJEE, DIRECTOR SHAHIR GUINDI, DIRECTOR GURPARTAP SINGH SACHDEVA, DIRECTOR

QUICK ANALYSIS FLAGS

OFAC:	No
Global Sanctions:	No
Bankruptcy Debtor or Creditor:	No
MSB:	No
Other Listings Linked to Business Phone:	No



Disclaimers | Help

Source: Google Maps

Related Information:

Investext Results

EXHIBIT 8

WESTLAW

JUBILANT PHARMA LIMITED

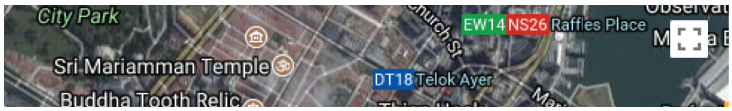
80 RAFFLES PL 26-01 UOB PLZ
048624

JUBILANT PHARMA LIMITED

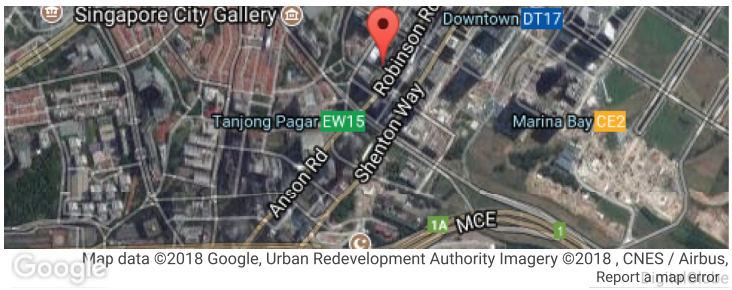
Location Of Incorporation:	SG, Singapore
NAICS Code:	325411
CIK(s):	0001526258
Officers/Directors/Contacts:	SHANKER IYER, DIRECTOR

QUICK ANALYSIS FLAGS

OFAC:	No
Global Sanctions:	No
Bankruptcy Debtor or Creditor:	No
MSB:	No
Other Listings Linked to Business	No
Phone:	

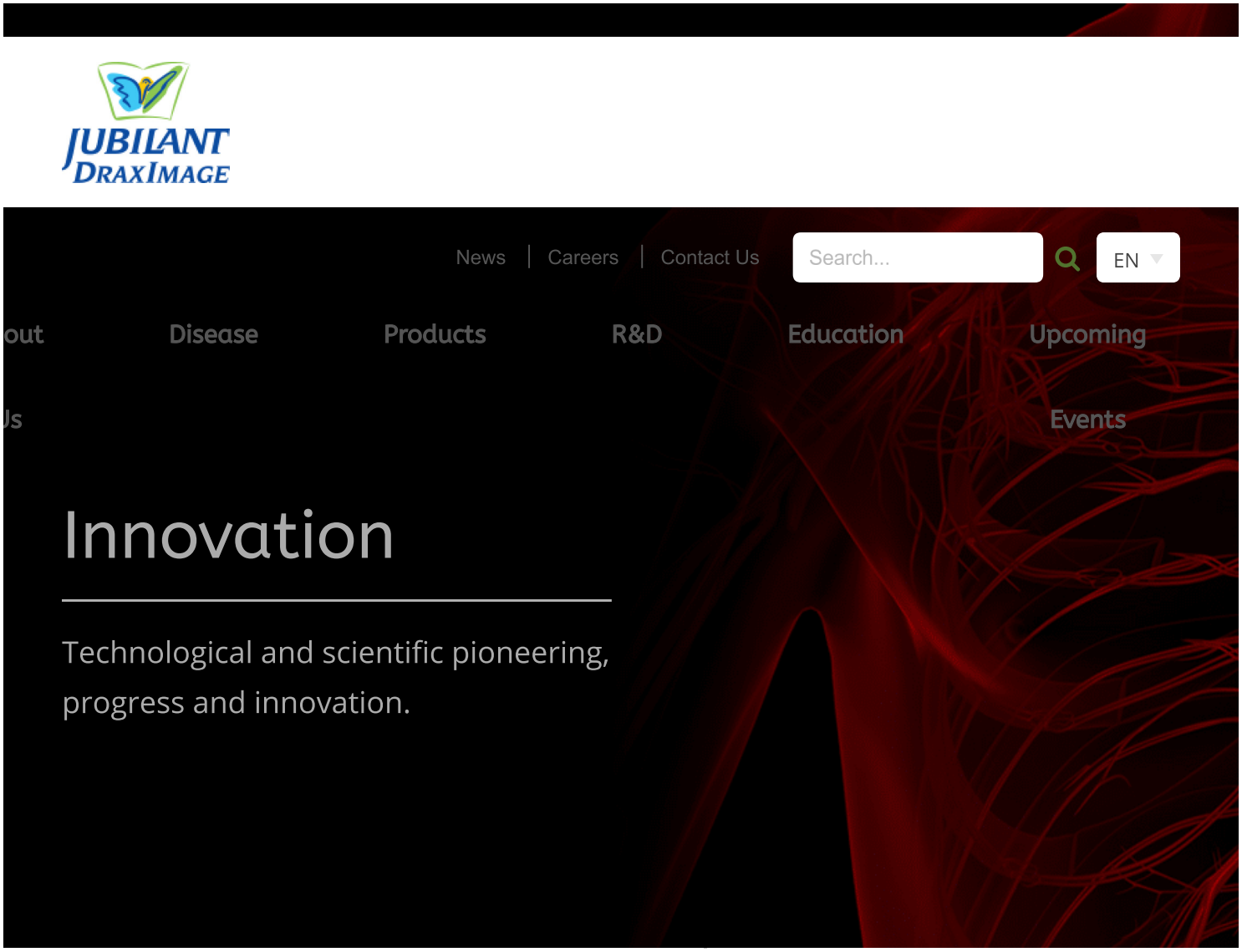


Disclaimers | Help



Source: Google Maps

EXHIBIT 9



News

JDI RECEIVES FDA APPROVAL FOR NEW PULMONARY INDICATIONS FOR DRAXIMAGE® DTPA ▸ DECEMBER 30, 2017

JDI TO ATTEND MIAMI THYROID ONCOLOGY SYMPOSIUM 2018 ▸ NOVEMBER 6, 2017

JUBILANT DRAXIMAGE RECEIVES FDA APPROVAL FOR 12-HOUR SHELF-LIFE FOR DRAXIMAGE® MAA ▸ OCTOBER 27, 2017

About Jubilant DraxImage

We develop, manufacture and commercialize radiopharmaceuticals used for the diagnosis and treatment of diseases. We serve customers and through them patients, globally with high quality and reliable products and services.

Jubilant DraxImage is a subsidiary of Jubilant Pharma.

EXHIBIT 10

JUBILANT DRAXIMAGE RECEIVES FDA APPROVAL FOR RUBY-FILL® RUBIDIUM 82 GENERATOR AND ELUTION SYSTEM

RUBY-FILL® is an approved cutting edge technology for PET myocardial perfusion imaging (MPI) under rest and pharmacological stress conditions to evaluate regional myocardial perfusion in adult patients with suspected or existing coronary artery disease.

MONTREAL, Quebec – October 3, 2016 - Jubilant DraxImage Inc., ("DraxImage") a wholly Owned Subsidiary of Jubilant Pharma Ltd, announced today that the U.S. Food and Drug Administration has approved RUBY-FILL®, an innovative technology for Positron Emission Tomography (PET) myocardial perfusion imaging (MPI). Comprised of a Rubidium-82 (Rb-82) Generator and precedent setting Elution System, RUBY-FILL® is used to produce a personalized patient dose of Rubidium Rb 82 chloride used to evaluate regional myocardial perfusion in adult patients with suspected or existing coronary artery disease (CAD) which is an important component of diagnosing CAD.

"We are proud to bring to the US market a groundbreaking, state-of-the-art technology for myocardial perfusion imaging. RUBY-FILL® expands DraxImage's nuclear medicine portfolio and is a part of our commitment to provide healthcare providers and their patients with innovative health care solutions for those with suspected or existing coronary artery disease," **comments GP Singh, CEO of Jubilant Pharma Ltd.**

"Our knowledge of the role and value of PET nuclear cardiology, specifically Rb- 82 Chloride PET in known or suspected coronary artery disease, advanced significantly as we progressed through the comprehensive and rigorous FDA review process," **said Norman LaFrance, MD, Chief Medical Officer and Senior VP, Medical & Regulatory Affairs, for Jubilant Pharma and Jubilant DraxImage**. "With its advanced weight based dose accuracy and multiple infusion options, among other product capabilities, RUBY-FILL® will enhance the way patients with known or suspected coronary artery disease are both diagnosed and managed."

Commercial launch plans for RUBY-FILL® is expected to be in the October-December 2016 quarter.

RUBY-FILL® Rubidium 82 Generator and RUBY Rubidium Elution System

The RUBY-FILL® Generator contains an accelerator produced Strontium-82, which decays to Rubidium-82. When the generator is eluted with saline it produces a sterile, non-pyrogenic solution of Rb-82 Chloride.

Due to the short half-life (75 s) of Rb-82, the use of an elution system is required for delivery of the Rb-82 Chloride into a patient for the purposes of performing Myocardial Perfusion Imaging with PET. PET imaging with Rb-82 Chloride may be performed under rest and/or stress conditions.

The Rubidium Elution System has been exclusively designed to be used with the RUBY-FILL® generator and to deliver accurate doses of Rb-82 Chloride to patients.

For more information, please contact:

Medical & Regulatory Affairs - medicalaffairs@jdi.jubl.com

or visit http://www.draximage.com/en/pipeline/cardiovascular-pet.html

Important Safety Information

WARNING: UNINTENDED STRONTIUM 82 (Sr 82) AND STRONTIUM 85 (Sr 85) RADIATION EXPOSURE

Please see full prescribing information for complete boxed warning

- Unintended radiation exposure occurs when the levels of Sr 82 or Sr 85 in the rubidium Rb 82 chloride injection exceed specific limits.
- Perform generator eluate tests:
  1) Determine Rb 82, Sr 82, Sr 85 levels in the eluate:
     - Once daily, prior to any drug administration, and
     - With additional daily tests after detection of an Alert Limit.
  2) Stop use of the generator at its Expiration Limit.

About Jubilant DraxImage

Jubilant DraxImage Inc., a wholly Owned Subsidiary of Jubilant Pharma Ltd, which is held by Jubilant Life Sciences Ltd, develops, manufactures and commercializes radiopharmaceuticals used for the diagnosis and treatment of diseases. The company is dedicated to nuclear medicine and serves customers and through them patients, globally, with high quality and reliable products and services. The company is the market leader in North America for I-131 products (diagnosis and treatment of thyroid disorder and cancer, MAA (lung perfusion imaging), DTPA (renal and brain imaging) and MDP (bone imaging), and also markets other products such as Sestamibi, Xenon and Gluceptate. The company has a strong development pipeline of new products and commitment in bringing new products to market. For more info: www.draximage.com

About Jubilant Life Sciences

Jubilant Life Sciences Limited is an integrated global Pharmaceutical and Life Sciences Company engaged in Pharmaceuticals, Life Science Ingredients and Drug Discovery Solutions. The Pharmaceuticals segment, through its wholly owned subsidiary Jubilant Pharma Ltd, is engaged in manufacture and supply of APIs, Solid Dosage Formulations, Radiopharmaceuticals, Allergy Therapy Products and Contract Manufacturing of Sterile and Non Sterile products through 6 USFDA approved facilities in India, US and Canada. The Life Science Ingredients segment is engaged in Specialty Intermediates, Nutritional Products and Life Science Chemicals through 5 manufacturing facilities in India. The Drug Discovery Solutions segment provides proprietary in-house innovation and collaborative research and partnership for out-licensing through 3 world class research centres in India and US. Jubilant Life Sciences Ltd has a team of around 6,500 multicultural people across the globe and is committed to deliver value to its customers

spread across over 100 countries. The Company is well recognized as a ‘Partner of Choice’ by leading pharmaceuticals and life sciences companies globally. For more info: www.jubl.com.

EXHIBIT 11

DIAGNOSIS & INTERVENTION

- E-Z-DISK
- E-Z-HD
- E-Z-PASTE
- E-Z-PAQUE
- Liquid E-Z-PAQUE
- Liquid POLIBAR PLUS
- VARIBAR
- SINOGRAFIN
- CYSTOGRAFIN
- Related Fluoroscopy

Associated products

NEXO [DOSE]

Contrast Enhanced Ultrasound
- LUMASON
- related Contrast Enhanced Ultrasound

Myelography
- ISOVUE-M
- Related Myelography

Products and Solutions

R & D

R&D Centers and Partnerships
- Bracco Imaging R&D objectives

- R&D Pipeline
- Clinical Development

Reimbursement

Congresses
- Past Events
- Upcoming Events

Education

Educational Portfolio
- National MDCT Symposium

- Diagnostic Industry Support
- Professional Societies
- Upcoming Events

- Careers

Press Room

Contacts

Bracco Diagnostics Inc. Launches Web Site on CardioGen-82® (Rubidium Rb 82 Generator)

Princeton, NJ , 05/28/2005

"www.CardioGen.com" to Feature Updated Information on Cardiac PET

Bracco Diagnostics Inc. announced today the launch of a new Web site with content focused on the myocardial perfusion agent CardioGen-82. CardioGen-82 is used for

cardiac PET (Positron Emission Tomography), a diagnostic procedure that detects coronary artery disease.

The new site at www.CardioGen.com features comprehensive product information, related information on PET technology, and other resources for medical professionals. Content will be regularly updated to help users stay in tune with the latest trends and technologies relative to cardiac PET.

About CardioGen-82

CardioGen-82 is the only FDA approved generator-based PET perfusion agent reimbursed for the evaluation of coronary artery disease.

As in the use of any radioactive material, care should be taken to minimize radiation exposure to the patient consistent with proper patient management and to ensure minimum radiation exposure to occupational workers. Radiopharmaceuticals should be used only by physicians who are qualified by training and experience in the safe use and handling of radionuclides and whose experience and training have been approved by the appropriate government agency authorized to license the use of radionuclides. Please see full prescribing information available with this release.

About Bracco

The Bracco Group is a world leading provider of global diagnostic imaging solutions, with net sales of about $1.25 billion. Bracco has operations in 115 countries and about 3,300 employees, around 600 of whom work in R&D. Bracco invests approximately 15% of its annual turnover in R&D and has a portfolio of 1,500 patents worldwide.

The Bracco Group is a leader in the diagnostic imaging market with an integrated product offering from a diverse roster of subsidiary companies. While Bracco is recognized internationally as a definitive market leader in its core business of contrast media, Bracco also markets key diagnostic imaging resources through the following companies: Esaote, which is one of the world's primary producers of magnetic resonance and ultrasound imaging systems; ACIST Medical Systems, a manufacturer of advanced contrast media injection systems; EBIT-AET, which creates and markets medical application software, and Singapore-based Volume Interactions, which also produces advanced medical software.

Bracco also operates a high-level international research network, with three centers (Milan, Geneva, and Princeton). These centers develop products of the latest-generation diagnostic techniques, from X-ray and computed tomography (CT) to magnetic resonance imaging (MRI) and echocontrast.

This press release may include some products' commercial brands, which are not to be used unless by media addressed to the medical community.

Please click **here** for the CardioGen-82 Package Insert.

Kirk Deeter
Bracco Diagnostics Inc. Press Office
303-838-8708

MODALITY

CT & CT Colonography

Magnetic Resonance Imaging

Injectors & Informatics

Nuclear Medicine & Radiopharmaceuticals

MODALITY

Cardiac Catheterization and Interventional Radiology

Fluoroscopy

Contrast Enhanced Ultrasound

Myelography

R&D

R&D Centers and Partnerships

R&D Pipeline

Clinical Development

CONTACTS

Local Contacts

Worldwide Contacts

Find your Rep

Find a Wholesaler

EXHIBIT 12

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use RUBY-FILL safely and effectively. See full prescribing information for RUBY-FILL.

RUBY-FILL (rubidium Rb 82 generator)
To produce rubidium Rb 82 chloride injection, for intravenous use
Initial U.S. Approval: 1989

WARNING: UNINTENDED STRONTIUM 82 (Sr 82) AND STRONTIUM 85 (Sr 85) RADIATION EXPOSURE

Please see full prescribing information for complete boxed warning

- **Unintended radiation exposure occurs when the levels of Sr 82 or Sr 85 in the rubidium Rb 82 chloride injection exceed specific limits. (5.1)**
- **Perform generator eluate tests:**
  1) Determine Rb 82, Sr 82, Sr 85 levels in the eluate:
  - **Once daily, prior to any drug administration, and**
  - **With additional daily tests after detection of an Alert Limit. (2.6)**
  2) Stop use of the generator at its Expiration Limit. (2.7)

INDICATIONS AND USAGE

RUBY-FILL is a closed system used to produce rubidium Rb 82 chloride injection for intravenous use. Rubidium Rb 82 chloride injection is a radioactive diagnostic agent indicated for Positron Emission Tomography (PET) imaging of the myocardium under rest or pharmacologic stress conditions to evaluate regional myocardial perfusion in adult patients with suspected or existing coronary artery disease. (1)

DOSAGE AND ADMINISTRATION

Use RUBY-FILL with a specific Elution System. (2.4)

- The recommended weight-based dose of rubidium Rb 82 is between 10-30 Megabecquerels (MBq)/kg [0.27-0.81 millicuries (mCi)/kg]. (2.2)
- Do not exceed a single dose of 2220 MBq (60 mCi) per rest or stress component of a procedure. (2.2)
- Administer the single dose at a rate of 15-30 mL/minute through a catheter inserted into a large peripheral vein; do not exceed an infusion volume of 60 mL. (2.2)
- Use the lowest dose necessary to obtain adequate cardiac visualization and individualize the dose depending on multiple factors, including, patient weight, imaging equipment and acquisition type used to perform the procedure. (2.2)
- Start imaging acquisition 60-90 seconds after completion of the infusion; if a longer circulation time is anticipated, wait for 120 seconds. Acquisition may be started immediately post-injection if dynamic imaging is needed. Image acquisition is typically 3-7 minutes long. (2.3)
- To obtain rest and stress images, wait 10 minutes after completion of the rest image acquisition then administer the pharmacologic stress agent in accordance with its prescribing information. After administration of the pharmacologic stress agent, infuse the second dose of Rb 82, at the time interval according to the prescribing information of the pharmacological stress agent and complete the stress image acquisition. (2.3)

DOSAGE FORMS AND STRENGTHS

RUBY-FILL consists of Sr 82 adsorbed on a hydrous stannic oxide column with an activity of 3145 – 4255 MBq (85 – 115 mCi) Sr 82 at calibration time. (3)

CONTRAINDICATIONS

None. (4)

WARNINGS AND PRECAUTIONS

- Unintended radiation exposure occurs when Sr 82 and Sr 85 levels in rubidium Rb 82 chloride injection exceed specified generator eluate limits. (5.1)
- Pharmacologic induction of cardiovascular stress: May be associated with serious adverse reactions such as myocardial infarction, arrhythmia, hypotension, bronchoconstriction, and cerebrovascular events. Perform testing only in setting where cardiac resuscitation equipment and trained staff are readily available. (5.2)

ADVERSE REACTIONS

To report SUSPECTED ADVERSE REACTIONS, contact Jubilant DRAXIMAGE Inc. at 1-888-633-5343 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

USE IN SPECIFIC POPULATIONS

- Lactation: Do not resume breastfeeding until at least one hour after completion of RUBY-FILL infusion. (8.2)

See 17 for PATIENT COUNSELING INFORMATION.

Revised: 11/2016

FULL PRESCRIBING INFORMATION: CONTENTS*

*Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

WARNING: UNINTENDED STRONTIUM 82 (Sr 82) AND STRONTIUM 85 (Sr 85) RADIATION EXPOSURE

Unintended radiation exposure occurs when the levels of Sr 82 or Sr 85 in the rubidium Rb 82 chloride injection exceed specified limits *[see Warnings and Precautions (5.1)]*.
Perform generator eluate tests:
1) The system automatically generates a record and saves the data for each generator eluate volume, including flushing and test volumes. Total cumulative eluate volumes are also recorded and saved for the life of the generator *[see Dosage and Administration (2.5)]*.
2) Determine Rb 82, Sr 82, Sr 85 in the generator eluate:
- **Once a day, prior to any drug administration, and**
- **At additional daily tests after detection of an Alert Limit. Alert Limits are:**
  - **20 L for the generator's cumulative eluate volume, or**
  - **An eluate Sr 82 level of 0.004 µCi/ mCi (kBq/MBq) Rb 82, or**
  - **An eluate Sr 85 level of 0.04 µCi/ mCi (kBq/MBq) Rb 82.**
- **Perform additional daily tests every 4 patients after detection of an alert limit *[see Dosage and Administration (2.6)]*.**

3) Stop use of a generator at any of the following Expiration Limits. Expiry Limits are:
- **30 L for the generator's cumulative eluate volume, or**
- **Expiration date of the generator (60 days post-manufacturing)**
- **An eluate Sr 82 level of 0.01 µCi /mCi (kBq/MBq) Rb 82, or**
- **An eluate Sr 85 level of 0.1 µCi /mCi (kBq/MBq) Rb 82 *[see Dosage and Administration (2.7)]*.**

1 INDICATIONS AND USAGE

RUBY-FILL is a closed system used to produce rubidium Rb 82 chloride injection for intravenous administration. Rubidium Rb 82 chloride injection is indicated for Positron Emission Tomography (PET) imaging of the myocardium under rest or pharmacologic stress conditions to evaluate regional myocardial perfusion in adult patients with suspected or existing coronary artery disease.

2 DOSAGE AND ADMINISTRATION

2.1 Radiation Safety – Drug Handling

Rubidium Rb 82 is a radioactive drug and should be handled with appropriate safety measures to minimize radiation exposure during administration *[see Warnings and Precautions (5.3)]*.

- Use waterproof gloves and effective shielding when handling rubidium Rb 82 chloride injection and the RUBY Rubidium Elution System.
- Use aseptic techniques in all drug handling.
- Visually inspect the drug for particulate matter and discoloration prior to administration whenever solution and container permit. Do not administer eluate from the generator if there is any evidence of foreign matter.

2.2 Recommended Dose and Administration Instructions

- The recommended weight-based dose of rubidium Rb 82 chloride to be administered per rest or stress component of a PET myocardial perfusion imaging (MPI) procedure is between 10-30 Megabecquerels (MBq)/kg [0.27-0.81 millicuries (mCi)/kg].
- Do not exceed a single dose of 2220 MBq (60 mCi).
- Use the lowest dose necessary to obtain adequate cardiac visualization and individualize the weight-based dose depending on multiple factors, including, patient weight, imaging equipment and acquisition type used to perform the procedure. For example, 3D imaging acquisition may require doses at the lower end of the recommended range compared to 2D imaging.
- Administer the single dose at a rate of 15 – 30 mL/minute through a catheter inserted into a large peripheral vein; do not exceed an infusion volume of 60 mL.
- Instruct patients to void as soon as a study is completed and as often as possible thereafter for at least one hour.
- The maximum available activity (delivery limit) will decrease as the generator ages *[see Dosage and Administration (2.8)]*.

2.3 Image Acquisition Guidelines

For Rest Imaging:

- Administer a single ("rest") rubidium Rb 82 chloride dose;
- Start imaging 60-90 seconds after completion of the infusion of the rest dose and acquire images for 3-7 minutes.

For Stress Imaging:

- Begin the study 10 minutes after completion of the resting dose infusion, to allow for sufficient Rb 82 decay;
- Administer a pharmacologic stress agent in accordance with its prescribing information;
- After administration of the pharmacological stress agent, administer the second dose of Rb 82 at the time interval according to the prescribing information of the pharmacological stress agent;
- Start imaging 60-90 seconds after completion of the stress rubidium Rb 82 chloride dose infusion and acquire images for 3-7 minutes.

For Both Rest and Stress Imaging:

- If a longer circulation time is anticipated (e.g., in a patient with severe left ventricular dysfunction), start imaging 120 seconds after the rest dose.
- Acquisition may be started immediately post-injection if dynamic imaging is needed.

2.4 Elution System

- Use RUBY-FILL Rubidium Rb 82 Generator only with an elution system specifically designed for use with the generator (RUBY Rubidium Elution System) and capable of accurate measurement and delivery of doses of rubidium Rb 82 chloride injection.
- The generator used with the elution system provides ± 10% accuracy for rubidium Rb 82 chloride doses between 370-2220 MBq (10-60 mCi)
- Follow instructions in the RUBY Rubidium Elution System User Manual for the set up and intravenous infusion of rubidium Rb 82 chloride injection dose.

2.5 Directions for Eluting Rubidium Rb 82 Chloride Injection

- Allow at least 10 minutes between elutions for regeneration of Rb 82.
- Elute with additive-free 0.9% Sodium Chloride Injection USP only. Additives (particularly calcium ions, to which strontium ions are chemically analogous), may cause the release of substantial amounts of Sr 82 and/or Sr 85 into the eluate regardless of the age or prior use of the generator.
- The system will automatically discard the first 75 mL eluate each day the generator is first eluted.
- The RUBY Rubidium Elution System automatically generates records and saves data of all eluate volumes (from flushing, QC testing, patient infusions), representing the cumulative volume of eluate from the generator.

2.6 Eluate Testing Protocol

- **Elute with additive-free 0.9% Sodium Chloride Injection USP only.**
- Use the ionization chamber-type dose calibrator that is integrated into the elution system (used specifically with the RUBY-FILL Rubidium Rb 82 Generator) for eluate testing.
- Perform **Mandatory Eluate Testing** (i.e. Quality Control test) to determine Rb 82, Sr 82, and Sr 85 levels:
  1. Daily – Before administering rubidium Rb 82 chloride injection to the first patient each day.
  2. Repeat every 4 patients after an **Alert Limit** has been detected.

  Alert Limits:
  - 20 L total elution volume has passed through the generator column, or
  - Sr 82 level reaches 0.004 µCi per mCi (kBq per MBq) Rb 82, or
  - Sr 85 level reaches 0.04 µCi per mCi (kBq per MBq) Rb 82.

  3. Immediately after detection of the volume alert limit (20 L).
- The elution system will automatically indicate when alert limits have been reached and require that additional tests be performed.

When the Quality Control test is performed as described in the User Manual, the system automatically performs the following eluate testing:

Rubidium Eluate Testing:

1. The dose calibrator is automatically set for Rb 82 within the Elution System.
2. The Quality Control test begins by automatically initiating a generator flush using 75 mL of 0.9% Sodium Chloride Injection USP. This eluate is by default diverted towards the waste container and is ultimately discarded.
3. After the generator flush, the system waits approximately 15.2 minutes to accomplish a complete generator recharge of 12 Rb 82 half-lives
4. The system then elutes a calibration sample (35 mL of 0.9% Sodium Chloride Injection USP at 20 mL/min). Using the dose calibrator, the system automatically quantifies the activity of Rb 82 in the calibration sample (Rb 82 decay does not need to be corrected for because of a real-time automated measurement).

Strontium Eluate Testing (Strontium Breakthrough):

1. Using the calibration sample obtained from the Rb 82 eluate testing, the system allows the sample to stand for 30 minutes to allow for the complete decay of Rb 82.
2. The system measures the activity of the sample to automatically determine the total Sr 82 and Sr 85 activity.
3. The system automatically determines the ratio (R) on the day (post calibration) of the measurement using the ratio of Sr 85/Sr 82 on the day of calibration provided on the generator label and the Sr 85/Sr 82 ratio factor from the Sr 85/Sr 82 ratio based on generator age using the following equation:

$$R = \frac{[Sr\,85]}{[Sr\,82]} \text{ on calibration date X Ratio Factor on the day (post-calibration) of measurement}$$

4. The system uses a correction factor (F) of 0.48 to compensate for the contribution of Sr 85 to the reading.

5. The system calculates the amount of Sr 82 in the sample using the following equation:

In Empirical Units (µCi):

$$Sr\,82\ (\mu Ci) = \frac{\text{dose calibration reading } (\mu Ci)}{[1 + (R)(F)]}$$

Example: dose calibrator reading (µCi) = 0.8
Sr 85/Sr 82 ratio (R) = (1.48)
correction factor (F) = 0.48

$$Sr\,82\ (\mu Ci) = \frac{0.8\ \mu Ci}{[1 + (1.48)(0.48)]} = 0.47\ \mu Ci$$

In International Units (kBq):

$$Sr\,82\ (kBq) = \frac{\text{dose calibration reading } (kBq)}{[1 + (R)(F)]}$$

Example: dose calibrator reading (kBq) = 29.6 kBq
Sr 85/Sr 82 ratio (R) = (1.48)
correction factor (F) = 0.48

$$Sr\,82\ (kBq) = \frac{29.6\ kBq}{[1 + (1.48)(0.48)]} = 17.3\ kBq$$

6. The system determines if Sr 82 in the eluate exceeds an Alert or Expiration Limit by dividing the µCi (or kBq) of Sr 82 by the mCi (or MBq) of Rb 82 at End of Elution (see below for further instructions based on the Sr 82 level)

In Empirical Units (µCi):

Example: 0.47 µCi of Sr 82; 50 mCi of Rb 82

$$\frac{0.47\ \mu Ci\ Sr\ 82}{50\ mCi\ Rb\ 82} = 0.0094\ \mu Ci\ Sr\ 82/mCi\ Rb\ 82$$

(Sr 82 is above Alert Limit of 0.004 µCi/mCi; additional daily eluate testing must be performed)

In International Units (kBq):

Example: 17.3 kBq of Sr 82; 1850 MBq of Rb 82

$$\frac{17.3\ kBq\ Sr\ 82}{1850\ MBq\ Rb\ 82} = 0.0094\ kBq\ Sr\ 82/MBq\ Rb\ 82$$

(Sr 82 is above Alert Limit of 0.004 kBq/MBq; additional daily eluate testing must be performed)

7. The system determines if Sr 85 in the eluate exceeds an Alert or Expiration Limit by multiplying the result obtained in step 6 by (R) as calculated in step 3 (above).

In Empirical Units (µCi):

Example: 0.0094 x 1.48 = 0.014 µCi Sr 85/mCi Rb 82
(Sr 85 test result is below Alert and Expiration Limits)

In International Units (kBq):

Example: 0.0094 x 1.48 = 0.014 kBq Sr 85/MBq Rb 82
(Sr 85 test result is below Alert and Expiration Limits)

The system uses Table 1 to calculate the decay factor for Rb 82

TABLE 1

Physical Decay Chart: Rb 82 half-life 75 seconds

Seconds	Fraction Remaining	Seconds	Fraction Remaining
0*	1.00	165	0.218
15	0.871	180	0.190
30	0.758	195	0.165
45	0.660	210	0.144
60	0.574	225	0.125
75	0.500	240	0.109
90	0.435	255	0.095
105	0.379	270	0.083
120	0.330	285	0.072
135	0.287	300	0.063
150	0.250		

*Elution time

The system uses Table 2 to calculate the ratio (R) of Sr 85/Sr 82.

TABLE 2

Sr 85/Sr 82 Ratio Chart (Sr 85 $T_{\frac{1}{2}}$ = 65 days, Sr 82 $T_{\frac{1}{2}}$ = 25 days)

Days	Ratio Factor	Days	Ratio Factor	Days	Ratio Factor
0*	1.00	21	1.43	42	2.05
1	1.02	22	1.46	43	2.08
2	1.03	23	1.48	44	2.12
3	1.05	24	1.51	45	2.15
4	1.07	25	1.53	46	2.19
5	1.09	26	1.56	47	2.23
6	1.11	27	1.58	48	2.27
7	1.13	28	1.61	49	2.30
8	1.15	29	1.64	50	2.34
9	1.17	30	1.67	51	2.38
10	1.19	31	1.70	52	2.43
11	1.21	32	1.73	53	2.47
12	1.23	33	1.76	54	2.51
13	1.25	34	1.79	55	2.55
14	1.27	35	1.82	56	2.60
15	1.29	36	1.85	57	2.64
16	1.31	37	1.88	58	2.69
17	1.34	38	1.91	59	2.73
18	1.36	39	1.95	60	2.78
19	1.38	40	1.98		
20	1.41	41	2.01		

* Day of calibration.

2.7 RUBY-FILL Expiration

Stop use of the RUBY-FILL Rubidium Rb 82 Generator once any one of the following **Expiration Limits** is reached:

- A total elution volume of 30 L has passed through the generator column, or
- Expiration date of the generator (60 days post-manufacturing), or
- An eluate Sr 82 level of 0.01 µCi/mCi (kBq/MBq) Rb 82, or
- An eluate Sr 85 level of 0.1 µCi/mCi (kBq/MBq) Rb 82.

2.8 RUBY-FILL Dose Delivery Limit

The maximum available activity (delivery limit) will decrease as the generator ages. Certain doses, including the maximum recommended dose [60 mCi (2220 MBq)], are not achievable for the entire shelf-life of the generator. Table 3 provides an estimate of the maximum available activity of Rubidium Rb 82 (Delivery Limit) as a function of generator age.

Table 3 Rubidium Rb 82 Dose Delivery Limit Based on Generator Age[1]

Generator Age (days) [2]	Maximum Rubidium Dose (Delivery Limit)
0-17	60 mCi (2220 MBq)
24	50 mCi (1850 MBq)
32	40 mCi (1480 MBq)
42	30 mCi (1110 MBq)
57	20 mCi (740 MBq)

[1] Estimate is based on a 100 mCi (3700 MBq) Sr 82 generator at calibration.
[2] Generator age at which delivery limit is reached varies with generator activity at release. For example, an 85 mCi (3145 MBq) generator and a 115 mCi (4255 MBq) generator will reach a delivery limit < 60 mCi at ≥ 12 days and ≥ 23 days, respectively.

2.9 Radiation Dosimetry

The estimated radiation absorbed dose coefficients for Rb 82, Sr 82, and Sr 85 from an intravenous injection of rubidium Rb 82 chloride are shown in Table 4.

Table 4
Adult absorbed dose per radioisotope activity associated with injection

Organ	^{82}Rb[1] (µGy/MBq)	^{82}Sr[2] (µGy/kBq)	^{85}Sr[2] (µGy/kBq)
Adrenals	2.4	2.9	1.4
Bone surfaces	0.42	29	2.7
Brain	0.14	2.2	0.8
Breast	0.19	1.9	0.5
Gallbladder wall	0.72	2.3	0.8
Gastrointestinal tract			
Esophagus[3]	1.5	2.1	0.6
Stomach wall	0.83	2.1	0.6
Small intestine wall	2.0	2.6	1.1
Colon wall	1.1	9.7	1.2
(ULI wall)	1.1	6.4	1.0
(LLI wall)	1.1	14	1.4
Heart wall	4.0	2.2	0.7
Kidneys	9.3	2.5	0.7
Liver	1.0	2.2	0.7
Lungs	2.6	2.2	0.8
Muscles	0.23	2.2	0.7
Ovaries	0.50	2.8	1.2
Pancreas	2.6	2.5	0.9
Red marrow	0.38	25	2.7
Skin	0.18	1.9	0.5
Spleen	0.18	2.2	0.7
Testes	0.26	2.0	0.5
Thymus	1.5	2.1	0.6
Thyroid	0.31	2.2	0.7
Urinary bladder wall	0.18	5.9	0.8
Uterus	1.0	2.5	0.9
Remaining organs	0.31	–	–
Effective dose per unit activity	1.1 µSv/MBq	6.3 µSv/kBq	1.1 µSv/kBq

[1] Rb- 82 doses are averages of rest and stress dosimetry data. To calculate organ doses (µGy) from Rb- 82, multiply the dose coefficient for each organ by the administered activity in MBq.
[2] To calculate organ doses attributable to Sr-82 and Sr-85, multiply those dose coefficients by the respective strontium activities associated with the injection.
[3] The absorbed dose to the thymus is used as a substitute.

3 DOSAGE FORMS AND STRENGTHS

RUBY-FILL is a closed system used to produce rubidium Rb 82 chloride injection for intravenous use. RUBY-FILL consists of Sr 82 adsorbed on a hydrous stannic oxide column with an activity of 3145-4255 MBq (85-115 mCi) Sr 82 at calibration time.

4 CONTRAINDICATIONS

None.

5 WARNINGS AND PRECAUTIONS

5.1 Unintended Sr 82 and Sr 85 Radiation Exposure

Unintended radiation exposure occurs when the Sr 82 and Sr 85 levels in rubidium Rb 82 chloride injections exceed the specified generator eluate limits. To minimize the risk of unintended radiation exposure, strict adherence to a daily eluate testing protocol is required. Stop using the rubidium generator when the expiration limits are reached *[see Dosage and Administration (2.6) and (2.7)]*.

5.2 Risks Associated with Pharmacologic Stress

Pharmacologic induction of cardiovascular stress may be associated with serious adverse reactions such as myocardial infarction, arrhythmia, hypotension, bronchoconstriction, and cerebrovascular events. Perform pharmacologic stress testing in accordance with the pharmacologic stress agent's prescribing information and only in the setting where cardiac resuscitation equipment and trained staff are readily available.

5.3 Radiation Risks

RUBY-FILL use contributes to a patient's overall long-term cumulative radiation exposure. Long-term cumulative radiation exposure is associated with an increased risk for cancer. Ensure safe handling to minimize radiation exposure to the patient and health care providers. Encourage patients to void as soon as a study is completed and as often as possible thereafter for at least one hour *[see Dosage and Administration (2.1) and (2.2)]*.

6 ADVERSE REACTIONS

The following serious adverse reaction associated with the use of rubidium Rb 82 chloride was identified in clinical trials or post marketing reports. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Unintended Sr 82 and Sr 85 Radiation Exposure: Unintended radiation exposure has occurred in some patients who received rubidium Rb 82 chloride injection at clinical sites where generator eluate testing appeared insufficient *[see Boxed Warning, Warnings and Precautions (5.1), Dosage and Administration (2.6)]*.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

There are no data available on the use of rubidium Rb 82 in pregnant women. Animal reproduction studies with rubidium Rb 82 chloride have not been conducted. However, all radiopharmaceuticals have the potential to cause fetal harm depending on the fetal stage of development and the magnitude of the radiation dose. If considering rubidium Rb 82 chloride injection administration to a pregnant woman, inform the patient about the potential for adverse pregnancy outcomes based on the radiation dose from Rb 82 and the gestational timing of exposure.

The estimated background risk of major birth defects and miscarriage for the indicated population is unknown. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2-4% and 15-20%, respectively.

8.2 Lactation

Risk Summary

There is no information regarding the presence of Rb 82 chloride in human milk, the effects on the breastfed infant or the effects on milk production. Due to the short half-life of Rb 82 chloride (75 seconds), exposure of a breast fed infant through breast milk can be minimized by temporary discontinuation of breastfeeding [See Clinical Considerations]. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for Rb 82, any potential adverse effects on the breastfed child from Rb 82 or from the underlying maternal condition.

Clinical considerations

Minimizing Exposure

Exposure to Rb 82 chloride through breast milk can be minimized if breastfeeding is discontinued when Rb 82 chloride injection is administered. Do not resume breastfeeding until at least one hour after completion of RUBY-FILL infusion.

8.4 Pediatric Use

The safety and effectiveness of rubidium Rb 82 chloride injection in pediatric patients have not been established.

8.5 Geriatric Use

In elderly patients with a clinically important decrease in cardiac function, lengthen the delay between infusion and image acquisition *[see Dosage and Administration (2.3)]*. Observe for the possibility of fluid overload from the infusion.

11 DESCRIPTION

11.1 Chemical Characteristics

RUBY-FILL Rubidium Rb 82 Generator contains accelerator-produced Sr 82 adsorbed on stannic oxide in a lead-shielded column and provides a means for obtaining sterile non-pyrogenic solutions of rubidium Rb 82 chloride injection. The chemical form of Rb 82 is $^{82}RbCl$.

The amount (mCi) of Rb 82 obtained in each elution will depend on the potency of the generator. When used with the RUBY Rubidium Elution System, the generator provides ± 10% accuracy for rubidium Rb 82 chloride doses between 370-2220 MBq (10-60 mCi).

When eluted at a rate of 15-30 mL/minute, each generator eluate at the end of elution should not contain more than 0.02 µCi (0.74 kBq) of Sr 82 and not more than 0.2 µCi (7.4 kBq) of Sr 85 per mCi of rubidium Rb 82 chloride injection, and not more than 1 µg of tin per mL of eluate.

11.2 Physical Characteristics

Rb 82 decays by positron emission and associated gamma emission with a physical half-life of 75 seconds. Table 5 shows the annihilation photons released following positron emission which are useful for detection and imaging studies.

The decay modes of Rb 82 are: 95.5% by positron emission, resulting in the production of annihilation radiation, i.e., two 511 keV gamma rays; and 4.5% by electron capture, resulting in the emission of "prompt" gamma rays of predominantly 776.5 keV. Both decay modes lead directly to the formation of stable Kr 82.

TABLE 5
Principal Radiation Emission Data

Radiation	Mean Percent Per Disintegration	Mean Energy (keV)
Annihilation photons (2)	191.01	511 (each)
Gamma rays	13 to 15	776.5

The specific gamma ray constant for Rb-82 is 6.33 R cm^2 / mCi h (1.23×10^{-12} C m^2 / kg MBq s). The first half-value layer is 0.53 cm of lead (Pb). Table 6 shows a range of values for the relative attenuation of the radiation emitted by this radionuclide that results from interposition of various thicknesses of Pb. For example, the use of a 6.15 cm thickness of Pb will attenuate the radiation emitted by a factor of about 1,000.

TABLE 6
Radiation Attenuation by Lead Shielding

Shield Thickness (Pb) cm	Attenuation Factor
0.53	0.5
1.68	10^{-1}
3.55	10^{-2}
6.15	10^{-3}
9.3	10^{-4}

Sr 82 (half-life of 25 days; 600 hrs.) decays to Rb 82. To correct for physical decay of Sr 82, Table 7 shows the fractions that remain at selected intervals after the time of calibration.

TABLE 7
Physical Decay Chart: Sr 82 half-life 25 days

Days	Fraction Remaining	Days	Fraction Remaining	Days	Fraction Remaining
0*	1.000	21	0.559	41	0.321
1	0.973	22	0.543	42	0.312
2	0.946	23	0.529	43	0.304
3	0.920	24	0.514	44	0.295
4	0.895	25	0.500	45	0.287
5	0.871	26	0.486	46	0.279
6	0.847	27	0.473	47	0.272
7	0.824	28	0.460	48	0.264
8	0.801	29	0.448	49	0.257
9	0.779	30	0.435	50	0.250
10	0.758	31	0.423	51	0.243
11	0.737	32	0.412	52	0.237
12	0.717	33	0.401	53	0.230
13	0.697	34	0.390	54	0.224
14	0.678	35	0.379	55	0.218
15	0.660	36	0.369	56	0.212
16	0.642	37	0.358	57	0.206
17	0.624	38	0.349	58	0.200
18	0.607	39	0.339	59	0.195
19	0.591	40	0.330	60	0.189
20	0.574				

* Calibration time

To correct for physical decay of Rb 82, Table 1 shows the fraction of Rb 82 remaining in all 15 second intervals up to 300 seconds after time of calibration *[see Dosage and Administration (2.6)]*.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Rb 82 is analogous to potassium ion (K^+) in its biochemical behavior and is rapidly extracted by the myocardium proportional to the blood flow. Rb^+ participates in the sodium-potassium (Na^+/K^+) ion exchange pumps that are present in cell membranes. The intracellular uptake of Rb 82 requires maintenance of ionic gradient across cell membranes. Rb 82 radioactivity in viable myocardium is higher than in infarcted tissue, reflecting intracellular retention.

12.2 Pharmacodynamics

In human studies, myocardial activity was noted within the first minute after peripheral intravenous injection of Rb 82. When areas of infarction or ischemia are present in the myocardium, they are visualized within 2-7 minutes after injection as photon-deficient, or "cold", areas on the myocardial perfusion scan. In patients with reduced cardiac function, transit of the injected dose from the peripheral infusion site to the myocardium may be delayed.

Blood flow brings Rb 82 to all areas of the body during the first pass of circulation. Accordingly, visible uptake is observed in highly vascularized organs, such as the kidneys, liver, spleen and lungs.

12.3 Pharmacokinetics

With a physical half-life of 75 seconds, Rb 82 is converted by radioactive decay into stable Kr 82 gas, which is passively expired by the lungs.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

No long-term studies have been performed to evaluate carcinogenic potential, mutagenicity potential, or to determine whether rubidium Rb 82 chloride injection may affect fertility in males or females.

14 CLINICAL STUDIES

In a descriptive, prospective, blinded image interpretation study of adult patients with known or suspected coronary artery disease, myocardial perfusion deficits in stress and rest PET images obtained with ammonia N 13 (n = 111) or Rb 82 (n = 82) were compared to changes in stenosis flow reserve (SFR) as determined by coronary angiography. PET perfusion defects at rest and stress for seven cardiac regions (anterior, apical, anteroseptal, posteroseptal, anterolateral, posterolateral, and inferior walls) were graded on a scale of 0 (normal) to 5 (severe). Values for stenosis flow reserve, defined as flow at maximum coronary vasodilatation relative to rest flow, ranged from 0 (total occlusion) to 5 (normal). With increasing impairment of flow reserve, the subjective PET defect severity increased. A PET defect score of 2 or higher was positively correlated with flow reserve impairment (SFR < 3).

A systematic review of published literature was conducted using pre-defined inclusion/exclusion criteria which resulted in identification of 10 studies evaluating the use of Rb 82 PET myocardial perfusion imaging (MPI) for the identification of coronary artery disease as defined by catheter-based angiography. In these studies, the patient was the unit of analysis and 50% stenosis was the threshold for clinically significant coronary artery disease (CAD). Of these 10 studies, 9 studies were included in a meta-analysis for sensitivity (excluding one study with 100% sensitivity) and 7 studies were included in a meta-analysis of specificity (excluding 3 studies with 100% specificity). A random effects model yielded overall estimates of sensitivity and specificity of 92% (95% CI: 89% to 95%) and 81% (95% CI: 76% to 86%), respectively. The use of meta-analysis in establishing performance characteristics is limited, particularly by the possibility of publication bias (positive results being more likely to be published than negative results) which is difficult to detect especially when based on a limited number of small studies.

16 HOW SUPPLIED/STORAGE AND HANDLING

16.1 How Supplied

RUBY-FILL Rubidium Rb 82 Generator consists of Sr 82 adsorbed on a hydrous stannic oxide column with an activity of 3145-4255 MBq (85-115 mCi) Sr 82 at calibration time. A lead shield encases the generator. The container label provides complete assay data for each generator. Use RUBY-FILL Rubidium Rb 82 Generator only with an appropriate, properly calibrated Elution System (RUBY Rubidium Elution System) labeled for use with the generator.

16.2 Storage and Handling

- Store the generator at 20-25 °C (68-77 °F).
- Receipt, transfer, possession, storage, disposal or use of this product is subject to the radioactive material regulations and licensing requirements of the U.S. Nuclear Regulatory Commission (NRC), Agreement States or Licensing States as appropriate. Do not dispose of the generator in regular refuse systems.
- For questions about the disposal of the RUBY-FILL Rubidium Rb 82 Generator, contact Jubilant DraxImage Inc. at 1-888-633-5343.

17 PATIENT COUNSELING INFORMATION

Pregnancy

Advise a pregnant woman of the potential risk to a fetus.

Lactation

Advise lactating women that exposure to Rb 82 chloride through breast milk can be minimized if breastfeeding is discontinued when Rb 82 chloride injection is administered. Advise lactating women not to resume breastfeeding for at least one hour after completion of rubidium Rb 82 infusion.

General Safety Precautions

Advise patients to void after completion of each image acquisition session and as often as possible for one hour after completion of the PET scan.

Manufactured by:

Jubilant DRAXIMAGE Inc.
16751 TransCanada Highway
Kirkland, Québec, Canada
H9H 4J4

Version: 1

EXHIBIT 13

Jubilant Life Sciences

Ethanol a positive surprise in otherwise inline Quarter

Q3FY18 Result Update

January 18, 2018

Surajit Pal
surajitpal@plindia.com
+91-22-66322259

Rating	**Accumulate**
Price	Rs921
Target Price	Rs861
Implied Upside	-6.5%
Sensex	35,082
Nifty	10,789

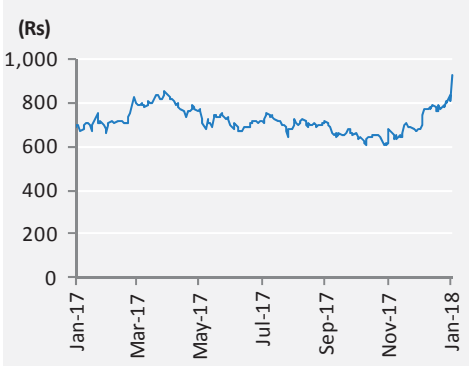
(Prices as on January 17, 2018)

Trading data	
Market Cap. (Rs bn)	142.3
Shares o/s (m)	154.5
3M Avg. Daily value (Rs m)	380.8
Major shareholders	
Promoters	56.25%
Foreign	19.38%
Domestic Inst.	5.28%
Public & Other	19.09%

Stock Performance			
(%)	**1M**	**6M**	**12M**
Absolute	35.4	29.4	32.8
Relative	30.5	20.0	4.0

How we differ from Consensus			
EPS (Rs)	**PL**	**Cons.**	***% Diff.***
2019	52.4	55.3	*-5.3*
2020	60.7	67.2	*-9.6*

Price Perf. (RIC: JULS.BO, BB: JUBILANT IN)



Source: Bloomberg

- **Ex-Ethanol Sales, EBITDA, PAT in line**: JUBL sales, EBITDA and PAT after adjusting one-off Ethanol sales are more or less in line with our estimates. Ex-ethanol sales were below estimates by 4% YoY while EBITDA and PAT were up 4% and 2% above estimates. Triad sales (post acquisition) of US$47.5m with 5% operating loss were on expected lines. EBITDA margin was 16.5% vs our estimates of 15.2% as there was improvement in margin in core LSI business. With increase in demand and favourable price in Vitamins, pyridine and acetyls, JUBL's EBITDA margin in LSI business grew to 19% in Q3FY18 from 17.7% in Q2FY18. Ex-Triad, Pharma sales increased by 3% QoQ despite 9% QoQ growth in specialty pharma business in US. The reason for tepid growth in pharma was 11% decline in generic business, driven by channel consolidation in US generics and lower offtake of clients in API business. JUBL secured tender business of Rs3bn for supplying Ethanol to the GOI's petrol-blending program over 12 months with initial supply beginning in Q3FY18.
- **Ruby-Fill yet to take off:** JUBL completed installation of Ruby-fill (first NDA product) in three sites while management believes that the drug will take longer time before seeing any critical contribution in revenues and operating margin. JOL plans to launch another NDA drug Drax Exametazime in the US in FY19E. We believe Ruby-Fill sales to remain lacklustre in near term due to installation of costly machinery of PET-CT technology.
- **Valuation-Maintain 'Accumulate', TP increased to Rs861**: While there are improvement seen in LSI, we have reduced sales and EBITDA estimates due to a)lower growth and margin in pharma sales and b) high LSI base in Q4FY17. JUBL's EBITDA margin of Pharma is expected to have lower margin due to addition of low margin business of Traid Isotopes post acquisition. This will result in 11% CAGR in EBITDA during FY17-20E. Net Debt decreased to Rs34.5bn in Q3FY18 from Rs36.6bn in Q2FY18. We roll forward our earnings to FY20E and assigned 12x EV/EBITDA on pharma and 5x of EV/EBITDA on LSI, leading to increase in valuation by 22%. We maintain our recommendation of 'Accumulate' and increase TP to Rs861 (from earlier Rs707)

Key financials (Y/e March)	2017	2018E	2019E	2020E
Revenues (Rs m)	57,653	71,879	86,362	97,267
Growth (%)	*2.1*	*24.7*	*20.2*	*12.6*
EBITDA (Rs m)	12,491	13,262	15,459	17,265
PAT (Rs m)	5,756	6,315	8,164	9,457
EPS (Rs)	37.0	40.5	52.4	60.7
Growth (%)	*46.6*	*9.7*	*29.3*	*15.8*
Net DPS (Rs)	3.1	3.1	3.1	3.1

Profitability & Valuation	2017	2018E	2019E	2020E
EBITDA margin (%)	*21.7*	*18.5*	*17.9*	*17.8*
RoE (%)	*18.0*	*17.0*	*18.6*	*18.1*
RoCE (%)	*10.8*	*10.9*	*12.6*	*13.1*
EV / sales (x)	3.1	2.5	2.0	1.7
EV / EBITDA (x)	14.4	13.3	11.1	9.7
PE (x)	24.9	22.7	17.6	15.2
P / BV (x)	4.2	3.6	3.0	2.5
Net dividend yield (%)	*0.3*	*0.3*	*0.3*	*0.3*

Source: Company Data; PL Research

Key takeaways from Conference call

- With major growth in Specialty Pharma Injectables, JUBL's Pharma segment sales were at Rs11bn, grew 40% YoY and 28% QoQ in In Q3FY18. Management guided that the Pharma revenues and profitability increased 5% YoY ex-Triad business
- LSI business grew 39% YoY and 28% QoQ to Rs9.2bn. JOL won a new contract which will help generate revenues worth Rs3bn from Dec 2017 to Nov 2018. EBITDA margin for LSI business increased to 22.3% on favourable pricing regime and due to greater availability of molasses with better pricing. Growth in LSI business was driven equally by increase in volumes and prices
- Management soft launched gCardiogen-82 (branded as Ruby-Fill) in Q3FY17 and successfully completed its installation at three sites is USA by Q3FY18. The company expects Ruby-Fill market to expand to US$250m by FY21E. Management maintained guidance for achieving at least 30-40% market share of the product over 5 years
- Management guided to launch 5 new products in the Radiopharmaceuticals segment in 3-4 years. The company received 2 approvals and filed 4 ANDAs in Q3FY18 in the injectable segment
- JUBL received approval for new indication for Draximage DTPA in US in Q3FY18. Management guided to launch Drax Exametazime in FY19E in US for which it has received approval in Q3FY18
- The company incurred capex of Rs700m in Q3FY18. R&D expenditure was 4.6% of segment sales at Rs510m in Q3FY18. Of which, Rs380m was charged to P/L and balance being capitalized as product development expenditure which will be amortized over a period of 5 years.
- Management guided for capex at Rs4bn (to be financed through internal accruals) and maintained R&D expenses to be at 8.5% of segment sales in FY18E. Management maintained guidance for capitalisation of Rs1.4-1.7bn on R&D expenditures.
- Ttax rate is expected to be lower at 25% in FY18E due to reduction in US federal tax rates from 35% to 21%, which has helped JUBL to reduce US$10m in tax outflow
- Management guided to maintain overall EBITDA margin in a range of 20-21% and to maintain LSI EBITDA margin at 17-18% in H2FY18E
- JOL decreased net debt by Rs1.59bn in Q3FY18. Its current net debt is Rs34.8bn. Going forward, management has guided to maintain focus on reducing debt and improving the return ratios
- Management guided that capacity enhancement for acetic anhydride is underway at SEZ Bharuch facility. With target completion date in FY19, JOL expects to achieve revenues of Rs3bn at full capacity utilization

Exhibit 1: Change in Estimates

Year	Sales (Rs m)			EBITDA (Rs m)			EPS (Rs)		
	Old	New	Diff (%)	Old	New	Diff (%)	Old	New	Diff (%)
FY18E	72,739	71,879	(1.2)	14,177	13,262	(6.5)	44.3	40.5	(8.5)
FY19E	89,764	86,362	(3.8)	16,145	15,459	(4.2)	55.8	52.4	(6.1)

Source: PL Research

Exhibit 2: Q3FY18 Result Overview (Rs m)

Y/e March	Q3FY18	Q3FY17	YoY gr. (%)	Q2FY18	9MFY18	9MFY17	YoY gr. (%)
Net Sales	**20,678**	**14,916**	***38.6***	**16,420**	**53,059**	**43,649**	***21.6***
Raw Material	9,065	6,058	*49.6*	7,107	23,310	17,175	*35.7*
% of Net Sales	*43.8*	*40.6*		*43.3*	*43.9*	*39.3*	
Personnel Cost	4,229	3,092	*36.8*	3,688	11,021	9,065	*21.6*
% of Net Sales	*20.5*	*20.7*		*22.5*	*20.8*	*20.8*	
Others	3,215	2,449	*31.3*	2,565	8,123	6,668	*21.8*
% of Net Sales	*15.5*	*16.4*		*15.6*	*15.3*	*15.3*	
Total Expenditure	16,509	11,598	*42.3*	13,360	42,453	32,908	*29.0*
EBITDA	**4,168**	**3,318**	***25.6***	**3,061**	**10,605**	**10,742**	***(1.3)***
Margin (%)	*20.2*	*22.2*		*18.6*	*20.0*	*24.6*	
Depreciation	818	727	*12.6*	790	2,333	2,162	*7.9*
EBIT	**3,350**	**2,592**	***29.3***	**2,271**	**8,272**	**8,580**	***(3.6)***
Other Income	32	51	*(37.1)*	71	171	143	*19.5*
Interest	771	982	*(21.5)*	660	2,118	2,609	*(18.8)*
PBT	**2,612**	**1,661**	***57.2***	**1,681**	**6,325**	**6,114**	***(3.5)***
Minority Interest	(3)	13	*(123.3)*	(28)	(59)	(2)	
Total Taxes	483	480	*0.7*	427	1,505	1,520	*(1.0)*
ETR (%)	*18.5*	*28.9*		*25.4*	*23.8*	*24.9*	
Reported PAT	**2,125**	**1,194**	***78.0***	**1,283**	**4,879**	**4,596**	***(6.2)***
Other Comprehensive Income	(409)	(98)		802	787	(216)	
Total Comprehensive Income	**1,716**	**1,096**	***56.6***	**2,084**	**5,667**	**4,380**	***(29.4)***

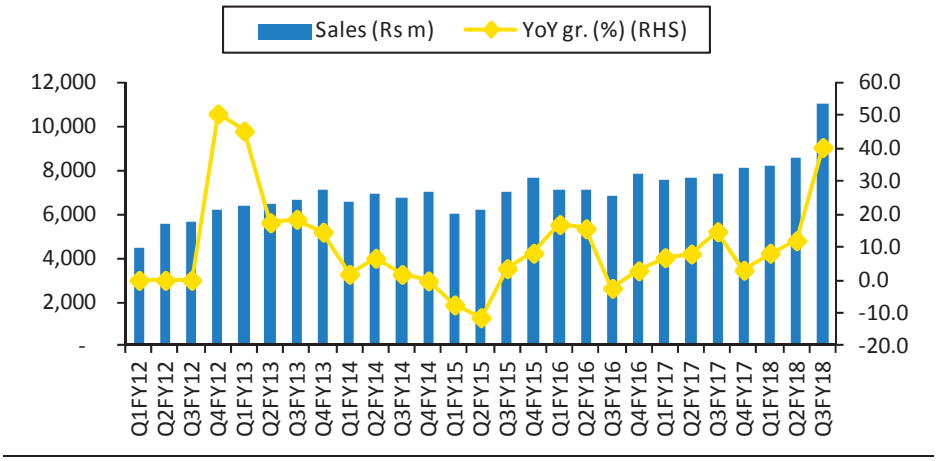
Source: Company Data, PL Research

Exhibit 3: Major Sources of Revenues (Rs m)

Y/e March	Q3FY18	Q3FY17	YoY gr. (%)	Q2FY18	9MFY18	9MFY17	YoY gr. (%)
Pharmaceuticals	11,007	7,846	*40.3*	8,593	27,765	23,065	*20.4*
% of Net Sales	*53.2%*	*52.6%*		*52.3%*	*52.3%*	*52.8%*	
Life Science ingredients	9,225	6,633	*39.1*	7,385	23,993	19,274	*24.5*
% of Net Sales	*44.6%*	*44.5%*		*45.0%*	*45.2%*	*44.2%*	
Drug Discovery Solutions	446	437	*2.0*	443	1,300	1,311	*(0.8)*
% of Net Sales	*2.2%*	*2.9%*		*2.7%*	*2.5%*	*3.0%*	
Gross Sales	**20,678**	**14,916**	*38.6*	**16,420**	**53,059**	**43,649**	*21.6*

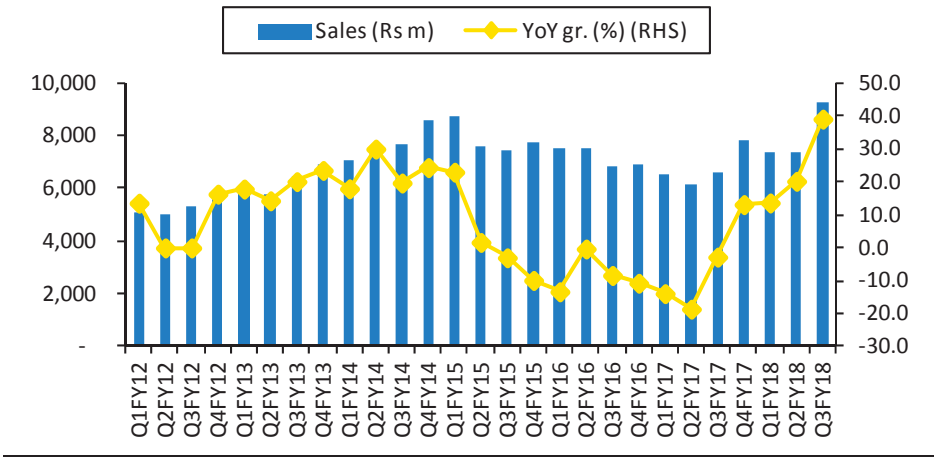
Source: Company Data, PL Research

Exhibit 4: Pharma sales and growth



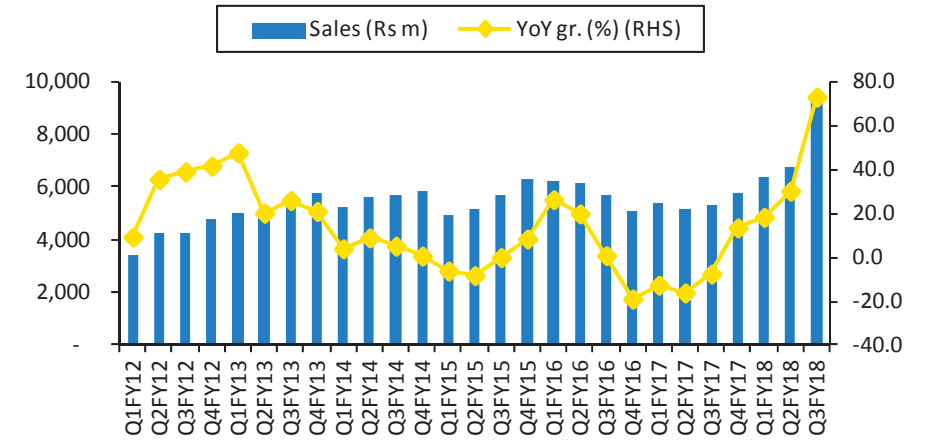
Source: Company Data, PL Research

Exhibit 5: LSI Sales and Growth



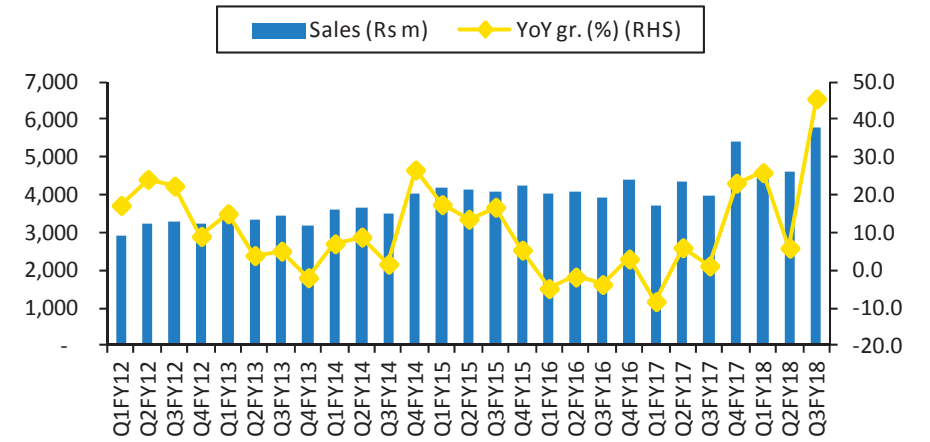
Source: Company Data, PL Research

Exhibit 6: US Sales and Growth



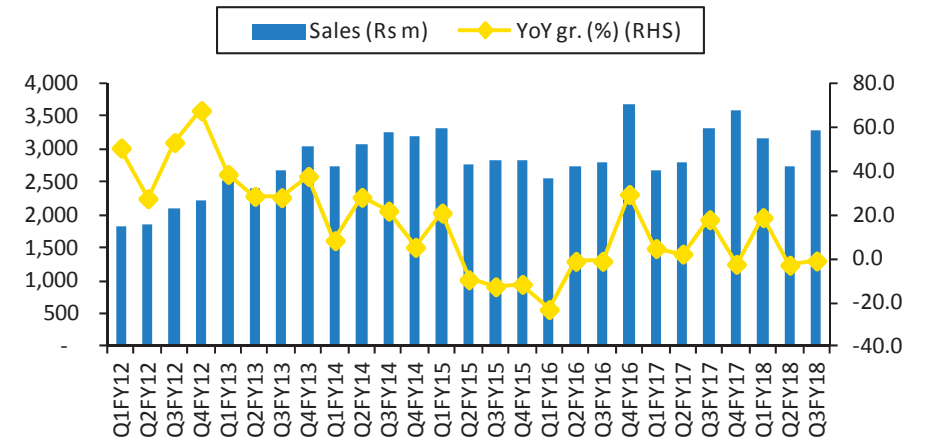
Source: Company Data, PL Research

Exhibit 7: India Sales and Growth



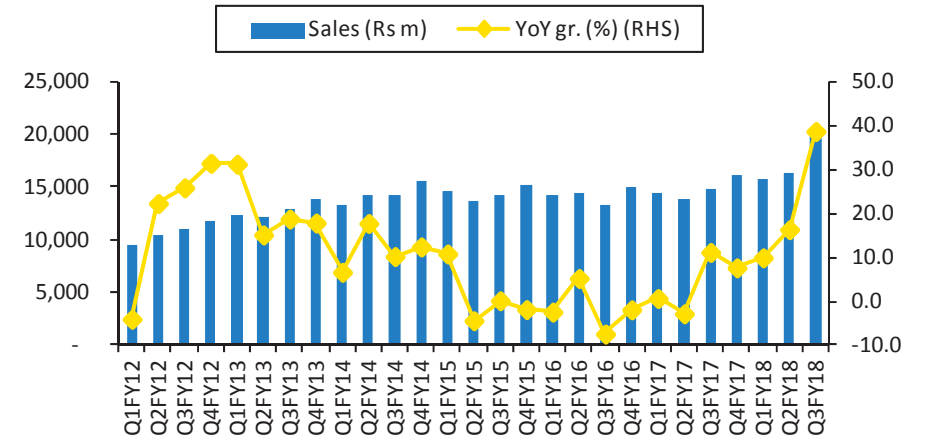
Source: Company Data, PL Research

Exhibit 8: EU, Japan: Sales and Growth



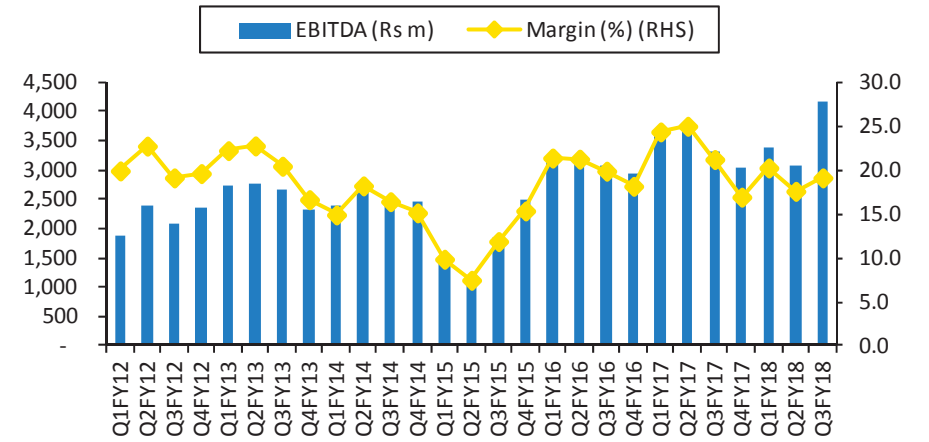
Source: Company Data, PL Research

Exhibit 9: Overall Sales and Growth



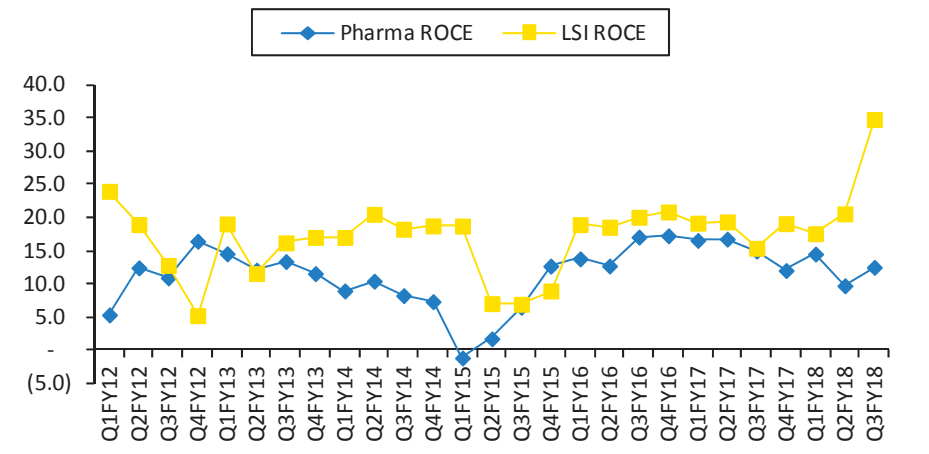
Source: Company Data, PL Research

Exhibit 10: EBITDA and Margin: Pharma and LSI



Source: Company Data, PL Research

Exhibit 11: ROCE: Pharma and LSI



Source: Company Data, PL Research

Income Statement (Rs m)

Y/e March	2017	2018E	2019E	2020E
Net Revenue	**57,653**	**71,879**	**86,362**	**97,267**
Raw Material Expenses	19,995	27,314	33,250	37,448
Gross Profit	37,657	44,565	53,113	59,819
Employee Cost	12,309	15,454	17,920	20,426
Other Expenses	12,857	15,849	19,734	22,128
EBITDA	**12,491**	**13,262**	**15,459**	**17,265**
Depr. & Amortization	2,914	3,224	3,547	4,071
Net Interest	3,411	2,803	2,457	2,169
Other Income	1,210	1,184	1,430	1,585
Profit before Tax	**7,376**	**8,420**	**10,885**	**12,610**
Total Tax	1,630	2,105	2,721	3,152
Profit after Tax	**5,746**	**6,315**	**8,164**	**9,457**
Ex-Od items / Min. Int.	(10)	—	—	—
Adj. PAT	**5,756**	**6,315**	**8,164**	**9,457**
Avg. Shares O/S (m)	**155.8**	**155.8**	**155.8**	**155.8**
EPS (Rs.)	**37.0**	**40.5**	**52.4**	**60.7**

Cash Flow Abstract (Rs m)

Y/e March	2017	2018E	2019E	2020E
C/F from Operations	12,685	9,808	11,915	10,814
C/F from Investing	(4,504)	(3,478)	(3,478)	(4,478)
C/F from Financing	(6,859)	(7,434)	(6,672)	(6,587)
Inc. / Dec. in Cash	1,322	(1,104)	1,766	(251)
Opening Cash	3,393	4,715	3,611	5,377
Closing Cash	4,715	3,611	5,377	5,125
FCFF	7,790	1,374	5,038	5,141
FCFE	3,310	(2,682)	1,399	1,298

Key Financial Metrics

Y/e March	2017	2018E	2019E	2020E
Growth				
Revenue (%)	2.1	24.7	20.2	12.6
EBITDA (%)	9.1	6.2	16.6	11.7
PAT (%)	46.9	9.7	29.3	15.8
EPS (%)	46.6	9.7	29.3	15.8
Profitability				
EBITDA Margin (%)	21.7	18.5	17.9	17.8
PAT Margin (%)	10.0	8.8	9.5	9.7
RoCE (%)	10.8	10.9	12.6	13.1
RoE (%)	18.0	17.0	18.6	18.1
Balance Sheet				
Net Debt : Equity	1.0	0.8	0.6	0.4
Net Wrkng Cap. (days)	150	129	116	122
Valuation				
PER (x)	24.9	22.7	17.6	15.2
P / B (x)	4.2	3.6	3.0	2.5
EV / EBITDA (x)	14.4	13.3	11.1	9.7
EV / Sales (x)	3.1	2.5	2.0	1.7
Earnings Quality				
Eff. Tax Rate	22.1	25.0	25.0	25.0
Other Inc / PBT	16.4	14.1	13.1	12.6
Eff. Depr. Rate (%)	5.1	5.2	5.3	5.7
FCFE / PAT	57.5	(42.5)	17.1	13.7

Source: Company Data, PL Research.

Balance Sheet Abstract (Rs m)

Y/e March	2017	2018E	2019E	2020E
Shareholder's Funds	34,360	40,100	47,689	56,571
Total Debt	40,453	36,397	32,757	28,913
Other Liabilities	2,817	2,862	2,716	1,754
Total Liabilities	**77,631**	**79,359**	**83,161**	**87,238**
Net Fixed Assets	57,905	57,081	58,135	58,563
Goodwill	—	—	—	—
Investments	1,027	1,027	1,027	1,027
Net Current Assets	18,124	19,565	23,403	27,039
Cash & Equivalents	*4,596*	*3,611*	*5,377*	*5,125*
Other Current Assets	*24,885*	*26,925*	*28,500*	*32,200*
Current Liabilities	*11,357*	*10,970*	*10,473*	*10,286*
Other Assets	574	585	596	608
Total Assets	**77,631**	**78,259**	**83,161**	**87,238**

Quarterly Financials (Rs m)

Y/e March	Q4FY17	Q1FY18	Q2FY18	Q3FY18
Net Revenue	**16,414**	**15,961**	**16,420**	**20,678**
EBITDA	**3,050**	**3,376**	**3,061**	**4,168**
% of revenue	*18.6*	*21.2*	*18.6*	*20.2*
Depr. & Amortization	752	725	790	818
Net Interest	802	617	560	571
Other Income	105	(2)	(29)	(168)
Profit before Tax	**1,601**	**2,032**	**1,681**	**2,612**
Total Tax	111	595	427	483
Profit after Tax	**1,501**	**1,471**	**1,283**	**2,125**
Adj. PAT	**1,501**	**1,471**	**1,283**	**2,125**

Key Operating Metrics (Rs m)

Y/e March	2017	2018E	2019E	2020E
Pharmaceuticals	32,987	40,641	51,318	57,820
LSI	27,076	32,165	36,210	40,760

Source: Company Data, PL Research.

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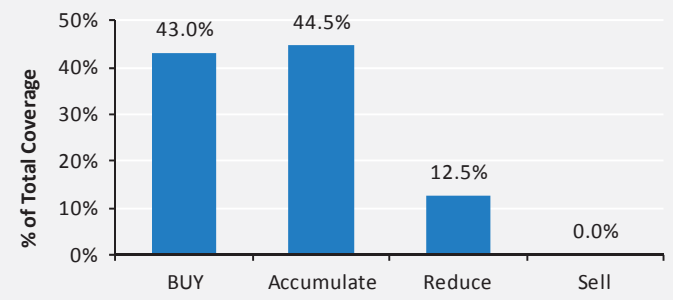

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BUY	:	Over 15% Outperformance to Sensex over 12-months
Accumulate	:	Outperformance to Sensex over 12-months
Reduce	:	Underperformance to Sensex over 12-months
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Trading Buy	:	Over 10% absolute upside in 1-month
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22nd Annual Scientific Session
American Society of Nuclear Cardiology

Sept. 14–17, 2017 | Kansas City, Missouri

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and RUBY Rubidium Elution System

Elution Evolution

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Advancing cardiac PET imaging to be:

Precise	Constant-activity infusion option Maintains consistent activity rate profiles throughout the life cycle of the generator[1-3]
Flexible	Accurate patient-specific dosing Long shelf life—60 days
Efficient	Automated daily quality control Built-in safety controls

Leap forward with RUBY-FILL®

Indication and Important Safety Information

RUBY-FILL® Rubidium Rb 82 Generator is a closed system used to produce rubidium Rb 82 chloride injection for intravenous use. Rubidium Rb 82 chloride injection is a radioactive diagnostic agent indicated for Positron Emission Tomography (PET) imaging of the myocardium under rest or pharmacologic stress conditions to evaluate regional myocardial perfusion in adult patients with suspected or existing coronary artery disease.

WARNING: UNINTENDED STRONTIUM-82 (Sr-82) AND STRONTIUM-85 (Sr-85) RADIATION EXPOSURE

Please see full prescribing information for complete boxed warning

- **Unintended radiation exposure occurs when the levels of Sr-82 or Sr-85 in the rubidium Rb 82 chloride injection exceed specific limits.**
- **Perform generator eluate tests:**
  - **1) Determine Rb-82, Sr-82, Sr-85 levels in the eluate:**
    - **Once daily, prior to any drug administration, and**
    - **With additional daily tests after detection of an Alert Limit.**
  - **2) Stop use of the generator at its Expiration Limit.**

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/safety/medwatch, or call 1-800-FDA-1088.

References: 1. Epstein JN, Ziadi MC, Benelfassi A, Beanlands RS, deKemp RA. An 82Rb infusion system for quantitative perfusion imaging with 3D PET. *Appl Radiat Isot*. 2004;60(6):921-927. **2.** Klein R, Adler A, Beanlands RS, deKemp RA. Precision-controlled elution of a 82Sr/82Rb generator for cardiac perfusion imaging with positron emission tomography. *Phys Med Biol*. 2007;52(3):659-673. **3.** Klein R, Renaud JM, Ziadi MC, et al. Intra- and inter-operator repeatability of myocardial blood flow and myocardial flow reserve measurements using rubidium-82 pet and a highly automated analysis program. *J Nucl Cardiol*. 2010;17(4): 600-616.

RUBY RUBIDIUM ELUTION SYSTEM

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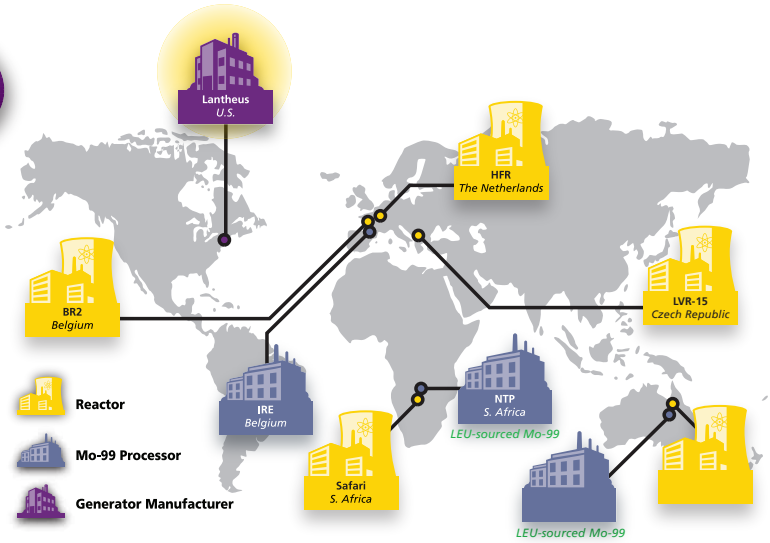

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1. Data on file, Lantheus Medical Imaging, Inc.

President's Welcome

As ASNC President, it is my pleasure to welcome you to Kansas City for ASNC2017. Nuclear cardiology continues to play a critical and cost-effective role in the diagnosis of heart disease and risk stratification in our patients. ASNC2017 showcases what nuclear cardiology has to offer in providing the best care for our patients.

This year's program will allow physicians and technologists to refine their diagnostic and technical acumen and to focus on patient-centered imaging – choosing the right test for the right patient and affording the lowest radiation dose possible. Sessions on multimodality imaging will provide an important perspective for attendees, particularly in providing essential diagnostic information in an environment of health care cost containment. State-of-the-art innovations in cardiac PET and SPECT imaging, including perfusion imaging, quantification of myocardial blood flow reserve, and the diagnosis of inflammatory and infiltrative cardiomyopathies, will be highlighted in the meeting. Be sure to attend our first-ever disease-based, rapid-fire abstract session focused on cardiac amyloid during the opening reception.

We are delighted to have world-renowned experts in cardiology in sessions covering a variety of disease-specific imaging topics. In a unique session on heart failure, long-time ASNC member Dr. Rory Hachamovitch will share his perspective as a patient rather than a physician. In addition, we are pleased to have ASNC past president, Dr. Leslee Shaw, deliver the 2017 Verani Lecture "Evolving, Innovating and Revolutionary Changes in Cardiovascular Imaging – We Have Only Begun!".

Our industry partners will exhibit the latest advancements in imaging hardware and software, radiopharmaceuticals, pharmacologic stress agents, and many other products essential to provide high quality patient care. I encourage you to visit the Exhibit Hall to meet with our industry partners and learn more about these exciting advancements.

ASNC's continued growth and success depends on the support of our members, guests, and industry partners. I thank you not only for your attendance, but also for your continued support of ASNC and nuclear cardiology. Enjoy the meeting, have a great time in Kansas City, and don't forget to sample some KC barbecue!

Raymond Russell

Raymond Russell, MD, PhD, FASNC
ASNC2017 President

Chair's Welcome

On behalf of the American Society of Nuclear Cardiology, I would like to welcome you to ASNC2017, the 22nd Annual Scientific Session of ASNC. We are very excited to be visiting Kansas City, the HEART of America. This year's meeting will highlight disease specific sessions (sarcoidosis and amyloidosis), hands on reading with the experts, case-based sessions, new rapid fire ePoster presentations and lots of opportunities for networking and mentorship.

The educational program will consist of several exciting plenary sessions. Dr. Leslee Shaw will deliver the Mario Verani Memorial Lecture at the opening plenary. Dr. Shaw will be speaking on Evolving, Innovating and Revolutionary Changes in Cardiovascular Imaging – We Have Only Begun. Our second plenary will focus on heart failure and will open with the patient perspective (Dr. Rory Hachamovitch): experiencing a heart transplant.

In addition to the diverse plenary sessions there will be several multimodality imaging sessions, practical sessions on how to establish a PET program, PYP imaging, international sessions, and, as always, the engaging Controversies in Cardiology session which will be held in an exciting new format.

NEW for 2017 – be sure to find time to drop in to the Comprehensive Boot Camp for Heart Service Line Administrators, Laboratory Managers, and Nuclear Cardiologists on Thursday afternoon.

So whether this is your first time at an ASNC annual meeting or you are a regular attendee, we have designed an interactive and exciting program that we hope you will enjoy.

I would like to thank the members of the ASNC2017 Program Committee and specifically Vice Chair, Sharmila Dorbala, MD, FASNC for their time and commitment in preparing this program. I would also like to thank all of the individuals who agreed to participate as part of the faculty for ASNC2017.

Donna M. Polk

Donna M. Polk, MD, MPH, FASNC
ASNC2017 Program Chair

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ASNC Education

Program Design

- A scientific forum featuring panel discussions on focused areas of cutting-edge research
- State-of-the-art reviews of the key aspects of nuclear cardiology by the world's experts
- A basic core curriculum addressing practical issues in the performance of nuclear cardiology procedures to include opportunities for maintenance of certification credit
- Scientific sessions on advances in nuclear cardiology
- Ethics session will offer case-based scenarios dealing with ethical issues
- Educational track dealing with the pathophysiology of multimodality imaging
- Presentations addressing technical issues in nuclear cardiology
- Oral abstracts featuring the latest clinical studies in cardiovascular imaging as well as young investigator presentations
- Abstracts of original investigation programmed as poster presentations
- Commercial exhibits displaying the latest in nuclear cardiology technology and services
- Cost-related information in the practice and business of nuclear cardiology focused on developing a PET program
- Innovations in Technology session to cover expanding horizons for cardiac imaging
- Opportunities to convene and interact with experts in all aspects of nuclear cardiology and cardiovascular imaging

Statement of Need

In order to maintain competence and improve performance, imaging professionals must assimilate and integrate knowledge spanning multiple areas, including clinical data, technical aspects of imaging, and appropriate application of imaging (e.g., clinical guidelines and appropriate use criteria). Each of these areas is constantly evolving, particularly as innovative technologies and novel pharmacologic agents are introduced. ASNC2017 is an educational activity designed to help you and other imaging professionals obtain the latest information in clinical practice and review cutting-edge scientific advances in nuclear cardiology and cardiac imaging.

Disclosure

ASNC is pledged to ensure balance, independence, objectivity, and scientific rigor in all its supported educational activities through disclosure of relationships with commercial companies and resolution of conflict of interest. All planners, reviewers and presenters involved with this activity are expected to disclose financial interests with the manufacturer(s) of any commercial product(s) and/or providers of commercial services discussed in an educational presentation. A complete list of disclosures will be distributed to all attendees on site.

Accreditation and Continuing Education Credit

PHYSICIANS: The American Society of Nuclear Cardiology is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians.

The American Society of Nuclear Cardiology designates this live activity for a maximum of 31.75* AMA PRA Category 1 Credits™. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

TECHNOLOGISTS: The American Society of Nuclear Cardiology is a recognized provider of continuing education credit for technologists. ASNC's Continuing Education (ACE) credit is accepted by both NMTCB and ARRT. ASNC2017 has been approved for a maximum of 20.75* ARRT Category A Credits.

PHYSICIAN ASSISTANTS: The American Academy of Physician Assistants (AAPA) accepts certificates of participation for educational activities certified for AMA PRA Category 1 Credits™ from organizations accredited by ACCME.

NURSE PRACTITIONERS: The American Academy of Nurse Practitioners Certification Board (AANPCP) recognizes attendance at CE offerings which provide AMA PRA Category 1 Credits™ for the purpose of recertification.

**Subject to Change*

Target Audience

This course is intended for cardiologists, radiologists, nuclear medicine specialists, practice administrators, nuclear technologists, nurses and other health care professionals with an interest in the field of nuclear cardiology and cardiac CT imaging.

Overall Purpose

The overall goal of the meeting is to improve learner knowledge, competence and skills in applications about appropriate use criteria, radiation safety, reporting, and lab performance in using appropriate guidelines-based treatment.

General Learning Objectives

DEMONSTRATE improved skills in image interpretation and reporting

LEARN how to recognize and minimize technical problems and artifacts that may be associated with cardiac imaging

LEARN the appropriate use of cardiac imaging techniques based on current guidelines

EVALUATE new imaging technologies, software, and stress techniques

UNDERSTAND the role of nuclear and cardiac CT imaging in overall patient care

LEARN the importance of balancing radiation exposure with image quality

DESCRIBE future directions in cardiac PET, CT, and SPECT/CT in order to anticipate training and equipment needs

UNDERSTAND the clinical implication of multimodality cases and recognize the value and limitations in clinical cardiology

Program Tracks

The program will include the following tracks to allow attendees to customize their educational experience:

PL **PLENARY**
Sessions will include keynote presentations from leaders in the field covering areas such as emerging research, new technology, and advances in treatment.

AR **ABSTRACTS/RESEARCH**
To include poster, ePosters, Rapid Fire ePosters and oral abstract presentation including young investigator oral presentations.

A **ADVANCED**
This track includes sessions covering advances in the field of nuclear cardiology and potential clinical applications for these innovations.

CA **CASES WITH THE ACES: INTERACTIVE READING**
Small group sessions on how to read a scan with senior faculty using vendor software to demonstrate cases

C **CORE**
These didactic presentations review topics essential to the effective diagnosis and treatment of heart disease patients using imaging modalities.

I **INTERNATIONAL**
These sessions offer an opportunity to learn about multimodality imaging from the international community and how that view may differ from the US-based approach.

LL **LIFELONG LEARNING**
Participate in a dedicated study session offering the opportunity to weigh in through audience response and discussion with facilitators and fellow participants to identify the most appropriate answers to ABIM approved questions. In addition, many didactic sessions offer MOC. These are designated in the schedule program schedule.

MI **MULTIMODALITY IMAGING**
Sessions include important applications of nuclear cardiology along with other imaging modalities in current practice to deliver optimal care to patients

O **OTHER**
These sessions are general in nature with broad-based interest. They include a boot camp focusing on positioning your lab for the future, an ethics session, choosing wisely challenge and ImageGuide registry update.

P **PET**
These sessions will offer a broad-based review of the clinical value of pharmacologic PET, radiation exposure, modeling cost effectiveness and other areas

PP **POLICY AND PRACTICE**
Managing a cardiology practice has never been more challenging. In each presentation you will find programming that gets to the heart of today's challenges while preparing you for the cardiology practice of tomorrow.

RE **READ WITH THE EXPERTS**
Learn with the best practitioners in the field by walking through cases along with panelists and expert faculty. Audience response opportunities available.

T **TECHNOLOGY AND TECHNIQUES**
Sessions are instructive with regard to nuclear cardiology procedures. Information is intended to provide practical information for providing quality imaging services. These sessions are geared for the nuclear cardiology technologist.

ASNC2017 Schedule by Track

A ADVANCED

DAY	SESS#	SESSION TITLE	START	END	ROOM
Fri	205	Imaging to Guide Arrhythmia Management	10:30AM	12:00PM	New York
Sat	304	Cutting Edge Technologies	10:30AM	12:00PM	New York
Sat	315	Debate: Clash of the Titans	1:30PM	3:00PM	Exhibit Hall B
Sun	402	Approach to Known or Potential Ischemic Heart Disease	9:45AM	10:45AM	Atlanta

CA CASES WITH THE ACES

DAY	SESS#	SESSION TITLE	START	END	ROOM
Fri	203	Cases from the Cleveland Clinic	10:00AM	11:30AM	Empire B
Fri	210	Cases from St. Luke's Roosevelt/Mt. Sinai	12:00PM	1:30PM	Empire B
Fri	217	Cases from MMP MaineHealth Cardiology	3:00PM	4:30PM	Empire B
Sat	303	Cases from Brigham & Women's Hospital	10:00AM	11:30AM	Empire B
Sat	310	Cases from Brown University	12:00PM	1:30PM	Empire B
Sat	321	Cases from Mayo Clinic	3:00PM	4:30PM	Empire B

C CORE

DAY	SESS#	SESSION TITLE	START	END	ROOM
Thu	101	How to Incorporate Test Findings Beyond Perfusion	1:00PM	2:30PM	Chicago
Fri	206	Nuclear Cardiology Lab in 2017	10:30AM	12:00PM	Exhibit Hall B
Sat	305	Cardiac Amyloidosis in 2017	10:30AM	12:00PM	Exhibit Hall B
Sat	316	Patient Centered Myocardial Perfusion Imaging	1:30PM	3:00PM	New York
Sun	404	How Does Radionuclide Imaging Guide Clinical Decision Making?	11:00AM	12:00PM	Atlanta

I INTERNATIONAL

DAY	SESS#	SESSION TITLE	START	END	ROOM
Fri	225	IAEA Global Initiatives - Part 1	4:00PM	5:00PM	Atlanta
Fri	226	IAEA Global Initiatives - Part 2	5:15PM	6:15PM	Atlanta

LL LIFELONG LEARNING

DAY	SESS#	SESSION TITLE	START	END	ROOM
Thu	107	ASNC MOC Module 2	7:00PM	9:30PM	New York/Atlanta

MI MULTIMODALITY IMAGING

DAY	SESS#	SESSION TITLE	START	END	ROOM
Thu	103	CT, PET/CT and PET/MR Imaging to Assess Heart Disease	2:45PM	4:00PM	Chicago
Fri	207	Methods and Value of Cardiotoxicity Assessment in Oncologic Disease	10:30AM	12:00PM	Atlanta
Fri	221	Evaluation of Suspected Coronary Artery Disease in Women	4:00PM	5:30PM	New York
Sun	405	Multimodality Assessment of Complex Cardiovascular Disease	11:00AM	12:00PM	Chicago AB

O OTHER

DAY	SESS#	SESSION TITLE	START	END	ROOM
Thu	102	Positioning your Nuclear Cardiology Laboratory for Long-term Success - Part 1	1:00PM	2:30PM	Empire BC
Thu	104	Positioning your Nuclear Cardiology Laboratory for Long-term Success - Part 2	2:45PM	4:15PM	Empire BC
Fri	211	Ethics in Nuclear Cardiology: A Focus on Informed Consent	12:15PM	1:15PM	New York
Sat	300	ImageGuide Registry Informational Session	6:30AM	7:45AM	Chicago C
Sat	322	Choosing Wisely Challenge	3:15PM	4:15PM	New York

DAY	SESS#	SESSION TITLE	START	END	ROOM
P	**PET**				
Fri	222	How to Establish a Cardiac PET Program	4:00PM	5:30PM	Exhibit Hall B
Sat	306	Imaging in Sarcoidosis (Update on Guidelines)	10:30AM	12:00PM	Atlanta
Sat	317	How to Incorporate PET Myocardial Blood Flow Quantification into Practice	1:30PM	3:00PM	Atlanta
Sat	325	New Directions in Cardiovascular PET	4:00PM	5:30PM	Atlanta
PL	**PLENARY**				
Fri	201	Opening Plenary and Verani Lecture	7:45AM	9:30AM	Exhibit Hall B
Fri	215	Multimodality Imaging in the Diagnosis and Management of Heart Failure	1:30PM	3:00PM	Exhibit Hall B
Sat	301	The Emerging Clinical Challenge of Symptomatic Non-obstructive Coronary Artery Disease	7:55AM	9:30AM	Exhibit Hall B
Sun	401	Controversies in Clinical Cardiology and Cardiac Imaging	8:00AM	9:30AM	Atlanta
PP	**POLICY AND PRACTICE**				
Thu	105	The Changing Face of Medicare: Considerations in Practice and Payment	4:30PM	6:00PM	Chicago
AR	**ABSTRACTS/RESEARCH**				
Thu	106	Rapid Fire ePosters: Disease-based - Amyloidosis	6:15PM	7:15PM	Exhibit Hall A
Fri	202a	ePosters: New Developments in Quality and Appropriate Imaging	9:30AM	10:30AM	Exhibit Hall A
Fri	202b	Posters: Advances in PET Imaging	9:30AM	10:30AM	Exhibit Hall A
Fri	218a	ePosters: Advances in PET Imaging	3:00PM	4:00PM	Exhibit Hall A
Fri	218b	Posters: New Techniques in Myocardial Perfusion Imaging	3:00PM	4:00PM	Exhibit Hall A
Sat	302a	ePosters: New Techniques in Myocardial Perfusion Imaging	9:30AM	10:30AM	Exhibit Hall A
Sat	302b	Posters: New Developments in Quality and Appropriate Imaging	9:30AM	10:30AM	Exhibit Hall A
Sat	327	Featured Research Oral Abstracts	4:30PM	5:30PM	New York
Sat	330	Young Investigator Competition	5:45PM	6:45PM	Chicago C
RE	**READ WITH THE EXPERTS**				
Fri	208	99mcTc-PYP Amyloid Imaging; PET for Inflammation/Infection	10:30AM	12:00PM	Chicago AB
Fri	223	Appropriate Use of Nuclear Stress Imaging	4:00PM	5:30PM	Chicago AB
Sat	307	Imaging for the Detection or Risk Assessment of Stable CAD: Get with the Guidelines	10:30AM	12:00PM	Chicago AB
Sat	318	Viability Assessment (SPECT and PET)	1:30PM	3:00PM	Chicago AB
Sat	326	New Technology in SPECT (Attenuation Correction, CZT)	4:00PM	5:30PM	Chicago AB
Sun	403	PET Perfusion/Myocardial Blood Flow	9:45AM	10:45AM	Chicago AB
T	**TECHNOLOGY & TECHNIQUES**				
Fri	209	Not Just Pushing Buttons	10:30AM	12:00PM	Chicago C
Fri	216	Patients are Different - So are Protocols	1:30PM	3:00PM	Chicago C
Fri	224	RWTE for Technologists	4:00PM	5:30PM	Chicago C
Sat	308	Cardiac PET: Focus on Myocardial Perfusion Imaging	10:30AM	12:00PM	Chicago C
Sat	319	Nuclear Cardiology Beyond Plain Myocardial Perfusion Imaging	1:30PM	3:00PM	Chicago C
Sat	328	Multimodality Imaging	4:00PM	5:30PM	Chicago C

ASNC2017 Schedule by Time

Thursday, September 14, 2017

TYPE	SESS#	SESSION TITLE	START	END	ROOM
C	101	How to Incorporate Test Findings Beyond Perfusion	1:00PM	2:30PM	Chicago
O	102	Positioning your Nuclear Cardiology Laboratory for Long-term Success - Part 1	1:00PM	2:30PM	Empire BC
MI	103	CT, PET/CT and PET/MR Imaging to Assess Heart Disease	2:45PM	4:00PM	Chicago
O	104	Positioning your Nuclear Cardiology Laboratory for Long-term Success - Part 2	2:45PM	4:15PM	Empire BC
PP	105	The Changing Face of Medicare: Considerations in Practice and Payment	4:30PM	6:00PM	Chicago
AR	106	Rapid Fire ePosters: Disease-based - Amyloidosis	6:15PM	7:15PM	Exhibit Hall A
LL	107	ASNC MOC Module 2	7:00PM	9:30PM	New York/Atlanta

Friday, September 15, 2017

PL	201	Opening Plenary and Verani Lecture	7:45AM	9:30AM	Exhibit Hall B
AR	202a	ePosters: New Developments in Quality and Appropriate Imaging	9:30AM	10:30AM	Exhibit Hall A
AR	202b	Posters: Advances in PET Imaging	9:30AM	10:30AM	Exhibit Hall A
CA	203	Cases from the Cleveland Clinic	10:00AM	11:30AM	Empire B
A	205	Imaging to Guide Arrhythmia Management	10:30AM	12:00PM	New York
C	206	Nuclear Cardiology Lab in 2017	10:30AM	12:00PM	Exhibit Hall B
MI	207	Methods and Value of Cardiotoxicity Assessment in Oncologic Disease	10:30AM	12:00PM	Atlanta
RE	208	99mcTc-PYP Amyloid Imaging; PET for Inflammation/Infection	10:30AM	12:00PM	Chicago AB
T	209	Not Just Pushing Buttons	10:30AM	12:00PM	Chicago C
CA	210	Cases from St. Luke's Roosevelt/Mt. Sinai	12:00PM	1:30PM	Empire B
O	211	Ethics in Nuclear Cardiology: A Focus on Informed Consent	12:15PM	1:15PM	Chicago AB
PL	215	Multimodality Imaging in the Diagnosis and Management of Heart Failure	1:30PM	3:00PM	Exhibit Hall B
T	216	Patients are Different - So are Protocols	1:30PM	3:00PM	Chicago C
CA	217	Cases from MMP MaineHealth Cardiology	3:00PM	4:30PM	Empire B
AR	218a	ePosters: Advances in PET Imaging	3:00PM	4:00PM	Exhibit Hall A
AR	218b	Posters: New Techniques in Myocardial Perfusion Imaging	3:00PM	4:00PM	Exhibit Hall A
MI	221	Evaluation of Suspected Coronary Artery Disease in Women: A Comparison of the Different Imaging Modalities	4:00PM	5:30PM	New York
P	222	How to Establish a Cardiac PET Program	4:00PM	5:30PM	Exhibit Hall B
RE	223	Appropriate Use of Nuclear Stress Imaging	4:00PM	5:30PM	Chicago AB
T	224	RWTE for Technologists	4:00PM	5:30PM	Chicago C
I	225	IAEA Global Initiatives - Part 1	4:00PM	5:00PM	Atlanta
I	226	IAEA Global Initiatives - Part 2	5:15PM	6:15PM	Atlanta

TYPE	SESS#	SESSION TITLE	START	END	ROOM

Saturday, September 17, 2017

O	300	ImageGuide Registry Informational Session	6:30AM	7:45AM	Chicago C
PL	301	The Emerging Clinical Challenge of Symptomatic Non-obstructive Coronary Artery Disease	7:55AM	9:30AM	Exhibit Hall B
AR	302a	ePosters: New Techniques in Myocardial Perfusion Imaging	9:30AM	10:30AM	Exhibit Hall A
AR	302b	Posters: New Developments in Quality and Appropriate Imaging	9:30AM	10:30AM	Exhibit Hall A
CA	303	Cases from Brigham & Women's Hospital	10:00AM	11:30AM	Empire B
A	304	Cutting Edge Technologies	10:30AM	12:00PM	New York
C	305	Cardiac Amyloidosis in 2017	10:30AM	12:00PM	Exhibit Hall B
P	306	Imaging in Sarcoidosis (Update on Guidelines)	10:30AM	12:00PM	Atlanta
RE	307	Imaging for the Detection or Risk Assessment of Stable CAD: Get with the Guidelines	10:30AM	12:00PM	Chicago AB
T	308	Cardiac PET: Focus on Myocardial Perfusion Imaging	10:30AM	12:00PM	Chicago C
CA	310	Cases from Brown University	12:00PM	1:30PM	Empire B
A	315	Debate: Clash of the Titans	1:30PM	3:00PM	Exhibit Hall B
C	316	Patient Centered Myocardial Perfusion Imaging	1:30PM	3:00PM	New York
P	317	How to Incorporate PET Myocardial Blood Flow Quantification into Practice	1:30PM	3:00PM	Atlanta
RE	318	Viability Assessment (SPECT and PET)	1:30PM	3:00PM	Chicago AB
T	319	Nuclear Cardiology Beyond Plain Myocardial Perfusion Imaging	1:30PM	3:00PM	Chicago C
CA	321	Cases from Mayo Clinic	3:00PM	4:30PM	Empire B
O	322	Choosing Wisely Challenge	3:15PM	4:15PM	New York
P	325	New Directions in Cardiovascular PET	4:00PM	5:30PM	Atlanta
RE	326	New Technology in SPECT (Attenuation Correction, CZT)	4:00PM	5:30PM	Chicago AB
AR	327	Featured Research Oral Abstracts	4:30PM	5:30PM	New York
T	328	Multimodality Imaging	4:00PM	5:30PM	Chicago C
AR	330	Young Investigator Competition	5:45PM	6:45PM	Chicago C

Sunday, September 17, 2017

PL	401	Controversies in Clinical Cardiology and Cardiac Imaging	8:00AM	9:30AM	Atlanta
A	402	Approach to Known or Potential Ischemic Heart Disease	9:45AM	10:45AM	Atlanta
RE	403	PET Perfusion/Myocardial Blood Flow	9:45AM	10:45AM	Chicago AB
C	404	How Does Radionuclide Imaging Guide Clinical Decision Making?	11:00AM	12:00PM	Atlanta
MI	405	Multimodality Assessment of Complex Cardiovascular Disease	11:00AM	12:00PM	Chicago AB

ASNC Organized Ancillary Sessions

SATURDAY, SEPTEMBER 16

Saturday, 6:30AM – 7:45AM | Chicago C

ImageGuide Registry Informational Session & Discussion

Join us for an informational session on the latest updates for the ImageGuide Registry and how it can be used to improve quality, demonstrate value, and fulfill requirements under The Merit-based Incentive Payment System (MIPS).

FACULTY: Peter Tilkemeier, MD, FASNC
Georgia Lawrence
Joe Reyes
Emmett Chapital, MD, MBBS, FASNC

Saturday, 3:15PM – 4:15PM | New York

Vote for the Winner of the Nuclear Cardiology Choosing Wisely® Challenge

Come listen to live presentations of the three finalists from ASNC's Choosing Wisely® Challenge. Audience voting will combine with a judging panel to select the top prize winner!

- **Minimizing Radiation Exposure from Myocardial Perfusion Imaging**
  Debra Mahlum, CNMT; Maureen Van der Kooy, CNMT; Steven Port, MD
- **A Simplified Approach to Stress-first Nuclear Myocardial Perfusion Imaging: Implementation of ASNC Choosing Wisely Recommendations**
  Randy Jeffrey MD, David E. Winchester MD, FASNC, David C. Wymer MD, Vicente Taasan MD
- **Advanced Protocol Planning in Nuclear Cardiology to Enhance Care Delivery**
  Sarah Cuddy, MB, BCh, BAO, Yin Ge, MD, Ron Blankstein, MD, FASNC, Marcelo DiCarli, MD, Sharmila Dorbala, MD, MPH, FASNC

FACULTY: Raymond R. Russell, III, MD, PhD, FASNC

JUDGES: Renee Bullock-Palmer, MD, FASNC
Maria G. Sciammarella, MD

This activity is supported by Bracco Diagnostics Inc.