The use of the shielding assembly in claim 34 permits to provide in an alternative way an access to the compartment.

In conclusion, the groups of claims are not linked by common or corresponding special technical features and define 4 different inventions not linked by a single general inventive concept. Therefore the application claims 4 inventions not so linked to form a single general inventive concept. The requirement of unity is not fulfilled, according to Rule 13 PCT.

Re Item V

Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1 Reference is made to the following documents:

D1	WO 2005/002971 A1
D2	US 2003/004463 A1
D3	JP 2000 350783 A
D4	WO 2008/037939 A2
D5	WO 2008/082966 A2
D6	EP 0 102 121 A1
D7	JP 2006 325826 A

Novelty Article 33(2) PCT

Invention 1: Claims 1 - 15,37

2 The present application does not meet the criteria of Article 33 (1) PCT, because the subject-matter of **claim 1** is not new in the sense of Article 33(2) PCT.

2.1 The document D1 is regarded as being the closest prior art and discloses (the references in parentheses applying to this document) discloses a shielding assembly for an infusion system, the shielding assembly being mounted within a cabinet structure comprising (figure 1-4):

- a first compartment (30) sized to contain one or more radioisotope generators (34) of the infusion system, the first compartment being enclosed by a first sidewall (sidewall 31) that forms a barrier to radioactive radiation, the first sidewall including an opening extending therethrough and a lid (32), the lid mating with the opening to alternately enclose the first compartment and provide access to the first compartment, via the opening, and the opening being oriented upward and located at a first elevation, with respect to a lowermost portion of the cabinet structure;

- a second compartment (2) sized to contain a portion of an infusion tubing circuit (tubing 57) of the infusion system that is downstream of the one or more generators, the second compartment being enclosed by a second sidewall that forms a barrier to radioactive radiation, the second sidewall including a base portion and a lid portion (9), the lid portion mating with the base portion to alternately enclose the second compartment and provide access to the second compartment; and

- a third compartment (52) sized to contain a waste bottle (53) of the infusion system, the third compartment being enclosed by a third sidewall that forms a barrier to radioactive radiation, the third sidewall including an opening, extending through the third sidewall, and a lid (41), the lid of the third sidewall mating with the opening of the third sidewall to alternately enclose the third compartment and provide access to the third compartment, via the opening of the third sidewall, the opening of the third sidewall being oriented upward and located at a second elevation, with respect to the lowermost portion of the cabinet structure, and the second elevation being greater than the first elevation of the opening of the first sidewall.

The subject matter of claim 1 is not novel document D1.

2.2 The technical feature of claim 37 is also disclosed in Document D1.

2.3 The technical feature of claims 1 and 37 is shown in Documents D2 and D3.

Invention 2: Claims 22-26

3 The present application does not meet the criteria of Article 33 (1) PCT, because the subject-matter of **claim 22** is not new in the sense of Article 33(2) PCT.

3.1 The document D4 is regarded as being the closest prior art and discloses (the references in parentheses applying to this document) discloses a shielding assembly for an infusion system (6) comprising (figure 1-2):

- a plurality of compartments (2a,2b,2c) and providing a radioactive radiation barrier for the compartments, the assembly further comprising:

- a first door (2b) to alternately enclose and provide access to a first compartment of the plurality of compartments, the first compartment sized to contain one or more radioisotope generators (11) of the infusion system; and

- second door (41) to alternately enclose and provide access to a second compartment (2) of the plurality of compartments, the second compartment being separate from, and outside of, the first compartment, the second compartment being sized to contain a portion of an infusion tubing circuit (22) of the infusion system that is downstream of the one or more generators, and the second door, when enclosing the second compartment, preventing the first door from opening to provide access to the first compartment.

The subject matter of claim 22 is not new over document D4.

3.2 The technical feature of claim 1 is revealed in Document D3.

Invention 3: Claims 27-33

4 The present application does not meet the criteria of Article 33 (1) PCT, because the subject-matter of **claim 27** is not new in the sense of Article 33(2) PCT.

4.1 The document D4 is regarded as being the closest prior art and discloses (the references in parentheses applying to this document) discloses an infusion system comprising (figure 1-2):

- a cabinet structure (figure 2) including a shell defining an interior space thereof, the shell including a first opening (21), a second opening (2b) and an access panel (41), the access panel mating with the second opening and being removable therefrom;

- a lock reversibly (it is implicit that the access panel has a lock) engaging the access panel to secure access to the interior space of the cabinet structure;

- an eluant source (16);

- a shielding assembly located within the interior space of the cabinet structure, the shielding assembly including a sidewall defining a plurality of compartments and providing a barrier to radioactive radiation for the compartments, the shielding assembly further including a corresponding plurality of doors (41,2b), each door, when open, providing access to the corresponding compartment via an opening in the sidewall, and, when closed, providing further barrier to radioactive radiation for the corresponding compartment;

- one or more radioisotope generators (11) contained within a first compartment of the plurality of compartments (2c) of the shielding assembly and being accessible through the second opening (2b) of the shell of the cabinet structure, when the access panel (41) is unlocked, and when a first door (2b) of the plurality of doors, which corresponds to the first compartment, is open;

- an eluant line (23) coupled to the eluant source and to the one or more generators; an eluate line coupled to the one or more generators; and a patient line (17) coupled to the eluate line and extending out from the interior space of the cabinet structure through the first opening of the shell.

The subject matter of claim 27 is not new over Document D4.

4.2 The technical feature of claim 27 is disclosed in Document D3.

Invention 4: Claims 34-36

5 The present application does not meet the criteria of Article 33 (1) PCT, because the subject-matter of **claim 34** is not new in the sense of Article 33(2) PCT.

5.1 The document D1 is regarded as being the closest prior art and discloses (the references in parentheses applying to this document) discloses a shielding assembly comprising (figure 1-4):

- a plurality of compartments (2,30) having sidewalls providing barriers to radioactive radiation for the compartments;

- a corresponding plurality of doors (9,32), each door, when open, providing access to the corresponding compartment via an opening in its sidewall, and, when closed, providing further barrier to radioactive radiation for the corresponding compartment;

-a first compartment (2) of the plurality of compartments enclosed by a first sidewall of the sidewalls and sized to contain one or more radioisotope generators (62) of the infusion system, the first sidewall including a first sidewall opening oriented upward and aligned with a first upper opening through a shell of the cabinet structure;

- wherein an upper surface of the shell is located at an elevation, with respect to a lowermost portion of the cabinet structure, such that the elevation of the upper surface is substantially greater than that of the first sidewall opening and the first upper opening (see figure 1)

The subject matter of claim 34 is not new over Document D1.

5.2 Furthermore the technical features of claims 34 are revealed by documents D2,D3 and D6.

Inventive step Article 33(3) PCT

Invention 1: Claims 1 - 15,37

6 The present application does not meet the criteria of Article 33 (1) PCT, because the subject-matter of **claims 2 to 15** does not seem to involve an inventive step in the sense of Article 33(3) PCT. Document D1 is the closest prior art.

In claims 2 to 15 a slight constructional change in the shielding assembly is defined which comes within the scope of the customary practice followed by persons skilled in the art, especially as the advantages thus achieved can readily be foreseen. Consequently, the subject-matter of these claims also lacks an inventive step.

Invention 2: Claims 22-26

7 The present application does not meet the criteria of Article 33 (1) PCT, because the subject-matter of **claims 23 to 26** does not seem to involve an inventive step in the sense of Article 33(3) PCT. Document D4 is the closest prior art.

In claims 23 to 26 a slight constructional change in the shielding assembly is defined which comes within the scope of the customary practice followed by persons skilled in the art, especially as the advantages thus achieved can readily be foreseen. Consequently, the subject-matter of these claims also lacks an inventive step.

Invention 3: Claims 27-33

8 The present application does not meet the criteria of Article 33 (1) PCT, because the subject-matter of **claims 28 to 33** does not seem to involve an inventive step in the sense of Article 33(3) PCT. Document D4 is the closest prior art.

The features of claims 28 to 33 are merely one of several straightforward possibilities from which the skilled person would select, in accordance with circumstances, without the exercise of inventive skill, in order to solve the problem posed. (see Document D7 for using a latch component) Consequently, the subject-matter of these claims also lacks an inventive step.

Invention 4: Claims 34-36

9 The present application does not meet the criteria of Article 33 (1) PCT, because the subject-matter of **claims 35 and 36** does not seem to involve an inventive step in the sense of Article 33(3) PCT. Document D1 is the closest prior art.

In claims 35 and 36 a slight constructional change in the shielding assembly (elevation) is defined which comes within the scope of the customary practice followed by persons skilled in the art, especially as the advantages thus achieved can readily be foreseen. Consequently, the subject-matter of these claims also lacks an inventive step.

Further comments

Invention 1: Claims 1 - 15,37

10 Contrary to the requirements of Rule 5.1(a)(ii) PCT, the **relevant background** art disclosed in the documents D1-D4 are not mentioned in the description, nor are these documents identified therein.

11 Independent claim 1 is not in the **two-part form** in accordance with Rule 6.3 (b) PCT, which in the present case would be appropriate, with those features known in combination from the prior art (document D1) being placed in the preamble (Rule 6.3(b)(I) PCT) and with the remaining features being included in the characterising part (Rule 6.3(b)(ii) PCT).

12 The features of the claims are not provided with **reference signs** placed in parentheses (Rule 6.2(b) PCT).

13 The unit employed in claims 4 and 5 and in description is not recognised in international practice, contrary to the requirements of Rule 10.1(d) PCT.

Invention 2: Claims 22-26

14 Contrary to the requirements of Rule 5.1(a)(ii) PCT, the **relevant background** art disclosed in the documents D3,D4 and D6 are not mentioned in the description, nor are these documents identified therein.

15 Independent claim 22 is not in the **two-part form** in accordance with Rule 6.3 (b) PCT, which in the present case would be appropriate, with those features known in combination from the prior art (document D4) being placed in the preamble (Rule 6.3(b)(I) PCT) and with the remaining features being included in the characterising part (Rule 6.3(b)(ii) PCT).

16 The features of the claims are not provided with **reference signs** placed in parentheses (Rule 6.2(b) PCT).

Invention 3: Claim 27-33

17 Contrary to the requirements of Rule 5.1(a)(ii) PCT, the **relevant background** art disclosed in the documents D3,D4 and D7 are not mentioned in the description, nor are these documents identified therein.

18 Independent claim 27 is not in the **two-part form** in accordance with Rule 6.3 (b) PCT, which in the present case would be appropriate, with those features known in combination from the prior art (document D4) being placed in the preamble (Rule 6.3(b)(I) PCT) and with the remaining features being included in the characterising part (Rule 6.3(b)(ii) PCT).

19 The features of the claims are not provided with **reference signs** placed in parentheses (Rule 6.2(b) PCT).

Invention 4: Claim 34-36

20 Contrary to the requirements of Rule 5.1(a)(ii) PCT, the **relevant background** art disclosed in the documents D1,D2,D3 and D6 are not mentioned in the description, nor are these documents identified therein.

21 Independent claim 34 is not in the **two-part form** in accordance with Rule 6.3 (b) PCT, which in the present case would be appropriate, with those features known in combination from the prior art (document D1) being placed in the preamble (Rule 6.3(b)(I) PCT) and with the remaining features being included in the characterising part (Rule 6.3(b)(ii) PCT).

22 The features of the claims are not provided with **reference signs** placed in parentheses (Rule 6.2(b) PCT).

23 The unit employed in claims 35 and 36 and in description is not recognised in international practice, contrary to the requirements of Rule 10.1(d) PCT.

Re Item VI

Certain documents cited

Certain published documents

Application No Patent No	Publication date *(day/month/year)*	Filing date *(day/month/year)*	Priority date *(valid claim)* *(day/month/year)*
WO2008082966	10.07.2008	20.12.2007	31.10.2007

Document D5 discloses the technical feature of claims 1,22,27 and 34. This document will be considered during the European phase.

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference 56782.1.6.1	**FOR FURTHER ACTION**	see Form PCT/ISA/220 as well as, where applicable, item 5 below.
International application No. PCT/US2009/047030	International filing date *(day/month/year)* 11/06/2009	(Earliest) Priority Date *(day/month/year)* 11/06/2008
Applicant BRACCO DIAGNOSTICS INC.		

This international search report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This international search report consists of a total of 6 sheets.

[X] It is also accompanied by a copy of each prior art document cited in this report.

1. **Basis of the report**
   a. With regard to the **language**, the international search was carried out on the basis of:
      - [X] the international application in the language in which it was filed
      - [ ] a translation of the international application into ______, which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1(b))

   b. [ ] This international search report has been established taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 (Rule 43.6*bis*(a)).

   c. [ ] With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, see Box No. I.

2. [ ] **Certain claims were found unsearchable** (See Box No. II)

3. [X] **Unity of invention is lacking** (see Box No III)

4. With regard to the **title**,
   - [X] the text is approved as submitted by the applicant
   - [ ] the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,
   - [X] the text is approved as submitted by the applicant
   - [ ] the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority

6. With regard to the **drawings**,
   a. the figure of the **drawings** to be published with the abstract is Figure No. 1d
      - [ ] as suggested by the applicant
      - [X] as selected by this Authority, because the applicant failed to suggest a figure
      - [ ] as selected by this Authority, because this figure better characterizes the invention

   b. [ ] none of the figures is to be published with the abstract

Form PCT/ISA/210 (first sheet) (April 2007)

International application No
PCT/US2009/047030

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61M5/00
ADD. A61M5/14

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

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
A61M

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

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, INSPEC

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	FR 2 867 084 A1 (GEN ELECTRIC [US]) 9 September 2005 (2005-09-09) figures 1-12 page 6, line 16 - page 30, line 11	1-2,5-9
X	EP 0 102 121 A1 (BYK MALLINCKRODT CIL BV [NL]) 7 March 1984 (1984-03-07) figures 1-4 page 9, line 15 - page 12, line 11	1,5-9, 17-25, 27-32, 36-38
X	WO 99/56117 A1 (GEN HOSPITAL CORP [US]; LAYFIELD DOMINICK [US]; VENEGAS JOSE [US]) 4 November 1999 (1999-11-04) page 4, line 20 - page 16, line 13; figures 1-6	1-3, 15-17, 31-38

-/--

[X] Further documents are listed in the continuation of Box C.

[X] See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
10 February 2010	17/02/2010

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Reinbold, Sylvie

2

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 0 160 303 A2 (SQUIBB & SONS INC [US]) 6 November 1985 (1985-11-06) figures 1-12 page 7, line 28 - line 15	1-2
X	JP 2000 350783 A (SUMITOMO HEAVY INDUSTRIES) 19 December 2000 (2000-12-19) paragraph [0014] - paragraph [0032]; figures 1-5	18-25, 27-30
X	US 2008/093564 A1 (TARTAGLIA DANIEL [CA] ET AL) 24 April 2008 (2008-04-24) figures 1-7 paragraph [0023] - paragraph [0035]	18-30
X	WO 2007/149108 A2 (MALLINCKRODT INC [US]; POLLARD RALPH E JR [US]) 27 December 2007 (2007-12-27) figures 1-18 paragraph [0031] - paragraph [0053]	18-30
X	US 2003/004463 A1 (REILLY DAVID M [US] ET AL) 2 January 2003 (2003-01-02) paragraph [0049] - paragraph [0072]; figures 1-4	31-38

2

INTERNATIONAL SEARCH REPORT	International application No. PCT/US2009/047030

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. [X] As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fees, this Authority did not invite payment of additional fees.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.

☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.

[X] No protest accompanied the payment of additional search fees.

Form PCT/ISA/210 (continuation of first sheet (2)) (April 2005)

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-17

   These claims essentially define an infusion system comprising an eluant source, a shielding assembly having a plurality of compartments and plurality of doors, a radioisotope generator, a eluate line and a patient line. (technical effect: to provide an infusion system to infuse an radioactive eluate)

   ---

2. claims: 18-30

   These claims essentially define a shielding assembly comprising a sidewall defining a plurality of compartments, a first passageway formed in an upper surface of a first portion of the sidewall and defining a first compartment sized to contain a radioisotope and a second passageway with a second compartment.
   (technical effect: to provide a shielding assembly to permit a more effective operation)

   ---

3. claims: 31-38

   These claims essentially define a disposable infusion circuit subassembly comprising: an eluate line, a patient line, a waste line, a valve member and a support frame. (technical effect: to facilitate the positioning of the components of a portion of infusion circuit in an infusion system)

Information on patent family members

International application No
PCT/US2009/047030

Patent document cited in search report		Publication date	Patent family member(s)			Publication date
FR 2867084	A1	09-09-2005	DE	102005010152	A1	15-09-2005
			DE	102005010154	A1	15-09-2005
			FR	2867294	A1	09-09-2005
			JP	2005326398	A	24-11-2005
			JP	2005324007	A	24-11-2005
			US	2008242915	A1	02-10-2008
EP 0102121	A1	07-03-1984	NONE			
WO 9956117	A1	04-11-1999	EP	1075654	A1	14-02-2001
			US	6773673	B1	10-08-2004
EP 0160303	A2	06-11-1985	AU	581218	B2	16-02-1989
			CA	1250504	A1	28-02-1989
			CA	1233274	A2	23-02-1988
			DE	3581653	D1	14-03-1991
			JP	2568169	B2	25-12-1996
			JP	60241454	A	30-11-1985
			US	4562829	A	07-01-1986
JP 2000350783	A	19-12-2000	NONE			
US 2008093564	A1	24-04-2008	WO	2009003290	A1	08-01-2009
WO 2007149108	A2	27-12-2007	CA	2627429	A1	27-12-2007
			CN	101253577	A	27-08-2008
			EP	1938339	A2	02-07-2008
			JP	2009506343	T	12-02-2009
			US	2008224065	A1	18-09-2008
US 2003004463	A1	02-01-2003	US	2005238576	A1	27-10-2005
			US	2003216609	A1	20-11-2003

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY
(PCT Rule 43*bis*.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/US2009/047030	11.06.2009	11.06.2008

International Patent Classification (IPC) or both national classification and IPC
INV. A61M5/00
ADD. A61M5/14

Applicant
BRACCO DIAGNOSTICS INC.

1. This opinion contains indications relating to the following items:

☒ Box No. I Basis of the opinion
☐ Box No. II Priority
☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
☒ Box No. IV Lack of unity of invention
☒ Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
☐ Box No. VI Certain documents cited
☐ Box No. VII Certain defects in the international application
☒ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notifed the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:	Date of completion of this opinion	Authorized Officer
European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Fax: +49 89 2399 - 4465	see form PCT/ISA/210	Reinbold, Sylvie Telephone No. +49 89 2399-7918

Form PCT/ISA/237 (Cover Sheet) (April 2005)

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of:

   ☒ the international application in the language in which it was filed

   ☐ a translation of the international application into , which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1 (b)).

2. ☐ This opinion has been established taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 (Rule 43bis.1(a))

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

   a. type of material:

      ☐ a sequence listing

      ☐ table(s) related to the sequence listing

   b. format of material:

      ☐ on paper

      ☐ in electronic form

   c. time of filing/furnishing:

      ☐ contained in the international application as filed.

      ☐ filed together with the international application in electronic form.

      ☐ furnished subsequently to this Authority for the purposes of search.

4. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

5. Additional comments:

Box No. IV Lack of unity of invention

1. ☒ In response to the invitation (Form PCT/ISA/206) to pay additional fees, the applicant has, within the applicable time limit:

   ☒ paid additional fees

   ☐ paid additional fees under protest and, where applicable, the protest fee

   ☐ paid additional fees under protest but the applicable protest fee was not paid

   ☐ not paid additional fees

2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose not to invite the applicant to pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rule 13.1, 13.2 and 13.3 is

   ☐ complied with

   ☒ not complied with for the following reasons:

   see separate sheet

4. Consequently, this report has been established in respect of the following parts of the international application:

   ☐ all parts.

   ☒ the parts relating to claims Nos. 1-38

Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	4, 10-14, 24-26, 29-30, 33, 35
	No:	Claims	1-3, 5-9, 15-23, 27-28, 31-32, 34, 36-38
Inventive step (IS)	Yes:	Claims	4, 10-14
	No:	Claims	1-3, 5-9, 15-38
Industrial applicability (IA)	Yes:	Claims	1-38
	No:	Claims	

2. Citations and explanations

see separate sheet

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

Re Item IV

Lack of unity of invention

The inventions in this international application, as follows:

1. Claims 1 - 17

These claims essentially define an infusion system comprising an eluant source, a shielding assembly having a plurality of compartments and plurality of doors, a radioisotope generator, a eluate line and a patient line.

(technical effect: to provide an infusion system to infuse an radioactive eluate)

2. Claims 18-30:

These claims essentially define a shielding assembly comprising a sidewall defining a plurality of compartments, a first passageway formed in an upper surface of a first portion of the sidewall and defining a first compartment sized to contain a radioisotope and a second passageway with a second compartment.

(technical effect: to provide a shielding assembly to permit a more effective operation)

3. Claims 31-38:

These claims essentially define a disposable infusion circuit subassembly comprising: an eluate line, a patient line, a waste line, a valve member and a support frame.

(technical effect: to facilitate the positioning of the components of a portion of infusion circuit in an infusion system)

The only common concept between the invention 1 and 2 is a shielding assembly having a plurality of compartments. This is already known from the person skilled in the art. (FR2867084)

The only common concept between the invention 1 and 3 is an eluate line and a patient line. This is already know from the person skilled in the art. (FR2867084)

There is no common concept between the invention 2 and 3.

The special technical features are not identical. The effects of both compounds are different. The problems posed when using a shielding assembly and a disposable infusion circuit subassembly are also quite different. Consequently the special technical features cannot be regarded as being corresponding. Therefore the application claims 3 inventions not so linked to form a single general inventive concept. The requirement of unity is not fulfilled, according to Rule 13PCT.

Re Item V

Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1 Reference is made to the following documents:

D1 FR 2 867 084 A1

D2	EP 0 102 121 A1
D3	WO 99/56117 A1
D4	EP 0 160 303 A2
D5	JP 2000 350783 A
D6	US 2008/093564 A1
D7	WO 2007/149108 A2
D8	US 2003/004463 A1

Novelty Article 33(2) PCT

Invention 1: Claims 1 - 17

2 The present application does not meet the criteria of Article 33 (1) PCT, because the subject-matter of claims **1-3,5-9 and 15-17** is not new in the sense of Article 33(2) PCT.

2.1 The document D1 is regarded as being the closest prior art and discloses (the references in parentheses applying to this document) discloses an infusion system comprising:

- a cabinet structure (page 20 line 25-30) including a shell defining an interior space thereof;

- an eluant source (412)

- a shielding assembly (509+404) located within the interior space of the cabinet structure, the shielding assembly including a sidewall defining a plurality of compartments (509,404,418) and providing a barrier to radioactive radiation for the compartments, the shielding assembly further including a corresponding plurality of doors, each door, when open, providing access to the corresponding compartment via an opening in the sidewall, and, when closed, providing further barrier to radioactive radiation for the corresponding compartment;

- radioisotope generator (502)contained within a first compartment (509) of the plurality of compartments of the shielding assembly;

- an eluant line (figure 6)coupled to the eluant source (412) and to the generator (104,502), the eluant line extending from the eluant source to the generator, through the shielding assembly, at a first location between the sidewall and a first door of the plurality of doors, which first door corresponds to the first compartment;

- an eluate line coupled to the generator and extending out from the first compartment and into a second compartment (418) of the plurality of compartments of the shielding assembly, at a second location between the sidewall and both the first door and a second door of the plurality of doors, which corresponds to the second compartment, the second compartment being located immediately adjacent the first compartment;

- a patient line (428) coupled to the eluate line, within the second compartment, the patient line extending out from the second compartment at a third location between the sidewall and the second door, and out from the interior space through an opening in the shell of the cabinet structure.

The subject matter of claim 1 is not novel document D1.

2.2 Document D1 shows the technical features of claims 2 and 5 to 9.

2.3 Furthermore document D2 reveals the technical features of claims 1,5-9 and 17. (figure 1 to 4)

2.4 The technical features of claims 1-3 and 15-17 are disclosed in document D3.

2.5 Finally document D4 shows the technical features of claims 1 and 2.

Invention 2: Claims 18-30

3 Furthermore, the above-mentioned lack of clarity notwithstanding, the subject-matter of **claim 18-23 and 27-28** is not new in the sense of Article 33(2) PCT, and therefore the criteria of Article 33(1) PCT are not met.

3.1 The document D5 is regarded as being the closest prior art and discloses (the references in parentheses applying to this document) discloses a shielding assembly (40+84) comprising:

- a sidewall defining a plurality of compartments and providing a radioactive radiation barrier for the compartments;

- a first passageway (bore between wagon (40) and casing (52)) formed in an upper surface of a first portion of the sidewall, the first portion of the sidewall defining a first compartment (62) of the plurality of compartments, the first compartment being sized to contain a radioisotope generator (30) of the infusion system, and the first passageway (bore) being sized to accommodate routing of an eluate line (see figure 2) from the generator;

- a second passageway (passage for the tube 80) formed along a second portion of the sidewall, the second portion of the sidewall extending upward relative to the first portion of the sidewall and defining a second compartment (84) of the plurality of compartments, the second compartment (84) being sized to accommodate a waste bottle (82) of the infusion system and the second compartment being located on a side of the second portion of the sidewall that is opposite the second passageway, and the second passageway being sized to accommodate routing of at least one extension of the eluate line (see figure 5) from the generator.

The subject matter of claim 18 is not novel document D5.

3.2 Document D5 shows the technical features of claims 18-23,27 and 28.

3.3 The document D2 discloses a shielding assembly (41+26) comprising:

- a sidewall defining a plurality of compartments and providing a radioactive radiation barrier for the compartments;

- a first passageway (bore 32) formed in an upper surface of a first portion of the sidewall, the first portion of the sidewall defining a first compartment (26) of the plurality of compartments, the first compartment being sized to contain a radioisotope generator (31) of the infusion system, and the first passageway (32) being sized to accommodate routing of an eluate line (see figure 1) from the generator;

- a second passageway (passage between the shield (26) and cover (43)) formed along a second portion of the sidewall, the second portion of the sidewall extending upward relative to the first portion of the sidewall and defining a second compartment (41) of the plurality of compartments, the second compartment (41) being sized to accommodate a waste bottle (12a) of the infusion system and the second compartment being located on a side of the second portion of the sidewall that is opposite the second passageway, and the second passageway being sized to accommodate routing of at least one extension of the eluate line (see figure 1) from the generator.

The subject matter of claim 18 is not novel document D2.

3.4 Document D2 shows the technical features of claims 18-21,27 and 28.

3.5 Furthermore documents D6 and D7 reveal the technical features of claim 18.

Invention 3: Claims 31-38

4 The present application does not meet the criteria of Article 33 (1) PCT, because the subject-matter of **claims 31,32,34 and 36-38** is not new in the sense of Article 33(2) PCT.

4.1 The document D8 is regarded as being the closest prior art and discloses (the references in parentheses applying to this document) discloses a disposable infusion circuit comprising (figures 1-5):

- an eluate line (line from the syringe (20)) ;

- a patient line (100);

- a waste line (line in connection with waste (161));

- a valve member (171) coupling the patient line and the waste line to the eluate line; and

- a support frame (15) including a perimeter edge, the support frame holding the valve member (16) and a portion of each of: the eluate line, the patient line and the waste line in approximately fixed relation with respect to the perimeter edge;

- wherein the perimeter edge of the support frame is sized to fit within a compartment of a shielding assembly (18) of the infusion system; and

- an end of each of the eluate line, the patient line and the waste line extends out from the perimeter edge.

Therefore the subject matter of claim 31 is not novel over document D8.

4.2 Document D8 shows the technical features of claims 32,34 and 36-38.

4.3 Furthermore documents D2 and D3 reveal the technical features of claims 31,32 and 36-38.

Document D2: (figures 1 to 5), eluate line (6), patient line (line next to the valve 4b), waste line (11a), valve member (4b), support frame (operating block 46)

Document D3: (figures 1 to 56, eluate line (saline), patient line (to patient), waste line (dump), valve member (27), support frame (figure 5a-5c)

Inventive step Article 33(3) PCT

Invention 1: Claims 1 - 17

5 The present application does not meet the criteria of Article 33 (1) PCT, because the subject- matter of **claims 4 and 10 to 14** does not seem to involve an inventive step in the sense of Article 33(3) PCT. Document D1 is the closest prior art. In claims 4 and 10 to 14 a slight constructional change in the infusion system is defined which comes within the scope of the customary practise followed by persons skilled in the art, especially as the advantages thus achieved can readily be foreseen. Consequently, the subject- matter of these claims also lacks an inventive step.

Invention 2: Claims 18-30

6 The present application does not meet the criteria of Article 33 (1) PCT, because the subject- matter of **claims 24-26,29 and 30** does not seem to involve an inventive step in the sense of Article 33(3) PCT. Document D2 is the closest prior art. In claims 24-26,29 and 30 a slight constructional change in the shielding assembly is defined which comes within the scope of the

customary practise followed by persons skilled in the art, especially as the advantages thus achieved can readily be foreseen. Consequently, the subject-matter of these claims also lacks an inventive step.

Invention 3: Claims 31-38

7 The present application does not meet the criteria of Article 33 (1) PCT, because the subject-matter of **claims 33 and 35** does not seem to involve an inventive step in the sense of Article 33(3) PCT. Document D8 is the closest prior art. In claims 33 and 35 a slight constructional change in the disposable infusion circuit (eluant line extends out from a third side of the perimeter edge) is defined which comes within the scope of the customary practise followed by persons skilled in the art, especially as the advantages thus achieved can readily be foreseen. Consequently, the subject- matter of these claims also lacks an inventive step.

Further comments

Invention 1: Claims 1 - 17

8 Contrary to the requirements of Rule 5.1(a)(ii) PCT, the **relevant background** art disclosed in the documents D1-D4 are not mentioned in the description, nor are these documents identified therein.

9 Independent claim 1 is not in the **two-part form** in accordance with Rule 6.3 (b) PCT, which in the present case would be appropriate, with those features known in combination from the prior art (document D1) being placed in the preamble (Rule 6.3(b)(I) PCT) and with the remaining features being included in the characterising part (Rule 6.3(b)(ii) PCT).

10 The features of the claims are not provided with **reference signs** placed in parentheses (Rule 6.2(b) PCT).

Invention 2: Claims 18-30

11 Contrary to the requirements of Rule 5.1(a)(ii) PCT, the **relevant background** art disclosed in the documents D2,D5-D7 are not mentioned in the description, nor are these documents identified therein.

12 Independent claim 18 is not in the **two-part form** in accordance with Rule 6.3 (b) PCT, which in the present case would be appropriate, with those features known in combination from the prior art (document D5) being placed in the preamble (Rule 6.3(b)(I) PCT) and with the remaining features being included in the characterising part (Rule 6.3(b)(ii) PCT).

13 The features of the claims are not provided with **reference signs** placed in parentheses (Rule 6.2(b) PCT).

Invention 3: Claims 31-38

14 Contrary to the requirements of Rule 5.1(a)(ii) PCT, the **relevant background** art disclosed in the documents D2,D3 and D8 are not mentioned in the description, nor are these documents identified therein.

15 Independent claim 31 is not in the **two-part form** in accordance with Rule 6.3 (b) PCT, which in the present case would be appropriate, with those features known in combination from the prior art (document D8) being placed in the preamble (Rule 6.3(b)(I) PCT) and with the remaining features being included in the characterising part (Rule 6.3(b)(ii) PCT).

16 The features of the claims are not provided with **reference signs** placed in parentheses (Rule 6.2(b) PCT).

Re Item VIII

Certain observations on the international application

Invention 2: Claims 18-30

Clarity Article 6 PCT

17 Although **claims 18 and 27** have been drafted as separate independent claims, they appear to relate effectively to the same subject-matter and to differ from each other only with regard to the definition of the subject-matter for which protection is sought.

The aforementioned claims therefore lack conciseness. Moreover, lack of clarity ofthe claims as a whole arises, since the plurality of independent claims makes it difficult, if not impossible, to determine the matter for which protection is sought, and places an undue burden on others seeking to establish the extent of the protection.

Hence, these claims do not appear to meet the requirements of Article 6 PCT.

It appears to be appropriate to file an amended set of claims taking account of the above comments and Article 34(2)(b) PCT. The revelant subjecr-matter should be defined in **a single independent claim** followed by dependent claims covering features which are merely optional (Rules 6.3 and 6.4 PCT)

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference 56782.1.7.1	**FOR FURTHER ACTION** see Form PCT/ISA/220 as well as, where applicable, item 5 below.	
International application No. PCT/US2009/047031	International filing date *(day/month/year)* 11/06/2009	(Earliest) Priority Date *(day/month/year)* 11/06/2008
Applicant BRACCO DIAGNOSTICS INC.		

This international search report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This international search report consists of a total of 7 sheets.

[X] It is also accompanied by a copy of each prior art document cited in this report.

1. **Basis of the report**
   a. With regard to the **language**, the international search was carried out on the basis of:
      [X] the international application in the language in which it was filed
      [ ] a translation of the international application into ____________, which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1(b))
   b. [ ] This international search report has been established taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 (Rule 43.6*bis*(a)).
   c. [ ] With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, see Box No. I.

2. [X] **Certain claims were found unsearchable** (See Box No. II)

3. [X] **Unity of invention is lacking** (see Box No III)

4. With regard to the **title**,
   [ ] the text is approved as submitted by the applicant
   [X] the text has been established by this Authority to read as follows:
   INFUSION SYSTEMS INCLUDING COMPUTER-FACILITATED MAINTENANCE AND/OR OPERATION

5. With regard to the **abstract**,
   [X] the text is approved as submitted by the applicant
   [ ] the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority

6. With regard to the **drawings**,
   a. the figure of the **drawings** to be published with the abstract is Figure No. 1d
      [ ] as suggested by the applicant
      [X] as selected by this Authority, because the applicant failed to suggest a figure
      [ ] as selected by this Authority, because this figure better characterizes the invention
   b. [ ] none of the figures is to be published with the abstract

Form PCT/ISA/210 (first sheet) (April 2007)

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61M5/00
ADD. A61M5/14

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

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
A61M

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

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, INSPEC

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 0 310 148 A2 (SQUIBB & SONS INC [US]) 5 April 1989 (1989-04-05) figures 1-6 column 3, line 37 - column 15, line 43	1-5
X	US 2007/140958 A1 (DEKEMP ROBERT A [CA]) 21 June 2007 (2007-06-21) figures 1-5 paragraph [0003] paragraph [0018] - paragraph [0035]	1-5
X	WO 2006/129301 A2 (SPECTRUM DYNAMICS [IL]; ROUSSO BENNY [IL]; BEN-HAIM SHLOMO [GB]; BRONS) 7 December 2006 (2006-12-07) figures 1-14 page 40, line 3 - page 41, line 16 page 90, line 10 - page 97, line 26	1

-/--

[X] Further documents are listed in the continuation of Box C.

[X] See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance
"E" earlier document but published on or after the international filing date
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed

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

Date of the actual completion of the international search	Date of mailing of the international search report
12 February 2010	01/03/2010

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Reinbold, Sylvie

2

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2007/213848 A1 (DEKEMP ROBERT A [CA] ET AL) 13 September 2007 (2007-09-13) figures 1-8 paragraph [0006] paragraph [0024] - paragraph [0056] -----	1-7, 32-35
X	NEIL J. EPSTEIN, AHMED BENELFASSI, ROB S.B. BEANLANDS, ROBERT A. DEKEMP: "A Rb82 infusion system for quantitative perfusion imaging with 3D PET" APPLIED RADIATION AND ISOTOPES, vol. 60, 9 February 2004 (2004-02-09), pages 921-927, XP002557544 DOI: 10.1016/j.apradiso.2004.02.002 the whole document -----	1-7, 32-35
X	R KLEIN, A ADLER, R S BEANLANFS AND R A DEKEMP: "Precision controlled elution of a Sr82/Rb82 generator for cardiac perfusion imaging with positron emission tomography" PHYSICS IN MEDICINE AND BIOLOGY, vol. 52, 11 January 2007 (2007-01-11), pages 659-673, XP002557545 DOI: 10.1088/0031-9155/52/3/009 the whole document -----	1-7, 32-35
X	WO 2008/028165 A2 (CATHOLIC HEALTHCARE WEST D B A [US]; DESHMUKH VIVEK R [US]; CRAWFORD N) 6 March 2008 (2008-03-06) paragraph [0060]; figures 1-5 -----	30-31

2

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box II.1

Claims Nos.: 8-29, 36

The methods of claims 8 to 29 for operating an infusion system is carried out within a human body. As stated in the claims, the method is during a medical therapy. Furthermore the method of claim 36 for purging a tubing circuit of an infusion system with air is carried out within a human body. As stated in the claim, the method is during a medical therapy. These methods are forming part of a therapeutic procedure and can therefore not be regarded as an invention which is susceptible of industrial application. The application does not meet the requirement of Rule 39.1 (iv), because these claims are a method of treatment of the human body.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2009/047031

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.: 8-29, 36
because they relate to subject matter not required to be searched by this Authority, namely:

see FURTHER INFORMATION sheet PCT/ISA/210

2. [ ] Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. [X] As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fees, this Authority did not invite payment of additional fees.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.

[ ] The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.

[X] No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-5

   These claims essentially define an infusion system with an eluant reservoir, a pump, a radioisotope generator, an activity detector, a waste bottle, a computer,an eluant line and an user interface.
   (technical effect: to provide an infusion pump which permits a quality control of a dose)

   ---

2. claims: 6-7

   These claims essentially define an infusion system with an eluate line, a pump, an activity sensor, a waste bottle, a computer, a patient line, a by pass line coupled to the eluant line via a divergence valve and a radiosotope generator.
   (technical effect: to provide an infusion system which permits to flush or to push any eluate remaining in patient line)

   ---

3. claims: 30-35

   These claims essentially define a computer readable medium.
   (technical effect: to execute computer instructions)

International application No
PCT/US2009/047031

Patent document cited in search report		Publication date	Patent family member(s)			Publication date
EP 0310148	A2	05-04-1989	AT	53305	T	15-06-1990
			AU	570429	B2	17-03-1988
			CA	1237539	A1	31-05-1988
			DE	3482410	D1	12-07-1990
			EP	0117752	A2	05-09-1984
			JP	5249245	A	28-09-1993
			JP	1856747	C	07-07-1994
			JP	5062314	B	08-09-1993
			JP	59163584	A	14-09-1984
			US	4585941	A	29-04-1986
			US	4585009	A	29-04-1986
US 2007140958	A1	21-06-2007	AU	2006326814	A1	28-06-2007
			CA	2562340	A1	21-06-2007
			WO	2007071022	A1	28-06-2007
			EP	1973624	A1	01-10-2008
			JP	2009520953	T	28-05-2009
WO 2006129301	A2	07-12-2006	CA	2610256	A1	07-12-2006
			EP	1891597	A2	27-02-2008
US 2007213848	A1	13-09-2007	AU	2007224955	A1	20-09-2007
			CA	2562453	A1	10-09-2007
			WO	2007104133	A1	20-09-2007
			EP	1996276	A1	03-12-2008
			JP	2009529682	T	20-08-2009
			KR	20090071512	A	01-07-2009
WO 2008028165	A2	06-03-2008	NONE			

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To: see form PCT/ISA/220	PCT WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY (PCT Rule 43*bis*.1)
	Date of mailing *(day/month/year)* see form PCT/ISA/210 (second sheet)
Applicant's or agent's file reference see form PCT/ISA/220	**FOR FURTHER ACTION** See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/US2009/047031	11.06.2009	11.06.2008

International Patent Classification (IPC) or both national classification and IPC
INV. A61M5/00
ADD. A61M5/14

Applicant
BRACCO DIAGNOSTICS INC.

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☒ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☒ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notifed the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:	Date of completion of this opinion	Authorized Officer
European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Fax: +49 89 2399 - 4465	see form PCT/ISA/210	Reinbold, Sylvie Telephone No. +49 89 2399-7918

Form PCT/ISA/237 (Cover Sheet) (April 2005)

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US2009/047031

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of:

   ☒ the international application in the language in which it was filed

   ☐ a translation of the international application into , which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1 (b)).

2. ☐ This opinion has been established taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 (Rule 43bis.1(a))

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

   a. type of material:

      ☐ a sequence listing

      ☐ table(s) related to the sequence listing

   b. format of material:

      ☐ on paper

      ☐ in electronic form

   c. time of filing/furnishing:

      ☐ contained in the international application as filed.

      ☐ filed together with the international application in electronic form.

      ☐ furnished subsequently to this Authority for the purposes of search.

4. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

5. Additional comments:

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US2009/047031

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of

☐ the entire international application

☒ claims Nos. 8-29, 36

because:

☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international search *(specify)*:

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed *(specify)*:

☒ no international search report has been established for the whole application or for said claims Nos. 8-29, 36

☐ a meaningful opinion could not be formed without the sequence listing; the applicant did not, within the prescribed time limit:

- ☐ furnish a sequence listing on paper complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Searching Authority in a form and manner acceptable to it.
- ☐ furnish a sequence listing in electronic form complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Searching Authority in a form and manner acceptable to it.
- ☐ pay the required late furnishing fee for the furnishing of a sequence listing in response to an invitation under Rules 13*ter*.1(a) or (b).

☐ a meaningful opinion could not be formed without the tables related to the sequence listings; the applicant did not, within the prescribed time limit, furnish such tables in electronic form complying with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions, and such tables were not available to the International Searching Authority in a form and manner acceptable to it.

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in electronic form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See Supplemental Box for further details

Box No. IV Lack of unity of invention

1. ☒ In response to the invitation (Form PCT/ISA/206) to pay additional fees, the applicant has, within the applicable time limit:

   ☒ paid additional fees

   ☐ paid additional fees under protest and, where applicable, the protest fee

   ☐ paid additional fees under protest but the applicable protest fee was not paid

   ☐ not paid additional fees

2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose not to invite the applicant to pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rule 13.1, 13.2 and 13.3 is

   ☐ complied with

   ☒ not complied with for the following reasons:

   see separate sheet

4. Consequently, this report has been established in respect of the following parts of the international application:

   ☒ all parts.

   ☐ the parts relating to claims Nos. 1-5

Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	7, 35
	No:	Claims	1-6, 30-34
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-7, 30-35
Industrial applicability (IA)	Yes:	Claims	1-7, 30-35
	No:	Claims	

2. Citations and explanations

   see separate sheet

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

Re Item III

Non- establishment of opinion with regard to novelty, inventive step and industrial applicability

The methods of **claims 8 to 29** for operating an infusion system is carried out within a human body. As stated in the claims, the method is during a medical therapy.

Furthermore the method of **claim 36** for purging a tubing circuit of an infusion system with air is carried out within a human body. As stated in the claim, the method is during a medical therapy.

These methods are forming part of a therapeutic procedure and can therefore not be regarded as an invention which is susceptible of industrial application. The application does not meet the requirement of Rule 39.1 (iv), because these claims are a method of treatment of the human body. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject matter of theses claims. (Article 34 (4)(a)(i)PCT)

Re Item IV

Lack of unity of invention

The inventions in this international application, as follows:

1. Claims 1-5

These claims essentially define an infusion system with an eluant reservoir, a pump, a radioisotope generator, an activity detector, a waste bottle, a computer,an eluant line and an user interface. (technical effect: to provide an infusion pump which permits a quality control of a dose)

2. Claims 6-7

These claims essentially define an infusion system with an eluate line, a pump, an activity sensor, a waste bottle, a computer, a patient line, a by pass line coupled to the eluant line via a divergence valve and a radioisotope generator. (technical effect: to provide an infusion system which permits to flush or to push any eluate remaining in patient line)

3. Claims 30-35:

These claims essentially define a computer readable medium. (technical effect: to execute computer instructions)

The only common concept between the invention 1 and 2 is an infusion system comprising an eluant reservoir, a pump, a radioisotope generator, an activity detector, a waste bottle, a computer and an eluant line. This is already known from the person skilled in the art. (EP0310148)

There is no common concept between the invention 1 and 3 and 2 and 3.

The special technical features are not identical. The effects of both compounds are different. The use of the infusion system in claim 6 is to flush or push any eluate remaining in the patient line. The use of a computer readable medium is to execute computer instructions.

The groups of claims are not linked by common or corresponding special technical features and define 3 different inventions not linked by a single general inventive concept. Therefore the application claims 3 inventions not so linked to form a single general inventive concept. The requirement of unity is not fulfilled, according to Rule 13 PCT.

Re Item V

Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1 Reference is made to the following documents:

D1	EP 0 310 148
D2	US 2007/140958
D3	WO 2006/129301
D4	US 2007/213848
D5	NEIL J. EPSTEIN "A Rb82 infusion system for quantitative perfusion imaging with 3D PET"
D6	R KLEIN "Precision controlled elution of a Sr82/Rb82 generator for cardiac perfusion imaging with positron emission tomography"
D7	WO2008/028165

Novelty Article 33(2) PCT

Invention 1: Claims 1 - 5

2 Furthermore, the above-mentioned lack of clarity notwithstanding, the subject-matter of **claims 1 to 5** is not new in the sense of Article 33(2) PCT, and therefore the criteria of Article 33(1) PCT are not met.

2.1 The document D1 is regarded as being the closest prior art and discloses (the references in parentheses applying to this document) an infusion system comprising (figure 1-6):

-an eluant reservoir (10) , a pump (64) coupled to the reservoir, an infusion tubing circuit (26,30,44,38), a radioisotope generator (28), an activity detector (58), a waste bottle (42) and a computer (60);

- the infusion tubing circuit including an eluant line (26) coupled to the pump and to the generator and an eluate line (30) coupled to the generator and to the activity detector; and the computer being coupled to a user interface (figure 2), to the pump and to the activity detector and being preprogrammed to receive input from a user of the system, via the user interface, to collect information, from the pump and the activity detector, and to provide output to the user, via the user interface (column 6 line 12 to 42), according to a method, the method comprising

- activating the pump to pump a volume of eluant from the reservoir, through the eluant line and through the generator, in order to generate a sample or a dose of eluate in the eluate line, via an elution within the generator, the sample (probe 58) being intended for a quality control measurement, and the dose being intended for diagnostic imaging;

- providing an indication, via the computer interface, that the elution is completed, when the pump has completed pumping the volume of eluant through the generator; and

- providing an indication, via the computer interface, of a time lapse since the elution was completed.

The subject matter of claim 1 is not novel document D1.

2.2 Document D1 shows the technical features of claims 2 to 5.

2.3 The technical features of claims 1 to 5 are also disclosed in Documents D2 to D6.

Invention 2: Claims 6-7

3 Furthermore, the above-mentioned lack of clarity notwithstanding, the subject-matter of **claim 6** is not new in the sense of Article 33(2) PCT, and therefore the criteria of Article 33(1) PCT are not met.

3.1 The document D4 is regarded as being the closest prior art and discloses (the references in parentheses applying to this document) an infusion system comprising (figure 1-8):

- an eluant reservoir (4), a pump (6) coupled to the reservoir, an infusion tubing circuit, a radioisotope generator (8), an activity detector (20), a waste bottle (26) and a computer (28); the infusion tubing circuit including an eluant line coupled to the pump and to the generator (figure 6), an eluate line coupled to the generator and to the activity detector, a patient line coupled to the eluate line, a by-pass line (18) coupled to the eluant line, via a divergence valve (16), and to the patient line, the by-pass line (18) accommodating flow of eluant to the patient line, when the divergence valve is set to direct the flow to by-pass the generator; and the computer being coupled to the pump and to the activity detector and being pre-programmed to collect information, from the pump and the activity detector and to control the divergence valve and the pump (paragraph 29 to 32) according to a method, the method comprising:

- activating the pump a first time to pump a portion of a volume of eluant from the reservoir, through the eluant line and through the generator at a first flow rate, in order to generate eluate in the eluate line, via an elution within the generator, and to push a dose of the eluate into the patient line (figure 6c);

- setting the divergence valve (16) to direct flow through the by-pass line, once the dose has been pushed into the patient line (figure 6d); and

- activating the pump a second time to pump a second portion of the volume of eluant from the reservoir, through the eluant line, through the by-pass line and into the patient line to inject the dose out from the patient line (figure 6d);

- wherein the pump, when activated the second time, is controlled to pump the second portion of the volume of eluant at a second flow rate, the second flow rate being higher than the first flow rate, in order to increase a flow rate of the injection of the dose. (the flow rate can be variable: desired flow)

The subject matter of claim 6 is not novel document D4.

3.2 The technical feature of claim 6 is also disclosed in Documents D5 (figure 1) and D6. (figure 1)

Invention 3: Claims 30-35

4 Furthermore, the above-mentioned lack of clarity notwithstanding, the subject-matter of **claims 30-34** is not new in the sense of Article 33 (2) PCT, and therefore the criteria of Article 33(1) PCT are not met.

4.1 The document D7 is regarded as being the closest prior art and discloses (the references in parentheses applying to this document) a computer readable medium (106) comprising (figure 1-5):

- having computer executable instructions for executing a method for maintaining an infusion system (18), the method comprising:

- tracking a portion of a volume of eluant (saline) that is pumped from a reservoir (38) of the system and through a generator of the system, in order to generate, via elution, an eluate; providing an indication of the volume of eluant within the reservoir to a user of the system; tracking a volume of the eluate that is diverted from the generator to a waste bottle (120) of the system; and providing an indication to the user that the waste bottle needs to be emptied (paragraph 60).

The subject matter of claim 30 is not novel document D7.

4.2 Document D7 also reveals the technical feature of claim 31.

4.3 The document D4 is regarded as being the closest prior art and discloses (the references in parentheses applying to this document) a computer readable medium (28) comprising (figure 1-8) computer executable instructions for executing a method of calibrating an activity detector (20) of an infusion system. (see paragraph 29-32 and paragraph 55). The subject matter of claim 32 is not novel over document D4.

4.4 Moreover Document D4 shows the technical features of claims 33 and 34.

4.5 Finally the technical features of claims 32 to 34 are also disclosed in Documents D5 and D6.

__Inventive Step Article 33(3) PCT__

Invention 2: Claims 6-7

5 The present application does not meet the criteria of Article 33 (1) PCT, because the subject-matter of **claim 7** does not seem to involve an inventive step in the sense of Article 33(3) PCT. Document D4 is the prior art. In **claim 7** a slight constructional change (flow rate) in device of D4 is defined which comes within the scope of the customary practice followed by persons skilled in the art, especially as the advantages thus achieved can readily be foreseen. Consequently, the subject-matter of this claim also lacks an inventive step.

Invention 3: Claims 30-35

6 The present application does not meet the criteria of Article 33 (1) PCT, because the subject-matter of **claim 35** does not seem to involve an inventive step in the sense of Article 33(3) PCT. Document D4 is the prior art. In **claim 35** a slight constructional change (time period) in device of D4 is defined which comes within the scope of the customary practice followed by persons skilled in the art, especially as the advantages thus achieved can readily be foreseen. Consequently, the subject-matter of this claim also lacks an inventive step.

__Further comments__

Invention 1: Claims 1 - 5

7 Contrary to the requirements of Rule 5.1(a)(ii) PCT, the **relevant background** art disclosed in the documents D1-D3 are not mentioned in the description, nor are these documents identified therein.

8 Independent claim 1 is not in the **two-part form** in accordance with Rule 6.3 (b) PCT, which in the present case would be appropriate, with those features known in combination from the prior art (document D1) being placed in the preamble (Rule 6.3(b)(I) PCT) and with the remaining features being included in the characterising part (Rule 6.3(b)(ii) PCT).

9 The features of the claims are not provided with **reference signs** placed in parentheses (Rule 6.2(b) PCT).

Invention 2: Claims 6-7

10 Contrary to the requirements of Rule 5.1(a)(ii) PCT, the **relevant background** art disclosed in the documents D4- D6 are not mentioned in the description, nor are these documents identified therein.

11 Independent claim 6 is not in the **two-part form** in accordance with Rule 6.3 (b) PCT, which in the present case would be appropriate, with those features known in combination from the prior art (document D4) being placed in the preamble (Rule 6.3(b)(I) PCT) and with the remaining features being included in the characterising part (Rule 6.3(b)(ii) PCT).

12 The features of the claims are not provided with **reference signs** placed in parentheses (Rule 6.2(b) PCT).

Invention 3: Claims 30-35

13 Contrary to the requirements of Rule 5.1(a)(ii) PCT, the **relevant background** art disclosed in the documents D4- D7 are not mentioned in the description, nor are these documents identified therein.

14 Independent claim 30 is not in the **two-part form** in accordance with Rule 6.3 (b) PCT, which in the present case would be appropriate, with those features known in combination from the prior art (document D7) being placed in the preamble (Rule 6.3(b)(I) PCT) and with the remaining features being included in the characterising part (Rule 6.3(b)(ii) PCT).

15 The features of the claims are not provided with **reference signs** placed in parentheses (Rule 6.2(b) PCT).

Re Item VIII

Certain observations on the international application

Clarity Article 6 PCT

Invention 1: Claims 1 - 5

16 Some of the features in the apparatus **claim 1** relate to a method of using the apparatus (method comprising activating the pump, providing an indication and providing an indication) rather than clearly defining the apparatus in terms of its technical features. The intended limitations are therefore not clear from this claim, contrary to the requirements of Article 6 PCT.

Furthermore such a method of using an infusion system is not allowed because this is a method of treatment of the human body. (Rule 39.1 (iv))

Invention 2: Claims 6-7

17 Some of the features in the infusion system **claim 6** relate to a method of using the apparatus (method comprising activating the pump, setting the valve and providing an indication) rather than clearly defining the apparatus in terms of its technical features. The intended limitations are therefore not clear from this claim, contrary to the requirements of Article 6 PCT.

Furthermore such a method of using an infusion system is not allowed because this is a method of treatment of the human body. (Rule 39.1 (iv)). The method is carried out within a human body, because a dose of eluate is injected to the patient line into the patient.

Invention 3: Claims 30-35

18 Although **claims 30,32 and 33** have been drafted as separate independent claims, they appear to relate effectively to the **same subject-matter** and to differ from each other only with regard to the definition of the subject-matter for which protection is sought.

The aforementioned claims therefore lack conciseness. Moreover, lack of clarity of the claims as a whole arises, since the plurality of independent claims makes it difficult, if not impossible, to determine the matter for which protection is sought, and places an undue burden on others seeking to establish the extent of the protection. Hence, these claims do not meet the requirements of Article 6 PCT.

19 Some of the features in the computer readable medium of **claim 30** relate to a method for maintaining an infusion system rather than clearly defining the apparatus in terms of its technical features. The intended limitations are therefore not clear from this claim, contrary to the requirements of Article 6 PCT.

Furthermore such a method for maintaining an infusion system is not allowed because this is during a method of treatment of the human body. (Rule 39.1 (iv)). It is implicit that to generate an eluate, the infusion pump is activated and is during a method of treatment of the human body.

20 Some of the features in the computer readable medium of **claim 32** relate to a method for calibrating an activity detector of an infusion system, rather than clearly defining the apparatus in terms of its technical features. The intended limitations are therefore not clear from this claim, contrary to the requirements of Article 6 PCT.

Furthermore such a method for calibrating an activity detector of an infusion system is not allowed because this is during a method of treatment of the human body. (Rule 39.1 (iv)). It is implicit that to generate an eluate, the infusion pump is activated and is during a method of treatment of the human body.

21 Some of the features in the computer readable medium of **claim 33** relate to a method for conducting a breakthrough test of a radioisotope generator of an infusion system rather than clearly defining the apparatus in terms of its technical features. The intended limitations are therefore not clear from this claim, contrary to the requirements of Article 6 PCT.

Furthermore such a method for conducting a breakthrough test of a radioisotope generator of an infusion system is not allowed because this is during a method of treatment of the human body. (Rule 39.1 (iv)). It is implicit that to generate an eluate, the infusion pump is activated and is during a method of treatment of the human body.

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference 56782.1.8.1	**FOR FURTHER ACTION** see Form PCT/ISA/220 as well as, where applicable, item 5 below.	
International application No. PCT/US2009/047034	International filing date *(day/month/year)* 11/06/2009	(Earliest) Priority Date *(day/month/year)* 11/06/2008
Applicant BRACCO DIAGNOSTICS INC.		

This international search report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This international search report consists of a total of 6 sheets.

[X] It is also accompanied by a copy of each prior art document cited in this report.

1. **Basis of the report**
   a. With regard to the **language**, the international search was carried out on the basis of:
      [X] the international application in the language in which it was filed
      [ ] a translation of the international application into ______, which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1(b))
   b. [ ] This international search report has been established taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 (Rule 43.6*bis*(a)).
   c. [ ] With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, see Box No. I.
2. [ ] **Certain claims were found unsearchable** (See Box No. II)
3. [X] **Unity of invention is lacking** (see Box No III)
4. With regard to the **title,**
   [X] the text is approved as submitted by the applicant
   [ ] the text has been established by this Authority to read as follows:
5. With regard to the **abstract,**
   [X] the text is approved as submitted by the applicant
   [ ] the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority
6. With regard to the **drawings,**
   a. the figure of the **drawings** to be published with the abstract is Figure No. 1c
      [ ] as suggested by the applicant
      [X] as selected by this Authority, because the applicant failed to suggest a figure
      [ ] as selected by this Authority, because this figure better characterizes the invention
   b. [ ] none of the figures is to be published with the abstract

Form PCT/ISA/210 (first sheet) (April 2007)

International application No
PCT/US2009/047034

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61M5/14 A61G12/00
ADD. A61M5/00

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

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
A61M G21F

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

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, INSPEC

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	JP 2000 350783 A (SUMITOMO HEAVY INDUSTRIES) 19 December 2000 (2000-12-19) figures 1-5 paragraph [0013] - paragraph [0032]	1-35
X	WO 2008/037939 A2 (LEMER PROT ANTI X PAR ABREVIAT [FR]; LEMER PIERRE-MARIE [FR]) 3 April 2008 (2008-04-03) figures 1-2 page 5, line 27 - page 11, line 19	1-23
X	EP 0 102 121 A1 (BYK MALLINCKRODT CIL BV [NL]) 7 March 1984 (1984-03-07) figures 1-4 page 9, line 16 - page 12, line 11	1,8-10, 12, 14-16, 19,22-23

-/--

[X] Further documents are listed in the continuation of Box C.

[X] See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
11 February 2010	25/02/2010

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31–70) 340–2040, Fax: (+31–70) 340–3016	Reinbold, Sylvie

3

Form PCT/ISA/210 (second sheet) (April 2005)

International application No
PCT/US2009/047034

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	JP 2006 325826 A (UNIVERSAL GIKEN KK; SD GIKEN KK) 7 December 2006 (2006-12-07) figures 1-10 paragraph [0020] - paragraph [0069]	1-23
X	FR 2 867 084 A1 (GEN ELECTRIC [US]) 9 September 2005 (2005-09-09) figures 1-12 page 13, line 23 - page 27, line 9	1,8-12, 14-15, 17,19
X	WO 2006/074473 A2 (ATLAS SYSTEMS INC [US]; LIVENGOOD AMY L [US]; LIVENGOOD JOSEPH C [US];) 13 July 2006 (2006-07-13) figures 1-6 page 16, line 4 - page 27, line 4	24-35
X	US 5 590 648 A (MITCHELL ANDREW [US] ET AL) 7 January 1997 (1997-01-07) figures 1-9 column 3, line 65 - column 8, line 5	24,28-35
X	WO 02/096335 A2 (HILL ROM SERVICES INC [US]; GALLANT DENNIS J [US]; LANCI DENNIS M [US]) 5 December 2002 (2002-12-05)	24, 28-29, 33-34
A	figure 18 page 22, line 6 - page 23, line 3	35
X	WO 96/15337 A1 (NILSSON AGNE [CY]) 23 May 1996 (1996-05-23) figures 1-26 page 4, line 4 - page 12, line 34	28-35

3

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2009/047034

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☒ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fees, this Authority did not invite payment of additional fees.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.

☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.

☒ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-23

These claims essentially define a cabinet structure for an infusion system comprising:
- a platform
- a shell, wherein the shell comprises a first upper opening, a second upper opening and an access panel
- the access panel mating with the upper opening and being removable therefrom
- the upper opening is sized and oriented to allow a lowering of one or more radioisotope generators
- the upper opening being located at an elevation which is substantially lower than an elevation of an uppermost portion of the upper surface

(technical problem: to provide a better ergonomic)

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2. claims: 24-35

These claims essentially define a cabinet structure for an infusion system comprising:
- a platform
- a shell
- at least one external recess

(technical problem: to provide a cabinet structure to hold articles pertaining to operation of the infusion system)

International application No
PCT/US2009/047034

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
JP 2000350783 A	19-12-2000	NONE	
WO 2008037939 A2	03-04-2008	AU 2007301772 A1	03-04-2008
		CA 2664760 A1	03-04-2008
		CN 101516420 A	26-08-2009
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		US 2008242915 A1	02-10-2008
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		AU 2002309987 A1	09-12-2002
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		JP 2005515800 T	02-06-2005
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		DE 69533965 D1	03-03-2005
		EP 0797712 A1	01-10-1997
		JP 10508770 T	02-09-1998
		JP 4061657 B2	19-03-2008
		US 6089518 A	18-07-2000

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY
(PCT Rule 43*bis*.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/US2009/047034	11.06.2009	11.06.2008

International Patent Classification (IPC) or both national classification and IPC
INV. A61M5/14 A61G12/00
ADD. A61M5/00

Applicant
BRACCO DIAGNOSTICS INC.

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☒ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☒ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notifed the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:	Date of completion of this opinion	Authorized Officer
European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Fax: +49 89 2399 - 4465	see form PCT/ISA/210	Reinbold, Sylvie Telephone No. +49 89 2399-7918

Form PCT/ISA/237 (Cover Sheet) (April 2005)

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US2009/047034

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of:

   ☒ the international application in the language in which it was filed

   ☐ a translation of the international application into , which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1 (b)).

2. ☐ This opinion has been established taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 (Rule 43bis.1(a))

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

   a. type of material:

      ☐ a sequence listing

      ☐ table(s) related to the sequence listing

   b. format of material:

      ☐ on paper

      ☐ in electronic form

   c. time of filing/furnishing:

      ☐ contained in the international application as filed.

      ☐ filed together with the international application in electronic form.

      ☐ furnished subsequently to this Authority for the purposes of search.

4. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

5. Additional comments:

Box No. IV Lack of unity of invention

1. ☒ In response to the invitation (Form PCT/ISA/206) to pay additional fees, the applicant has, within the applicable time limit:

   ☒ paid additional fees

   ☐ paid additional fees under protest and, where applicable, the protest fee

   ☐ paid additional fees under protest but the applicable protest fee was not paid

   ☐ not paid additional fees

2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose not to invite the applicant to pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rule 13.1, 13.2 and 13.3 is

   ☐ complied with

   ☒ not complied with for the following reasons:

   see separate sheet

4. Consequently, this report has been established in respect of the following parts of the international application:

   ☒ all parts.

   ☐ the parts relating to claims Nos. 1-23

Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	2-7, 13, 20-21, 26-27
	No:	Claims	1, 8-12, 14-19, 22-25, 28-35
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-35
Industrial applicability (IA)	Yes:	Claims	1-35
	No:	Claims	

2. Citations and explanations

   see separate sheet

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US2009/047034

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

Re Item IV

Lack of unity of invention

The inventions in this international application, as follows:

1. Claims 1 - 23

These claims essentially define a cabinet structure for an infusion system comprising:

- a platform, a shell, wherein the shell comprises a first upper opening, a second upper opening and an access panel
- the access panel mating with the upper opening and being removable therefrom
- the upper opening is sized and oriented to allow a lowering of one or more radioisotope generators
- the upper opening being located at an elevation which is substantially lower than an elevation of an uppermost portion of the upper surface

(technical problem: to provide a better ergonomic)

2. Claims 24-35:

These claims essentially define a cabinet structure for an infusion system comprising:

- a platform, a shell
- at least one external recess

(technical problem: to provide a cabinet structure to hold articles pertaining to operation of the infusion system)

The only common concept between the invention 1 and 2 is a cabinet structure for an infusion system having a platform and a shell. This is already known from the person skilled in the art. (see JP200350783).

The special technical features are not identical. The effects of both compounds are different. The use of the cabinet structure in claim 24 or 28 permit to hold articles pertaining to operation of the infusion system.

In conclusion, the groups of claims are not linked by common or corresponding special technical features and define 2 different inventions not linked by a single general inventive concept. Therefore the application claims 2 inventions not so linked to form a single general inventive concept. The requirement of unity is not fulfilled, according to Rule 13 PCT.

Re Item V

Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1 Reference is made to the following documents:

D1	JP 2000 350783
D2	WO 2008/037939
D3	EP 0 102 121
D4	JP 2006 325826
D5	FR 2 867 084
D6	WO 2006/074473
D7	US 5 590 648
D8	WO 02/096335
D9	WO 96/15337

Novelty Article 33(2) PCT

Invention 1: claims 1 - 23

2 The present application does not meet the criteria of Article 33 (1) PCT, because the subject-matter of claims **1,8-12,14-19,22 and 23** is not new in the sense of Article 33(2) PCT.

2.1 The document D1 is regarded as being the closest prior art and discloses (the references in parentheses applying to this document) discloses a cabinet structure for an infusion system comprising (figure 1-5):

- a platform on which the infusion system is mounted; and

- a shell (40+74) surrounding an interior space of the structure, the interior space containing at least a portion of the infusion system;

- wherein the shell comprises a first upper opening (84) into the interior space, a second upper opening (opening where the panel (64) is fixed) into the interior space and an access panel;

- the access panel (64) mates with the second upper opening and is removable therefrom;

- the first upper opening is sized to provide access to a waste bottle (syringe) of the infusion system within the interior space; and

- the second upper opening is sized and oriented to allow a lowering of one or more radioisotope generators, for the system, into the interior space, and a lifting of the one or more generators out from the interior space, the second upper opening being located at an elevation, with respect to a lowermost portion of the cabinet structure, which is lower than an elevation, with respect to the lowermost portion of the cabinet structure, of the first upper opening (see figure 2).

The subject matter of claim 1 is not novel over document D1.

2.2 Document D1 shows the technical features of claims 8,10,11,12,14,15,17-19, 22 and 23.

2.3 The technical feature of claims 1,8-12,14-19,22 and 23 is disclosed in Documents D2,D3,D4 and D5.

Invention 2: claims 24 - 35

3 The present application does not meet the criteria of Article 33 (1) PCT, because the subject-matter of claims **24,25 and 28-35** is not new in the sense of Article 33(2) PCT.

3.1 The document D6 is regarded as being the closest prior art and discloses (the references in parentheses applying to this document) discloses a cabinet structure (100) for an infusion system (124, page 16 line 21), the structure comprising (figures 1-15):

- a platform (120) on which the infusion system is mounted; and

- a shell (204) surrounding an interior space of the structure and including an upper surface (112) in which at least one opening (138,124) and an external recess (192) is formed;

- wherein the interior space contains at least a portion of the infusion system (IV pump);

- the at least one opening provides a passageway (138) for a tubing line of the infusion system to extend out from the interior space; and the external recess (192) is sized to contain a spill from the infusion system.

Therefore the subject matter of claim 24 is not novel over document D6.

3.2 Document D6 also shows the technical features of claims 25 and 28 to 35.

3.3 Moreover the technical feature of **claims 24,25 and 28-35** is disclosed in Documents D1,D7,D8 and D9.

<u>Inventive step Article 33(3) PCT</u>

Invention 1: claims 1 - 23

4 The present application does not meet the criteria of Article 33 (1) PCT, because the subject- matter of **claims 2-7,13 and 20-21** does not seem to involve an inventive step in the sense of Article 33(3) PCT. Document D1 is the closest prior art.

In claims 2-7,9,13 and 20-21 a slight constructional change in the cabinet structure is defined which comes within the scope of the customary practice followed by persons skilled in the art, especially as the advantages thus achieved can readily be foreseen. Consequently, the subject-matter of these claims also lacks an inventive step.

Invention 2: claims 24 - 35

5 The present application does not meet the criteria of Article 33 (1) PCT, because the subject-matter of **claims 26 and 27** does not seem to involve an inventive step in the sense of Article 33(3) PCT. Document D6 is the closest prior art.

In claims 26 and 27 a slight constructional change in the cabinet structure is defined which comes within the scope of the customary practice followed by persons skilled in the art, especially as the advantages thus achieved can readily be foreseen. Consequently, the subject- matter of these claims also lacks an inventive step.

Further comments

Invention 1: claims 1 - 23

6 Contrary to the requirements of Rule 5.1(a)(ii) PCT, the **relevant background** art disclosed in the documents D1-D4 are not mentioned in the description, nor are these documents identified therein.

7 Independent claim 1 is not in the **two-part form** in accordance with Rule 6.3 (b) PCT, which in the present case would be appropriate, with those features known in combination from the prior art (document D1) being placed in the preamble (Rule 6.3(b)(I) PCT) and with the remaining features being included in the characterising part (Rule 6.3(b)(ii) PCT).

8 The features of the claims are not provided with **reference signs** placed in parentheses (Rule 6.2(b) PCT).

Invention 2: claims 24 - 35

9 Contrary to the requirements of Rule 5.1(a)(ii) PCT, the **relevant background** art disclosed in the documents D1, D6 to D9 are not mentioned in the description, nor are these documents identified therein.

10 Independent claim 24 is not in the **two-part form** in accordance with Rule 6.3 (b) PCT, which in the present case would be appropriate, with those features known in combination from the prior art (document D1) being placed in the preamble (Rule 6.3(b)(I) PCT) and with the remaining features being included in the characterising part (Rule 6.3(b)(ii) PCT).

11 The features of the claims are not provided with **reference signs** placed in parentheses (Rule 6.2(b) PCT).

Re Item VIII

Certain observations on the international application

Clarity Article 6 PCT

Invention 1: claims 1 - 23

12 Although **claims 1 and 19** have been drafted as separate independent claims, they appear to relate effectively to the **same subject-matter** and to differ from each other only with regard to the definition of the subject-matter for which protection is sought.

The aforementioned claims therefore lack conciseness. Moreover, lack of clarity of the claims as a whole arises, since the plurality of independent claims makes it difficult, if not impossible, to determine the matter for which protection is sought, and places an undue burden on others seeking to establish the extent of the protection.

Hence, these claims do not meet the requirements of Article 6 PCT.

It appears to be appropriate to file an amended set of claims taking account of the above comments and Article 34(2)(b) PCT. The relevant subject-matter should be defined in **a single independent claim** followed by dependent claims covering features which are merely optional (Rules 6.3 and 6.4 PCT).

Invention 2: claims 24 - 35

13 Although **claims 24 and 28** have been drafted as separate independent claims, they appear to relate effectively to the **same subject-matter** and to differ from each other only with regard to the definition of the subject-matter for which protection is sought.

The aforementioned claims therefore lack conciseness. Moreover, lack of clarity of the claims as a whole arises, since the plurality of independent claims makes it difficult, if not impossible, to determine the matter for which protection is sought, and places an undue burden on others seeking to establish the extent of the protection.

Hence, these claims do not meet the requirements of Article 6 PCT.

It appears to be appropriate to file an amended set of claims taking account of the above comments and Article 34(2)(b) PCT. The relevant subject-matter should be defined in **a single independent claim** followed by dependent claims covering features which are merely optional (Rules 6.3 and 6.4 PCT).

Electronic Acknowledgement Receipt

EFS ID:	7196788
Application Number:	12137363
International Application Number:	
Confirmation Number:	7372
Title of Invention:	INFUSION SYSTEM CONFIGURATIONS
First Named Inventor/Applicant Name:	Charles R. Quirico
Customer Number:	22859
Filer:	Elisabeth Lacy Belden
Filer Authorized By:	
Attorney Docket Number:	56782.1.6
Receipt Date:	12-MAR-2010
Filing Date:	11-JUN-2008
Time Stamp:	12:32:38
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	no

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1		5thSIDS_56782-1-6.pdf	858287 6b8050909459ff1ebe4b116a4b3d3555a129f847	yes	5

	Multipart Description/PDF files in .zip description		
	Document Description	**Start**	**End**
	Information Disclosure Statement (IDS) Filed (SB/08)	1	3
	Transmittal Letter	4	5

Warnings:

Information:

2	Foreign Reference	WO9615337A1.pdf	1486044 3f0a489957d75fe17b634665cba1dca9a555959d	no	36

Warnings:

Information:

3	Foreign Reference	WO02096335A2.pdf	2874922 0123b0873d007d1e9c2963ddeec35337455e36de	no	57

Warnings:

Information:

4	Foreign Reference	WO2006074473A2.pdf	3009340 b2dd51851cfeee42a881fc6b1edbf0729b389e96	no	79

Warnings:

Information:

5	Foreign Reference	WO2008028165A2.pdf	1831913 875573dee4f641eff4007e9ffa8ce768088784bc	no	45

Warnings:

Information:

6	NPL Documents	Article-Epstein.pdf	1242548 4d1ae76a39290b7146438b33486c7d98821ec552	no	7

Warnings:

Information:

7	NPL Documents	Article-Klein.pdf	2007175 3e644852e664ae035f2776e9ac7322fa45a539c5	no	15

Warnings:

Information:

8	NPL Documents	ISR-WO_56782_1_5_1.pdf	3081572 773bbb06586bc6dbfbafe2f645d6b37ceaebe442	no	22

Warnings:

Information:

9	NPL Documents	ISR-WO_56782_1_6_1.pdf	2732881 70698277b5883d4af6d71695b799561e78095ddb	no	17
Warnings:					
Information:					
10	NPL Documents	ISR-WO_56782_1_7_1.pdf	3013153 08067db8c7b81d3142e5ad89e5ab72e32d751231	no	20
Warnings:					
Information:					
11	NPL Documents	ISR-WO_56782_1_8_1.pdf	2323105 384268c2cb35b512f07968afccebbccf9cf908b3	no	15
Warnings:					
Information:					
			Total Files Size (in bytes):	24460940	

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

<u>New Applications Under 35 U.S.C. 111</u>
If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

<u>National Stage of an International Application under 35 U.S.C. 371</u>
If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

<u>New International Application Filed with the USPTO as a Receiving Office</u>
If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
12/137,363	06/11/2008	Charles R. Quirico	56782.1.6	7372

22859 7590 03/04/2010
INTELLECTUAL PROPERTY GROUP
FREDRIKSON & BYRON, P.A.
200 SOUTH SIXTH STREET, SUITE 4000
MINNEAPOLIS, MN 55402

EXAMINER	
ZHANG, JENNA	

ART UNIT	PAPER NUMBER
3763	

MAIL DATE	DELIVERY MODE
03/04/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

PTOL-90A (Rev. 04/07)

Office Action Summary	Application No.	Applicant(s)	
	12/137,363	QUIRICO ET AL.	
	Examiner	Art Unit	
	JENNA ZHANG	3763	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *1* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 June 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-36* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-36* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Restriction to one of the following inventions is required under 35 U.S.C. 121:

   I. **Claims 1-15**, drawn to an infusion system, classified in class 604, subclass 93.01.

   II. **Claims 16-28**, drawn to different shielding assemblies, classified in class 604, subclass 410.

   III. **Claims 29-36**, drawn to a disposable infusion circuit, classified in class 604, subclass 236.

2. The inventions are distinct, each from the other because of the following reasons:

Inventions I and II are related as combination and subcombination. Inventions in this relationship are distinct if it can be shown that (1) the combination as claimed does not require the particulars of the subcombination as claimed for patentability, and (2) that the subcombination has utility by itself or in other combinations (MPEP § 806.05(c)). In the instant case, the combination as claimed does not require the particulars of the subcombination as claimed because Invention I requires a plurality of compartments with corresponding plurality of doors whereas Invention II specify that the compartments are defined by passageways with no doors. The subcombination has separate utility such as serving as a multi-compartment chamber for storing a radioactive material.

Inventions I and III are related as combination and subcombination. Inventions in this relationship are distinct if it can be shown that (1) the combination as claimed does not require the particulars of the subcombination as claimed for patentability, and (2) that the subcombination has utility by itself or in other combinations (MPEP § 806.05(c)). In the instant case, the combination as claimed does not require the particulars of the subcombination as claimed because Invention III requires a valve member that Invention I does not. Furthermore, Invention I is more specific about the assembly of the different lines. The subcombination has separate utility such as serving as the circuitry for an intravenous delivery bag.

The examiner has required restriction between combination and subcombination inventions. Where applicant elects a subcombination, and claims thereto are subsequently found allowable, any claim(s) depending from or otherwise requiring all the limitations of the allowable subcombination will be examined for patentability in accordance with 37 CFR 1.104. See MPEP § 821.04(a). Applicant is advised that if any claim presented in a continuation or divisional application is anticipated by, or includes all the limitations of, a claim that is allowable in the present application, such claim may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application.

Inventions II and III are directed to related devices. The related inventions are distinct if: (1) the inventions as claimed are either not capable of use together or can have a materially different design, mode of operation, function, or effect; (2) the inventions do not overlap in scope, i.e., are mutually exclusive; and (3) the inventions as claimed are not obvious variants. See MPEP § 806.05(j). In the instant case, the inventions as claimed can have a materially different design, mode of operation, function, or effect. Furthermore, the inventions as claimed do not encompass overlapping subject matter and there is nothing of record to show them to be obvious variants.

Restriction for examination purposes as indicated is proper because all these inventions listed in this action are independent or distinct for the reasons given above and there would be a serious search and examination burden if restriction were not required because one or more of the following reasons apply:

(a) the inventions have acquired a separate status in the art in view of their different classification;

(b) the inventions have acquired a separate status in the art due to their recognized divergent subject matter;

(c) the inventions require a different field of search (for example, searching different classes/subclasses or electronic resources, or employing different search queries);

(d) the prior art applicable to one invention would not likely be applicable to another invention;

(e) the inventions are likely to raise different non-prior art issues under 35 U.S.C. 101 and/or 35 U.S.C. 112, first paragraph.

Applicant is advised that the reply to this requirement to be complete must include (i) an election of a invention to be examined even though the requirement may be traversed (37 CFR 1.143) **and (ii) identification of the claims encompassing the elected invention**.

3. The election of an invention may be made with or without traverse. To reserve a right to petition, the election must be made with traverse. If the reply does not distinctly and specifically point out supposed errors in the restriction requirement, the election shall be treated as an election without traverse. Traversal must be presented at the time of election in order to be considered timely. Failure to timely traverse the requirement will result in the loss of right to petition under 37 CFR 1.144. If claims are added after the election, applicant must indicate which of these claims are readable on the elected invention.

If claims are added after the election, applicant must indicate which of these claims are readable upon the elected invention.

Should applicant traverse on the ground that the inventions are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the inventions to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

4. A telephone call was made to Elizabeth Balden on February 17, 2010 to request an oral election to the above restriction requirement, but did not result in an election being made.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

5. Any inquiry concerning this communication or earlier communications from the examiner should be directed to JENNA ZHANG whose telephone number is (571)270-5369. The examiner can normally be reached on Monday-Thursday 8AM - 5PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Nicholas Lucchesi can be reached on 571-272-4977. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/J. Z./
Examiner, Art Unit 3763
2/17/2010

/Nicholas D Lucchesi/
Supervisory Patent Examiner, Art Unit 3763

Index of Claims	Application/Control No. 12137363	Applicant(s)/Patent Under Reexamination QUIRICO ET AL.
	Examiner JENNA ZHANG	Art Unit 3763

✓	Rejected	-	Cancelled	N	Non-Elected	A	Appeal
=	Allowed	÷	Restricted	I	Interference	O	Objected

☐ Claims renumbered in the same order as presented by applicant ☐ CPA ☐ T.D. ☐ R.1.47

CLAIM		DATE								
Final	Original	02/17/2010								
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APPLICATION NUMBER	FILING OR 371(C) DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO./TITLE
12/137,363	06/11/2008	Charles R. Quirico	56782.1.6

CONFIRMATION NO. 7372

PUBLICATION NOTICE

OC000000039282054

22859
INTELLECTUAL PROPERTY GROUP
FREDRIKSON & BYRON, P.A.
200 SOUTH SIXTH STREET, SUITE 4000
MINNEAPOLIS, MN 55402

Title:INFUSION SYSTEM CONFIGURATIONS

Publication No.US-2009-0309465-A1
Publication Date:12/17/2009

NOTICE OF PUBLICATION OF APPLICATION

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	Application Number	12137363
	Filing Date	2008-06-11
	First Named Inventor	Charles R. Quirico
	Art Unit	3637
	Examiner Name	
	Attorney Docket Number	56782.1.6

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	2	20050002971	WO		2005-01-13	Iphase Technologies		☐

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	Filing Date	2008-06-11
	First Named Inventor	Charles R. Quirico
	Art Unit	3637
	Examiner Name	
	Attorney Docket Number	56782.1.6

	3	2006129301	WO		2006-12-07	Spec-Trum Dynamics		☐
	4	2008037939	WO		2008-04-03	Lemer Protection		☐
	5	2008082966	WO		2008-07-10	Medrad, Inc.		☐
	6	0160303	EP		1985-11-06	E.R. Squibb		☐
	7	0310148	EP		1989-04-05	E.R. Squibb		☐
	8	2867084	FR		2005-09-09	General Electric Company		☐
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	Filing Date	2008-06-11
	First Named Inventor	Charles R. Quirico
	Art Unit	3637
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	Attorney Docket Number	56782.1.6

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☐ See attached certification statement.

☐ Fee set forth in 37 CFR 1.17 (p) has been submitted herewith.

☒ None

SIGNATURE

A signature of the applicant or representative is required in accordance with CFR 1.33, 10.18. Please see CFR 1.4(d) for the form of the signature.

Signature	/Elisabeth L. Belden/	Date (YYYY-MM-DD)	2009-10-16
Name/Print	Elisabeth L. BELDEN	Registration Number	50,751

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INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 6 : G01N 24/00, 37/00

A1

(11) International Publication Number: WO 99/56117

(43) International Publication Date: 4 November 1999 (04.11.99)

(21) International Application Number: PCT/US99/08981

(22) International Filing Date: 26 April 1999 (26.04.99)

(30) Priority Data:
60/083,133 27 April 1998 (27.04.98) US

(63) Related by Continuation (CON) or Continuation-in-Part (CIP) to Earlier Application
US 60/083,133 (CON)
Filed on 27 April 1998 (27.04.98)

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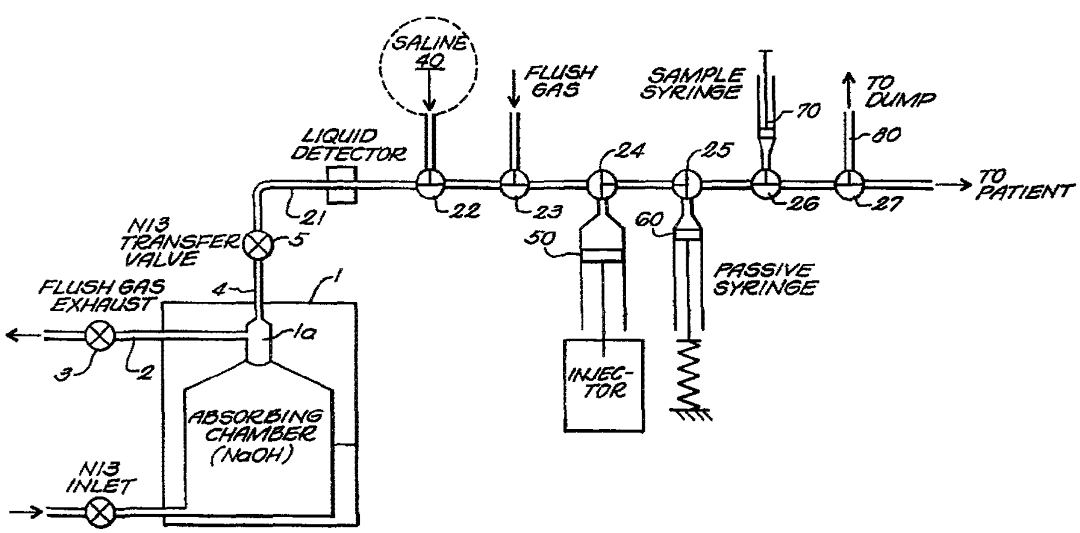
(81) Designated States: JP, US, European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE).

Published
With international search report.

(54) Title: RADIATION HANDLING SYSTEM AND SET



(57) Abstract

A radioactive material such as an unstable isotopic gas is provided to a receiving chamber (1) directly from a source to form a purified or enriched bubble. The bubble is passed to a fluid handling set for preparation of the reagent or other delivery system. In an exemplary embodiment trace amounts of nitrogen-13 are concentrated in a receiving chamber and passed into a small bubble of carrier gas. The carrier gas is then delivered into a fluid handling set. The fluid handling set connects to a pressure syringe (50) and a passive syringe (60), and further includes a plurality of flushable valves (22-27) interconnected as a closed unit by tubing (21) to form a switchable or finite state flow network in which the pressure syringe may back flush the tubing, mix the isotope in a delivery liquid, and transfer the mixed liquid to an output for diagnostic imaging or other use.

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RADIATION HANDLING SYSTEM AND SET

CROSS-REFERENCE TO RELATED APPLICATIONS

Not Applicable.

STATEMENT REGARDING FEDERALLY SPONSORED RESEARCH

Not Applicable.

BACKGROUND OF THE INVENTION

The present invention relates to the preparation and use of radioactive isotopes for biological purposes such as labeling, marking, imaging and diagnostics. Such applications generally utilize a single element containing minor amounts of an unstable isotope, which must be generally formed into a simple compound that is incorporated into a solution or reagent which undergoes a known or predictable interaction with the biological system being studied. Thus, for example, radionuclides are often added as labels to a substance that binds to a nucleic acid to indicate the presence of a particular substrate, termination or functional group. Similarly, materials which are taken up by particular biological systems may be labeled for treatment or imaging purposes. Aerosols or radio-labeled fluids may also be used for blood flow or lung function diagnostic imaging studies.

In general, it is necessary that radioactive materials be handled in such a way as to not expose the operator to radiation. Thus they are preferably handled under robotic control or automated conditions. It is desirable that the radioisotopes involved have a short half life, so as to automatically limit the exposure of the subject to radiation, and to facilitate proper disposal. However, materials with a short half life cannot be compounded in advance or stored for lengthy times. Such radionuclides must therefore be manufactured at or near to the site of intended use. In these cases the purification and preparation of the radionuclide in a suitable delivery system must also be accomplished locally. The brevity of the nuclide half life may further complicate its handling and processing. These factors have sometimes prevented the acceptance or use of otherwise worthwhile radionuclide-based procedures.

It would therefore be desirable to provide a convenient system for preparing radionuclides for biological use.

It would also be desirable to provide such a system for handling a radionuclide in an automated fashion without exposing the operator to radiation.

It would further be desirable to provide such a system useful for short-lived materials or small batches to enable the routine use of such materials in individual procedures.

SUMMARY OF THE INVENTION

These and other desirable features are achieved in a system in accordance with the present invention by providing a radioactive marker material such as an unstable isotopic gas to a receiving chamber directly from a source to undergo initial cleansing or concentration, and passing the material into a fluid handling set for automated preparation of the reagent or actual delivery system. In an exemplary embodiment, trace amounts of ^{13}N, created by proton bombardment of a target at a cyclotron, pass to a receiving chamber, are cleansed and pass into a small bubble of carrier gas. The carrier gas is then delivered into a fluid handling set. The fluid handling set includes or connects to a pressure syringe and a passive syringe, and further includes a plurality of flushable valves interconnected by tubing in a closed unit to form a flow network in which the pressure syringe may back-flush the tubing, mix the isotope in a delivery liquid, and transfer the mixed liquid to an output for diagnostic imaging or other use. The fluid handling set, which is a closed and preferably sterile unit, may include the receiving chamber 1, and it mounts in a fixed console of operating motors and condition sensors to control the various steps of fluid handling and delivery, and to effect safety functions which enable the system to connect directly to a catheter or to a vascular injection system for use on human beings.

In a preferred embodiment, the receiving chamber 1 is substantially rigid, but has a region of limited or unidirectional compliance. The chamber receives a flow of trace isotope in a bulk gas, operating to remove the bulk gas while the radionuclide accumulates in a bubble at the outlet port of the chamber. Compliance of the receiving chamber may be effected by means of an elastic wall tensioned against a rigid support such that the wall flexes outwardly under pressure to accommodate the inflow of carrier gas but may not bow inwardly. This maintains the chamber volume above a fixed minimum, and prevents liquid from leaving the chamber when suction is applied at the top. In an illustrative system, nitrogen-13 is generated by cyclotron bombardment of a target with accelerated particles, and when the target has attained a sufficient level of radioactivity, the sample is passed to the receiving chamber and the CO_2 with trace ^{13}NN is bubbled into a sodium hydroxide solution. The one-way compliant wall allows a large flow to be received and maintained under pressure to accommodate the different rates of carrier delivery and carrier removal effected at this stage. The CO_2 reacts with and is effectively taken up by the sodium hydroxide solution, while the desired nuclide concentrates at a gas-filled plenum at the top of the receiving chamber, where it is accessed at the outlet port using a closed sterile set to effect transfer, mixing and delivery in a form useful for medical imaging. The fluid handling set includes a plurality of three way valves or medical infusion stopcocks that are preconnected together via small bore tubing to form a flow path. Two of the stopcocks each have a third port, which are attached to syringe bodies. One operates as an active bidirectional pump, while various motors and sensors in the console operate and control the position of the stopcock handles to achieve transfer, mixing and delivery of the radionuclide.

BRIEF DESCRIPTION OF THE DRAWINGS

The invention will be more fully understood from the following detailed description taken in conjunction with the accompanying drawings, in which:

Figure 1 is a flow chart illustrating major steps of the preparation process of the present system:

Figure 1A illustrates the system showing representative components in use for positron emission tomography;

Figure 2 illustrates system architecture as applied to a nitrogen 13 radionuclide;

Figure 3 illustrates a preferred construction of a receiving chamber for the system of Figure 2;

Figures 4A through 4D illustrate details of valve operation and flow for transfer of the radionuclide into a fluid handling set of the present invention;

Figure 5 illustrates an operating console for the set of the invention;

Figures 5A-5C illustrate stopcock mounting and control blocks of the console for use with a closed sterile set; and

Figure 6 illustrates another embodiment of the system and set.

DETAILED DESCRIPTION OF THE DRAWINGS

In accordance with a principal aspect of the present invention, there is provided a system for automated and isolated handling of a hazardous material, such as a radionuclide, for biological or medical use. The system includes a sterile set defining the path of the nuclide from a source or process chamber to its end use which, in the illustrated embodiment, involves injection into a patient. Other potential end uses may include specialized labeling, microanalytic or synthesis applications. As shown in Figure 1 for a representative system, the radionuclide, which in this case is nitrogen-13, passes from a source to a conditioning or purification chamber 1 which produces a small mass or bubble of the concentrated radionuclide for delivery to the preparation portion 10 of the system. The preparation portion 10 dissolves the nuclide in a saline solution for injection in a patient, and may directly inject the prepared solution into the patient.

By way of technical background for this embodiment, the use of nitrogen-13 in gaseous form for medical imaging procedures was pioneered at the Hammersmith Hospital, in London, several decades ago. The radionuclide is produced by bombardment in a cyclotron using a number of possible target systems and sweep gases. Further details may be found in the text Short-lived Radioactive Gases for Clinical Use of J. C. Clark and P. D. Buckingham (Butterworth, London and Boston) pp 190-200. That text is hereby incorporated herein by reference. Nitrogen-13 is only very slightly soluble in blood, and when injected in solution in the blood stream, quickly leaves the blood and accumulates at the blood-air exchange interface in the lung. Its decay creates positrons which may provide excellent three dimensional PET images of the lung, for evaluation of both perfusion and ventilation. However, the difficulties of using this radionuclide have effectively prevented its adoption in hospital settings. Much of the discussion below is applicable to other gaseous radionuclides such as oxygen-15, or radionuclides incorporated in a gaseous medium, or in a liquid with appropriate modifications. However, the preparation and use of nitrogen-13 presents a number of technical difficulties and will therefore be discussed more fully to illustrate aspects of a system and components of the present invention.

In accordance with a principal aspect of the present invention the source radionuclide is provided in a relatively crude or bulk form, for example in a sweep gas or target fluid from a cyclotron, or in other primitive or intermediate form, and flows through the system to directly enter the patient or be applied to some other sterile or purified application such as marking, analysis or synthesis of a pure product. As shown in Figure 1A it is generally contemplated that the system 20 will be a small cabinet, desktop or other stand-alone unit containing the sub-assemblies 1, 10 (Figure 1), and which attaches to the source and to the patient either directly or via a small intermediate assembly. For example, the unit 20 may connect to the source through a filtration unit or the like, and to the patient via an infusion line, port or pressurized timed injector or the like. However, most preferably the connection to the source and to the patient are as direct as possible so that little dead space, wasted volume, delay time or regions of radiation exposure are interposed between the source and the patient.

As further shown in Figure 1A, the invention generally contemplates that the unit 20 will be controlled as to several parameters discussed below by a connection to a keyboard/processor assembly 21. Also the specific nitrogen-13 embodiment is used in conjunction with an imaging or detection assembly 25. The assembly 25 of Figure 1A is a detector array which encircles the patient and is configured for positron emission tomography, to simultaneously detect the pair of annihilation photons emitted in opposite directions by positron-electron annihilations as the radionuclide decays. The detector 25 provides its detection signals to a processor for construction of a three dimensional image of the distribution of the positron-emitting radionuclide. Other suitable detectors include single-sided detector arrays, or even photographic plate cameras which register and record the received annihilation photons on a plate of film. However, a positron emission tomography (PET) instrument is the preferred detection instrument for the illustrated process.

Figure 2 illustrates functional component of the units 1, 10 of Figure 1. As shown, the unit 1 for carrying out preliminary cleansing or refinement of the radionuclide in this case includes an absorbing chamber through which the nitrogen-13 bubbles to remove the CO_2 sweep or residual target gas as the material arrives from the cyclotron source. The absorbing chamber 1 is filled with sodium hydroxide solution and is shaped with an inverted funnel cap that channels unabsorbed gas upward to a plenum 1a at the top of the chamber. Plenum 1a connects on the one hand to an exhaust port 2 controlled by an exhaust valve 3 and, on the other hand, to an outlet port 4 controlled by transfer valve 5. The outlet port connects to the main process line 21 of the sub-assembly 10, which as noted above resides within the preparation console 20 (Figure 1A) forming an inlet thereof and extending therethrough to the patient or end use. As described further below, chamber 1 may also be located within the console 20.

As further shown in Figure 2, the functional flow control and handling units appearing in the preparation console 20 include in addition to the flow line 21 a plurality of sterile three-way valves or stopcocks 22,... 27 each of which has two of its three ports connected to the line 21, and its third port connected to an inlet, outlet or syringe. The distal end of line 21 forms the output path from console 20. Each of the stopcocks 22-27 may be identical, and advantageously the stopcocks together with tube 21 are connected together and initially provided as a closed and sterile unit packaged in a manner similar, for example, to a medical infusion set. Each stopcock thus has one "free" port which is connected to allow material to enter, leave, or be moved along line 21. These third ports are attached to a source of sterile saline fluid 40, an active injector syringe 50, a source of flush fluid, and a passive holding syringe 60. In addition, a sample syringe 70 connects at stopcock 26, and an outlet line 80 to a dump, or waste vessel, extends from stopcock 27. These elements may also be connected as part of the set, although, as will be understood from the discussion below, variations are possible. The function of the sample syringe may be implemented instead by providing a small plenum with a pierceable septum connected to the third port of stopcock 26, and the line 80 may simply terminate with a spike port for attaching to a suitable collection vessel or transfer mechanism.

As further illustrated in Figure 2, the passive syringe is spring loaded so that it is normally biased to a non-extended, closed or minimal volume configuration. Thus, when a pressurized flow appears along line 21 and is directed into the syringe 60 by stopcock 25, its piston moves outwardly to form an adaptive chamber that changes volume under pressure for receiving the fluid in the line 21.

In accordance with a principal aspect of the present invention, the sterile set 21 includes a set of connected stopcocks and a syringe 50 all configured to fit within the control console (described further below) and to be manipulated by servomotor elements therein to carry out the radionuclide preparation and delivery to the patient. In a representative preparation and delivery protocol, the stopcocks are set to positions such that one or more stopcocks block the inlet, outlet or intermediate portion of the set, while one or more stopcocks are open to interconnect various portions of the path for receiving, preparing or delivering the radionuclide. In particular, the set 21 defines a finite state flow path formed of sterile single use disposable elements that fit within a console adapted to secure and control both sets of elements. Advantageously, the console 20 may be configured as a cabinet having separate compartments and which may, for example, be hinged to open for inserting and changing the set. In the prototype, the receiving chamber 1 is housed in the back half with its outlet line 4 (Figure 1A) connecting through the middle wall of the cabinet so that the fluid line 21 (Figure 2), runs through an array of stopcock or syringe receiving recesses and control elements laid out along a path in the front half of the cabinet.

In this embodiment, the apparatus is conveniently divided into those parts that do not contact the sterile solution, and those parts which do. The parts which contact the saline directly are sterile, and are assembled from disposable medical components. These include all of the tubing downstream of the liquid detector, the stopcocks, and the three syringes 50, 60, 70 which are disposable, and are to be replaced for each patient. These components are mounted on the front panel of the main unit, so that they can be changed quickly. The remaining parts of the system do not contact the saline, and may advantageously be made of reusable components. Thus the absorbing chamber 1, and the various solenoid valves and tubing that connect to it may be permanently installed. Preferably, the system is enclosed in a cabinet which is connected to a high flow-rate vacuum to maintain a steady flow into the cabinet through its small openings, so that any leaks of radioactivity within the system are contained and the radioactive material is removed.

The cabinet is divided into three compartments. The rear compartment, accessible via a rear door, contains the absorbing chamber and a dump tank. This compartment is watertight so that a catastrophic failure of the absorbing chamber will not result in escape of sodium hydroxide. A central compartment houses all of the electronics of the apparatus, and is protected from contact with any liquid that may leak from a failing component or connection. The front of the cabinet forms a door which encloses the front panel, allowing easy access to components of the system that need to be changed frequently. Preferably the syringes mount on this panel.

Figure 3 shows a preferred construction for the receiving chamber 1, which may be formed of a strong medical grade polymer. As shown, the receiving vessel 1 is configured with a rigid housing 101 which may for example be formed of a hard plastic and having an interior with a major lower portion configured with a sloped roof leading to a chimney-like upper portion or outlet plenum 109 of defined volume. The vessel 101 is configured to fit on a magnetic base such as a stand having an internally mounted rotating permanent magnet driver mechanism positioned below the chamber support surface, and a magnetic stirring rod 107 is positioned in the bottom of the vessel 1. The main chamber communicates through a passage 102 to a secondary chamber 101a bounded by a flexible elastic membrane or wall 104 positioned over the passage 102. This serves as a compliant chamber; the membrane 104 bends outwardly as pressure increases in the chamber 1 and fluid flows through the passage into the secondary chamber. However, housing 101 is rigid and the passage 102 is relatively small, or else may consist of a number of small passages such that the wall below the flexible sheet 104 forms a perforated plate that supports the sheet and effectively prevents the sheet 104 from moving inwardly in response to negative pressure. This arrangement provides a stable volume within chamber 1, and accommodates a large influx of fluid so that when radioactive material from the cyclotron enters the inlet, a large bolus of material may be received, increasing the pressure and allowing the material to more effectively react in the absorbing chamber at the slower process rate of absorption therein. As discussed briefly above for the illustrated CO_2/nitrogen-13 material, chamber 1 is filled with a sodium hydroxide solution and is gently stirred by a magnetic stirring rod, so the solution quickly reacts with and effectively removes all the CO_2 while the unreactive nitrogen tracer rises into the outlet plenum 109 at the top of the chamber.

Preferably, for this process, the plenum 109 is initially loaded with a small volume, e.g. a few cubic centimeters, of a carrier gas in which the nitrogen-13 is soluble. This carrier may, for example, be nitrous oxide or other suitable biocompatible gas. It is also advantageous that the carrier be highly soluble in blood or aqueous solutions, so that as discussed further below, problems of bubble formation or potential danger of bends are avoided. Thus, operation of the receiving chamber 1 is such that the sweep gas or target predecessor material from the source is removed, and the cleansed or concentrated radionuclide resides in the plenum 109 with a carrier gas for transfer through the transfer valve to the flow path 21. The architecture of vessel 1 therefore retains the pocket of gas at the top of the chamber intact. In this way, no liquid infiltrates the tubing leading to the rest of the apparatus, where small droplets of liquid might cause false triggering of the liquid detector or blocking of the hydrophobic filter.

An important aspect of the design of the compliant compartment is that it is only compliant to positive volumes. That is, volume can be added to the chamber, but not withdrawn. Once the carbon dioxide is absorbed, and the bubble of nitrogen withdrawn, the membrane wall lies flat against the side wall of the chamber, and the chamber becomes rigid. Thus it is impossible to suck significant volumes of sodium hydroxide out of the absorbing chamber and into the rest of the system.

Skipping ahead to Figure 5, there is shown a representative front panel of the console assembly 20 with the radionuclide entry port and elements of the flow path 21 laid out thereon. As shown, the flow line 21 first passes through a liquid detector which detects the arrival of liquid in the flow line from the chamber 1 and provides a control signal used, as described further below, for switching the states of the various stopcocks and transporting the bubble of radionuclide through the processing stages of the preparation assembly 10.

As further shown in Figure 5 a hydrophobic filter 29b is placed in the flow line 21 as a barrier to entry of liquid from chamber 1 into the system 10. As shown, the fluid preparation line 21 or set, is positioned in the console 20 such that each of the stopcocks 22-27 fits within a corresponding receiving block 22a through 27a, and the injection syringe 50 and passive syringe 60 fit within a driver mounting 50a and a syringe support 60a, respectively. By way of example, the driver assembly for the injector syringe may be that of, or similar to, a manual or programmed contrast agent injector system capable of operation to drive a standard disposable syringe at high pressures through one or more precisely timed and controlled displacements to inject preset doses or volumes into the vascular system of a patient. The mounting 60a for the passive syringe may include a spring-loaded or counter-weighted platform or pushing member against which the distal end of the plunger of the injection syringe rides, so that the biased member returns the piston to its upper position (as shown) when the state of the stopcocks allows flow and the pressure in line 21 drops below the spring bias threshold.

In the prototype embodiment, the injector drive consisted of a MedRad radiographic contrast injection instrument, and the remainder of the cabinet and control mechanism of unit 20 was built atop the injector mount so that the active syringe was conveniently located in immediate proximity to the other elements shown in Figure 2. The stopcock mounting assemblies were prepared as shown in Figures 5A through 5C, by constructing shaped plastic receiving blocks having recesses each shaped to accept a standard disposable stopcock assembly therein and to mount on a plate so that each stopcock engages a position reporting actuator mechanism, which turns the handle of the stopcock. The stopcock was placed into the housing with the handle facing forward and the housing was designed to grip the three fluid connecting stubs of the stopcock, thus securely holding the stopcock body in a fixed position that allowed stopcock position to be controlled to within about one degree. A molded coupling was used to connect the stopcock handle to a standard servomotor, which in turn was controlled by a microcontroller board connected via a serial line to a computer used to control the apparatus. The computer was programmed to control operation of the stopcocks to define different segments for receiving, transferring, mixing and delivering the material. It was also programmed to control the injection regimen of the syringe for delivery of prepared doses to the patient.

In the prototype embodiment, the servomotor assemblies were modified so that the output of an internal potentiometer was passed to an A/D converter on the microcontroller board, and this output was used to calibrate the stopcock positions and then continuously monitor the position of each stopcock. Control software in the microprocessor with a graphical user interface allowed the user to set the position of the stopcock and displayed the position on the screen, signaling an alarm if a motor fails to drive a stopcock element to the programmed position. For preparing the nitrogen-13 tracer, the program was written to effect a sequence of control steps as described below, and delivery steps were controlled by using the injector both to control the preparation of the solution and the injection into the patient.

Figure 4 illustrates a particular sequence for transfer of the tracer bubble from the absorbing chamber 1 into the mixing syringe, which is performed by encapsulating the tracer bubble with a saline solution. In broad terms, the operating sequence proceeded as follows. Before gas is received from the cyclotron the system is readied for production. The tubing from the absorbing chamber is flushed with a gas and the remainder of the apparatus is flushed and filled with de-gassed saline solution. One suitable flush gas is nitrous oxide but many other gases may be used. The chief requirements are that the gas be biologically safe, soluble in water and be non-reactive with the reagents used (sodium hydroxide, in this case). The radioactive gas is then admitted to the absorbing chamber and is stirred with a magnetic stirrer until all carbon dioxide is absorbed. Stirring is performed gently to avoid generation of droplets which might clog the hydrophobic filter 29b (Figure 5). The bubble of remaining gas at the top of the absorbing chamber is then transferred to the injector syringe which is otherwise filled with an appropriate amount of de-gassed saline for the contemplated infusion regiment or for the amount or available radionuclide. The mixture in the injector is next dissolved by repeatedly ejecting it into the passive syringe allowing its return and again ejecting it, so that by the vigorous flow and atomizing action of ejection the tracer is quickly dissolved in the saline solution. This process of vigorous atomization mixing by repeated passage through a flow segment between syringes in a closed set thus effectively addresses the difficult problem of preparing the radionuclide solution in a manner that is both safe and quick.

Next, with the stopcocks reset to define a different flow segment, a sample of the injectate so prepared is expelled from the syringe into the sampling syringe 80. Preferably a pH sensor is also present in the apparatus downstream of the injector syringe to detect any sodium hydroxide contamination which may have occurred, and to actuate a shutdown in that event. The strength of the prepared solution is determined and this data is entered in suitable program for the injection control or image processing. The stopcock configurations are again changed, and the injector then gives a rapid bolus of tracer solution along its output line into the patient.

Returning now to Figure 4, there is shown a representative sequence of states of the finite state flow segment operating sequence of the device, illustrating in this case the initial radionuclide transfer from the receiving chamber 1 into the preparation set 10. After the initial system preparation and cleansing in chamber 1 are completed, the state of the apparatus is as depicted in Figure 4A. The upstream tubing (on the left) of stopcock 22 is filled with flush gas and the downstream tubing (to the right) is filled with degassed saline. The syringe 50 is then operated to draw along line 21 so that, as shown in Figure 4B the bubble of radioactive gas is drawn out of the pocket 109 (Figure 3), and toward the injector syringe 50. Sodium hydroxide solution is also drawn out of the absorbing chamber 1 at the trailing edge of the bubble of carrier/tracer gas. A liquid detector 29a is installed in the assembly 10 about the line 21 just upstream of the first stopcock 22 to provide a signal when the sodium hydroxide reaches this point. The transfer valve (Figure 3) is then closed, and the controller moves the first stopcock (Figure 4C) to connect the saline reservoir and fill in behind the bubble with saline solution from the reservoir. The bubble of tracer is thus "encapsulated" by saline solution as shown in Figure 4D. This allows controlled transfer through the apparatus by operation of the injector syringe. A slight amount of tracer gas still residing in the first stopcock and liquid detector is wasted. However, it will be understood that all tubing interconnecting the various components in the processing section 10 is of small size (under one millimeter), of the type customarily used for transfer of small volumes of fluid, and thus the wasted tracer represents a very small proportion of the carrier/tracer bubble being processed.

After the bubble of gas is completely drawn into the injector syringe, the stopcocks are moved to define a new flow/transfer segment such that the injector outlet communicates only with the adjacent passive syringe. The mixture is then vigorously expelled into the passive syringe, then again drawn back into the active syringe and re-expelled. This process of repeated ejection promotes dissolution of the gas in several ways. Firstly, the surface area of the interface is increased exponentially by atomizing the fluid and in subsequent ejections breaking bubbles of gas into many smaller bubbles. Secondly, the ejection occurs at elevated pressure, thus enhancing the mechanisms of diffusion. Finally, the strong current and highly turbulent flow during ejection mixes the liquid very well, reducing any concentration gradients that might otherwise limit the process.

After the mixing process is complete, the stopcocks are again repositioned and the syringe 50 is operated to expel to the dump a volume equal to the volume of gas originally drawn into the syringe. This assures that any undissolved gas is ejected from the system. The lines to the patient are then flushed with the prepared tracer solution, and a small (1 ml) sample is taken. For the illustrated system, the sample is used primarily to assess the activity of the solution, but it could be additionally analyzed to check the composition of the injectate, or when applied to other radionuclide systems could determine other relevant conditions or parameters.

The pH of the solution is preferably measured by a sensor installed on the line to the dump tank. Any sodium hydroxide contamination is detected at this point, before injection to a patient.

In the foregoing system, it is important that the solution injected into the patient not be super-saturated and not contain any gas bubbles. If the solution were super-saturated, there would be a risk that bubbles could spontaneously appear in the solution before infusion or that microbubbles of nitrogen would form in the bloodstream causing an artificially-induced form of decompression sickness ('the bends'). To assure that supersaturation does not occur, the volume of nitrogen withdrawn from the absorbing chamber is limited to that volume which is known to dissolve in the volume of saline being prepared, and following dissolution, the mixture is allowed to equilibrate at atmospheric pressure. Thus, even if the solution is super-saturated, excess gas will diffuse out of the solution. Further, when, following the mixing described above, the volume at least as great as the volume of gas originally drawn in from the absorbing chamber is ejected from the top of the injector syringe to dump, both the excess undissolved gas and the gas that has come out of solution are expelled.

Preferably, an ultrasonic bubble detector is also installed on the line to the patient, as well as a bubble-trap filter. Prior to injection, the lines are flushed, and a final, visual check for microbubbles is performed.

Figure 6 illustrates another embodiment of the system and set of the present invention. In this embodiment, the compliance chamber or flexible-walled side chamber may be actively pressed. This may be done to assure complete return of the flexible wall, and thus further guard against expulsion of the sodium hydroxide solution. Furthermore, the stopcocks are located somewhat differently to provide a short direct infusion path to the patient, and to separate or shift other paths or path segments. As in the first embodiment, the pressure syringe is centrally located, and serves as a hub for drawing, expelling or moving fluid along the various segment defined by the states of the stopcock valves. Advantageously, the pressure syringe mounts vertically, so that it initially receives and segregates the gas, and subsequently expels residual bubbles to the dump.

For operation of the system, the saline may be drawn from a USP-standard infusion bag, and all parts of the apparatus that contact the solution are assembled using aseptic technique from sterile, disposable medical components. Microporous filters are installed on the line entering the system from the saline bag, and on the line out of the system to the patient. Preferably a batch of tracer solution is prepared before the batch intended for infusion, and a sample is assayed.

Preferably, the bolus infusion of tracer is given by the injector under computer control, with the computer programmed to accurately control the infusate volume and rate, to effectively synchronize with a PET camera, and to automatically adjust dosage as the tracer decays. However, preferably the hardware is designed so that if necessary, the injector can be disconnected and operated manually. In the prototype embodiment using an existing, manually-operated contrast media injector, the addition of a microprocessor-based controller and other modifications made to the injector were such that all of its safety-features function normally, and when manually-operated, the injector was fundamentally the same device as an unmodified, FDA-approved original. The series architecture of the treatment vessel and mixing assembly, together with the unique bubble transfer mechanism and multiple redundant stops and operation safety checks thus forms a system that is safely interposed between a cyclotron target and the patient's vasculature. Repetitive ejection between syringes produces a highly effective mixing/solution mechanism using fungible disposables. Moreover, the provision of a closed, disposable set for handling and compounding the radionuclide in an automated negative pressure safety cabinet allows the operator to maintain a safe distance from radiation, and provides a convenient system for the remote handling and preparation of diverse medicines, reagents and tracer materials.

The invention has been described above in a particular application for receiving, preparing and injecting a gaseous radionuclide for pulmonary PET imaging. However, the unique remote handling, sterile mixing, and volumetric control achieved by the set and the operating console are applicable with slight changes to compounding and delivering medications, marking and synthesizing materials and other radiation-handling tasks. Thus, it should be understood that the invention is not to be limited by the particular embodiments shown and discussed above, but may take other forms and be embodied in diverse systems for preparing, reacting, formulating or delivering radionuclides or biologically active materials. The invention and its principals of operation being thus disclosed, one skilled in the art will appreciate further features and advantages of the invention, and will be lead to further variations and modifications of the invention. Accordingly, all such variations and modifications are considered to be within the spirit and scope of applicant's invention as defined by claims appended hereto and equivalents thereof. All publications and references cited herein are expressly incorporated herein by reference in their entirety.

Claims

1. A system for preparation and delivery of a biologically active, hazardous or radioactive fluid, the system comprising

a receiving system having a first port for receiving said fluid and a second port positioned for delivering said fluid

a fluid handling set including a syringe and a plurality of flushable valves interconnected as a closed unit by tubing extending to an outlet

the syringe connecting via said fluid handling set to said second port and to said outlet for drawing the fluid into the tubing and transferring said fluid to the outlet as a prepared liquid

and the fluid handling set being configured for operation of said valves to define a finite set of flow segments at different times in said set such that the syringe flushes, fills, prepares and delivers the prepared fluid without exposing the operator to radiation.

2. A system for preparation and delivery of a biologically active, hazardous or radioactive material such as a gas, the system comprising

a receiving chamber having a first port for receiving said fluid and a second port positioned for accessing an active gas present in said material

an operating assembly for mounting a fluid handling set including a pressure syringe, a passive syringe and a plurality of flushable valves interconnected as a closed unit by tubing such that the tubing connects to said second port, and the operating assembly being configured to secure and operate the pressure syringe and the plurality of valves in sequence such that the pressure syringe draws the material into the pressure syringe and transfers the material with liquid to said passive syringe so as to form a prepared liquid, and furtheroperating said valves to define a finite set of flow segments at different times in said set for flushing, filling, preparing and delivering the prepared liquid, to receive the material from a source and provide the prepared liquid to a patient.

3. A system for preparation and delivery of a biologically active, hazardous or radioactive material, the system comprising

a receiving chamber having a first port for receiving said material and a second port positioned for accumulating a desired portion of the material

a fluid handling set including a plurality of flushable valves interconnected as a closed unit by tubing and configured for automated remote operation of said valves to form a finite state flow path effective to receive and encapsulate said desired portion as a bubble, prepare said portion in a delivery liquid and transfer the delivery liquid to an output.

4. The system of claim 3, wherein said valves define flow segments at different times in said set for flushing, filling, preparing and delivering the material such that the set receives the material as a gas from a source and safely delivers the delivery liquid to the bloodstream of a patient.

5. The system of claim 4, wherein the fluid handling set includes a pressure syringe operable for drawing the material into the set, mixing the delivery liquid, and delivering the delivery liquid into the bloodstream of a patient.

6. The system of claim 3 or 4, wherein the system prepares a gaseous radionuclide for injection to perform positron emission tomographic images of the patient.

7. The system of claim 3, wherein the fluid handling set is sterile assembly and further comprises and active syringe connected to one of said valves, and a passive syringe connected to another of said valves for receiving liquid such that the set is operable to prepare said portion in said delivery liquid by ejecting said portion and delivery liquid from the active syringe into the passive syringe.

8. A system for sterile preparation of a fluid radionuclide for use, such system comprising a sterile flow set including an inlet, an outlet, a plurality of stopcocks arranged in a sequence along a flow line to define a plurality of fluid transport segments, and first

and second syringes connected to the flow line being operable to form a sterile liquid solution of said radionuclide while it remains in the flow set by repeated ejection from said first syringe to said second syringe and return to said first syringe.

9. A system according to claim 8, wherein the sterile flow set includes at least five stopcocks.

10. A system according to claim 8, wherein at least one of said syringes attaches directly to a port of one of the stopcocks.

11. A fluid handling set for use in receiving a hazardous fluid material and forming a delivery liquid, such set comprising a plurality of at least five stopcocks and tubing interconnecting said plurality of stopcocks to form a closed transport path for handling the hazardous fluid material, each stopcock further having a port for admitting material to or expelling material from said closed transport path.

12. A device for receiving a hazardous fluid material and forming a delivery liquid such as a reagent, medicine or imaging agent containing said fluid material, such device comprising

a plurality of stopcock receptacles arranged along a path,

a corresponding plurality of servomotors positioned and configured for individually controlling a stopcock each being positioned in one of the receptacles,

a syringe driver, and

a controller operative to control said servomotors to form a set of flow segments along a closed transport path for handling the hazardous fluid material, and to control said syringe driver to drive a syringe so that the syringe draws said fluid material into the transport path and moves the fluid material along ones of said flow segments so as to prepare and deliver the delivery fluid.

13. The device of claim 12, further comprising a flow set including a plurality of stopcocks interconnected by tubing to form a sterile flow path, an active syringe connected to said flow path, and a passive syringe connected to said flow path.

14. The device of claim 13, wherein the controller is operative to control said servomotors to define a path between the active syringe and the passive syringe, and to prepare the fluid material by repeated ejection of the material from the active syringe to the passive syringe.

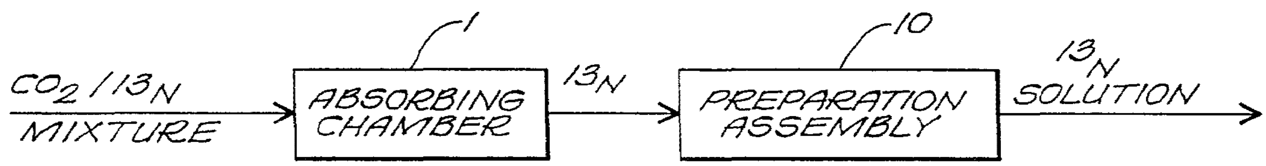

1
10
CO_2 / 13N MIXTURE
ABSORBING CHAMBER
13N
PREPARATION ASSEMBLY
13N SOLUTION

FIG. 1

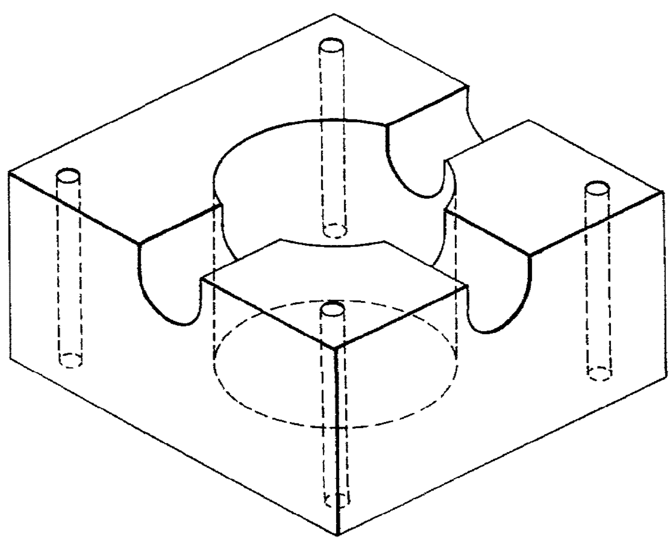


FIG. 5A

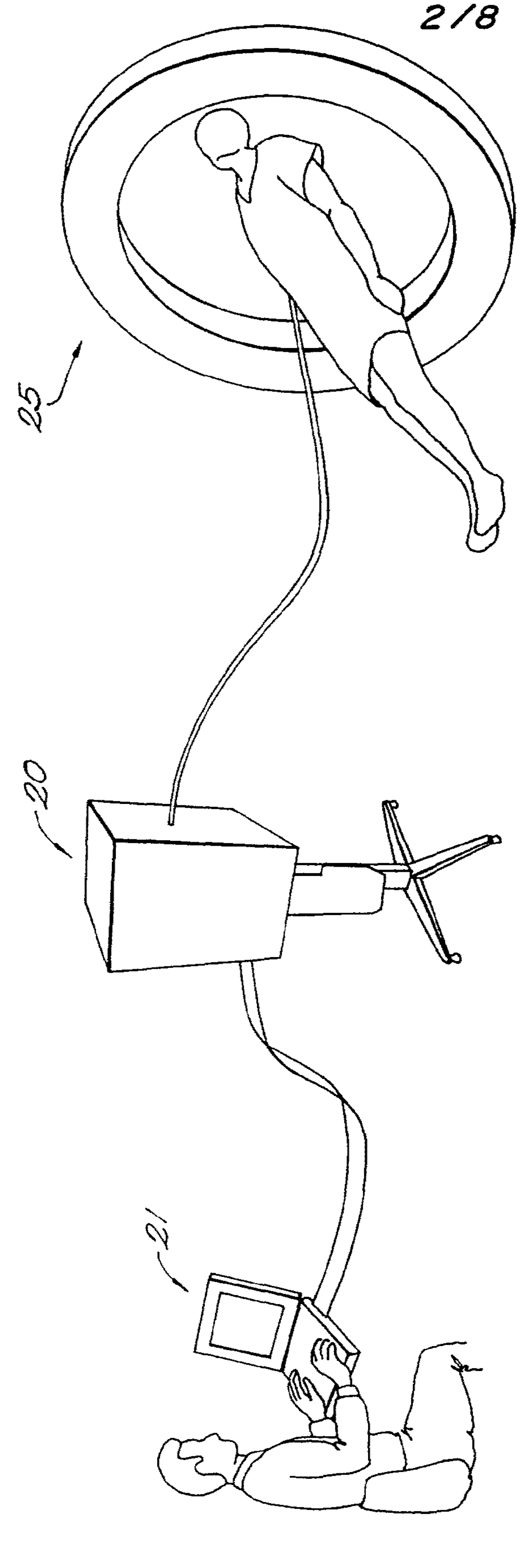


FIG. 1A

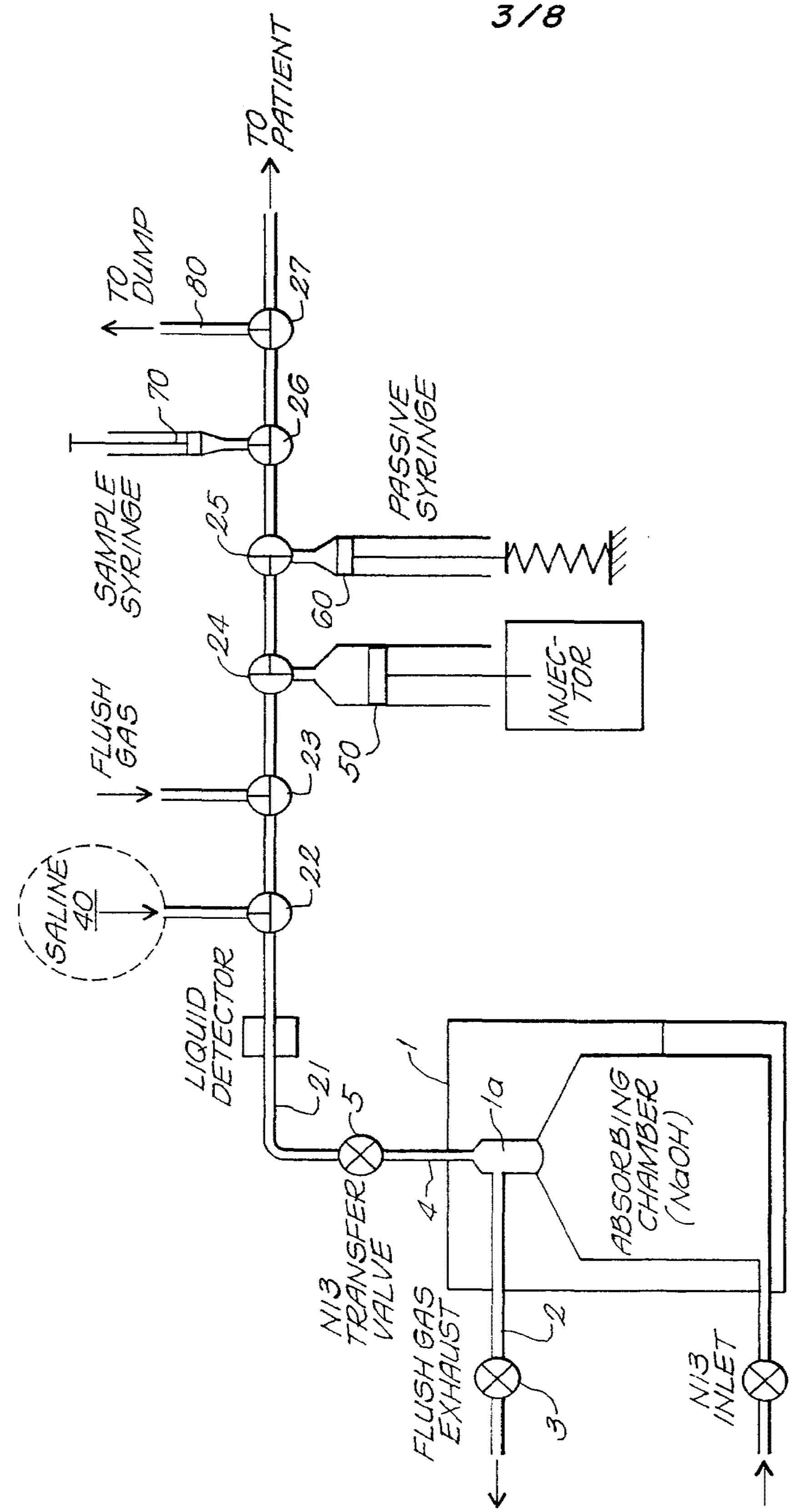

TO PATIENT
TO DUMP
80
27
70
26
SAMPLE SYRINGE
PASSIVE SYRINGE
25
60
24
INJEC-TOR
FLUSH GAS
23
50
SALINE 40
22
LIQUID DETECTOR
21
5
1
1a
ABSORBING CHAMBER (NaOH)
N13 TRANSFER VALVE
4
FLUSH GAS EXHAUST
2
3
N13 INLET

FIG. 2

4/8

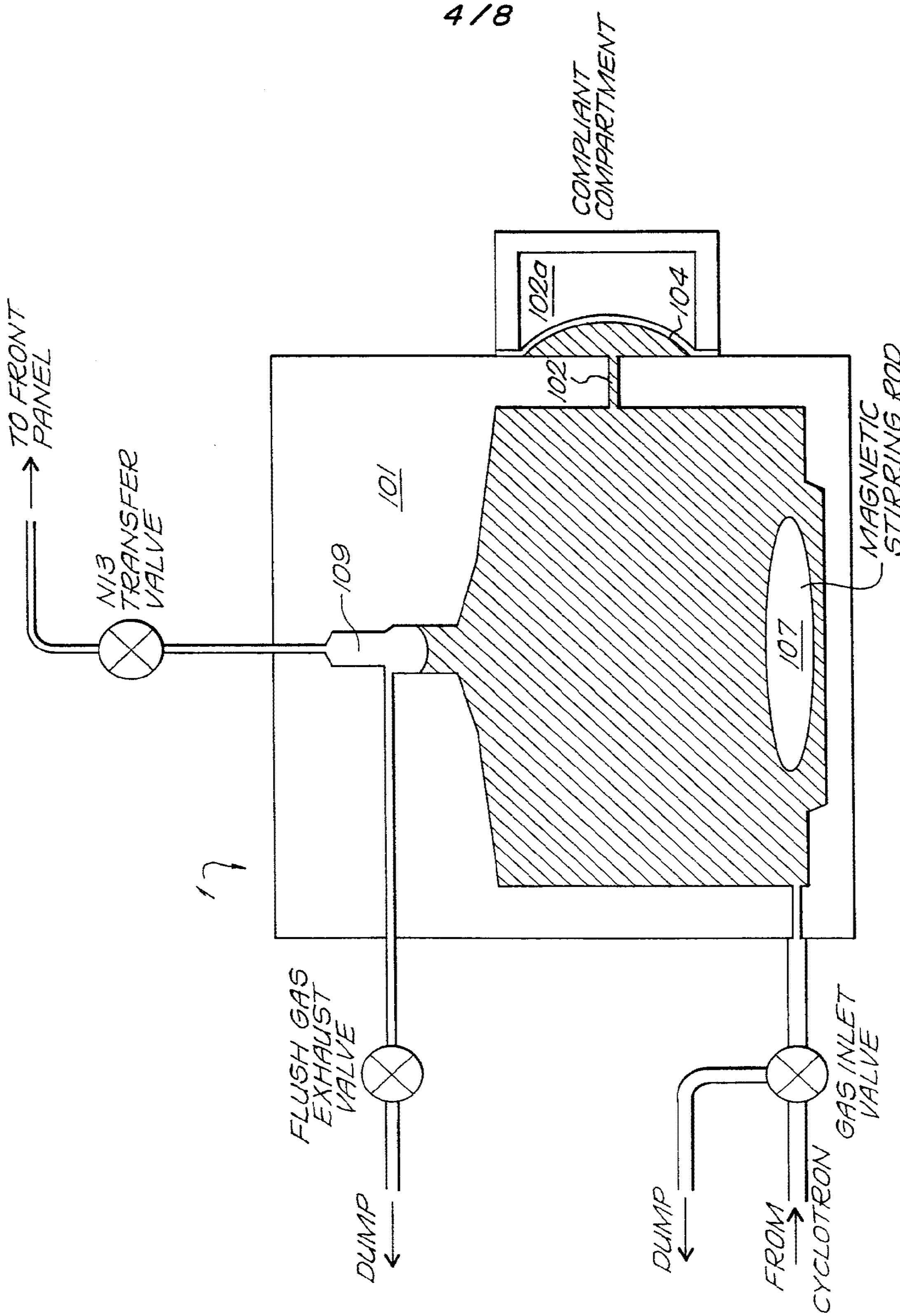

COMPLIANT COMPARTMENT
102a
104
102
TO FRONT PANEL
N13 TRANSFER VALVE
101
109
MAGNETIC STIRRING ROD
107
1
FLUSH GAS EXHAUST VALVE
DUMP
GAS INLET VALVE
DUMP
FROM CYCLOTRON

FIG. 3

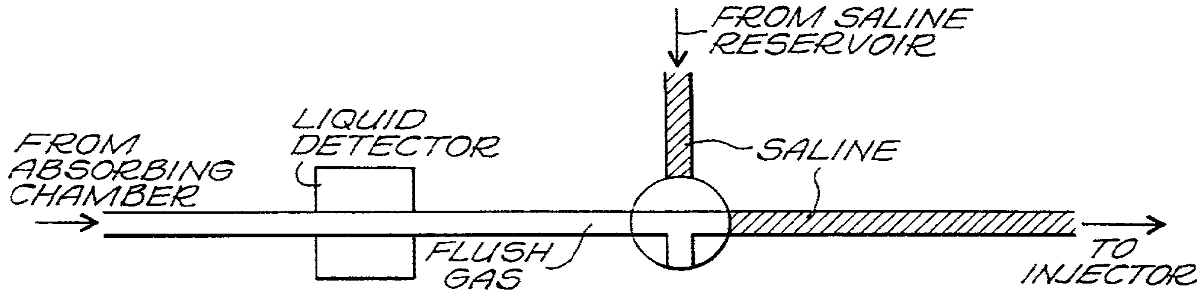


FIG. 4A

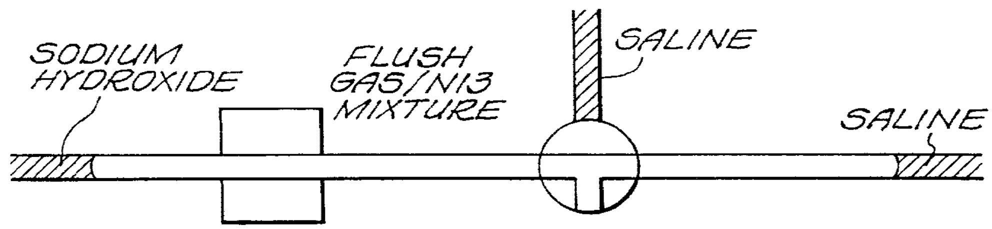


FIG. 4B

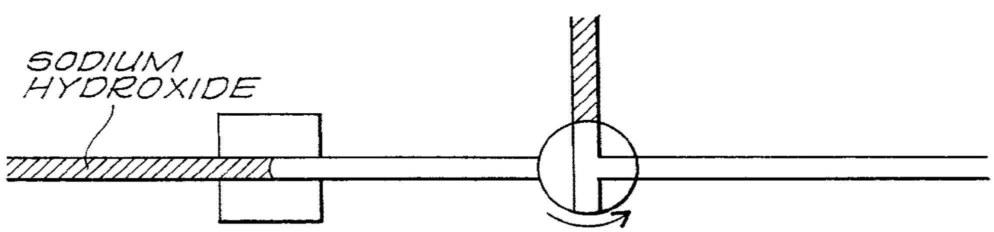


FIG. 4C

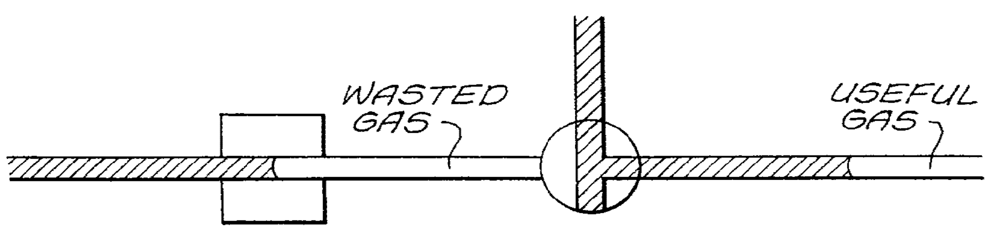


FIG. 4D

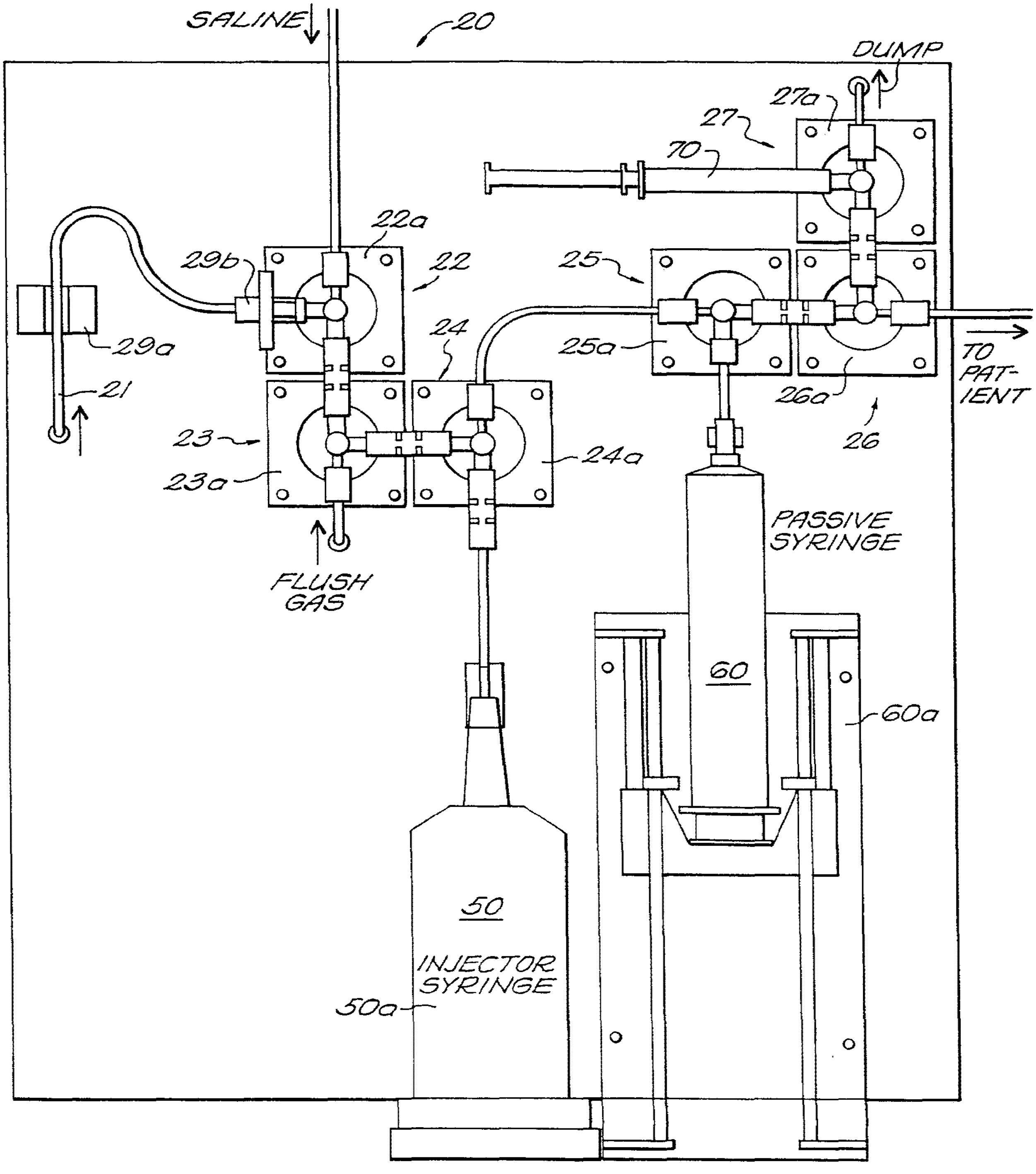

SALINE
20
DUMP
27a
27
70
22a
29b
22
25
29a
24
25a
TO PATIENT
21
26a
26
23
24a
23a
PASSIVE SYRINGE
FLUSH GAS
60
60a
50
INJECTOR SYRINGE
50a

FIG. 5

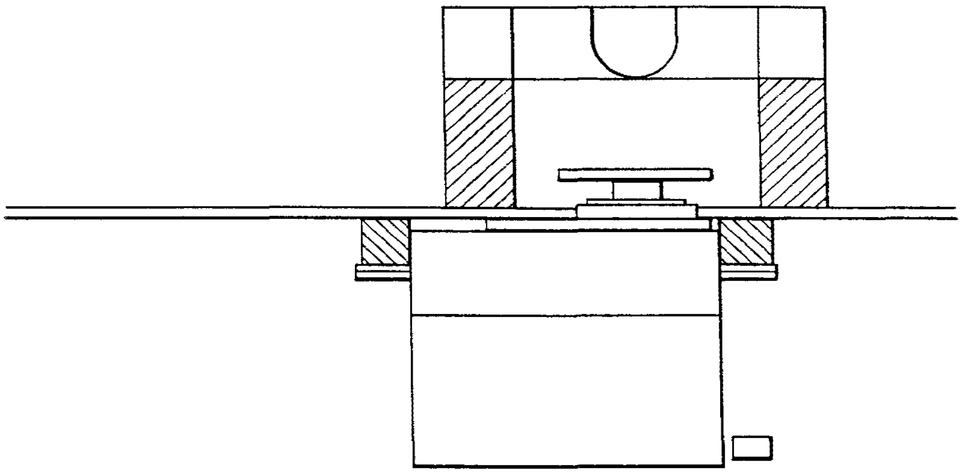


FIG. 5B

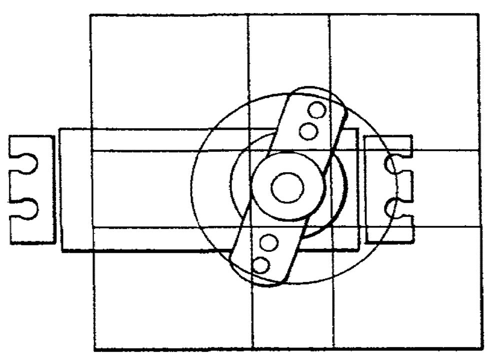
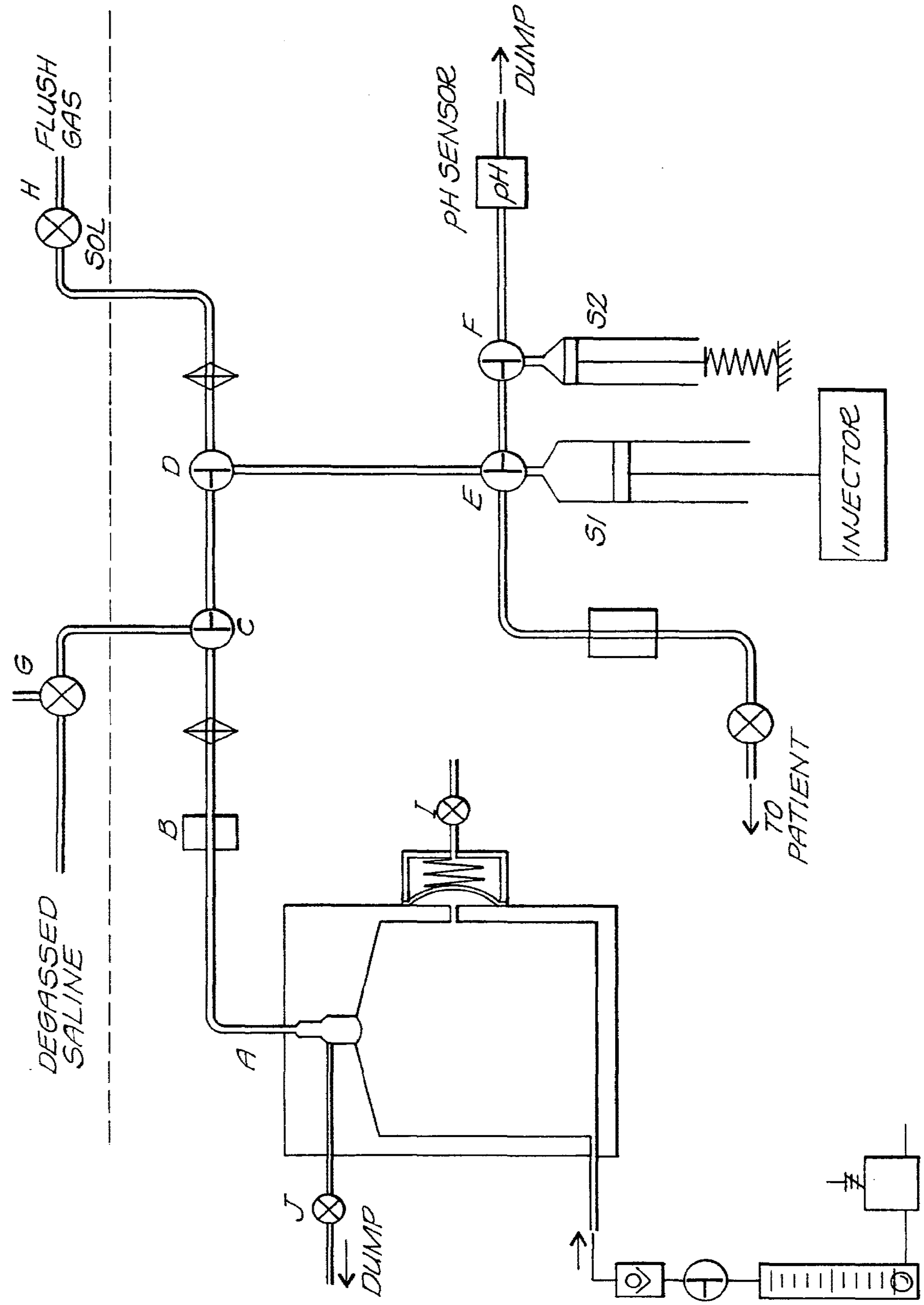


FIG. 5C



FLUSH GAS
H
SOL
DEGASSED SALINE
G
B
A
C
D
E
F
S1
S2
pH SENSOR
pH
DUMP
INJECTOR
TO PATIENT
I
J
DUMP

FIG. 6

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US99/08981

A. CLASSIFICATION OF SUBJECT MATTER

IPC(6) :G01N 24/00, 37/00
US CL :436/57, 174, 180; 422/81, 100, 903
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 436/57, 174, 180; 422/81, 100, 903

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

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

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 5,482,865 A (FERRIERI et al) 09 January 1996, entire document.	1-14
A	US 5,514,071 A (SIELAFF, JR. et al) 07 May 1996, entire document.	1-14
A	US 5,468,355 A (SHEFER et al) 21 November 1995, entire document.	1-14
A	US 5,223,434 A (KANNO et al) 29 June 1993, entire document.	1-14

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

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
19 JULY 1999	19 AUG 1999

Name and mailing address of the ISA/US
Commissioner of Patents and Trademarks
Box PCT
Washington, D.C. 20231
Facsimile No. (703) 305-3230

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Form PCT/ISA/210 (second sheet)(July 1992)★

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
13 January 2005 (13.01.2005)

PCT

(10) International Publication Number
WO 2005/002971 A1

(51) International Patent Classification[7]: B65B 3/30

(21) International Application Number: PCT/AU2004/000897

(22) International Filing Date: 2 July 2004 (02.07.2004)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
2003903404 2 July 2003 (02.07.2003) AU

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(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

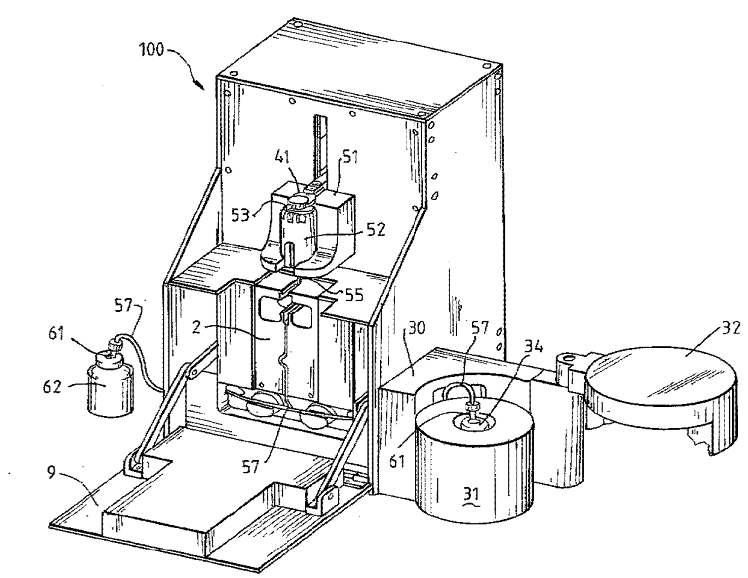
(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Declarations under Rule 4.17:

— *as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii)) for the following designations AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS,*

[Continued on next page]

(54) Title: PROCESS AND DEVICE FOR THE DOSE DISPENSING OF A RADIOACTIVE SOLUTION



(57) Abstract: A method of and a device (100) for automatically dispensing radioactive doses by filling a container (53), being a vial or disposable syringe, with a required radioactive dose in a sterile environment, the device (100) being stand alone and radiation shielded. The device (100) further includes control means to accurately dispense and dilute the requested radioactive dose using an on-line radioactivity measurement without any need for knowledge of the volumetric radioactivity of the stock solution.

WO 2005/002971 A1

JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, ARIPO patent (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG)

— *as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii)) for the following designations AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, ARIPO patent (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG)*

— *of inventorship (Rule 4.17(iv)) for US only*

Published:

— *with international search report*

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

PROCESS AND DEVICE FOR THE DOSE DISPENSING OF A RADIOACTIVE SOLUTION

Area Of The Invention

This invention relates to apparatus used in nuclear medicine and in particular to a means whereby a radioactive dose required can be provided to a syringe in an automated fashion which obviates the need for a person to actually handle the radioactive material.

Background To The Invention

Radioactive solutions called radiotracers or radiopharmaceuticals, have found applications in various medical fields, in particular in medical diagnostic and therapeutic fields. In recent years the advance of Positron Emission Tomography (PET), which use radionuclides (radioisotopes) of significant higher radiation energy than more conventional nuclear medicine isotopes, has raised some concerns about hand and body radiation exposure received by the persons preparing the dose.

The dangers of ionising radiation are well known and apply to all persons being exposed to radiation, including the staff involved in the preparation of radioactive solutions. Dose fractionation of the radioactive solutions is usually a manual process, performed behind a lead shielded screen to minimal exposure to radiation. However, the performance of this task is time consuming, as the operator needs to withdraw by successive iterations, small volumes of the radiotracer, until he reaches the targeted dose.

After each withdrawal the needle needs to be re-capped and the syringe placed in a dose calibrator to determine if more or less of the radioactive solution should be processed in or out of the syringe. When the targeted dose has been achieved (within ± 10%), the syringe may be topped up with saline to obtain a reasonable volume.

Before being released or dispatched for clinical use, the syringe is placed again in the dose calibrator to print out the accurate dose record. To date, very little attempt has been made by manufacturers to design automated equipment capable of withdrawing a dedicated radioactive dose into a disposable sterile syringe or vial.

The very few systems currently on the market are expensive and bulky and are not widely available. Other more affordable systems are either not technically practical or do not achieve efficient radiation protection and need to be operated in a shielded environment. In addition, most of these apparatus rely on the pre-requisite knowledge of the volumetric radioactivity (Ci/mL or Bq/mL) of the stock solution to determine the corresponding volume and hence the radioactive dose to be dispensed.

Outline of The Invention

It is an object of this invention to provide an accurate means of automatically dispensing individual doses of a radioactive solution into vials or syringes under aseptically controlled conditions while minimising the exposure to radiation of an operator which would otherwise be associated with the manipulation of radioactive solutions.

The invention in one aspect is a radioactive dose dispensing device for automatically filling a container with a required radioactive dose in a sterile environment, said device being stand alone and radiation shielded and including control means to control a mix of radioactive stock solution and dilution stock solution, the radioactivity of which mix is monitored by radiation detection means.

The invention in a second aspect is a method of automatically dispensing a dose of a radioactive solution using a software controlled lead shielded device which includes the steps of

- providing the device with a radioactive stock solution and a dilution stock solution
- using a computer software interface to the device to control the dose dispensed automatically into a syringe or vial in the device.

It is preferred that the radioactive dose dispensing device be used for filling a disposable syringe. It is further preferred that a shielded receptacle be provided to receive the syringe.

It is also preferred that a fork shaped arm be provided to actuate the plunger of the disposable shielded syringe. It is further preferred that a high precision linear drive mechanism to move either the syringe or its plunger in a vertical direction.

It is preferred that a customised disposable T shaped tubing assembly be used to provide a sterile fluid pathway. It is further preferred that pinch valves be provided to switch between the radioactive stock solution and the dilution stock solution.

It is also preferred that the automation of the device be controlled by a programmable logic controller (PLC) in association with a radiation detector which monitors on-line the radioactive dose passing through the tubing and being dispensed into the syringe.

It is further preferred that the PLC controls the automation tasks and relevant mathematical calculations for dispensing a requisite dose and that this be operable by computer means with an associated printer although any desired arrangement could be used.

In order that the invention may be more readily understood an embodiment of it will be described herein by way of non limiting example with reference to the accompanying drawings

Brief Description Of The Drawing Figures

Fig. 1 Shows a perspective view of the components of the radioactive dose dispensing device of the invention in its "open" orientation;

Fig. 2 Shows a cross-section though the device of the invention as shown in Figure 1.;

Fig. 3 Shows the pre assembled sterile disposable tubing kit used in the device;

Fig. 4 Shows the device of the invention in its "closed" orientation;

Brief Description of an Embodiment of the Invention

The invention 100 in one embodiment is a device for the automatic filling of disposable syringes with a radioactive solution (radiopharmaceutical) for injection or infusion into a patient.

The device 100 is a stand alone equipment that does not require any additional lead shielding and can be directly used on a bench or inside a conventional, unshielded, laminar flow cabinet.

The device includes a concave lead block 30 and a swinging lead lid 32 designed to accommodate standard lead shielded pots 31 commonly used for the transport of radioactive solutions. It also includes a receptacle 51 that can accommodate various shapes of commercially available tungsten syringe shields and provides an easy and safe installation of the syringe shield 52.

The device further includes a fork-shape arm 41 that can hold or release the plunger of the syringe and an electro-actuator that can link the linear drive 36 to the receptacle 51, and drive up/down the syringe and its needle 55 to pierce the Luer Slip Injection Site 59.

The device provides a permanent link between the linear drive 36 and the fork-shape arm 41 and allows both the radioactive solution and the diluting solution to be drawn at a constant fluid flow rate through the tubing and into the syringe.

The Luer Slip Injection Site 59 is attached to the upper tubing assembly and two Luer-lock fittings 61 (with needles) are attached to the lower tubes assembly (see Fig.3 for view of the pre-assembled sterile disposable kit).

The tubing assembly is held in its appropriate position by a small groove and a dedicated shaped recess 2 to accurately position the Luer Slip Injection Site 59, in regard to the needle 55.

The device is provided with both radioactive and diluting stock solutions which are dispensed from their respective vials 34 and 62, up to the syringe by passing through a disposable, sterile and non-pyrogenic fluid pathway with the radioactive amount controlled by a radiation detector 63, which in this embodiment of the invention is a Geiger-Muller tube or PIN photodiode and located behind a portion of the tube assembly leading to the injection site (behind the plate holder 2).

The device is automated via a programmable PLC and is connected to a computer serving as a user interface, and preferably is provided with a printer to print the syringe or vial label showing the activity, date, time, batch, patient name, etc. or whatever may be required.

The dispensing of the radioactive dose is done on-line by measuring the true amount of radioactivity passing in front of the radiation detector 63 and the total volume required into the syringe is automatically adjusted by dilution.

The device also includes a safety cross-evaluation of the delivered radioactive dose which is automatically performed using the traditional volumetric dispensing method, and the volumetric method can also be used as the main dispensing method.

It is further envisaged that the device of the invention may include a built-in sterile air flow, designed to allow the device to be operated on a bench in a conventional room but still maintaining full compliance with a 3.5 class (A class) dispensing environment, characterized by a sterile air flow directed towards the Luer Slip Injection Site 59 and needle 55.

It is also envisaged that in another embodiment of the invention a sterile disposable double check-valve could be located between the syringe 53 and needle 55, or underneath the Luer Slip Injection Site 59 to allow the transfer of an accurate dose of radioactive solution through a tube, to externally located vials or containers.

Operation of the device

When the device is being operated the user opens the door 9 of the device and installs a new tubing kit 57 onto the tubing holder 2. The Luer Slip Injection Site 59 attached to the upper T-shape tube is slid into the appropriate recess and both needles 61 attached to the lower T-shape tubes are fed through each lead channel and connected to the radioactive stock solution 34 and the dilution stock solution 62.

The user then rotates the lid 32 and closes the door 9 and introduces a disposable syringe 53 with its appropriate needle 55 into a tungsten syringe shield 52. At this point the needle is un-capped and the tungsten syringe shield is placed onto the receptacle 51 on the front face of the device. The operator then enters on the computer the requested radioactive dose and total volume.

The device lowers the receptacle 51 enabling the syringe to pierce the Luer Slip Injection Site with the needle. The filling sequence will automatically dispense the desired radioactive dose into the syringe and dilute it to match the requested volume by actuation of the syringe plunger. Once the syringe has been filled (less than one minute), the syringe and syringe shield are lifted away from the Luer Slip Injection Site, and the syringe and syringe shield is removed from the device and needle re-capped. At the end of the process, a syringe label is printed with the appropriate dose data.

Summary of the embodiment of invention

Traditionally the accurate knowledge of the volumetric radioactivity (specific activity: Ci/mL or Bq/mL) of a radioactive stock solution is required for the accurate dispensing of any radioactive dose.

For example, a dose of 3mCi (111MBq) of a radioactive solution with a volumetric radioactivity of 50 mCi/mL (1850MBq/mL) will be precisely achieved by dispensing a volume of 0.06mL. However, volumetric radioactivity of solutions is not always determined with great accuracy at the time of the manufacturing of the product, and post measurement of the volumetric radioactivity at the customer site is regarded as a critical operation.

The invention has the novel feature in that it can accurately dispense a requested radioactive dose without any knowledge of the volumetric radioactivity of the stock solution by an on-line radioactivity measurement and without exposing an operator to the radiation.

In the invention, a radiation detector 63 being a Geiger-Muller tube, a PIN photodiode or other fast measuring device is located behind a portion of the tubing leading to the injection site 59 and then to the syringe 53. The radiation detector continuously monitors the radioactive dose passing through the tube and into the syringe at a very constant liquid flow rate and the PLC 11 determines the appropriate switching sequence of the valves to dispense the requested dose and volume.

The program also calculates online the corresponding radioactivity contained in the dead volume of the tubing which will be inevitably added-on during the dilution phase of the syringe filling. That corresponding radioactivity is subtracted from the required dose by the PLC 11 to identify the amount of radioactivity allowed to pass the radiation detector 63. At the end of the filling process, the sum of the amount of activity allowed to pass by the detector before the dilution phase and the resultant activity gained during the dilution phase due to the dead volume of the tubing kit, translates to the required dose.

Below is the formula used to determine how much of the stock solution needs to be drawn-up into the syringe to achieve the desired dose (this calculation is performed continuously during the filling process):

Let RD = Requested dose

ADV = Activity contained in the dead volume of the tubing

RMT = Radioactivity measured passing through the tubing

VA = Volumetric activity of the stock solution

DV = Dead volume of the tubing

SA = Volumetric radioactivity

VSW = Volume of stock solution withdrawn from vial

Therefore the radioactive amount of stock solution to draw-up into syringe:

= RD – ADV

= RD – (DV x SA)

= RD – (DV x (RMT/(VSW-DV))

Using the above method of filling a syringe with a radioactive solution, it is not necessary to know the specific activity of the stock solution prior to the filling process, as it is calculated during the filling process.

The accuracy of the dose dispensed is a function of the volumetric radioactivity of the radioactive stock solution, and experiments have shown accuracy better than 5% for volumetric radioactivity in the range of 0-50 mCi/mL (0-1850MBq/mL) and better than 10% for volumetric radioactivity in the range of 50-100 mCi/mL (0-3700MBq/mL).

The invention lies in an automated means of preparing a dose of a radiopharmaceutical into a disposable syringe under computer control by means of a radiation detector to determine the radioactive dosage and dilution by a non radioactive solution to achieve a desired volume. By this means such a dose can be prepared without unnecessary radiation exposure occurring to the person preparing the dose.

The precise components of the apparatus of the invention may be varied provided they achieve the method of the invention as described. It is further envisaged that other embodiments of the invention will exhibit any number of and any combination of the features of those previously described and whilst we have described herein one specific embodiment of the invention it is to be understood that variations and modifications in this can be made without departing from the spirit and scope thereof.

The claims defining the invention are as follows:

1. A radioactive dose dispensing device for automatically filling a container with a required radioactive dose in a sterile environment, said device being stand alone and radiation shielded and including control means to control a mix of radioactive stock solution and dilution stock solution, the radioactivity of which mix is monitored by radiation detection means.

2. A radioactive dose dispensing device as claimed in claim 1 wherein the container is a plunger operated disposable syringe.

3. A radioactive dose dispensing device as claimed in claim 2 wherein a shielded receptacle is provided in the device to receive the syringe.

4. A radioactive dose dispensing device as claimed in claim 3 wherein drive means are provided to actuate the plunger of the syringe.

5. A radioactive dose dispensing device as claimed in claim 4 wherein the drive means is a linear drive mechanism adapted to move either the syringe or its plunger relative to one and other.

6. A radioactive dose dispenser device as claimed in any one of claims 1 to 5 wherein a disposable tubing assembly is used to provide a sterile fluid pathway for the stock solutions.

7. A radioactive dose dispenser device as claimed in claim 6 wherein pinch valves are provided to switch between the radioactive stock solution and the dilution stock solution.

8. A radioactive dose dispenser device as claimed in any one of claims 1 to 7 wherein the automation of the device and its calculation of a requisite dose is controlled by a programmable logic controller (PLC) in association with a radiation detector which controls the radioactive dose passing through the tubing and being dispensed into the syringe.

9. A radioactive dose dispenser device as claimed in claim 8 wherein the device and its PLC are operable by means of a computer interface.

10. A method of automatically dispensing a dose of a radioactive solution using a software controlled lead shielded device which includes the steps of
   - providing the device with a radioactive stock solution and a dilution stock solution
   - using a computer software interface to the device to control the dose dispensed automatically into a syringe or vial in the device.

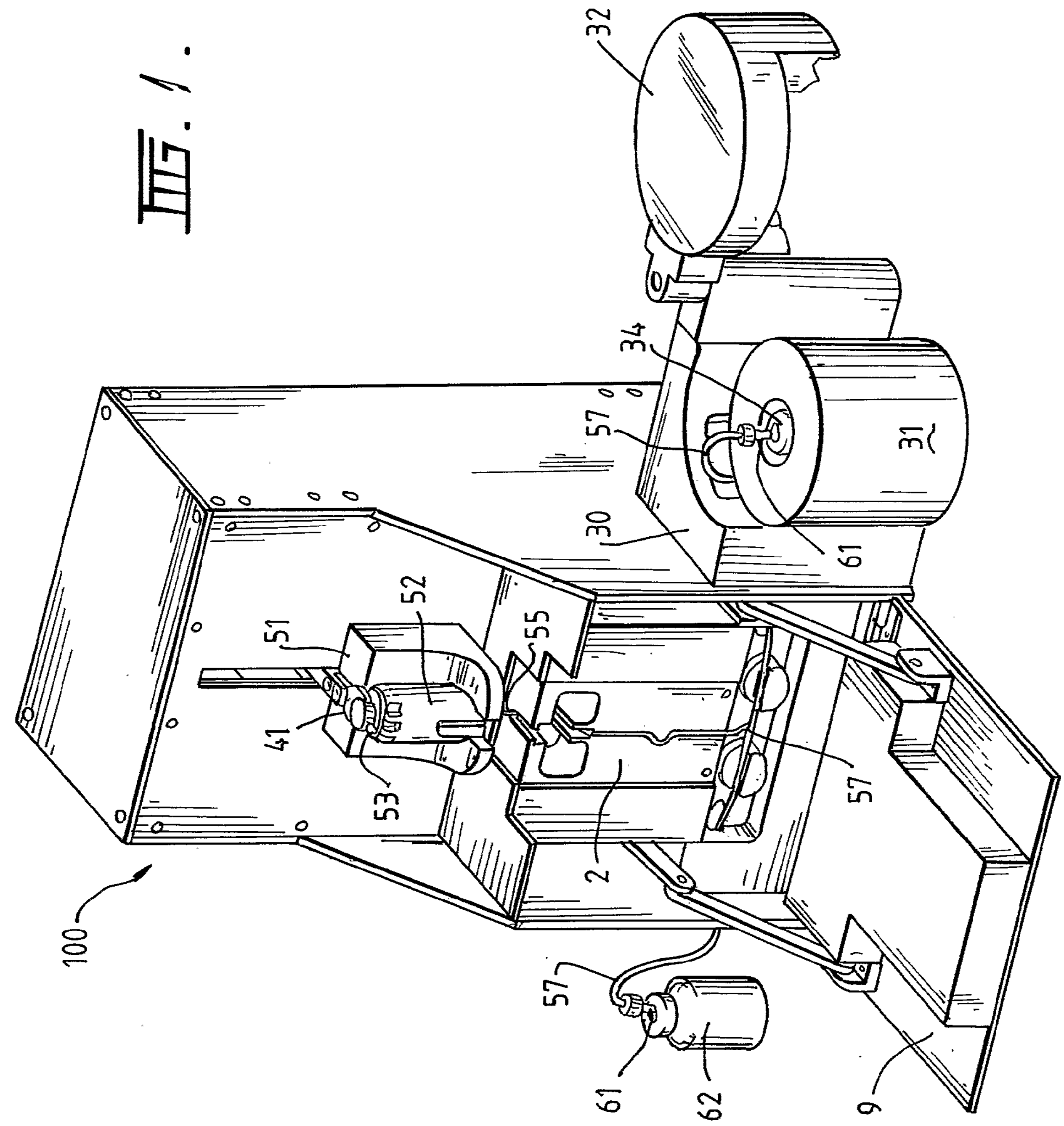


FIG. 1.

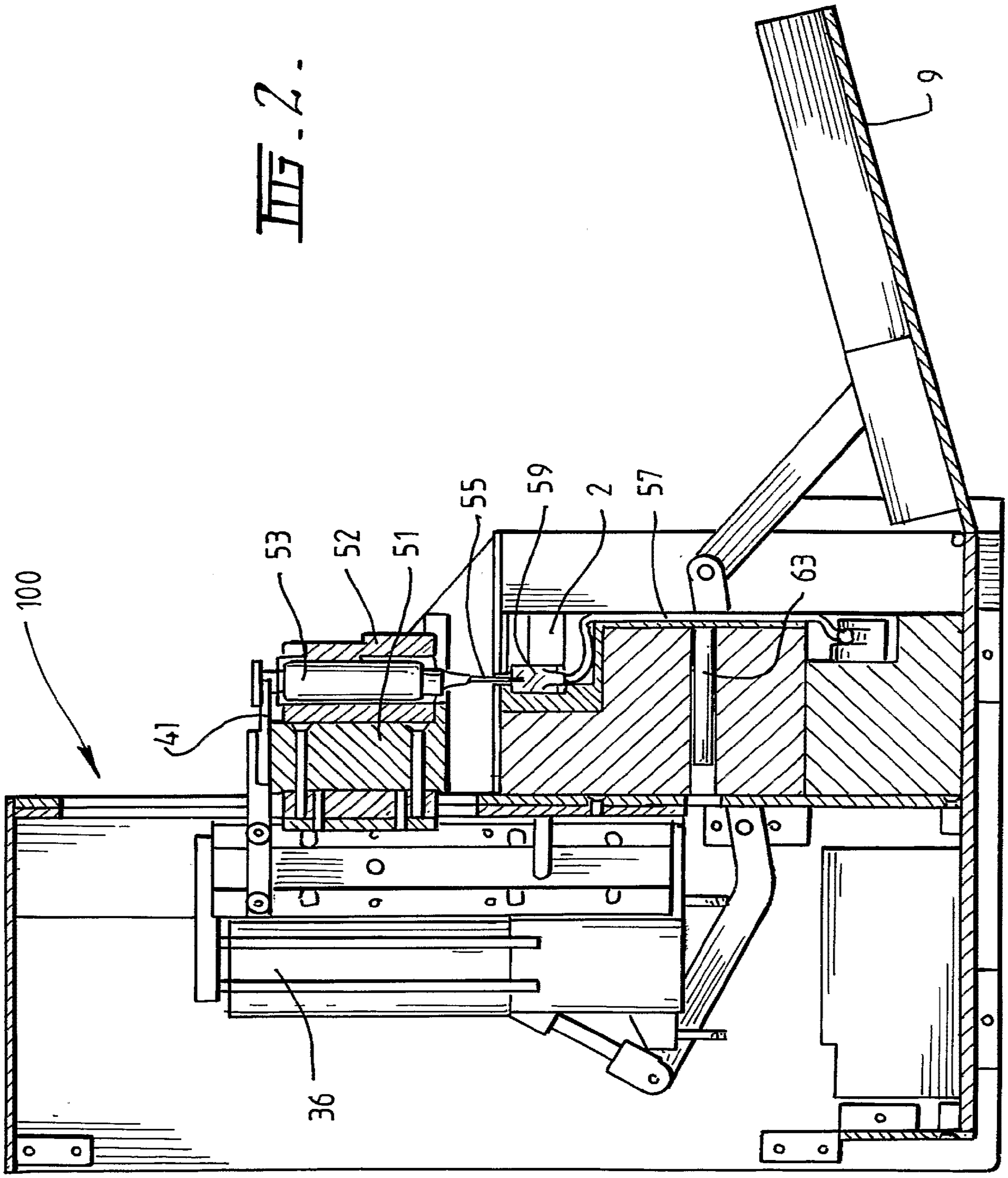


FIG. 2.

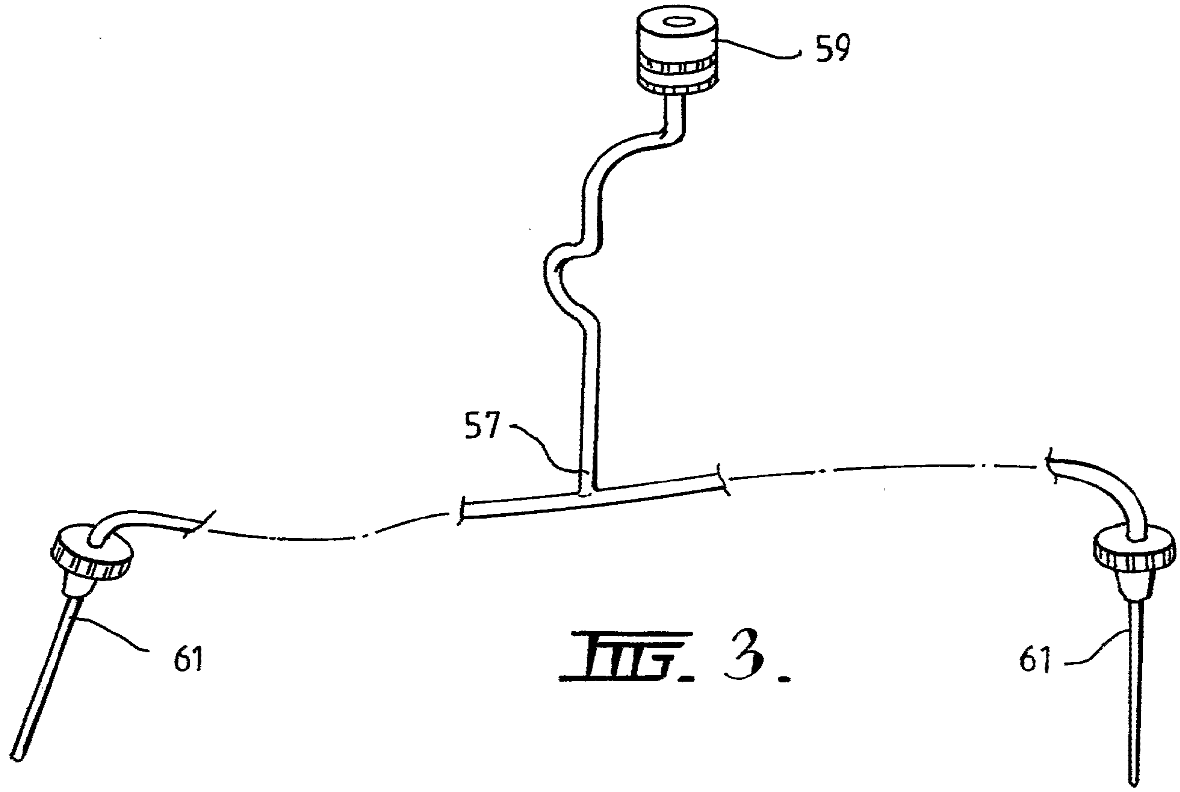


FIG. 3.

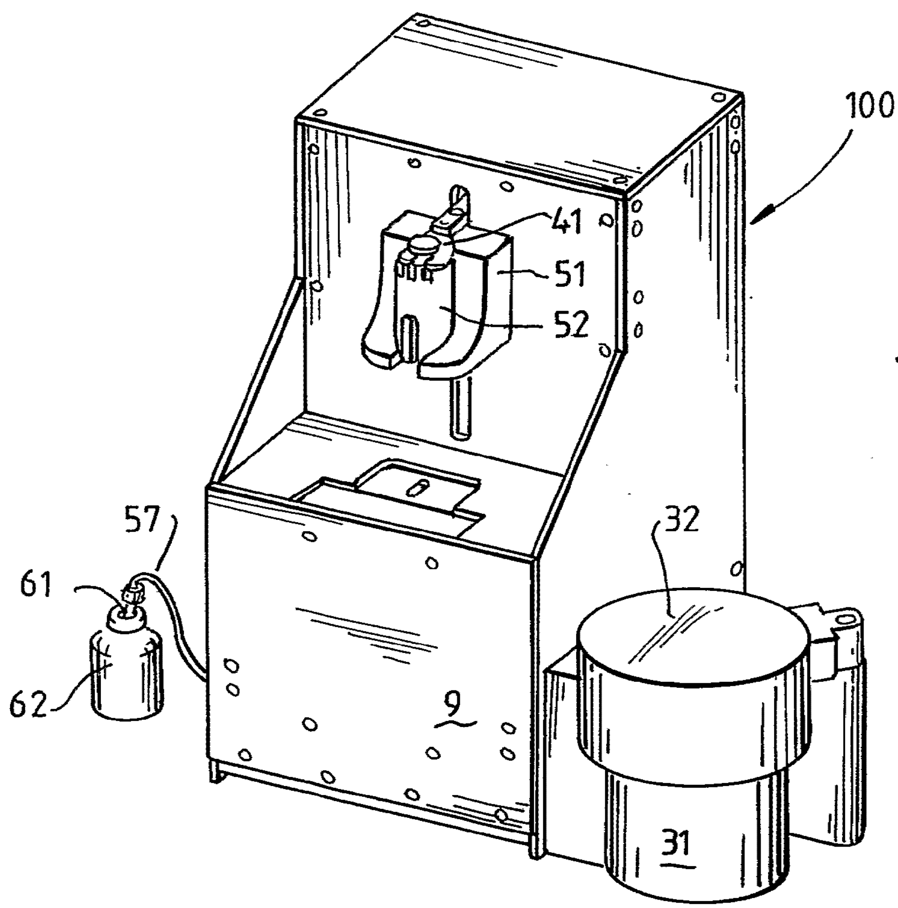


FIG. 4.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/AU2004/000897

A. CLASSIFICATION OF SUBJECT MATTER

Int. Cl. [7]: B65B 3/30

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

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
See below under "Electronic database consulted"

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
USPTO

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
DWPI: IPC : B65B 3/- with keywords: radioactive, nuclear

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
	US 5911252A (CASSEL) 15 June 1999	
X	The whole document	10
Y	The whole document	1-9
	US 4041994A (HORWITZ et al.) 16 August 1977	
Y	The whole document	1-9
A	US 4662231A (SCHAARSCHMIDT et al.) 5 May 1987	1-10
A	GB 1415804A (COMMISSARIAT A L'ENERGIE ATOMIQUE) 26 November 1975	1-10

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

* Special categories of cited documents:

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier application or patent but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed
- "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
- "&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
22 July 2004	- 3 AUG 2004

Name and mailing address of the ISA/AU

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INTERNATIONAL SEARCH REPORT

International application No.
PCT/AU2004/000897

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
   because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
   because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☐ Claims Nos.:
   because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a)

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:
See the Supplemental Box

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☒ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest ☐ The additional search fees were accompanied by the applicant's protest.
☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/AU2004/000897

Supplemental Box
(To be used when the space in any of Boxes I to VIII is not sufficient)

Continuation of Box No: III

The international application does not comply with the requirements of unity of invention because it does not relate to one invention or to a group of inventions so linked as to form a single general inventive concept. In coming to this conclusion the International Searching Authority has found that there are different inventions as follows:

1. Claims 1-9 is directed to a radioactive dose dispensing device including control means to control a mix of radioactive stock solution and dilution solution. It is considered that the monitoring the radioactivity of a mix by radiation detection means comprises a first “special technical feature”.

2. Claim 10 is directed to a method of automatically dispensing a dose of radioactive solution. It is considered that the steps providing the device with a radioactive stock solution and dilution solution and using a computer software interface to control the dispensed dose comprises a second “special technical feature”.

These groups are not so linked as to form a single general inventive concept, that is, they do not have any common inventive features, which define a contribution over the prior art. The common concept linking together these groups of claims is controlling a mix of radioactive stock solution and dilution solution in a dispensing device. However this concept is not novel in the light of US 5911252A. Therefore these claims lack unity a posteriori.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/AU2004/000897

This Annex lists the known "A" publication level patent family members relating to the patent documents cited in the above-mentioned international search report. The Australian Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

Patent Document Cited in Search Report		Patent Family Member					
US	5911252						
US	4041994						
US	4662231	BE	900719	BE	902407	BR	8405970
		BR	8505220	DE	3342470	DE	3438303
		FR	2555746	FR	2572179	GB	2151780
		GB	2167736	JP	60179624	JP	61099836
		US	4665758				
GB	1415804	BE	805777	CH	576845	FR	2205038

Due to data integration issues this family listing may not include 10 digit Australian applications filed since May 2001.

END OF ANNEX

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
7 December 2006 (07.12.2006)

PCT

(10) International Publication Number
WO 2006/129301 A2

(51) International Patent Classification: Not classified

(21) International Application Number: PCT/IL2006/000562

(22) International Filing Date: 11 May 2006 (11.05.2006)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:

PCT/IL2005/000572	1 June 2005 (01.06.2005)	IL
PCT/IL2005/000575	1 June 2005 (01.06.2005)	IL
60/691,780	20 June 2005 (20.06.2005)	US
60/700,318	19 July 2005 (19.07.2005)	US
60/700,299	19 July 2005 (19.07.2005)	US
60/700,317	19 July 2005 (19.07.2005)	US
60/700,753	20 July 2005 (20.07.2005)	US
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60/750,294	13 December 2005 (13.12.2005)	US
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60/750,334	15 December 2005 (15.12.2005)	US
PCT/IL2006/000059	15 January 2006 (15.01.2006)	IL
67/763,458	31 January 2006 (31.01.2006)	US

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(81) **Designated States** *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) **Designated States** *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

— *without international search report and to be republished upon receipt of that report*

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) **Title:** UNIFIED MANAGEMENT OF RADIOPHARMACEUTICAL DISPENSING, ADMINISTRATION, AND IMAGING

(57) **Abstract:** Apparatus is provided for use with at least one labeled radiopharmaceutical agent, the apparatus including a container (22) containing the at least one labeled radiopharmaceutical agent, and a portable computer-communicatable data carrier (120, 24) associated with the container (22), the data carrier (120, 24) containing imaging protocol information for use with the at least one labeled radiopharmaceutical agent. Other embodiments are also described.

WO 2006/129301 A2

UNIFIED MANAGEMENT OF RADIOPHARMACEUTICAL DISPENSING, ADMINISTRATION, AND IMAGING

CROSS-REFERENCES TO RELATED APPLICATIONS

The present patent application is a continuation-in-part of:

(i) International Application PCT/IL2005/001215, filed November 16, 2005; and

(ii) International Application PCT/IL2005/001173, filed November 9, 2005, which:

(a) claims the benefit of the following US Provisional Patent Applications:

- 60/625,971, filed November 9, 2004;
- 60/628,105, filed November 17, 2004;
- 60/630,561, filed November 26, 2004;
- 60/632,236, filed December 2, 2004;
- 60/632,515, filed December 3, 2004;
- 60/635,630, filed December 14, 2004;
- 60/636,088, filed December 16, 2004;
- 60/640,215, filed January 3, 2005;
- 60/648,385, filed February 1, 2005;
- 60/648,690, filed February 2, 2005;
- 60/675,892, filed April 29, 2005;
- 60/691,780, filed June 20, 2005;
- 60/700,318, filed July 19, 2005;
- 60/700,299, filed July 19, 2005;
- 60/700,317, filed July 19, 2005;
- 60/700,753, filed July 20, 2005;
- 60/700,752, filed July 20, 2005;

- 60/702,979, filed July 28, 2005;
- 60/720,034, filed September 26, 2005;
- 60/720,652, filed September 27, 2005; and
- 60/720,541, filed September 27, 2005, and

(b) is a continuation-in-part of the following International Patent Applications:

- PCT/IL2005/000572, filed June 1, 2005; and
- PCT/IL2005/000575, filed June 1, 2005.

The present patent application claims the benefit of the following US Provisional Applications:

- 60/750,287, filed December 13, 2005;
- 60/750,334, filed December 15, 2005; and
- 60/750,597, filed December 15, 2005.

The present patent application is related to a US provisional patent application filed on even date herewith, entitled, "Imaging protocols."

All of the above-mentioned applications are assigned to the assignee of the present application and are incorporated herein by reference.

FIELD OF THE INVENTION

The present invention relates generally to pharmaceutical management and control, and specifically to systems and methods for radiopharmaceutical dispensing, administration, and imaging.

BACKGROUND OF THE INVENTION

US Patent Application Publication 2005/0277833 to Williams, Jr., which is incorporated herein by reference, describes techniques for handling, mixing, dispensing and/or injecting a mixture into an individual during a medical procedure. The mixture contains pharmaceutical agents and/or radiopharmaceutical agents. Also described is a mixing device capable of diluting a radiopharmaceutical agent with, for instance, a diluent, for altering a radiation dose emitted by the radiopharmaceutical agent.

US Patent Application Publication 2005/0203389 to Williams, Jr., which is incorporated herein by reference, describes techniques for an operator to control an injection device and imaging equipment from a common control console. The injection device may be used to administer a contrast medium into a patient so that imaging equipment can acquire internal images of the patient. An injection system is bundled with software and/or hardware that is used to modify an existing imaging control console so that it can be used to operate both the injection device and imaging device. In one embodiment, the common control console can access stored protocols that can contain operational parameters for the injection device, the imaging device, or both.

US Patent 4,679,142 to Lee, which is incorporated herein by reference, describes techniques for dispersing quantities of radioactive material at a user location. Billing is accomplished by monitoring the decay of material and the degree of activity following each user withdrawal.

US Patent Application Publication 2005/0261938 to Silverbrook et al., which is incorporated herein by reference, describes a method for authenticating a pharmaceutical product, the pharmaceutical product being associated with packaging having disposed thereon or therein coded data including a number of coded data portions, each coded data portion being indicative of an identity of the pharmaceutical product and at least part of a digital signature of at least part of the identity. The method includes having a computer system receive indicating data from a sensing device, the sensing device being responsive to sensing of the coded data to generate indicating data at least partially indicative of the identity of the pharmaceutical product and the signature part. The computer system determines the identity at least one determined signature part and uses these to authenticate the pharmaceutical product.

US Patent Application Publication 2005/0261936 to Silverbrook et al., which is incorporated herein by reference, describes a method for allowing a user to interact with a pharmaceutical product, the pharmaceutical product associated with packaging having disposed thereon or therein coded data, at least some of the coded data being indicative of at least an identity. The method includes having a computer system receive indicating data from a sensing device, in response to sensing of the coded data, and determine, using the indicating data, at least one action. The computer system then performs the action associated with the pharmaceutical product, the action including at least one of providing information to a user; updating tracking information relating to the pharmaceutical product; performing a transaction relating to the pharmaceutical product; authenticating the pharmaceutical product; and receiving feedback from the user.

US Patents 5,882,338 and 6,019,745 to Gray, which are incorporated herein by reference, describe a medical syringe comprising a cylindrical barrel having therein a plunger which can be axially driven by a plunger rod. The plunger rod passes through an aperture in the center of a finger grip having two finger grip projections at opposite sides thereof. A data carrier means in the form of an electrically or magnetically operable device is mounted near the end of one of the two finger grip projections, with preferably a device mounted near the end of each finger grip projection. The device carries data relating to the medicament contained or to be contained within the syringe, and can be read by a suitably adapted syringe pump when the syringe is mounted thereon to be driven by the syringe pump.

US Patent 6,970,735 to Uber, III et al., which is incorporated herein by reference, describes a system for producing a contrast-enhanced medical image of a patient, including a source of a contrast or enhancement medium, a pressurizing unit in fluid connection with the source of contrast or enhancement medium, an energy source operable to apply energy to a region of the patient, an imaging unit providing a visual display of an internal view of the patient based upon a signal resulting from the energy applied to the region of the patient, and a control unit. In an embodiment, the signal is affected by a condition of the contrast or enhancement medium in the patient. To control an imaging procedure, the control unit adjusts the condition of the contrast or enhancement medium in the patient based upon the signal. A communication interface preferably enables information between an injector subsystem and an imaging subsystem.

US Patents 5,781,442, 6,671,563, 6,915,170, and 6,731,989 to Engleson et al., which are incorporated herein by reference, describe a care management system in which the management of the administration of care for patients is automated. Hospital information systems are monitored and the information from those systems is used in verifying the administrations of care to patients. The care management system monitors ongoing administrations for progress and automatically updates records and provides alarms when necessary. The care management system is modular in nature but is fully integrated among its modules. Particular lists of data, such as the termination times of all ongoing infusions, provide hospital staff current information for increased accuracy and efficiency in planning. Features include the automatic provision of infusion parameters to pumps for accurate and efficient configuration of the pump, and providing an alarm when an unscheduled suspension of an infusion exceeds a predetermined length of time. A passive recognition system for identifying patients and care givers is described.

US Patent Application Publication 2003/0055685 to Cobb et al., which is incorporated herein by reference, describes techniques for monitoring administration of a medical product within a delivery device using a medicine data storage device attached to the delivery device, which includes a product identifier identifying the medical product and an intended patient identifier identifying a patient intended to receive the medical product. Before administering the medical product to an individual patient, the product identifier and the intended patient identifier are uploaded into a reader, and a patient identifier is accessed from the reader's memory or uploaded from a patient identification device associated with the individual patient into the reader. The patient identifier is compared with the intended patient identifier to determine whether the individual patient is intended to receive the medical product. Once it is confirmed that the individual patient is intended to receive the medical product, the medical product is administered to the individual patient.

US Patent Application Publication 2005/0131270 to Weil et al., which is incorporated herein by reference, describes a system including a radiation treatment agent to treat tissue in response to received X-ray radiation and an identifier associated with the radiation treatment agent. The identifier may be usable to identify a radiation treatment plan. In some embodiments, a radiation treatment plan associated with a patient is generated, the radiation treatment plan is associated with an identifier and a patient identifier identifying the patient, a radiation treatment agent is prepared for delivery to the patient according to the radiation treatment plan, and the radiation treatment agent is associated with the identifier.

US Patent 6,985,870 to Martucci et al., which is incorporated herein by reference, describes a medication delivery system comprising a medical container holding a prescribed medication to be delivered to a patient, a tag adapted to be worn by the patient, a handheld computing device, and an electronic medication delivery device. Data on the medication is contained in a first label on the medication container. The first label also contains the instruction on how the medication is delivered to the patient, including the appropriate settings for an electronic medication delivery device for delivering the medication to the patient. Patient data is contained in a second label on the tag worn by the patient. The medication data, medication delivery instruction, and patient data are provided in machine readable formats. The handheld computing device reads the medication data and the medication delivery instruction on the medication container and the patient data on the patient tag. The handheld computing device stores the information obtained and performs a matching check to confirm that the medication data matches with the patient data. Upon a confirmed match, it transmits the medication delivery instruction to the electronic medication delivery device, which downloads the instruction, programs the delivery device, and prompts an operator to begin delivering the medication to the patient according to the downloaded instruction.

US Patent Application Publication 2005/0029277 to Tachibana, which is incorporated herein by reference, describes a drug container having an identification tag fixed or detachably provided at a predetermined position of the container, the tag having recorded thereon drug data on a kind and a concentration of a drug, and upper and/or lower limits of a flow rate for continuous infusion, or time and flow rate for one-shot administration.

US Patent Application Publication 2005/0277911 to Stewart et al., which is incorporated herein by reference, describes techniques for programming a medical therapy in a medical device. The medical device has a controller, a memory, a processor, and an input device. The memory is preloaded with at least one of a plurality of patient profiles and condition profiles. The memory is further preloaded with an associated medication therapy for a plurality of the profiles. The input device receives profile data, comprising at least one of a patient profile data and a condition profile data for a specific patient, and the processor processes the received profile data and provides as output one of the preloaded medication therapies based on the processed profile data.

US Patent 6,506,155 to Sluis, which is incorporated herein by reference, describes an ultrasound imaging system including a data entry device that reads storage media that is assigned to each patient on which the system is to be used or the operator of the system to obtain ultrasound images. The storage media, which comprises a barcode, smartcard, or personal digital assistant, contains patient identifying information. The patient or procedure identifying information is used to access a digital requisition that is referenced by the patient identifying information. The digital requisition is stored in a disk drive included in the ultrasound imaging system or in a clinical information system accessed through a communication link included in the ultrasound imaging system. The digital requisition includes information pertaining to an ultrasound examination procedure that is to be performed on the patient, which is used to automatically set up the ultrasound imaging system. The digital requisition may also include the patient's medical history or information about the patient that can be associated with ultrasound images obtained from the patient.

US Patent Application Publication 2005/0121505 to Metz et al., which is incorporated herein by reference, describes patient-centric data acquisition protocol selection systems and methods, and identification tags therefor. A patient-centric data acquisition protocol selection system comprises a programmable identification tag capable of allowing predetermined information about a patient to be stored therein and retrieved therefrom; a medical imaging system capable of communicating with the programmable identification tag; and programming associated with the medical imaging system for selecting an optimal data acquisition protocol. The medical imaging system reads information from the programmable identification tag and then the programming selects an optimal data acquisition protocol based, at least in part, on the predetermined information about the patient that is stored in the programmable identification tag.

PCT Publication WO 04/004787 to Van Naemen et al., which is incorporated herein by reference, describes a method for dispensing individual doses of a radiopharmaceutical solution, which consists of a radioactive parent solution diluted with a diluting solution. Also described is a computer-generated dose dispenser for dispensing individual doses of a radiopharmaceutical solution at a specified speed. The method and device are described as being particularly suitable for use in the field of nuclear medicine, and more in particular for use for PET scan applications.

US Patent 6,032,155 to de la Huerga, which is incorporated herein by reference, describes techniques for administering a prescribed medication to a patient. A medication administration system and apparatus dispense the prescribed medication, verify that the medication is given to a correct patient by an authorized healthcare worker, and track and record the administration of the medication. The system utilizes a workstation connected to a database containing prescribed medication dose information for various patients. A healthcare worker uses the workstation to manually or automatically dispenses the medication the portable container. An information device is secured to the portable container during transport and administration of the medication to the intended patient. The information device prevents access to the medication or warns the healthcare worker of a potential error if the medication is delivered to the wrong patient or administered by an unauthorized healthcare worker. The information device records actual consumption information, and delivers this information back the workstation database or to a hospital or pharmacy database.

US Patent 5,317,506 to Coutre et al., which is incorporated herein by reference, describes an infusion management and pumping system. Infusion prescriptions are generated and monitored by a pharmacy management system. Labels for each infusion to be given to a patient are generated and printed in a barcode format. Each label contains data regarding a prescribed infusion program, including the drug or drugs to be infused, the infusion regimen, the expiration date, and the patient to whom the infusion is to be administered. The management system checks for incompatibilities between drugs that are being prescribed for simultaneous infusion. Each label generated by the management system is attached to the container which holds the infusion solution. The data on the label is transferred to an infusion pumping system by a barcode reader at the infusion pumping system. The pumping system checks that all necessary data has been entered. During operation, the pumping system checks for a variety of alarm conditions and stores any alarms in a ranking according to urgency. The infusion pumping system is responsive to remote or biofeedback instructions to alter the planned infusion program. Central computer records processing receives infusion data and provides infusion, inventory, and use analysis.

US Patent 5,039,863 to Matsuno et al., which is incorporated herein by reference, describes an automatic radioisotope filling apparatus, which is equipped with a radioisotope vial containing a radioisotope solution, a saline vial containing a physiological saline solution, a dilution vial to which a predetermined amount of the radioisotope solution and a predetermined amount of the physiological saline solution are to be transferred to prepare a diluted radioisotope solution, a radiation detector for measuring the radioactive intensity of the diluted radioisotope solution prepared in the dilution vial, and a plurality of label vials containing a drug to be labeled.

US Patent Application Publication 2004/0051368 to Caputo et al., which is incorporated herein by reference, describes a system for delivering medical fluid to a patient. The system includes a medical container including a Radio Frequency Identification (RFID) tag storing data related to the medical fluid therein. A RF reader receives data signals transmitted from the RFID tag that include a desired flow rate for delivering the fluid to the intended patient. A pump coupled to the reader includes a pumping mechanism for pumping the medical fluid from the container, and a pump controller for receiving the data including the desired flow rate from the reader. The pump controller automatically controls the pumping mechanism to pump the medical fluid from the medical container at the desired flow rate based upon the data.

US Patent Application Publication 2005/0171815 to Vanderveen, which is incorporated herein by reference, describes a centralized medication management system for monitoring, managing and controlling medication delivery from a central location. A central computer displays medication orders and ongoing medication administrations for a health care facility. The central computer checks medication delivery against a database of medication administration guidelines, including guidelines for medication interactions with other medications and with patient conditions, and provides an indication of any detected incompatibilities. A clinician at the central location may adjust the medication administration parameters in response to detected incompatibilities and communicate with a caregiver at the point of care to provide decision support. In an embodiment, the central location is a pharmacy at the healthcare facility.

US Patent Application Publication 2005/0240441 to Suzuki, which is incorporated herein by reference, describes a hospital information system. The system enables an RF reader, comprising a personal digital assistant (PDA), to read tag information recorded by RF tags either attached to, or embedded in, various types of a patient wrist bands, injection medicine bottles, patient charts, and medical instrument cases. The PDA transmits a query to a server via a wireless LAN for confirmation from the server. The server collates the query with the content of a medical practice order recorded in its data base, and registers a completion of instructed operation for an instructed item in the database, and replies with a notification if the transmitted readout data from the PDA is correct. If the readout data is incorrect, the PDA is notified and instructed to perform another reading.

US Patent Application Publication 2001/0049608 to Hochman, which is incorporated herein by reference, describes an automated drug administering system such an injection device or infusion pump, which is provided with means for reading information from a container holding the drug. The information is then checked for accuracy before the administration of the drug. Optionally, an ID tag on the patient and/or the health care professional providing the drug may also be scanned and checked. The information thus gathered is sent to another station where it is logged for future use and analyzed.

US Patent 6,743,202 to Hirschman et al., which is incorporated herein by reference, describes apparatus for sharing information on syringe configuration between syringes and injector systems, comprising a storage system to store encoded information on syringe configuration. The encoded information is readable by a detection circuit in an injector. In one embodiment, the storage system is an electronic storage system in which information relevant to the syringe configuration is encoded. A method comprises the step of conveying syringe configuration information to a detector in an injector for use with the syringe.

US Patent Application Publication 2005/0148869 to Masuda, which is incorporated herein by reference, describes a liquid syringe having various kinds of data items recorded in a two-dimensional code format. A liquid injector optically reads the two-dimensional codes, decodes them, and executes a predetermined operations corresponding to the decoded results. Recording, for example, a variable pattern for the liquid of interest in the two-dimensional code format on the liquid syringe makes it possible for the liquid injector to inject the liquid in accordance with the predetermined variable pattern.

US Patent 6,346,886 de la Huerga, which is incorporated herein by reference, describes an electronic identification apparatus having data storage memory on board a removable transceiver device. The transceiver device also includes a processor and a transponder for receiving information pertaining to the object/person to which it is attached and storing the information in memory. The transceiver also transmits stored data to a control computer or the external devices. The transceiver is mounted on a base, such as a wristband, and the apparatus includes an attachment sensor indicating whether the transceiver is attached to the base. If the transceiver has been removed from the base, the processor performs one or more lockdown operations to prevent the stored data from being used in connection with another object or person. The lockdown operations include clearing the contents of the memory, disabling access to the memory, suppressing the display of stored data and activating an alarm.

US Patent Application Publication 2004/0156081 to Bril et al., which is incorporated herein by reference, describes a color-coded signature, for securing documents or encrypting images. The encrypted image comprises an array of printed positions formed using a group of inks each of which has a predetermined spectrum. The positions are selected to form a predetermined image, either real or virtual, when the image is viewed through an optical processor. The optical processor may further use a distorted grating or a distorted lens. The correct image is the spectrum, as distorted by the optical processor. An image formed using inks having the same colors as experienced by the human eye, or even by a standard spectrometer will fail to form the correct predetermined image.

The following patents and patent application publications, all of which are incorporated herein by reference, may be of interest:

US Patent Applications 2005/0131579 and 2005/0088306, and US Patent 6,935,560, all to Andreasson

US Patent 6,851,615 to Jones

US Patent application 2005/0131397 and US Patent 6,861,954 to Levin

US Patent 6,519,569 to White et al.

US Patent 5,692,640 to Caulfield et al.

US Patents 6,475,192 and 6,733,478 to Reilly et al.

US Patent 6,958,053 to Reilly

US Patent Application Publications 2005/0261937 and 2005/0261938 to Silverbrook et al.

US Patent 6,994,249 to Peterka et al.

US Patent 6,843,357 to Bybee et al.

US Patent 6,425,174 to Reich

US Patent 6,722,499 to Reich

US Patent 5,536,945 to Reich

US Patent RE36,693 to Reich

US Patent 5,519,931 to Reich

US Patent Application Publication 2005/0198800 to Reich

US Patent 6,576,918 to Fu et al.

US Patent Application Publication 2005/0247893 to Fu et al.

US Patent 5,927,351 to Zhu et al.

US Patent 5,828,073 to Zhu et al.

US Patent 6,162,198 to Coffey et al.

US Patents 6,338,007 and 6,116,461 to Broadfield et al.

US Patent 5,944,190 to Edelen

PCT Publication WO 04/032151 to Besing et al.

US Patent Application Publication 2005/0234424 to Besing et al.

US Patent 4,296,785 to Vitello et al.

US Patent 3,446,965 to Ogier et al.

US Patent 6,355,024 to Small et al.

US Patent 6,468,261 to Small et al.

US Patent 5,580,541 to Wells et al.

US Patent 3,535,085 to Shumate

US Patent 4,853,546 to Abe et al.

US Patent 5,329,976 to Haber et al.

US Patent 5,304,165 to Haber et al.

US Patent 5,911,252 to Cassel

US Patent 5,475,232 to Powers et al.

PCT Publication WO 05/002971 to Tochon-Danguy et al.

US Patent Application Publication 2005/0278066 to Graves

US Patent 5,479,969 to Hardie et al.

US Patent 5,309,959 to Shaw et al.

US Patent 6,870,175 to Dell et al.

US Patent 6,767,319 to Reilly et al.

US Patent 6,976,349 to Baldwin et al.

US Patent 6,957,522 to Baldwin et al.

US Patent 6,915,619 to Baldwin

US Patent 6,813,868 to Baldwin et al.

US Patent 5,893,397 to Peterson et al.

US Patents 5,885,216, 5,806,519, and 6,901,283 to Evans, III et al.

US Patent Application Publication 2004/0084340 to Morelle et al.

US Patent 6,269,340 to Ford et al.

US Patent Application Publication 2004/0193453 to Butterfield et al.

US Patent 4,476,381 to Rubin

US Patent 6,643,537 to Zatezalo et al.

US Patent Application Publication 2005/0108044 to Koster

US Patent 6,851,615 to Jones

US Patent 5,840,026 to Uber, III et al.

US Patent 6,685,678 to Evans et al.

US Patent Application Publication 2003/0183226 to Brand et al.

US Patent Application Publications 2005/0107914 and 2005/0113945 to Engleson et al.

US Patent Application Publication 2002/0198738 to Osborne

US Patent Application Publication 2002/0099334 to Hanson et al.

US Patents 6,317,648 and 6,522,945 to Sleep et al.

US Patent 6,155,485 and 6,318,630 to Coughlin et al.

US Patent 6,202,923 to Boyer et al.

US Patent 6,915,823 to Osborne et al.

US Patent Application Publication 2004/0205343 to Forth et al.

US Patent 5,493,805 to Penuela et al.

US Patent 5,973,598 to Beigel

US Patent Application Publication 2005/0149350 to Kerr et al.

US Patent 5,884,457 to Ortiz et al.

The following patents and patent application publications, which describe gamma cameras and imaging processing techniques, and which are incorporated herein by reference, may be of interest:

US Patent Application Publication 2005/0205792 to Rousso et al.

PCT Publication WO 05/118659 to Dichterman et al.

PCT Publication WO 05/119025 to Nagler et al.

US Patent Application Publication 2004/0204646 to Nagler et al.

PCT Publication WO 04/042546 to Kimchy et al.

US Patent Application Publication 2004/0054248 to Kimchy et al.

US Patent Application Publication 2004/0015075 to Kimchy et al.

US Patent Application Publication 2004/0054278 to Kimchy et al.

US Patent Application Publication 2005/0266074 to Zilberstein et al.

US Patents 5,939,724, 5,587,585, and 5,365,069 to Eisen et al.

US Patent 6,943,355 to Shwartz et al.

US Patents 6,242,743 and 5,757,006 to DeVito et al.

US Patent 6,137,109 to Hayes

US Patent 6,388,258 to Berlad et al.

US Patent 6,429,431 to Wilk

US Patent 6,838,672 to Wagenaar et al.

US Patents 6,740,882, 6,545,280, 6,229,145, 5,519,221, and 5,252,830 to Weinberg

US Patent 6,713,766 to Garrard et al.

US Patent 6,765,981 to Heumann

US Patent 6,664,542 to Ye et al.

US Patent 6,080,984 to Friesenhahn

US Patent 5,818,050 to Dilmanian et al.

US Patent 6,728,583 to Hallett

US Patent 5,481,115 to Hsieh et al.

US Patent 6,723,988 to Wainer

US Patent 6,940,070 to Tumer

US Patent 6,635,879 to Jimbo et al.

US Patent 6,353,227 to Boxen

US Patent 6,184,530 to Hines et al.

US Patent Application Publication 2005/0145797 to Oaknin et al.

US Patent Application Publication 2004/0251419 to Nelson et al.

US Patent Application Publication 2003/0001098 to Stoddart et al.

PCT Publication WO 98/16852 to DeVito et al.

PCT Publication WO 05/059840 to Nielsen et al.

SUMMARY OF THE INVENTION

In some embodiments of the present invention, an end-to-end automated system for medical imaging comprises a plurality of integrated elements that are configured to electronically exchange information among one another. The elements include an automated radiopharmaceutical dispensing system, a portable information-bearing radiopharmaceutical agent container, a patient management system, a portable patient-specific data carrier, an automated administration system, and an automated imaging system. The systems perform their respective automated functions at least in part responsively to the exchanged information. The elements typically authenticate one another via the exchanged information, in order to ensure that only authorized elements participate in the system, and that the systems perform only authorized and appropriate functions.

The exchanged information typically includes patient-specific data, radiopharmaceutical agent-specific data, and/or patient- or radiopharmaceutical agent-specific imaging protocol data. Such data enable the systems to customize their respective automated functions for specific patients, radiopharmaceutical agents, indications, and/or imaging procedures. For some applications, the exchanged information includes commercial license information relating to the use of a specific protocol with a specific radiopharmaceutical agent, and one or more of the systems are configured to verify the license information before performing their respective functions.

In some embodiments of the present invention, the information-bearing radiopharmaceutical agent container and/or the patient-specific data carrier is configured to contain protocol information for performing an imaging procedure using the labeled radiopharmaceutical agent held by the container. For some applications, the protocol information includes SPECT imaging protocol information, and the imaging system uses the protocol information to perform a SPECT imaging procedure using the labeled radiopharmaceutical agent contained in the container. For some applications, the agent container contains a single dose of the labeled radiopharmaceutical agent, which dose is appropriate for use with the imaging protocol.

In some embodiments of the present invention, the information-bearing radiopharmaceutical agent container or the patient-specific data carrier is configured to contain at least one kinetic parameter of the labeled radiopharmaceutical agent contained in the container. The imaging system uses the kinetic parameter to perform a dynamic SPECT imaging procedure.

In some embodiments of the present invention, the information-bearing radiopharmaceutical agent container contains radiopharmaceutical information regarding the labeled radiopharmaceutical agent contained in the container. The portable patient-specific data carrier is configured to contain patient information regarding the patient, and imaging protocol information for use with the labeled radiopharmaceutical agent, such as SPECT imaging protocol information. The imaging system uses the protocol information to perform an imaging procedure, such as a dynamic SPECT imaging procedure. For some applications, the patient-specific data carrier comprises a coupling mechanism configured to be coupled to the patient. For example, the coupling mechanism may comprise a bracelet, a watch, a necklace, or another wearable article.

In some embodiments of the present invention, the information-bearing radiopharmaceutical agent container contains a first identifier value, and the patient-specific data carrier contains a second identifier value. The imaging system is configured to perform an imaging procedure responsively to a detection of a correspondence between the first and second identifier values. For some applications, the first identifier value equals the second identifier value, while for other applications the values do not equal one another, but instead correspond to one another based on information provided by an element of the end-to-end system. For some applications, the first and/or second identifier values are arbitrarily assigned, or pre-loaded into the data carrier my a manufacturer or distributor, while for other applications at least one of the identifier values comprises a patient identifier, or another meaningful value. For some applications, at least one of the information-bearing agent container and the patient-specific data carrier performs the detection of the correspondence, while for other applications the imaging system or another element of the end-to-end system performs the detection of the correspondence.

In some embodiments of the present invention, the imaging system comprises a SPECT imaging system configured to utilize the information contained in the labeled radiopharmaceutical agent container and/or the patient-specific data carrier to customize at least one function of the system selected from the group consisting of: administration of the labeled radiopharmaceutical agent, acquisition of a SPECT image of the patient to whom the labeled radiopharmaceutical agent is administered, reconstruction of the SPECT image, analysis of the SPECT image, and diagnosis of a condition of the patient based at least in part on the analysis.

The integration of the elements of the end-to-end system, and the exchange of authenticatable information among the elements generally increase patient safety, by ensuring that each patient receives the prescribed labeled radiopharmaceutical agent and dosage, and undergoes the desired imaging protocol. For some applications, one or more elements of the end-to-end system are configured to perform their respective function only upon being triggered by another element of the system. For example, the administration or imaging system may perform its function only upon being triggered by the information-bearing radiopharmaceutical agent container, by the patient-specific data carrier, and/or, in the case of the administration system, by the imaging system.

In some embodiments of the present invention, the automated radiopharmaceutical dispensing system comprises an information manager that is configured to receive radiopharmaceutical information regarding a labeled radiopharmaceutical agent and patient information regarding a patient. Responsively to the information, the dispensing system automatically dispenses a dose of the labeled radiopharmaceutical agent to an agent container, and stores the radiopharmaceutical information and at least a portion of the patient information in a data carrier associated with the container. For some applications, the radiopharmaceutical information is selected from the group consisting of: imaging protocol information for use with the labeled radiopharmaceutical agent, such as a SPECT imaging protocol; at least one kinetic parameter useful for performing a dynamic SPECT imaging procedure using the at least one labeled radiopharmaceutical agent; and authenticatable information regarding a commercial license for use of a SPECT imaging protocol with the at least one labeled radiopharmaceutical agent.

In some embodiments of the present invention, the dispensing system is configured to receive a mother vial containing a labeled radiopharmaceutical agent in a quantity sufficient for preparation of a plurality of doses of the labeled radiopharmaceutical agent. Associated with the mother vial is a data carrier containing information regarding the labeled radiopharmaceutical agent, such as the formulation, radioactivity information, and protocol information. The information manager of the dispensing system receives at least a portion of the labeled radiopharmaceutical agent information from the data carrier.

In some embodiments of the present invention, use of the end-to-end automated system enables customization of one or more aspects of the imaging process, from dispensing to diagnosis. Customization typically includes one or more of the following:

- The dispensing system customizes the dispensed dose for a specific patient, based on radiopharmaceutical information and patient-specific information. Typically, the dispensing system customizes the dispensed dose (e.g., the radioactivity level thereof) based in part on the scheduled time of the scheduled time of administration of the dose, and/or the scheduled time of the imaging procedure to be performed using the dose.

- The administration system customizes the administered dose for a specific patient, based on radiopharmaceutical information and patient-specific information. For some applications in which the administration system customizes the administered dose, the radiopharmaceutical agent container contains a standard, non-customized dose.
- The imaging system customizes image acquisition, image reconstruction, image analysis, and/or diagnosis, based on radiopharmaceutical information and patient-specific information, such as patient physiology and/or known and/or suspected disease of the patient.

Such customization is typically based at least in part on information provided by the manufacturer or distributor of the radiopharmaceutical agent. Such information may be in the form of lookup tables and/or expert system rules.

As used in the present application, including in the claims, "labeled" means radiolabeled, and "unlabeled" means not radiolabeled.

There is therefore provided, in accordance with an embodiment of the present invention, apparatus for use with at least one labeled radiopharmaceutical agent, the apparatus comprising:

a container containing the at least one labeled radiopharmaceutical agent; and

a portable computer-communicatable data carrier associated with the container, the data carrier containing imaging protocol information for use with the at least one labeled radiopharmaceutical agent.

For some applications, the apparatus comprises a device configured to write the imaging protocol information to the data carrier.

For some applications, the data carrier additionally contains administration protocol information useful for administering the at least one labeled radiopharmaceutical agent.

In an embodiment, the imaging protocol information comprises instructions for performing an imaging procedure using the at least one labeled radiopharmaceutical agent. Alternatively or additionally, the imaging protocol information comprises an identifier of an imaging protocol. Further alternatively or additionally, the imaging protocol information comprises a parameter of the at least one labeled radiopharmaceutical agent. Still further alternatively or additionally, the imaging protocol information comprises a parameter useful for configuring at least one aspect of an imaging procedure performed using the at least one labeled radiopharmaceutical agent.

In an embodiment, the container contains a single dose of the radiopharmaceutical agent, which dose is appropriate for use with the imaging protocol information. Alternatively, the container contains a plurality of labeled radiopharmaceutical agents mixed together. For some applications, the container is shaped so as to define a plurality of chambers, each of which contains a respective one of a plurality of labeled radiopharmaceutical agents.

In an embodiment, the data carrier comprises a first data carrier, which contains a first identifier value, the apparatus further comprises a second computer-communicatable data carrier, which contains a second identifier value, and the apparatus is configured to operate responsively to a detection of a correspondence between the first and second identifier values. For some applications, at least one of the first and second data carriers is configured to perform the detection of the correspondence. Alternatively or additionally, the apparatus comprises a correspondence-detection element configured to perform the detection of the correspondence.

In an embodiment, at least one of the first and second data carriers contains an identifier of a patient to whom the labeled radiopharmaceutical agent is to be administered.

For some applications, at least one of the first and second identifier values comprises an identifier of a patient to whom the labeled radiopharmaceutical agent is to be administered.

In an embodiment, exactly one of the first and second data carriers comprises a coupling mechanism configured to be coupled to a patient to whom the labeled radiopharmaceutical agent is to be administered.

In an embodiment, the apparatus comprises an imaging system comprising imaging functionality, the imaging system configured, responsively to the detection of the correspondence, to drive the imaging functionality to perform an imaging procedure using the at least one labeled radiopharmaceutical agent.

In an embodiment, the data carrier is physically coupled to the container. For some applications, the data carrier contains an identifier of a patient to whom the labeled radiopharmaceutical agent is to be administered, and the imaging protocol information comprises imaging protocol information selected for the patient. For some applications, the imaging protocol information comprises an identifier of an imaging protocol.

For some applications, the imaging protocol information comprises imaging protocol information customized for the patient.

In an embodiment, the imaging protocol information comprises SPECT imaging protocol information, such as dynamic SPECT imaging protocol information. For some applications, the SPECT imaging protocol information comprises at least one kinetic parameter of the at least one labeled radiopharmaceutical agent, the at least one kinetic parameter useful for performing a dynamic SPECT imaging procedure using the at least one labeled radiopharmaceutical agent.

In an embodiment, the apparatus comprises an imaging system, which comprises a communication element, configured to read the imaging protocol information from the data carrier; and a control unit, comprising imaging functionality, which is configured to perform an imaging procedure, and to configure the procedure at least in part responsively to the imaging protocol information read from the data carrier by the communication element.

In an embodiment, the imaging system comprises a camera, wherein the imaging functionality comprises image acquisition functionality, and wherein the image acquisition functionality is configured to perform an image acquisition procedure using the camera, and to configure the procedure at least in part responsively to the imaging protocol information read from the data carrier by the communication element. For some applications, the image acquisition functionality configures a total acquisition time of the image acquisition procedure at least in part responsively to the imaging protocol information. Alternatively or additionally, the camera comprises a plurality of detectors, and wherein the image acquisition functionality is configured to configure, at least in part responsively to the imaging protocol information, at least one motion of at least one of the detectors during the image acquisition procedure. For some applications, the control unit is configured to configure, at least in part responsively to the imaging protocol information, a waiting time between administration of the labeled radiopharmaceutical agent and commencement of the image acquisition procedure. For some applications, the image acquisition functionality is configured to perform a gated image acquisition procedure at least in part responsively to the imaging protocol information.

In an embodiment, the imaging functionality comprises image reconstruction functionality, and wherein the image reconstruction functionality is configured to perform an image reconstruction procedure, and to configure the procedure at least in part responsively to the imaging protocol information read from the data carrier by the communication element.

In an embodiment, the imaging functionality comprises image analysis functionality, and wherein the image analysis functionality is configured to perform an image analysis procedure, and to configure the procedure at least in part responsively to the imaging protocol information read from the data carrier by the communication element.

In an embodiment, the imaging functionality comprises diagnosis functionality, and wherein the diagnosis functionality is configured to perform a diagnostic procedure, and to configure the procedure at least in part responsively to the imaging protocol information read from the data carrier by the communication element.

In an embodiment, the imaging procedure includes a three-dimensional dynamic imaging study, and wherein the imaging functionality is configured to perform the three-dimensional dynamic imaging study, and to configure the study at least in part responsively to the imaging protocol information read from the data carrier by the communication element.

In an embodiment, the data carrier is not physically coupled to the container, and wherein the data carrier contains an identifier of a patient to whom the labeled radiopharmaceutical agent is to be administered. For some applications, the data carrier comprises a coupling mechanism configured to be coupled to the patient. In an embodiment, the data carrier comprises a first data carrier, and wherein the apparatus further comprises a second computer-communicatable data carrier physically coupled to the container, the second data carrier containing radiopharmaceutical information regarding the at least one labeled radiopharmaceutical agent.

There is also provided, in accordance with an embodiment of the present invention, apparatus for use with at least one labeled radiopharmaceutical agent, the apparatus comprising:

a container containing the at least one labeled radiopharmaceutical agent; and

a computer-communicatable data carrier associated with the container, the data carrier containing authenticatable information regarding a commercial license for use of SPECT imaging protocol information with the at least one labeled radiopharmaceutical agent.

In an embodiment, the apparatus comprises an imaging system, which comprises:

a communication element, configured to read the authenticatable license information from the data carrier;

a control unit, comprising imaging functionality, the control unit configured to:

authenticate the authenticatable license information, and

only upon authentication, drive the imaging functionality to perform an imaging procedure using the SPECT imaging protocol information.

For some applications, the apparatus comprises a device configured to write the authenticatable license information to the data carrier.

For some applications, the data carrier is physically coupled to the container.

There is further provided, in accordance with an embodiment of the present invention, apparatus comprising a portable computer-communicatable data carrier containing authenticatable information regarding a commercial license for use of SPECT imaging protocol information.

For some applications, the data carrier additionally contains patient information regarding a patient upon whom an imaging procedure using the SPECT imaging protocol information is to be performed.

For some applications, the authenticatable license information is encrypted.

In an embodiment, the apparatus comprises an imaging system, which comprises:

a communication element, configured to read the authenticatable license information from the data carrier;

a control unit, comprising imaging functionality, the control unit configured to:

authenticate the authenticatable license information, and

only upon authentication, drive the imaging functionality to perform an imaging procedure using the SPECT imaging protocol information.

For some applications, the apparatus comprises a device configured to write the authenticatable license information to the data carrier.

For some applications, the data carrier comprises a coupling mechanism configured to be coupled to a patient upon whom an imaging procedure using the SPECT imaging protocol information is to be performed.

There is still further provided, in accordance with an embodiment of the present invention, apparatus comprising:

a first portable computer-communicatable data carrier containing a first identifier value;

a second portable computer-communicatable data carrier containing a second identifier value; and

an imaging system comprising imaging functionality, the imaging system configured, responsively to a detection of a correspondence between the first and second identifier values, to drive the imaging functionality to perform an imaging procedure on a patient.

For some applications, at least one of the first and second data carriers is configured to perform the detection of the correspondence. Alternatively or additionally, the imaging system comprises a correspondence-detection element configured to perform the detection of the correspondence.

For some applications, at least one of the first and second data carriers contains an identifier of a patient to whom the labeled radiopharmaceutical agent is to be administered.

For some applications, at least one of the first and second identifier values comprises an identifier of a patient to whom the labeled radiopharmaceutical agent is to be administered.

In an embodiment, one of the first and second data carriers comprises a coupling mechanism configured to be coupled to a patient to whom the labeled radiopharmaceutical agent is to be administered.

For some applications,. the apparatus comprises a device configured to write at least one of the first and second identifier values to the respective first and second data carriers.

In an embodiment, at least one of the first and second data carriers contains radiopharmaceutical information regarding at least one labeled radiopharmaceutical agent, the imaging system comprises a communication element, configured to read the radiopharmaceutical information from the at least one of the data carriers, and the imaging system is configured to configure the imaging procedure at least in part responsively to the read radiopharmaceutical information. For some applications, the apparatus comprises a container containing the at least one labeled radiopharmaceutical agent. For some applications, one of the first and second data carriers is physically coupled to the container.

In an embodiment, the imaging functionality comprises a nuclear camera. For some applications, the nuclear camera comprises a SPECT camera.

There is yet further provided, in accordance with an embodiment of the present invention, apparatus for use with first and second portable computer-communicatable data carriers containing first and second identifier values, respectively, the apparatus comprising an imaging system, which comprises:

imaging functionality; and

a control unit configured to drive the imaging functionality to perform an imaging procedure on a patient, responsively to a detection of a correspondence between the first and second identifier values.

For some applications, the imaging system comprises a correspondence-detection element configured to perform the detection of the correspondence.

There is additionally provided, in accordance with an embodiment of the present invention, apparatus for use with at least one labeled radiopharmaceutical agent for administration to a patient, the apparatus comprising:

a container containing the at least one labeled radiopharmaceutical agent;

a first computer-communicatable data carrier physically coupled to the container, the first data carrier containing radiopharmaceutical information regarding the at least one labeled radiopharmaceutical agent; and

a second portable computer-communicatable data carrier containing patient information regarding the patient, and imaging protocol information for use with the at least one labeled radiopharmaceutical agent.

For some applications, the imaging protocol information comprises SPECT imaging protocol information.

For some applications, the patient information comprises an identifier of the patient.

For some applications, the second data carrier comprises a coupling mechanism configured to be coupled to the patient.

For some applications, the first data carrier contains a first patient identifier, the patient information contained in the second data carrier comprises a second patient identifier, and the apparatus comprises an administration system, which comprises:

a first communication element, configured to read the first patient identifier from the first data carrier;

a second communication element, configure to read the second patient identifier from the second data carrier; and

a control unit, configured to compare the first patient identifier to the second patient identifier, and, upon detecting a match, generate an administration signal that triggers administration to the patient of the at least one labeled radiopharmaceutical agent contained in the container.

For some applications, the first data carrier contains a first protocol identifier, the imaging protocol information contained in the second data carrier comprises a second protocol identifier, and the apparatus comprises an administration system, which comprises:

a communication element, configured to read the first and second protocol identifiers from the first and second data carriers, respectively; and

a control unit, configured to compare the first protocol identifier to the second protocol identifier, and, upon detecting a match, generate an administration signal that triggers administration to the patient of the at least one labeled radiopharmaceutical agent contained in the container.

For some applications, the first data carrier contains a first protocol identifier, the imaging protocol information contained in the second data carrier comprises a second protocol identifier, and the apparatus comprises an administration system, which comprises:

a first communication element, configured to read the first protocol identifier from the first data carrier;

a second communication element, configured to read the second protocol identifier from the second data carrier; and

a control unit, configured to compare the first protocol identifier to the second protocol identifier, and, upon detecting a match, generate an administration signal that triggers administration to the patient of the at least one labeled radiopharmaceutical agent contained in the container.

In an embodiment, the apparatus comprises an administration system, which comprises:

a communication element; and

a control unit, configured to:

generate an administration signal that triggers administration to the patient of the at least one labeled radiopharmaceutical agent contained in the container, and

drive the communication element to transmit information regarding the administration to the second data carrier.

For some applications, the apparatus comprises a device configured to write the imaging protocol information to the first data carrier. Alternatively or additionally, the apparatus comprises a device configured to write the patient information to the second data carrier.

In an embodiment, the imaging protocol information comprises imaging protocol information selected for the patient. For some applications, the imaging protocol information comprises an identifier of an imaging protocol. For some applications, the imaging protocol information comprises imaging protocol information customized for the patient.

In an embodiment, the first data carrier contains a first patient identifier, the patient information contained in the second data carrier includes a second patient identifier, and the apparatus comprises an administration system, which comprises:

a communication element, configured to read the first and second patient identifiers from the first and second data carriers, respectively; and

a control unit, configured to compare the first patient identifier to the second patient identifier, and, upon detecting a match, generate an administration signal that triggers administration to the patient of the at least one labeled radiopharmaceutical agent contained in the container.

For some applications, the administration system comprises an automated administration device, configured to administer the at least one labeled radiopharmaceutical agent to the patient upon being triggered by the administration signal.

For some applications, the control unit is configured to generate the administration signal to trigger the administration of the at least one labeled radiopharmaceutical agent by instructing a healthcare worker to administer the at least one labeled radiopharmaceutical agent to the patient.

There is yet additionally provided, in accordance with an embodiment of the present invention, apparatus for use with at least one labeled radiopharmaceutical agent for administration to a patient, the apparatus comprising:

a container containing the at least one labeled radiopharmaceutical agent;

a computer-communicatable data carrier associated with the container, the data carrier containing data regarding at least one of: the labeled radiopharmaceutical agent and the patient; and

a SPECT imaging system comprising:

a communication element, configured to read the data; and

a control unit, configured to utilize the read data to customize at least one function of the system selected from the group consisting of: administration of the labeled radiopharmaceutical agent, acquisition of a SPECT image of the patient to whom the labeled radiopharmaceutical agent is administered, reconstruction of the SPECT image, analysis of the SPECT image, and diagnosis of a condition of the patient based at least in part on the analysis.

For some applications, the data carrier contains the data regarding the labeled radiopharmaceutical agent. Alternatively or additionally, the data carrier contains the data regarding the patient.

For some applications, the control unit is configured to utilize the read data to customize the administration of the labeled radiopharmaceutical agent. Alternatively or additionally, the control unit is configured to utilize the read data to customize the acquisition of a SPECT image of the patient to whom the labeled radiopharmaceutical agent is administered. Further alternatively or additionally, control unit is configured to utilize the read data to customize the reconstruction of the SPECT image. Still further alternatively or additionally, the control unit is configured to utilize the read data to customize the analysis of the SPECT image. Alternatively or additionally, the control unit is configured to utilize the read data to customize the diagnosis of a condition of the patient based at least in part on the analysis.

For some applications, the apparatus comprises a device configured to write the data to the data carrier.

There is also provided, in accordance with an embodiment of the present invention, a SPECT imaging system for use with a container containing at least one labeled radiopharmaceutical agent for administration to a patient, and data regarding at least one of: the labeled radiopharmaceutical agent and the patient, the system comprising:

a communication element, configured to read the data; and

a control unit, configured to utilize the read data to customize at least one function of the system selected from the group consisting of: administration of the labeled radiopharmaceutical agent, acquisition of a SPECT image of the patient to whom the labeled radiopharmaceutical agent is administered, reconstruction of the SPECT image, analysis of the SPECT image, and diagnosis of a condition of the patient based at least in part on the analysis.

For some applications, the system comprises a device configured to write the data to the container.

There is further provided, in accordance with an embodiment of the present invention, an automated radiopharmaceutical dispensing system for use with a container and a computer-communicatable container data carrier associated with the container, the system comprising:

a robot, configured to manipulate the container;

a communication element; and

a control unit, configured to:

receive radiopharmaceutical information regarding at least one labeled radiopharmaceutical agent, the radiopharmaceutical information selected from the group consisting of: imaging protocol information for use with the at least one labeled radiopharmaceutical agent, and authenticatable information regarding a commercial license for use of an imaging protocol with the at least one labeled radiopharmaceutical agent,

receive patient information regarding a patient,

drive the robot to automatically dispense a dose of the labeled radiopharmaceutical agent to the container, and

drive the communication element to transmit to the container data carrier at least a portion of the radiopharmaceutical information and at least a portion of the patient information.

For some applications, the control unit is configured to receive the radiopharmaceutical information regarding a plurality of labeled radiopharmaceutical agents, and drive the robot to automatically dispense respective doses of the labeled radiopharmaceutical agents to the container.

For some applications, the patient information includes an identifier of an imaging protocol assigned to the patient for performance using the dose, and wherein the control unit is configured to drive the communication element to transmit the imaging protocol identifier to the container data carrier.

For some applications, the control unit is configured to drive the communication element to transmit to the container data carrier at least one of: a time of dispensing of the labeled radiopharmaceutical agent to the container, and information regarding a radioactivity of the dose at the time of dispensing.

In an embodiment, the apparatus comprises:

a mother vial that contains the labeled radiopharmaceutical agent prior to dispensing thereof; and

a computer-communicatable mother vial data carrier associated with the mother vial, which mother vial data carrier contains the radiopharmaceutical information,

wherein the control unit is configured to receive the radiopharmaceutical information from the mother vial data carrier.

For some applications, the radiopharmaceutical information comprises the imaging protocol information. For some applications, the imaging protocol information comprises SPECT imaging protocol information, which may comprise at least one kinetic parameter of the at least one labeled radiopharmaceutical agent.

In an embodiment, the radiopharmaceutical information comprises the authenticatable information regarding the commercial license. For some applications, the information regarding the commercial license comprises information regarding the commercial license for use of a SPECT imaging protocol with the at least one labeled radiopharmaceutical agent. For some applications, the control unit is configured to authenticate the authenticatable license information, and to drive the robot to automatically dispense the dose only upon authentication.

There is still further provided, in accordance with an embodiment of the present invention, apparatus for use with a container, the apparatus comprising:

a mother vial having a volume of at least 10 ml, which contains at least 5 ml of a non-diluted labeled radiopharmaceutical agent, and at least 5 ml of saline solution; and

an automated radiopharmaceutical dispensing system, configured to contain the mother vial, and to dispense at least one dose from the mother vial to the container.

There is additionally provided, in accordance with an embodiment of the present invention, a method comprising:

placing at least one labeled radiopharmaceutical agent in a container;

associating a portable computer-communicatable data carrier with the container; and

writing, to the data carrier, imaging protocol information for use with the at least one labeled radiopharmaceutical agent.

There is yet additionally provided, in accordance with an embodiment of the present invention, a method comprising:

placing at least one labeled radiopharmaceutical agent in a container;

associating a computer-communicatable data carrier with the container; and

writing, to the data carrier, authenticatable information regarding a commercial license for use of SPECT imaging protocol information with the at least one labeled radiopharmaceutical agent.

There is also provided, in accordance with an embodiment of the present invention, a method comprising:

providing a portable computer-communicatable data carrier; and

writing, to the data carrier, authenticatable information regarding a commercial license for use of SPECT imaging protocol information.

There is further provided, in accordance with an embodiment of the present invention, a method comprising:

writing first and second identifier values to first and second computer-communicatable data carriers, respectively;

detecting a correspondence between the first and second identifier values; and

perform an imaging procedure on a patient responsively to the detecting.

There is still further provided, in accordance with an embodiment of the present invention, a method for use with at least one labeled radiopharmaceutical agent for administration to a patient, the method comprising:

placing at least one labeled radiopharmaceutical agent in a container;

physically coupling a first computer-communicatable data carrier to the container;

writing, to the first data carrier, radiopharmaceutical information regarding the at least one labeled radiopharmaceutical agent; and

writing, to a second portable computer-communicatable data carrier, patient information regarding the patient, and imaging protocol information for use with the at least one labeled radiopharmaceutical agent.

There is additionally provided, in accordance with an embodiment of the present invention, a method comprising:

placing, in a container, at least one labeled radiopharmaceutical agent for administration to a patient;

associating a computer-communicatable data carrier with the container;

writing data to the data carrier regarding at least one of: the labeled radiopharmaceutical agent and the patient;

reading the data from the data carrier at a SPECT imaging system;

utilizing the read data to customize at least one function of the system selected from the group consisting of: administration of the labeled radiopharmaceutical agent, acquisition of a SPECT image of the patient to whom the labeled radiopharmaceutical agent is administered, reconstruction of the SPECT image, analysis of the SPECT image, and diagnosis of a condition of the patient based at least in part on the analysis.

There is yet additionally provided, in accordance with an embodiment of the present invention, a method for use with a container containing at least one labeled radiopharmaceutical agent for administration to a patient, and data regarding at least one of: the labeled radiopharmaceutical agent and the patient, the method comprising:

reading the data at a SPECT imaging system; and

utilizing the read data to customize at least one function of the system selected from the group consisting of: administration of the labeled radiopharmaceutical agent, acquisition of a SPECT image of the patient to whom the labeled radiopharmaceutical agent is administered, reconstruction of the SPECT image, analysis of the SPECT image, and diagnosis of a condition of the patient based at least in part on the analysis.

There is also provided, in accordance with an embodiment of the present invention, a method for use with a container and a computer-communicatable container data carrier associated with the container, the method comprising:

receiving, by an automated radiopharmaceutical dispensing system, radiopharmaceutical information regarding at least one labeled radiopharmaceutical agent, the radiopharmaceutical information selected from the group consisting of: imaging protocol information for use with the at least one labeled radiopharmaceutical agent, and authenticatable information regarding a commercial license for use of an imaging protocol with the at least one labeled radiopharmaceutical agent;

receiving, by the dispensing system, patient information regarding a patient;

automatically robotically dispensing, by the dispensing system, a dose of the labeled radiopharmaceutical agent to the container; and

transmitting to the container data carrier, by the dispensing system, at least a portion of the radiopharmaceutical information and at least a portion of the patient information.

There is further provided, in accordance with an embodiment of the present invention, a method for automatically dispensing a labeled radiopharmaceutical agent to a container, comprising:

providing a mother vial having a volume of at least 10 ml;

filling the mother vial with at least 5 ml of a non-diluted labeled radiopharmaceutical agent, and with at least 5 ml of saline solution;

placing the mother vial in an automated radiopharmaceutical dispensing system; and

dispensing at least one dose from the mother vial to the container.

There is also provided, in accordance with an embodiment of the present invention, a method for setting a dose of a labeled radiopharmaceutical agent for use for performing an imaging procedure on a patient for studying a physiological characteristic of the patient, the method including:

selecting the radiopharmaceutical agent;

receiving information regarding a medical parameter of the patient not directly related to the physiological characteristic of the patient; and

setting the dose at least in part responsively to the received information.

There is further provided, in accordance with an embodiment of the present invention, a substance associated with a time-dependent substance intake program generated by a computer controlled functionality employing a machine readable multi-parameter human physiological profile including at least one of a kinetic and intra-body location dependent parameter and a machine readable multi-parameter substance profile, including at least one kinetic parameter.

There is still further provided, in accordance with an embodiment of the present invention, a computer controlled functionality employing a machine readable multi-parameter human physiological profile including at least one of a kinetic and intra-body location dependent parameter and a machine readable multi-parameter substance profile, including at least one kinetic parameter, for indicating a time-dependent substance intake program.

There is yet further provided, in accordance with an embodiment of the present invention, a substance associated with a time-dependent substance intake program generated by a computer controlled functionality employing a machine readable multi-parameter human physiological profile including at least one of a kinetic and intra-body location dependent parameter and a machine readable multi-parameter substance profile, including at least one kinetic parameter.

There is also provided, in accordance with an embodiment of the present invention, a time-dependent substance intake program generated by a computer controlled functionality employing a machine readable multi-parameter human physiological profile including at least one of a kinetic and intra-body location dependent parameter and a machine readable multi-parameter substance profile, including at least one kinetic parameter.

There is further provided, in accordance with an embodiment of the present invention, a substance formulated in accordance with a time-dependent substance intake program generated by a computer controlled functionality employing a machine readable multi-parameter human physiological profile including at least one of a kinetic and intra-body location dependent parameter and a machine readable multi-parameter substance profile, including at least one kinetic parameter.

There is still further provided, in accordance with an embodiment of the present invention, an apparatus, method, and/or functionality for generation of a machine readable multi-parameter human physiological profile including at least one of a kinetic and intra-body location dependent parameter, including providing a time-dependent substance intake program; a data acquisition system which acquires data from the patient passing through the intake program; and a computerized analysis using a machine readable multi-parameter substance profile, including at least one kinetic parameter.

There is yet further provided, in accordance with an embodiment of the present invention, an apparatus, method, and/or functionality for generation of a human physiological profile, including providing a substance intake program; a data acquisition system which acquires data from the patient passing through the intake program; and a computerized analysis using a substance profile, including at least one kinetic parameter.

There is also provided, in accordance with an embodiment of the present invention, an interactive pharmaceutical-containing, machine-readable information-bearing, customized medicine module suitable for use in computerized customized medicine, said customized medicine module including a computerized customized medicine machine-interfaceable pharmaceutical-containing delivery module and a computerized individualized medicine machine-readable information-containing carrier containing at least data regarding said pharmaceutical which is required for use of said pharmaceutical in computerized customized medicine, said data being useful in computerized customized medicine machine actuation of said pharmaceutical-containing delivery module.

There is additionally provided, in accordance with an embodiment of the present invention, a computerized customized medicine machine including:

a computerized patient imager;

a computerized pharmaceutical deliverer employing a pharmaceutical-containing, machine-readable information-bearing, customized medicine module; and

a customized medicine protocol controller including:

an interactive patient imager interface including patient information receiving functionality and patient imaging actuation functionality; and

an interactive pharmaceutical deliverer interface including patient information receiving functionality and patient information-responsive pharmaceutical delivery actuation functionality.

There is also provided, in accordance with an embodiment of the present invention, an interactive pharmaceutical-containing, machine-readable authenticated, authenticated customized medicine module suitable for use in computerized customized medicine, said customized medicine module including a computerized customized medicine machine-interfaceable pharmaceutical-containing module and a computerized individualized medicine machine-readable authentication-containing carrier containing at least authentication data regarding said pharmaceutical which is required for use of said pharmaceutical in computerized customized medicine, said data being useful in said computerized customized medicine machine.

There is further provided, in accordance with an embodiment of the present invention, a computerized customized medicine preparation machine including:

a computerized patient information manager;

a computerized customized medicine pharmaceutical information manager;

a computerized authenticated customized medicine module authenticator; and a computerized pharmaceutical-containing, machine-readable information-bearing, customized medicine module generator including:

a computerized generator protocol manager operative to receive patient information from said patient information manager, to receive authentication of an authenticated customized medicine module from said authenticator, to receive customized medicine pharmaceutical information relating to at least one pharmaceutical contained in said authenticated customized medicine module from said pharmaceutical information manager and to prepare customized medicine information to be included in said customized medicine module; and

a computerized pharmaceutical-containing, machine-readable information-bearing, customized medicine module preparer operative to associate said customized medicine information prepared by said protocol manager in an authenticatable machine readable form with a quantity of said pharmaceutical contained in said authenticated customized medicine module, thereby providing a pharmaceutical-containing, machine-readable information-bearing, customized medicine module.

There is still further provided, in accordance with an embodiment of the present invention, an interactive pharmaceutical-containing, machine-readable information-bearing, individualized medicine module suitable for use in computerized individualized medicine, said individualized medicine module including a computerized individualized medicine machine actuable pharmaceutical-containing delivery module and a computerized individualized medicine machine-readable information-containing carrier containing at least data regarding said pharmaceutical which is required for use of said pharmaceutical in computerized individualized medicine, said data being useful in computerized individualized medicine machine actuation of said pharmaceutical-containing delivery module.

For some applications, said data is in an encrypted format, readable by said computerized individualized medicine machine upon receipt of a predetermined authentication.

There is also provided, in accordance with an embodiment of the present invention, a computerized individualized medicine machine including:

a computerized patient imager;

a computerized pharmaceutical deliverer employing a pharmaceutical-containing, machine-readable information-bearing, individualized medicine module; and

an individualized medicine protocol controller including:

an interactive patient imager interface including patient image receiving functionality and patient imaging actuation functionality; and

an interactive pharmaceutical deliverer interface including patient image receiving functionality and patient image-responsive pharmaceutical delivery actuation functionality.

There is further provided, in accordance with an embodiment of the present invention, use of a high definition, high sensitivity camera for determination of an optimal parameter for a labeled radiopharmaceutical agent, the optimal parameter selected from the group consisting of: optimal dose, optimal mode of administration, optimal mode of acquisition of data with respect to the labeled radiopharmaceutical agent, optimal mode of data processing with respect to the labeled radiopharmaceutical agent, and optimal mode of presentation of information acquired with respect to the labeled radiopharmaceutical agent.

There is still further provided, in accordance with an embodiment of the present invention, a labeled radiopharmaceutical agent that is manufactured or designed or indicated for use with or sold with any one of the above techniques.

The present invention will be more fully understood from the following detailed description of embodiments thereof, taken together with the drawings, in which:

BRIEF DESCRIPTION OF THE DRAWINGS

Fig. 1 is a schematic illustration of an end-to-end automated system for medical imaging, in accordance with an embodiment of the present invention;

Fig. 2 is a flow chart showing an end-to-end method for medical imaging, in accordance with an embodiment of the present invention;

Fig. 3 is a schematic illustration of a patient-specific data carrier, in accordance with an embodiment of the present invention;

Fig. 4 is a schematic illustration of a patient management system, in accordance with an embodiment of the present invention;

Fig. 5 is a schematic illustration of a radiopharmaceutical dose calculation system, in accordance with an embodiment of the present invention;

Figs. 6A-E are tables showing exemplary preconfigured SPECT protocols and parameters thereof, in accordance with respective embodiments of the present invention;

Fig. 7 is a schematic illustration of a mother vial and attached data carrier, in accordance with an embodiment of the present invention;

Fig. 8 is a schematic illustration of a data carrier coupled to a radiopharmaceutical agent container, in accordance with an embodiment of the present invention;

Figs. 9A-H are schematic illustrations of respective embodiments of a radiopharmaceutical agent container and data carrier coupled thereto, in accordance with respective embodiments of the present invention;

Fig. 10 is a schematic illustration of an administration system, in accordance with an embodiment of the present invention;

Fig. 11 is a schematic illustration of an imaging system, in accordance with an embodiment of the present invention;

Fig. 12 is a schematic illustration of an automated radiopharmaceutical dispensing system, in accordance with an embodiment of the present invention;

Figs. 13A-C are schematic illustrations of a system for carrying out a data transfer process, in accordance with an embodiment of the present invention;

Fig. 14 is a schematic illustration of a radioisotope automatic elution system, in accordance with an embodiment of the present invention;

Fig. 15 is a schematic illustration of a mother vial preparation system, in accordance with an embodiment of the present invention;

Figs. 16A-B are illustrations of color spectra and a color-coded signature, respectively, in accordance with an embodiment of the present invention;

Fig. 17 is a schematic illustration of a computer-readable medium, a portion of which is shaped so as to define a physical key, in accordance with an embodiment of the present invention; and

Fig. 18 is a graph showing particle energy vs. photon count at a detector of a camera, in accordance with an embodiment of the present invention.

DETAILED DESCRIPTION OF EMBODIMENTS

Fig. 1 is a schematic illustration of an end-to-end automated system 10 for medical imaging, in accordance with an embodiment of the present invention. System 10 comprises a plurality of integrated elements that are configured to electronically exchange information among one another. The elements include an automated radiopharmaceutical dispensing system 20, a portable information-bearing radiopharmaceutical agent container 22, a portable patient-specific data carrier 24, an automated administration system 26, and an automated imaging system 28. The systems perform their respective automated functions at least in part responsively to the exchanged information. The elements typically authenticate one another via the exchanged information, in order to ensure that only authorized elements participate in the system, and that only authorized and appropriate functions are performed. Each of the elements is described in detail hereinbelow.

End-to-end imaging method

Fig. 2 is a flow chart showing an end-to-end method for medical imaging, in accordance with an embodiment of the present invention. At a radiopharmaceutical provisioning step 100, a manufacturer 102 (Fig. 1) or distributor provides a mother vial 104 (Fig. 1) containing an unlabeled radiopharmaceutical agent, and information associated with the radiopharmaceutical agent. Such an unlabeled radiopharmaceutical agent typically comprises a pharmaceutical substance, for example an antibody such as Capromab Pendetide marketed by Cytogen Corp. under the name ProstaScint and used in the detection of prostate cancer metastases, or sestamibi used in cardiac perfusion studies and marketed under the name of Cardiolite by Bristol Meyers Squibb Corporation, an ion, or another biological metabolized substance, or a substance which is not metabolized but nevertheless undergoes an interaction with the body. The information is stored in a mother vial data carrier 106 associated with mother vial 104, as described hereinbelow with reference to Fig. 7. For some applications, data carrier 106 is physically coupled to mother vial 104, while for other applications the data carrier is provided as a separate element associated with the mother vial. As described hereinbelow with reference to Fig. 7, the information stored in data carrier 106 typically includes information regarding the radiopharmaceutical agent, such as the formulation, pharmacologic kinetic parameters, radioactivity information, and/or protocol information.

At a labeling step 110, the unlabeled radiopharmaceutical agent is labeled with an appropriate radioisotope, to produce a labeled radiopharmaceutical agent. Such labeling is typically performed using conventional methods, including mixing the agent with a solution containing the radioisotope, heating the mixture, and performing quality testing on the labeled radiopharmaceutical agent. For some applications, step 110 is performed using conventional radiopharmacy labeling techniques, while for other applications system 10 comprises a mother vial preparation system 700, which automatically performs all or a portion of the labeling, as described hereinbelow with reference to Fig. 15. The radioisotopes are provided by a radioisotope supplier 111, such as a conventional radiopharmacy or an automatic elution system 600, described hereinbelow with reference to Fig. 14. Data carrier 106 is typically updated with radioactivity-related information, including the time of labeling, the radioactivity of the radioisotope at the time of labeling, and the volume of the labeled radiopharmaceutical agent, as described hereinbelow with reference to Fig. 7.

For some applications, the only active constituent of the labeled radiopharmaceutical agent is the radioisotope; in other words, the radioisotope is not bound to a biologically active substance. For example, the labeled radiopharmaceutical agent may consist essentially of thallium (as well as pH-balancing constituents, salt ions, and preservatives). As used in the present application, including in the claims, a "labeled radiopharmaceutical agent" means either: (a) an agent comprising a diagnostic radioisotope, such as thallium, or (b) an agent comprising a radioisotope bound to a biologically active substance, such as an antibody, a pharmaceutical compound, an ion, or another biological metabolized substance, or a substance which is not metabolized but nevertheless undergoes an interaction with the body.

At a patient registration and imaging protocol assignment step 112, a healthcare worker 206 uses a patient management system 160 to register a patient into system 10, and to assign appropriate administration and imaging protocols for the patient, as described in detail hereinbelow with reference to Fig. 4. At an information transfer step 114, patient management system 160 assigns a portable patient-specific data carrier 24 to the patient, and transmits information to data carrier 24, including at least a patient identifier (typically, the patient's identification code and/or name), and the assigned administration and imaging protocols. Additional patient data parameters recorded may include physiological data such as girth, height and weight. The patient management system additionally transmits an order for one or more patient-specific doses of the appropriate labeled radiopharmaceutical agent(s) to dispensing system 20 or a conventional radiopharmacy.

At a dose dispensing step 116, dispensing system 20 dispenses the ordered customized dose of the labeled radiopharmaceutical agent from mother vial 104, as described in detail hereinbelow with reference to Fig. 12. Prior to dispensing the dose, dispensing system 20 typically authenticates the mother vial using information stored in mother vial data carrier 106. For some applications, dispensing system 20 verifies the authenticity of a commercial license contained in data carrier 106. Typically, all or a portion of the information used for such verification is encrypted, and dispensing system 20 decrypts the information during the verification procedure. Alternatively or additionally, dispensing system 20 accesses, over a network, information stored at a remote site, and utilizes the information for such verification. The dispensing system dispenses the dose based on patient-specific prescription information, radiopharmaceutical agent-related information stored in data carrier 106, and/or patient-specific information provided by an element of system 10. Such patient-specific information may include, for example, age, weight, Body Mass Index (BMI), body dimensions, metabolic rate, hemodynamic state, and/or kinetic parameters of the labeled radiopharmaceutical agent as determined during previous imaging procedures performed on the patient. For some applications, dosage information is provided directly or indirectly by patient management system 160 and/or a radiopharmaceutical dose calculation system 152, which are described hereinbelow with reference to Figs. 4 and 5, respectively.

At an information transfer step 118, dispensing system 20 transfers patient-specific information and radiopharmaceutical-related information to a data carrier 120 physically coupled to container 22, as described hereinbelow with reference to Figs. 9A-H and 10. "Physically coupled," as used in the present application, including the claims, includes both direct and indirect physical coupling. For example, data carrier 120 may be indirectly physically coupled to container 22 via shielding of container 22, or shielding of a cylinder in which container 22 is stored during transport and handling thereof. The patient-specific information includes the patient's identification code and/or name, and the assigned administration and imaging protocols. The radiopharmaceutical-related information typically includes: (a) all or a portion of the information provided by the manufacturer in data carrier 106, such as described hereinbelow with reference to Fig. 7, e.g., intended use, formulation, pharmacologic kinetic parameters, and protocol information; (b) information regarding the radioactivity and volume of the dose; and (c) time of dispensing, as described in detail hereinbelow with reference to Fig. 8. In addition, the dispensing system typically prints and attaches a conventional information label to container 22, such as in order to comply with regulatory labeling requirements. For applications in which the labeled radiopharmaceutical agent(s) is dispensed using conventional radiopharmacy techniques, dispensing system 20, or another element of system 10, such as dose calculation system 152, typically transfers the radiopharmaceutical-related information to data carrier 120. Alternatively, all or a portion of the information is transferred directly from mother vial data carrier 106 to container data carrier 120.

At an administration step 122, administration system 26 receives radiopharmaceutical agent container 22, and administers the labeled radiopharmaceutical agent contained therein to the appropriate patient. As described hereinbelow with reference to Fig. 10, for some applications, administration system 26 comprises an automated administration device, which is configured to administer the labeled radiopharmaceutical agent, while for other applications, a healthcare worker manually administers the agent upon receiving a signal to do so from system 26. Prior to administration, system 26 authenticates container 22 and verifies the identity of the patient, using information provided by patient-specific data carrier 24 and container data carrier 120, and, optionally, another element of system 10, such as a physician station 115. Typically, all or a portion of the information used for such verification is encrypted, and administration system 26 decrypts the information during the verification procedure. Alternatively or additionally, administration system 26 accesses, over a network, information stored at a remote site, and utilizes the information for such verification. Administration system 26 verifies that the patient identification codes contained in patient-specific data carrier 24 and container data carrier 120 match one another, and, typically, verifies that the administration and/or imaging protocols contained in the data carriers match one another. Typically, at least a portion of the information stored in data carrier 120 of container 22 is transferred to data carrier 24, either directly, via administration system 26, or via a communication element. For some applications, system 26 generates a signal for a healthcare worker confirming that a proper match has been made between agent container 22 and the patient. The system also typically verifies that the current time is the proper administration time, as per the administration protocol, and that container 22 contains the proper dose, as per the selected protocol. Optionally, system 26 is configured to administer the labeled radiopharmaceutical agent only if such matches are confirmed by the system. For some applications, administration system 26 verifies the authenticity of a commercial license contained in data carrier 120, and performs the administration only upon verification of the authenticity.

For some applications, administration system 26 customizes the administration of the labeled radiopharmaceutical agent using information provided by data carrier 24, data carrier 120, physician station 115, and/or patient management system 160. For example, system 26 may customize a time-dependent administration profile of the labeled radiopharmaceutical agent, such as a rate of administration. Alternatively or additionally, system 26 may administer less than the entire dose of the labeled radiopharmaceutical agent, e.g., based on feedback from imaging system 28 during an imaging procedure.

For some applications, such as dynamic studies, administration system 26 administers the labeled radiopharmaceutical agent during an imaging procedure performed by imaging system 28. For these applications, the administration system is in communication with the imaging system during the administration, in order to assure information regarding time-dependent administration is accurately communicated between the administration system and the imaging system. For some applications, imaging system 28 reads information from patient-specific data carrier 24, and transmits at least a portion of the information to administration system 26, thereby obviating the need for the administration system to directly read such information from the data carrier. For some applications, imaging system 28 triggers the commencement of administration. (It is to be understood that although the imaging system triggers administration of the agent, for some applications the agent is not administered until a healthcare worker provides a final authorization to do so, such as to comply with regulatory safety requirements.) For some applications, the labeled radiopharmaceutical agent(s) is administered in a closed loop with an imaging procedure performed by imaging system 28; administration system 28 modifies one or more parameters of the administration in real time based on feedback received from imaging system 28, and/or based on real-time measurements of physiological parameters of the patient (e.g., systemic blood concentrations) during the imaging procedure. For some protocols, the administration system administers a preliminary bolus injection, and, based on feedback from imaging system 28 and/or on physiological parameters of the patient, configures one or more parameters of a subsequent administration of the same or a different labeled radiopharmaceutical agent.

At an information transfer step 123, before, during and/or after administration of the labeled radiopharmaceutical agent, system 26 electronically updates patient-specific data carrier 24 with details of the administration, such as:

- an identification code of container 22 and/or an administration device;
- an identification code of the patient to which the labeled radiopharmaceutical agent was dispensed, which should match the patient code already stored in data carrier 24;
- the administered labeled radiopharmaceutical agent;
- the volume of the labeled radiopharmaceutical agent administered;
- the time of administration;
- the time profile of administration;
- the radioactivity of the labeled radiopharmaceutical agent at the time of administration;
- the radioactivity of the labeled radiopharmaceutical agent when dispensed to container 22;
- the time of measurement of the radioactivity when dispensed to container 22; and/or
- at least a portion of the radiopharmaceutical information provided by data carrier 106 of mother vial 104.

For some applications, data carrier 120 of container 22 communicates administration information to patient-specific data carrier 24, either directly or via administration system 26. For some applications, system 26 provides similar updates to other elements of system 10, such as patient management system 160, management control component 150, physician station 115, and/or imaging system 28. Alternatively or additionally, a healthcare worker manually updates one or more of the data carrier and/or system elements. Typically, for safety purposes, after administration system 26 has read all necessary information from data carrier 120, administration system 26 permanently disables data carrier 120 of container 22, in order to ensure that the data carrier is not accidentally reused for another patient.

Reference is still made to Fig. 2. After or during administration of the labeled radiopharmaceutical agent, imaging system 28 performs an imaging procedure on the patient, at an imaging step 124. Imaging system 28 is described hereinbelow with reference to Fig. 11. Prior to performing the imaging procedure, system 28 verifies one or more of the following:

- the identity of the patient, using information provided by patient-specific data carrier 24;
- the authenticity of patient-specific data carrier 24, typically using information provided by the data carrier itself, a coded signature 256, as described hereinbelow in the section entitled "Signature," and/or a key 852, as described hereinbelow with reference to Fig. 17;
- that patient-specific data carrier 24 has been brought within a certain distance of imaging system 28, e.g., within about 30 cm;
- the identity of the manufacturer or distributor of the radiopharmaceutical agent, using information stored in data carrier 120;
- that a selected camera of imaging system 28, imaging protocol, and patient identification code, as provided to imaging system 28 by one or more elements of system 10, match those stored in patient-specific data carrier 24;
- the authenticity of a commercial license contained in patient-specific data carrier 24. For some applications, system 28 verifies that the license has not been previously used, for example by verifying that a registration code associated with the license has not been previously received by system 28 and/or system 10; and/or

- that administration system 26 used (or is about to use, for procedures in which administration occurs during imaging) the correct container 22 and associated data carrier 120 for the prescribed imaging procedure, and administered (or is about to administer) the appropriate dose of the labeled radiopharmaceutical agent(s) at time(s) appropriate for performance of the imaging procedure.

Typically, all or a portion of the information used for such verification is encrypted, and imaging system 28 decrypts the information during the verification procedure. Alternatively or additionally, imaging system 28 accesses, over a network, information stored at a remote site, and utilizes the information for such verification.

For some applications, system 28 generates a signal for a healthcare worker confirming that a proper match has been made between the patient and one or more of the components described above. Optionally, system 28 is configured to perform the imaging procedure only if such a match is confirmed by the system.

Typically, system 28 customizes the imaging procedure using information provided by administration system 26, data carrier 24, and/or physician station 115. Such information typically includes information regarding the time of labeled radiopharmaceutical administration, the labeled radiopharmaceutical agent (e.g., radioactive strength, time of preparation, and/or kinetic parameters), patient-specific physiological information, and/or imaging protocol information. Parameters of the imaging procedure that are typically customized include, but are not limited to: total acquisition time; detector motions, such as detector angular and translational motions, detector step size (i.e., the density of the step size, typically expressed in degrees), and detector dwell time at each view; type of study, such as standard, active vision (as described in the above-mentioned International Application PCT/IL2005/001173), or gated; definition of the region of interest (ROI), for example, based on the size of the heart; and/or attenuation correction parameters, which are typically based on physiological parameters such as body mass, BMI, and girth.

At an image reconstruction step 126, imaging system 28 uses the acquired imaging data for image reconstruction. For some applications, system 28 customizes the image reconstruction procedure using information provided by administration system 26, data carrier 24, and/or physician station 115.

Imaging system 28 analyzes the reconstructed image, at an analysis step 128. For some applications, system 28 customizes the analysis procedure using information provided by administration system 26, data carrier 24, and/or physician station 115.

The imaging system, or a separate diagnostic system of system 10, assists with developing a diagnosis based on the analysis, at a diagnosis step 130. Typically, system 28 customizes the diagnostic procedure using information provided by administration system 26, data carrier 24, and/or physician station 115. For some applications, authentication is performed to verify that the imaging was performed as intended. Reconstruction and analysis are preferably based on lookup tables and expert system rules, for example, as provided by the radiopharmaceutical manufacturer, and may be patient customized, taking into account known patient physiology and/or suspected disease. Alternatively or additionally, the lookup tables and/or expert system diagnostic rules are configured to provide such customization. For some applications, customization and/or diagnostic techniques are performed that are described in the above-mentioned International Application PCT/IL2005/001173.

The diagnosis and/or the results of the imaging procedure are typically transmitted to physician station 115, for use by an attending healthcare worker 206. Alternatively or additionally, the diagnosis and/or the results of the imaging procedure are transmitted to a database 132 (Fig. 1). The accumulated results of a number of such imaging procedures for a large population are analyzed in order to develop, optimize, update, or otherwise re-evaluate imaging protocols, and update appropriate lookup tables and/or expert system rules for the use of the radiopharmaceutical agent. For example, the database may contain quantitative data regarding absolute blood flow measurements from healthy patients and patients with varying level of diseases. For some applications, such data is used to obtain disease-specific tissue signatures by performing quantitative analysis of normal and diseased tissue. Alternatively or additionally, the information in database 132 is used for: (a) comparing the results of an imaging procedure (images, and/or quantitative information and/or analyses) with historical results of the patient, in order to classify disease state and/or (b) comparing the results of an imaging procedure with similar results from a patient population, in order to classify disease state.

Typically, physician station 115 comprises one or more standard personal computers or servers with appropriate memory, communication interfaces and software for carrying out the functions prescribed by relevant embodiments of the present invention. This software may be downloaded to the physician station in electronic form over a network, for example, or it may alternatively be supplied on tangible media, such as CD-ROM.

During or after steps 124 through 128, imaging system 28 updates the data stored in patient-specific data carrier 24 and/or other elements of system 10, such as patient information system 160, and/or physician station 115, to reflect details of the imaging procedure performed. In addition, for some applications, imaging system 28 transfers data to the specific camera used for the procedure, such as patient details, radiopharmaceutical information, and/or administration information, which information is received from data carrier 24, or from other elements of system 10.

The patient-specific data carrier

Reference is made to Fig. 3, which is a schematic illustration of patient-specific data carrier 24, in accordance with an embodiment of the present invention. Data carrier 24 is configured to be held or worn by the patient, and, for some applications, comprises a coupling mechanism configured to be coupled to the patient, which coupling mechanism, comprises, for example, a bracelet, watch, or necklace (Fig. 3A shows the data carrier integrated into a watch or bracelet 170). Data carrier 24 is computer-communicatable, and typically comprises an RFID tag, smart card, disk-on-key (e.g., a USB key), or other electronic memory, as described below. Data carrier 24 is configured to hold information regarding the patient and a selected imaging procedure, as described immediately hereinbelow with reference to Fig. 4.

One or more communication elements 240 are provided for reading data from and transmitting data to data carrier 24 e.g., using a proprietary or standard wireless protocol, e.g., Bluetooth, WiFi, W-LAN, or IEEE 802.11. Alternatively, the communication element is brought into physical contact with data carrier 24, and reads and/or writes the information using an electrical contact, or other coupling technique, such as inductive coupling. Respective communication elements 240 are typically in data communication with patient management system 160, physician station 115, dispensing system 20, administration system 26, and/or imaging system 28. For some applications, communication elements 240 comprise one or more coils for transmitting and receiving electromagnetic radiation. Typically, the communication elements are configured to have a short effective transmission range, e.g., no more than between about 20 and 40 cm, such as about 30 cm. Such a short range reduces the likelihood of accidental communication with a data carrier other than the intended data carrier.

For some applications, a portion of the patient information stored in the data carrier is also printed in human- and/or machine-readable form on the data carrier. For example, a name 172 and identification code 174 of the patient, and/or a barcode 176 may be printed on the data carrier.

Data carrier 24 comprises circuitry 178, which comprises memory and logic. For some applications, data carrier 24 is passive, in which case it is configured to receive energy from communication element 240. For other applications, data carrier 24 comprises a power source (not shown). For some applications in which the data carrier comprises a power source, the data carrier comprises a communication element for communicating and/or energizing another electronic apparatus. Alternatively or additionally, the data carrier comprises a communication element configured for wireless communication.

For some applications, data carrier 24 further comprises a user output 180 for outputting information to the patient or healthcare workers. For example, output 180 may comprise a display screen, light, and/or sound generator, which circuitry 178 drives to communicate information, such as when communications have been established with other elements of system 10, e.g., data carrier 120, administration system 26, imaging system 28, and/or patient management system 160. For some applications, circuitry 178 is configured to additionally function as an alarm clock; for example, the circuitry may drive display 180 to alert the patient prior to a scheduled administration or imaging procedure.

Typically, for safety purposes, upon completion of all the imaging procedures associated with a given patient-specific data carrier 24, system 10 permanently disables the data carrier, in order to ensure that the data carrier is not accidentally reused for another patient.

The patient management system

Reference is made to Fig. 4, which is a schematic illustration of patient management system 160, in accordance with an embodiment of the present invention.

Patient management system 160 manages patient-related administrative and medical information, and typically comprises at least one workstation 200 in communication with one or more servers 202. Typically, workstation 200 and servers 202 comprise standard personal computers and/or computer servers with appropriate memory, communication interfaces and software for carrying out the functions prescribed by relevant embodiments of the present invention. This software may be downloaded to the workstation and servers in electronic form over a network, for example, or it may alternatively be supplied on tangible media, such as CD-ROM.

System 160 performs the following functions:

- receives and registers new patients into system 10, typically into management and control component 150 thereof;
- assigns patient identification codes;
- assigns, issues, and transfers information to patient-specific data carriers 24;
- receives and tracks patient prescriptions for radiopharmaceuticals, and communicates the prescriptions to other elements of system 10, such as dispensing system 20, administration system 26, and/or management and control component 150; and/or
- suggests and assigns imaging protocols based on the patient's imaging needs and patient-specific information.

During reception of a new patient 204, healthcare worker 206 manually enters patient information into workstation 200. Alternatively or additionally, all or a portion of the patient information is provided electronically by another healthcare system or electronic information source. System 160 typically verifies the healthcare worker's identity and access privileges by interrogating a computer-commuticatable identity tag 208 held by the worker, and/or by checking the validity of a password entered into workstation 200 by the healthcare worker.

The patient information provided to system 160 typically includes:

- the patient's general details, such as name, age, gender, address, telephone number, profession, attending and/or treating physician, health insurance plan, and next of kin;

- the patient's medical profile, such as medical condition, medical history, family medical history, BMI, weight, allergies, sensitivity to one or more chemical compounds, metabolic rate, and other physiological conditions;
- medications prescribed to the patient;
- the patient's imaging history; and/or
- information regarding the desired imaging, including reason for imaging, type of imaging, body structure or organ to be imaged, and known or suspected pathology.

In an embodiment of the present invention, upon entry of such patient information into patient management system 160, the system automatically suggests one or more imaging protocols that may be appropriate for the patient's imaging needs and medical condition. When making such suggestion, the system takes into consideration, in addition to the information regarding the desired imaging, such factors as the patient's general details, medical profile, imaging history, and guidelines for medication interactions. The system typically selects the suggested protocol(s) from a database of preconfigured protocols, which is described hereinbelow with reference to Figs. 6A-E. Healthcare worker 206 selects one of the suggested protocols, or selects another non-suggested protocol directly from the protocol database.

For some applications, the system suggests one or more customizations of the selected protocol, as described hereinbelow with reference to Figs. 6A-E, which the healthcare worker may accept, decline, or modify, in whole or in part. These suggested customizations are typically based on (a) physiological parameters of the patient, such as age, weight, BMI, metabolic rate, and/or hemodynamic state, and/or kinetic parameters of the radiopharmaceutical agent as determined during previous imaging procedures performed on the patient, and/or (b) a medical profile group to which the patient is assigned, such as high, normal, or low BMI, or high BMI - diabetic, or high BMI - normal metabolic rate. (For some applications, such profile groups are stored in a database of management and control component 150.) Alternatively or additionally, the healthcare worker may customize the protocol manually.

Upon selection and customization of the protocol, patient management system 160 schedules, typically automatically:

- a specific imaging system 28 capable of performing the selected imaging procedure;
- a date and time for performing the imaging procedure; and
- a date(s) and time(s) for administration of labeled radiopharmaceutical agent(s).

Patient management system 160 transmits the entered and generated patient-specific information, including the selected protocol, to the patient's patient-specific data carrier 24. The transmitted patient-specific information typically includes:

- the patient's identification code and name;
- an identifier of the selected imaging protocol(s), such as a name and/or an identification code thereof, and/or additional imaging protocol information, such as described hereinbelow with reference to Figs. 6A-E;
- an identifier of the selected administration protocol(s), such as a name and/or an identification code thereof;
- the scheduled imaging system 28;
- the scheduled imaging date and time;
- the scheduled administration date(s) and time(s);
- the patient's personal details;
- the patient's medical profile; and/or
- the patient's imaging history.

The patient management system transmits an order for one or more patient-specific doses of the appropriate labeled radiopharmaceutical agent(s) to dispensing system 20, such as via management and control component 150. Typically, the patient management system additionally transmits at least a portion of the entered and generated patient-specific information to one or more of: (a) management and control component 150, (b) dose calculation system 152, (c) administration system 26, and/or (d) imaging system 28. Typically, a different subset of the information is transmitted to each of these entities.

As described hereinabove with reference to Fig. 3, for some applications, a portion of the patient information stored in data carrier 24 is also printed in human- and/or machine-readable form on the data carrier. For example, a name 172 and identification code 174 of the patient, and/or a barcode 176 may be printed on the data carrier. For such applications, system 160 comprises a printer 210, which is configured to print the information directly on data carrier 24, or to print the information on an adhesive label, which healthcare worker 206 attaches to data carrier 24. For some applications, printer 210 comprises communication element 240, and the printer is configured to both print the information on the data carrier and transmit the information to the data carrier, typically generally at the same time.

In an embodiment of the present invention, system 10 comprises at least one web server, which is configured to accept orders for an imaging procedure over an intranet or the Internet, placed by a physician or other healthcare worker. Such orders can typically be modified up until a deadline, such as midnight before the day of the scheduled imaging procedure.

The management and control component

Reference is again made to Fig. 1. In an embodiment of the present invention, system 10 comprises management and control component 150, which coordinates a portion of the interaction and communication among the elements of system 10. The remainder of the interaction and communication occurs directly between the elements of the system, and/or via other elements of the system. For some applications, component 150 issues a password and/or computer-communicatable identity tags 208 to healthcare workers 206 authorized to interact with one or more elements of system 10. For example, tag 208 may comprise an RFID tag, smart card, disk-on-key (e.g., a USB key), minidisk, or other electronic memory, or a machine-readable code, e.g., a barcode. As appropriate, healthcare workers 206 may be assigned various permission levels, such as permission to view or modify particular system and/or patient data.

Typically, management and control component 150 comprises one or more standard personal computers or servers with appropriate memory, communication interfaces and software for carrying out the functions prescribed by relevant embodiments of the present invention. This software may be downloaded to the management and control component in electronic form over a network, for example, or it may alternatively be supplied on tangible media, such as CD-ROM.

The dose calculation system

Reference is made to Fig. 5, which is a schematic illustration of radiopharmaceutical dose calculation system 152, in accordance with an embodiment of the present invention. The dose calculation system manages and tracks, typically automatically, radiopharmaceutical inventory, ordering, dose dispensing, and disposal. Typically, the dose calculation system comprises one or more standard personal computers or servers with appropriate memory, communication interfaces and software for carrying out the functions prescribed by relevant embodiments of the present invention. This software may be downloaded to the dose calculation system in electronic form over a network, for example, or it may alternatively be supplied on tangible media, such as CD-ROM. The dose calculation system receives information from dispensing system 20 regarding doses drawn from the inventory.

Dose calculation system 152 typically comprises:

- an ordering sub-system 154, which orders radiopharmaceutical products from radiopharmaceutical manufacturers, distributors, and/or radiopharmacies, typically automatically, such as when the dose calculation system identifies that inventories of a given radiopharmaceutical are lower than needed;
- a receipt and verification sub-system 155, which manages the receipt and registration of radiopharmaceutical products. The receipt and verification sub-system checks the received products against orders placed by the ordering sub-system, and typically performs license management. When a received mother vial 104 includes a mother vial data carrier 106, the sub-system reads information contained in the data carrier to verify that the order has been accurately fulfilled, and, typically, verifies the authenticity of the mother vial;
- a dose calculation sub-system 156, which calculates customized doses of labeled radiopharmaceutical agents for patients based on patient-specific information, protocol information, and/or prescription information, and communicates the customized doses to patient management system 160

and/or dispensing system 20; and/or

- a waste-disposal sub-system 157, which tracks radioactive waste disposal by system 10, such as disposal of radioactive materials contained in waste container 512, described hereinbelow with reference to Fig. 12. For some applications, sub-system 157 additionally tracks radioactive waste disposal of materials in the clinical environment not associated with system 10.

Ordering sub-system 154 and waste-disposal sub-system 157 typically operate in accordance with per country requirements for radiopharmaceutical use. A reporting sub-system reports to relevant nuclear regulatory commissions as required, based on information obtained from the other sub-systems.

In an embodiment of the present invention, dose calculation sub-system 156 designs a cocktail of labeled radiopharmaceutical agents or a series of labeled radiopharmaceutical agents to carry out the desired imaging. When designing such a cocktail or series, the sub-system considers constraints imposed by the physical properties of the agents and by the patient history, and other requirements, such as safety and efficacy requirements. The sub-system determines an appropriate dose for the specific patient having particular physiological parameters (e.g., weight, BMI, and age), and determines the times at which multiple agents are to be administered to the patient in order to achieve optimal imaging.

For some applications, sub-system 156 determines that a plurality of labeled radiopharmaceutical agents are to be administered together and thus must be combined in a single preparation, i.e., a cocktail. For other applications, the sub-system determines that a plurality of labeled radiopharmaceutical agents are to be administered separately at different times and thus must be contained in separate containers 22. As appropriate, sub-system 156 takes into consideration differing half-lives of the plurality of labeled radiopharmaceutical agents, in conjunction with the prescribed time of the imaging procedure. For example, a simultaneous imaging protocol is provided for assessing cardiac perfusion using a cocktail comprising Tc-99m sestamibi injected at rest, and thallium-201 injected at stress, wherein the desired activities at imaging time of the Tc-99m sestamibi and the thallium are 6 mCi and 4 mCi, respectively. When calculating the necessary activity of the dispensed dose, sub-system 156 accounts for the respective half-lives of Tc-99m (6 hours) and thallium-201 (64 hours) in view of the planned time interval between the dispensing time and administration time. For example, if dispensing is performed 24 hours before administration, sub-system 156 calculates the activities of the Tc-99m and thallium-201 at the time of dispensing to be 96 mCi and 5.5 mCi, respectively.

Protocol information

Reference is made to Figs. 6A-E, which is a table showing exemplary preconfigured SPECT protocols and parameters thereof, in accordance with respective embodiments of the present invention. These protocols are appropriate, for example, for use with the SPECT imaging methods and apparatus described hereinbelow with reference to Fig. 11, and/or in the co-assigned patent applications and/or patent application publications incorporated herein by reference hereinabove. For some applications, the techniques described herein utilize additional protocols described in above-mentioned International Application PCT/IL2005/001173, International Application PCT/IL2005/001215, filed November 16, 2005, above-mentioned US Provisional Patent Application 60/628,105, above-mentioned US Provisional Patent Application 60/675,892, or in one or more of the other co-assigned patent applications and/or patent application publications incorporated herein by reference. Alternatively or additionally, the techniques described herein utilize protocols for non-SPECT imaging modalities, such as PET or CT, or other imaging modalities known in the art. The preconfigured protocols are stored in a database, which is typically used by patient management system 160 for suggesting protocols and/or by dose calculation sub-system 156, as described hereinabove with reference to Figs. 4 and 5, respectively.

For each of the exemplary protocols shown in Fig. 6A, the table indicates general parameters for a rest phase and a stress phase of the protocol. For example, for the "single isotope / low dose / fast imaging" protocol, the table shows that the radiopharmaceutical (RP) for the rest phase of the protocol is less than 0.3 mCi of Thallium, that the waiting time after injection of the radiopharmaceutical is 2 minutes, and that the image acquisition duration is 15 minutes. Parameters for the stress phase are similarly indicated, with the addition of the type of stress (exercise, e.g., treadmill or bicycle, or pharmaceutical, e.g., adenosine). The "thallium stress perfusion" and "simultaneous dual isotope stress perfusion" protocols are optionally dynamic.

For each of the exemplary protocols shown in Figs. 6B-E, the table indicates administration parameters, detector parameters, scanning parameters, and analysis parameters for the protocol. For example, for Protocol A of Figs. 6B-C ("Cardiac mapping"), the table indicates:

- the labeled radiopharmaceutical agent is Tc-99-sestamibi (MIBI);
- the protocol is a fast protocol, with image acquisition completed prior to substantial uptake of the agent by the liver;
- the injection is by a single bolus;
- image acquisition begins either about 2 minutes after injection, or during or immediately administration, for applications in which the administration is performed while the patient is already placed at camera 452 (Fig. 11);
- the detected photon energy is 140 KeV with an energy resolution of 15%, i.e., the total range of energy levels detected by the detectors 454 of camera 452 (Fig. 11) is set to be 15% of the emitted energy level of the labeled radiopharmaceutical agent (140 Kev). Typically, this range is not centered around the emitted energy level, but instead is shifted towards lower energy levels;
- the total scan time is 120 seconds;
- four detectors 454 of camera 452 are assigned as outer (distal) detectors, and six detectors 454 are assigned as inner (proximal) detectors, as described hereinbelow with reference to Fig. 11;
- each of the inner detectors has an angular range of between 90 and 120 degrees, and each of the outer detectors has an angular range of between 40 and 60 degrees;
- the total number of angular orientations assumed by the detectors in aggregate is 1200, i.e., 10 detectors times 120 orientations each;
- each angular step of the inner detectors is one degree, and each angular step of the outer detectors is 0.3 to 0.5 degrees (corresponding to the range of 40 to 60 degrees described above);
- the dwell time at each step is one second, for both the inner and outer detectors;

- the imaging procedure is gated using 16 to 32 frames;
- the analyses to be performed include intensity image and ejection fraction.

For some applications, the protocol information includes additional information not shown in Figs. 6B-E, such as:

- additional scanning parameters, such as whether the detectors perform multiple scans (in all the protocols shown in the table, the detectors typically perform a single scan); and
- additional analysis parameters, such as:
  - saturation handling (in the first cardiac mapping protocol shown in the table, no saturation handling is performed, while in the second cardiac mapping protocol shown in the table, the analysis is configured to dismiss saturated pixels);
  - whether the analysis handles scatter from multiple sources (in the protocols shown in the table, the analysis does not handle scatter from multiple sources);
  - reconstruction resolution (in all of the protocols shown in the table, the image reconstruction resolution is 2.5 mm in the z-direction, and 5 mm in the x- and y-directions); and
  - parameters that provide the diagnosis system (e.g., expert system) with information regarding how to interpret the results of the imaging study, such as kinetic parameters, predefined pathological values, or patient-specific physiological parameters (e.g., BMI, age, or a group to which the patient is assigned).

Reference is made to Protocol E of Figs. 6B-C. In this cardiac mapping protocol, simultaneous image acquisition is performed using, typically using full conventional doses of both thallium and MIBI-Tc. The detected photon energy of the thallium is 167 KeV, rather than the 72 KeV that is conventionally detected during nuclear imaging procedures. Unlike conventional SPECT cameras, the camera described hereinbelow with reference to Fig. 11 is sufficiently sensitive to detect a clinically-relevant count of the relatively low percentage (8%) of photons emitted at the 167 KeV energy level.

(Detection of 72 KeV energy is generally not practical when a conventional dose of MIBI-Tc is used, because the scatter from the 140 KeV energy level of MIBI-Tc masks the 72 KeV photons emitted by the thallium.)

Reference is made to Protocol I of Figs. 6D-E. In this cardiac dynamic mapping protocol, image acquisition typically begins prior to administration of the radiopharmaceutical agent, such as at one minute prior to administration, as shown in the table. This allows the imaging system to complete one full scan of the region of interest prior to administration of the radiopharmaceutical agent, in order to ensure that the imaging system is able to acquire photons of radiation beginning immediately after the radiopharmaceutical agent is administered.

Typically, a selected preconfigured protocol is customized based on physiological parameters of the specific patient, and/or a medical profile group of the patient, as described hereinabove with reference to Fig. 4. Such customization typically includes customization of the radiopharmaceutical agent, administration parameters, and/or imaging parameters.

For some applications, one or more of the following parameters of the radiopharmaceutical agent are customized:

- the dose, or for multiple radiopharmaceutical agents, the respective doses;
- the radioactivity;
- for cocktails, the ratio of the different radiopharmaceutical agents; and/or
- the volume of the dose, or for multiple radiopharmaceutical agents, the volumes of the respective doses.

For some applications, one or more of the following parameters of the administration are customized:

- the dose administered, or for multiple radiopharmaceutical agents, the respective doses per administration;
- the type of administration, e.g., a single bolus, a plurality of boluses (e.g., two boluses), pulsatile administration, or constant drip administration;
- the labeled radiopharmaceutical agent for each administration, whether a single agent or a cocktail of agents;

- the time of the administration with respect to the time of imaging;
- the timings of multiple administrations with respect to each other and with respect to other activities, such as rest or stress (physical or pharmacological);
- the administration device, e.g., a syringe, a dual-needle syringe, a pump, or an IV line; and/or
- the mode of administration, e.g., manual, automatic, or computer driven.

For some applications, one or more of the following parameters of the imaging procedure are customized. For some applications, such parameters are separately specified for individual components of camera 452 of imaging system 28, or groups of components, such as for individual detectors 454 or groups of detectors of camera 452, described hereinbelow with reference to Fig. 11.

- total acquisition time, and/or acquisition time for a plurality of phases of acquisition;
- detector scanning plan, including detector motions, such as detector angular and translational motions, detector step size (i.e., the density of the step size, typically expressed in degrees), number of detectors utilized for image acquisition, and detector dwell time at each view;
- detector sensitivity;
- detection energy resolution;
- detector calibration plan;
- definition of the region of interest (ROI);
- gating parameters;
- energy bands, i.e., a plurality of non-overlapping energy windows;
- collimator positioning, shape, structure, and orientation;
- multiple/interlaced scans;
- zooming parameters;
- uniformity/non-uniformity of scan;

- Compton scatter map calculation and correction parameters;
- optimal energy window;
- optimal energy resolution, i.e., the range of energy level windows for which detection is enabled; and/or
- adaptivity of scan pattern to acquired counts, e.g., active vision parameters (as described in the above-mentioned International Application PCT/IL2005/001173).

In an embodiment of the present invention, system 10 uses high definition protocols in conjunction with SPECT imaging techniques to enable personalized functional imaging at higher speeds and resolutions than can be achieved using conventional radiopharmaceutical protocols and imaging technology, using imaging techniques described herein and/or incorporated herein by reference. Alternatively or additionally, the system uses low dose protocols that enable personalized functional imaging at higher resolutions but with substantially lower doses than possible using conventional methods.

In an embodiment of the present invention, system 10 uses a protocol pursuant to which a patient undergoes a rest thallium (Tl-201-thallous chloride) and stress Tc-99-sestamibi (MIBI) study having a total study duration of between about 60 and about 90 minutes, and a total image acquisition duration of between about 0.5 and about 6 minutes, e.g., about four minutes. For example, pursuant to the protocol:

- about 3 mCi of thallium may be administered to the patient as a bolus IV injection,
- the patient may rest for between about 10 and about 15 minutes,
- an image acquisition having a duration of about two minutes may be performed,
- the patient may be physically stressed,
- about 20-30 mCi of Tc-99-sestamibi may be administered as a bolus IV injection, and
- a second image acquisition having a duration of about two minutes may be performed.

Such dual-isotope imaging is generally useful for assessing myocardial perfusion of patients with suspected ischemic syndromes and a variety of other conditions. Alternatively, in an embodiment, the rest phase is performed using an approximately 8 to 10 mCi dose of Tc-99-sestamibi, in which case image acquisition typically commences about 30 minutes after injection of the sestamibi. Further alternatively, in an embodiment, image acquisition for the rest phase is performed about two minutes after injection of the thallium, the stress is pharmacological (e.g., using adenosine), and image acquisition for the stress phase is performed essentially immediately after injection of the sestamibi. Still further alternatively, in an embodiment, the rest phase is performed using Tc-99-sestamibi, and image acquisition commences essentially immediately upon injection of a dose of about 8 to 10 mCi.

In accordance with respective embodiments of the present invention, dual-radiopharmaceutical protocols include the administration and simultaneous imaging of the following combinations of labeled radiopharmaceutical agents. Typically, the labeled radiopharmaceutical agents are administered as a mixture (i.e., a cocktail) before or during a simultaneous imaging procedure; alternatively, the labeled radiopharmaceutical agents are administered separately before or during a simultaneous imaging procedure.

- (a) I-123 BMIPP, a fatty acid imaging agent that has been available in Japan for many years, and is currently in Phase III clinical trials in the United States, and (b) a myocardial perfusion agent (e.g., Tc-99m sestamibi, Tc-99m tetrofosmin, or Tl-201-thallous chloride), for simultaneously studying myocardial perfusion and fatty acid metabolism;
- (a) Tl-201-thallous chloride and (b) Tc-99m pertechnetate, for differentiating an organ from its anatomical surroundings, such as differentiating parathyroid glands from the thyroid gland;
- (a) In-111 DTPA, and (b) Tc-99m-MAG3, for differentiating pathological processes in a given organ, such as performing differential diagnosis of a hypo-perfused kidney, e.g., to study true glomerular filtration rate and tubular secretion simultaneously;
- a cocktail of labeled radiopharmaceutical agents, for studying cancer, including simultaneous diagnosis, prediction of therapy response, and

monitoring of therapy, such as simultaneously identifying a tumor, and characterizing tumor perfusion and metabolic activity, e.g., in order to provide a disease signature; and

- the combinations shown in the following table.

TABLE 1

First radiopharmaceutical	First application	Second radiopharmaceutical	Second application
^{201}Tl	Myocardial perfusion	Tc-99m-teboroxime	Myocardial perfusion
		Tc-99m-sestamibi	
		Tc-99m-tetrophosmin	
^{201}Tl	Myocardial perfusion	Tc-99m-PYP	Infarct Imaging
^{201}Tl	Myocardial perfusion	Tc-99m-Annexin	Apoptosis
^{201}Tl	Myocardial perfusion	^{123}I-BMIPP	Hypoxia
Tc-99m-teboroxime	Myocardial perfusion	^{111}In-Annexin	Apoptosis
Tc-99m-teboroxime	Myocardial perfusion	^{123}I-Fatty acid	Metabolism
^{111}In-WBC	Infection	Tc-99m-SC	Bone Marrow
^{111}In-DTPA	Kidney (GFR)	Tc-99m-MAG3	Kidney (tubular secretion)
Tc-99m-RBC	Blood pool	^{111}In-Prostascint	Prostate cancer
Tc-99m-HMPAO	Cerebral blood flow	^{123}I-IBZM	Dopamine D2 receptors

In an embodiment of the present invention, system 10 uses protocols for studying the kinetics of thallium. For some applications, such protocols provide dynamic information regarding myocardial function, such as blood flow, rate of thallium uptake, thallium accumulation/redistribution, thallium metabolism, and/or thallium and/or metabolite secretion and/or wash-out (active or passive). Kinetic perfusion radiopharmaceutical modeling provides absolute myocardial perfusion measurements, coronary flow reserve, and parametric representation of cellular function.

In accordance with respective embodiments of the present invention, thallium protocols include:

- protocols using a conventional dose of thallium, with a substantially reduced SPECT image acquisition duration, e.g., less than about 6 minutes, such as less than about 2 minutes, e.g., about 0.5 minutes. By way of comparison, conventional thallium SPECT imaging procedures generally have image acquisition durations of between about 10 and about 20 minutes. For some applications, the thallium protocol is customized for a specific patient, as described hereinabove;
- protocols using a conventional dose of thallium and a conventional image acquisition duration, with a substantially increased image resolution. For some applications, acquired photon counts are at least 5 times greater than those acquired using conventional SPECT techniques, e.g., at least 10 times greater, resulting in an image with substantially higher resolution; and
- dynamic protocols for myocardial perfusion studies that provide absolute quantitative measurements. For example, images of the heart may be reconstructed from list mode data, with a temporal resolution of 5-10 seconds. This temporal resolution is typically appropriate for the measurement of the kinetics of uptake and wash-out of thallium from the myocardium, as well as those of an input bolus as it passes through the left ventricle. Such data enables the measurement of absolute myocardial blood flow at rest and during peak stress.

In an embodiment of the present invention, system 10 uses protocols for cardiac stress testing studies, using, for example, Tc99m-sestamibi, Tc-99m tetrofosmin, or thallium. Such protocols differentiate between healthy cardiac tissue and scarred or poorly perfused cardiac tissue. Perfusion defects that appear after exercise or pharmacologic stress suggest either vascular occlusion or myocardial infarction. For some applications, such studies are performed gated to the patient's ECG, in order to study cardiac wall motion. Wall motion studies allow calculation of key cardiac function parameters, such as ejection fraction and estimated cardiac output.

In accordance with respective embodiments of the present invention, cardiac stress testing protocols, which use, for example, Tc99m-sestamibi, Tc-99m tetrofosmin, or thallium, include:

- protocols using a conventional dose, with a substantially reduced SPECT image acquisition duration, e.g., less than about 6 minutes, such as less than about 2 minutes, e.g., about 0.5 minutes. By way of comparison, conventional cardiac stress testing SPECT imaging procedures generally have image acquisition durations of between about 10 and about 20 minutes. For some applications, the protocol is customized for a specific patient, as described hereinabove. For some applications, such as when the protocol uses Tc99m-sestamibi, image acquisition is performed immediately following administration of the labeled radiopharmaceutical agent, before the agent reaches the liver, thereby reducing interference by the liver on the resulting images.
- protocols using a dose of the labeled radiopharmaceutical agent that is substantially lower than conventional SPECT protocols using the agent. For example, the dose may be between about 50% and about 90% lower than a conventional dose, e.g., about 50% lower than a conventional dose. By using the image acquisition techniques described herein and/or incorporated herein by reference, even at such reduced doses, acquired photon counts are typically at least 5 times greater than those acquired using conventional SPECT techniques at conventional SPECT doses, e.g., at 10 times greater, and image acquisition duration is typically about 50% less than conventional durations, e.g., about 80% less (such as four minutes instead of 20 minutes). Alternatively, the dose may be reduced by about 90%, and the image acquisition duration is approximately the same as conventional image acquisition durations.

In an embodiment of the present invention, system 10 uses Tc-99m teboroxime for performing a SPECT myocardial perfusion study. This radiopharmaceutical is extracted by the myocardium in proportion to myocardial blood flow throughout the entire range of achievable flow rates. When conventional imaging techniques are used, the wash-out rate of Tc-99m teboroxime from cardiac tissue is so rapid that there is inadequate time for imaging, because the radiopharmaceutical rapidly and avidly accumulates in the liver, which emits gamma rays that blind the imaging of the heart. By using the imaging techniques described herein and/or incorporated herein by reference, sufficient photon counts are obtained in an image acquisition period of no more than approximately two minutes, immediately following administration. The use of such a short period enables the completion of image acquisition prior to substantial uptake of the radiopharmaceutical by the liver, thereby enabling the effective clinical use of Tc-99m teboroxime for cardiac imaging.

In an embodiment of the present invention, a dynamic multiple isotope combination protocol is provided for studying different pathological processes of the same organ, such as studying acute myocardial ischemia. In accordance with this protocol, the following labeled radiopharmaceutical agents are administered as bolus IV injections:

(a) an approximately 2 mCi dose of I-123-BMIPP, followed by a wait of about 48 hours;

(b) an approximately 1 mCi dose of Tl-201-thallous chloride; and

(c) either (i) an approximately 10 mCi dose of Tc-99m-sestamibi or (ii) an approximately 10 mCi dose of Tc-99m-teboroxime.

Agents (b) and (c) are administered as a cocktail, or as separate injections at approximately the same time. Simultaneous image acquisition of all three radiopharmaceutical agents is performed during or soon after administration of agents (b) and (c), typically using an up to about 30 minute acquisition time, such as between about 5 and about 15 minutes, which is faster than that of standard imaging protocols. Typically, camera 452 of imaging system 28, described hereinbelow with reference to Fig. 11, performs image acquisition using an energy window of between about 2% and about 10% of the emitted energy levels of the radiopharmaceutical agents. Typically, detectors 454 of camera 452 sweep the region of interest once every approximately 10 to approximately 15 seconds. The I-123-BMIPP identifies the ischemic/infarcted area of the myocardium, while the other radiopharmaceutical agents identify the perfused area of the myocardium. Simultaneous imaging provides more accurate identification of myocardial perfusion pathologies than is generally possible using conventional imaging techniques and protocols.

In an embodiment of the present invention, system 10 uses one or more of the protocols described in the above-mentioned US provisional application filed on even date herewith, entitled, "Imaging protocols."

In some embodiments of the present invention, the protocols described herein (including those shown in Figs. 6A-E), and in the co-assigned patent applications incorporated herein by reference, are performed using values that vary from those provided in the protocols by +/- 20%, e.g., +/- 5%, +/- 10%, or +/- 15%. Furthermore, in some embodiments, the protocols are performed with a range of doses from 50%, 75%, 90%, or 100% of the dosage value given for the respective protocol, up to 10 times the dosage value given for the respective protocol (such as up to 2, 4, 6, or 8 times the given dosage value). For example, a dose shown as 3 mCi for a given protocol may, in some embodiments, have a range of 1.5 mCi to 30 mCi, or from 2.7 mCi to 6 mCi. Similarly, in some embodiments, the protocols are performed with a range of acquisition durations (total scan times) from 50%, 75%, 90%, or 100% of the duration value given for the respective protocol, up to 5 times the duration value given for the respective protocol, such as up to 1.5, 2, 3, or 4 times the given duration value. Other protocol values, such as waiting times, energy windows/resolution, angular range, angular step, and dwell time, may also have a range from 50%, 75%, 90%, or 100% of the value given for the respective protocol, up to 5 times the value given for the respective protocol, such up to 1.5, 2, 3, or 4 times the given value.

In respective embodiments of the present invention, all of the protocols described herein and/or in the co-assigned patent applications incorporated herein by reference are enabled to generate clinically-valuable images. A "clinically-valuable image" is an image of an intra-body region of interest (ROI) containing the labeled radiopharmaceutical agent(s), which image fulfills one or more of the following criteria:

- the image is generated according to a protocol, including at the radiopharmaceutical dose specified by the protocol, using a high-definition SPECT camera, for example, camera 452 of imaging system 28, described hereinbelow with reference to Fig. 11, which camera, during the imaging of the ROI, is capable of acquiring at least one of 5000 photons emitted from the ROI during the image acquisition procedure, such as at least one of 4000, 3000, 2500, 2000, 1500, 1200, 1000, 800, 600, 400, 200, 100, or 50 photons emitted from the ROI. In one particular embodiment, the camera is capable of acquiring at least one of 2000 photons emitted from the ROI during the image acquisition procedure;

- the image is generated according to a protocol, including at the radiopharmaceutical dose and image acquisition duration specified by the protocol, using a high-definition SPECT camera, for example, camera 452, which, during the imaging of the ROI, is capable of acquiring at least 200,000 photons, such as at least 500,000, 1,000,000, 2,000,000, 3,000,000, 4,000,000, 5,000,000, 8,000,000, or 10,000,000 photons, emitted from a portion of the ROI having a volume of no more than 500 cc, such as a volume of no more than 500 cc, 400 cc, 300 cc, 200 cc, 150 cc, 100cc, or 50 cc. In one particular embodiment, the camera is capable of acquiring at least 1,000,000 photons emitted from a volume of the ROI having a volume of no more than 200 cc;

- the image has a resolution of at least 7x7x7 mm, such as at least 6x6x6 mm, 5x5x5 mm, 4x4x4 mm, 4x3x3 mm, or 3x3x3 mm, in at least 50% of the reconstructed volume, wherein the labeled radiopharmaceutical agent as distributed within the ROI has a range of emission-intensities R (which is measured as emitted photons / unit time / volume), and wherein at least 50% of the voxels of the reconstructed three-dimensional emission-intensity image of the ROI have inaccuracies of less than 30% of range R, such as less than 25%, 20%, 15%, 10%, 5%, 2%, 1%, or 0.5% of range R. For example, the agent may emit over a range from 0 photons/second/cc to 10^5 photons/second/cc, such that the range R is 10^5 photons/second/cc, and at least 50% of the voxels of the reconstructed three-dimensional intensity image of the ROI have inaccuracies of less than 15% of range R, i.e., less than 1.5 x 10^4 photons/second/cc. For some applications, the study produce a parametric image related to a physiological process occurring in each voxel. In one particular embodiment, the image has a resolution of at least 5x5x5 mm, and at least 50% of the voxel have inaccuracies of less than 15% of range R;

- the image is generated according to a protocol, including at the radiopharmaceutical dose and image acquisition duration specified by the protocol, the image has a resolution of at least 7x7x7 mm, such as at least 6x6x6 mm, 5x5x5 mm, 4x4x4 mm, 4x3x3 mm, or 3x3x3 mm, wherein the labeled radiopharmaceutical agent has a range of intensities R (photons / unit time / volume), and wherein at least 50% of the voxels of the reconstructed three-dimensional intensity image of the ROI have inaccuracies of less than 30% of range R, such as less than 25%, 20%, 15%, 10%, 5%, 2%, 1%, or 0.5% of range R. For some applications, the study produce a parametric image related to a physiological process occurring in each voxel; and/or
- the image has a resolution of at least 20x20x20 mm, such as at least 15x15x15 mm, 10x10x10 mm, 7x7x7 mm, 5x5x5 mm, 4x4x4 mm, 4x3x3 mm, or 3x3x3 mm, wherein values of parameters of a physiological process modeled by a parametric representation have a range of physiological parameter values R, and wherein at least 50% of the voxels of the reconstructed parametric three-dimensional image have inaccuracies less than 100% of range R, such as less than 70%, 50%, 40%, 30%, 25%, 20%, 15%, 10%, 5%, 2%, 1%, or 0.5% of range R. For example, the physiological process may include blood flow, the values of the parameters of the physiological process may have a range from 0 to 100 cc / minute, such that the range R is 100 cc / minute, and at least 50% of the voxels of the reconstructed parametric three-dimensional image have inaccuracies less than 25% of range R, i.e., less than 25 cc / minute. In one particular embodiment, the image has a resolution of at least 5x5x5 mm, and at least 50% of the voxels have inaccuracies of less than 25% of range R.

The mother vial

Reference is made to Fig. 7, which is a schematic illustration of mother vial 104 and attached data carrier 106, in accordance with an embodiment of the present invention. Data carrier 106 is computer-communicatable, and typically comprises an RFID tag, smart card, disk-on-key (e.g., a USB key), compact disc, minidisk, disposable computer-readable medium, or other electronic memory, or a machine-readable code, e.g., a barcode. Mother vial 104 is shown contained within shielding 272, to which data carrier 106 is attached. Alternatively, the data carrier is attached directly to the mother vial, or otherwise associated with the mother vial, such as by being stored in proximity to the mother vial, e.g., in a tray that also contains the mother vial.

Data carrier 106 typically contains at least some of the following information:

- a coded signature 256, for authenticating mother vial 104;
- radiopharmaceutical information, a portion of which is typically supplied by the manufacturer, and a portion of which is typically generated by dispensing system 20 in conjunction with dispensing the radiopharmaceutical agent(s). For some applications, a portion of the information is generated by mother vial preparation system 700, described hereinbelow with reference to Fig. 15, in conjunction with preparing the radiopharmaceutical. The information includes, for example:
    - the name of and/or information regarding the manufacturer;
    - the indicated use(s) (e.g., "Formulation for Cardiac Dynamic Studies");
    - the pre-labeled composition;
    - the time of preparation of the labeled radiopharmaceutical agent(s);
    - the radioactivity at the time of preparation;
    - the total solution volume;
    - the pre-labeled-composition expiration date;
    - the appropriate labeling isotope(s);
    - the decay scheme(s) of the appropriate labeling isotope(s);
    - the radiopharmaceutical biodistribution as a function of time;
    - the radiopharmaceutical clearance rate;
    - the percent clearance by the liver;
    - the percent clearance by the kidneys;
    - the breakdown rate;

- the liver uptake as a function of time; and/or
- radiopharmaceutical kinetic parameters, such as described hereinbelow, which parameters may be stored in one or more lookup tables;

- administration protocol information, such as described hereinbelow;
- image acquisition protocol information, such as described hereinbelow;
- image reconstruction protocol information, such as described hereinbelow;
- image analysis protocol information, such as described hereinbelow;
- expert system protocol information, such as described hereinbelow;
- radiolabeling information, which, for some applications, is generated by mother vial preparation system 700, described hereinbelow with reference to Fig. 15. Such information includes, for example:
  - the labeling radioisotope(s), e.g., Tc-99m;
  - time of labeling;
  - activity of the radioisotope(s) per volume at the time of labeling;
  - total solution volume in the mother vial; and/or
  - ratio of radioisotopes (e.g., Tc-99m to Tc-99) at the time of labeling.

If the labeled radiopharmaceutical agent stored in the mother vial is radiolabeled by mother vial preparation system 700, as described hereinbelow with reference to Fig. 15, the labeling information is provided by the mother vial preparation system. Otherwise, the labeling information is provided by the pharmacist and/or conventional labeling system that radiolabels the unlabeled radiopharmaceutical agent.

The radiopharmaceutical kinetic parameters are used by imaging system 28 for performing dynamic imaging studies, for example as described in the above-mentioned International Patent Application PCT/IL2005/001173, and/or in the above-mentioned US provisional application filed on even date herewith, entitled, "Imaging protocols". For some applications, respective sets of these parameters are provided for:

- different patient populations, such as a healthy population and populations which suffer from various pathologies;

- different organs and/or tissue types, for example, brain tissue, cardiac tissue, liver tissue, and tumor tissue;
- different pathologies;
- different patient physiologies;
- different organs, according to the physiology of the specific patient;
- different patient groups, as expected according to the physiology of the specific patient;
- different pathologies, as expected according to the physiology of the specific patient;
- different organs, as measured for the specific patient;
- different patient groups, as measured for the specific patient; and/or
- different pathologies, as measured for the specific patient.

Such kinetic parameters may include, for example:

- volume of blood in a voxel;
- density of blood in a tissue within a voxel;
- labeled radiopharmaceutical agent concentration in the blood within a voxel;
- labeled radiopharmaceutical agent concentration in a tissue within a voxel;
- total labeled radiopharmaceutical agent concentration in a voxel;
- labeled radiopharmaceutical agent concentration in the systemic blood circulation;
- linearity with blood flow;
- receptor binding for molecular radiotracers;
- labeled radiopharmaceutical accumulation/redistribution in tissue;
- labeled radiopharmaceutical metabolic rate;
- diffusion coefficient from the blood to the tissue (i.e., rate of wash-out,

passive or active);

- diffusion coefficient from the tissue to the blood (i.e., rate of uptake, passive or active); and/or
- accumulation rate in a tissue within a voxel.

The administration protocol information is used by administration system 26 to set parameters of administration of the labeled radiopharmaceutical agent(s) contained in container 22. This protocol information may include, for example:

- the dose administered, or for multiple radiopharmaceutical agents, the respective doses per administration;
- the type of administration, e.g., a single bolus, a plurality of boluses (e.g., two boluses), pulsatile administration, or constant drip administration;
- the labeled radiopharmaceutical agent for each administration, whether a single agent or a cocktail of agents;
- the time of the administration with respect to the time of imaging;
- the timings of multiple administrations with respect to each other and with respect to other activities, such as rest or stress (physical or pharmacological);
- the administration device, e.g., a syringe, a dual-needle syringe, a pump, or an IV line;
- the mode of administration, e.g., manual, automatic, or computer driven; and/or
- an algorithm for customizing the administration based on physiological parameters of the specific patient.

The image acquisition protocol information is used by imaging system 28 to set parameters of the image acquisition process. For some applications, such parameters are separately specified for individual components of camera 452 of imaging system 28, or groups of components, such as for individual detectors 454 or groups of detectors. Such acquisition protocol information may include, for example:

- the name(s) and/or identification code(s) of one or more protocols for which the radiopharmaceutical agent contained in mother vial 104 is suitable;

- total acquisition time, and/or acquisition time for a plurality of phases of acquisition;
- detector scanning plan, including detector motions, such as detector angular and translational motions, detector step size (typically expressed in degrees), and detector dwell time at each view;
- detector sensitivity;
- detector energy resolution;
- detector calibration plan;
- definition of the region of interest (ROI);
- gating parameters;
- energy bands, i.e., a plurality of non-overlapping energy windows;
- collimator positioning, shape, structure, and orientation;
- multiple/interlaced scans;
- zooming parameters;
- uniformity/non-uniformity of scan;
- Compton scatter map calculation and correction parameters;
- optimal energy window;
- optimal energy resolution, i.e., the range of energy window levels detected; and/or
- adaptivity of scan pattern to acquired counts, e.g., active vision parameters (as described in the above-mentioned International Application PCT/IL2005/001173).

For some applications, the optimal energy window is set at least in part responsively to the BMI of the patient. For example, the width of the energy window (i.e., the energy resolution) may be inversely related to the BMI, because the tissue of patients with higher BMIs tends to create more scatter. To compensate for narrower energy windows, a longer acquisition time and/or a higher dose of radiopharmaceutical agent is typically used. For some applications, the protocol information includes a look-up table of BMIs and associated energy windows. For some applications, the energy window is non-symmetrical around a peak of the energy curve.

The image reconstruction protocol information is used by imaging system 28 to set parameters of the image reconstruction process. Such parameters may include, for example:

- calibration parameters;
- timing of acquisition;
- reconstruction parameters and algorithms;
- priors, i.e., mathematical constants signifying pre-imaging phase knowledge about system behavior;
- multi-resolution reconstruction parameters;
- non-uniform reconstruction grid;
- filters;
- noise modeling and handling;
- mode selection;
- information derived during image acquisition and/or gating;
- protocols for handling interfering organs;
- protocols describing the precise procedure to be followed in radiopharmaceutical administration, time management, patient activity status, imaging process, and other parameters that can affect imaging results;
- optimization parameters per dose and/or cocktail of doses; and/or
- attenuation correction parameters, which are typically based on physiological parameters such as body mass, BMI, and girth.

For some applications, imaging system 28 uses one or more of these parameters to perform the image reconstruction process using techniques described in one or more of the co-assigned patent applications incorporated herein by reference.

The image analysis protocol information includes analysis algorithms and/or parameters of the image analysis process, which are used by imaging system 28 for performing diagnostic analysis of the reconstructed image. For some applications, such analysis includes tracer kinetics analysis. Such parameters may include, for example:

- information for selection of a model of tracer kinetics;
- information for selection of one or more time scales for tracer kinetics;
- tracer parameters;
- information for analysis of multiple time points;
- information for analysis regarding the clinical meaning of radiation distribution within the patient's body for the purpose of making a clinical diagnosis regarding the patient's health state;
- information for identifying the signatures of multiple labeled radiopharmaceutical agents; and/or
- optimization parameters per dose and/or cocktail of doses.

The expert system protocol information, such as expert system rules, is used by imaging system 28 to set parameters of the expert system used for assisting with diagnosis. For some applications, the expert system is implemented using techniques described in the above-mentioned International Application PCT/IL2005/001173, or in one or more of the other co-assigned patent applications incorporated by reference. Such parameters may include, for example:

- classification of the patient into a patient population;
- multi-parameter vectors of radiopharmaceutical kinetic parameters for different patient populations, such as a healthy population and populations which suffer from various pathologies, and for different tissue types, for example, brain tissue, cardiac tissue, liver tissue, or tumor tissue;
- patient history;
- multi-dimensional thresholds for defining healthy-disease state;
- disease signature classifications per pathology and/or organ (typically per

patient population); and/or

- optimization parameters per dose and/or cocktail of doses.

The portable information-bearing radiopharmaceutical agent container

Fig. 8 is a schematic illustration of data carrier 120, in accordance with an embodiment of the present invention. As mentioned above, data carrier 120 is physically coupled to radiopharmaceutical agent container 22. Data carrier 120 is computer-communicatable, and typically comprises an RFID tag, smart card, disk-on-key (e.g., a USB key), compact disc, minidisk, disposable computer-readable medium, or other electronic memory, or a machine-readable code, e.g., a barcode. One or more communication elements 240 are provided for reading data from and transmitting data to data carrier 24. Respective communication elements 240 are typically in data communication with dispensing system 20 and administration system 26. For some applications, communication elements 240 comprise one or more coils for transmitting and receiving electromagnetic radiation. Typically, the communication elements are configured to have a short effective transmission range, e.g., no more than between about 20 and 40 cm, such as about 30 cm. Such a short range reduces the likelihood of accidental communication with a data carrier other than the intended data carrier.

Data carrier 120 comprises circuitry 250, which comprises memory and logic. For some applications, data carrier 120 is passive, in which case it is configured to receive energy from communication element 240. For other applications, data carrier 120 comprises a power source (not shown). For some applications in which the data carrier comprises a power source, the data carrier comprises a communication element for communicating and/or energizing another electronic apparatus. Alternatively or additionally, the data carrier comprises a communication element 252 configured for wireless communication. For some applications, data carrier 24 further comprises a user output 254 for outputting information to the patient or healthcare workers. For example, output 254 may comprise a display screen, light, and/or sound generator, which the circuitry drives to communicate information, such as when communications have been established with other elements of system 10, e.g., data carrier 120, administration system 26, or imaging system 28. For some applications, data carrier 120 further comprises coded signature 256, which is typically encrypted, color-coded, or both encrypted and color-coded, as described hereinbelow in the section entitled "Signature."

The information contained in data carrier 120 typically includes some or all of the following:

- an administration-device identification code;
- an identifier, such as an identification code and/or name, of the patient for which the specific attached radiopharmaceutical agent container 22 is intended;
- the formulation of the labeled radiopharmaceutical agent(s) contained in attached container 22;
- the time of dispensing of the labeled radiopharmaceutical agent(s) to container 22;
- activity of the labeled radiopharmaceutical agent(s), at the time of dispensing of the labeled radiopharmaceutical agent(s) to container 22;
- the assigned protocol(s) for use with the labeled radiopharmaceutical agent(s) contained in attached container 22;
- the intended time(s) and date(s) of administration of the labeled radiopharmaceutical agent(s) contained in container 22;
- the intended activity(ies) of the labeled radiopharmaceutical agent(s) at the time of administration thereof;
- the intended time profile of administration (single bolus, slow-drip administration, or any other form of administration);
- the identification code of mother vial 104 from which the labeled radiopharmaceutical agent(s) contained in container 22 were dispensed; and/or
- at least a portion of the radiopharmaceutical information stored in data carrier 106 of mother vial 104, as described hereinabove with reference to Fig. 7. This information is typically electronically transferred from data carrier 106 during dispensing of the labeled radiopharmaceutical agent(s) to container 22, as described hereinabove with reference to step 118 of Fig. 2 and hereinbelow with reference to Fig. 12.

As mentioned above, for some applications, all or a portion of the information contained in patient-specific data carrier 24 is alternatively or additionally stored in data carrier 120. Such information is described hereinabove with reference to Fig. 7. For some applications, a portion of the information stored in the data carrier is also printed in human- and/or machine-readable form on the data carrier and/or on the container, for example as a barcode 260, as shown below in Figs. 9A-H.

In an embodiment of the present invention, radiopharmaceutical agent container 22 comprises all or a portion of a drug administration device, such as a syringe or an inhalation device, packaging for an oral dosage form, or radiopharmaceutical packaging.

Reference is made to Figs. 9A-H, which are schematic illustrations of respective embodiments of radiopharmaceutical agent container 22 and data carrier 120, in accordance with respective embodiments of the present invention. In all of these embodiments, data carrier 120 is physically coupled to agent container 22.

Fig. 9A is a schematic illustration of radiopharmaceutical agent container 22 comprising a manual syringe 270, in accordance with an embodiment of the present invention. Syringe 270 is protected by shielding 272, to which data carrier 120 is coupled. Alternatively, the data carrier is coupled directly to an exposed portion of the syringe, such as the end of the plunger of the syringe, as shown in the figure.

Fig. 9B is a schematic illustration of radiopharmaceutical agent container 22 comprising an automatic administration device 280, in accordance with an embodiment of the present invention. Device 280 comprises a chamber 282 for containing the labeled radiopharmaceutical agent(s), a needle 283, a controller 284, a drive 286, and a power source 288. For some applications, controller 284 is preprogrammed with administration instructions, while for other applications, the controller is coupled to administration system 26 and receives an administration signal therefrom prior to administration, or in real time during administration. Administration device 280 typically includes an interlock 290 to prevent administration without verification, for example, of the patient's identity. For some applications, device 180 comprises a flow meter 292, which measures the volume of labeled radiopharmaceutical agent administered. Controller 284 uses this flow information for regulating parameters of the administration, such as rate of administration and total amount of agent administered. Shielding 272 protects medical personnel from the radioactivity of the labeled radiopharmaceutical agent.

Fig. 9C is a schematic illustration of a multi-chamber embodiment of radiopharmaceutical agent container 22, in accordance with an embodiment of the present invention. In this embodiment, container 22 comprises a plurality of chambers in fluid isolation from one another, each of which chambers contains a labeled radiopharmaceutical agent. In the embodiment shown in Fig. 9C, the container comprises two such chambers, a first chamber 282A and a second chamber 282B. Alternatively, the container comprises more than two chambers (configuration not shown). For some multi-chamber applications, container 22 comprises automatic administration device 280, as shown in Fig. 9C, while for other multi-chamber applications, container 22 comprises a plurality of manual syringes 270, as described hereinabove with reference to Fig. 9A (multi-chamber configuration not shown). For some applications, a separate needle 283 is provided for each injection, while for other applications, container 22 is configured to utilize a single needle 283 for the plurality of injections. For example, needle 283 may be configured to slide along a needle mount 294, so as to service the plurality of chambers.

Fig. 9D is a schematic illustration of another configuration of radiopharmaceutical agent container 22, in accordance with an embodiment of the present invention. In this embodiment, container 22 comprises automatic administration device 280, as described hereinabove with reference to Fig. 9B, and controller 284 is configured to perform all or a portion of the functions of data carrier 120. For some applications, one or more of the elements of data carrier 120 are provided separately from the controller. For example, communication element 252 or user output 254 may be provided separately from the controller.

Figs. 9E-G are schematic illustrations of another configuration of radiopharmaceutical agent container 22 comprising manual syringe 270, in accordance with an embodiment of the present invention. In this embodiment, syringe 270 comprises a transmitter 296 fixed with respect to a plunger 298 of the syringe, and shielding 272 is configured so as to modulate effective transmission by transmitter 296. For example, shielding 272 may be shaped so as to define a longitudinal slot 300 along a portion of the shielding. This modulation serves to send, from syringe 270 to administration system 26 and/or imaging system 28, a signal indicative of a time of administration of the labeled radiopharmaceutical agent(s) contained in container 22. The techniques of this embodiment are typically useful when registration of the time of administration with imaging system 28 is important, such as for dynamic studies.

Figs. 9E-G respectively illustrate three steps for administration using these techniques. Fig. 9E shows a first step, during which transmitter 296 is exposed, and therefore effectively transmits a signal. Fig. 9F shows a second step, during which transmitter 296 is shielded by shield 272. Fig. 9G shows a third step, in which transmitter 296 is again exposed. This sequence of exposing, shielding, and again exposing the transmitter serves to signal that administration has occurred. The receiver of the signal (administration system 26 and/or imaging system 28) records the time that this signal is detected. For some applications, other techniques are used to automatically transmit an indication of when the labeled radiopharmaceutical agent(s) are administered. For example, a transmitter may be mounted on shield 272, and may send a signal when electrical contact is established between electrodes (not shown) on plunger 298 and shield 272 at the end of complete motion of the plunger into syringe 270.

Fig. 9H is a schematic illustration of a syringe adaptor 320, in accordance with an embodiment of the present invention. Adaptor 320 comprises shielding 272 and data carrier 120 coupled thereto. The adaptor is configured to placed on a standard administration device, such as a standard syringe. In an embodiment of the present invention, an adaptor similar to adaptor 320 is provided for use with other components of an end-to-end imaging system, such as Tc-99m vials, mother vials, dispensing tools, and dilution containers. Alternatively or additionally, data carrier 120 is configured to be couplable to such other components.

In an embodiment of the present invention, data carrier 120 is configured to be couplable to a standard administration device, such as a syringe. For example, the data carrier may be couplable to the barrel, plunger, or conventional shielding of a conventional syringe, or another syringe known in the art.

The administration system

Reference is made to Fig. 10, which is a schematic illustration of administration system 26, in accordance with an embodiment of the present invention. Administration system 26 comprises a control unit 350, at least one communication element 240, and, for some applications, an automated administration device 352. Typically, control unit 350 comprises a standard personal computer or server with appropriate memory, communication interfaces and software for carrying out the functions prescribed by relevant embodiments of the present invention. This software may be downloaded to the control unit in electronic form over a network, for example, or it may alternatively be supplied on tangible media, such as CD-ROM. For some applications, administration system 26 comprises a single communication element 240 that communicates with both patient-specific data carrier 24 and data carrier 120 of container 22, while for other applications the administration system comprises separate communication elements 240 for communicating with data carriers 120 and 24 respectively. For example, a communication element for communicating with data carrier 120 may be integrated into or coupled to automated administration device 352.

Upon authenticating container 22, verifying the identity of the patient, and performing additional verifications, as described hereinabove with reference to step 122 of Fig. 2, control unit 350 generates an administration signal that triggers administration to the patient of the labeled radiopharmaceutical agent(s) stored in container 22. For applications in which administration system 26 comprises automated administration device 352, container 22 is operatively coupled to device 352, and the signal drives administration device 352 to administer the labeled radiopharmaceutical agent(s) stored therein to the patient. Automated administration device 352 is configured to perform intravenous (IV) injection, intramuscular (IM) injection, subcutaneous injection, transdermal application, oral administration, nasal administration, inhalation, transcervical application, transrectal administration, or another type of administration known in the art. (It is to be understood that although the administration signal triggers administration of the agent, for some applications automated administration device 352 does not administer the agent until a healthcare worker provides a final authorization to do so, such as to comply with regulatory safety requirements.) For applications in which administration system 26 does not comprise automated administration device 352, the administration signal triggers administration of the agent by instructing a healthcare worker to manually administer the agent to the patient.

For some applications, based on administration protocol information received from data carrier 120 of radiopharmaceutical agent container 22 and/or patient-specific data carrier 24, control unit 350 customizes the administration of the labeled radiopharmaceutical agent(s) contained in agent container 22. Such administration protocol information typically includes all or a portion of the administration protocol information described hereinabove with reference to Fig. 7. For some applications, administration system 26 administers a plurality of labeled radiopharmaceutical agents, either sequentially or premixed together within a single agent container 22 (i.e., as a cocktail).

For some applications, administration system 26 administers the labeled radiopharmaceutical agent(s) responsively at least in part to acquisition of a signal associated with the agent(s). For example, acquisition of the signal may comprise detection of photons emitted from the agent(s), in order to determine a radioactivity level.

For some applications, administration system 26 monitors uptake and/or clearance of the labeled radiopharmaceutical agent(s) by (a) measuring physiological parameters, e.g., from samples of blood, saliva, or secretions, e.g., urine, breath, feces, or sweat, or (b) by performing an imaging procedure using imaging system 28. For some applications, these measurements are used to estimate pharmacokinetics of the radiopharmaceutical agent(s) in organs, and/or to predict optimal imaging timing (the optimal time to perform the imaging, and/or the optimal timing parameters of the imaging procedure). For some applications, based on these estimates, an expected level of uptake of the radiopharmaceuticals in a target organ is determined, enabling diagnosis of pathologies based on absolute uptake levels in the target organ.

The imaging system

Reference is made to Fig. 11, which is a schematic illustration of imaging system 28, in accordance with an embodiment of the present invention. Imaging system 28 comprises a control unit 450, a communication element 240, a camera 452, and an imaging workstation 453. Typically, control unit 450 and imaging workstation 453 comprise one or more standard personal computers or servers with appropriate memory, communication interfaces and software for carrying out the functions prescribed by relevant embodiments of the present invention. This software may be downloaded to the control unit and imaging workstation in electronic form over a network, for example, or it may alternatively be supplied on tangible media, such as CD-ROM.

Control unit 450 typically comprises: (a) image acquisition functionality, which is configured to drive camera 452 to perform image acquisition of the patient; (b) image reconstruction functionality, which is configured to perform an image reconstruction procedure on the acquired image; (c) image analysis functionality, which is configured to perform an image analysis procedure on the reconstructed image; and (d) diagnosis functionality, which is configured to perform a diagnostic procedure using the results of the image analysis procedure. It will be appreciated that control unit 450 may comprise a plurality of personal computers or servers, each of which performs one or more of these procedures, and that one or more of these computers or servers may be located remotely from camera 452. Imaging workstation 453 displays the reconstructed images and allows the attending healthcare worker to view and manipulate the images.

As mentioned above with reference to steps 124 through 130 of Fig. 2, imaging system 28 typically customizes one or more of these procedures at least in part responsively to imaging protocol information and/or patient-specific information read by communication element 240 from patient-specific data carrier 24.

For some applications, camera 452 comprises a commercially available diagnostic structural or functional camera, such as a SPECT or PET camera, and/or utilizes imaging techniques described in one or more of the patents and patent applications described hereinabove in the section entitled "Background of the Invention." Alternatively, camera 452 utilizes techniques described in the above-mentioned International Application PCT/IL2005/001173, in above-mentioned PCT Publication WO 05/119025, and/or in the other above-mentioned co-assigned patent applications and/or patent application publications.

In an embodiment of the present invention, camera 452 comprises a plurality of detectors 454, each of which is coupled to a respective angular orientator 456. Each of the detectors comprises a plurality of gamma ray sensors, such as a pixelated CZT array, and a collimator. For example, the array may include 16x64 pixels. Control unit 450 drives, typically separately, each of the orientators to orient its respective detector in a plurality of orientations with respect to a region of interest (ROI). Control unit 450 produces a SPECT image from a plurality of radiation acquisitions acquired with the detectors in different relative orientations.

In an embodiment of the present invention, camera 452 is configured to begin an image acquisition procedure by performing a relatively brief, preliminary scan, and, based on the results of this preliminary scan, to determine one or more parameters of the full image acquisition procedure, such as dwell time per orientation of each detector 454. Typically, this determination further takes into account imaging protocol and/or patient-specific information received by imaging system 28 from patient-specific data carrier 24, such as the activity of the labeled radiopharmaceutical agent at the time of administration, the time of administration, the patient's BMI (which may be used to estimate a perfusion percentage), and the pharmacokinetics of the labeled radiopharmaceutical agent.

In an embodiment of the present invention, camera 452 is configured to individually set a total angular range of each of detectors 454 responsively to the detector's orientation with respect to the ROI. For example, at least one detector closer to the ROI (a "proximal detector" or an "inner detector") may have a greater total angular range than at least one detector further from the ROI (a "distal detector" or an "outer detector"). The distal detectors are typically located nearer to the ends of a frame holding the detectors, while the proximal detectors are typically located nearer to center of the frame. The use of narrower angular ranges for some of the detectors generally reduces the photon acquisition time spent by these detectors in orientations aimed outside of the ROI. Alternatively, at least one distal detector has a greater total angular range than at least one proximal detector. In order to reduce the total angular range for a given detector, camera 452 typically drives the associated angular orientator 456 to: (a) increase the dwell time of the detector in at least a portion of its orientations, and/or (b) reduce the angle by which the detector is moved during each orienting of the detector. For some applications, camera 452 sets the angular range of the detectors based on protocol information received by imaging system 28 from patient-specific data carrier 24. For example, the number of distal and proximal detectors, and their respective angular ranges, may be specified by the protocol information, as described hereinabove with reference to Figs. 6B-E.

In an embodiment of the present invention, camera 452 comprises a plurality of detectors 454, each of which is coupled to a respective angular orientator 456. Each of the detectors comprises a plurality of gamma ray sensors, such as a pixelated CZT array, and a collimator. Control unit 450 drives, typically separately, each of the orientators to orient its respective detector in a plurality of orientations with respect to a region of interest (ROI). Control unit 450 produces a SPECT image from a plurality of radiation acquisitions acquired with the detectors in different relative orientations.

In an embodiment, camera 452 is configured to drive one of orientators 456 to move its respective detector 454 through a plurality of sequential angular positions, e.g., positions 1, 2, 3, ..., 18, 19, and 20. Typically, a linear relationship relates the sequential positions, such that, for example, positions 1, 2, 3, ..., 20 represent 1°, 2°, 3°, ..., 20°, or, 2°, 4°, 6°, ..., 40°. Alternatively, a non-linear relationship relates the sequential positions. Higher or lower angular resolutions are typically obtainable, as well.

For some applications, camera 452 steps the orientator in a first pass through a subset of the positions spanning most of the range of positions, and in a second pass the camera steps the orientator through a different subset of the positions. At each position, data are acquired by the detector. For example, during the first pass, the camera may drive the orientator to step through positions 1, 5, 9, 13, and 17, and the detector acquires data at each of these positions. During the second pass, the orientator steps through positions 2, 6, 10, 14, and 18. During two subsequent passes, data are acquired at the remainder of the positions. In this manner, a single-direction interlaced scan of the data is acquired by camera 452.

In an embodiment, a back-and-forth interlaced scan is acquired in which data are sampled when the orientator is moving in both directions. For example, during the first pass, the camera may drive the orientator to step through positions 1, 5, 9, 13, and 17. During the second pass, the orientator steps through positions 18, 14, 10, 6, and 2. During the third pass, the orientator steps through positions 3, 7, 11, 15, and 19, while during the fourth pass, the orientator steps through positions 20, 16, 12, 8, and 4. Fifth and higher passes, if desired, typically repeat the motions used in the earlier passes.

For some applications, the positions in a pass are not ordered from lowest-to-highest or highest-to-lowest. For example the positions of a pass may be 1, 15, 11, 19, and 17. Typically, the positions are, however, distributed generally evenly throughout the range of positions, in order to acquire photon counts representative of the entire region of interest.

As appropriate for a given scanning protocol using interlaced scanning, one or more, or even all of orientators 456 are driven to step through their respective positions in an interlaced fashion.

Typically, execution of an interlaced scan as provided by these embodiments of the present invention allows an operator of camera 452, such as an imaging technician or other healthcare worker, to acquire a high-resolution image of the ROI in about 105% to 115% of the amount of time as would be used if orientator 456 were stepped through the positions sequentially. (Typically, each orientation takes between about 50 and about 200 msec, depending upon the angle of the step.) The high-resolution image is completely acquired after the orientator has stepped through each of its positions. In some cases, additional value is attained by interlacing the scanning, however, as this allows the performance of dynamic studies, in which a plurality of images are acquired during a respective plurality of the time periods, i.e., during each complete pass of the orientator. Although each these images is typically of lower resolution than the high-resolution image acquired using photon counts acquired during all of the passes, the images nevertheless have sufficient resolution to produce clinically-meaningful data for each time period of a dynamic study.

For some applications, interlacing the scanning allows an operator to see an initial, lower-resolution scan of the ROI. If, for example, an adjustment of any form is desired, this can often be seen within the first few seconds of a scan. The present scan is terminated, the adjustment made, and a second scan initiated. In the absence of interlacing, it is typically necessary to wait until a scan has completed until an assessment of the scan's results can be made.

For some applications, it is desirable to know whether the patient has moved during a scan. Patient movement is one reason for lower quality images, and when identified it can typically be corrected by suitable instruction and then a second scanning procedure initiated. Interlaced scanning, as provided by these embodiments of the present invention, allows the operator to immediately assess whether there has been patient movement between one pass and a subsequent pass. In an embodiment, the imaging system displays to an operator the scans obtained from the various passes in rapid succession at the same location on a monitor. As appropriate, the imaging system cycles quickly through the scans repeatedly (e.g., pass 1, pass 2, pass 3, pass 4, pass 1, pass 2, pass 3, pass 4...), e.g., displaying each scan for between about 0.2 and about 2 seconds, allowing an operator to see whether there is jitter between successive scans. If so, patient movement is typically the cause and image acquisition is repeated. For some applications, the scan is acquired in exactly two passes, e.g., the orientator steps through positions 1, 3, 5, …, 19 during a first pass, and through positions 2, 4, 6, …., 20 during a second pass, or through positions 20, 18, 16, ..., 2 during the second pass.

Images acquired using these techniques, or other non-interlacing techniques described herein, are generally used to perform one or more of the following image reconstructions: (a) reconstruction of intensity image, (b) reconstruction of intensity over time, followed by fitting a model of the kinetics (which describe for each voxel a parameter set describing its time curve), and followed by presenting a three-dimensional map of the parameters, and/or (c) direct reconstruction of a three-dimensional parametric representation, without performing a reconstruction of an intensity map, typically by plugging an equation of a kinetic model into a reconstruction algorithm, and generating a result directly in terms of the value of the parameters per voxel (the parameters may include, for example, flow, diffusion coefficients, metabolism rate, or bio-clearance rate).

The radiopharmaceutical dispensing system

Reference is made to Fig. 12, which is a schematic illustration of automated radiopharmaceutical dispensing system 20, in accordance with an embodiment of the present invention. System 20 comprises a control unit 500, at least one robot 502, and at least one communication element 504, which, for some applications, is coupled to robot 502. Control unit 500 typically comprises a conventional personal computer running a conventional operating system, such as Windows XP, with appropriate memory, communication interfaces and software for carrying out the functions described herein. This software may be downloaded to the control unit in electronic form over a network, for example, or it may alternatively be supplied on tangible media, such as CD-ROM. Control unit 500 is in communication with other elements of system 10, for example via management and control component 150. The control unit notifies appropriate elements of the system upon successful completion of dispensing of a dose.

At least one radiolabeled mother vial 104 is placed in a shielded vials complex 505 of dispensing system 20. Control unit 500 authenticates the mother vial, by actuating communication element 504 to read authentication information stored in data carrier 106, and/or by verifying a coded signature 256 coupled to the mother vial, as described hereinbelow in the section entitled "Signature." Upon successful authentication, control unit 500 actuates communication element 504 to read radiopharmaceutical-related information from data carrier 106 of the mother vial, including the radiopharmaceutical agent type, isotope type, batch, lot, radiochemical purity (RCP), preparation time, and half-life information. Dispensing system 20 assays the radioactivity per unit volume of the labeled radiopharmaceutical agent contained in the mother vial. Robot 502 picks up an empty syringe 506 from a syringe tray 508, draws a predetermined amount of solution from mother vial 104, and brings the syringe to a dose calibrator 510. The syringe used for the assaying is typically discarded into a waste container 512. Typically, robot 502 brings the mother vial to a weighing station 507 for verification that the vial contains the indicated solution volume.

Dispensing system 20 receives a patient-specific dose request for at least one specific labeled radiopharmaceutical agent, having a specific dose, radioactivity, and solution volume. Such a dose is typically calculated by dose calculation sub-system 156 of dose calculation system 152, as described hereinabove with reference to Fig. 5, and/or by patient management system 160, described hereinabove with reference to Fig. 4. Alternatively or additionally, dispensing system 20 is configured to customize, modify, or verify the dose. Further alternatively, dispensing system 20 receives the order from another hospital or radiopharmacy information system, or the order is manually inputted into system 20.

To fill the request, control unit 500 calculates a required volume of the labeled radiopharmaceutical agent and a required volume of saline solution for dilution, if any. To perform this calculation, control unit 500 uses (a) information read from data carrier 106 (such as the half-life of the labeling isotope of the labeled radiopharmaceutical agent), and (b) the assayed radioactivity of the labeled radiopharmaceutical agent. Alternatively, dose calculation sub-system 156 performs all or a portion of this calculation.

For some applications, control unit 500 authenticates mother vial license information read from data carrier 106, in order to verify that a license is available for dispensing the requested dose. Dispensing proceeds only if a license is available and authenticated. The use of such a license generally provides increased quality control of the imaging process, by verifying that only approved manufacturers (or distributors) are able to provide radiopharmaceutical agents for use with system 10. A lack of precision in any aspect of an imaging procedure, which may result from the use of an agent that has not been tested and approved for use with system 10, often causes a deterioration of the resultant image quality and/or ability to make accurate and/or quantitative diagnoses.

Control unit 500 actuates robot 502 to pick up an empty radiopharmaceutical agent container 22 from tray 508. Typically, but not necessarily, container 22 comprises a syringe, such as described hereinabove with reference to Figs. 9A-H. Container 22 has coupled thereto a data carrier 120. For some applications, syringes 506 and containers 22 are stored in a single tray, as shown in Fig. 12, while for other applications, they are stored in separate trays. Robot 502 typically authenticates container 22, by actuating communication element 504 to read authentication information stored in data carrier 120 and/or verifying coded signature 245 coupled to the container, as described hereinbelow in the section entitled "Signature."

Robot 502 removes the needle cap from container 22, turns the container over, and brings container 22 to the appropriate mother vial 104. The robot actuates the container to draw the calculated volume of labeled radiopharmaceutical agent from the mother vial, typically by inserting the needle of container 22 through a membrane of mother vial 104, and withdrawing a plunger of container 22 until the desired volume of agent has been drawn from the mother vial. The robot typically brings the syringe to dose calibrator 510 for quality control assaying of radioactivity. If necessary, robot 502 brings container 22 to a saline vial 514, and actuates the container to draw the required volume of saline solution into the container. Robot 502 replaces the needle cap on the container, and turns the container over. Alternatively, saline solution is drawn prior to drawing the labeled radiopharmaceutical agent from mother vial 104. For some applications, a needle of the container 22 is changed between drawings.

For dispensing a cocktail of labeled radiopharmaceutical agents, each having a respective dose, robot 502 repeats these steps for a plurality of mother vials 104, typically changing the needle of container 22 between drawings. During dispensing of such a cocktail, robot 502 typically draws first from the mother vial containing the lower or lowest radiation labeled radiopharmaceutical agent, such as to reduce any effect the assaying of the first agent may have on the assaying of the subsequent agent(s).

System 20 typically performs a quality control check on the dispensed radiopharmaceutical solution to confirm that the solution contains the desired dose(s) of the radiopharmaceutical agent(s) and radioactivity level.

Control unit 500 activates communication element 504 to write radiopharmaceutical information to data carrier 120 of container 22, as described hereinabove with reference to Fig. 8 and step 118 of Fig. 2. For some applications, the data carrier is coupled to the container prior to placement of the container in dispensing system 20, while for other applications, robot 502 couples a data carrier to each container during or after the dispensing process. Similarly, for some applications in which coded signature 256 is provided, the coded signature is attached to container 22 prior to placement of the container in dispensing system 20, while for other applications, robot 502 couples a coded signature to each container during or after the dispensing process.

Robot 502 brings the filled container to a shield body tray 530, and inserts the container into a container shield 532. The robot picks up a shield cap 534 from a shield cap tray 536, and secures it to container shield 532. For some applications, data carrier 120 is coupled to shield 532 or cap 534, rather than directly to container 22. Alternatively, separate data carriers 120 are coupled to the container and the shield or cap.

In an embodiment of the present invention, dispensing system 20 comprises a print area 540, at which dispensing system 20 prints and attaches at least one conventional label to container 22, shield 532, and/or cap 534, in order to comply with regulatory labeling requirements. The dispensing system typically prints yet another conventional label for placement on a basket that holds a plurality of containers 22 for transport within or between healthcare facilities.

After the dispensing of container 22 has been completed, robot 502 brings the container to a completed container tray (tray not shown in the figure).

In an embodiment of the present invention, dispensing system 20 comprises at least one diluted mother vial which has a greater volume than a conventional mother vial. For example, the diluted mother vial may have a volume of at least about 10 ml, e.g., at least about 20 ml, such as 21 ml, while a conventional mother vial may have a volume of less than 10 ml, e.g., less than 7 ml, such as 5.8 ml. The labeled radiopharmaceutical agent solution from a conventionally-sized mother vial 104 is transferred to the diluted mother vial, and the balance of the additional volume of the diluted mother vial is filled with saline solution. The resulting diluted solution is used by dispensing system 20 to fill containers 22 with low-dose labeled radiopharmaceutical agents useful for performing low-dose imaging procedures, such as those described in the above-mentioned International Application IL/2005/001173, in above-mentioned PCT Publication WO 05/119025, or in one or more of the other co-assigned patent applications incorporated herein by reference. Alternatively, the resulting lower-dose solution is used for time-dependent administration protocols, pursuant to which a desired total dose is divided into several sub-doses for sequential administration over time. For mechanical handling and administration reasons, each sub-dose must have a minimum volume, e.g., at least 1 ml.

The information contained in data carrier 106 of conventionally-sized mother vial 104 is transferred to a data carrier 106 of the dilution mother vial, with appropriate adjustments to reflect the diluted dose of the labeled radiopharmaceutical agent.

In an embodiment of the present invention, a method for automatically dispensing a labeled radiopharmaceutical agent comprises providing a mother vial having a volume of at least 10 ml, e.g., at least 20 ml; filling the mother vial with at least 5 ml of a non-diluted labeled radiopharmaceutical agent, and with at least 5 ml of saline solution; placing the mother vial in automated radiopharmaceutical dispensing system 20; and dispensing at least one dose from the mother vial to a container. For some applications, dispensing system 20 further dilutes the dose by dispensing saline solution to the container from a saline solution container.

It is noted that dispensing system 20 is theoretically able to dispense similar low doses to containers 22 by drawing a small volume of labeled radiopharmaceutical agent from a conventionally-sized mother vial, and diluting the agent with saline solution drawn from saline vial 512, as described above. However, the drawing of such a small volume may present mechanical challenges for achieving precise volumes within acceptable variations.

Reference is made to Figs. 13A-C, which are schematic illustrations of a system for carrying out a data transfer process, in accordance with an embodiment of the present invention. In this embodiment, information is transferred directly from data carrier 106 of mother vial 104 to data carrier 120 of container 22 while container 22 draws the labeled radiopharmaceutical agent from mother vial 104. As shown in Fig. 13A, container 22 is lowered to mother vial 104 (which is contained within shielding 520 of vials complex 505), as indicated by an arrow 522. As shown in Fig. 13B, as container 22 draws labeled radiopharmaceutical solution from mother vial 104, data carrier 120 of the container is positioned in a vicinity of data carrier 106 of the mother vial. Container 22 is raised from mother vial 104, as indicated by an arrow 524 in Fig. 13C. Information transfer takes place during one or more of the steps illustrated in Figs. 13A-C.

For some applications, information is transferred to data carrier 120 of container 22 during assaying of the contents of the container at dose calibrator 510.

In an embodiment of the present invention, dispensing system 20 is configured to dispense to a plurality of containers 22 for a single patient, or to a plurality of independent chambers within a single container 22 (such as first and second chambers 282A and 282B, described hereinabove with reference to Fig. 9C). For some applications, the plurality of containers are permanently coupled to one another, while for other applications the plurality of containers are removably coupled to one another. Alternatively, the plurality of containers are not coupled to one another, in which case they may be stored in association with one another, e.g., in a single tray.

For some applications, dispensing system 20 utilizes one or more of the dispensing techniques described in the references mentioned hereinabove in the Background of the Invention section, *mutatis mutandis*.

In an embodiment of the present invention, system 10 does not comprise dispensing system 20. System 10 is instead electronically or manually interfaced with a conventional radiopharmacy. Patient management system 160 places orders with the radiopharmacy for a particular dose of a labeled radiopharmaceutical agent for a particular patient. Upon dispensing of the dose into a conventional container, such as a syringe, data carrier 120 is physically coupled to the container, and information is written to the data carrier, such as the identity of the labeled radiopharmaceutical agent, the time of dispensing, the measured radioactivity level, and/or other information described herein as being contained in the data carrier, such as with reference to Fig. 8. For some applications, system 10 comprises a module for automatically measuring the radioactivity level and recording the information in the data carrier. Optionally, the module is in communication with system 10, such as via management control component 150, and receives additional patient-specific or protocol-related information from system 10, and records the information in data carrier 120. For some applications, the radiopharmacy dispenses the labeled radiopharmaceutical agent to one of the novel radiopharmaceutical agent containers 22 described herein.

The radioisotope elution system

Reference is made to Fig. 14, which is a schematic illustration of a radioisotope automatic elution system 600, in accordance with an embodiment of the present invention. System 600 automatically elutes a radioisotope, such as technetium Tc-99m, into radioisotope vials 610. The radioisotope is used for radiolabeling the unlabeled radiopharmaceutical agent, as described hereinabove with reference to step 110 of Fig. 2. Vials 610 are coupled to radioisotope data carriers 612 containing information about the radioisotope, such as a vial code, the time of preparation, the activity at the time of preparation, and total solution volume. Labels 612 are computer-communicatable, and typically comprise an RFID tag, smart card, disk-on-key (e.g., a USB key), compact disc, minidisk, disposable computer-readable medium, or other electronic memory, or a machine-readable code, e.g., a barcode. For some applications, information contained in data carrier 612 is encrypted for enabling authentication. Alternatively or additionally, data carrier 612 and/or vial 610 comprise coded signature 256, as described hereinabove. The coded signature typically comprises an encrypted signature and/or a color-coded signature, as described hereinbelow in the section entitled "Signature."

The automatic elution process typically begins with a determination by dose calculation system 152 (Fig. 5) of an optimal elution frequency, for example:

- 18 hours, 6 hours, 18 hours, 6 hours, ... ,;
- 23 hours, 1 hour, 23 hours, 1 hour, ... ,;
- 18 hours, 1 hour, 5 hours, 18 hours, 1 hour, 5 hours, ... ,; or
- 18 hours, 6 hours, 23 hours, 1 hour, 18 hours, 6 hours, 23 hours, 1 hour, ... ,.

Dose calculation system 152 electronically notifies a control system 616 of elution system 600 of the desired elution frequency. For applications in which the radioisotope comprises Tc-99m, it will be appreciated that the ratio of Tc-99 to Tc-99m, which is determined by the elution frequency, is important for molecular imaging by an antibody, and there is generally an optimal range of the ratio of Tc-99 to Tc-99m, which should be taken into consideration when preparing Tc-99m with an antibody. Typically, control system 616 comprises one or more standard personal computers or servers with appropriate memory, communication interfaces and software for carrying out the functions prescribed by relevant embodiments of the present invention. This software may be downloaded to the control system in electronic form over a network, for example, or it may alternatively be supplied on tangible media, such as CD-ROM.

Sterile, empty vials 610 of predetermined volumes (e.g., 10 ml or 20 ml), and typically comprising caps 618, are placed on a conveyor belt 620. A first robot 622 places a shield 624 on each vial 610. Alternatively, the vials 610 are manually shielded. Conveyor belt 620 moves shielded vial 610 into position under a radioisotope generator 626, such as a TC-99m generator. At a required elution time, a second robot 628 lifts the shielded empty vial 610, and, under sterile conditions, removes cap 618 and engages the shielded empty vial 610 with generator 626.

Upon engagement of vial 610 with generator 626, both a first electronic valve 630 of a saline tank 632 and a second electronic valve 634 of generator 626 open, and vial 610 is filled, while a flow meter 636 monitors the amount of saline flow. After flow of a predetermined volume, control system 616 automatically shuts first electronic valve 630 of saline tank 632 and second electronic valve 634 of generator 626.

Filled, shielded vial 610 is automatically disengaged from generator 626, and is automatically sealed under sterile conditions with a shielded seal 638. Filled, shielded vial 610 is lowered back to conveyor belt 620. The conveyor belt moves filled, shielded vial 610 past an assaying and labeling station 640, which assays and labels the vial with data carrier 612, a barcode 642, and/or coded signature 256. For some applications, coded signature 256 is placed on data carrier 612, while for other applications it is placed on vial 610. For still other applications, separate coded signatures 256 are placed on both vial 610 and data carrier 612, and are used to match the vial with the data carrier. For example, a color-coded signature may be printed on vial 610, either prior to the elution or together with the application of data carrier 612, and an encrypted signature may be stored in the data carrier 612. Alternatively, the encrypted signature may be printed.

It will be appreciated that the elution process is subject to modifications and alterations based on communication and information that is received from system 10. For example, a log book of elution system 600 may specify a Tc-99m vial of 1000 mCi, yet a communication request from dose calculation system 152 may modify the order to be a Tc-99m vial of 200 mCi, based on new requirements, e.g., low-dose administration.

The mother vial preparation system

Reference is made to Fig. 15, which is a schematic illustration of a mother vial preparation system 700, in accordance with an embodiment of the present invention. System 700 automatically labels mother vials 104, containing unlabeled radiopharmaceutical agents, with appropriate radioisotopes. System 700 attaches a data carrier 106 to each mother vial 104, and writes the information to the data carrier that is described hereinabove with reference to Fig. 7. Alternatively, the manufacturer or distributor attaches data carrier 106 to mother vial 104, and writes at least a portion of the information to the carrier.

Prior to beginning the radiolabeling process, a control unit 702 of system 700 authenticates radioisotope vial 610 and mother vial 104, and verifies that radioisotope vial 610 contains the correct radioisotope at the correct radioactivity, and that mother vial 104 contains the correct unlabeled radiopharmaceutical agent. For some applications, such authentication and/or verification is performed by authenticating coded signature 256 of data carrier 612 of radioisotope vial 610. For some applications, such authentication includes authentication of a commercial license associated with the use of mother vial 104. Typically, control unit 702 comprises one or more standard personal computers or servers with appropriate memory, communication interfaces and software for carrying out the functions prescribed by relevant embodiments of the present invention. This software may be downloaded to the control unit in electronic form over a network, for example, or it may alternatively be supplied on tangible media, such as CD-ROM.

Conveyor belt 620 carries shielded radioisotope vial 610 from radioisotope automatic elution system 600 to mother vial preparation system 700. Alternatively, for embodiments in which elution system 600 is not provided, the radioisotope vial is manually placed on conveyor belt 620. The conveyor belt brings vial 610 to a radioisotope filling point 710.

System 700 typically comprises a plurality of dose preparation platforms 712, each of which contains premixed mother vials 104 containing unlabeled radiopharmaceutical agents that require radiolabeling with the radioisotope contained in radioisotope vial 610, e.g., Tc-99m. In the example shown in Fig. 15, preparation platforms 712 comprise a Tc-99m-teboroxime dose preparation platform, a Tc-99m-pertechnetate dose preparation platform, a Tc-99m-sestamibi dose preparation platform, and a Tc-99m-MDP dose preparation platform.

A robot 720 picks up a syringe 722 from a first syringe platform 724, or a micro-syringe 726 from a second syringe platform 728, and travels along a second conveyer belt 730 to filling point 710. It will be appreciated that other types syringes and/or other dispensing tools may also be used. Upon reaching filling point 710, syringe

722 or 726 draws a predetermined amount of radioisotope solution from radioisotope vial 610. The robot typically travels to an assay station 732, which assays the radioisotope solution. Syringe 722 or 726 is then discarded at a discard station 734.

Robot 720 picks up another syringe 722 or 726 from the platform 724 or 728, fills the syringe with a predetermined amount of the radioisotope from vial 610, and travels along second conveyor belt 730 to one of dose preparation platforms 712. At the dose preparation platform, the syringe injects a predetermined amount of radioisotope into mother vial 104 of the dose preparation platform, thereby labeling the unlabeled radiopharmaceutical agent contained in the mother vial.

Robot 720 discards the syringe at discard station 734, picks up a new syringe, draws a predetermined amount of solution from labeled mother vial 104, and assays the solution at assay station 732, in order to determine the radioactivity of the labeled radiopharmaceutical agent contained in mother vial 104. Following the assaying, robot 720 discards the syringe at discard station 734. Typically, system 700 performs one or more quality control procedures on the labeled radiopharmaceutical agent.

System 700 updates data carrier 106 of mother vial 104 with radiolabeling information, such as the time of labeling, and the activity of the radioisotope at the time of labeling, the total solution volume in the mother vial, and the ratio of radioisotopes (e.g., Tc-99m to Tc-99) at the time of labeling, for applications in which the unlabeled radiopharmaceutical agent is labeled with more than one radioisotope.

It is noted that system 700 is configurable to vary a radioactivity of the radioisotope used to label a given radiopharmaceutical agent in order to produce labeled radiopharmaceutical agents of various levels of radioactivity (for example, Tc-99m-teboroxime of 500 mCi and Tc-99m-teboroxime of 50 mCi). For some applications, system 700 comprises at least one cocktail dose preparation platform 736, for labeling a cocktail of radiopharmaceutical agents (for example, Tl-201-thallous chloride, Tc-99m-sestamibi, and I-123-BMIPP).

It will be appreciated that the mother vial preparation process is subject to modifications and alterations based on communication and information that is received from system 10. For example, a log book of system 700 may specify a mother vial of 500 mCi, yet a communication request from dose calculation system 152 may modify the order to be a mother vial of 200 mCi, based on new requirements, e.g., low-dose administration.

The exercise room

In an embodiment of the present invention, system 10 comprises at least one exercise room, which comprises one or more pieces of exercise equipment, typically including at least one treadmill. The exercise room, and the equipment therein, is typically in communication with one or more elements of system 10, such as patient-specific data carrier 24, management and control component 150, administration system 26, data carrier 120 of radiopharmaceutical agent container 22, and/or imaging system 28. For example, the exercise room may report the duration, time, and type of exercise to imaging system 28, administration system 26, and/or management control component 150, for synchronizing the exercise with administration and imaging. For some applications, the exercise room receives instructions regarding the duration, time, and/or type of exercise to be performed for a given patient, and schedules an appropriate exercise session in a log book. For some applications, the exercise room sends the patient an SMS-like message notifying the patient of the scheduled session, and/or reminding the patient about a scheduled session. For some applications in which data carrier 24 is integrated into watch or bracelet 170, as described hereinabove with reference to Fig. 3, watch or bracelet 170 is configured to receive and display the SMS-like message to the patient.

Signature

In accordance with an embodiment of the present invention, coded signature 256 comprises a signature encrypted using an encryption algorithm, which is either proprietary or known in the art, e.g., Advanced Encryption Standard (AES), Data Encryption Standard (DES), or Triple DES (3DES). Typically, the encryption algorithm utilizes a symmetric key cipher, as is known in the art.

For some applications, coded signature 256 is stored in one of the data carriers described herein. Alternatively or additionally, the coded signature is printed on the apparatus, e.g., as a barcode.

For some applications, coded signature 256 comprises a color-coded signature, which is implemented using techniques described in the above-mentioned US Patent Application Publication 2004/0156081 to Bril et al. Techniques described in the '081 publication include the use of an encrypted image comprising an array of printed positions formed using a group of inks each of which has a predetermined spectrum. The positions are selected to form a predetermined image, either real or virtual, when the image is viewed through an optical processor. The optical processor may further use a distortion, such as a distorted grating or a distorted lens. The correct image is the spectrum, as distorted by the optical processor. An image formed using inks having the same colors as experienced by the human eye, or even by a standard spectrometer, will fail to form the correct predetermined image. Alternatively or additionally, special inks may be used, so that no two ink combinations are exactly alike, and only registered ink combinations provide the correct spectrum. Furthermore, the special inks may be mixtures of 5 or more colors.

Fig. 16A illustrates color spectra 800 of several dyes, for example dyes B, D1, G, D2, and R, each having a well-defined spectral peak, as described in the '081 publication. When dye B and dye G are mixed, the human eye may see a color substantially the same as the color of dye D1. When dye D1 and dye D2 are mixed, the human eye may see a color substantially the same as the color of dye G.

Fig. 16B illustrates a color-coded signature 802, as described in the '081 publication. A color patch 804, which to the human eye may seem a plain orange, for example, may have a first portion 806A, consisting of dye B and dye G, combined to form a hue which is substantially the same as that of dye D1, and a second portion 806B, consisting of dye D1. To the human eye, the color-coded signature 802 appears as a homogeneous patch.

An optical processor 820 comprises an imaging spectrograph, which comprises a grating 822 and, typically, a lens 824. In the example shown in Fig. 16B, the spectrograph produces three structures: a structure 821 formed by diffraction of dye D1 through the grating, a structure 823 formed by diffraction of dye G, and a structure 825 formed by diffraction of dye B. Optical processor 220 thus reveals the authentic spectra of the color-coded signature 802.

For some applications, optical processor 820 comprises two lenses 824 of substantially equal power, one to create a parallel beam at the input to the grating, just before the grating, and one to create an image at the focal point after the grating. Alternatively, a single lens 824, having twice the power of the two lenses, may be placed just before or just after the grating.

For some applications, a more complex color coding is achieved by using a distorted lens or a distorted grating, such that spectral structure 821, 823, and 825 may be reproduced only when an optical processor having the exact distortion is used. It will be appreciated that a single hue may be produced by mixing several dyes, for example, 3, 5, or 10. It will be appreciated that each printing house may be allocated only a specific mix of dyes, so that no two printing houses may have identical dye combinations, and no two printing houses may reproduce the same color-coded signatures 802.

For some applications, color-coded signature 802 is printed directly on an element of system 10, for example, on radiopharmaceutical agent container 22 (Fig. 1), or on radioisotope vial 610 (Fig. 14). Alternatively or additionally, a label, for example, mother vial data carrier 106 or data carrier 120 (Fig. 1) is color-coded, or includes a color-coded patch or pattern, operative as color-coded signature 802.

For some applications, an encrypted signature 256 and a color-coded signature 802 are combined. The resulting color-coded machine-readable signature 256 is authenticated by optical processor 820. For example, an encrypted signature may be provided on a label colored with a coded color. Alternatively or additionally, encrypted signature 256 is printed on a color-coded background, or with color-coded dyes. Alternatively or additionally, coded signature 256 comprises a color-coded barcode. For some applications, the color-coded barcode may appear black or another color to the eye, but reveal a unique spectrum to optical processor 820. For some applications, the color-coded machine-readable signature further comprises a date, to prevent the recycling or re-use of signatures.

Physical key

Reference is made to Fig. 17, which is a schematic illustration of a computer-readable medium 850, a portion of which is shaped so as to define a physical key 852, in accordance with an embodiment of the present invention. A communication element 854 is shaped so as to define a dedicated slot 856 having a geometry matching that of key 852. Only keys having the particular geometry of slot 856 can be inserted into the slot. Key 852 thus enables authentication of computer-readable medium 850. Computer-readable medium 850 may comprise, for example, a disk-on-key apparatus or a chip, having, for example, a USB-type connector.

For some applications, patient-specific data carrier 24 comprises computer-readable medium 850, and a communication element of imaging system 28 and/or administration system 26 is shaped so as to define slot 856. Alternatively or additionally, healthcare worker identity tag 208 comprises computer-readable medium 850, and workstation 200, elution system 600, dispensing system 20, administration system 26, and/or imaging system 28 is shaped so as to define slot 856. For some applications, computer-readable medium 850 further comprises coded signature 256, as described hereinabove, while for other applications, key 852 is relied upon in lieu of coded signature 256.

For some applications, authentication, as described herein, is alternatively or additionally based on additional parameters, such as a manufacturer's attribute.

In an embodiment of the present invention, information is transferred from one element of system 10 to another element thereof by physically transferring an electronic information-carrying chip from one element to the other. For example, upon administration of the labeled radiopharmaceutical agent contained in container 22, information may be transferred from data carrier 120 to patient-specific data carrier 24 by physically transferring a memory chip of data carrier 120 to data carrier 24.

Managing Compton residuals

Reference is made to Fig. 18, which is a graph showing particle energy vs. photon count at a detector 454 of camera 452 of imaging system 28 (Fig. 11), in accordance with an embodiment of the present invention. In this embodiment, dose calculation sub-system 156 of radiopharmaceutical dose calculation system 152, described hereinabove with reference to Fig. 5, takes Compton residuals into consideration when calculating doses of a first and a second labeled radiopharmaceutical agent to be mixed together in a cocktail, or to be separately administered for the same image acquisition procedure. If the first agent were to be provided at a relatively high dose and the second agent were to be provided at a lower dose, the first agent would produce a first peak 900A around a first energy level E^1, and the second agent would produce a second peak 902 around a second energy level E^2. A Compton residual 904A produced by the first agent at least partially masks second peak 902. For some applications, in order to prevent such masking, dose calculation sub-system 156 reduces the dose of the first agent, thereby producing a first peak 900B and a corresponding Compton residual 904B having lower counts than initial first peak 900A and Compton residual 904A, respectively. Compton residual 904B is sufficiently low so as not to mask second peak 902. By using techniques described hereinabove and/or incorporated herein by reference, camera 452 is sufficiently sensitive to acquire sufficient counts emitted from the lower dose of the second agent. For example, the first and second agents may comprise MIBI-Tc and thallium, respectively, which emit energy at 140 KeV and 72 KeV, respectively.

Alternatively, calculation sub-system 156 determines that the dose of the first labeled radiopharmaceutical agent cannot be reduced sufficiently to prevent such Compton masking. To make such a determination, the sub-system typically takes into consideration constraints applied by the physical properties of the first agent, patient-specific information, and/or camera 452. The sub-system may thus determine that the two agents must be prepared as separate doses for non-simultaneous administration. Alternatively, the sub-system determines that the dose of the second agent is to be increased, so as to prevent the masking. To make such a determination, the sub-system typically takes into consideration constraints applied by the physical properties of the first agent, patient-specific information, camera 452, and/or safety and/or regulatory requirements.

Information-bearing radiopharmaceuticals

In an embodiment of the present invention, a portion of the patient, radiopharmaceutical, and/or protocol information described herein is chemically stored together with a labeled radiopharmaceutical agent in a container, such as radiopharmaceutical agent container 22 or mother vial 104. For some applications, such information is chemically stored by providing a chemical indicative of and/or encoding the information, and mixing the chemical with the radiopharmaceutical agent. Alternatively, such information is chemically stored by attaching a chemical marker indicative of the information to the radiopharmaceutical agent, or otherwise chemically modifying the radiopharmaceutical agent to store the information. The information-indicative chemical indicator (i.e., chemical or chemical marker) has properties which are machine-readable, for example, using optical, spectral, fluorescence, or isotope emission techniques.

For some applications, the information is stored by setting a level of a parameter of the chemical indicator, such as concentration or radioactivity, which level is indicative of the information. For example, a plurality of concentrations 0, A_1, A_2, A_3, ..., A_{max} may be defined, each of which represents a respective value. At all of the defined concentrations, the chemical indicator is biologically inert and/or safe in the body, and does not affect the sterility and/or properties of the radiopharmaceutical agent. The plurality of concentrations are sufficiently different from one another so as to be independently measurable and identifiable, such as by measuring a spectral signature of the chemical indicator. For some applications, a plurality of different chemical indicators are used, each of which has defined levels of a parameter representing respective values. The values represented by the plurality of chemical indicators together represent the information.

For some applications, the level of the parameter of the chemical indicator changes over time, e.g., the radioactivity of the chemical indicator declines because of radioactive decay, thereby providing an indication of elapsed time. Such elapsed time may be used, for example, to determine the timing of preparation of the radiopharmaceutical agent and/or subsequent processes, as well as validating whether such timing is within an allowed time window.

For some applications, dispensing system 20 applies the code to the labeled radiopharmaceutical agent and/or container 22 during the dispensing process, and administration system 26 and/or imaging system 28 reads and verifies the stored information. A dedicated reader may be provided for such reading, or a camera of imaging system 28 may be configured to perform such reading.

The scope of the present invention includes embodiments described in the following applications, which are assigned to the assignee of the present application and are incorporated herein by reference. In an embodiment, techniques and apparatus described in one or more of the following applications are combined with techniques and apparatus described herein:

- International Application PCT/IL2005/001173, filed November 9, 2005;
- International Application PCT/IL2005/000572, filed June 1, 2005;
- International Application PCT/IL2005/000575, filed June 1, 2005;

- International Application PCT/IL2005/001215, filed November 16, 2005;
- US Provisional Application 60/625,971, filed November 9, 2004;
- US Provisional Application 60/628,105, filed November 17, 2004;
- US Provisional Application 60/630,561, filed November 26, 2004;
- US Provisional Application 60/632,236, filed December 2, 2004;
- US Provisional Application 60/632,515, filed December 3, 2004;
- US Provisional Application 60/635,630, filed December 14, 2004;
- US Provisional Application 60/636,088, filed December 16, 2004;
- US Provisional Application 60/640,215, filed January 3, 2005;
- US Provisional Application 60/648,385, filed February 1, 2005;
- US Provisional Application 60/648,690, filed February 2, 2005;
- US Provisional Application 60/675,892, filed April 29, 2005;
- US Provisional Application 60/691,780, filed June 20, 2005;
- US Provisional Application 60/700,318, filed July 19, 2005;
- US Provisional Application 60/700,299, filed July 19, 2005;
- US Provisional Application 60/700,317, filed July 19, 2005;
- US Provisional Application 60/700,753, filed July 20, 2005;
- US Provisional Application 60/700,752, filed July 20, 2005;
- US Provisional Application 60/702,979, filed July 28, 2005;
- US Provisional Application 60/720,034, filed September 26, 2005;
- US Provisional Application 60/720,652, filed September 27, 2005;
- US Provisional Application 60/720,541, filed September 27, 2005;
- US Provisional Application 60/750,287, filed December 13, 2005;
- US Provisional Application 60/750,334, filed December 15, 2005; and/or
- US Provisional Application 60/750,597, filed December 15, 2005.

As used in the present application, including in the claims, a "clinical environment" means any facility or institution in which at least one of radiopharmaceutical preparation, dispensing, and administration occur, including, for example, a radiopharmaceutical manufacturing facility, a pharmacy, a hospital, a doctor's clinic, a day clinic, an out-patient clinic, a laboratory, and a geriatric center.

It will be appreciated by persons skilled in the art that the present invention is not limited to what has been particularly shown and described hereinabove. Rather, the scope of the present invention includes both combinations and subcombinations of the various features described hereinabove, as well as variations and modifications thereof that are not in the prior art, which would occur to persons skilled in the art upon reading the foregoing description.

CLAIMS

1. Apparatus for use with at least one labeled radiopharmaceutical agent, the apparatus comprising:

a container containing the at least one labeled radiopharmaceutical agent; and

a portable computer-communicatable data carrier associated with the container, the data carrier containing imaging protocol information for use with the at least one labeled radiopharmaceutical agent.

2. The apparatus according to claim 1, wherein the apparatus comprises a device configured to write the imaging protocol information to the data carrier.

3. The apparatus according to claim 1, wherein the data carrier additionally contains administration protocol information useful for administering the at least one labeled radiopharmaceutical agent.

4. The apparatus according to claim 1, wherein the imaging protocol information comprises instructions for performing an imaging procedure using the at least one labeled radiopharmaceutical agent.

5. The apparatus according to claim 1, wherein the imaging protocol information comprises an identifier of an imaging protocol.

6. The apparatus according to claim 1, wherein the imaging protocol information comprises a parameter of the at least one labeled radiopharmaceutical agent.

7. The apparatus according to claim 1, wherein the imaging protocol information comprises a parameter useful for configuring at least one aspect of an imaging procedure performed using the at least one labeled radiopharmaceutical agent.

8. The apparatus according to claim 1, wherein the container contains a single dose of the radiopharmaceutical agent, which dose is appropriate for use with the imaging protocol information.

9. The apparatus according to claim 1, wherein the container contains a plurality of labeled radiopharmaceutical agents mixed together.

10. The apparatus according to claim 1, wherein the container is shaped so as to define a plurality of chambers, each of which contains a respective one of a plurality of labeled radiopharmaceutical agents.

11. The apparatus according to any one of claims 1-10,

wherein the data carrier comprises a first data carrier, which contains a first identifier value,

wherein the apparatus further comprises a second computer-communicatable data carrier, which contains a second identifier value, and

wherein the apparatus is configured to operate responsively to a detection of a correspondence between the first and second identifier values.

12. The apparatus according to claim 11, wherein at least one of the first and second data carriers is configured to perform the detection of the correspondence.

13. The apparatus according to claim 11, wherein the apparatus comprises a correspondence-detection element configured to perform the detection of the correspondence.

14. The apparatus according to claim 11, wherein at least one of the first and second data carriers contains an identifier of a patient to whom the labeled radiopharmaceutical agent is to be administered.

15. The apparatus according to claim 11, wherein at least one of the first and second identifier values comprises an identifier of a patient to whom the labeled radiopharmaceutical agent is to be administered.

16. The apparatus according to claim 11, wherein exactly one of the first and second data carriers comprises a coupling mechanism configured to be coupled to a patient to whom the labeled radiopharmaceutical agent is to be administered.

17. The apparatus according to claim 11, wherein the apparatus comprises an imaging system comprising imaging functionality, the imaging system configured, responsively to the detection of the correspondence, to drive the imaging functionality to perform an imaging procedure using the at least one labeled radiopharmaceutical agent.

18. The apparatus according to any one of claims 1-10, wherein the data carrier is physically coupled to the container.

19. The apparatus according to claim 18, wherein the data carrier contains an identifier of a patient to whom the labeled radiopharmaceutical agent is to be administered, and wherein the imaging protocol information comprises imaging protocol information selected for the patient.

20. The apparatus according to claim 19, wherein the imaging protocol information comprises an identifier of an imaging protocol.

21. The apparatus according to claim 19, wherein the imaging protocol information comprises imaging protocol information customized for the patient.

22. The apparatus according to any one of claims 1-10, wherein the imaging protocol information comprises SPECT imaging protocol information.

23. The apparatus according to claim 22, wherein the SPECT imaging protocol information comprises dynamic SPECT imaging protocol information.

24. The apparatus according to claim 23, wherein the SPECT imaging protocol information comprises at least one kinetic parameter of the at least one labeled radiopharmaceutical agent, the at least one kinetic parameter useful for performing a dynamic SPECT imaging procedure using the at least one labeled radiopharmaceutical agent.

25. The apparatus according to any one of claims 1-10, comprising an imaging system, which comprises:

a communication element, configured to read the imaging protocol information from the data carrier; and

a control unit, comprising imaging functionality, which is configured to perform an imaging procedure, and to configure the procedure at least in part responsively to the imaging protocol information read from the data carrier by the communication element.

26. The apparatus according to claim 25, wherein the imaging system comprises a camera, wherein the imaging functionality comprises image acquisition functionality, and wherein the image acquisition functionality is configured to perform an image acquisition procedure using the camera, and to configure the procedure at least in part responsively to the imaging protocol information read from the data carrier by the communication element.

27. The apparatus according to claim 26, wherein the image acquisition functionality configures a total acquisition time of the image acquisition procedure at least in part responsively to the imaging protocol information.

28. The apparatus according to claim 26, wherein the camera comprises a plurality of detectors, and wherein the image acquisition functionality is configured to configure, at

least in part responsively to the imaging protocol information, at least one motion of at least one of the detectors during the image acquisition procedure.

29. The apparatus according to claim 26, wherein the control unit is configured to configure, at least in part responsively to the imaging protocol information, a waiting time between administration of the labeled radiopharmaceutical agent and commencement of the image acquisition procedure.

30. The apparatus according to claim 26, wherein the image acquisition functionality is configured to perform a gated image acquisition procedure at least in part responsively to the imaging protocol information.

31. The apparatus according to claim 25, wherein the imaging functionality comprises image reconstruction functionality, and wherein the image reconstruction functionality is configured to perform an image reconstruction procedure, and to configure the procedure at least in part responsively to the imaging protocol information read from the data carrier by the communication element.

32. The apparatus according to claim 25, wherein the imaging functionality comprises image analysis functionality, and wherein the image analysis functionality is configured to perform an image analysis procedure, and to configure the procedure at least in part responsively to the imaging protocol information read from the data carrier by the communication element.

33. The apparatus according to claim 25, wherein the imaging functionality comprises diagnosis functionality, and wherein the diagnosis functionality is configured to perform a diagnostic procedure, and to configure the procedure at least in part responsively to the imaging protocol information read from the data carrier by the communication element.

34. The apparatus according to claim 25, wherein the imaging procedure includes a three-dimensional dynamic imaging study, and wherein the imaging functionality is configured to perform the three-dimensional dynamic imaging study, and to configure the study at least in part responsively to the imaging protocol information read from the data carrier by the communication element.

35. The apparatus according to any one of claims 1-10, wherein the data carrier is not physically coupled to the container, and wherein the data carrier contains an identifier of a patient to whom the labeled radiopharmaceutical agent is to be administered.

36. The apparatus according to claim 35, wherein the data carrier comprises a coupling mechanism configured to be coupled to the patient.

37. The apparatus according to claim 35, wherein the data carrier comprises a first data carrier, and wherein the apparatus further comprises a second computer-communicatable data carrier physically coupled to the container, the second data carrier containing radiopharmaceutical information regarding the at least one labeled radiopharmaceutical agent.

38. Apparatus for use with at least one labeled radiopharmaceutical agent, the apparatus comprising:

a container containing the at least one labeled radiopharmaceutical agent; and

a computer-communicatable data carrier associated with the container, the data carrier containing authenticatable information regarding a commercial license for use of SPECT imaging protocol information with the at least one labeled radiopharmaceutical agent.

39. The apparatus according to claim 38, comprising an imaging system, which comprises:

a communication element, configured to read the authenticatable license information from the data carrier;

a control unit, comprising imaging functionality, the control unit configured to:

authenticate the authenticatable license information, and

only upon authentication, drive the imaging functionality to perform an imaging procedure using the SPECT imaging protocol information.

40. The apparatus according to claim 38, wherein the apparatus comprises a device configured to write the authenticatable license information to the data carrier.

41. The apparatus according to any one of claims 38-40, wherein the data carrier is physically coupled to the container.

42. Apparatus comprising a portable computer-communicatable data carrier containing authenticatable information regarding a commercial license for use of SPECT imaging protocol information.

43. The apparatus according to claim 42, wherein the data carrier additionally contains patient information regarding a patient upon whom an imaging procedure using the

SPECT imaging protocol information is to be performed.

44. The apparatus according to claim 42, wherein the authenticatable license information is encrypted.

45. The apparatus according to claim 42, wherein the apparatus comprises a device configured to write the authenticatable license information to the data carrier.

46. The apparatus according to claim 42, wherein the data carrier comprises a coupling mechanism configured to be coupled to a patient upon whom an imaging procedure using the SPECT imaging protocol information is to be performed.

47. The apparatus according to any one of claims 42-46, comprising an imaging system, which comprises:

a communication element, configured to read the authenticatable license information from the data carrier;

a control unit, comprising imaging functionality, the control unit configured to:

authenticate the authenticatable license information, and

only upon authentication, drive the imaging functionality to perform an imaging procedure using the SPECT imaging protocol information.

48. Apparatus comprising:

a first portable computer-communicatable data carrier containing a first identifier value;

a second portable computer-communicatable data carrier containing a second identifier value; and

an imaging system comprising imaging functionality, the imaging system configured, responsively to a detection of a correspondence between the first and second identifier values, to drive the imaging functionality to perform an imaging procedure on a patient.

49. The apparatus according to claim 48, wherein at least one of the first and second data carriers is configured to perform the detection of the correspondence.

50. The apparatus according to claim 48, wherein the imaging system comprises a correspondence-detection element configured to perform the detection of the correspondence.

51. The apparatus according to claim 48, wherein at least one of the first and second

data carriers contains an identifier of a patient to whom the labeled radiopharmaceutical agent is to be administered.

52. The apparatus according to claim 48, wherein at least one of the first and second identifier values comprises an identifier of a patient to whom the labeled radiopharmaceutical agent is to be administered.

53. The apparatus according to claim 48, wherein one of the first and second data carriers comprises a coupling mechanism configured to be coupled to a patient to whom the labeled radiopharmaceutical agent is to be administered.

54. The apparatus according to claim 48, wherein the apparatus comprises a device configured to write at least one of the first and second identifier values to the respective first and second data carriers.

55. The apparatus according to any one of claims 48-54,

wherein at least one of the first and second data carriers contains radiopharmaceutical information regarding at least one labeled radiopharmaceutical agent,

wherein the imaging system comprises a communication element, configured to read the radiopharmaceutical information from the at least one of the data carriers, and

wherein the imaging system is configured to configure the imaging procedure at least in part responsively to the read radiopharmaceutical information.

56. The apparatus according to claim 55, wherein the apparatus comprises a container containing the at least one labeled radiopharmaceutical agent.

57. The apparatus according to claim 56, wherein one of the first and second data carriers is physically coupled to the container.

58. The apparatus according to any one of claims 48-54, wherein the imaging functionality comprises a nuclear camera.

59. The apparatus according to claim 58, wherein the nuclear camera comprises a SPECT camera.

60. Apparatus for use with first and second portable computer-communicatable data carriers containing first and second identifier values, respectively, the apparatus comprising an imaging system, which comprises:

imaging functionality; and

a control unit configured to drive the imaging functionality to perform an imaging procedure on a patient, responsively to a detection of a correspondence between the first and second identifier values.

61. The apparatus according to claim 60, wherein the imaging system comprises a correspondence-detection element configured to perform the detection of the correspondence.

62. Apparatus for use with at least one labeled radiopharmaceutical agent for administration to a patient, the apparatus comprising:

a container containing the at least one labeled radiopharmaceutical agent;

a first computer-communicatable data carrier physically coupled to the container, the first data carrier containing radiopharmaceutical information regarding the at least one labeled radiopharmaceutical agent; and

a second portable computer-communicatable data carrier containing patient information regarding the patient, and imaging protocol information for use with the at least one labeled radiopharmaceutical agent.

63. The apparatus according to claim 62, wherein the imaging protocol information comprises SPECT imaging protocol information.

64. The apparatus according to claim 62, wherein the patient information comprises an identifier of the patient.

65. The apparatus according to claim 62, wherein the second data carrier comprises a coupling mechanism configured to be coupled to the patient.

66. The apparatus according to claim 62, wherein the first data carrier contains a first patient identifier, wherein the patient information contained in the second data carrier comprises a second patient identifier, and comprising an administration system, which comprises:

a first communication element, configured to read the first patient identifier from the first data carrier;

a second communication element, configure to read the second patient identifier from the second data carrier; and

a control unit, configured to compare the first patient identifier to the second patient identifier, and, upon detecting a match, generate an administration signal that triggers administration to the patient of the at least one labeled radiopharmaceutical agent contained in the container.

67. The apparatus according to claim 62, wherein the first data carrier contains a first protocol identifier, wherein the imaging protocol information contained in the second data carrier comprises a second protocol identifier, and comprising an administration system, which comprises:

a communication element, configured to read the first and second protocol identifiers from the first and second data carriers, respectively; and

a control unit, configured to compare the first protocol identifier to the second protocol identifier, and, upon detecting a match, generate an administration signal that triggers administration to the patient of the at least one labeled radiopharmaceutical agent contained in the container.

68. The apparatus according to claim 62, wherein the first data carrier contains a first protocol identifier, wherein the imaging protocol information contained in the second data carrier comprises a second protocol identifier, and comprising an administration system, which comprises:

a first communication element, configured to read the first protocol identifier from the first data carrier;

a second communication element, configured to read the second protocol identifier from the second data carrier; and

a control unit, configured to compare the first protocol identifier to the second protocol identifier, and, upon detecting a match, generate an administration signal that triggers administration to the patient of the at least one labeled radiopharmaceutical agent contained in the container.

69. The apparatus according to claim 62, comprising an administration system, which comprises:

a communication element; and

a control unit, configured to:

generate an administration signal that triggers administration to the patient of the at least one labeled radiopharmaceutical agent contained in the container, and

drive the communication element to transmit information regarding the administration to the second data carrier.

70. The apparatus according to claim 62, wherein the apparatus comprises a device configured to write the imaging protocol information to the first data carrier.

71. The apparatus according to claim 62, wherein the apparatus comprises a device configured to write the patient information to the second data carrier.

72. The apparatus according to any one of claims 62-71, wherein the imaging protocol information comprises imaging protocol information selected for the patient.

73. The apparatus according to claim 72, wherein the imaging protocol information comprises an identifier of an imaging protocol.

74. The apparatus according to claim 72, wherein the imaging protocol information comprises imaging protocol information customized for the patient.

75. The apparatus according to any one of claims 62-71, wherein the first data carrier contains a first patient identifier, wherein the patient information contained in the second data carrier includes a second patient identifier, and comprising an administration system, which comprises:

a communication element, configured to read the first and second patient identifiers from the first and second data carriers, respectively; and

a control unit, configured to compare the first patient identifier to the second patient identifier, and, upon detecting a match, generate an administration signal that triggers administration to the patient of the at least one labeled radiopharmaceutical agent contained in the container.

76. The apparatus according to claim 75, wherein the administration system comprises an automated administration device, configured to administer the at least one labeled radiopharmaceutical agent to the patient upon being triggered by the administration signal.

77. The apparatus according to claim 75, wherein the control unit is configured to generate the administration signal to trigger the administration of the at least one labeled radiopharmaceutical agent by instructing a healthcare worker to administer the at least one labeled radiopharmaceutical agent to the patient.

78. Apparatus for use with at least one labeled radiopharmaceutical agent for administration to a patient, the apparatus comprising:

a container containing the at least one labeled radiopharmaceutical agent;

a computer-communicatable data carrier associated with the container, the data carrier containing data regarding at least one of: the labeled radiopharmaceutical agent and the patient; and

a SPECT imaging system comprising:

a communication element, configured to read the data; and

a control unit, configured to utilize the read data to customize at least one function of the system selected from the group consisting of: administration of the labeled radiopharmaceutical agent, acquisition of a SPECT image of the patient to whom the labeled radiopharmaceutical agent is administered, reconstruction of the SPECT image, analysis of the SPECT image, and diagnosis of a condition of the patient based at least in part on the analysis.

79. The apparatus according to claim 78, wherein the data carrier contains the data regarding the labeled radiopharmaceutical agent.

80. The apparatus according to claim 78, wherein the data carrier contains the data regarding the patient.

81. The apparatus according to claim 78, wherein the control unit is configured to utilize the read data to customize the administration of the labeled radiopharmaceutical agent.

82. The apparatus according to claim 78, wherein the control unit is configured to utilize the read data to customize the acquisition of a SPECT image of the patient to whom the labeled radiopharmaceutical agent is administered.

83. The apparatus according to claim 78, wherein the control unit is configured to utilize the read data to customize the reconstruction of the SPECT image.

84. The apparatus according to claim 78, wherein the control unit is configured to utilize the read data to customize the analysis of the SPECT image.

85. The apparatus according to claim 78, wherein the control unit is configured to utilize the read data to customize the diagnosis of a condition of the patient based at least in part on the analysis.

86. The apparatus according to any one of claims 78-85, wherein the apparatus comprises a device configured to write the data to the data carrier.

87. A SPECT imaging system for use with a container containing at least one labeled radiopharmaceutical agent for administration to a patient, and data regarding at least one of: the labeled radiopharmaceutical agent and the patient, the system comprising:

a communication element, configured to read the data; and

a control unit, configured to utilize the read data to customize at least one function of the system selected from the group consisting of: administration of the labeled radiopharmaceutical agent, acquisition of a SPECT image of the patient to whom the labeled radiopharmaceutical agent is administered, reconstruction of the SPECT image, analysis of the SPECT image, and diagnosis of a condition of the patient based at least in part on the analysis.

88. The system according to claim 87, wherein the system comprises a device configured to write the data to the container.

89. An automated radiopharmaceutical dispensing system for use with a container and a computer-communicatable container data carrier associated with the container, the system comprising:

a robot, configured to manipulate the container;

a communication element; and

a control unit, configured to:

receive radiopharmaceutical information regarding at least one labeled radiopharmaceutical agent, the radiopharmaceutical information selected from the group consisting of: imaging protocol information for use with the at least one labeled radiopharmaceutical agent, and authenticatable information regarding a commercial license for use of an imaging protocol with the at least one labeled radiopharmaceutical agent,

receive patient information regarding a patient,

drive the robot to automatically dispense a dose of the labeled radiopharmaceutical agent to the container, and

drive the communication element to transmit to the container data carrier at least a portion of the radiopharmaceutical information and at least a portion of the patient information.

90. The system according to claim 89, wherein the control unit is configured to receive the radiopharmaceutical information regarding a plurality of labeled

radiopharmaceutical agents, and drive the robot to automatically dispense respective doses of the labeled radiopharmaceutical agents to the container.

91. The system according to claim 89, wherein the patient information includes an identifier of an imaging protocol assigned to the patient for performance using the dose, and wherein the control unit is configured to drive the communication element to transmit the imaging protocol identifier to the container data carrier.

92. The system according to claim 89, wherein the control unit is configured to drive the communication element to transmit to the container data carrier at least one of: a time of dispensing of the labeled radiopharmaceutical agent to the container, and information regarding a radioactivity of the dose at the time of dispensing.

93. The system according to claim 89, comprising:

a mother vial that contains the labeled radiopharmaceutical agent prior to dispensing thereof; and

a computer-communicatable mother vial data carrier associated with the mother vial, which mother vial data carrier contains the radiopharmaceutical information,

wherein the control unit is configured to receive the radiopharmaceutical information from the mother vial data carrier.

94. The system according to any one of claims 89-93, wherein the radiopharmaceutical information comprises the imaging protocol information.

95. The system according to claim 94, wherein the imaging protocol information comprises SPECT imaging protocol information.

96. The system according to claim 95, wherein the imaging protocol information comprises at least one kinetic parameter of the at least one labeled radiopharmaceutical agent.

97. The system according to any one of claims 89-93, wherein the radiopharmaceutical information comprises the authenticatable information regarding the commercial license.

98. The system according to claim 97, wherein the information regarding the commercial license comprises information regarding the commercial license for use of a SPECT imaging protocol with the at least one labeled radiopharmaceutical agent.

99. The system according to claim 97, wherein the control unit is configured to

authenticate the authenticatable license information, and to drive the robot to automatically dispense the dose only upon authentication.

100. Apparatus for use with a container, the apparatus comprising:

a mother vial having a volume of at least 10 ml, which contains at least 5 ml of a non-diluted labeled radiopharmaceutical agent, and at least 5 ml of saline solution; and

an automated radiopharmaceutical dispensing system, configured to contain the mother vial, and to dispense at least one dose from the mother vial to the container.

101. A method comprising:

placing at least one labeled radiopharmaceutical agent in a container;

associating a portable computer-communicatable data carrier with the container; and

writing, to the data carrier, imaging protocol information for use with the at least one labeled radiopharmaceutical agent.

102. The method according to claim 101, comprising writing, to the data carrier, administration protocol information useful for administering the at least one labeled radiopharmaceutical agent.

103. The method according to claim 101, wherein writing the imaging protocol information comprises writing instructions for performing an imaging procedure using the at least one labeled radiopharmaceutical agent.

104. The method according to claim 101, wherein writing the imaging protocol information comprises writing an identifier of an imaging protocol.

105. The method according to claim 101, wherein writing the imaging protocol information comprises writing a parameter of the at least one labeled radiopharmaceutical agent.

106. The method according to claim 101, wherein writing the imaging protocol information comprises writing a parameter useful for configuring at least one aspect of an imaging procedure performed using the at least one labeled radiopharmaceutical agent.

107. The method according to claim 101, wherein placing comprises placing a single dose of the radiopharmaceutical agent in the container, which dose is appropriate for use with the imaging protocol information.

108. The method according to claim 101, wherein placing comprises placing, in the container, a plurality of labeled radiopharmaceutical agents mixed together.

109. The method according to claim 101, wherein the container is shaped so as to define a plurality of chambers, and wherein placing the at least one labeled radiopharmaceutical agent in the container comprises placing a plurality of labeled radiopharmaceutical agents in respective chambers.

110. The method according to any one of claims 101-109, wherein associating the data carrier comprises associating a first data carrier with the container, and wherein the method comprises:

writing a first identifier value to the first data carrier;

writing a second identifier to a second computer-communicatable data carrier;

detecting a correspondence between the first and second identifier values; and

performing an operation responsively to the detecting.

111. The method according to claim 110, wherein detecting comprises detecting the correspondence by at least one of the first and second data carriers.

112. The method according to claim 110, wherein detecting comprises detecting by a correspondence-detection element separate from the first and second data carriers.

113. The method according to claim 110, comprising writing, to at least one of the first and second data carriers, an identifier of a patient to whom the labeled radiopharmaceutical agent is to be administered.

114. The method according to claim 110, wherein writing at least one of the first and second identifier values comprises writing an identifier of a patient to whom the labeled radiopharmaceutical agent is to be administered.

115. The method according to claim 110, comprising coupling exactly one of the first and second data carriers to a patient to whom the labeled radiopharmaceutical agent is to be administered.

116. The method according to claim 110, wherein performing the operation comprises, responsively to the detecting of the correspondence, performing an imaging procedure using the at least one labeled radiopharmaceutical agent.

117. The method according to any one of claims 101-109, wherein associating the data carrier with the container comprises physically coupling the data carrier to the container.

118. The method according to claim 117, wherein the data carrier contains an identifier of a patient to whom the labeled radiopharmaceutical agent is to be administered, and wherein writing the imaging protocol information comprises writing imaging protocol information selected for the patient.

119. The method according to claim 118, wherein writing the imaging protocol information comprises writing an identifier of an imaging protocol.

120. The method according to claim 118, wherein writing the imaging protocol information comprises writing imaging protocol information customized for the patient.

121. The method according to any one of claims 101-109, wherein writing the imaging protocol information comprises writing SPECT imaging protocol information.

122. The method according to claim 121, wherein writing the SPECT imaging protocol information comprises writing dynamic SPECT imaging protocol information.

123. The method according to claim 122, wherein writing the SPECT imaging protocol information comprises writing at least one kinetic parameter of the at least one labeled radiopharmaceutical agent, the at least one kinetic parameter useful for performing a dynamic SPECT imaging procedure using the at least one labeled radiopharmaceutical agent.

124. The method according to any one of claims 101-109, comprising:

reading the imaging protocol information from the data carrier; and

performing an imaging procedure, and configuring the procedure at least in part responsively to the imaging protocol information read from the data carrier.

125. The method according to claim 124, wherein performing the imaging procedure comprises performing an image acquisition procedure, and configuring the procedure at least in part responsively to the imaging protocol information read from the data carrier.

126. The method according to claim 125, wherein performing the image acquisition procedure comprises configuring a total acquisition time of the image acquisition procedure at least in part responsively to the imaging protocol information.

127. The method according to claim 125, wherein performing the image acquisition procedure comprises performing the image acquisition procedure using a camera having a plurality of detectors, and configuring, at least in part responsively to the imaging protocol information, at least one motion of at least one of the detectors during the image

acquisition procedure.

128. The method according to claim 125, wherein performing the image acquisition procedure comprises configuring, at least in part responsively to the imaging protocol information, a waiting time between administration of the labeled radiopharmaceutical agent and commencement of the image acquisition procedure.

129. The method according to claim 125, wherein performing the image acquisition procedure comprises performing a gated image acquisition procedure at least in part responsively to the imaging protocol information.

130. The method according to claim 124, wherein performing the imaging procedure comprises performing an image reconstruction procedure, and configuring the procedure at least in part responsively to the imaging protocol information read from the data carrier.

131. The method according to claim 124, wherein performing the imaging procedure comprises performing an image analysis procedure, and configuring the procedure at least in part responsively to the imaging protocol information read from the data carrier.

132. The method according to claim 124, wherein performing the imaging procedure comprises performing a diagnostic procedure, and configuring the procedure at least in part responsively to the imaging protocol information read from the data carrier.

133. The method according to claim 124, wherein performing the imaging procedure comprises performing a three-dimensional dynamic imaging study, and configuring the study at least in part responsively to the imaging protocol information read from the data carrier.

134. The method according to any one of claims 101-109, wherein associating the data carrier with the container does not comprise physically coupling the data carrier to the container, and comprising writing, to the data carrier, an identifier of a patient to whom the labeled radiopharmaceutical agent is to be administered.

135. The method according to claim 134, comprising coupling the data carrier to the patient.

136. The method according to claim 134, wherein associating the data carrier comprises associating a first data carrier with the container, and comprising writing, to a second computer-communicatable data carrier, radiopharmaceutical information regarding the at least one labeled radiopharmaceutical agent, and physically coupling the second data

carrier to the container.

137. A method comprising:

placing at least one labeled radiopharmaceutical agent in a container;

associating a computer-communicatable data carrier with the container; and

writing, to the data carrier, authenticatable information regarding a commercial license for use of SPECT imaging protocol information with the at least one labeled radiopharmaceutical agent.

138. The method according to claim 137, comprising:

reading the authenticatable license information from the data carrier;

authenticating the authenticatable license information; and

only upon authentication, performing an imaging procedure using the SPECT imaging protocol information.

139. The method according to any one of claims 137-138, wherein associating comprises physically coupling the data carrier to the container.

140. A method comprising:

providing a portable computer-communicatable data carrier; and

writing, to the data carrier, authenticatable information regarding a commercial license for use of SPECT imaging protocol information.

141. The method according to claim 140, comprising writing, to the data carrier, patient information regarding a patient upon whom an imaging procedure using the SPECT imaging protocol information is to be performed.

142. The method according to claim 140, wherein writing the authenticatable license information comprises encrypting the authenticatable license information.

143. The method according to claim 140, comprising:

reading the authenticatable license information from the data carrier;

authenticating the authenticatable license information; and

only upon authentication, performing an imaging procedure using the SPECT imaging protocol information.

144. The method according to any one of claims 140-143, comprising coupling the data carrier to a patient upon whom an imaging procedure using the SPECT imaging protocol

information is to be performed.

145. A method comprising:

writing first and second identifier values to first and second computer-communicatable data carriers, respectively;

detecting a correspondence between the first and second identifier values; and

perform an imaging procedure on a patient responsively to the detecting.

146. The method according to claim 145, wherein detecting comprises detecting the correspondence by at least one of the first and second data carriers.

147. The method according to claim 145, wherein detecting comprises detecting by a correspondence-detection element separate from the first and second data carriers.

148. The method according to claim 145, comprising writing, to at least one of the first and second data carriers, an identifier of a patient to whom the labeled radiopharmaceutical agent is to be administered.

149. The method according to claim 145, wherein writing at least one of the first and second identifier values comprises writing an identifier of a patient to whom the labeled radiopharmaceutical agent is to be administered.

150. The method according to claim 145, comprising coupling one of the first and second data carriers to a patient to whom the labeled radiopharmaceutical agent is to be administered.

151. The method according to any one of claims 145-150, comprising:

writing, to at least one of the first and second data carriers, radiopharmaceutical information regarding at least one labeled radiopharmaceutical agent;

reading the radiopharmaceutical information from the at least one of the data carriers; and

configuring the imaging procedure at least in part responsively to the read radiopharmaceutical information.

152. The method according to claim 151, comprising placing the at least one labeled radiopharmaceutical agent in a container.

153. The method according to claim 152, comprising physically coupling one of the first and second data carriers to the container.

154. The method according to any one of claims 145-150, wherein performing the imaging procedure comprises performing a nuclear imaging procedure.

155. The method according to claim 154, wherein performing the nuclear imaging procedure comprises performing a SPECT imaging procedure.

156. A method for use with at least one labeled radiopharmaceutical agent for administration to a patient, the method comprising:

placing at least one labeled radiopharmaceutical agent in a container;

physically coupling a first computer-communicatable data carrier to the container;

writing, to the first data carrier, radiopharmaceutical information regarding the at least one labeled radiopharmaceutical agent; and

writing, to a second portable computer-communicatable data carrier, patient information regarding the patient, and imaging protocol information for use with the at least one labeled radiopharmaceutical agent.

157. The method according to claim 156, wherein writing the imaging protocol information comprises writing SPECT imaging protocol information.

158. The method according to claim 156, wherein writing the patient information comprises writing an identifier of the patient.

159. The method according to claim 156, comprising coupling the second data carrier to the patient.

160. The method according to claim 156, wherein writing the patient information to the second data carrier comprises writing a second patient identifier to the second data carrier, and comprising:

writing a first patient identifier to the first data carrier;

reading the first and second patient identifiers from the first and second data carriers, respectively; and

comparing the first patient identifier to the second patient identifier, and, upon detecting a match, generating an administration signal that triggers administration to the patient of the at least one labeled radiopharmaceutical agent contained in the container.

161. The method according to claim 156, wherein writing the imaging protocol information to the second data carrier comprises writing a second protocol identifier to the second data carrier, and comprising:

writing a first protocol identifier to the first data carrier;

reading the first and second protocol identifiers from the first and second data carriers, respectively; and

comparing the first protocol identifier to the second protocol identifier, and, upon detecting a match, generating an administration signal that triggers administration to the patient of the at least one labeled radiopharmaceutical agent contained in the container.

162. The method according to claim 156, comprising:

generating an administration signal that triggers administration to the patient of the at least one labeled radiopharmaceutical agent contained in the container; and

transmitting information regarding the administration to the second data carrier.

163. The method according to any one of claims 156-162, wherein writing the imaging protocol information to the second data carrier comprises writing imaging protocol information selected for the patient.

164. The method according to claim 163, wherein writing the imaging protocol information comprises writing an identifier of an imaging protocol.

165. The method according to claim 163, wherein writing the imaging protocol information comprises writing imaging protocol information customized for the patient.

166. The method according to any one of claims 156-162, wherein writing the patient information to the second data carrier comprises writing a second patient identifier to the second data carrier, and comprising:

writing a first patient identifier to the first data carrier;

reading the first and second patient identifiers from the first and second data carriers, respectively; and

comparing the first patient identifier to the second patient identifier, and, upon detecting a match, generating an administration signal that triggers administration to the patient of the at least one labeled radiopharmaceutical agent contained in the container.

167. The method according to claim 166, comprising automatically administering the at least one labeled radiopharmaceutical agent to the patient upon triggering by the administration signal.

168. The method according to claim 166, wherein generating the administration signal comprises instructing a healthcare worker to administer the at least one labeled

radiopharmaceutical agent to the patient.

169. A method comprising:

placing, in a container, at least one labeled radiopharmaceutical agent for administration to a patient;

associating a computer-communicatable data carrier with the container;

writing data to the data carrier regarding at least one of: the labeled radiopharmaceutical agent and the patient;

reading the data from the data carrier at a SPECT imaging system;

utilizing the read data to customize at least one function of the system selected from the group consisting of: administration of the labeled radiopharmaceutical agent, acquisition of a SPECT image of the patient to whom the labeled radiopharmaceutical agent is administered, reconstruction of the SPECT image, analysis of the SPECT image, and diagnosis of a condition of the patient based at least in part on the analysis.

170. The method according to claim 169, wherein writing the data comprises writing the data regarding the labeled radiopharmaceutical agent.

171. The method according to claim 169, wherein writing the data comprises writing the data regarding the patient.

172. The method according to claim 169, wherein utilizing the read data comprises utilizing the read data to customize the administration of the labeled radiopharmaceutical agent.

173. The method according to claim 169, wherein utilizing the read data comprises utilizing the read data to customize the acquisition of a SPECT image of the patient to whom the labeled radiopharmaceutical agent is administered.

174. The method according to claim 169, wherein utilizing the read data comprises utilizing the read data to customize the reconstruction of the SPECT image.

175. The method according to claim 169, wherein utilizing the read data comprises utilizing the read data to customize the analysis of the SPECT image.

176. The method according to any one of claims 169-175, wherein utilizing the read data comprises utilizing the read data to customize the diagnosis of a condition of the patient based at least in part on the analysis.

177. A method for use with a container containing at least one labeled radiopharmaceutical agent for administration to a patient, and data regarding at least one of: the labeled radiopharmaceutical agent and the patient, the method comprising:

reading the data at a SPECT imaging system; and

utilizing the read data to customize at least one function of the system selected from the group consisting of: administration of the labeled radiopharmaceutical agent, acquisition of a SPECT image of the patient to whom the labeled radiopharmaceutical agent is administered, reconstruction of the SPECT image, analysis of the SPECT image, and diagnosis of a condition of the patient based at least in part on the analysis.

178. The method according to claim 177, comprising writing the data to the container.

179. A method for use with a container and a computer-communicatable container data carrier associated with the container, the method comprising:

receiving, by an automated radiopharmaceutical dispensing system, radiopharmaceutical information regarding at least one labeled radiopharmaceutical agent, the radiopharmaceutical information selected from the group consisting of: imaging protocol information for use with the at least one labeled radiopharmaceutical agent, and authenticatable information regarding a commercial license for use of an imaging protocol with the at least one labeled radiopharmaceutical agent;

receiving, by the dispensing system, patient information regarding a patient;

automatically robotically dispensing, by the dispensing system, a dose of the labeled radiopharmaceutical agent to the container; and

transmitting to the container data carrier, by the dispensing system, at least a portion of the radiopharmaceutical information and at least a portion of the patient information.

180. The method according to claim 179, wherein receiving the radiopharmaceutical information comprises receiving the radiopharmaceutical information regarding a plurality of labeled radiopharmaceutical agents, and wherein dispensing comprises dispensing respective doses of the labeled radiopharmaceutical agents to the container.

181. The method according to claim 179, wherein the patient information includes an identifier of an imaging protocol assigned to the patient for performance using the dose, and wherein transmitting comprises transmitting the imaging protocol identifier to the container data carrier.

182. The method according to claim 179, wherein transmitting comprises transmitting to the container data carrier at least one of: a time of dispensing of the labeled radiopharmaceutical agent to the container, and information regarding a radioactivity of the dose at the time of dispensing.

183. The method according to claim 179, wherein receiving the radiopharmaceutical information comprises:

providing, to the dispensing system, a mother vial that contains the labeled radiopharmaceutical agent prior to dispensing thereof, and a computer-communicatable mother vial data carrier associated with the mother vial, which mother vial data carrier contains the radiopharmaceutical information; and

receiving the radiopharmaceutical information from the mother vial data carrier.

184. The method according to any one of claims 179-183, wherein receiving the radiopharmaceutical information comprises receiving the imaging protocol information.

185. The method according to claim 184, wherein receiving the imaging protocol information comprises receiving SPECT imaging protocol information.

186. The method according to claim 185, wherein receiving the imaging protocol information comprises receiving at least one kinetic parameter of the at least one labeled radiopharmaceutical agent.

187. The method according to any one of claims 179-183, wherein receiving the radiopharmaceutical information comprises receiving the authenticatable information regarding the commercial license.

188. The method according to claim 187, wherein receiving the information regarding the commercial license comprises receiving information regarding the commercial license for use of a SPECT imaging protocol with the at least one labeled radiopharmaceutical agent.

189. The method according to claim 187, wherein dispensing comprises authenticating the authenticatable license information, and dispensing the dose only upon authentication.

190. A method for automatically dispensing a labeled radiopharmaceutical agent to a container, comprising:

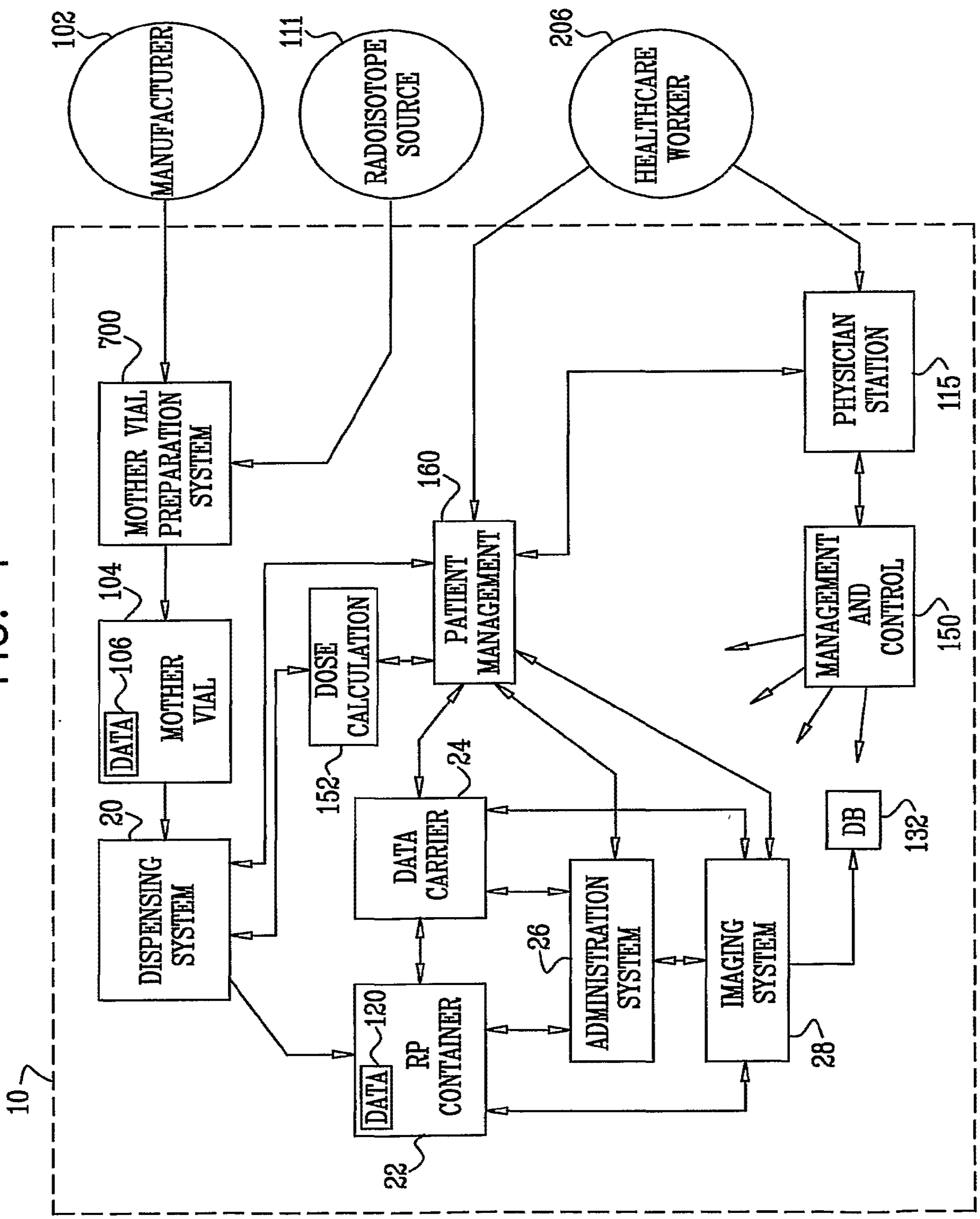
providing a mother vial having a volume of at least 10 ml;

filling the mother vial with at least 5 ml of a non-diluted labeled radiopharmaceutical agent, and with at least 5 ml of saline solution;

placing the mother vial in an automated radiopharmaceutical dispensing system; and

dispensing at least one dose from the mother vial to the container.

FIG. 1



MANUFACTURER
102
RADIOISOTOPE SOURCE
111
HEALTHCARE WORKER
206
MOTHER VIAL PREPARATION SYSTEM
700
DATA
MOTHER VIAL
104
106
DISPENSING SYSTEM
20
DOSE CALCULATION
152
PATIENT MANAGEMENT
160
DATA CARRIER
24
DATA
RP CONTAINER
120
22
ADMINISTRATION SYSTEM
26
IMAGING SYSTEM
28
DB
132
PHYSICIAN STATION
115
MANAGEMENT AND CONTROL
150
10

FIG. 2

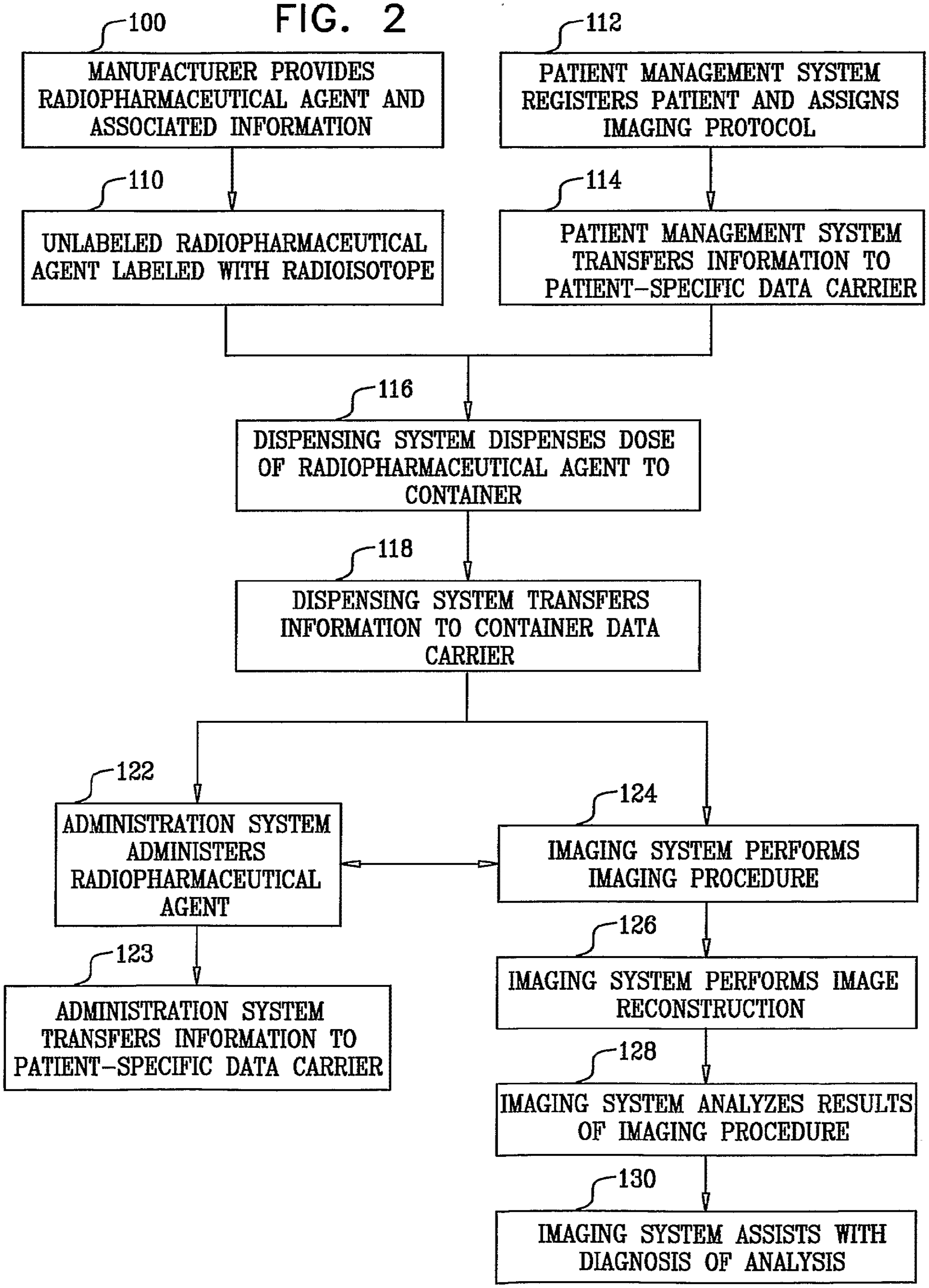

100
MANUFACTURER PROVIDES RADIOPHARMACEUTICAL AGENT AND ASSOCIATED INFORMATION
112
PATIENT MANAGEMENT SYSTEM REGISTERS PATIENT AND ASSIGNS IMAGING PROTOCOL
110
UNLABELED RADIOPHARMACEUTICAL AGENT LABELED WITH RADIOISOTOPE
114
PATIENT MANAGEMENT SYSTEM TRANSFERS INFORMATION TO PATIENT-SPECIFIC DATA CARRIER
116
DISPENSING SYSTEM DISPENSES DOSE OF RADIOPHARMACEUTICAL AGENT TO CONTAINER
118
DISPENSING SYSTEM TRANSFERS INFORMATION TO CONTAINER DATA CARRIER
122
ADMINISTRATION SYSTEM ADMINISTERS RADIOPHARMACEUTICAL AGENT
124
IMAGING SYSTEM PERFORMS IMAGING PROCEDURE
123
ADMINISTRATION SYSTEM TRANSFERS INFORMATION TO PATIENT-SPECIFIC DATA CARRIER
126
IMAGING SYSTEM PERFORMS IMAGE RECONSTRUCTION
128
IMAGING SYSTEM ANALYZES RESULTS OF IMAGING PROCEDURE
130
IMAGING SYSTEM ASSISTS WITH DIAGNOSIS OF ANALYSIS

FIG. 3

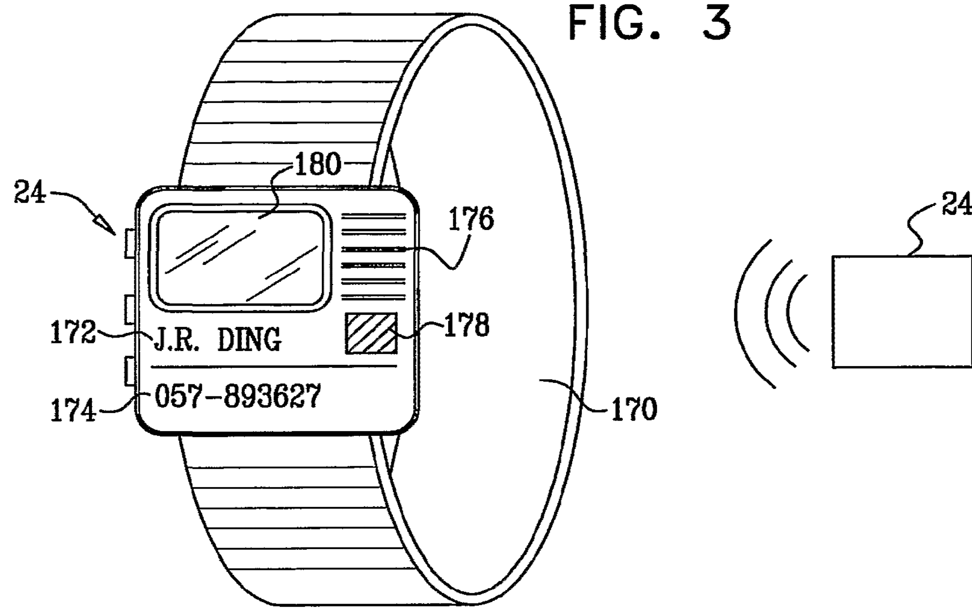

180
24
176
240
172
J.R. DING
178
174
057-893627
170

FIG. 4

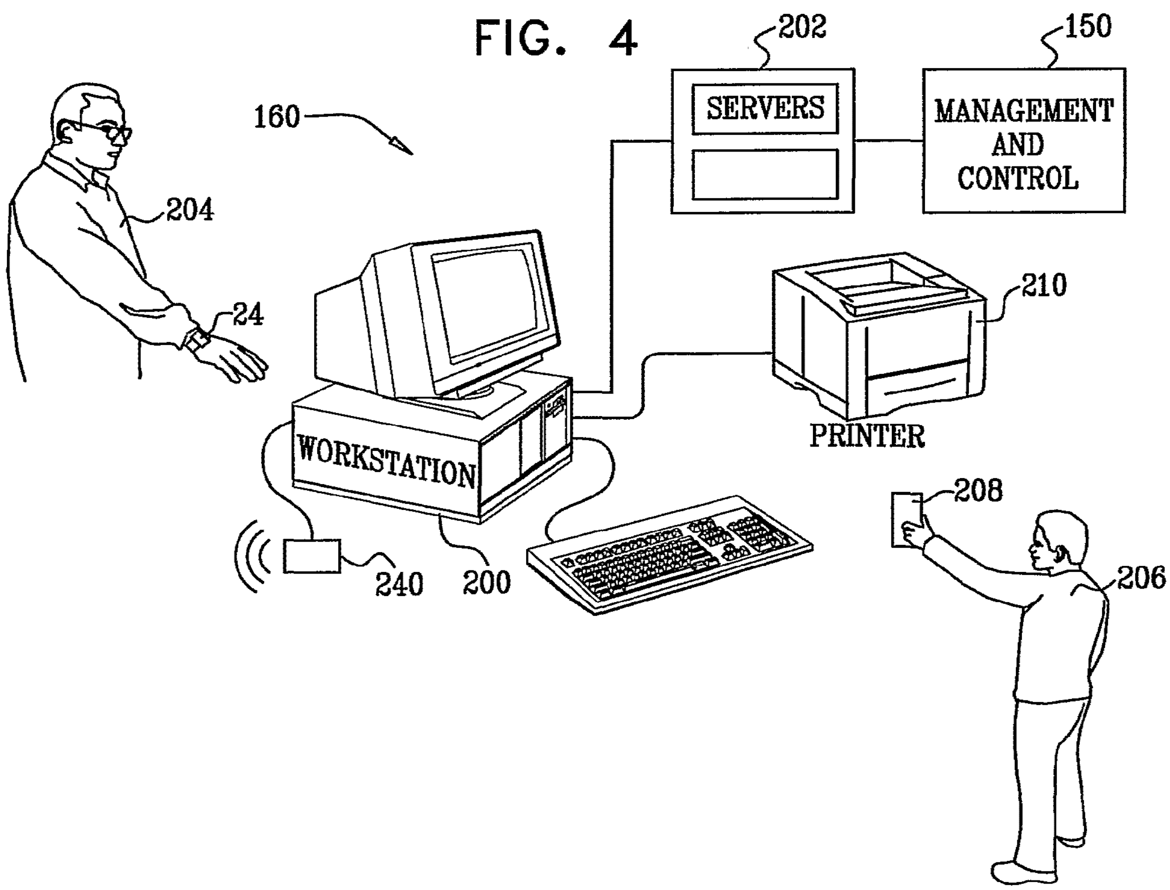

202
150
SERVERS
MANAGEMENT AND CONTROL
160
204
24
210
PRINTER
WORKSTATION
208
206
240
200

FIG. 5

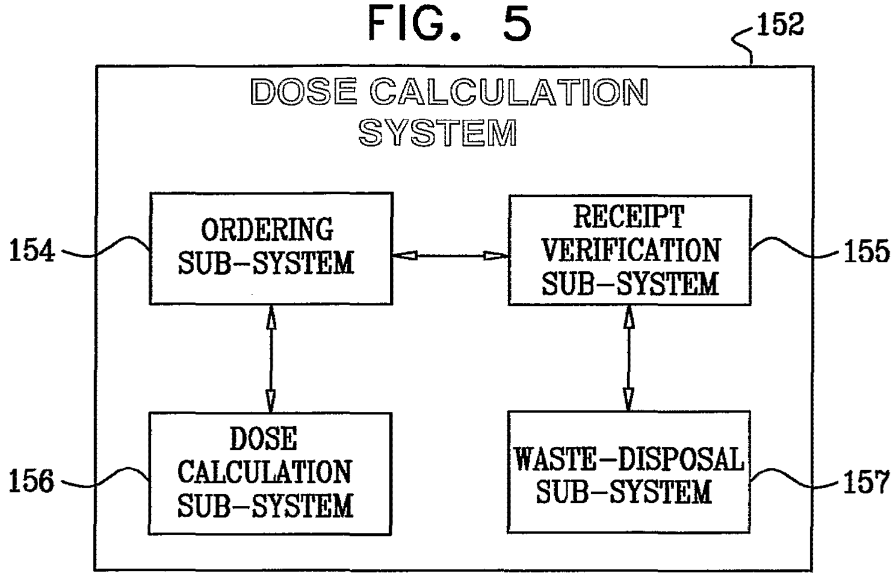

152
DOSE CALCULATION SYSTEM
154
ORDERING SUB-SYSTEM
RECEIPT VERIFICATION SUB-SYSTEM
155
156
DOSE CALCULATION SUB-SYSTEM
WASTE-DISPOSAL SUB-SYSTEM
157

FIG. 6A

	REST PHASE				STRESS PHASE				
	INJECTION		WAITING TIME [MIN]	ACQUISITION DURATION [MIN]	STRESS	INJECTION		WAITING TIME [MIN]	GATED ACQUISITION DURATION [MIN]
	RP	DOSE [mCi]				RP	DOSE [mCi]		
SINGLE ISOTOPE/ LOW DOSE/FAST IMAGING	TL	<0.3	2	15	EXERCISE	TL	<3	10–15	1.5
DUAL ISOTOPE/ LOW DOSE/FAST IMAGING	TL	<0.3	2	15	EXERCISE	Tc–MIBI	30	30–60	1.5
GATED REST THALLIUM (STUNNING)	TL	1.5	2	5 (GATED)	EXERCISE	Tc–MIBI	30	30–60	1.5
THALLIUM STRESS PERFUSION	Tc–MIBI	3	30	1.5	PHARMA	TL	3	0	10 (DYNAMIC)
SIMULTANEOUS DUAL ISOTOPE STRESS PERFUSION	Tc–MIBI	3	20		EXERCISE/PHARMA	TL	3		10 (DYNAMIC)
DYNAMIC IMAGING	TL	0.3			PHARMA (ADENOSINE)	TL	3		10 (DYNAMIC)

FIG. 6B

NO.	PROTOCOL NAME	KEY FEATURES AND PROPERTIES	ADMINISTRATION PARAMETERS			DETECTOR PARAMETERS
			DOSE (mCi)	INJECTION PROFILE	INJECT TO ACQUISITION TIME	DETECTED PHOTON ENERGY / RESOLUTION
A	CARDIAC MAPPING	MIBI-TC, FAST, BEFORE LIVER UPTAKE	20-40	BOLUS	2 MIN, OR ADMIN UNDER THE CAMERA	140 KeV / 15%
B	CARDIAC MAPPING	MIBI-TC AFTER LIVER UPTAKE	20-40	BOLUS	30+ MIN	140 KeV / 15%
C	CARDIAC MAPPING	SIMULTANEOUS FAST DUAL-ISOTOPE TL-201+ LOW DOSE MIBI-TC	TL-201: 3.5-5; MIBI-Tc-99m: 4-8	2 BOLUS (BEFORE AND AT PEAK STRESS)	TL INJECTED PREVIOUSLY AT REST, TC UNDER CAMERA OR 2 MIN	Tc-140 KeV, Tl-72 KeV / 15%
D	CARDIAC MAPPING	SIMULTANEOUS DUAL-ISOTOPE TL-201+ LOW DOSE MIBI-TC	TL-201: 3.5-5; MIBI-Tc-99m: 4-8	2 BOLUS (BEFORE AND AT PEAK STRESS)	SAME AS ONE OF FIRST 2 CARDIAC MAPPING PROTOCOLS	Tc-140 KeV, Tl-72 KeV / 15%
E	CARDIAC MAPPING	SIMULTANEOUS DUAL-ISOTOPE FULL TL-201+ FULL DOSE MIBI-TC	TL-201: 3.5-5; MIBI-Tc-99m: 20-40	2 BOLUS (BEFORE AND AT PEAK STRESS)	SAME AS ONE OF PROTOCOLS A OR B	Tc-140 KeV, Tl-167 KeV / 10%
F	CARDIAC MAPPING - UNDERWEIGHT (**BMI<18.5**)	MIBI-TC-99M AFTER LIVER UPTAKE	15-20	BOLUS	30+ MIN	140 KeV / 15%
G1	CARDIAC MAPPING - NORMAL (**18.6<BMI<24.9**)	MIBI-TC-99M AFTER LIVER UPTAKE	20-30	BOLUS	30+ MIN	140 KeV / 10%
G2	CARDIAC MAPPING - OVERWEIGHT (**25<BMI<29.9**)	MIBI-TC-99M AFTER LIVER UPTAKE	30-35	BOLUS	30+ MIN	140 KeV / 10%

FIG. 6C

NO.	SCANNING PARAMETERS						ANALYSIS PARAMETERS	
	TOTAL SCAN TIME	COLUMNS DIFFERENCES / UNIFORM SCAN	ANGULAR RANGE	TOTAL # ANGULAR ORIENT-TATIONS	ANGULAR STEP / INTERLACE	DWELL TIME	GATED ANALYSIS OF VOLUMES	ANALYSIS ALGORITHM / PARAMETERS
A	120 SEC	a) 4 X OUTER b) 6 X INNER	a) 40-60 DEG b) 90-120 DEG	120X10	a) 0.3-0.5 DEG b) 0.75-1 DEG	1 SEC	YES, 16-32 FRAMES	INTENSITY IMAGE, EJECTION FRACTION
B	120 SEC	a) 4 X OUTER b) 6 X INNER	a) 40-60 DEG b) 90-120 DEG	120X10	a) 0.3-0.5 DEG b) 0.75-1 DEG	1 SEC	YES, 16-32 FRAMES	INTENSITY IMAGE, EJECTION FRACTION
C	120 SEC	a) 4 X OUTER b) 6 X INNER	a) 40-60 DEG b) 90-120 DEG	120X10	a) 0.3-0.5 DEG b) 0.75-1 DEG	1 SEC	YES, 16-32 FRAMES	INTENSITY IMAGE, EJECTION FRACTION
D	120 SEC	a) 4 X OUTER b) 6 X INNER	a) 40-60 DEG b) 90-120 DEG	120X10	a) 0.3-0.5 DEG b) 0.75-1 DEG	1 SEC	YES, 16-32 FRAMES	INTENSITY IMAGE, EJECTION FRACTION
E	UP TO 1200 SEC	a) 4 X OUTER b) 6 X INNER	a) 40-60 DEG b) 90-120 DEG	240X10	a) 0.15-0.25 DEG b) 0.375-0.5 DEG	5 SEC	YES, 16-32 FRAMES	INTENSITY IMAGE, EJECTION FRACTION
F	90 SEC	a) 4 X OUTER b) 6 X INNER	a) 20-35 DEG b) 45-60 DEG	60X10	a) .3-.75 DEG b) 0.75-1DEG	1 SEC	YES, 16-32 FRAMES	INTENSITY IMAGE, EJECTION FRACTION
G1	120 SEC	a) 4 X OUTER b) 6 X INNER	a) 30-45 DEG b) 75-90 DEG	120X10	a) 0.5-0.75 DEG b) 0.625-1 DEG	1.5 SEC	YES, 16-32 FRAMES	INTENSITY IMAGE, EJECTION FRACTION
G2	120 SEC	a) 4 X OUTER b) 6 X INNER	a) 40-60 DEG b) 90-120 DEG	120X10	a) 0.3-0.5 DEG b) 0.75-1 DEG	2 SEC	YES, 16-32 FRAMES	INTENSITY IMAGE, EJECTION FRACTION

FIG. 6D

NO.	PROTOCOL NAME	KEY FEATURES AND PROPERTIES	ADMINISTRATION PARAMETERS			DETECTOR PARAMETERS
			DOSE (mCi)	INJECTION PROFILE	INJECT TO ACQUISITION TIME	DETECTED PHOTON ENERGY / RESOLUTION
H	CARDIAC MAPPING - OBESE (BMI>30)	MIBI-TC AFTER LIVER UPTAKE	35-40	BOLUS	30+ MIN	140 KeV / 6%
I	CARDIAC DYNAMIC MAPPING	TEBOROXIME-TC	20-40	BOLUS	-1 MIN (IMAGE BEFORE INJECT), OR SIMULTANEOUSLY WITH INJECT	140 KeV / 15%
J	CARDIAC DYNAMIC MAPPING (2-STEP)	TEBOROXIME-TC	20-40	(i) INITIAL SMALL BOLUS FOR IDENTIFYING ROI, (ii) FULL BOLUS FOR DYNAMIC STUDY	(i) 5+ MIN (ii) -1 MIN (IMAGE BEFORE INJECT)	140 KeV / 15%
K	TUMOR SCAN (MULTIPLE BODY SEGMENTS - HEAD TO LEGS)	MDP-TC-99M AFTER LIVER UPTAKE	20-40	BOLUS	30+ MIN	140 KeV / 15%
L	TUMOR SCAN (MULTIPLE BODY SEGMENTS - HEAD TO LEGS), FOCUSED SCAN	MDP-TC-99M AFTER LIVER UPTAKE	20-40	BOLUS	30+ MIN	140 KeV / 15%
M	TUMOR SCAN WITH COCKTAIL (MULTIPLE BODY SEGMENTS - HEAD TO LEGS), FOCUSED SCAN	FDG (METABOLISM), MIBI-TC-99M AND TL (PERFUSION)	TL-201: 3.5-5; MIBI-TC-99M: 20-40; 18-F FDG 10-30	BOLUS	30+ MIN	Tc-140 KeV, Tl-72 KeV, FDG 511 KeV / 10%

FIG. 6E

NO.	SCANNING PARAMETERS						ANALYSIS PARAMETERS	
	TOTAL SCAN TIME	COLUMNS DIFFERENCES / UNIFORM SCAN	ANGULAR RANGE	TOTAL # ANGULAR ORIENT-TATIONS	ANGULAR STEP / INTERLACE	DWELL TIME	GATED ANALYSIS OF VOLUMES	ANALYSIS ALGORITHM / PARAMETERS
H	180 SEC	a) 4 X OUTER b) 6 X INNER	a) 40-60 DEG b) 90-120 DEG	160X10	a) 0.25-0.375 DEG b) 0.6-0.75 DEG	1.2 SEC	YES, 8-16 FRAMES	INTENSITY IMAGE, EJECTION FRACTION
I	<= 600 SEC	a) 2 X OUTER b) 8 X INNER	a) 40-60 DEG b) 90-120 DEG	600X10	a) continuous b) continuous INTERLACED SCAN	1 SEC	YES, 8 FRAMES	KINETIC PARAMETES, PREDEFINED PATHOLOGICAL VALUES
J	(i) 60 SEC FOR IDENTIFYING ROI (ii) 600 SEC DYNAMIC STUDY	a) 2 X OUTER b) 8 X INNER	a) 40-60 DEG b) 90-120 DEG	(i) 60X10 (ii) 600X10	(i) a) 0.75-1 DEG b) 0.75-0.75-1 DEG (ii) a) continuous b) continuous INTERLACED SCAN	1 SEC	YES, 8 FRAMES	KINETIC PARAMETES, PREDEFINED PATHOLOGICAL VALUES
K	240 SEC PER BODY SEGMENT	16	40-60 DEG	120X16	0.3-0.5 DEG	2 SEC	NO	INTENSITY IMAGE, PREDEFINED PATHOLOGICAL VALUES
L	(i) 120 SEC PER BODY SEGMENT (ii) 60 SEC PER ROI	16	(i) 45-60 DEG (ii) 15-20 DEG	(i) 120X16 (ii) 60x16	(i) 0.375-0.5 DEG (ii) 0.25-0.3	1 SEC	NO	INTENSITY IMAGE, PREDEFINED PATHOLOGICAL VALUES
M	(i) 120 SEC PER BODY SEGMENT (ii) 60 SEC PER ROI	16	(i) 45-60 DEG (ii) 15-20 DEG	(i) 120X16 (ii) 60x16	(i) 0.375-0.5 DEG (ii) 0.25-0.4	1 SEC	NO	INTENSITY IMAGE, PREDEFINED PATHOLOGICAL VALUES

FIG. 7

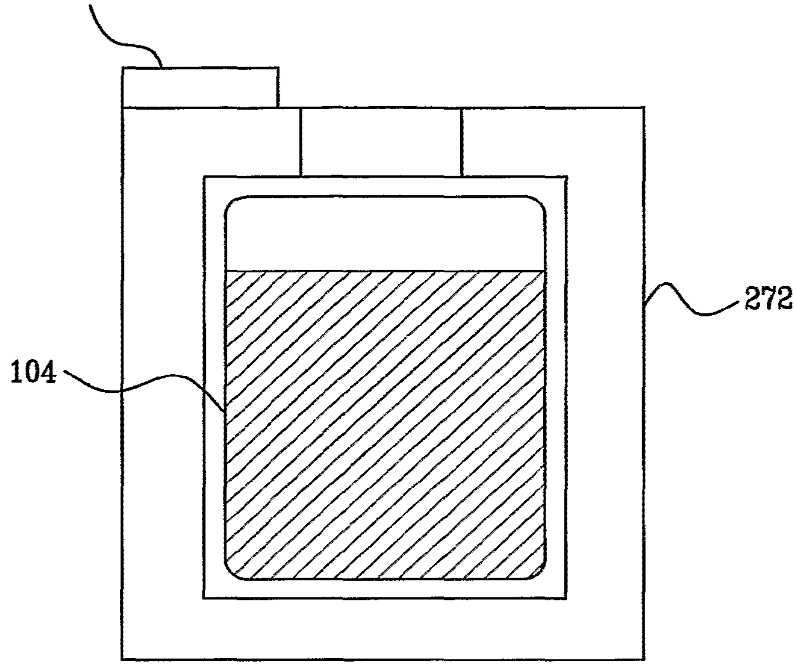


FIG. 8

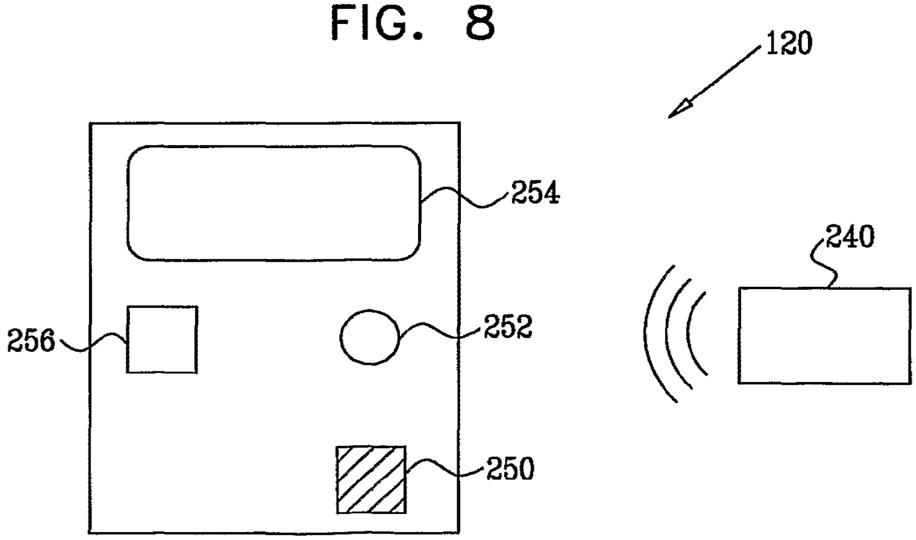


FIG. 9A

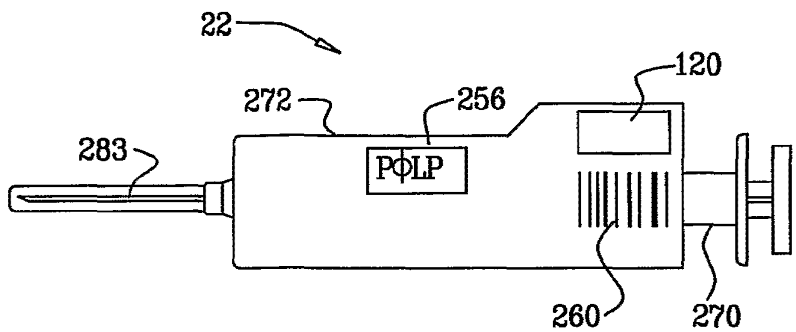


FIG. 9B

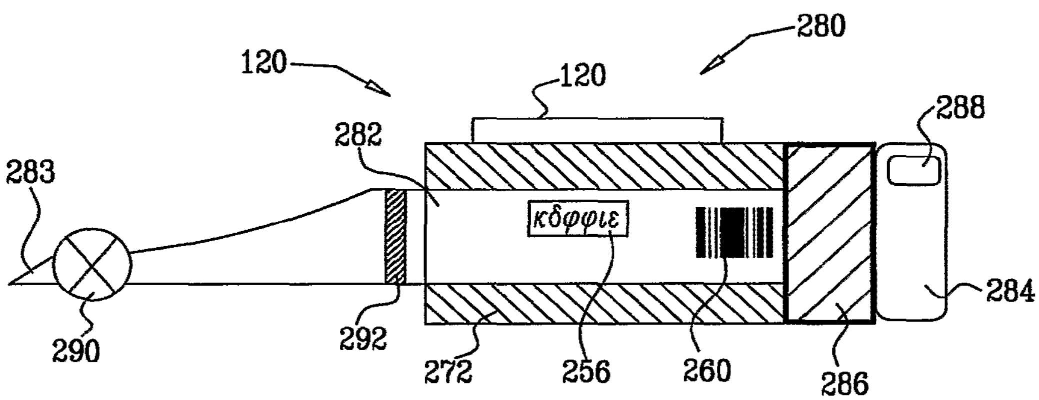


FIG. 9C

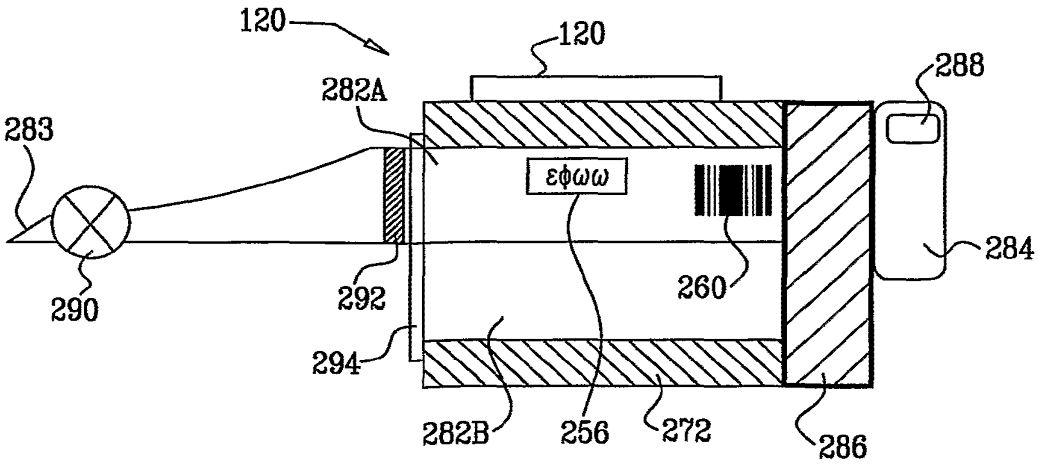


FIG. 9D

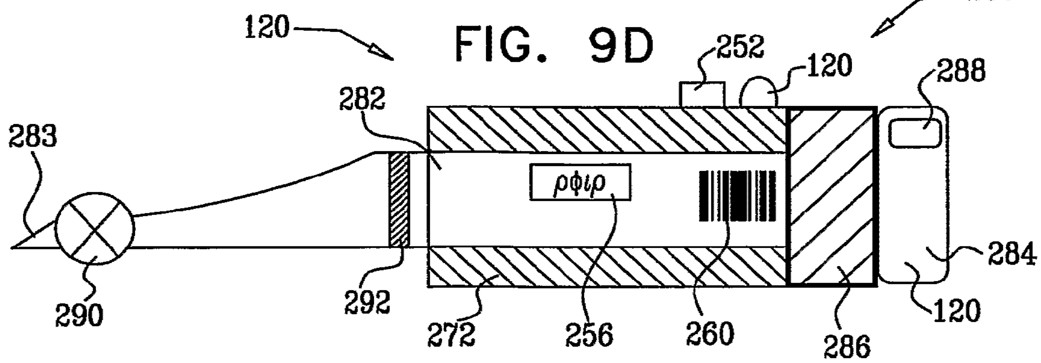


FIG. 9E

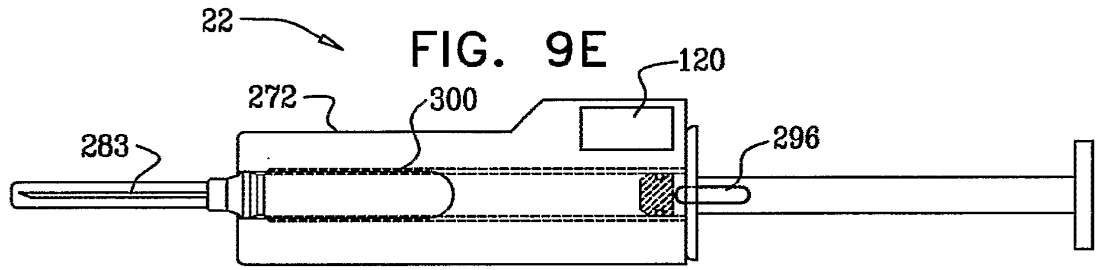


FIG. 9F

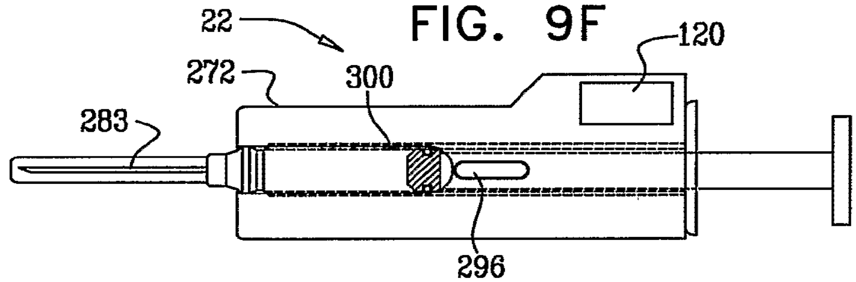


FIG. 9G

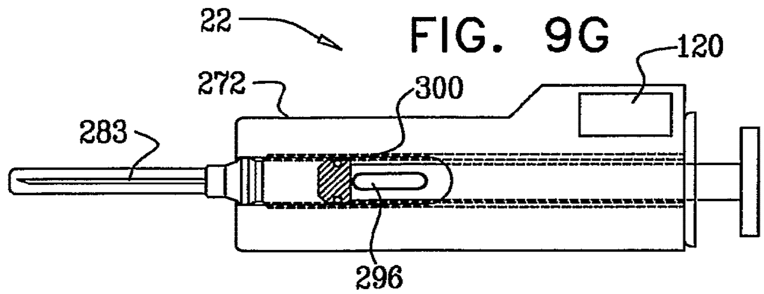


FIG. 9H

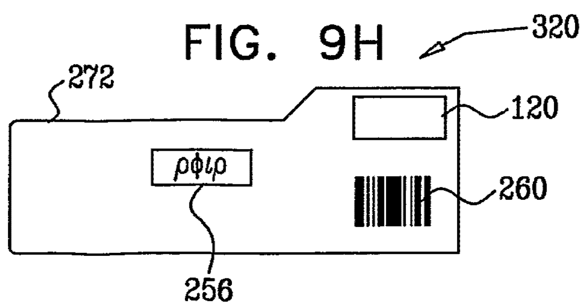


FIG. 10

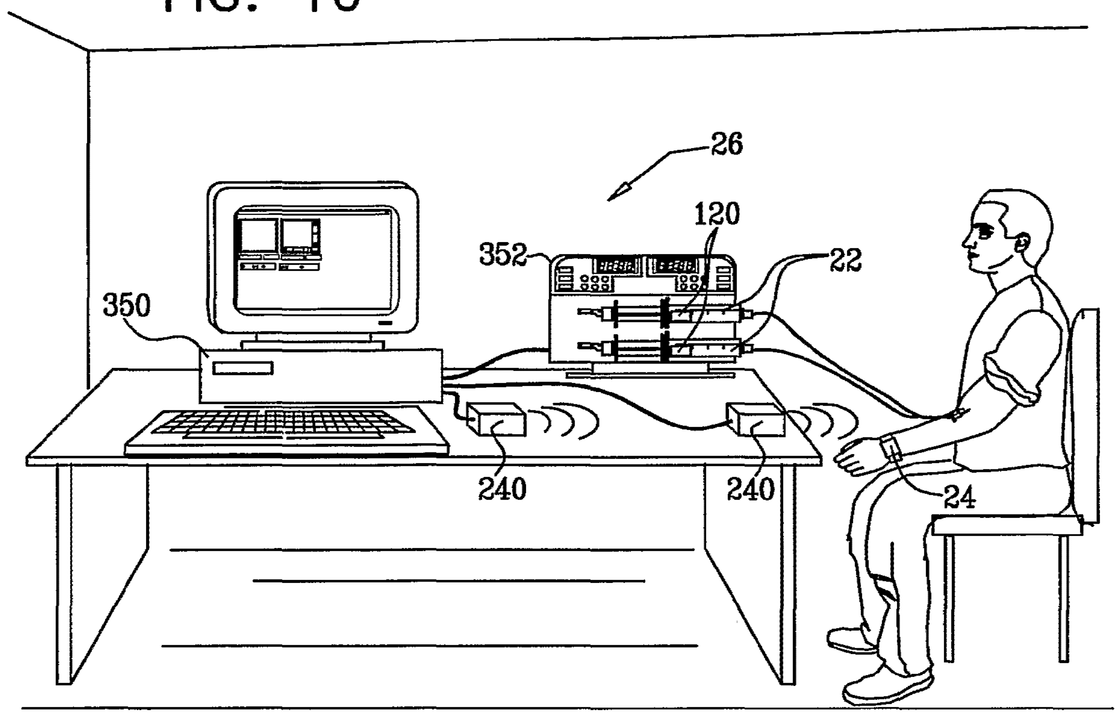
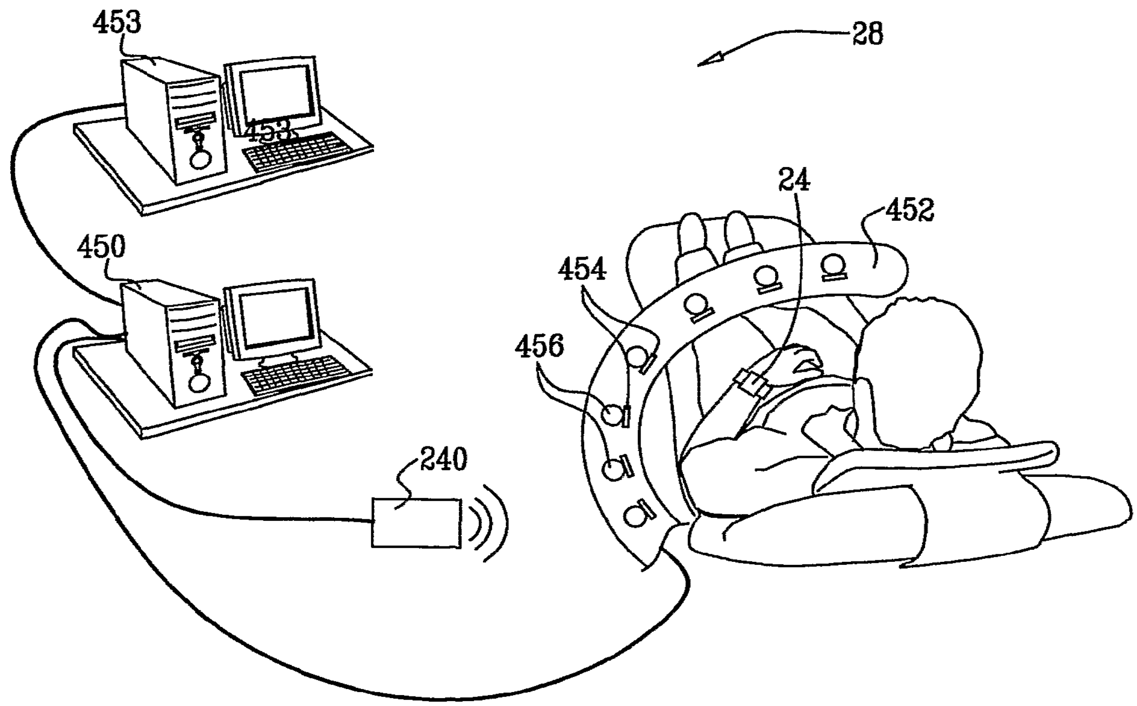


FIG. 11



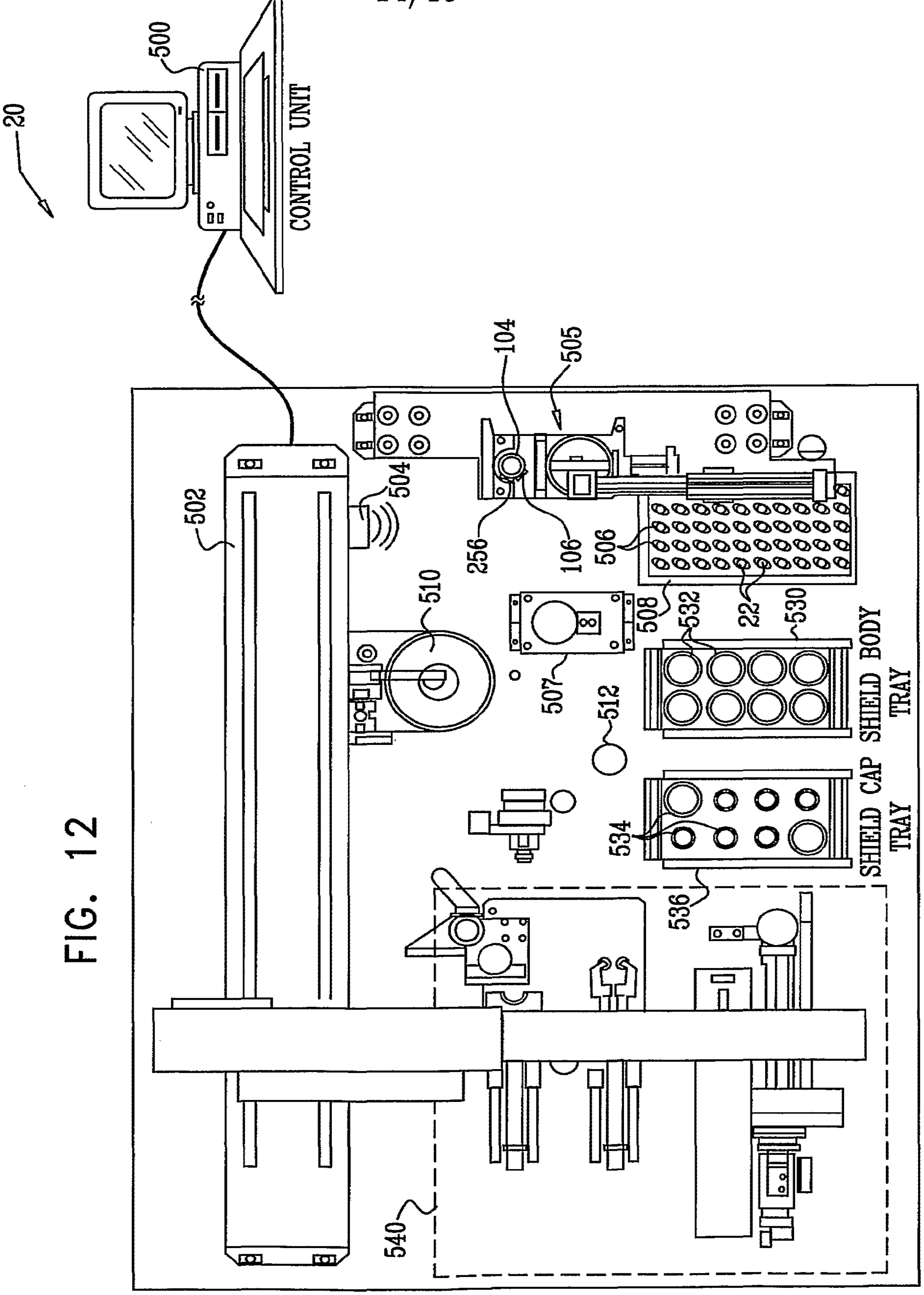

20
500
CONTROL UNIT
104
505
504
502
256
106
506
510
508
532
22
530
SHIELD BODY TRAY
507
512
SHIELD CAP TRAY
534
536
540

FIG. 12

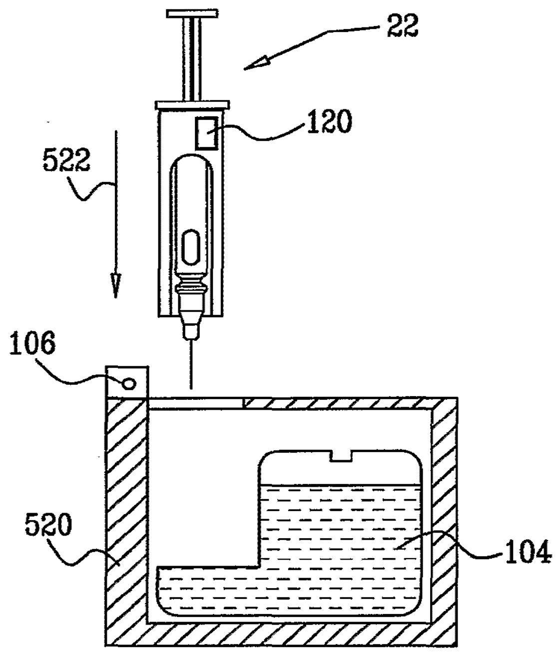


FIG. 13A

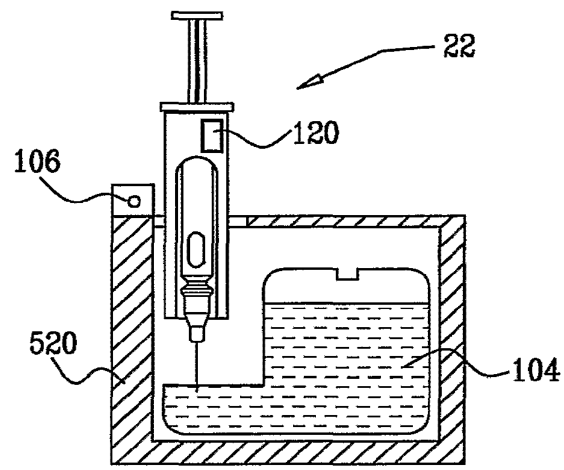


FIG. 13B

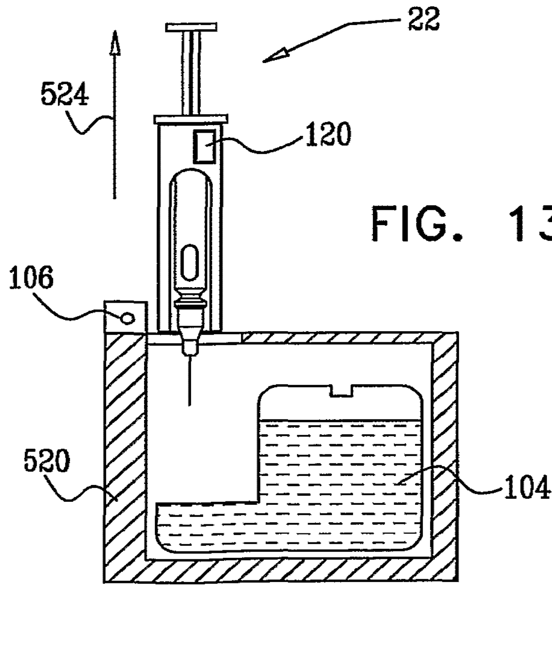


FIG. 13C

FIG. 14

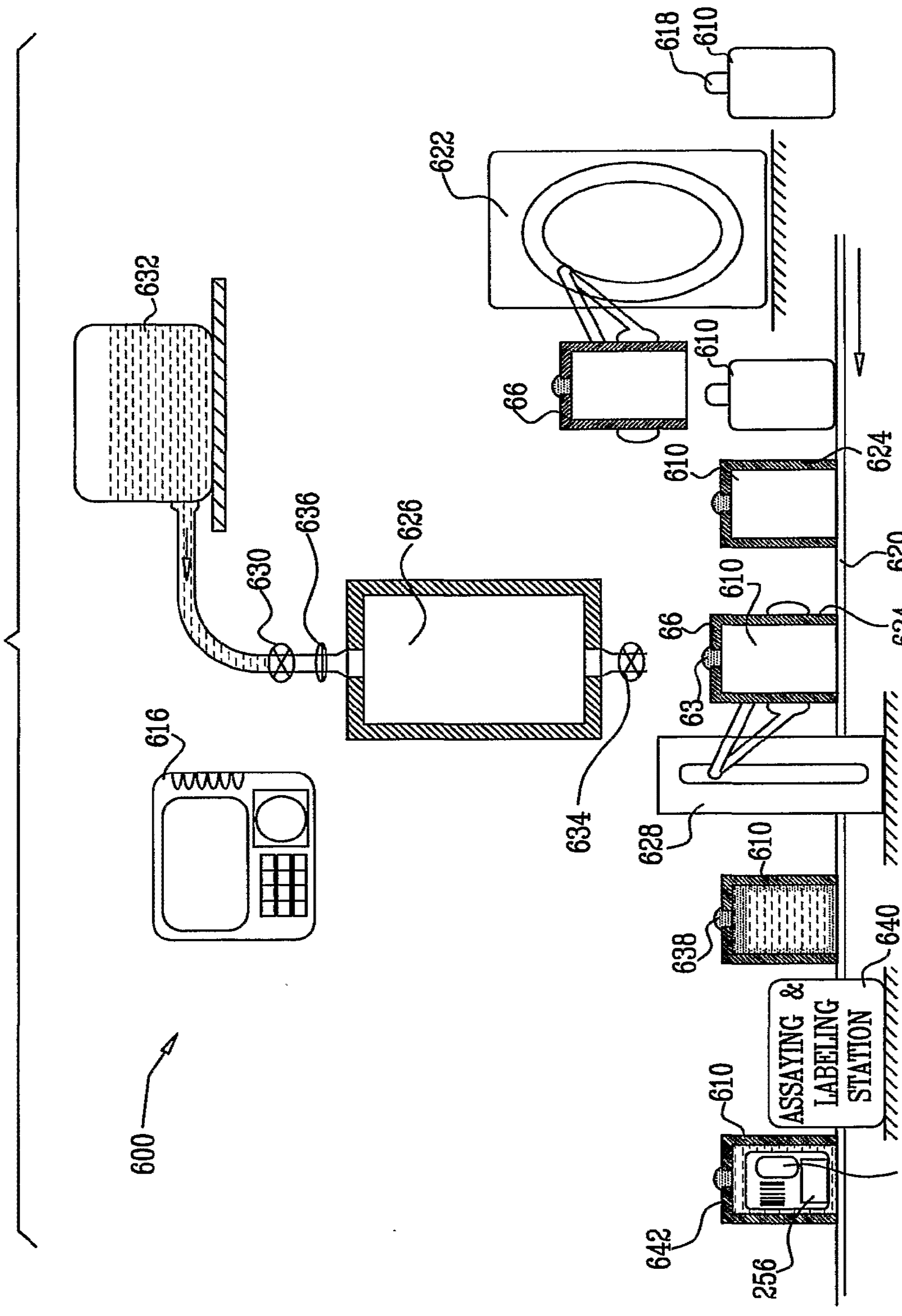

600
616
632
630
636
626
634
622
66
610
618
624
620
63
628
638
640
ASSAYING & LABELING STATION
612
642
256

FIG. 15

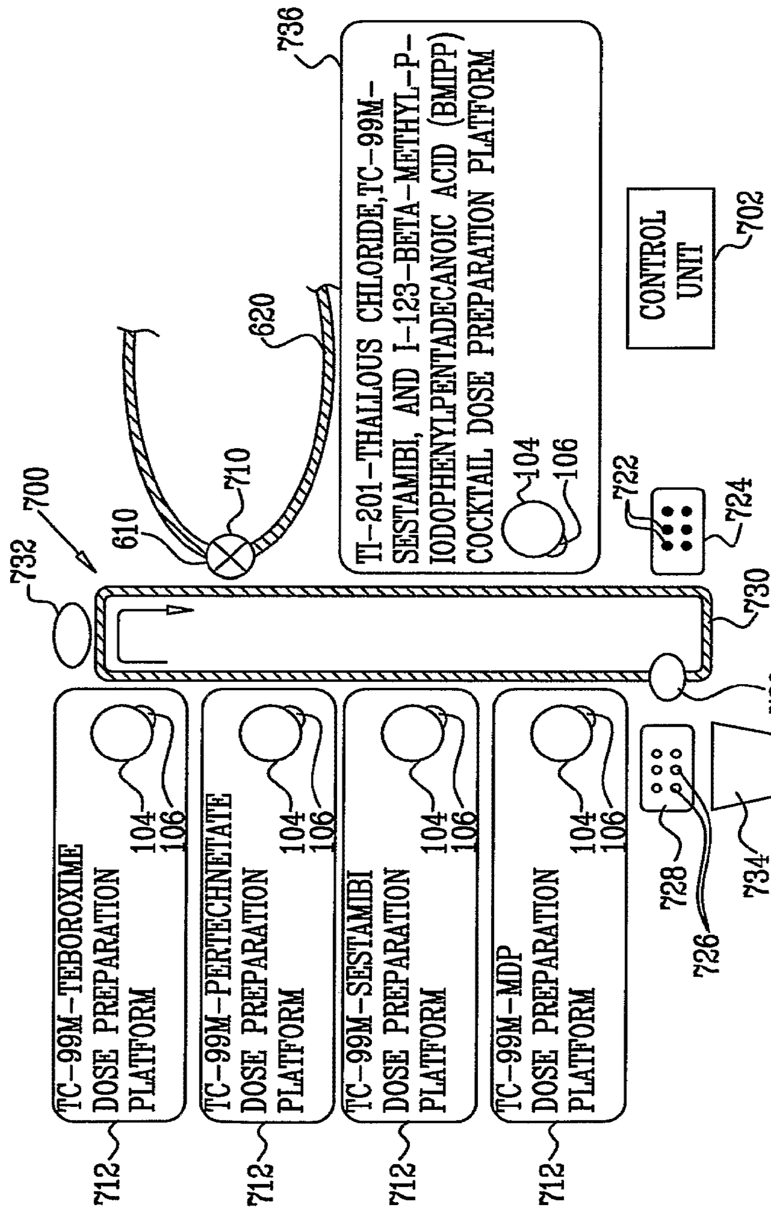

700
732
610
710
620
736
TI-201-THALLOUS CHLORIDE,TC-99M-SESTAMIBI, AND I-123-BETA-METHYL-P-IODOPHENYLPENTADECANOIC ACID (BMIPP) COCKTAIL DOSE PREPARATION PLATFORM
104
106
CONTROL UNIT
702
722
724
730
720
TC-99M-TEBOROXIME DOSE PREPARATION PLATFORM
TC-99M-PERTECHNETATE DOSE PREPARATION PLATFORM
TC-99M-SESTAMIBI DOSE PREPARATION PLATFORM
TC-99M-MDP DOSE PREPARATION PLATFORM
712
728
726
734

FIG. 16A

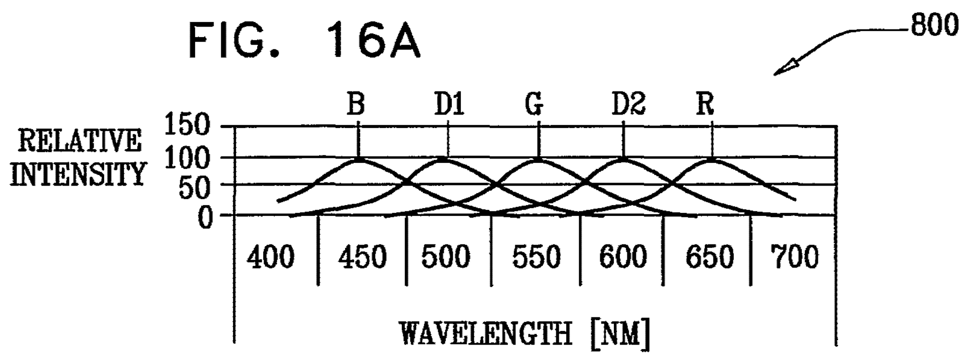


FIG. 16B

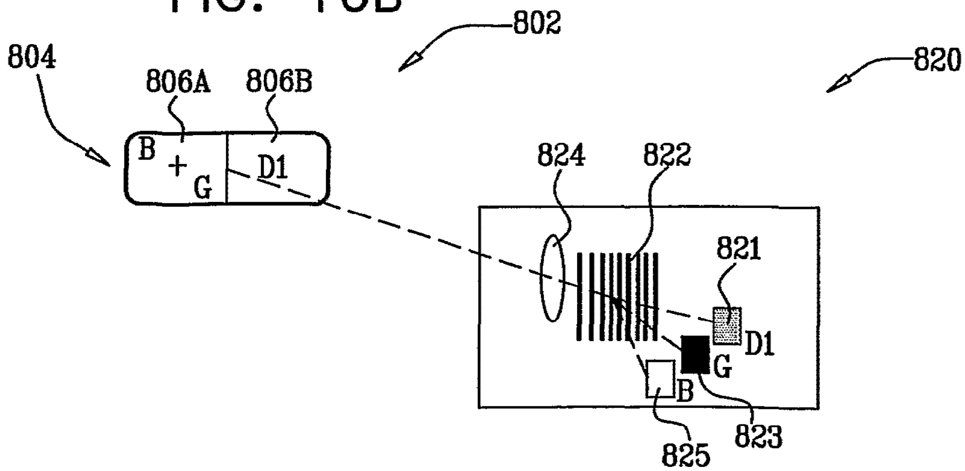


FIG. 17

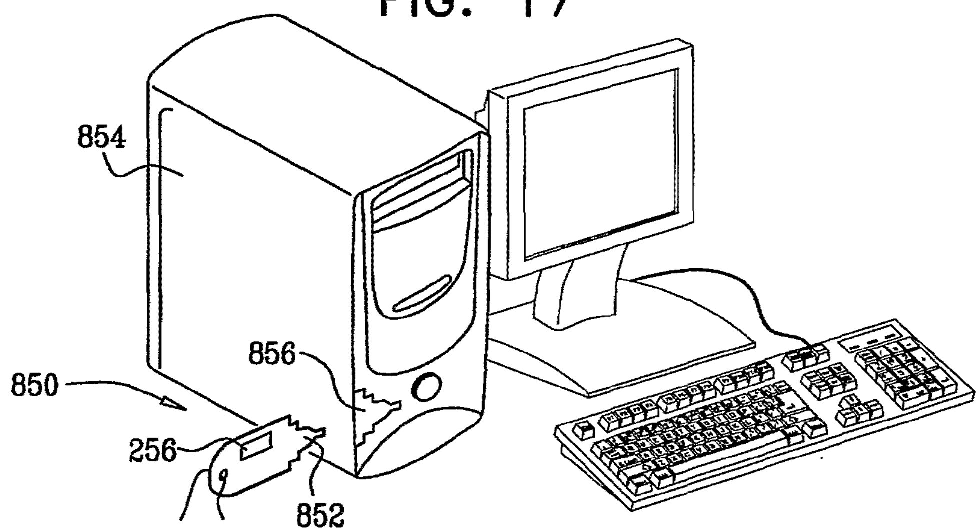
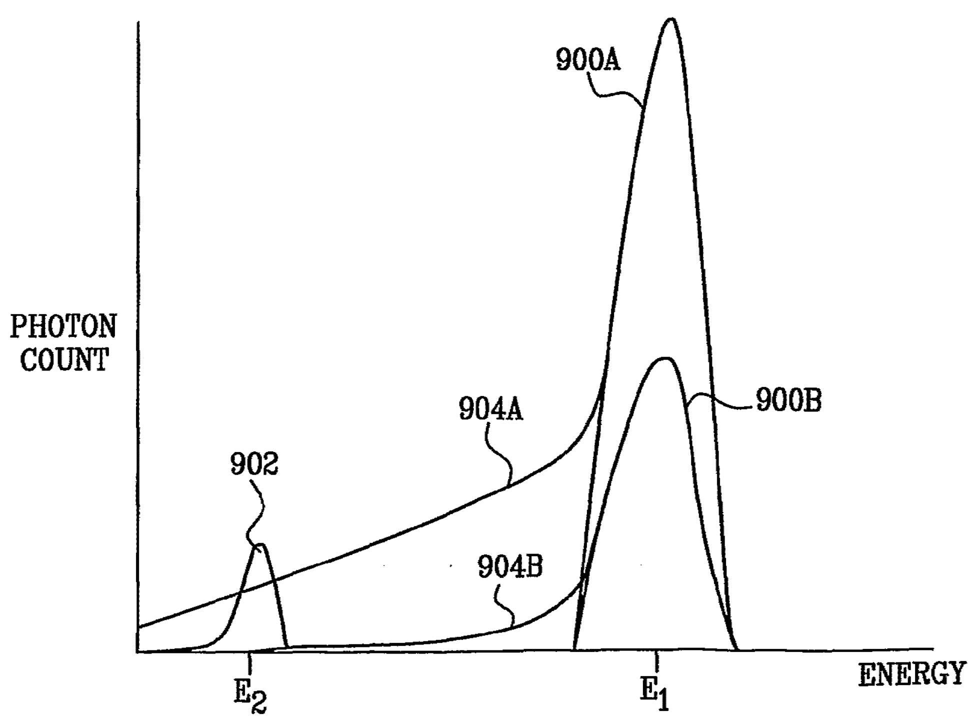

854
856
850
256
852

FIG. 18


900A
PHOTON COUNT
904A
900B
902
904B
E2
E1
ENERGY

(12) DEMANDE INTERNATIONALE PUBLIÉE EN VERTU DU TRAITÉ DE COOPÉRATION EN MATIÈRE DE BREVETS (PCT)

(19) **Organisation Mondiale de la Propriété Intellectuelle**
Bureau international

(43) **Date de la publication internationale**
3 avril 2008 (03.04.2008)

PCT

(10) **Numéro de publication internationale**
WO 2008/037939 A2

(51) **Classification internationale des brevets :**
A61M 5/14 (2006.01) ***G21F 5/00*** (2006.01)
A61M 5/168 (2006.01) ***G01T 1/161*** (2006.01)

(21) **Numéro de la demande internationale :** PCT/FR2007/052048

(22) **Date de dépôt international :** 28 septembre 2007 (28.09.2007)

(25) **Langue de dépôt :** français

(26) **Langue de publication :** français

(30) **Données relatives à la priorité :**
0608586 29 septembre 2006 (29.09.2006) FR

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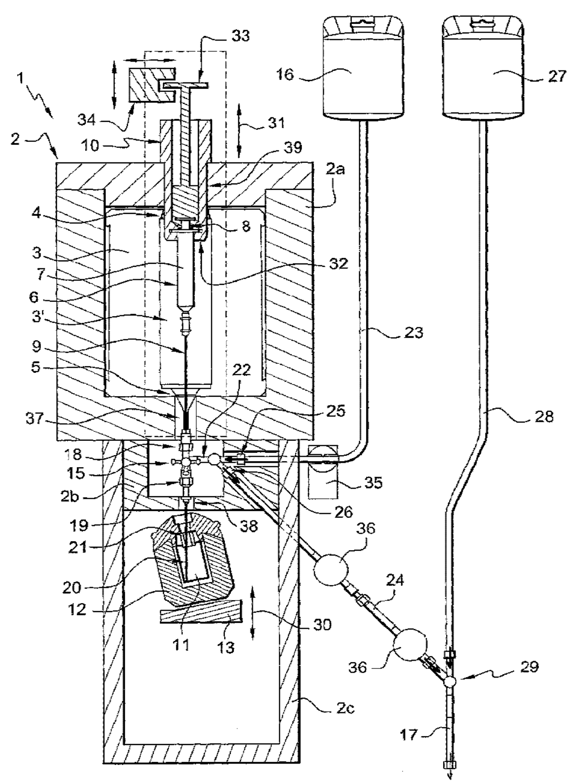
(81) **États désignés** *(sauf indication contraire, pour tout titre de protection nationale disponible)* : AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

[Suite sur la page suivante]

(54) Title: MEDICAL UNIT FOR THE COLLECTION, CALIBRATION, DILUTION AND/OR INJECTION OF AN INJECTABLE RADIOACTIVE PRODUCT

(54) Titre : UNITE MEDICALE POUR LE PRELEVEMENT, LE CALIBRAGE, LA DILUTION ET/OU L'INJECTION D'UN PRODUIT RADIOACTIF INJECTABLE



(57) Abstract: The medical unit according to the invention comprises a shielded enclosure (2) that accommodates means (13) for supporting a container (12) comprising a source or a generator of radioactive product (11), means (10) for supporting a syringe (6), a device of the activity meter type (3), and a system of conduits (9, 23, 24) joined to at least one valve (15). The syringe support (10), the valve (15) and the radioactive source support (13) are arranged vertically relative to one another, each facing downwards, said syringe support (10) being designed to support said syringe (6) with its plunger (8) oriented upwards. The valve (15) and the syringe plunger (8) can be manoeuvred for performing the operations of collection, dilution and injection.

(57) Abrégé : L'unité médicale selon l'invention comporte une enceinte blindée (2) dans laquelle sont logés : des moyens (13) support d'un conteneur (12) comprenant une source ou un générateur de produit radioactif (11); des moyens (10) pour le support d'une seringue (6); un dispositif de type activimètre (3); et un système de conduites (9, 23, 24) associé à au moins une vanne (15). Le support de seringue (10), la vanne (15) et le support de source radioactive (13) sont agencés verticalement les uns par rapport aux autres, respectivement du haut vers le bas, ledit support de seringue (10) étant agencé pour supporter ladite seringue (6) avec son piston (8) orienté vers le haut. La vanne (15) et le piston de seringue (8) sont manoeuvrables pour assurer les opérations de prélèvement, de dilution et d'injection.

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(84) États désignés *(sauf indication contraire, pour tout titre de protection régionale disponible)* **:** ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), eurasien (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), européen (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Déclaration en vertu de la règle 4.17 :

— *relative à la qualité d'inventeur (règle 4.17.iv))*

Publiée :

— *sans rapport de recherche internationale, sera republiée dès réception de ce rapport*

UNITE MEDICALE POUR LE PRELEVEMENT, LE CALIBRAGE, LA DILUTION ET/OU L'INJECTION D'UN PRODUIT RADIOACTIF INJECTABLE

La présente invention concerne le domaine général de la médecine nucléaire. Elle concerne plus particulièrement une unité médicale employée pour le prélèvement, le calibrage, la dilution et/ou l'injection d'une substance radioactive destinée à être injectée à un patient.

Certaines substances radioactives sont particulièrement utiles dans le domaine médical, par exemple dans les procédures d'imagerie, à titre d'agents de contraste, ou comme agents thérapeutiques.

Pour limiter les doses de radiations reçues par le patient et par le personnel chargé des manipulations, on utilise des radioéléments de courtes demi-vies à usage médical, c'est-à-dire que le niveau de radiation émis par ces produits radioactifs décroît rapidement avec le temps.

Mais de tels produits radioactifs à courte demi-vie rendent problématique l'administration d'une dose appropriée au patient. Le dosage correspondant doit en effet être très précis ; il doit tenir compte du temps nécessaire pour la préparation de la dose à injecter, et aussi du temps susceptible de séparer le moment de la préparation de la dose de produit et le moment de l'injection proprement dite de cette dose au patient.

En outre, malgré le type de produits mis en œuvre (courte demi-vie), une autre contrainte à prendre en compte concerne la radioprotection du personnel médical chargé de préparer la dose radioactive et de l'injecter au patient. Cette radioprotection doit aussi être effective pour le patient.

De manière classique, les doses à injecter sont prélevées dans une seringue munie d'un blindage approprié, placée elle-même dans une enceinte blindée équipée de moyens de mesure et de contrôle appropriés, permettant de prélever dans la seringue la dose de produit radioactif recherchée. Ensuite, un opérateur récupère la seringue blindée et il se rend auprès du patient pour réaliser l'injection.

Cependant, cette manière d'opérer n'offre pas une sécurité optimale, tant sur le plan de la radioprotection pour l'opérateur que sur le plan de la précision de la dose injectée au patient.

Le document US-6 767 319 décrit un matériel de calibrage et d'injection de produit radioactif visant à limiter l'exposition du personnel à la substance radioactive et aussi optimiser la sécurité du patient.

L'installation correspondante comprend trois enceintes radioprotectrices indépendantes, contenant respectivement :

- des moyens pour le support d'une source en produit radioactif injectable,
- des moyens pour le support d'une seringue, qui sont équipés de moyens pour la manœuvre automatique de son piston, et qui sont associés à un dispositif de type activimètre pour la mesure en temps réel de l'activité radio-isotopique émise par le produit contenu dans la seringue, et
- un système de vannes.

Ce système de vannes est raccordé hydrauliquement, par le biais de tubulures, à l'enceinte contenant la source mère radioactive, à l'enceinte contenant la seringue, à une source de sérum physiologique et à un cathéter d'injection destiné à être connecté au patient.

Ce matériel comprend encore des moyens destinés à piloter le système de vannes et les moyens de manœuvre du piston de seringue, cela de manière adaptée pour assurer, dans un premier temps, le prélèvement d'une dose de produit radioactif et/ou de sérum physiologique au sein de la seringue, et dans un second temps l'éjection au travers du cathéter d'injection, du produit radioactif et/ou du sérum physiologique préalablement prélevés. La dose de produit radioactif est mesurée par le dispositif activimètre au cours du prélèvement dans la seringue.

Dans ce matériel, les tubulures reliant l'enceinte contenant le système de vannes et celles contenant la seringue ou la source radioactive, ne sont pas protégées et sont source d'émissions radioactives dans l'environnement.

De plus, du fait de sa structure, le matériel correspondant est encombrant. En outre, la complexité du réseau de tubulures entraîne la présence de volumes morts importants.

La présente invention propose une unité médicale originale de calibration et d'injection de produits radioactifs, très compacte, permettant le prélèvement, la mesure et l'injection des produits avec une grande précision, en toute sécurité, et avec des volumes morts réduits.

Cette unité médicale est du type comprenant :

- des moyens pour le support d'un conteneur en matériau radioprotecteur dans lequel est logée une source ou un générateur de produit radioactif injectable,
- des moyens pour le support d'une seringue équipée d'un piston,
- un dispositif de type activimètre pour la mesure en temps réel de l'activité radio-isotopique émise par le contenu de ladite seringue, et

- un système de conduites associé à au moins une vanne pour le raccordement hydraulique de ladite source radioactive, de ladite seringue, d'une source de sérum physiologique et d'un cathéter d'injection destiné à être connecté au patient,

ladite vanne et ledit piston de seringue étant manœuvrables pour assurer, d'une part, une aspiration dudit produit radioactif ou dudit sérum physiologique au sein de ladite seringue, et d'autre part, une éjection dudit produit radioactif, dudit sérum physiologique ou d'un mélange de ces deux produits, préalablement aspirés au sein de ladite seringue, cela au travers dudit cathéter d'injection, la dose de produit radioactif prélevée et injectée par ladite seringue étant mesurée par ledit activimètre.

Conformément à l'invention, l'unité médicale comporte encore une enceinte blindée réalisée en au moins un matériau radioprotecteur, dans laquelle sont logés le support de source radioactive, au moins une partie des moyens support de la seringue, l'activimètre, la vanne, et au moins une partie du système de conduites.

De plus, le support de seringue, la vanne et le support de source radioactive sont agencés verticalement les uns par rapport aux autres, respectivement du haut vers le bas, le support de seringue étant agencé pour porter la seringue verticalement avec son piston orienté vers le haut.

Cet agencement particulier permet à la seringue de prélèvement/injection et à la source de produit radioactif d'être très proches de la vanne, pour obtenir un ensemble très compact, avec des volumes morts minimisés.

Selon une caractéristique de réalisation, la vanne consiste en une vanne trois voies comprenant :

- une voie supérieure, destinée à être raccordée à la seringue de prélèvement et d'injection,
- une voie inférieure, destinée à être raccordée à la source de produit radioactif injectable, et
- une voie latérale, destinée à être raccordée à une première conduite connectée à la source de sérum physiologique et à une seconde conduite connectée au cathéter d'injection, lesdites conduites étant équipées chacune d'un clapet anti-retour convenablement orienté.

Dans ce cas, l'activimètre a avantageusement une forme générale tubulaire délimitant un puits central, d'axe vertical, destiné à contenir la seringue, ledit activimètre étant muni de deux ouvertures, l'une supérieure et l'autre inférieure, cette dernière étant orientée en regard de la vanne trois voies et du support de la source radioactive.

Pour réduire les volumes morts dans les conduits de ce matériel, la voie supérieure de la vanne, destinée à être raccordée à la seringue, comporte avantageusement un opercule hermétique destiné à être percé par l'aiguille équipant ladite seringue montée sur son support ; de même, la voie inférieure de la vanne, destinée à être raccordée à la source de produit radioactif est avantageusement prolongée par une aiguille destinée à percer un opercule obturant le flacon contenant ladite source radioactive.

Encore selon une caractéristique de réalisation de l'invention, les supports de source radioactive et de seringue sont portés chacun par des moyens assurant leur(s) déplacement(s) selon un axe vertical ou sensiblement vertical, cela entre deux positions :

- une première position, dans laquelle un opérateur peut charger la source radioactive et la seringue sur leurs supports respectifs, ou à l'inverse les décharger, et
- une seconde position dans laquelle la source radioactive et la seringue sont raccordées à la vanne.

Selon cette caractéristique, les moyens de déplacement du support de seringue permettent avantageusement son cheminement verticalement au travers d'un orifice ménagé dans l'enceinte blindée, entre :

- une position supérieure de chargement/déchargement, dans laquelle ledit support se situe au moins partiellement hors de ladite enceinte, et
- une position inférieure de raccordement, dans laquelle la seringue se positionne au sein du logement central de l'activimètre et est raccordée à la vanne.

De plus, le support de source radioactive chemine avantageusement au sein de l'enceinte blindée entre ses positions de chargement/déchargement et de raccordement ; cette enceinte est encore munie d'une trappe frontale pour permettre l'accès d'un opérateur au support de source radioactive au moins dans sa position de chargement/déchargement.

Encore selon une autre caractéristique, l'unité médicale comprend des moyens de commande informatiques et/ou électroniques aptes à piloter la vanne et les moyens de manœuvre du piston de seringue, cela de manière à mettre en œuvre les opérations de prélèvement et d'éjection par la seringue. De même, les moyens de commande informatiques/électroniques pilotent également éventuellement les moyens de déplacement du support de seringue et du support de source radioactive.

Dans ce cas, les moyens de manœuvre du piston de la seringue sont avantageusement de type motoréducteur débrayable, contrôlés par les moyens informatiques/électroniques, pour assurer, d'une part, le prélèvement automatique d'une dose déterminée de produit radioactif au sein de la seringue et, d'autre part, pour assurer l'injection de cette dose au patient, soit automatiquement, soit manuellement. L'opérateur peut en effet, s'il le souhaite, débrayer les moyens motoréducteurs et contrôler manuellement l'injection de la dose radioactive au patient.

Selon toujours une forme de réalisation intéressante, l'enceinte se compose de trois sous-enceintes alignées verticalement les unes par rapport aux autres, à savoir :

- une sous-enceinte supérieure contenant la seringue et l'activimètre,
- une sous-enceinte intermédiaire contenant la vanne, et
- une sous-enceinte inférieure contenant la source de produit radioactif.

Ces sous-enceintes sont raccordées deux à deux par des ouvertures traversantes au travers desquelles passent certaines des conduites de raccordement hydraulique.

Pour optimiser encore le traitement des données des médicales, les moyens de commande informatiques/électroniques sont pourvus d'une connectique pour l'envoi et/ou la réception de données, en particulier pour les échanges avec un serveur informatique.

L'unité médicale selon l'invention peut être rendue mobile. Pour cela, elle est montée sur des roues avantageusement motorisées ; elle intègre éventuellement un système de géolocalisation, par exemple de type GPS.

L'invention sera encore illustrée, sans être aucunement limitée, par la description suivante d'un mode de réalisation particulier, donné uniquement à titre d'exemple et représenté sur les dessins annexés dans lesquels :

- la figure 1 est une représentation schématique, en coupe, d'une unité médicale conforme à l'invention ;
- la figure 2 est une vue en perspective de la structure externe d'une forme de réalisation possible de l'unité médicale illustrée figure 1.

Tel que représenté sur la figure 1, l'unité médicale 1 conforme à l'invention comprend une enceinte blindée 2 réalisée en matériau radioprotecteur dans laquelle on trouve un dispositif 3 pour la mesure en temps réel de l'activité radio-isotopique (activimètre de type ACAD (marque déposée)), de forme générale cylindrique d'axe vertical, muni d'une ouverture supérieure 4 et d'une ouverture inférieure 5.

Une seringue classique 6, comprenant un corps 7, un piston 8 et une aiguille 9, est installée dans le puits de mesure 3' de l'activimètre 3 (connectée à une unité de traitement appropriée) ; cette seringue 6 est montée verticalement sur un support supérieur 10, son piston 8 étant orienté vers le haut, et donc son aiguille 9 étant orientée vers le bas.

Une source ou générateur 11 de produit radioactif est placé sous l'activimètre 3, en regard de son ouverture inférieure 5. Cette source de produit radioactif 11 est contenue dans un flacon conditionné dans un conteneur blindé 12 réalisé en matériau radioprotecteur. Le conteneur blindé 12 est logé dans l'enceinte blindée 2, posé sur un support 13.

Une vanne trois voies motorisée 15, logée dans l'enceinte blindée 2 entre la seringue 6 et le flacon de source radioactive 11, assure une connexion hydraulique appropriée entre ladite seringue 6, ledit flacon de source radioactive 11, une poche de sérum physiologique 16 (extérieure à l'enceinte blindée 2) et un cathéter 17 d'injection au patient (également extérieur à l'enceinte blindée 2). Cette vanne 15 est localisée en regard de l'ouverture inférieure 5 de l'activimètre 3, et en regard de la source radioactive 11.

La voie supérieure 18 de cette vanne trois voies 15 comporte un opercule hermétique destiné à être percé par l'aiguille 9 de la seringue 6. La voie inférieure 19 de la vanne 15 se prolonge par une aiguille 20 destinée à percer l'opercule hermétique 21 qui obture le flacon de source radioactive 11. La voie latérale 22 de la vanne 15 est connectée, par un raccordement en Y, à une tubulure 23 aboutissant à la poche de sérum physiologique 16, et à une tubulure 24 aboutissant au cathéter d'injection 17.
La tubulure 23 est équipée d'un clapet anti-retour 25 empêchant un retour de liquide en direction de la poche de sérum physiologique 16. La tubulure 24 est également équipée d'un clapet anti-retour 26 imposant le passage de liquide en direction du patient.

Sur la figure 1, on remarque que le cathéter 17 est également en communication avec une seconde poche 27 de sérum physiologique, par le biais d'une tubulure 28 et d'un raccordement en Y 29.

La vanne trois voies 15 a deux positions principales : - une première mettant en communication ses voies supérieure 18 et inférieure 19 (permettant la mise en communication de la seringue 6 avec la source de produit radioactif 11 pour assurer le prélèvement d'une dose de produit radioactif dans le corps de seringue 7), et - une seconde position, mettant en communication la voie supérieure 18 et la voie latérale 22 (soit pour aspirer du sérum physiologique venant de la poche 16 dans le corps de seringue 7, lors d'une opération d'aspiration par la seringue 6, soit pour éjecter le

liquide contenu dans le corps de seringue 7 dans le cathéter d'injection 17, par une manœuvre de vidange du corps de seringue 7).
Une troisième position possible de la vanne 15 consiste à mettre en communication la source de radioéléments 11 et les tubulures 23 et 24, cela pour casser la dépression du flacon de source radioactive 11 en autorisant l'aspiration du sérum physiologique provenant de la poche 16.

La vanne trois voies 15 est montée fixe à l'intérieur de l'enceinte 2 sur l'axe vertical ou sensiblement sur l'axe vertical passant par la seringue 6 et la source 11 de produit radioactif.

Le support 13 de la source de produit radioactif 11 est mobile verticalement, conformément à la flèche d'orientation 30, sous l'action de moyens mécaniques appropriés (non représentés) actionnés manuellement (ou au pied), ou par des moyens moteurs (également non représentés) de manière à permettre l'intégration de l'aiguille 20 dans le flacon de source radioactive 11, ou le retrait de cette aiguille 20 dudit flacon.
L'opérateur manœuvre le support mobile 13 dans cette dernière position « extraite » lorsqu'il souhaite changer la source de produit radioactif.

D'autre part, le support 10 de la seringue 6 est également mobile verticalement, conformément à la flèche d'orientation 31, sous l'action de moyens mécaniques appropriés (non représentés) actionnés manuellement ou par des moyens moteurs (également non représentés), de manière à permettre l'intégration de l'aiguille 9 de la seringue 6 dans la vanne trois voies 15, ou l'extraction de la seringue 6 au-dessus de l'activimètre 3 et hors du conteneur blindé 2, pour réaliser les opérations de mise en place et de retrait de la seringue 6.

Le support 10 de la seringue 6 est également structuré pour permettre une manœuvre du piston 8 de la seringue depuis l'extérieur du conteneur blindé 2, alors que ladite seringue 6 est centrée dans le puits de mesure 3' de l'activimètre 3.
Pour cela, le support 10 comporte une partie cylindrique 32 en prise avec la partie arrière du corps de seringue 7, et une partie centrale 33, en forme de piston coulissant dans la partie cylindrique 32, en prise avec la partie arrière du piston de seringue 8.

Lorsque le corps de seringue 7 est en position dans le puits de mesure 3' de l'activimètre 3, l'extrémité supérieure du piston coulissant 33 est accessible depuis l'extérieur de l'enceinte blindée 2. Cette extrémité supérieure de piston 33 est associée à une motorisation débrayable 34 qui, une fois embrayée, permet l'actionnement automatique du piston de seringue 8 et qui, lorsqu'elle est débrayée, permet l'actionnement manuel de ce piston 8.

Cette particularité offre à l'opérateur un choix de gestion, automatique ou manuelle, du prélèvement de produit radioactif par la seringue 6 et/ou de l'éjection du produit dans le cathéter 17.

Sur la figure 1, on remarque encore la présence d'une électrovanne à pincement 35, positionnée sur la tubulure 23 de la poche de sérum physiologique 16. Cette électrovanne 35 a pour fonction d'empêcher la circulation intempestive de sérum physiologique au travers de la tubulure 23, avant la connexion du cathéter d'injection 17 au patient.

Sur la tubulure 24 d'alimentation du cathéter 17, on remarque aussi la présence de deux moyens anti-bulles/antibactérien 36 qui se présentent, par exemple, sous la forme de filtres, garantissant la stérilité du processus d'injection.

Toujours sur la figure 1, on remarque que l'enceinte blindée 2 se présente sous la forme de trois sous-ensembles blindés :

- un premier ensemble 2a intègre l'activimètre 3 et une partie du support de seringue 10,
- un second ensemble 2b cloisonne la vanne trois voies motorisée 15, et
- un troisième ensemble 2c cloisonne le support mobile 13 avec son conteneur blindé 12.

Les trois sous-enceintes 2a, 2b et 2c sont superposées ; la connexion entre la seringue 6 et la vanne 15 s'effectue au travers d'une ouverture 37 ménagée entre lesdits sous-ensembles 2a et 2b. La connexion entre la vanne 15 et la source de produit radioactif 11 est réalisée au travers d'une ouverture 38 ménagée entre les sous-ensembles 2b et 2c.

Le support 10 de la seringue 6 est réalisé en matériau radioprotecteur. Ses dimensions sont ajustées au mieux dans une ouverture 39 ménagée dans la partie supérieure du sous-ensemble 2a, pour obtenir une continuité de blindage en position abaissée (c'est-à-dire lorsque la seringue 6 est centrée dans le puits de mesure 3' de l'activimètre 3).

L'enceinte blindée 2 comporte encore des ouvertures appropriées pour le passage des tubulures 23 et 24 reliées, respectivement, à la poche de sérum physiologique 16 et au cathéter 17.

Les principales étapes mises en œuvre au sein de l'unité médicale 1, pour la préparation d'une dose déterminée de produit radioactif, puis son injection au patient, sont détaillées ci-dessous.

Tout d'abord, la dose de produit radioactif à injecter au patient est préparée au sein de la seringue 6.

Pour cela, la seringue 6 (avec son piston 8 en position basse) et la source de produit radioactif 11 sont connectées à la vanne trois voies 15 ; ensuite, cette vanne 15 est pilotée de sorte que ses voies supérieure 18 et inférieure 19 soient raccordées hydrauliquement, permettant la mise en communication respectivement de l'aiguille de seringue 9 avec la source 11 de produit radioactif.

Le piston de seringue 8 est ensuite manœuvré, vers le haut, pour aspirer la dose voulue de produit radioactif dans le corps de seringue 7, qui est mesurée en temps réel par l'activimètre 3. Cette dose est notamment fonction du poids du patient.

La dose préparée au sein de la seringue peut ensuite être administrée au patient.

A cet effet, la vanne 15 est à nouveau pilotée, cela de sorte que ses voies supérieure 18 et latérale 22 soient respectivement en communication avec l'aiguille de seringue 9, et avec les tubulures 23 et 24 (connectées à la poche 16 de sérum physiologique et au cathéter d'injection 17).

Avant la phase d'injection proprement dite, le piston de seringue 8 peut, si nécessaire, être piloté (vers le haut) pour aspirer un volume complémentaire de sérum physiologique provenant de la poche 16 ; ce volume de sérum permet de diluer le produit radioactif, et aussi d'obtenir un volume d'injection suffisant.

La seringue 6 est ensuite vidangée par le déplacement adapté du piston de seringue 8 (vers le bas). Le produit radioactif, éventuellement dilué par le volume complémentaire de sérum physiologique, chemine alors au travers de la tubulure 24 où il est filtré par les dispositifs 36, puis le long du cathéter d'injection 17 jusqu'au patient.

Suite à cette phase d'injection, l'opérateur peut éventuellement mettre en œuvre une phase complémentaire de rinçage du corps de seringue 7, de la vanne 15, et des conduites aval 17 et 24, avec un volume adapté de sérum physiologique pour assurer l'administration au patient de la totalité de la dose radioactive souhaitée.

A cet effet, le piston de seringue 8 est manœuvré successivement en aspiration (vers le haut) pour prélever un volume déterminé de sérum physiologique en provenance de la poche 16, puis manœuvré en éjection (vers le bas) pour éjecter ce volume au travers de la conduite 24 et du cathéter d'éjection 17.

Lorsque l'opérateur souhaite remplacer la seringue 6 ou la source de produit radioactif 11, il lui suffit de manœuvrer leurs structures supports respectives 10 et 13.
A titre indicatif, la seringue 6 et la vanne 15 avec ses différentes conduites peuvent être remplacées suite à chaque injection. La seringue 6, d'une part, et la vanne 15 avec son aiguille 20, ses tubulures 23, 24, la poche de sérum physiologique 16 et le cathéter 17, d'autre part, constituent un ensemble stérile à usage unique, remplaçable très facilement après chaque utilisation.

Les différents cycles précités de prélèvement, de dilution et d'injection de ce matériel sont gérés par des moyens de commande électroniques/informatiques de type automate programmable, aptes à piloter automatiquement les moyens de manœuvre 34 du piston de seringue 8 et la vanne trois voies 15, de manière appropriée.
L'ensemble de ces cycles peut être totalement automatisé. En fonction des besoins, ou des souhaits de l'utilisateur, l'injection de la dose radioactive au patient peut aussi être réalisée manuellement grâce aux moyens débrayables du motoréducteur 34.

Une forme particulièrement intéressante de l'unité médicale illustrée schématiquement sur la figure 1, est représentée sur la figure 2.

Sur cette figure 2, l'enceinte blindée 2 qui intègre l'ensemble du matériel fonctionnel décrit ci-dessus, est montée sur un châssis équipé de quatre roues 40. De préférence, certaines au moins des roues 40 sont associées à une motorisation, constituant une simple assistance aux déplacements, ou assurant elle-même le déplacement autonome de l'unité mobile, pilotée à distance par un boîtier à manette adapté.

L'unité mobile 1 peut aussi intégrer un système de géolocalisation, par exemple de type GPS, pour connaître en permanence son positionnement à distance dans un bâtiment.

Dans la partie inférieure de l'enceinte 2, on remarque la présence d'une trappe blindée 41 donnant accès à l'intérieur de la sous-enceinte 2c, pour le chargement ou le déchargement sur son support 13 du conteneur blindé 12 renfermant la source de produit radioactif 11 (en particulier lorsque ce support 13 est en position basse de chargement/déchargement).

Dans la partie supérieure, on remarque le support de seringue 10, la poche de sérum physiologique 16 accrochée à un support 42, ainsi qu'un tableau 43 de commande et de visualisation, à écran tactile, intégrant l'automate programmable de gestion des cycles, ou en relation directe avec celui-ci (par exemple déporté au sein du châssis de l'unité). Ce tableau de commande, de dialogue et de visualisation 43 permet d'effectuer les opérations de calibration (mesure d'activité), et la visualisation en temps réel des diverses phases de préparation du transfert (dilution ...) et d'injection du produit radioactif.

Les moyens de commande électroniques/informatiques correspondants sont équipés d'une connectique 44 pour l'envoi et/ou la réception de données, en particulier pour réaliser certains échanges avec un serveur informatique situé à proximité ou à distance (par exemple par l'intermédiaire d'un réseau intranet ou du réseau internet), notamment pour réaliser une télémaintenance à distance et collecter certaines données concernant le patient (nécessaires notamment à la détermination de la dose de radioéléments qui doit lui être administrée).

Le châssis de l'unité 1 porte également des moyens propres d'énergie, par exemple de type batteries rechargeables, assurant l'alimentation électrique notamment des roues motorisées 40 et des moyens de commande électroniques/informatiques.

Cette unité mobile blindée 1 constitue une unité autonome permettant la calibration et l'injection de tous produits radioactifs (en particulier de FDG). Elle est très compacte du fait de la superposition de l'activimètre, de la vanne trois voies et de la source de produit radioactif sur le même axe vertical ou sensiblement sur le même axe vertical, et du fait de la superposition des sous-enceintes 2a, 2b et 2c. Cette unité permet un prélèvement, une mesure et une injection en toute sécurité.

- REVENDICATIONS -

1.- Unité médicale pour le prélèvement, le calibrage, la dilution et/ou l'injection d'un produit radioactif, injectable à un patient, laquelle unité (1) comprend au moins :

- des moyens (13) pour le support d'un conteneur (12) en matériau radioprotecteur dans lequel est logée une source ou un générateur de produit radioactif injectable (11),

- des moyens (10) pour le support d'une seringue (6) équipée d'un piston (8),

- un dispositif (3) de type activimètre pour la mesure en temps réel de l'activité radio-isotopique émise par le contenu de ladite seringue (6), et

- un système de conduites (9, 20, 23, 24) associé à au moins une vanne (15) pour le raccordement hydraulique de ladite source radioactive (11), de ladite seringue (6), d'une source de sérum physiologique (16) et d'un cathéter d'injection (17) destiné à être connecté au patient,

ladite vanne (15) et ledit piston de seringue (8) étant manœuvrables pour assurer, d'une part, une aspiration dudit produit radioactif (11) ou dudit sérum physiologique (16) au sein de ladite seringue (6), et d'autre part, une éjection dudit produit radioactif (11), dudit sérum physiologique ou d'un mélange de ces deux produits, préalablement aspiré(s) au sein de ladite seringue (6), cela au travers dudit cathéter d'injection (17), la dose de produit radioactif prélevée et injectée par ladite seringue (6) étant mesurée par ledit activimètre (3),

caractérisée en ce qu'elle comporte une enceinte blindée (2) réalisée en au moins un matériau radioprotecteur, dans laquelle sont logés ledit support (13) de source radioactive (11), au moins une partie des moyens supports (10) de la seringue (6), ledit activimètre (3), ladite vanne (15) et au moins une partie dudit système de conduites (9, 20, 23, 24), et en ce que ledit support de seringue (10), ladite vanne (15) et ledit support (13) de source radioactive (11) sont agencés verticalement les uns par rapport aux autres, respectivement du haut vers le bas, ledit support de seringue (10) étant agencé pour porter ladite seringue (6) avec son piston (8) orienté vers le haut.

2.- Unité médicale selon la revendication 1, caractérisée en ce que la vanne (15) consiste en une vanne trois voies comprenant :

- une voie supérieure (18), destinée à être raccordée à la seringue (6) de prélèvement et d'injection,

- une voie inférieure (19), destinée à être raccordée à la source de produit radioactif injectable (11), et

- une voie latérale (22), destinée à être raccordée à une première conduite (23) connectée à la source de sérum physiologique (16) et à une seconde conduite (24) connectée au cathéter d'injection (17), lesdites conduites (23, 24) étant équipées chacune d'un clapet anti-retour (25, 26) convenablement orienté.

3.- Unité médicale selon la revendication 2, caractérisée en ce que l'activimètre (3) a une forme générale tubulaire délimitant un puits central (3') d'axe vertical, destiné à contenir la seringue (6), ledit activimètre (3) étant muni de deux ouvertures, l'une supérieure (4) et l'autre inférieure (5), cette dernière étant orientée en regard de la vanne trois voies (15) et du support (13) de la source radioactive (11).

4.- Unité médicale selon l'une quelconque des revendications 2 ou 3, caractérisée en ce que la voie supérieure (18) de la vanne (15), destinée à être raccordée à la seringue (6), comporte un opercule hermétique destiné à être percé par l'aiguille (9) équipant ladite seringue (6).

5.- Unité médicale selon l'une quelconque des revendications 2 à 4, caractérisée en ce que la voie inférieure (19) de la vanne (15), destinée à être raccordée à la source de produit radioactif injectable (11), est prolongée par une aiguille (20) destinée à percer un opercule (21) obturant le flacon contenant ladite source radioactive (11).

6.- Unité médicale selon l'une quelconque des revendications 1 à 5, caractérisée en ce que les supports (13, 10) de source radioactive (11) et de seringue (6) sont portés chacun par des moyens assurant leur(s) déplacement(s) selon un axe vertical ou sensiblement vertical, cela entre deux positions :

- une première position, dans laquelle un opérateur peut charger la source radioactive (11) et la seringue (6) sur leurs supports respectifs (13, 10), ou à l'inverse les décharger, et
- une seconde position dans laquelle la source radioactive (11) et la seringue (6) sont raccordées à la vanne (15).

7.- Unité médicale selon la revendication 6, caractérisée en ce que les moyens de déplacement du support de seringue (10) permettent son cheminement verticalement au travers d'un orifice (39) ménagé dans l'enceinte blindée (2), entre :

- une position supérieure de chargement/déchargement, dans laquelle ledit support (10) se situe au moins partiellement hors de ladite enceinte (2), et
- une position inférieure de raccordement, dans laquelle la seringue (6) se positionne au sein du puits central (3') de l'activimètre (3) et est raccordée à la vanne (15).

8.- Unité médicale selon l'une quelconque des revendications 6 ou 7, caractérisée en ce que le support (13) de source radioactive (11) chemine au sein de l'enceinte blindée (2) entre ses positions de chargement/déchargement et de raccordement, ladite enceinte (2) étant encore munie d'une trappe (41) frontale pour permettre l'accès d'un opérateur audit support (13) de source radioactive (11) au moins dans sa position de chargement/déchargement.

9.- Unité médicale selon l'une quelconque des revendications 1 à 8, caractérisée en ce qu'elle comprend encore des moyens de commande informatiques et/ou électroniques aptes à piloter la vanne (15) et les moyens (33, 34) de manœuvre du piston de seringue (8), cela de manière à mettre en œuvre les opérations de prélèvement et d'éjection par ladite seringue (6), lesquels moyens de commande informatiques/électroniques pilotent également éventuellement les moyens de déplacement du support de seringue (10) et du support de source radioactive (13).

10.- Unité médicale selon la revendication 9, caractérisée en ce que les moyens de manœuvre du piston (8) de la seringue (6) sont de type motoréducteurs débrayables (34), contrôlés par les moyens de commande informatiques/électroniques, pour assurer, d'une part, le prélèvement automatique d'une dose déterminée de produit radioactif au sein de ladite seringue (6), et d'autre part, pour assurer l'injection de cette dose au patient, soit automatiquement, soit manuellement.

11.- Unité médicale selon l'une quelconque des revendications 1 à 10, caractérisée en ce que l'enceinte (2) se compose de trois sous-enceintes (2a, 2b, 2c) alignées verticalement les unes par rapport aux autres, à savoir - une sous-enceinte supérieure (2a) contenant la seringue (6) et l'activimètre (3), - une sous-enceinte intermédiaire (2b) contenant la vanne (15), et - une sous-enceinte inférieure (2c) contenant la source de produit radioactif (11), lesquelles sous-enceintes (2a, 2b, 2c) sont raccordées deux à deux par des ouvertures traversantes (37, 38) au travers desquelles passent certaines des conduites (9, 20) de raccordement hydraulique.

12.- Unité médicale selon l'une quelconque des revendications 1 à 11, caractérisée en ce que les moyens de commande informatiques/électroniques sont pourvus d'une connectique (44) pour l'envoi et/ou la réception de données, en particulier pour les échanges avec un serveur informatique.

13.- Unité médicale selon l'une quelconque des revendications 1 à 12, caractérisée en ce qu'elle est montée sur des roues (40) pour la rendre mobile, et en ce qu'elle intègre éventuellement un système de géolocalisation, par exemple de type GPS.

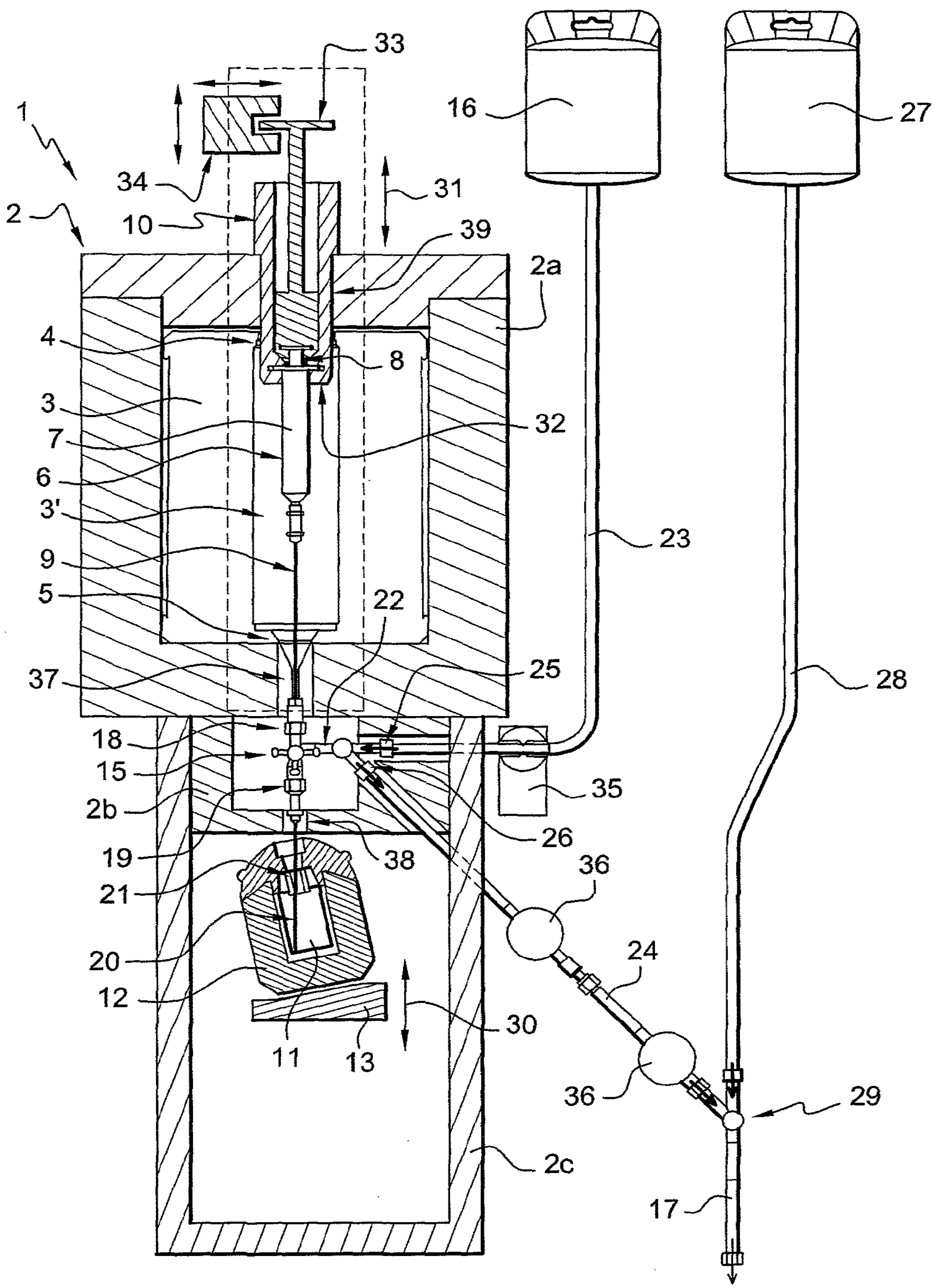
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Fig. 1

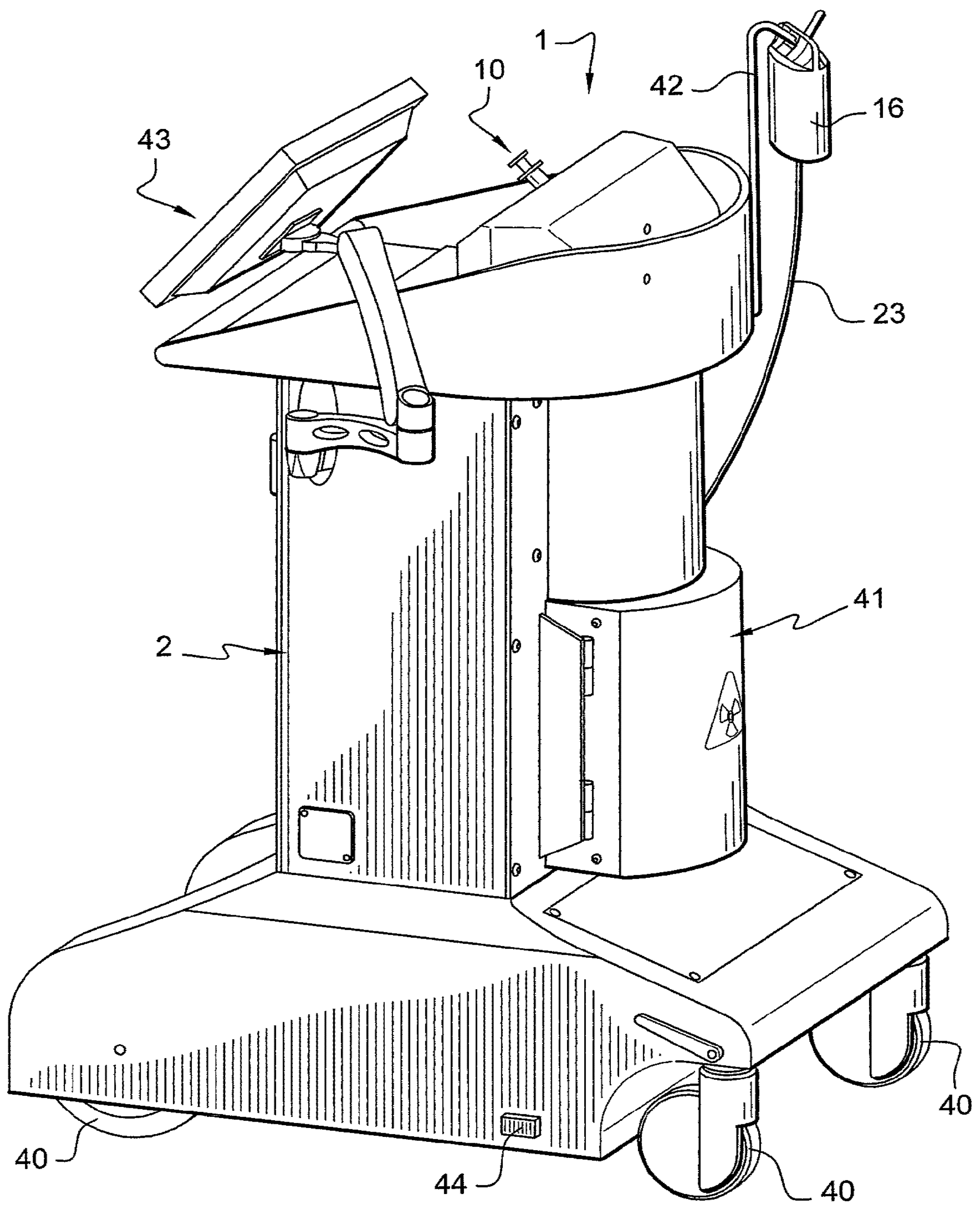

Fig. 2

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
10 July 2008 (10.07.2008)

PCT

(10) International Publication Number
WO 2008/082966 A2

(51) International Patent Classification:
A61M 36/08 (2006.01)

(21) International Application Number:
PCT/US2007/088028

(22) International Filing Date:
20 December 2007 (20.12.2007)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:

60/878,304	1 January 2007 (01.01.2007)	US
60/979,541	12 October 2007 (12.10.2007)	US
11/981,429	31 October 2007 (31.10.2007)	US

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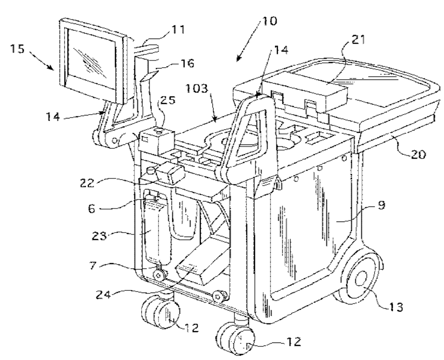
(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:
— *without international search report and to be republished upon receipt of that report*

(54) **Title:** RADIOPHARMACEUTICAL ADMINISTRATION METHODS, FLUID DELIVERY SYSTEMS AND COMPONENTS THEREOF



(57) **Abstract:** A fluid path set for a fluid delivery system includes a tube coil that is designed to optimally position one or more volumes of a pharmaceutical within an ionization chamber to optimally measure and prepare a pharmaceutical dose for administration to a patient. The tube coil may be maintained in a desired dimensional geometry by means of a core structure around which the tube coil is positioned. Novel developments in radiopharmaceutical administration methods and systems include, but are not limited to, the configuration and layout of a fluid path set for use in a fluid delivery system, arrangements for piercing and drawing fluid from a pharmaceutical container (such as a vial), arrangements for optimizing the positioning of a tube coil within an ionization chamber, a handling system for transporting vial shields that maintain an operator's hand and fingers at a safe distance from a pharmaceutical vial, a method for calibrating a radiopharmaceutical delivery system in which the difference between the expected and measured activities of two radioisotopes are used to calculate an estimated error in the measured activity of a third radioisotope and a vial access system that ensures an optimal draw of fluid from a radiopharmaceutical container.

WO 2008/082966 A2

RADIOPHARMACEUTICAL ADMINISTRATION METHODS, FLUID DELIVERY SYSTEMS AND COMPONENTS THEREOF

BACKGROUND OF THE INVENTION

[1] The present invention relates to methods, systems and components thereof for delivering pharmaceutical substances to patients for imaging procedures and, more particularly, for delivering radiopharmaceuticals to patients for positron emission tomography (PET) or single-photon emission computerized tomography (SPECT) procedures.

[2] PET and SPECT are noninvasive, three-dimensional, imaging procedures that provide information regarding physiological and biochemical processes in patients. PET and SPECT images of, for example, the brain or another organ, are produced by injecting the patient with a dose of a radiopharmaceutical (using, for example, fluid delivery systems such as those disclosed in U.S. Patent No. 6,767,319, JP Publication Nos. 2000-350783 and 2002-306609 and PCT Publication Nos. WO 2004/091688, WO 2006/007750 and 2004/004787, the disclosures of which are incorporated herein by reference) and then creating an image based on the radiation emitted by the radiopharmaceutical. The radiopharmaceutical generally includes a radioactive substance, such as a radioisotope, that can be absorbed by certain cells in the brain or other organs, concentrating it there.

[3] Radioisotopes, especially those with short half-lives, can be relatively safely administered to patients in the form of a labeled substrate, ligand, drug, antibody, neurotransmitter or other compound or molecule that is normally processed or used by the body (for example, glucose). The radioisotope acts as a tracer of specific physiological or biological processes. For example, fluorodeoxyglucose (FDG) is a normal molecule of glucose, the basic energy fuel of cells, to which is attached a radioisotope or radioactive fluor (i.e., F-18). The F-18 radioisotope is produced in a cyclotron equipped with a unit to synthesize the FDG molecule.

[4] Cells (for example, in the brain) that are more active in a given period of time after an injection of FDG will absorb more FDG because they have a higher metabolism and require more energy. The F-18 radioisotope in the FDG molecule experiences a radioactive decay, emitting a positron. When a positron collides with an electron, annihilation occurs, liberating a burst of energy in the form of two beams of gamma rays in opposite directions. The PET scanner detects the emitted gamma rays to compile a three dimensional image.

[5] To allow for cell uptake of the radiopharmaceutical, the patient typically rests for a period of time (45-90 minutes for FDG) after the radiopharmaceutical is injected. After sufficient time for cell uptake has elapsed, the patient is typically placed on a movable bed that slides into the PET (or SPECT or other suitable) scanner. The PET scanner includes several rings of radiation detectors. Each detector emits a brief pulse of light every time it is struck with a gamma ray coming from the radioisotope within the patient's body. The pulse of light is amplified, by for example a photomultiplier, and the information is sent to the computer for forming images of the patient.

[6] To minimize the radiation dose to patients, radiopharmaceuticals containing radioisotopes, such as Flourine-18, Technetium-99, Carbon-11, Copper-64, Gallium-67, Iodine-123, Nitrogen-13, Oxygen-15, Rubidium-82, Thallium-201, Chromium-51, Iodine-131, Iodine-151, Iridium-192, Phosphorus-32, Samarium-153, and Yttrium-90, having relatively short half-lives are typically used for PET and SPECT imaging procedures and other radio-therapies. F-18, for example, has a half-life of 109.7 minutes.

[7] Because of its short half-life, the radioactivity level of the radioisotope will quickly decrease after it is manufactured in a cyclotron or a reactor. Consequently, the elapsed time (and corresponding decrease in radioactivity level of the radioisotope) after synthesis of the radiopharmaceutical must be factored into calculating the volume of radiopharmaceutical required to be injected into the patient to deliver the desired radioactivity dose. If the time delay after synthesis is long in relation to the radioisotope's half-life or if the calculated volume of radiopharmaceutical to be injected into the patient is insufficient to deliver the desired radioactivity dose, the delivered radioactivity dose may be too low to provide diagnostic-quality images, resulting in wasted time and effort and exposing the patient and medical personnel to unnecessary radiation.

[8] Further, long-term radiation exposure to technologists and other personnel working in the scanner room can pose a significant health risk. Although the half-life of the radiopharmaceutical is rather short and the applied dosages are considered an acceptable risk to the patient, under current procedures administering personnel are exposed each time they work with the radiopharmaceuticals and other contaminated materials, such as tubing and syringes, used to inject the radiopharmaceuticals into patients. Constant and repeated exposure over an extended period of time can be harmful.

[9] A number of techniques are used to reduce radiation exposure to medical personnel, including minimizing the time of exposure of personnel, maintaining distance between personnel and the source of radiation and shielding personnel from the source of radiation. In general, the radiopharmaceuticals are typically delivered to a nuclear medicine hospital suite or other medical facility from a radiopharmaceutical synthesis facility (within or outside the hospital or medical facility) equipped with a cyclotron in, for example, a lead-shielded container (often called a "PIG"). Often, the radiopharmaceutical is manually drawn from such containers into a shielded syringe. See, for example, U.S. Pat. No. 5,927,351, disclosing a drawing station for handling radiopharmaceuticals for use in syringes. Remote injection mechanisms can also be used to maintain distance between the operator and the radiopharmaceutical. See, for example, U.S. Pat. No. 5,514,071, disclosing an apparatus for remotely administering radioactive material from a lead encapsulated syringe. Nevertheless, these current procedures and systems still result in unnecessary and repeated exposure of technicians and other medical personnel to radiation.

[10] It has long been recognized as very desirable to develop devices, systems, components and methods for calculating and delivering accurate and effective doses of radiopharmaceuticals to patients, while reducing the exposure of administering or other medical personnel to such hazardous pharmaceuticals.

SUMMARY OF THE INVENTION

[11] The present invention broadly contemplates and provides devices, systems, components and methods for accurately calculating or delivering effective doses of pharmaceuticals to patients.

[12] In a first aspect, the invention provides a fluid path set including a tube coil that is designed to optimally position one or more volumes of a pharmaceutical within an ionization chamber to optimally measure and prepare a pharmaceutical dose for administration to a patient. The tube coil may be maintained in a desired dimensional geometry by means of a core structure around which the tube coil is positioned or coiled.

[13] The fluid path set includes a medical fluid component comprising a first tubing section for connection to a source of a medical fluid, a pharmaceutical component comprising a second tubing section for connection to a source of a pharmaceutical, a coil assembly component comprising a tube coil having a height of approximately 1.53 inches, a diameter of approximately 1.95 inches and a volume capacity of

approximately 12.5 ml, and a connector comprising a first port for connecting the first tubing section of the medical fluid component, a second port for connecting the second tubing section of the pharmaceutical component and a third port for connecting the tube coil of the coil assembly component.

[14] In a second aspect, the present invention provides a vial access system for inserting a cannula into a pharmaceutical container, such as a vial. The vial access system includes structures that shields the operator from exposure to hazardous pharmaceuticals, such as radiopharmaceuticals, and is designed with an inclined bottom surface to tilt the pharmaceutical container from the horizontal and thereby allow the cannula to optimally extract the pharmaceutical from the container.

[15] The vial access system includes a base portion comprising a substantially horizontal lower surface and a sloped upper surface adapted to support a vial comprising a bottom wall and a substantially cylindrical wall connected thereto. The sloped upper surface is adapted to ensure that a residual volume of fluid in the vial gathers in an area defined at least partially by a portion of the junction between the bottom wall and the cylindrical wall of the vial.

[16] In a third aspect, the present invention provides a vented cannula for insertion into a pharmaceutical container, such as a vial. The vented cannula may be used in the vial access system of the present invention or may be fluidly connected to a shielded syringe to provide an alternate fluid delivery system.

[17] The vented cannula includes a main hub comprising two opposed lateral sides and defining a fluid port and a vent, a fluid draw needle in connection with the fluid port and adapted to be placed within the container, a vent needle in connection with the vent and adapted to be placed within the container; and two resilient arms connected to the opposed lateral sides of the main hub. Each of the two arms includes a top edge and a hook member formed thereon and extending outwardly therefrom.

[18] In a fourth aspect, the present invention provides a fluid delivery system having a retractable shielded cover to shield operators of the system from the fluid path components and the pharmaceutical contained therein. In another aspect, the fluid path components and the pharmaceutical may be disposed in a slidable drawer that may be removed from the shielded system to allow access thereto.

[19] The fluid delivery system includes a housing having an upper surface defining a plurality of recessed portions for accommodating one or more components of a fluid path set, a cover movably connected to the housing and a locking mechanism

associated with the cover. The cover is adapted to move between a first position that exposes the upper surface and a second position that overlies the upper surface, and the locking mechanism is adapted to lock the cover in the second position.

[20] In another aspect, the fluid delivery system includes a syringe comprising a body defining a discharge outlet and a plunger movably disposed within the body, a connector comprising a valve member and defining first, second and third ports, a first tubing segment connected between the discharge outlet of the syringe and the first port of the connector, a cannula defining a fluid port, a second tubing segment connected between the fluid port of the cannula and the second port of the connector, a third tubing segment comprising a first end connected to the third port of the connector and a second end comprising a second connector, and a per-patient tubing set comprising a first end that is adapted to be connected to the second connector on the second end of the third tubing segment and a patient end that is adapted to be connected to venous access device in a patient.

[21] In a fifth aspect, the present invention provides a method of priming the fluid path components of the fluid delivery system to remove air therefrom and to prepare the system to administer a pharmaceutical dose to a patient.

[22] A method of priming at least a portion of a fluid path set in a fluid delivery system includes: (1) placing a tubing section of the fluid path set in fluid connection with a source of a radiopharmaceutical; (2) placing a portion of the tubing section within a dose calibrator of the fluid delivery system; (3) pumping a volume of the radiopharmaceutical through the tubing section; (4) monitoring the dose calibrator to determine if a measured activity level is substantially equal to or above a predetermined activity level; and (5) if the measured activity level is substantially equal to or above the predetermined activity level, then concluding that the tubing section of the fluid path set has been primed.

[23] In a sixth aspect, the present invention provides a carrying system for connecting to and transporting a vial shield (containing a pharmaceutical vial). The carrying system may be used to transport the vial shield to and place the vial shield within the fluid delivery system of the present invention. In another aspect, the carrying system may be used to position the vial shield within the vial access device of the present invention.

[24] The vial shield carrying system includes a collar unit adapted to removably engage a flange on the vial shield and a handle unit adapted to engage the collar unit. The collar unit defines two elongated slots formed in a top surface thereof, each of the

slots including a pin disposed therein and extending between two opposing walls thereof. The handle unit includes a handle connected to a U-shaped cross piece that defines two, downwardly extending arms having hook members formed therein. The open ends of the hook members are formed on opposite ends of the arms and are adapted to engage the pins in the slots of the collar unit through rotation of the handle.

[25] In a seventh aspect, the present invention provides a system and a method for calibrating a radiopharmaceutical delivery system in which the difference between the expected (based on decay from the initial activity) and measured activities of two radioisotopes are used to calculate an estimated error in the measured activity of a third radioisotope. In response to a difference between the expected and measured activity of the first or the second radioisotope, the gain of the ionization chamber is adjusted to eliminate or reduce the error for that radioisotope. When the estimated error of the third radioisotope falls within an acceptable range, the activity of the third radioisotope is measured to check that the actual error between the expected and measured activity of the third radioisotope is substantially similar to the estimated error.

[26] Preferably, the energy levels of the first, second and third radioisotopes are less than, greater than, and relatively close to, respectively, the energy level of the radioisotope to be delivered by the system to the patient. In addition, the operator may take consecutive measurements of the first and second radioisotopes (i.e., in an iterative fashion) and adjust the gain of the ionization chamber in response thereto, before measuring the activity of the third radioisotope and comparing it against the estimated error of the third radioisotope.

[27] A method of calibrating includes (1) measuring an activity level of a first radioisotope in an ionization chamber of the fluid delivery system, the first radioisotope having an energy level less than that of the radioisotope to be delivered to the patient; (2) comparing the measured activity level of the first radioisotope to an expected activity level of the first radioisotope; (3) adjusting the gain of the ionization chamber to compensate for the difference, if any, between the measured activity and the expected activity of the first radioisotope; (4) measuring an activity level of a second radioisotope in the ionization chamber of the fluid delivery system, the second radioisotope having an energy level similar to or greater than that of the radioisotope to be delivered to the patient; (5) comparing the measured activity level of the second radioisotope to an expected activity level of the second radioisotope; (6) adjusting the gain of the ionization chamber to compensate for the difference, if

any, between the measured activity and the expected activity of the second radioisotope; and (7) calculating an estimated error in a measured activity of a third radioisotope based on the differences, if any, between the measured activity and the expected activity of the first radioisotope and the measured activity and the expected activity of the second radioisotope.

[28] Broadly contemplated herein are improvements in radiopharmaceutical administration methods and systems. These inventions include, but are not limited to, the configuration and layout of a fluid path set for use in a fluid delivery system, arrangements for piercing and drawing fluid from a radiopharmaceutical container (such as a vial), arrangements for optimizing the positioning of a tube coil within an ionization chamber, a handle / carrying system for transporting vial shields or "pigs" that keeps an operator's hand and fingers at a safe distance from a vial access cap, and a vial access system that ensures an optimal draw of fluid from a radiopharmaceutical container.

[29] The novel features which are considered characteristic of the present invention are set forth herebelow. The invention itself, however, both as to its construction and its method of operation, together with additional objects and advantages thereof, will be best understood from the following description of the specific embodiments when read in connection with the accompanying drawings.

BRIEF DESCRIPTION OF THE DRAWINGS

[30] For the present invention to be clearly understood and readily practiced, the present invention will be described in conjunction with the following figures, wherein like reference characters designate the same or similar elements, which figures are incorporated into and constitute a part of the specification.

[31] Fig. 1A is a perspective view of a fluid delivery system of the present invention.

[32] Fig. 1B is another perspective view of the fluid delivery system of Fig. 1A with the shielded cover thereof in a retracted position.

[33] Fig. 1C is a top plan view of the fluid delivery system shown in Figs. 1A and 1B with various fluid path components positioned therein.

[34] Fig. 1D is a cross-sectional view taken along line 1D-1D of Fig. 1A.

[35] Fig. 1E is a cross-sectional view taken along line 1E-1E of Fig. 1A.

[36] Fig. 2A is a schematic illustration of the multi-patient fluid path set and components thereof of the present invention.

[37] Fig. 2B is an exploded view showing the multi-patient fluid path set shown in Fig. 2A connected to a fluid source and disposed above the fluid delivery system shown in Figs. 1A-1E.

[38] Fig. 2C is a perspective view of an alternate embodiment of the multi-patient fluid path set of the present invention.

[39] Fig. 3A is an elevational view of a preferred embodiment of a coil assembly of the present invention.

[40] Fig. 3B is a partial cross-sectional view of Fig. 3A.

[41] Fig. 3C is a plan view (in partial cross-section) taken along line 3C-3C of Fig. 3A.

[42] Fig. 3D is a cross-sectional view taken along line 3D-3D of Fig. 3A.

[43] Fig. 3E is a perspective view of the core element of the coil assembly shown in Fig. 3A.

[44] Fig. 3F is an enlarged view of Fig. 1D showing the coil assembly in the ionization chamber of the fluid delivery system.

[45] Fig. 4A is an elevational view of preferred embodiments of a vial shield carrying system and a vial access system of the present invention.

[46] Fig. 4B is a perspective view showing the vial shield, the vial shield carrying system and the vial access system of Fig. 4A.

[47] Fig. 4C is an elevational view of a pharmaceutical vial that may be used in the fluid delivery system of the present invention.

[48] Figs. 5A-5D are various views of an alternate embodiment of a vial shield carrying system of the present invention.

[49] Fig. 6A is a bottom perspective view of a preferred embodiment of a vial access system of the present invention.

[50] Fig. 6B is a top perspective view of the vial access system shown in Fig. 6A.

[51] Fig. 6C is an exploded, perspective view of a preferred embodiment of the vented cannula of the multi-patient fluid path set of the present invention oriented to be connected to the cap of the vial access system shown in Figs. 6A-6B.

[52] Fig. 6D is a perspective view (similar to Fig. 4B) showing the vial access system and the vial-carrying shield disposed in a well of the fluid delivery system, and the vented cannula connected to the cap of the vial access system and in position to be lowered and inserted through the septum cap of the vial shield into the radiopharmaceutical vial.

[53] Fig. 6E is another perspective view (similar to Fig. 6D) showing the cap of the vial access system lowered into position and the vented cannula thereby inserted into the pharmaceutical vial.

[54] Fig. 6F is an enlarged view of Fig. 1E showing the vial access system and the vented cannula of the present invention.

[55] Fig. 6G is a perspective view of the vented cannula shown in Fig. 6C.

[56] Fig. 6H is an elevational view of the vented cannula shown in Fig. 6G.

[57] Fig. 6I is a left-side view of the vented cannula shown in Fig. 6H.

[58] Fig. 6J is a right-side view of the vented cannula shown in Fig. 6H.

[59] Fig. 7 shows a main screen of a graphical user interface of the present invention.

[60] Figs. 8, 9, 10, 11, 12A, 12B, 13, 14, 15, 16A, 16B, 17, 18, 19, 20, 21 and 22 are various depictions of a graphical user interface for use in system preparation tasks.

[61] Figs. 23, 24A-F, 25A, 25B, 26A, 26B, 27A, 27B, 28A, 28B, 29, 30A, 30B, 31, 32A and 32B are various depictions of a graphical user interface for use in patient treatment tasks.

[62] Figs. 33A-C, 34A and 34B are various depictions of a graphical user interface for use in injection history/recall operations or tasks.

[63] Figs. 35, 36, 37, 38, 39A, 39B, 40, 41, 42, 43, 44A-D, 45A-D and 46 are various depictions of a graphical user interface for use in system configuration tasks.

[64] Fig. 47A is a perspective view of the vented cannula shown in Figs. 6C and 6G-6J being utilized as part of a first alternate fluid delivery system.

[65] Fig. 47B is another perspective view showing the first alternate fluid delivery system of Fig. 47A.

[66] Fig. 47C is an elevational view of the first alternate fluid delivery system of Figs. 47A and 47B.

[67] Fig. 48 is a perspective view of the vented cannula shown in Figs. 6C and 6G-6J being utilized as part of a second alternate fluid delivery system.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

[68] As used herein, the term "pharmaceutical" refers to any substance or drug to be injected or otherwise delivered into the body (either human or animal) in a medical procedure and includes, but is not limited to, substances used in imaging procedures (for example, contrast media) and therapeutic substances. A number of such pharmaceutical substances pose a danger to both the patient and the personnel administering the substance if not handled and/or injected properly. Examples of hazardous pharmaceuticals include, but are not limited to, radiopharmaceuticals, biological pharmaceuticals, chemotherapeutic pharmaceuticals and gene therapeutic pharmaceuticals.

[69] Turning now to the drawings, Figs. 1A-1E show a preferred embodiment of the administration, injector or fluid delivery system 10 of the present invention. The fluid delivery 10 is preferably a cart-like apparatus 9 having wheels 13 and/or casters 12 for allowing the system to be movable. One or more of the wheels 13 may be lockable to prevent the system 10 from moving once it is in position. The system 10 also preferably includes one or more handles 14 for allowing an operator to move or position the system 10. Alternately, the fluid delivery system 10 may be a stand-alone or fixed-position apparatus.

[70] The fluid delivery system 10 includes a display or graphical user interface (GUI) 15 for programming and operating the system 10. The GUI display 15 is preferably attached to one of the handles 14 (as shown) of the system 10. The display 15 may be a color display and incorporate touch-screen capability, as known in the art, for ease of use. The display 15 may be fixed, but is preferably pivotally connected to the fluid delivery system 10 (as shown), by means of a movable arm 11 that is pivotally connected to a joint 16. Further, the display 15 may be tilted or swiveled with respect to the arm 11 to allow for optimal positioning of the display 15 by an operator.

[71] The fluid delivery system 10 preferably includes a retractable lid or cover 20 having a primary handle including a latch release 1 (see Figs. 1D and 1E) and a secondary handle 21. The lid 20 preferably covers an upper surface 103 that defines a number of recessed portions, such as wells and troughs, into which a vial or container (see 902 in Fig. 4C) of a pharmaceutical or a radiopharmaceutical (discussed in more detail below) and various components of a multi-patient fluid path set (hereinafter MPDS; discussed in more detail below) may be positioned during an injection procedure. A locking mechanism, such as a combination or a key lock (not shown), may be used to lock the lid 20 in a closed position to, for example, prevent use or access of the system 10 by unauthorized personnel. In another embodiment, the locking mechanism may be a software-implemented lock, such as a password-protected access point, that is accessible through the display 15 and is adapted to lock the cover in a closed position and/or to prevent unauthorized personnel from accessing or operating the system 10.

[72] The lid 20 is slidable or retractable (by, for example, using primary handle and latch release 1) with respect to the cart 9 to allow for insertion and removal of the vial or container 902 and MPDS from the fluid delivery system 10. The lid 20, upper surface 103 and various other portions of the cart 9 preferably include suitable radioactive shielding (such as lead) for minimizing potential radiation exposure from the radiopharmaceutical to the operator. In this manner, the radiopharmaceutical vial 902 and the components of the MPDS can lie below the plane of surface 103, whereupon the surface 103 or one or more portions thereof can be covered by the lid 20 during use to limit radiation exposure to the operator or other medical personnel. Further, instead of a retractable lid 20, surface 103 itself could be disposed on a portion of the injector apparatus 10 (e.g., a drawer-type mechanism) that slidably displaces with respect to a remainder of the injector apparatus 10.

[73] As further shown in Figs. 1A, 1B and 1D, the fluid delivery system 10 includes a pumping mechanism, such as a peristaltic pump 22, a removable/replaceable source of medical fluid 23 (such as saline), a printer 24 and an interrupt button 25. The peristaltic pump 22 is shown in a closed position in Fig. 1A, but may be opened (see Figs. 1B, 1C and 2B) to receive a length of tubing 27(see Figs. 1C and 2) in fluid connection with the source of medical fluid 23 to inject the fluid into a patient (discussed in more detail below). While a peristaltic pump 22 is currently preferred, any suitable type of pumping mechanism, such as a piston-driven syringe pump, gear pump, rotary pump or in-line pump, may be used.

[74] The printer 24 may be used to generate records of the injection and/or imaging procedures performed on patients, for inclusion in patients' medical records or for billing or inventory purposes. The printer 24 may be pivotally connected to the system 10 (see Fig. 1B) to allow an operator to load paper or labels into the printer 24.

[75] The interrupt button 25 allows an operator to quickly and easily pause or abort an injection procedure in the event of, for example, patient discomfort or an emergency, without having to resort to the GUI display 15 (which also can be manipulated to pause or abort an injection procedure). The interrupt button 25 may be connected to LEDs and/or a printed circuit board to provide visual and/or auditory alarms when the interrupt button 25 has been activated.

[76] Turning to Figs. 1C-1E, 2A and 2B, additional features and components of the fluid delivery system 10, including the upper surface 103, the MPDS 200, a vial access device 600 and a single-patient fluid path set 700 (hereinafter SPDS), will be discussed.

[77] As shown in Fig. 1C, the upper surface 103 generally defines wells and recesses or troughs into which various components of the MPDS are situated. Specifically, a first recess or trough 107 accommodates a first tubing section 204 of the MPDS 200 and a tubing holder 150 for holding the tubing section 204 and preventing it from getting kinked or tangled with, for example, the SPDS 700. The first tubing section 204 may also include the tubing length 27 that is placed within the peristaltic pump 22 and is in fluid connection with the medical fluid source 23.

[78] The first trough 107 leads into a second recess or trough 113 that accommodates a second pumping mechanism 180, such as a peristaltic pump, and a T-connector 205 (preferably including check valves 214, 215) of the MPDS 200. As shown in Fig. 1C, the second trough 113 also leads to a first well 111 that accommodates a vial access device 600 and a radiopharmaceutical vial or container 902 disposed in a vial shield or PIG 554 (discussed in more detail below) and to a second well 121 that accommodates a dose calibrator or ionization chamber 160 for the fluid delivery system 10. As shown in Figs. 1D and 3F, the ionization chamber 160 preferably accommodates a coil assembly 400 of the MPDS 200 (discussed in more detail below).

[79] A third recess or trough 125 extends from the second well 121 to a third well 127 and further along the surface 103 of the fluid delivery system 10. The trough 125 accommodates a T-connector 222 of the MPDS 200, two pinch valves 170, 172, an

air detector 174 and a mount or retainer 176 for holding the connector end 228 of the MPDS 200. The pinch valves are preferably powered and controlled by the fluid delivery system 10, but alternately could be manually-operated. In another alternate embodiment, the pinch valves 170, 172 and the T-connector 222 of the MPDS 200 may be replaced with a manual or automated 3-way stopcock.

[80] The third well 127 accommodates a waste receptacle or bag 224 for receiving medical fluid and/or pharmaceutical that is discarded during, for example, a priming procedure (discussed in more detail below) to prepare the system 10 for an injection procedure.

[81] As shown in Fig. 1C, the SPDS 700 includes a length of tubing (preferably coiled, as shown) having a first end 702 that is attachable to the connector end 228 of the MPDS 200 and a patient end 704 having a luer connector that is attachable to, for example, a catheter (not shown) placed in a venous structure of a patient. As discussed in more detail below, the MPDS 200 may be used for multiple patients but the SPDS 700 is intended to be used on a per-patient basis and discarded after use with a single patient to prevent, for example, cross-contamination between patients.

[82] As can be appreciated after reviewing Fig. 1A-1E, the secondary handle 21 of lid 20 overlies the tubing holder 150 and the mount 176 when the lid 20 and handle 21 are closed to cover the MPDS 200. The secondary handle 21 may be flipped open (from the closed position shown in Fig. 1A) without retracting the cover 20 to allow an operator to connect the SPDS 700 to the MPDS 200(as discussed in more detail below). As best shown in Fig. 1C, the SPDS 700 may be placed under the secondary handle 21 when it is closed.

[83] The fluid delivery system 10 further includes a system controller 5 (see Figs. 1D and 1E) in communication with the various components thereof, including the GUI 15, the pumps 22, 180, the dose calibrator or ionization chamber 160, the stop button 25, the air detector 176, the printer 24 and the motors 30, 31 (see Fig. 3F) for pinch valves 170, 172, respectively, for controlling the operation of the system 10. The system controller 5 is preferably a single-board computer, including a CPU having a main memory.

[84] As can be appreciated, the wells and troughs formed in the upper surface 103 can be sized, configured or arranged as suitable for the length, design or configuration of the MPDS 200 or other components thereof, including the radiopharmaceutical vial 902, vial shield 554, vial access device 600, ionization chamber 160, waste receptacle 224, etc.

[85] It should be understood that Fig. 1C in no way is intended to convey dimensions or relative dimensions of the aforementioned recessed portions or MPDS components; instead, Fig. 1C conveys general positional relationships of such recessed portions with respect to one another.

[86] It should further be understood and appreciated that the recessed portions shown and described with respect to Fig. 1C are preferably encased throughout with suitable radioactive shielding to further minimize exposure to an operator.

[87] Turning now to Figs. 2A and 2B, a preferred embodiment of the MPDS 200 and components thereof will be discussed. In addition, specific details of the coil assembly 400 employed in the MPDS 200 are shown and described with respect to Figs. 3A-3F and Fig. 1D.

[88] By way of a general overview, the MPDS 200 in accordance with at least one presently preferred embodiment of the present invention allows for FDG (or other radiopharmaceutical) to be drawn from a bulk radiopharmaceutical vial 902 and placed into a coil assembly 400 that allows an ionization chamber 160 to measure the amount of activity in the coil assembly 400. Once the system prepares a dose having the desired activity level, the fluid delivery system 10 will deliver the FDG dose to the patient (through the SPDS 700).

[89] Generally, the MPDS 200 can be considered in terms of four components: (1) a medical fluid or saline component; (2) an FDG or pharmaceutical component; (3) a coil assembly component; and (4) a waste component. The saline component preferably draws saline out of a bulk source 23 (e.g., via peristaltic pump 22). This is then used to prime the MPDS (i.e., remove air therefrom), position FDG in the coil assembly 400 in the ionization chamber 160, and then deliver the dose to the patient.

[90] The FDG component preferably serves to draw FDG out of a bulk radiopharmaceutical vial 902 (e.g., via peristaltic pump 180) and place the same into the fluid path to the ionization chamber 160.

[91] The coil assembly component preferably is employed to position the radiopharmaceutical to allow its radioactivity level to be optimally measured by the ionization chamber 160. Through the arrangement of the coil assembly 400 (as discussed in more detail below), the radiopharmaceutical can be optimally oriented and located within the "linear region" of the ionization chamber 160 to more accurately measure its activity level and prepare an optimal dose for injection into a patient.

[92] The waste component preferably holds the saline fluid and/or radiopharmaceutical that are discarded during the prime and dose preparation procedures, which are conducted to prepare the fluid path and the pharmaceutical dose for injection into a patient.

[93] Fig. 2A schematically illustrates the MPDS 200 in accordance with a preferred embodiment of the present invention. The MPDS shown in Fig. 2A may preferably be pre-connected as shown and may originally be stored in a sterile packet or container for use in an injector apparatus, such as fluid delivery system 10, when desired. For a non-restrictive and illustrative appreciation of a manner in which MPDS 200 can be incorporated in an injector apparatus, simultaneous reference may be made to Figs. 1A-1E and 2B (and the discussion thereof hereinabove).

[94] Primary components of MPDS 200 include, as shown, a spike 202 for connecting the MPDS to the medical fluid or saline source 23, a vented cannula 208 for connecting with a source of FDG or other radiopharmaceutical, a coil assembly 400, a T-connector 205 with check valves 214, 215 for fluidly connecting the saline source 23, the radiopharmaceutical source and the coil assembly 400, a waste bag 224, a connector end 228, and a T-connector 222 for fluidly connecting the coil assembly 400, the waste bag 224 and the connector end 228.

[95] In general, MPDS 200 and fluid delivery system 10 are configured for priming (i.e., purging air from) the MPDS 200, delivering pharmaceutical (e.g., FDG) to a patient, and providing a saline flush, while minimizing or eliminating exposure of administering or operating personnel to the detrimental effects of the pharmaceutical and minimizing or eliminating creation of contaminated waste. Moreover, MPDS 200 and other elements of the present invention also facilitate safe delivery of the pharmaceutical to multiple destinations (for example, dose delivery to a series of patients).

[96] A T-connector 205 and check valves 214, 215 preferably accommodate a first tubing section 204 that is in fluid connection with spike 202 and a second tubing section 210 in fluid connection with cannula 208. The check valves 214, 215 may be integrally formed with the T-connector 205 or may be separate components, or they could be combined into a single dual check valve. The check valves 214, 215 prevent saline from being pumped by peristaltic pump 22 into second tubing section 210 and the pharmaceutical from being pumped by peristaltic pump 180 into the first tubing section 204.

[97] A third tubing section 216 thence preferably leads to coil assembly 400 (including tube coil 444), and a fourth tubing section 220 preferably leads from the coil assembly 400 to the T-connector 222. As described below, in a preferred embodiment the tube coil 444 is formed from a tubing section 217 that has dimensions different from those of the third tubing section 216 and the fourth tubing section 220. In an alternate embodiment, the third tubing section 216, the tube coil 444 and the fourth tubing section 220 are formed from the same length of tubing.

[98] A fifth tubing section 226 leads from the T-connector 222 to the waste receptacle 224 and a sixth tubing section 230 leads from the T-connector 222 to the connector end 228. As shown above in Fig. 1C, the connector end 228 mates with the first end 702 of the SPDS 700 for delivery of a pharmaceutical to a patient.

[99] In a preferred embodiment, the connector end 228 is a swabable luer valve (Part No. 245204024 provided by Halkey-Roberts Corporation of St. Petersburg, FL) that is biased to close or seal off the connector end 228 of the MPDS 200 when the SPDS 700 is not connected thereto. The swabable luer valve prevents the MPDS 200 from being contaminated and allows an operator to swab or clean (by, for example, an alcohol wipe) the connector end 228 prior to connecting an SPDS 7000 thereto. Alternately, however, the connector end 228 may be a standard luer connector as known in the art.

[100] As schematically shown in Fig. 2A, the tubing length 27 of the first tubing section 204 can be placed within pump 22 (indicated by dotted lines) to pump saline or other medical fluid from source 23 and a portion of the second tubing section 210 can be placed within pump 180 (indicated by dotted lines) to pump a radiopharmaceutical from a radiopharmaceutical source.

[101] Absolute and relative dimensions of the components shown in Fig. 2A, including tubing, may be chosen to best suit the applications at hand. Preferably, the first tubing section 204 is approximately 56.75 inches in length, has an outer diameter (OD) of approximately 0.188 inches and an inner diameter (ID) of approximately 0.062 inches and has a 45 durometer, the third tubing section 216 is approximately 15 inches in length, has an OD of approximately 0.163 inches and an ID of approximately 0.062 inches and has a 60 durometer, the fourth tubing section 220 is approximately 12 inches in length, has an OD of approximately 0.163 inches and an ID of approximately 0.062 inches and has a 60 durometer, and the fifth tubing section 226 and the sixth tubing section 230 are each approximately 5 inches in length, have an OD of approximately 0.163 inches and an ID of approximately 0.062 inches and have a 60 durometer. The second tubing section 210 is approximately

8.75 inches in length and is formed of microbore tubing having an OD of about 0.094 inches and an ID of about 0.032 inches and a 45 durometer. The tubing in tube coil 444 preferably is approximately 41 inches in length, has an OD of about 0.218 inches and an ID of about 0.156 inches and an 80 durometer.

[102] Preferably, the microbore tubing of second tubing section 210 is formed of, for example, silicone, C-Flex, or silicone-like PVC material. Essentially, the use of microbore tubing in second tubing section 210 improves volume accuracy and thereby improves measured activity accuracy (i.e., of pharmaceutical delivered to the patient) and reduces radiopharmaceutical waste.

[103] By way of tubing material for the other tubing sections 204, 216, 220, 226, 230 and tube coil 444, essentially any suitable polymeric material, including standard PVC or pump tubing, may be employed.

[104] In an alternate embodiment of the MPDS 200' shown in Fig. 2C, a conventional manifold 228' or stopcock may be substituted for the connector end 228 of the MPDS 200 (all other components of the MPDS 200' may be identical or similar to those shown in Fig. 2A and are denoted in Fig. 2C by prime notations). As shown in Fig. 2C, the manifold 228' includes three outlet ports (preferably including swabable valves) to which respective first ends 702' of the SPDSs 700' are connected. By connecting the respective patient ends 704 of the SPDSs 700' to, for example, catheters placed in patients, pharmaceutical doses can be delivered sequentially or concurrently to three separate patients. While the manifold 228' shown in Fig. 2C includes three ports for connection to three SPDSs 700', two, four, five or any suitable number of ports may be included in manifold 228' for connection with a like number of SPDSs 700'.

[105] Referring again to Figs. 1A-2B, the placement of the MPDS 200 in the fluid delivery system 10 and the connection of the SPDS will now be discussed. To set up the system 10 at, for example, the beginning of the day, the operator lifts the secondary handle 21, grasps the primary handle and latch release 1 and retracts the lid 20 to reveal the upper surface 103 of the system 10. If a used MPDS 200 is present in the system 10, the operator will remove and discard it.

[106] A new MPDS 200 may be removed from its (typically sterile) packaging and placed in the system 10 as shown in Fig. 1C. This includes placing the waste receptacle 224 into well 127, placing coil assembly 400 into ionization chamber 160, placing second tubing section 210 into operative connection with pump 180, placing the tubing length 27 of the first tubing section 204 into operative connection with pump

22 and tubing holder 150, placing vented cannula 208 into fluid connection with radiopharmaceutical source or vial 902 located in well 111, placing fifth tubing section 226 in operative connection with pinch valve 170, and placing sixth tubing section 230 in operative connection with pinch valve 172, air detector 174 and mount 176. A saline source 23 may be hung on hook 6 (see Figs. 1A, 1B and 2B) or otherwise mounted on fluid delivery system 10, and spike 202 is inserted into port 7 (see Figs. 1A, 1B and 2B) of source 23 to fluidly connect the MPDS 200 to the source 23. Of course, this installation procedure does not need to completed in the order described above, but may be completed in any suitable order consistent with the description or drawings hereof.

[107] After the MPDS 200 is installed and preferably primed (as discussed below), the first end 702 of the SPDS 700 is connected to the connector end 228 of the MPDS 200 and the SPDS 700 is preferably primed to provide a wet connection at the patient end 704 of the SPDS 700, which is then connected to a catheter (not shown) located in a patient. The SPDS 700 is preferably a coiled tubing formed of standard PVC, approximately 60 inches in length and having an OD of approximately 0.100 inches and an ID of approximately 0.060 inches and a 90 durometer.

[108] As shown in Figs. 2A and 2B, the MPDS 200 includes a coil assembly 400. In the broadest sense, coil assembly 400 may include a section of tubing (including portions of third and fourth tubing sections 216, 220) that is simply gathered (in a coiled or an uncoiled, amorphous fashion) and placed inside ionization chamber 160.

[109] As shown in Figs. 3A-3F, however, a preferred embodiment of coil assembly 400 includes a (preferably thermoformed) core element or structure 446 that is preferably configured for allowing a tubing section 217 to be wrapped thereupon and to assume the coiled tube section indicated at 444. As such, the coiled tube section or tube coil 444 is preferably formed on the core element 446 to facilitate optimal positioning of the tube coil 444 within the ionization chamber 160.

[110] To facilitate positioning of the tube coil 444, the core element 446 preferably includes a tube channel 410 defined by shoulders 412, 414 (see Fig. 3B) that retain tube coil 444 therebetween to hold the tube coil 444 in position and to prevent tube kinking. Further, the upper surface 420 of core element 446 defines an inlet channel or groove 422 and an outlet channel or groove 424 to accommodate third tubing section 216 and fourth tubing section 220, respectively.

[111] In an alternate embodiment, the core element 446 could include a coiled tube channel (not shown) formed therealong to further guide and retain the tubing segments or turns that form tube coil 444 between shoulders 412, 414.

[112] The core element 446 preferably is self-centering when inserted into the sleeve 162 of the ionization chamber 160 of the fluid delivery system 10 to thereby facilitate optimal performance (see Fig. 3F). This may be achieved either through structural features of the coil assembly 400, the structure of core element 446 itself, or a combination thereof when used with the sleeve 162 of the ionization chamber 160.

[113] As best shown in Fig. 3E, the core element 446 is preferably formed by folding two elements (450, 452) together along an integral hinge 455. Suitable form-locking mechanisms can be molded onto the core element 446 to facilitate clasping of the elements 450, 452 together.

[114] Figs. 1C, 1D and 3F show coil assembly 400 positioned concentrically in the sleeve 162 of the ionization chamber 160. The core element 446 and the tube coil 444 are sized and dimensioned so that the coil assembly 400 is optimally positioned within the "linear region" of the ionization chamber 160 so that the ionization chamber 160 can accurately determine the activity level of one or more volumes of radiopharmaceutical that is located within the tube coil 444. The "linear region" of an ionization chamber is the region in which activity level measurements are repeatable and predictable. For the preferred ionization chamber (Model IK-102 Short Ionization Chamber provided by Veenstra Instruments) used in system 10, the "linear region" is located within a window of 5 mm to 65 mm measured from the base or bottom wall 160a of the ionization chamber 160 (see Fig. 3F).

[115] In a preferred embodiment, the tube coil 444 is comprised of approximately 7 turns (see Figs. 3A and 3B) formed from a length of tubing that is approximately 41.0 inches. As shown in Fig. 3B, the height H of the tube coil 444 is approximately 1.53 inches and the diameter D of the tube coil 444 is approximately 1.95 inches. The tube coil 444 is preferably formed from a tube having an OD of 0.218 inches and an ID of 0.156 inches. Further, based on the length and ID of the tubing, the tube coil 444 preferably has a volume capacity of approximately 12.5 ml.

[116] As discussed heretofore, a source, container or vial 902 (see Fig. 4C) of a pharmaceutical or radiopharmaceutical is placed into the fluid delivery system 10 (e.g., in well 111 formed in upper surface 103) to prepare and perform an injection procedure. A radiopharmaceutical container or vial 902 is typically placed in a conventional vial shield or PIG 554 for transport by personnel.

[117] Turning now to Figs. 4A and 4B, preferred embodiments of a vial shield carrying device or system 500 and a vial access system 600 of the present invention are shown. Vial access system 600 is removably disposed within well 111 of fluid delivery system 10 and operates to hold vial shield 554 and to access the contents of the vial 902 contained therein. (Vial access system 600 will be described in more detail below with reference to Figs. 6A-6J.

[118] As best shown in Fig. 4A, the vial shield 544 (containing a radiopharmaceutical vial 902) includes a flange 504 formed along a top end thereof and a removable septum cap 562 that is securely and removably engaged with the vial shield 544 (e.g., via threading) to allow insertion and removal of the vial 902 therefrom.

[119] As shown in Figs. 4A and 4B, the carrying system 500 includes a collar unit 502 that removably engages the flange 504 formed on the vial shield 554. The collar 502 may be formed in two pieces 506, 508 that are pivotally connected together (e.g., at one end thereof) to allow the collar 502 to engage and disengage the flange 504.

[120] The collar 502 includes two elongated slots 510 formed in a top surface therein. As best shown in Fig. 4B, the slots 510 each include a pin 512 disposed therein and extending between two opposing walls 514 thereof.

[121] The carrying system 500 further includes a handle unit 520 that engages with the collar unit 502 and the septum cap 562 to allow the vial shield 554 (and vial 902) to be carried and installed in the fluid delivery system 10. The handle unit 520 includes a handle 556 that is rigidly connected to a generally U-shaped cross piece 564a. The cross-piece 564a defines two, downwardly extending arms 530 having slots 532 formed thereon.

[122] The slots 523 each form a slight hook on the ends thereof and are adapted to engage and retain a second cross piece 564b that supports a plunger 566 having a generally frustoconical shape that mates with a generally frustoconical recess of the septum cap 562 (see Fig. 4B).

[123] The second cross piece 564b is also generally U-shaped and defines two downwardly extending arms 534 having hooks 536 formed therein. The open ends of the hooks 536 are formed on opposite ends of the arms 534 and are adapted to accept and retain the pins 512 in slots 510 of collar 502. The slots 510 are sized to provide sufficient clearance for the arms 534 to be inserted thereinto (in a downward direction) and for the hooks 536 to engage pins 512 (through rotation of handle 556).

[124] The plunger 566 is connected to the second cross piece 564b by means of a connector (such as a screw 540) and a spring 538. The plunger 566 is biased by spring 538 to ensure a tight fit between the plunger 566 and the septum cap 562.

[125] To engage and carry the vial shield 554, the collar 502 is connected to the flange 504 of the vial shield 554 as described above. The handle unit 520 is then moved into proximity to the vial shield 554 (by an operator grasping the handle 556 and moving the unit 520 into position) and the arms 534 are lowered into the slots 510 of the collar 502. At substantially the same time, the plunger 566 is engaged with the septum cap 562, with the spring 538 insuring a tight fit between the two. The operator then turns the handle unit 520 in a clockwise direction (see Arrow A in Fig. 4A) to seat the pins 512 in slots 510 into the hooks 536 of arms 534.

[126] The operator then lifts the combined vial shield 554 and vial carrying system 500 (by moving the handle unit 520 in an upward direction) and transports it to, for example, the fluid delivery system 10. The operator then lowers the vial shield 554 into the vial access system 600 disposed in well 111 (see Fig. 4A) and rotates the handle unit 520 in a counter-clockwise direction to disengage the hooks 536 from the pins 512. The operator then lifts the handle 556 in an upward direction to remove the arms 534 from the slots 510 and the plunger 566 from the septum cap 562, thereby leaving the vial shield 554 (with septum cap 562 and collar 502) in vial access device 600 in well 111 (see Fig. 4B).

[127] In a preferred embodiment, the plunger 566 includes radioactive shielding (such as lead) to shield the operator from radiation that would otherwise leak through or be emitted from the septum of the septum cap 562. Together with the vial shield 554 and the septum cap 562, the plunger 556 of the vial carrying system 500 shields the operator from the radiation emitted by the radiopharmaceutical and prevents unnecessary radiation exposure. Further by extending the handle 556 from the vial shield 554, the distance between the two functions to also lessen any possible radiation exposure to the operator.

[128] An alternate embodiment of the carrying system is shown in Figs. 5A-5D. As with the preferred embodiment described above with respect to Figs. 4A and 4B, the carrying system 1500 helps minimize operator exposure to radiation. Dimensions shown in Fig. 5A are for illustrative and non-restrictive purposes; here they are given in inches. As with Figs. 4A and 4B, generally contemplated here is an integral carrying system 1500 that enables the vial shield 1554 to be carried and placed in the fluid delivery system 10 with minimal operator finger/hand radiation exposure

because the design of the carrying system 1500 increases the distance from the vial 902 contained within the vial shield 1554.

[129] Shown in Figs. 5A and 5C is a vial shield 1554 with a plunger 1566 of the carrying/installation handle system 1500 engaged with the septum cap 1562 of the vial shield 1544. The septum cap 1562 engages securely with the vial shield 1554 (e.g., via threading) to provide suitable radioactive shielding.

[130] As shown in Figs. 5A-5D, a crosspiece 1564a with a central aperture is rigidly connected to handle 1556 and is preferably configured to slidably accommodate an extension tube 1558. At a free end of extension tube 1558, the plunger 1566 is preferably disposed to engage with septum cap 1562. Though this engagement may be embodied in essentially any suitable way, here plunger 1566 has a generally frustoconical shape that engages with a generally frustoconical recess of septum cap 1562.

[131] As further shown in Figs. 5A and 5B (and as can be better appreciated by the perspective views in Figs. 5C and 5D), handle 1556 preferably terminates in a ring 1564b that is configured for engaging with structural features of cap 1562 (to be described more fully below).

[132] As shown in Fig. 5B, plunger 1566 may be hingedly or pivotably connected to extension tube 1558 via a hinge or pivot connection 1568, which provides freedom of motion to allow the plunger 1566 to mate with the septum cap 1562 without the operator having to otherwise place her hand and fingers directly above the septum cap 1562 before it is covered by the plunger 1566 (thereby reducing the possibility of radiation exposure to the operator).

[133] While Figs. 5A-5C show handle 1556 in a retracted position, i.e., maximally displaced away from plunger 1566, Fig. 5D shows in perspective view a different stage of the engagement of handle 1556 with vial shield 1554. As such, Figs. 5A-5C shows handle 1556 maximally retracted from plunger 1566 (and, by extension, cap 1562), while Fig. 5D shows handle 1556 in a "fully engaged" configuration with respect to cap 1562.

[134] Preferably, plunger 1566 will initially mate with cap 1562. Thence, handle 1556 is preferably moved towards cap 1562 (conceptually progressing from Fig. 5B to 5D) such that slots 1570 on ring 1564b fit over and capture posts 1572 (through clockwise rotation of handle 1556) on cap 1562. The handle 1556 may then be lifted to carry and deposit the vial shield 1554 in the well 111, as described above.

The carrying system 1500 is disengaged from the vial shield 1554 through counter-clockwise rotation of the handle 1556 to disengage the capture posts 1572 from the slots 1570 on the ring 1564b. Of course, after the contents of the vial 902 are depleted, the carrying system 1500 can be attached to the vial shield 1554 as described above to remove the vial shield 1554 and the vial 902 from the fluid delivery system 10.

[135] As discussed above with respect to Figs. 4A-4B, the fluid delivery system 10 includes a vial access system 600 that is removably disposed within well 111 of fluid delivery system 10 and is adapted to hold vial shield 554, 1554 and to provide access to the contents of the vial 902 within vial shield 554, 1554.

[136] Because vials (such as vial 902 described herein) typically come in various sizes, such as 10 ml, 15 ml, 20 ml and 30 ml, the fluid delivery system 10 of the present invention is intended to accommodate various vial sizes. To do so, the fluid delivery system 10 may include one or more vial shields and vial access systems (varying primarily in size in relation to the preferred embodiment of the vial shields 554, 1554 and vial access system 600 disclosed and described herein) that are specifically sized to accommodate known vial sizes. In a preferred embodiment, three vial shields and vial access systems 600 are provided with the fluid delivery system 10, and the well 111 is configured and designed to accept each of the vial access systems 600. However, the fluid delivery system 10 can be provided with one, four, five or any suitable number of vial shields and vial access systems depending on evolving needs or changes in the size or shape of the vials. Thus, depending on the size of the vial used at a clinical site or for a particular procedure, an operator of the fluid delivery system 10 can select the appropriate vial shield and vial access system and place it in the well 111 of the fluid delivery system to enable a fluid injection procedure.

[137] Preferred embodiments of the vial access system 600 and the vented cannula 208 of the MPDS 200 are described below in relation to Figs. 6A-6J (and with reference to Figs. 4A and 4B). Generally, as best shown in Figs. 6A, 6B and 6F, the vial access system 600 includes a base portion 670 that preferably includes a sloped surface 672, the function of which will be more fully appreciated herebelow. Two (preferably removable and extendable) support members or pins 674 are provided to support and retain a vial shield 554 (i.e., enclosing a vial 902; see Fig. 4C) when it is placed on the sloped surface 672 (e.g., after being carried and disposed there using the vial shield carrying systems 500, 1500 discussed above).

[138] As shown, the vial access system 600 further includes a vertical support arm 676 that is disposed within a housing 678. A cap member 684 and a handle member 682 are connected to an upper end of the vertical support arm 676. The vertical support arm 676 is preferably slidably and rotationally displaceable with respect to the housing 678. That is, the arm 676 may slide and rotate with respect to the housing 678 (see e.g., Figs. 4B and 6D) to allow the vial shield 554 to be readily inserted and removed therefrom and to lower the vented cannula 208 into the vial 902 contained within the vial shield 554 (as discussed in more detail below).

[139] The handle 682 is used by an operator or technician to insert and remove the vial access system 600 from the well 111 of the fluid delivery system 10. The handle 682 is preferably connected to the vertical support arm 676 via a suitable pivot connection (such as a hinge or bolt connection) 680 to permit movement of the handle 682 between an extended, carrying position (see Fig. 6D) for carrying the vial access system 600 and a horizontal or operating position (see Figs. 6B and 6E) in which the handle 682 rests on top of the cap 684 (e.g., when the vial access system 600 is disposed in the well 111), thereby allowing the cover 20 of the fluid delivery system 10 to be closed.

[140] The cap 684 is preferably rigidly connected to the vertical support arm 676 via an arm 650 (see Figs. 6A and 6D), but it may be pivotally connected to the vertical support arm 676 via, for example, a pivot connection (not shown) or adjustably connected to the vertical support arm 676 via, for example, a slot (not shown) formed in the arm 650. As best shown in Figs. 6E and 6F, when the cap 684 is lowered (by sliding the vertical support arm 676 within the housing 678) to insert the cannula 208 into the vial 902 within the vial shield 554, and the handle 682 is pivoted to a horizontal position atop the cap 684, the cap 684 and the handle 682 (and thus the remainder of the vial access system 600) lies below or flush with the upper surface 103 of the fluid delivery system 10, thereby allowing the cover 20 to close over the upper surface 103 of the fluid delivery system 10 and the MPDS 200 installed therein. The cap 684 preferably includes or is formed with radioactive shielding material (e.g., lead) to minimize radiation exposure to personnel from the FDG or other radioactive solution contained within the vial 902 in the vial shield 554.

[141] As best shown in Figs. 6A and 6C, the underside of cap 684 includes a mounting mechanism 686 for accepting the cannula 208 (or other suitable type of spike, cannula or needle) for piercing the septum of a vial 902 or other pharmaceutical container in the vial shield 554. The mounting mechanism 686 preferably includes

two arms 687 that define a groove or slot 688 therebetween. Each of the arms 687 includes a tab member 690 extending downwardly therefrom.

[142] The vented cannula 208, in accordance with a preferred embodiment of the present invention, may be employed for spiking a pharmaceutical source (such as the radiopharmaceutical vial 902 discussed above) and preferably includes a main hub 332 to which are connected (or integrally formed) two, resilient spring arms 350. The spring arms 350 and the main hub 332 cooperate to define two U-shaped channels 352 on lateral sides of the main hub 332.

[143] As shown in Figs. 6C and 6G-6J, each of the spring arms 350 includes a flange or hook member 370 formed thereon and extending outwardly therefrom. The hook members 370 each defines an inclined surface or edge 372 formed thereon.

[144] The vented cannula 208 further includes a ledge or flange 338 that is connected to or integrally formed with the main hub 332 and is disposed in a horizontal plane above the two spring arms 350. The ledge 338 and the top edges of the spring arms 350 cooperate to define horizontal grooves or slots 360 therebetween for accommodating the arms 687 of the mounting mechanism 686 on the cap 684 of the vial access system 600.

[145] To connect the cannula 208 to the mounting mechanism 686 on the cap 684, the main hub 332 of the cannula 208 is aligned with the slot 688 of the mounting mechanism 686 and the arms 687 of the mounting mechanism 686 are aligned with the grooves 360 defined between the spring arms 350 and the top ledge 338 of the main hub 332. Once the structural elements of the cannula 208 and the mounting mechanism 686 are aligned, the cannula 208 is inserted into the mounting mechanism 686 until the hook members 370 of the spring arms 350 engage the front edges 691 of the tab members 690. Upon further insertion of the cannula 208, the front edges 691 of the tab members 690 engage and ride along the inclined surfaces 372 of the hook members 370, thereby moving the spring arms 350 in an inward direction (i.e., toward the vertical axis of cannula 208). This inward movement of the hook members 370 allows them to clear the front edges 691 of the tab members 690 and ride along the inner sides 693 thereof until the hook members 370 clear the tab members 690 and move or snap back into their original position to engage the rear edges 692 of the tab members 690. At this point, the cannula 208 is fully inserted into and retained by the mounting mechanism 686. To remove the cannula 208 from the mounting mechanism 686 (e.g., when the MPDS 200 is removed from the fluid delivery system 10), the operator pinches the hook members 370 together (i.e., moves them toward the vertical axis of the cannula 208) until they clear the

rear edges 692 of the tab members 690, and then slides the cannula 208 out of engagement with the mounting mechanism 686.

[146] Referring again to Figs. 6C and 6G-6J, the vented cannula 208 includes a longer, fluid draw needle 340 in fluid connection with the second tubing section 210 of the MPDS 200 via a fluid port 384 and a shorter, vent needle 342 in fluid connection with a vent 334. As known in the art, the vent 334 may include a suitable filter for filtering the ambient air that is drawn into the vial 902 to allow fluid to be drawn therefrom.

[147] The description now turns to the preferred operation and use of the vial access system 600 and the vented cannula 208 of the present invention. When a vial shield 554 (holding a pharmaceutical vial 902) is to be placed in the vial access system 600, the vertical support arm 676 is raised to an extended position and rotated (see Figs. 2B and 4A) to move the cap 684 out of its normal position above the sloped surface 672. The vial shield 554 is then inserted into the well 111 and placed on the sloped surface 672 (see Fig. 6F). The support pins 674 engage the vial shield 554 to hold it in position on the sloped surface 672.

[148] After the vial shield 554 is inserted into the vial access system 600 (see Fig. 4B), the vented cannula 208 of the MPDS 200 is inserted into the mounting mechanism 686 on the cap 684 and the cap 684 is rotated back into position (e.g., by turning the handle 682) above the septum cap 562 of the vial shield 554 (see Fig. 6D). Then the cap 684 is lowered (e.g., by using the handle 682 to urge the vertical support arm 676 into the housing 678) to insert the fluid draw needle 340 and the vent needle 342 of the cannula 208 through the septum of the septum cap 562 and into the pharmaceutical vial 902 (see Fig. 6F). The handle 682 is then rotated to lie in a substantially horizontal orientation on or above the cap 684 (see Figs. 1C and 6E), thereby allowing the cover 20 of the fluid delivery system 10 to be closed. While the preferred method of operating the vial access system 600 and the vented cannula 208 is provided above, the method and steps can be conducted in any suitable order or arrangement to achieve the desired results.

[149] As best shown in Fig. 6F, the support surface 672 is preferably configured such that when a vial is pierced by the fluid draw and vent needles 340, 342 of the cannula 208, the bottom end of the fluid draw needle 340 will be placed at or near the location where the cylindrical wall of the vial meets the bottom (floor) of the vial. Thus, to the extent that some vials may not have a completely flat bottom or floor (e.g., may have a rounded bump with a maximum height at the central longitudinal axis of the vial), the fluid draw needle 340 will be in a position to maximally draw

fluid from the vial as it collects at the junction of the vial's bottom and cylindrical wall (i.e., to avoid waste of the pharmaceutical). Or, even in a flat-bottomed vial, such an orientation of the vial will help ensure that fluid maximally gathers and is drawn in a closely defined area.

[150] As discussed above, the dimensions of the vial access system(s) 600 provided with the fluid delivery system 10 can preferably be chosen in accordance with dimensions of the vial shields and vials to be employed, to ensure that as much fluid from the vial is drawn as possible. By way of a non-restrictive example, the sloped surface 672 could be sloped at an angle of about 10-13 degrees with respect to the horizontal.

[151] Instead of being incorporated into and as part of the MPDS 200 for use with the fluid delivery system 10, the vented cannula 208 of the present invention may be used in other fluid delivery systems, including ones that use shielded syringes (see e.g., U.S. Patent Nos. 5,927,351 and 5,514,071, the contents of which are incorporated herein by reference), for injecting pharmaceuticals or other medical fluids into patients.

[152] As shown in Figs. 47A-C, the vented cannula 208 may be used with a hand-held syringe 380 (preferably held within a conventional lead-shielded container (not shown for ease of illustration)) having a discharge outlet 386 and a plunger 381 slidably disposed therein. The fluid draw needle 340 of the cannula 208 is in fluid connection with the shielded syringe 380 by means of a tube 383 connected between the discharge outlet 386 of the syringe 380 and the fluid port 384 of the cannula 208. The tube 383 preferably includes a connector 387, such as a standard luer connector, for removably connecting the tube 383 to the shielded syringe 380. The other end of the tube 383 may be non-removably attached to the fluid port 384 of the cannula 208 by use of, for example, an adhesive. Alternately, the tube 383 may include a connector (not shown) for removable connection to the fluid port 384 or may be press fit and held by friction forces onto the fluid port 384.

[153] The tube 383 may be fashioned in any length or diameter suitable for the application. In use, the fluid draw and vent needles 340, 342 of the cannula 208 are inserted into a vial (not shown) containing a pharmaceutical or other fluid. The plunger 381 is retracted (moved away from the discharge outlet 386 of the syringe 380) to aspirate fluid from the vial into the syringe 380. The connector 387 is disconnected from the shielded syringe 380 and the syringe 380 is then connected, generally via an intermediate tubing (not shown), to a catheter disposed in a patient.

The plunger 381 is then advanced (moved toward the discharge outlet 386) to inject fluid into the patient.

[154] As shown in Fig. 48, the vented cannula 208 may also be utilized as part of a second alternate fluid delivery system 399 including a shielded (not shown for ease of illustration), hand-held syringe 380' having a discharge outlet 386' and a plunger 381' slidably disposed therein. In addition to like elements shown in Figs 47A-C, the system 399 includes first, second and third tubing segments 390, 391, 392 that are connected via a T-connector 393 having an integral stopcock 394. The third tubing segment 392 also preferably includes a swabable valve 395 to which the first end 702 of the SPDS 700 described above could be connected. Instead of a swabable valve 395, it is contemplated that a conventional luer connector could be used for suitable applications.

[155] After the vented cannula 208 is placed in a pharmaceutical source (not shown), the stopcock 394 is actuated to open the fluid path between the vented cannula 208 and the syringe 380' and to close the path to the third tubing segment 392. The plunger is then retracted to aspirate fluid into the syringe 380' from the pharmaceutical source. The stopcock 394 is then actuated to open the fluid path between the syringe 380' and the third tubing segment 392 and to close the path to the second tubing segment 391. The first end 702 of the SPDS 700 is then preferably connected to the swabable valve or luer connector 395, and the plunger 381' is advanced to pump fluid to the patient end 704 of the SPDS 700 (e.g., to purge air from the tubing and to thereby provide a wet connection between the patient end 704 of the SPDS 700 and the catheter (not shown) in a patient). The patient end 704 is then connected to the catheter and the plunger 381' is advanced again to pump or deliver fluid through the SPDS 700 to the patient.

[156] After the fluid is delivered to the patient, the SPDS 700 is disconnected from the patient and the valve or luer connector 395 and is discarded. If another injection is to be performed, a new SPDS 700 can be connected to the valve or connector 395 and the system 399 can be primed to again provide a wet connection at the patient end 704 of the SPDS 700.

[157] The disclosure now turns to the operation of the fluid delivery system 10 and its various components. As known in the art, in injection procedures and other fluid delivery operations in which pharmaceuticals are delivered to a patient, air is purged from the fluid path by pumping an amount of the pharmaceutical and/or a diluent, such as saline, through the fluid path to the end of a tubing set (e.g., MPDS 200 or SPDS 700) before connecting the tubing set to a catheter in the patient. Such an air

purging or "priming" procedure is standard practice to prevent the occurrence of an air embolism in a patient, which can cause serious injury or death. Further, the dimensions (e.g., length and ID) of the SPDS 700 and the various tubing sections of the MPDS 200 (provided above) are necessary for accurate priming, activity measurement and delivery of the pharmaceutical to the patient because the system 10 relies on those dimensions to accurately determine and monitor the volume of pharmaceutical and saline that is required for those various operations.

[158] Referring again to Figs. 1C and 2A, once the MPDS 200 is installed in the fluid delivery system 10, the spike 202 is placed in fluid connection with the saline source 23 and the cannula 208 is inserted into the vial 902 and placed in fluid connection with the pharmaceutical therein, the MPDS 200 is primed to remove air therefrom.

[159] In a preferred method of priming the MPDS 200, the pump 22 is activated to draw saline out of source 23 and to move the saline through first tubing section 204, check valve 215, T-connector 205 and into third tubing section 216. The pump 180 is then activated to draw a small amount of pharmaceutical out of vial 902 and to move the pharmaceutical through second tubing section 210, check valve 214, T-connector 205 and into third tubing section 216. The pump 23 is then activated again to draw additional saline from saline source 23 to thereby move the volume of pharmaceutical present in third tubing section 216 into the tube coil 444 of coil assembly 400 located in the dose calibrator 160.

[160] To ensure that the second tubing section 210 is primed, the dose calibrator 160 is monitored to measure the level of radioactivity in the coil 444. If the dose calibrator measures no activity (or an activity level below a predetermined, baseline activity level), then the second tubing section 210 has not been appropriately primed and the priming process described above needs to be reinitiated by the operator. If the dose calibrator measures any activity level (or an activity level above the predetermined, baseline activity level), then the system 10 concludes that the second tubing section 210 has been correctly primed.

[161] After the second tubing section 210 is primed, the motor 30 is activated to open the pinch valve 170 and thereby open the fluid path from the fourth tubing section 220 through the T-connector 222 and the fifth tubing section 226 to the waste receptacle 224, the motor 31 is activated to close the pinch valve 172 and thereby close the fluid path along the sixth tubing section 230, and pump 22 is activated again to move the saline and the pharmaceutical in tube coil 444 through fourth tubing section 220, T-connector 222, fifth tubing section 226 and into waste receptacle 224.

[162] Subsequently, the first end 702 of the SPDS 700 is connected to the connector end 228 of the MPDS 200. The motor 30 is activated to close the pinch valve 170 (and thereby close the fluid path from the fourth tubing section 220 through the T-connector 222 and the fifth tubing section 226 to the waste receptacle 224), the motor 31 is activated to open the pinch valve 172 (and thereby open the fluid path along the sixth tubing section 230), and the pump 22 is activated again to move the saline through the T-connector 222 and the sixth tubing section 230 to the patient end 704 of the SPDS 700. At this point, the entire length of the MPDS 200 and the SPDS 700 is primed and the patient end 704 of the SPDS 700 can be connected to the catheter or other venous access device placed in a patient.

[163] In an alternate embodiment, after the pharmaceutical is moved into the waste receptacle 224, the remainder of the MPDS 200 is primed prior to the SPDS 700 being connected to connector end 228 of the MPDS 200. (This alternate priming method may be accomplished if the connector end 228 of the MPDS 200 is not the preferred swabable luer valve but rather is, for example, a standard luer connector or another connector that is not biased to a closed position when disconnected from the first end 702 of the SPDS 700.) Then, the first end 702 of the SPDS 700 is connected to the connector end 228 of the MPDS 200 and the SPDS 200 is primed to provide a wet connection at the patient end 704 of the SPDS 700.

[164] To accomplish this alternate priming method, the motor 30 is activated to close the pinch valve 170 (and thereby close the fluid path from the fourth tubing section 220 through the T-connector 222 and the fifth tubing section 226 to the waste receptacle 224), the motor 31 is activated to open the pinch valve 172 (and thereby open the fluid path along the sixth tubing section 230), and the pump 22 is activated again to move the saline through the T-connector 222 and the sixth tubing section 230 to the connector end 228 of the MPDS 200. Then, after the first end 702 of the SPDS 700 is connected to the connector end 228 of the MPDS 200, the pump 22 is activated again to move saline through the SPDS 700 to the patient end 704 thereof.

[165] After the MPDS 200 and the SPDS 700 are primed and the patient end 704 of the SPDS 700 is connected to the patient, the system 10 is ready for an injection procedure. While preferred and alternate methods of priming the MPDS 200 and the SPDS 200 are described above, other methods or steps may be employed or the steps above may be rearranged in any suitable manner to purge air from the MPDS 200 and the SPDS 700.

[166] In an alternate embodiment of the MPDS 200, the T-connector 205 and the check valves 214, 215 can be replaced with an automated, motor-driven stopcock. T-connector 222 also can be replaced with an automated stopcock as well.

[167] The disclosure now turns to embodiments of the present invention, as illustrated in Figures 7-46, that could conceivably be employed in programming and operating a fluid delivery system as broadly contemplated herein.

[168] Shown schematically in Figures 7-46 are various incarnations of a touch screen arrangement 1000 displayed on a graphical user interface, such as GUI 15, that could be employed with the fluid delivery system 10. As a non-restrictive example, such a touch screen arrangement could be utilized in conjunction with a system controller 5 and/or computer of any of a variety of fluid delivery systems as broadly contemplated herein.

[169] In order to clearly and unambiguously communicate to an operator the current status of the system 10, a graphical user interface with easily legible symbols and icons, including exceedingly user-friendly data entry mechanisms, is broadly contemplated. An operator will thus be able to intuitively understand and undertake various tasks for operating system 10.

[170] While a touch screen arrangement is contemplated in connection with Figures 7-46, it is to be understood that other types of data entry arrangements are conceivable that would achieve an equivalent purpose. For example, soft or hard key entry could be used, as well as trackball arrangements, mouse arrangements, or a cursor control touch pad (remote from the screen).

[171] The touch screen arrangement 1000 shown in Figures 7-46 can preferably be employed for four categories of tasks, namely: (1) system preparation, (2) patient treatment, (3) injection history (i.e., obtaining information regarding previous treatments) and (4) system configuration. Preferably, a touch screen arrangement 1000 will be flexibly and selectably manipulable to accommodate and undertake any and all of these tasks as desired.

System Preparation

[172] The "system preparation" category includes a number of tasks that are preferably performed in the following order to prepare the system 10 for a fluid injection or delivery procedure: (1) disposing of a used MPDS 200 and vial 902 from, for example, the previous day or previous use of the system 10 (if still present in the system 10); (2) conducting a quality control check or "daily QC" of the system 10;

(3) installing a new pharmaceutical vial 902 and a new MPDS 200 in the system 10; and (4) priming the MPDS 200 to remove air therefrom. While the above order is the preferred one for preparing the system 10, the tasks may be performed in any suitable manner and order for the intended application.

[173] Fig. 7 conveys a "main" screen visible on touch screen arrangement 1000, which may be an initial screen presented to an operator when the system 10 is initially activated.

[174] As such, and as shown in Fig. 7, touch screen arrangement 1000 preferably generally depicts at a very high level the fluid path (e.g., MPDS 200 and SPDS 700) of the fluid delivery system 10. It can be appreciated that touch screen 1000 can easily be "mapped" (i.e., provide a one-to-one correspondence) to major components of the MPDS 200, the SPDS 700 and other components of the system 10 such as that discussed and illustrated herein with respect to Figs. 1A-6J, but that level of detail is generally not required for programming and use of the system 10.

[175] As shown in Fig. 7, the touch screen shows a saline field 1002 (here in the stylized shape of an IV bag), a pharmaceutical or FDG field 1004 (here in the stylized shape of a vial) and an ionization chamber graphic 1010. A tubing graphic 1008, as shown, encompasses a three-way junction with branches leading, respectively, to saline field 1002, FDG field 1004 and ionization chamber graphic 1010. As shown, the tubing graphic 1008 is coiled inside the ionization chamber graphic 1010 to indicate the tube coil 444 described above.

[176] Touch screen arrangement 1000 in Fig. 7 shows the system 10 as being in an "idle" state. As such, no fluid is shown as being disposed in or moving through tubing graphic 1008 and ionization chamber graphic 1010. Further, saline and FDG fields 1002, 1004 in Fig. 7 both convey an "empty" status, to indicate that the system 10 has not yet been provided with information regarding the presence and/or amount of fluid in the saline source 23 and the vial 902.

[177] Indicated at 1006 is a touch field showing desired activity (currently displayed as 15.0 mCi) for an injection procedure to be performed. When the system 10 is activated, the desired activity field 1006 preferably displays a default activity value that can be pre-programmed into the system 10 or pre-set by the operator. Alternately, the desired activity field 1006 can default to the last activity level that was programmed into the system 10. Further, a display (read-only) system preparation field 1020 includes an associated "setup" button 1022a that, when activated, permits system preparation tasks to be performed.

[178] Indicated at 1012, 1014, 1016 and 1018, respectively, in Fig. 7 are circular status icons that provide quick and easy reference to different aspects of system status and, as such, will highlight when an aspect of system status is "on" or "active" or provide status information on the system 10. Thus, icons 1012-1018 from left to right, respectively, convey information on the following system aspects: activity present 1012, fluid motion / injection status 1014, check for air / priming status 1016, and system battery status 1018.

[179] The system battery (not shown) provides power to the system controller 5 and to the ionization chamber 160 (to maintain the ionization chamber at its normal operating state) in the event that the system 10 is disconnected from an AC power source. The system battery is charged while the system 10 is connected to an AC power source.

[180] Fig. 7 also shows four rectangular touch fields 1020-1023 along the bottom thereof. Reset button 1020 is activated to reset or clear information, such as case identification information, desired activity level, etc., from the treatment screens (as described in more detail below). Configuration button 1021 is activated to access the configuration screens for the system 10 (as described in more detail below). Records or Injection History button 1022 is activated to access information regarding prior injection procedures (as described in more detail below). Help button 1023 is activated to access searchable text, FAQs or other information that might be provided about the use and operation of the system 10.

[181] When the setup button 1022a is activated, the touch screen changes to that shown in Fig. 8. and "summary" 1030, "setup guide" 1032 and "daily QC" (quality control) 1034 touch fields preferably appear and the "summary" touch field 1030 is activated, prompting the appearance of a summary display 1038. As shown, summary display 1038 provides FDG and saline fields 1040, 1044, respectively, as well as MPDS tubing field 1048 and waste field 1050.

[182] In the saline field 1044, a "replace" button 1046 can be activated by the user to inform the system 10 that the saline source 23 has been replaced and to allow the user to input the volume of the saline source into the system 10 (see Fig. 13). After the saline volume is input via pop-up screen 1110 including keypad 1114 in Fig. 13, the saline volume is displayed as shown in Fig. 11. In a preferred embodiment, the saline source 23 is replaced at the same time that a new vial 902 is placed into the system 10.

[183] As part of the FDG field 1040 in Fig. 8, there are shown a number of informational displays (shown here as blank) regarding assay information that can be input by a

user into the system 10. An edit button 1042 can be activated by the user to facilitate the entry of such information. When the edit button 1042 is activated, the display shown in Fig. 10 appears. The user can then input the noted assay information (typically provided on the pharmaceutical vial 902) into the system 10. Specifically, a lot number can be entered into field 1072, while the activity and volume of, for example, FDG or other radiopharmaceutical in the vial can be entered into touch fields 1080 and 1082, respectively. In a manner well known to those of ordinary skill in the art, the activation of any of these fields can prompt a numerical keypad pop-up to assist in data entry, or data can be entered in essentially any other suitable manner (e.g., directly via a physical keyboard).

[184] Further, the assay date of the radiopharmaceutical in the vial is entered in field 1074 via a calendar button 1074a (which prompts the appearance of a pop-up calendar in known manner), or a simplified entry touch field 1074 which selectively permits the entry of a day such as "today" or "yesterday" (which is useful for radiopharmaceuticals, such as FDG, that have very short half-lives).

[185] The assay time is entered into touch field 1076 (via a pop-up time field or keyboard/keypad entry) and an AM/PM toggle field 1076a. Other functional buttons are present, such as "clear all" 1078, "cancel" 1084 and "OK" 1086 buttons, to facilitate entry, deletion and/or acceptance of inputted values of the requested assay information. When the OK button 1086 is activated to accept the assay information shown in Fig. 10, the display shown in Fig. 11 appears.

[186] Finally, as shown in both Figs. 8 and 11, information regarding the amount of radioactivity present in the MPDS tubing 200 is displayed at area 1048, while a waste field 1050 is preferably provided to graphically display the quantity of fluid and the activity level in the waste receptacle 224. Further, an "OK" button 1036 is activated to notify the system 10 that the system preparation tasks have been completed.

[187] Fig. 9 illustrates the display screen that is shown when the "setup guide" touch field 1032 shown in Fig. 8 is activated. As shown, setup guide 1032 prompts the appearance of a setup screen 1053 to assist an operator in physically preparing the system 10 for a procedure. Setup screen 1053 preferably includes four tabs 1054, 1056, 1058, 1060), which each, respectively, assist an operator in a different aspect of system setup (here, FDG removal, saline source installation, FDG installation, and MPDS installation, respectively).

[188] Fig. 9 also shows that FDG tab 1058 has been activated, prompting the appearance of display 1062. Up and down arrows 1066, 1068 preferably permit an operator to go through numbered procedure steps 1-4 as shown to install FDG vial 902 into the system 10, and a graphical image 1064 of the fluid delivery system 10 preferably graphically relates each of the numbered procedure steps. Here, for instance, "step 1" is shown graphically for the unlocking and opening of the cart. After the FDG vial 902 is installed in the system 10, status icon 1012a is highlighted (see Fig. 11) because activity is now present in the system 10.

[189] After the FDG vial 902, the saline source 23 and the MPDS 200 have been installed using, for example, the display shown in Fig. 9, and the FDG assay information and the saline volume information have been provided to the system (as shown in Fig. 11), the "purge air" button 1052 shown in Fig. 11 can be activated to prime the MPDS 200. When purge air button 1052 is activated, the "Prime MPDS" query prompt 1100 shown in Fig. 12A is displayed. When the "Yes" button 1101 in Fig. 12A is activated, the MPDS priming operation described in detail above is performed by the system 10 and a "Priming MPDS" status display 1102 is shown (see Fig. 12B) to indicate the status and completion of the MPDS priming operation to the user.

[190] After the MPDS 200 is primed by the system 10, a volume of fluid (i.e., a mixture of saline and a pharmaceutical (e.g., FDG)) is present in the waste receptacle 224 (as described in detail above). The outcome of the MPDS priming operation and the current status of the system 10 is displayed to the user, as shown in Fig. 14.

[191] As Fig. 14 shows, and as compared to the pre-MPDS priming system status shown in Fig. 11, the waste receptacle 224 contains 20 ml of waste (i.e., saline and pharmaceutical) and has an activity level of 15 mCi, the MPDS tubing has an activity level of 2 mCi, the saline source 23 contains 485 ml of saline (compared to 500 ml in Fig. 11) and the vial 902 contains 15 ml of FDG and has an activity level of 374 mCi (compared to 30 ml and an activity level of 700 mCi in Fig. 11).

[192] As shown in Fig. 14, the "Activity" (i.e., 700.0 mCi) listed in the Assay Information section of display 1038 is the amount of radioactivity provided by the radiopharmaceutical at the time it was assayed. The "Total Activity" (i.e., 415 mCi) shown next to the FDG display 1040 is the amount of radioactivity currently provided by the radiopharmaceutical present in the vial 902. The difference (i.e., 285 mCi) between the "Activity" and the "Total Activity" is calculated from the decay rate of the radioisotope and the elapsed time since the radiopharmaceutical was assayed. The activity level (i.e., 374 mCi) displayed within the FDG display

1040 is the 'extractable activity'; that is, the amount of activity that can be extracted from the vial 902. The "extractable activity" is less than the "total activity" because there is a small volume of radiopharmaceutical (e.g., approximately 1-2 ml) that cannot be extracted from pharmaceutical vials or containers and becomes discarded waste.

[193] Preferably prior to installing and priming the MPDS 200, the operator or other personnel should perform a quality control check on the fluid delivery system 10. In a preferred embodiment, the quality control check is performed daily, for example at the beginning of a work day, to ensure that the fluid delivery system 10 is in good working order. The quality control check is initiated by activating the "Daily QC" field or button 1034, as shown in Fig. 15. When activated, the "daily QC" touch field 1034 prompts the appearance of a QC display 1120 to assist an operator in performing a quality control check. A menu of checks to be performed preferably appears via the following touch fields: zero check (1122), bias adjustment (1124), background check (1126), constancy/accuracy test (1128) and ionization chamber battery (i.e., high voltage) measurement check (1130). In addition, the QC display 1120 provides a warning prompt 1121 to the operator that no activity (i.e., no radiopharmaceutical) should be inside the ionization chamber 160 when the quality control check is conducted.

[194] To the left of each touch field, preferably, is a "check box" or "pass/fail" indicator that preferably indicates one of the following four states, as appropriate: highlighted (if the corresponding touch field 1122-1130 is activated) to indicate an active test or check; not highlighted and blank to indicate an unexecuted test or check; checked with a checkmark to indicate a successful test or check; and an "X" to indicate a failed test or check.

[195] The QC display 1120 also includes a "Previous Test" button 1132 and a "Start" button 1134. The Previous Test button 1132 is activated to display the results of the previous quality control check of the system 10. When the Start button 1134 is activated, the tests or checks displayed in the QC display 1120 are initiated. Preferably, the checks are conducted in the order presented (i.e., from top to bottom) but they may be performed in any suitable order.

[196] Upon activating the Start button 1134, the "Zero Check" test 1122 is initiated. As shown in Fig. 16A, when the Zero Check test is initiated, the system 10 creates a pop-up 1136 that queries the operator as to whether there is activity (i.e., a radiopharmaceutical) inside of the ionization chamber 160 of the fluid delivery system 10. If the operator activates the "No" touch button 1137 in pop-up 1136,

system 10 "zeros out" the ionization chamber by automatically adjusting internal parameters so that the output from the ionization chamber indicates no activity. This check primarily accounts for environmental background radiation. When the check is completed, the system 10 displays a checkmark (see Fig. 16B) in the Zero Check display 1122.

[197] As shown in Fig. 17, the quality control check continues on to the Bias Adjustment check, which is similar to the Zero Check above but makes finer adjustments to internal biasing parameters to offset the effects of minor current fluctuations due to noise within the circuitry of the ionization chamber. The fine adjustments are made to ensure consistent activity readings from one measurement to the next. Fig. 17 shows a checkmark in the Bias Adjustment display 1124, thereby indicating that the system 10 has successfully adjusted the bias setting.

[198] Fig. 17 further shows that the Background Check is in progress. As such, field 1126 is highlighted and a progress bar 1126a indicates the degree of progress (here, 20%). The Background Check basically completes the ionization chamber "zeroing" steps conducted during the Zero and Bias Adjustment checks. The system 10 takes several readings (e.g., 10) from the ionization chamber and captures the average of those readings for display to the user. This allows the user to determine whether the ionization chamber has been sufficiently zeroed out.

[199] The next system check is the "Constancy/Accuracy" test, which is used to monitor the performance of the ionization chamber by measuring the same check source at intervals over a long period of time. The check source (e.g., Cs-137) is placed in the ionization chamber and the measured activity is compared to the expected activity based on the original assay information (decayed for time) of the check source. This ensures that the ionization chamber is providing accurate readings. The measured activity is also compared to previous readings of the same check source (decayed for time) by the ionization chamber. This ensures that the readings provided by the ionization chamber are consistent over time.

[200] When the system 10 initiates the "Constancy / Accuracy" test, a pop-up 1140 is generated (see Fig. 18) to prompt the operator to place a suitable pharmaceutical (in this example, Cs-137) in the ionization chamber 160 and to input information about the radiopharmaceutical (see data fields in pop-up 1140) into the system 10. In a preferred embodiment, the pop-up 1140 automatically includes the radiopharmaceutical information from the most recent "Constancy/Accuracy" test, and the operator activates the "Edit" button 1144 to input new and accurate

information when necessary. In an alternate embodiment the data fields in pop-up 1140 could be left blank for filling by the operator.

[201] After the pharmaceutical is placed in the ionization chamber 160 and the data fields in pop-up 1140 are complete and accurate, the operator activates the "OK" button 1146 to initiate the "Constancy/Accuracy" test. The "Constancy/Accuracy" display bar 1128 preferably includes a test progress bar (not shown) similar to bar 1126a in Fig. 17 that indicates the degree of progress to the operator. If the operator wishes to bypass the Constancy/Accuracy" test, she may activate the "Skip" button 1142 to bypass the test and proceed to the "Battery Measurement" test (discussed below with respect to Fig. 20). Once the "Constancy/Accuracy" test is completed, another pop-up 1148 is generated by the system 10 (see Fig. 19) to prompt the operator to remove the pharmaceutical from the ionization chamber 160. After the operator activates the "OK" button 1149 in pop-up 1148 to inform the system 10 that the radiopharmaceutical has been removed from the ionization chamber 160, the system 10 then initiates the ionization chamber "Battery Measurement" check.

[202] As shown in Fig. 20, the four previous system checks (see displays 1122-1128) are indicated by checkmarks as having been successfully completed. The ionization chamber "Battery Measurement" check measures the voltage output provided by a battery pack internal to the ionization chamber to ensure that the voltage output is sufficient to produce accurate readings from the ionization chamber. The ionization chamber "Battery Measurement" check is shown as being 84% completed by progress bar 1130a.

[203] After the "Battery Measurement" check is completed, the system 10 generates a "Summary" display screen 1150, as shown in Fig. 21, with specific results for all of the checks. If the "Constancy/Accuracy" test was bypassed by the operator (by activating Skip button 1142 in Fig. 18), the system 10 generates "Summary" display 1150a shown in Fig. 22, which indicates that the "Constancy/Accuracy" test was skipped.

[204] Screen 1150 also includes a print button 1152 that is activated to, for example, print out the test results (via printer 24 of system 10) for the system's maintenance file. In addition, the Summary display 1150 includes a New Test button 1154, which is activated by the operator to initiate a new series of quality control checks. When the New Test button is activated, the display 1120 shown in Fig. 15 is generated and the quality control check is conducted again by the system 10.

Patient Treatment

[205] The "Patient Treatment" category of tasks is described below in relation to Figs. 23-32B. The "Patient Treatment" category includes a number of tasks that are preferably performed in the following order to administer or inject a radiopharmaceutical into a patient: (1) setting the desired activity level to be delivered to the patient; (2) inputting patient and/or case identification information into the system 10; (3) connecting the first end 702 of the SPDS 700 to the connector end 228 of the MPDS 200; (4) priming the SPDS 700 to remove air therefrom; (5) connecting the patient end 704 of the SPDS 700 to the patient; (6) conducting a test injection to ensure the integrity of the fluid path to the patient; (7) preparing the radiopharmaceutical dose to be administered or injected into the patient; (8) measuring the activity level of the radiopharmaceutical dose in the dose calibrator 160 to ensure that it is equal or substantially equal to the desired activity level to be delivered to the patient; (9) discarding the radiopharmaceutical dose if, for example, the patient is experiencing discomfort or the measured activity level is not equal or substantially equal to the desired activity level; and (10) administering or injecting the radiopharmaceutical dose to the patient if the measured activity level is equal or substantially equal to the desired activity level. While the above order is the preferred one for the "Patient Treatment" tasks, the tasks may be performed in any suitable manner and order for the intended application.

[206] After the operator prepares the system 10 for a fluid delivery procedure by, for example, completing the steps set forth above in the "System Preparation" tasks, the system 10 generates the display 1000 shown in Fig. 23 which indicates in the upper left hand side thereof that the "System is ready." The saline field 1002 indicates that 500 ml of saline is available and the FDG field 1004 indicates that 700 mCi of FDG are available, as shown.

[207] As further shown in Fig. 23, the Desired Activity field 1006 indicates that 15.0 mCi is the current desired activity level. This 15.0 mCi activity level is preferably an operator-defined, default setting in the system 10, but also could be the desired activity level that was programmed for the last injection procedure.

[208] The desired activity level is preferably set by the operator in one of two ways: (1) manual input; or (2) a calculation based on patient weight. If the operator wants to set the desired activity level by manual input rather than by patient weight, the operator activates the "No" button 1202a in display 1006. In response thereto, the system 10 generates the display and keypad 1204 shown in Fig. 24A. The operator uses the keypad 1204 to input the desired activity level.

[209] If instead the operator wants to set the desired activity level based on patient weight, the operator activates the "Yes" button 1202b in Fig. 23. Upon activation of the "Yes" button 1202b, the system 10 generates the display 1000 and pop-up 1205 shown in Fig. 24B, which prompts the operator to "Enter patient weight" (displayed in pounds or kilograms in data field 1003) using pop-up 1205. Further, the operator can select the formula to be used in calculating the weight-based activity level by activating formula touch field 1011. When formula touch field 1011 is activated, the pop-up table 1013 shown in Fig. 24C is displayed and the operator is prompted to "Select formula." In a preferred embodiment the operator can select up to five operator-defined formulas. For example, as shown in Fig. 24C, the operator can select among three predefined formulas: (1) Standard (0.1 mCi/lb.); (2) Melanoma (0.13 mCi/lb.); and (3) Pediatric (0.07 mCi/lb.). However, the system 10 can include more than pre-set or predefined weight-based formulas. For example, the system 10 can also include formulas based on other patient parameters, such as glucose-level or cardiac output, or scanner parameters, such as acquisition time or crystal type.

[210] Once the formula is selected, the desired activity level is calculated using the formula and the patient's weight. The desired activity level (e.g., 13.5 mCi), the patient's weight (e.g., 135 lb.) and the formula (e.g., 0.1 mCi/lb.) are displayed in field 1006 and the screen display 100 indicates that the "System is ready", as shown in Fig. 24D.

[211] In addition, as displayed in display and keypad 1204 shown in Fig. 24A, in a preferred embodiment the system 10 includes pre-defined minimum and maximum activity levels that define the operating range (i.e., 5-25 mCi) of the system 10. The operating range of the system 10 cannot be altered by the operator, and the system 10 preferably will not accept a desired activity level (whether manually input or calculated based on patient weight or other patient or scanner parameter) that falls outside of the system's operating range. In a preferred embodiment, the system will default to the maximum or the minimum activity level (i.e., 25 mCi or 5 mCi) if the operator attempts to input or the system calculates a desired activity level that is greater than the maximum activity level or less than the minimum activity level, respectively.

[212] Furthermore, if desired for safety or medical practice or preference reasons, the operator preferably can define her own minimum and maximum desired activity levels for the system, as long as they fall within the operating range of the system 10. For example, the operator can define a minimum desired activity level of 10.0

mCi and a maximum desired activity level of 17.5 mCi for the system 10 because those two parameters fall within the 5-25 mCi operating range of the system 10. In such a case, as shown in Fig 24E, even though the operator inputted a patient weight of 5 lb. and chose a formula of 0.1 mCi/lb. (which would result in a calculated desired activity level of 0.5 mCi), the system 10 sets the desired activity level to the minimum desired activity level of 10.0 mCi. When the system 10 uses the minimum desired activity level instead of a manually input activity level or a calculated weight-based activity level, the system 10 indicates that to the operator by using, for example, the downward arrow icon 1006a shown in display field 1006 of Fig. 24E.

[213] Likewise, as shown in Fig. 24F, even though the operator inputted a patient weight of 999 lb. and chose a formula of 0.1 mCi/lb. (which would result in a calculated desired activity level of 99.9 mCi), the system 10 set the desired activity level to the maximum desired activity level of 17.5 mCi. When the system 10 uses the maximum desired activity level instead of a manually input activity level or a calculated weight-based activity level, the system 10 indicates that to the operator by using, for example, the upward arrow icon 1006b shown in display field 1006 of Fig. 24F.

[214] After the desired activity level is programmed or set by the system 10, preferably the operator inputs case information including patient identification and injection site information into the system 10, as shown in Figs. 25A and 25B. When the operator activates the Edit button 1208 in the Case ID field 1206 (see e.g., Fig. 23), the "Case Information" pop-up display 1217 shown in Fig. 25A appears. The display 1217 includes an "Identification" field 1217a and a keypad 1217j for inputting a patent or other identification number in field 1217a. In addition, the display 1217 includes a number of "Injection Site" touch buttons 1217b-1217i for identifying and recording in the system 10 the site on the patient at which the radiopharmaceutical will be administered or injected, including 'Left Antecubital' 1217b, 'Right Antecubital' 1217c, 'Left Hand' 1217d, 'Right Hand' 1217e, 'Left Foot' 1217f, 'Right Foot' 1217g, 'Access Port' 1217h and 'Other' 1217i.

[215] Once the Identification and Injection Site information is input into the system 10, the information is displayed in the Case ID field 1206, as shown in Fig. 25B. Further, as shown in Fig. 25B, after the requisite information is input into the system 10 and displayed in the Case ID field 1206, a Patient Preparation field 1210 including a Prime touch button 1212 is generated and displayed for the operator.

[216] Before the Prime button is 1212 is activated, the first end 702 of the SPDS 700 should be attached to the connector end 228 of the MPDS 200, as discussed in detail

above. When the SPDS 700 is connected to the MPDS 700, the operator can activate the prime button 1212 to cause the system 10 to prime the SPDS 700 to remove air therefrom.

[217] As shown in Fig. 26A, after the Prime button 1212 is activated the system 10 indicates that the system is "Priming" the SPDS 700 and generates a progress bar 1213 (which indicates in Fig. 26A that the priming operation is 17% completed). Further, the system 10 highlights the fluid path field 1008 and the coil field 1010 in display 1000 to indicate that saline is being pumped from saline source 23 (indicated by saline field 1002) through the MPDS 200 and the SPDS 700 to prime the SPDS 700. After the SPDS priming operation is completed, the system 10 generates a prompt display 1215, as shown in Fig. 26B, that queries the operator as to whether all air has been expelled or purged from the SPDS 700. If the "Yes" button 1215a is activated, the SPDS priming operation is completed and the system 10 is ready to conduct a test injection and/or to prepare the pharmaceutical dose for injection into the patient, as discussed in more detail below. If, on the other hand, the "No" button 1215b is activated, the SPDS priming operation is preferably conducted again.

[218] After the SPDS priming operation is completed, the patient end 704 of the SDPS 700 is connected to the patient (as described above) and the Patient Preparation display field 1210 on the touch screen 1000 includes a "Test Inject" button 1212a, as shown in Fig. 28A. If the operator desires to conduct a test injection to, for example, ensure the integrity of the fluid path along the MPDS 700, the SPDS 200 and the patient's vasculature, the operator activates the "Test Injection" button 1212a and the system 10 pumps saline from the saline source 23 through the MPDS 200 and the SPDS 700 to the patient. Concurrently, the system 10 generates the display shown in Fig. 27A to inform the operator that the system 10 is "Test Injecting" and highlights the fluid path display 1008 from the saline source icon 1002 to the ionization chamber display 1010. The display 1000 also includes a progress bar 1213a to indicate the degree of progress made (here 45%) in completing the test injection procedure.

[219] If the operator needs to pause the test injection due to, for example, patient discomfort or incorrect positioning of the catheter in the patient, she can activate the "Pause" button 1212d in the Patient Preparation" display 1210 (see Fig. 27A) to pause the procedure. When the test injection procedure is paused, the system 10 generates the display shown in Fig. 27B, indicating that the test injection is "Paused" and providing a "Resume" button 1212b and a "Stop" button 1212c in the Patient Preparation display 1210. To resume or stop the test injection, the operator

can activate the corresponding "Resume" and "Stop" buttons, 1212b, 1212c, respectively.

[220] In addition to using the various "Pause" and "Stop" buttons provided by the GUI display 15, an operator can also depress the interrupt button 25 on the cabinet 9 of the system 10 to at any time pause or stop a procedure or operation being conducted by the system.

[221] After the test injection is completed or terminated the system 10 generates the display 1000 shown in Fig. 28A, which includes an FDG Dose display 1216 and a corresponding "Prepare" button 1218. After the operator activates the "Prepare" button 1218, the system 10 generates the display shown in Fig. 28B and begins to pump a volume of FDG (or other suitable pharmaceutical or radiopharmaceutical) from the vial 902 through the MPDS 200 to the tube coil 444 thereof disposed in the ionization chamber 160. As shown in Fig. 28B, to reflect this operation the display 1000 informs the operator that the system 10 is "Measuring Dose" and highlights the fluid path display 1008 from the FDG source display 1004 to the ionization chamber display 1010. The display also includes a progress bar 1214a that shows the system's progress (here 78%) in measuring the pharmaceutical dose.

[222] In a preferred embodiment, the system 10 prepares the pharmaceutical dose in accord with the methodology described in PCT Publication No. WO 2006/007750, in which the activity level of a first amount of a radioactive liquid is measured and used to calculate a second amount of the radioactive liquid that is required for the combined amounts to have a pre-determined level of radioactivity to be delivered to a patient. The contents of PCT Publication No. 2006/007750 are incorporated herein by reference. The dimensions of the coil assembly 400 and the core structure 446, including the height, diameter and volume of the tube coil 444, the length, number of turns, OD and ID of the tubing that forms the tube coil 444, and the dimensional location of the "linear region" of the Veenstra IK-102 ionization chamber, provided above are necessary to optimally and accurately prepare the pharmaceutical dose, whether in accord with the preferred methodology described in PCT Publication No. WO 2006/007750 or using another suitable dose preparation methodology.

[223] The stated tube coil 444 dimensions are necessary to optimally position within the "linear region" of ionization chamber: (1) the volume(s) of pharmaceutical required to deliver the desired activity level to the patient; and (2) the volume of saline necessary to position the total volume of pharmaceutical in the tube coil. The tube coil 444 could be formed from tubing having a larger ID than that stated above (i.e.,

0.156 inches), but larger IDs tend to allow the radiopharmaceutical to be diffused with the saline (which is used to 'place' or 'position' the radiopharmaceutical within the tube coil 444), which may result in the radiopharmaceutical volume or a portion thereof being positioned outside of the tube coil 444 and thus outside of the "linear region" of the ionization chamber (resulting in inaccurate activity level measurements and delivery). Likewise, the tube coil 44 could be formed from tubing having a smaller ID than 0.156 inches (which would possibly further decrease or prevent the diffusion of the radiopharmaceutical with the saline), but the dimensions of the tube coil 444 (e.g., length of tubing, coil tube height, number of turns) required to maintain a tube coil volume of 12.5 ml would result in the tube coil 444 extending beyond the "linear region" of the ionization chamber (resulting in inaccurate activity level measurements and delivery).

[224] Further, the core structure 446 operates to maintain the desired tube coil geometry (e.g., tube coil diameter and height) and to properly position the tube coil 444 axially and vertically within the sleeve 162 so that the tube coil 444 thereby resides within the "linear region" of the ionization chamber 160 (see e.g., Fig. 3F).

[225] With specific reference to the dose preparation methodology described in PCT Publication No. WO 2006/007750, the 12.5 ml volume of the tube coil 444 is designed to accommodate two volumes of a radiopharmaceutical from vial 902 separated by a volume of saline from source 23, regardless of whether the dose is prepared shortly after the radiopharmaceutical was assayed (when a small volume of the radiopharmaceutical is required to deliver a desired activity level) or after a significant amount of time has passed (e.g., in relation to the radioisotope's half-life) since the radiopharmaceutical was assayed (when a greater volume of the radiopharmaceutical is required to deliver the same desired activity level). As a specific example of the above, the 12.5 ml tube coil 444 is designed to accommodate: (1) two 1/16 ml volumes or "slugs" of a pharmaceutical (for a total volume of 1/8 ml) at a concentration of 40 mCi/ml (i.e., highest concentration that the system 10 is designed to handle), separated by a calculated volume of saline necessary to fill or substantially fill the remaining tube coil volume; and (2) two 1.5 ml "slugs" of a pharmaceutical (for a total volume of 3 ml) at a concentration of 1.67 mCi/ml (i.e., lowest concentration that the system 10 is designed to handle), separated by a calculated volume of saline necessary to fill or substantially fill the remaining tube coil volume.

[226] After the dose is pumped by the system 10 into the tube coil 444 disposed within the ionization chamber 160, the activity level of the dose is measured by the system 10.

The measured activity level is then displayed to the operator and the ionization chamber display 1010 is highlighted, as shown in Fig. 29. A new display field 1006a is generated by the system, showing the measured "Calibrated Activity" (here 13.5 mCi) of the prepared dose. Just below field 1006a is a "plus/minus" range indicator 1224. Range indicator 1224, as shown, includes a center circle 1224a, flanked on each side by 10 rectangles. Left and right arrows are also included, respectively, at the far left and far right of indicator 1224. Preferably, as shown in Fig. 29, center circle highlights when the measured "Calibrated Activity" level is the same as the previously programmed, desired activity level (which is the case in Fig. 29). Otherwise, if the measured activity level is greater or lesser than the desired activity level, corresponding rectangles or, in some cases, arrows will highlight to the right of the center circle 1224a (for measured activity > desired activity) or to the left of the center circle 1224a (for measured activity < desired activity) to visually indicate to the operator the difference between the measured and desired activity levels.

[227] In a preferred embodiment, each of the rectangles represents a default value of a 1% discrepancy in the desired to measured activity level, such that three rectangles to the right of the center circle 1224a would be highlighted if the measured activity level was 3% greater than the desired activity level of 13.5 mCi. If the measured activity exceeds the desired activity by more than 10%, then all the rectangles to the right of the center circle 1224a and the right arrow would highlight. Preferably, the extent of the rectangles in indicator 1224 will convey an acceptable range within which the measured activity may fall. Thus, such an acceptable range could be plus or minus ten percent or could be another range as deemed appropriate, with each rectangle representing one tenth of the positive or negative extent of that range. Alternately, however, the default value of each rectangular could be pre-set to another value (such as 0.1 mCi) or could be changed by the operator to another value more suitable for the intended application.

[228] In addition to displaying the measured activity level, as shown in Fig. 29 the display 1000 also generates a "Discard" button 1222 and an "Inject" button 1220 in the FDG Dose display 1216. If for example the measured activity is outside of a clinically acceptable range for the intended procedure, the operator can activate the "Discard" button 1222 to have the system 10 discard the measured dose (i.e., by pumping the dose to the waste receptacle 224, as discussed in detail above) and to prepare another dose for delivery to the patient. Specifically, when the "Discard" button 1222 is activated the system generates the dialog box 1231 shown in Fig. 30A, which queries the operator to confirm that the measured dose is to be discarded. If the

operator confirms that the measured dose is to be discarded by activating the "Yes" button 1231a, the system 10 generates the display shown in Fig. 30B, which indicates to the operator that the system is "Discarding" and creates a progress bar 1233 that indicates the status of the "discarding" operation (here 86% completed). The display 1000 also highlights the fluid path display 1008 from the saline source display 1002 to the ionization chamber display 1010 to indicate that the system 10 is pumping saline through the MPDS 200 to push the dose from the tube coil 444 to the waste receptacle 224 (as described above).

[229] If, on the other hand, the operator activates the "No" button 1231b in Fig. 30A to inform the system 10 that she does not want to discard the measured dose, the system 10 reverts to the display shown in Fig. 29 and the "Discard" button 1222 and the "Inject" button 1220 are again made available to prompt the operator to decide whether to discard or to inject the measured pharmaceutical dose.

[230] If the operator desires to inject the measured dose and thus activates the "Inject" button 1220 shown in Fig. 29, the system 10 generates the display shown in Fig. 31 which indicates to the operator that the system 10 is "Injecting" and, via progress bar 1223, that the injection operation (in Fig. 31) is 27% completed. The fluid path display 1008 between the saline source display 1002 and through the ionization chamber display 1010 to the arrow at the end of the fluid path display 1008 is highlighted to indicate that the system 10 is pumping saline from the saline source 23 to push the dose in the ionization chamber 160 through the remainder of the MPDS 200 and the SPDS 700 to the patient (as described above). Further, the system 10 generates a "Pause" button 1230 in FDG Dose display 1216. As with the test injection operation discussed above (see Fig. 27A), the operator can activate the "Pause" button 1230 or the interrupt button 25 to pause the injection procedure.

[231] After the "Pause" button 1221 is activated, the display shown in Fig. 32A is generated and displayed to the operator. The display shown in Fig. 32A informs the operator that the system 10 is "Paused" and includes a "Discard" button 1222a and a "Resume" button 1230a in the FDG Dose display 1216.

[232] If the injection needs to be terminated, the operator activates the "Discard" button 1222a and the system reverts to that shown and described above with respect to Figs. 30A and 30B to discard the dose into the waste receptacle 224. However, if the procedure can be resumed, the operator activates the "Resume" button 1230a in Fig. 32A and the injection procedure continues to deliver the measured dose to the patient.

[233] When the injection procedure is completed, a pop-up 1240 preferably appears as shown in Fig. 32B. This pop-up 1240, as shown, preferably contains information about the activity and volume of the dose (e.g., FDG) just delivered to the patient, the total fluid delivered (which would include saline) and other identifying information including, for example, the patient identification number, radiopharmaceutical lot number and patient injection site (as shown on the right of pop-up 1240). Activating the "OK" button 1242 causes pop-up 1240 to disappear and the system to revert to an "Idle" state (as shown in Fig. 7) or a "Ready" state (as shown in Fig. 23), while activating the "print" button 1244 prompts the injection information to be printed out by the printer 24 for patient, billing, inventory or other suitable records.

[234] Other capabilities and functions not expressly discussed hereinabove or shown in the drawings are of course conceivable in accordance with the embodiments of the present invention. For instance, if the extraction of a pharmaceutical dose (e.g., FDG) from a vial is interrupted for an unforeseeable reason and is not prompted by a desired "pause", the system could alert the operator to discard the dose (and in that connection present a button for the purpose).

Injection History

[235] The disclosure now turns to a discussion of the injection history operations or tasks that can be performed using the display 1000, as depicted in Figs. 33A-C, 34A and 34B.

[236] The injection history operations or tasks may be prompted by activating the Records / Injection History button 1022, which is displayed when the system 10 is in an "Idle" state (see e.g., Fig. 7) or a "Ready" state (see e.g., Figs. 23, 24D and 28A). Activation of Records button 1022 preferably prompts the appearance of the calendar display 1302 shown in Fig. 33A (here 'October 2006'). Highlighted touch fields within the calendar display 1302 preferably correspond to those dates of the displayed month (here 'October 2006' in field 1309) on which the system 10 was used to perform an injection procedure, while those other days of the displayed month in which the system 10 was not used are not highlighted. Arrow buttons to the left 1309a and right (not shown), respectively, of field 1309 preferably permit the operator to scroll through different months to access and retrieve injection history information.

[237] The calendar display 1302 also includes a "Print Summary" button 1304, a "Print Days" button 1306 and a "Done" button 1308. Activation of the "Print Summary"

button 1304 provides a high-level summary of the injection procedures conducted for the specified month (here 'October 2006'), similar to the injection procedure information displayed in Fig. 34A. The "Print Days" button 1306 preferably prompts the appearance of the display 1302a shown in Fig. 33B. The "Done" button 1308 can be activated once the operator has completed the necessary injection history retrieval operation or task, and the display 1000 then preferably reverts to the "Idle" state display (see e.g., Fig. 7) or the "Ready" state display (see e.g., Figs. 23, 24D and 28A) as appropriate.

[238] Referring now to Fig. 33B (prompted by activation of "Print Days" button 1306), the display 1302a includes an "All Days" touch field 1330 (which is activated in Fig. 33B) including a "Print" button 1334, and a "Range" touch field 1332. If the operator mistakenly activated the "Print Days" button 1309 on display 1302 (see Fig. 33A), she can activate the "Cancel" button 1336 to return to the display 1302 shown in Fig. 33A. If the operator wishes to print the injection history information for all the days in the selected month (here 'October 2006'), "Print" button 1334 can be activated and the printer 24 will print the injection history records for the days in which the system 10 performed injection procedures. If the operator instead wants to access injection history information for a range of days in the selected month, the operator can activate the "Range" touch field 1332, which prompts the appearance of the display 1302b shown in Fig. 33C.

[239] As shown in Fig. 33C, the display 1302b includes a "From" touch field 1332a and a "To" touch field 1332b which the operator activates to select the "From" and "To" dates in the selected month to establish the range of dates for which injection history information is to be accessed. Once the date range is selected, the "Print" button 1334 is activated to prompt the printer 24 to print the injection history information.

[240] Referring back to Fig. 33A, in addition to activating the "Print Summary" button 1304 or the "Print Days" button 1306, the operator is also able to activate any of the highlighted calendar buttons to access injection history information for that day of the selected month. For example, if the operator wanted to retrieve injection history information for 10 October 2006, the operator would activate the "10" button 1340 shown in Fig. 33A and the system 10 would generate the display 1310 (including selected date field 1310a) shown in Fig. 34A.

[241] As shown in Fig. 34A, a series of display fields 1312 includes information on the lot number, case ID, delivery time and delivered activity of a given injection procedure conducted on the selected day (here '10 October 2006 (Tuesday)'). Page up 1316 and page down 1318 arrow buttons are provided to allow the operator to scroll

through the procedures conducted on the selected day. Page left 1350 and page right 1351 arrow buttons are also provided to allow the operator to scroll through and select dates prior to or subsequent to the selected '10 October 2006' date displayed in date field 1310a. A "Month View" button 1320 can be activated to revert to a "month view" as shown in Fig. 33A, while the "Print Day" button 1306a can be activated to print the injection history details of all injection procedures on the day in question (i.e., the day currently being displayed). Further, "magnifying glass" touch fields 1314 are provided for each procedure and, upon activation, preferably prompts a detailed injection history display 1360 (see Fig. 34B) for the selected procedure.

[242] As shown in Fig. 34B, the detailed injection history display 1360 provides details on the specific pharmaceutical injected (here "FDG"), the date (10 October 2006) and time (09:15) of injection and the activity level (15.1 mCi) and volume (5 ml) of the injected pharmaceutical. Further, the display 1360 indicates the total volume (35.0 ml) of injected fluid (pharmaceutical and saline), the Patient Identification number, the Lot number of the pharmaceutical and the IV Injection Site on the patient. The "Print" button 1363 is activated to print the injection details and the "OK" button 1362 is activated to revert to the display 1310 shown in Fig. 34A.

System Configuration

[243] The disclosure now turns to a discussion of system configuration tasks, as depicted in Figures 35-46. The configuration tasks are undertaken to permit an operator to set various system preferences, including but not limited to preferences related to the following: (1) Language; (2) Date / Time display; (3) Units; (4) Audio; (5) FDG / Pharmaceutical dose preparation formulas; (6) Saline volumes; (7) Case Information display; (8) Printing; (9) Daily QC isotope reference information; (10) Linearity measurement tests; (11) Calibration tests; and (12) Field Service reminders.

[244] The system configuration tasks may be prompted by activating the Configuration button 1021, which is displayed when the system 10 is in an "Idle" state (see e.g., Fig. 7) or a "Ready" state (see e.g., Figs. 23, 24D and 28A). Activation of Configuration button 1021 preferably prompts the appearance of the "System", "Treatment" and "Maintenance" touch fields (1402, 1404 and 1406, respectively) shown in Fig. 35, each of which when activated prompts the appearance of a distinct tabbed menu display 1400a-c (as explained in more detail below). An "OK" button 1418 may be activated when the system configuration tasks are completed, while a "default" button" 1416 may be activated to reset the system 10 to the default configuration settings.

[245] As shown in Fig. 35, the "System" touch field 1402 is activated and the tabbed menu display 1400a is provided. On menu display 1400a, tabs for language, date/time, units and audio are provided (1408, 1410, 1412, and 1414, respectively), and language tab 1408 is activated to prompt a language menu 1420. Preferably, language menu 1420 will permit the selection of any of a number of languages to be used with the system 10 in accordance with operator or local preferences.

[246] Fig. 36 shows date/time tab 1410 activated to prompt a date/time display 1422. Via a calendar button 1422a, a current date can be set, while date format preferences (e.g., European vs. American, etc.) can be set via touch field 1422b. A time display field 1422c preferably shows the current time and a time edit button 1422d may be activated to set the time as well as to select a 12- or 24-hour time format.

[247] Fig. 37 shows units tab 1412 activated to prompt a display 1424. Display 1424 preferably permits, via buttons 1426a, 1426b, 1428a, 1428b, a choice of units for weight (lbs. vs. kg) and activity (Curies vs. Becquerels), respectively.

[248] Fig. 38 shows audio tab 1414 activated to prompt a display 1444. "High", "normal" and "low" audio volumes (e.g., for prompts or alarms) can be selected via buttons 1444a, 1444b and 1444c, respectively.

[249] Fig. 39A shows the treatment touch field 1404 activated, which generates a second tabbed menu display 1400b. On menu display 1400b, tabs for "FDG", "saline", "case" and "printing" are provided (1450, 1452, 1454, and 1456, respectively). In Fig. 39A, FDG tab 1450 is activated to prompt a display 1460. Preferably, display 1460 includes an entry field 1462 for entering a default desired activity level (which may then automatically appear in field 1006 of Fig. 7).

[250] The display 1460 further includes a weight-based dosing sub-menu 1460a that includes on/off buttons 1464a, 1464b and an "Edit Formulas" button 1466. If the operator would like the system 10 to default to a weight-based calculation for desired activity level, the operator activates the "On" button 1464a. If a default, weight-based calculation for desired activity level is not desired, the operator can select the "Off" button 1464b (as shown in Fig. 39A). Further, upon activation of the "Edit Formulas" button 1466, the system 10 generates the pop-up edit display 1470 shown in Fig. 39B to allow the operator to edit existing or add new formulas for calculating desired activity level based on, for example, patient weight.

[251] As shown in Fig. 39B, the edit display 1470 may include a column of five buttons 1476, each preferably corresponding to a predetermined formula for a procedure

type that, for instance, may commonly be repeated. Here, a “Melanoma” button 1476a is activated to then present a sub-display 1478 which can afford an editing of any or all of the following: name of the formula (via button 1478a), multiplier to be used in calculating weight-based desired activity level (via touch field 1478b), and minimum and maximum desired activity levels (via touch fields 1478c and 1478d, respectively). Also, the entire formula can be deleted (via button 1478e) from the set 1476, if desired. Further, the operator may enter new formulas into the system 10 by activating the “New Formula” buttons 1476b

[252] Fig. 40 shows Saline tab 1452 activated to prompt a display 1480. Display 1480 preferably contains touch fields 1482, 1484 and 1486, respectively, for pre-selecting a default saline bulk size (here 500 ml) for the saline source 23 (if, for example, the facility generally uses or will use the same bulk size of saline), an additional saline flush volume (e.g., to account for the additional tubing length if the SPDS 700 is connected to an IV instead of directly to a catheter in a patient) and a test inject volume (here 30 ml). The Default Bulk Size volume entered in 1482, for example, can be a quantity that initially appears to an operator at a time when saline is installed in the system 10, which can be changed or left alone as appropriate. Any data entry in touch fields 1482, 1484, 1486 can be accomplished, e.g., via a keypad 1488.

[253] Fig. 41 shows case tab 1454 activated to prompt a display 1490. Display 1490 preferably permits the operator to set a default preference (via on/off buttons 1492) as to whether Case ID information (i.e., for a given patient) can be edited as appropriate. Further, the display 1490 allows the operator to set a default injection site for the system 10 by activating one of the injection site buttons 1494 provided in display 1490. Of course, the default injection site location can be changed by the operator during the preparation steps for the fluid delivery procedure if the actual injection site is different from the default injection site.

[254] Fig. 42 shows printing tab 1456 activated to prompt a display 1502 which allows an operator to establish an automatic printing of record labels (e.g., as may be printed at the end of an injection procedure) and the quantity of record labels to be printed.

[255] Finally, Fig. 43A shows maintenance touch field 1406 activated, which generates a third tabbed menu display 1400c. On menu display 1400c, tabs for “Daily QC”, “Linearity”, “Calibration” and “Field Service” (1510, 1512, 1514, 1516, respectively) are provided. The maintenance tabs relate to general maintenance and calibration of the system 10.

[256] As shown in Fig. 43, Daily QC tab 1510 is activated to prompt a display 1518. Display 1518 allows the operator to input information related to the radioisotope to be used to conduct daily QC tests (described above) of the system 10. Specifically, Isotope touch field 1520 and Lot Number touch field 1522 permit the operator to input the specific radioisotope to be used (here Cs-137) and the lot number thereof, respectively. Further, the operator can input the time and date that the radioisotope was created (e.g., in a cyclotron or a reactor), as well as the activity level of the radioisotope when it was created, in the Time and Activity touch fields 1526, 1524, respectively. The Edit button 1526a can be activated to edit the previously entered time and date information.

[257] Fig. 44A shows linearity tab 1512 activated to prompt a display 1530. Display 1530 prompts the operator for information and assists in conducting a linearity measurement for the system 10, which should be conducted every quarter (as noted in display 1530). Linearity measurements are based on the known decay of radioisotopes and are conducted to ensure that the ionization chamber 160 in the system 10 is reliably measuring the activity level of a radioisotope placed therein. Specifically, during a linearity measurement the measured activity level of a radioisotope is compared to the known activity level of the radioisotope (based on its half-life decay) at selected intervals (e.g., every 15 minutes) over a period of time (e.g., 24 hours) to determine whether the measured activity level falls within an acceptable error range.

[258] When the linearity tab 1512 is activated, details from the most recent linearity measurement are shown in sub-display 1532, while a button 1534 can be activated to prompt the appearance of a related graph (of, for example, measured vs. known activity level over the measurement period). To conduct a new linearity measurement, button 1536 is activated, which preferably generates the display 1540 shown in Fig. 44B.

[259] As shown in Fig. 44B, isotope field 1542 may be activated to identify the radioisotope to be used for the linearity measurement (here F-18). While isotope field 1542 preferably conveys the reference isotope, the activity level of the radioisotope (e.g., at the time it was drawn) can be input into activity level field 1544. In addition, the reference date and time for the activity level (e.g., the date and time that the radioisotope was drawn) is input into touch fields 1546 and 1548, respectively, by using, for example, a calendar button 1546a and a AM/PM time button 1548a. Once the requisite radioisotope information is inputted into display 1540, the operator can activate the "Begin Measurement" button 1543 to start the

linearity measurement. Of course, the operator can activate the "Cancel" button 1541 to cancel the linearity measurement and return to the display 1530 shown in Fig. 44A

[260] After the "Begin Measurement" button 1543 is activated, the pop-up display 1545 shown in Fig. 44C is generated to prompt the operator to confirm that the reference radioisotope has been placed in the ionization chamber 160. If the operator activates the "Yes" button 1545a (as shown in Fig. 44C) to confirm that the F-18 radioisotope has been placed in the ionization chamber 160, the system 10 will begin the linearity measurement.

[261] If the operator activates the "No" button 1545b, the display reverts to the display 1540 shown in Fig. 44B, and the operator can then load the reference radioisotope source into the ionization chamber and once again activate the "Begin Measurement" button 1543 to start the linearity measurement.

[262] After the operator activates the "Yes" button 1545a, the display 1547 shown in Fig. 44D is generated. In addition to displaying the radioisotope in field 1542 and the maximum allowable error for the linearity measurement in field 1552, the display 1547 also shows the estimated time for completion of the linearity measurement (here "23:15:03" hours) and the measured activity (in field 1554), the calculated activity (in field 1558) and the current error (in percentage format) (in field 1556). The linearity measurement may be aborted via an "Abort" button 1560 and the results of the linearity measurement, including a graph of the results, may be printed by selecting a "Print" button (not shown).

[263] As shown in Fig. 45A, activation of calibration tab 1514 prompts the system 10 to generate a calibration display 1570, which shows the results of a previous ionization chamber calibration routine. Ionization chamber calibration routines are preferably conducted upon installation of the system 10 (at, for example, a medical facility) and approximately once a year thereafter to ensure that the ionization chamber 160 of the system 10 is properly calibrated to operate over the range of energies and activity levels of the radiopharmaceuticals for which the ionization chamber 160 is intended to be used. In a preferred calibration routine, the gain of the ionization chamber is increased or decreased to best fit or adjust the measured activity levels of two or three radioisotopes (preferably having energy levels different from (e.g., lower than and greater than) the energy levels of the radiopharmaceuticals to be used with the system 10) against their known activity levels.

[264] By way of a specific example, the system 10 is currently intended to be used to administer FDG (which contains the radioisotope F-18) to patients. The energy level of F-18 is 511 KeV. In a first preferred embodiment, three radioisotopes are used to calibrate the ionization chamber 160: (1) Co-57 (energy level of 122 KeV; less than that of F-18); (2) Co-60 (energy level of 1333 KeV; greater than that of F-18); and (3) Cs-137 (energy level of 662 KeV; relatively close to that of F-18). In a second preferred embodiment, two radioisotopes are used for the calibration routine: (1) Co-57; and (2) Cs-137.

[265] Returning to Fig. 45A, the calibration display 1570 includes a sub-display 1571 conveying previous calibration results for Co-57 (field 1571a), Co-60 (field 1571b) and Cs-137 (field 1571c), while a button 1574 can be activated to begin a new calibration routine. Previous results can also be printed, e.g., via a button 1572.

[266] Upon activating button 1574, a display 1573 is generated (see Fig. 45B) that prompts the operator to place the radioisotope source (here Co-57) in the ionization chamber 160. The display 1573 includes a sub-display 1573a that lists various information about the isotope, including the isotope's name, the lot number, the date and time that the isotope was drawn and the activity level of the isotope when it was drawn. Further, the display 1573 includes "Cancel" button 1573b, "Edit" button 1573c and "OK" button 1573d. The cancel button 1573b is activated to cancel the calibration routine, the edit button 1573c is activated to edit the isotope information provided in sub-display 1573a and the OK button 1573d is activated (as shown in Fig. 45B) to commence the calibration routine with respect to the noted radioisotope (here Co-57), as discussed in more detail below.

[267] If the edit button 1573c in display 1573 is activated, the edit source display 1576 shown in Fig. 45C appears. The operator can edit the isotope information in display 1576 by entering the isotope name in field 1580, the lot number in field 1582, the activity level (at isotope creation) in field 1584 and the reference time and date (of isotope creation) in field 1586 via edit button 1586a. After the isotope information is entered, the operator activates the OK button 1578 and the display 1000 reverts to the display 1573 shown in Fig. 45B. If the isotope information is now correct, the operator can activate the OK button 1573d in display 1573 to commence the calibration routine for the noted radioisotope (here Co-57).

[268] After the OK button 1573d is activated, a tabbed calibration display 1590, including touch tabs for Co-57 (tab 1592), Co-60 (tab 1594) and Cs-137 (tab 1596), appears (as shown in Fig. 45D) and shows the results of the calibration routine for the noted radioisotope (here Co-57). Specifically, the display 1590a for Co-57 tab 1592

shows the target or expected activity for Co-57 (in field 1598), the actual measured activity for the Co-57 placed in the ionization chamber 160 (in field 1600) and the error between the target and measured activity (in field 1602). To thereafter compensate for the error (here 1%), the low gain of the ionization chamber (displayed in field 1604) is adjusted by using the 'plus' and 'minus' buttons 1606, respectively. Further, as shown in Fig. 45D, based on the error for Co-57 the system 10 calculates an estimated error (here 1%) for Cs-137 and displays it in field 1612. Based on the target or expected activity for Cs-137 (entered by the operator and displayed in field 1608) and the estimated error, the estimated measured activity is calculated by the system 10 and displayed in field 1610.

[269] The calibration routine is continued by thereafter activating the tab 1594 for the Co-60 isotope and repeating the steps described above with respect to Figs. 45B-45D. To compensate for the error (not shown) between the expected activity and the measured activity for Co-60, the high gain of the ionization chamber is adjusted (in the same way as shown in Fig. 45D for Co-57). The system 10 then uses the error for Co-60 to revise the estimated error for Cs-137, which is then displayed in field 1612 for the operator.

[270] The operator may continue the process above (i.e., iteratively conducting Co-57 and Co-60 activity measurements and adjusting the low and high gain of the ionization chamber) until the estimated error for Cs-137 (whose energy level of 662 KeV is relatively close to the 511 KeV energy level of F-18) is within an acceptable range (e.g., 1%). At that time, the operator activates the tab 1596 for the Cs-137 isotope and places the Cs-137 source in the ionization chamber to confirm that the difference between the expected and measured activity of the Cs-137 isotope is substantially similar to or within an acceptable range from the estimated error displayed in field 1612. At this point the calibration routine is completed, and the results may be printed and/or stored for later accessing by system maintenance personnel. As shown, an "abort" button 1614 for terminating the calibration procedure is provided for the operator.

[271] Finally, Fig. 46 shows field service tab 1516 activated to prompt a display 1620 which can be used to pre-set one or more future reminder dates to undertake preventative maintenance for the system 10.

[272] It is to be appreciated that the systems, devices and methods of the present invention can be used in a very wide variety of drug delivery and therapeutic procedures. In general, the systems, devices and methods of the present invention are particularly suited for use in connection with any hazardous pharmaceutical or substance to be

injected into a patient (human or animal). Even pharmaceuticals, such as contrast agents or thrombolytic agents, that are not considered to be especially hazardous can be beneficially administered via systems broadly contemplated herein and provide hospital personnel additional protection against adverse effects.

[273] To the extent that systems of the present invention can be applicable to radiotherapy drugs or pharmaceuticals wherein the drug or pharmaceutical itself is radioactive, it is to be appreciated that, as clear to one skilled in the art, maintaining containment of radiotherapy pharmaceuticals promotes safety. If the drug or pharmaceutical is radioactive, the use of radiation absorbing or leaded shielding will help protect the operator and patient from unnecessary radiation. Containment of radiotherapy pharmaceutical is discussed in U.S. Patent Application Publication No. 2003-0004463, the contents of which are incorporated herein by reference.

[274] While procedures discussed herein in accordance with embodiments of the present invention have generally been described with respect to liquid drugs, it is to be understood that they can also apply to powdered drugs with either a liquid or gaseous vehicle, or gaseous drugs that are to be delivered to a recipient.

[275] If not otherwise stated herein, it may be assumed that all components and/or processes described heretofore may, if appropriate, be considered to be interchangeable with similar components and/or processes disclosed elsewhere in the specification, unless an express indication is made to the contrary.

[276] If not otherwise stated herein, any and all patents, patent publications, articles and other printed publications discussed or mentioned herein are hereby incorporated by reference as if set forth in their entirety herein.

[277] It should be appreciated that the apparatus, systems, components and methods of the present invention may be configured and conducted as appropriate for any context at hand. The embodiments described above are to be considered in all respects only as illustrative and not restrictive.

WHAT IS CLAIMED IS:

1. A fluid path set for use in a fluid delivery system, the fluid path set comprising:

a medical fluid component comprising a first tubing section for connection to a source of a medical fluid;

a pharmaceutical component comprising a second tubing section for connection to a source of a pharmaceutical;

a coil assembly component comprising a tube coil having a height of approximately 1.53 inches, a diameter of approximately 1.95 inches and a volume capacity of approximately 12.5 ml; and

a connector comprising a first port for connecting the first tubing section of the medical fluid component, a second port for connecting the second tubing section of the pharmaceutical component and a third port for connecting the tube coil of the coil assembly component.

2. The fluid path set of Claim 1 wherein the tube coil comprises a tubing section having an outer diameter of approximately 0.218 inches, an inner diameter of approximately 0.156 inches and a length of approximately 41 inches.

3. The fluid path set of Claim 2 wherein the tube coil is formed in a helical coil of approximately 7 turns of the tubing section.

4. The fluid path set of Claim 3 wherein the coil assembly further comprises a core structure around which the tube coil is formed, the core structure comprising an upper shoulder and a lower shoulder that define a tube channel therebetween, the upper and lower shoulders adapted to retain the tube coil therebetween within the tube channel.

5. The fluid path set of Claim 4 wherein the core structure further comprises an upper surface defining an inlet for accommodating a first end of the tubing section and an outlet for accommodating a second end of the tubing section.

6. The fluid path set of Claim 5 wherein the coil assembly component further comprises a third tubing section connected to the third port of the connector and the first end of the tubing section and a fourth tubing section connected to the second end of the tubing section.

7. The fluid path set of Claim 6, further comprising:

a waste component comprising a fifth tubing section in connection with a waste receptacle;

a sixth tubing section having a connector end that is adapted to be connected to a single-patient tubing set; and

a second connector comprising a first port for connecting the fourth tubing section of the coil assembly component, a second port for connecting the fifth tubing section of the waste component and a third port for connecting the sixth tubing section.

8. The fluid path set of Claim 7 wherein the connector end comprises a swabable luer valve that is biased to a closed position when the single-patient tubing set is not connected thereto.

9. The fluid path set of Claim 7 wherein the connector end comprises a manifold or a stopcock each having two or more outlet ports for connection to respective single-patient tubing sets.

10. The fluid path set of Claim 7 wherein the first tubing section is approximately 56.75 inches in length and has an outer diameter of approximately 0.188 inches, an inner diameter of approximately 0.062 inches and a durometer of 45, the second tubing section is approximately 8.75 inches in length and has an outer diameter of approximately 0.094 inches, an inner diameter of approximately 0.032 inches and a durometer of 45, the third tubing section is approximately 15 inches in length and has an outer diameter of approximately 0.163 inches, an inner diameter of approximately 0.062 inches and a durometer of 60, the fourth tubing section is approximately 12 inches in length and has an outer diameter of approximately 0.163 inches, an inner diameter of approximately 0.062 inches and a durometer of 60, and the fifth tubing section and the sixth tubing section are each approximately 5 inches in length and have an outer diameter of approximately 0.163 inches, an inner diameter of approximately 0.062 inches and a durometer of 60.

11. The fluid path set of Claim 1 wherein the first tubing section comprises a first check valve and a spike for connecting to the source of a medical fluid and the second tubing

section comprises a second check valve and a vented cannula for connecting to the source of a pharmaceutical.

12. The fluid path set of Claim 1 wherein the second tubing section comprises a vented cannula comprising:

a main hub comprising two opposed lateral sides and defining a fluid port and a vent;

a fluid draw needle in connection with the second tubing section through the fluid port and adapted to be placed within the source of a pharmaceutical;

a vent needle in connection with the vent and adapted to be placed within the source of a pharmaceutical; and

two resilient arms connected to the opposed lateral sides of the main hub, each of the two arms comprising a top edge and a hook member formed thereon and extending outwardly therefrom.

13. The fluid path set of Claim 12 wherein the fluid draw needle is longer than the vent needle.

14. The fluid path set of Claim 12 wherein the vent comprises a filter.

15. The fluid path set of Claim 12 wherein the main hub of the vented cannula further comprises a ledge extending therefrom in a horizontal plane above the two arms, the ledge and the top edges of the two arms cooperating to define horizontal slots therebetween.

16. The fluid path set of Claim 15 wherein the hook members extend outwardly from the arms in a plane substantially normal to the horizontal plane of the ledge.

17. The fluid path set of Claim 12 wherein the main hub and each of the arms cooperate to define substantially U-shaped grooves extending along the lateral sides of the main hub.

18. A vented cannula for drawing fluid from a container, the vented cannula comprising:

a main hub comprising two opposed lateral sides and defining a fluid port and a vent;

a fluid draw needle in connection with the fluid port and adapted to be placed within the container;

a vent needle in connection with the vent and adapted to be placed within the container; and

two resilient arms connected to the opposed lateral sides of the main hub, each of the two arms comprising a top edge and a hook member formed thereon and extending outwardly therefrom.

19. The vented cannula of Claim 18 wherein the fluid draw needle is longer than the vent needle.

20. The vented cannula of Claim 18 wherein the vent comprises a filter.

21. The vented cannula of Claim 18 wherein the main hub of the vented cannula further comprises a ledge extending therefrom in a horizontal plane above the two arms, the ledge and the top edges of the two arms cooperating to define horizontal slots therebetween.

22. The vented cannula of Claim 21 wherein the hook members extend outwardly from the arms in a plane substantially normal to the horizontal plane of the ledge.

23. The vented cannula of Claim 18 wherein the main hub and each of the arms cooperate to define substantially U-shaped grooves extending along the lateral sides of the main hub.

24. A method of calibrating a fluid delivery system for delivering a pharmaceutical containing a radioisotope to a patient, the method comprising:

measuring an activity level of a first radioisotope in an ionization chamber of the fluid delivery system, the first radioisotope having an energy level less than that of the radioisotope to be delivered to the patient;

comparing the measured activity level of the first radioisotope to an expected activity level of the first radioisotope;

adjusting the gain of the ionization chamber to compensate for the difference, if any, between the measured activity and the expected activity of the first radioisotope;

measuring an activity level of a second radioisotope in the ionization chamber of the fluid delivery system, the second radioisotope having an energy level similar to or greater than that of the radioisotope to be delivered to the patient;

comparing the measured activity level of the second radioisotope to an expected activity level of the second radioisotope;

adjusting the gain of the ionization chamber to compensate for the difference, if any, between the measured activity and the expected activity of the second radioisotope; and

calculating an estimated error in a measured activity of a third radioisotope based on the differences, if any, between the measured activity and the expected activity of the first radioisotope and the measured activity and the expected activity of the second radioisotope.

25. The method of Claim 24, further comprising:

comparing the estimated error in a measured activity of the third radioisotope to a predetermined acceptable error or error range;

if the estimated error is the same as or similar to the predetermined acceptable error or is within the predetermined acceptable error range, then measuring an activity level of the third radioisotope in the ionization chamber of the fluid delivery system;

calculating the difference, if any, between the measured activity level of the third radioisotope and an expected activity level of the third radioisotope to derive an actual error; and

determining whether the actual error is the same or similar to the predetermined acceptable error or is within the predetermined acceptable error range.

26. The method of Claim 24 wherein the calculating step comprises:

calculating an initial estimated error in a measured activity of a third radioisotope based on the difference, if any, between the measured activity and the expected activity of the first radioisotope; and

calculating a revised estimated error in a measured activity of the third radioisotope based on the difference, if any, between the measured activity and the expected activity of the second radioisotope.

27. The method of Claim 26, further comprising:

comparing the revised estimated error in a measured activity of the third radioisotope to a predetermined acceptable error or error range;

if the revised estimated error is the same or similar to the predetermined acceptable error or is within the predetermined acceptable error range, then measuring an activity level of the third radioisotope in the ionization chamber of the fluid delivery system;

calculating the difference, if any, between the measured activity level of the third radioisotope and an expected activity level of the third radioisotope to derive an actual error; and

determining whether the actual error is the same or similar to the predetermined acceptable error or is within the predetermined acceptable error range.

28. The method of Claim 27, further comprising:

if the revised estimated error is not the same or similar to the predetermined acceptable error or is not within the predetermined acceptable error range, then remeasuring the activity level of the first radioisotope in the ionization chamber of the fluid delivery system;

comparing the remeasured activity level of the first radioisotope to the expected activity level of the first radioisotope;

adjusting the gain of the ionization chamber to compensate for the difference, if any, between the remeasured activity and the expected activity of the first radioisotope;

calculating a second revised estimated error in a measured activity of the third radioisotope based on the difference, if any, between the remeasured activity and the expected activity of the first radioisotope;

remeasuring the activity level of the second radioisotope in the ionization chamber of the fluid delivery system;

comparing the remeasured activity level of the second radioisotope to the expected activity level of the second radioisotope;

adjusting the gain of the ionization chamber to compensate for the difference, if any, between the remeasured activity and the expected activity of the second radioisotope; and

calculating a third revised estimated error in a measured activity of the third radioisotope based on the difference, if any, between the remeasured activity and the expected activity of the second radioisotope.

29. The method of Claim 28, further comprising:

comparing the third revised estimated error in a measured activity of the third radioisotope to a predetermined acceptable error or error range;

if the third revised estimated error is the same or similar to the predetermined acceptable error or is within the predetermined acceptable error range, then measuring an activity level of the third radioisotope in the ionization chamber of the fluid delivery system;

calculating the difference, if any, between the measured activity level of the third radioisotope and an expected activity level of the third radioisotope to derive an actual error; and

determining whether the actual error is the same or similar to the predetermined acceptable error or is within the predetermined acceptable error range.

30. The method of Claim 27, further comprising:

if the revised estimated error is not the same or similar to the predetermined acceptable error or is not within the predetermined acceptable error range, then remeasuring the activity level of the first radioisotope in the ionization chamber of the fluid delivery system;

comparing the remeasured activity level of the first radioisotope to the expected activity level of the first radioisotope;

adjusting the gain of the ionization chamber to compensate for the difference, if any, between the remeasured activity and the expected activity of the first radioisotope;

calculating a second revised estimated error in a measured activity of the third radioisotope based on the difference, if any, between the remeasured activity and the expected activity of the first radioisotope;

comparing the second revised estimated error in a measured activity of the third radioisotope to a predetermined acceptable error or error range;

if the second revised estimated error is the same or similar to the predetermined acceptable error or is within the predetermined acceptable error range, then measuring an activity level of the third radioisotope in the ionization chamber of the fluid delivery system;

calculating the difference, if any, between the measured activity level of the third radioisotope and an expected activity level of the third radioisotope to derive an actual error;

determining whether the actual error is the same or similar to the predetermined acceptable error or is within the predetermined acceptable error range;

if the second revised estimated error is not the same or similar to the predetermined acceptable error or is not within the predetermined acceptable error range, then remeasuring the activity level of the second radioisotope in the ionization chamber of the fluid delivery system;

comparing the remeasured activity level of the second radioisotope to the expected activity level of the second radioisotope;

adjusting the gain of the ionization chamber to compensate for the difference, if any, between the remeasured activity and the expected activity of the second radioisotope; and

calculating a third revised estimated error in a measured activity of the third radioisotope based on the difference, if any, between the remeasured activity and the expected activity of the second radioisotope.

31. The method of Claim 30, further comprising:

comparing the third revised estimated error in a measured activity of the third radioisotope to a predetermined acceptable error or error range;

if the third revised estimated error is the same or similar to the predetermined acceptable error or is within the predetermined acceptable error range, then measuring an activity level of the third radioisotope in the ionization chamber of the fluid delivery system;

calculating the difference, if any, between the measured activity level of the third radioisotope and an expected activity level of the third radioisotope to derive an actual error; and

determining whether the actual error is the same or similar to the predetermined acceptable error or is within the predetermined acceptable error range.

32. The method of Claim 24 wherein the radioisotope to be delivered to the patient is F-18.

33. The method of Claim 32 wherein the first radioisotope is Co-57, the second radioisotope is Co-60 and the third radioisotope is Cs-137.

34. The method of Claim 24 wherein the low gain of the ionization chamber is adjusted to compensate for the difference, if any, between the measured activity and the expected activity of the first radioisotope and the high gain of the ionization chamber is adjusted to compensate for the difference, if any, between the measured activity and the expected activity of the second radioisotope.

35. A vial access system comprising:

a base portion comprising a substantially horizontal lower surface and a sloped upper surface adapted to support a vial comprising a bottom wall and a substantially cylindrical wall connected thereto, the sloped upper surface adapted to ensure that a residual volume of fluid in the vial gathers in an area defined at least partially by a portion of the junction between the bottom wall and the cylindrical wall of the vial.

36. The vial access system of Claim 35, further comprising:

a housing extending vertically from the base portion;

a vertical support arm comprising an upper end, the vertical support arm movably disposed within the housing; and

a cap member connected to the upper end of the vertical support arm and adapted to overlie a septum of the vial.

37. The vial access system of Claim 36 wherein the cap member comprises a mounting mechanism disposed on an underside thereof, the mounting mechanism adapted to retain a cannula therein for insertion through the septum of the vial.

38. The vial access system of Claim 37 wherein the vertical support arm is slidably disposed within the housing to allow the cannula to be inserted into and removed from the vial.

39. The vial access system of Claim 38 wherein the vertical support arm is rotatably disposed within the housing to allow the cap member to be rotated into and out of a position that overlies the septum of the vial.

40. The vial access system of Claim 37 wherein the mounting mechanism comprises two arms that cooperate to define a slot therebetween, each of the two arms comprising a tab member extending downwardly therefrom, each of the tab members comprising a front edge and a rear edge.

41. The vial access system of Claim 36, further comprising a handle member pivotally connected to the upper end of the vertical support arm.

42. The vial access system of Claim 36 wherein the cap member includes or is formed from radioactive shielding material.

43. The vial access system of Claim 35, further comprising at least one support member connected to the base portion for retaining the vial on the sloped upper surface of the base portion.

44. The vial access system of Claim 43 wherein the at least one support member comprises two support pins that are connected to the sloped upper surface of the base portion.

45. The vial access system of Claim 35 wherein the vial is contained within a vial shield and the fluid is a radiopharmaceutical.

46. The vial access system of Claim 35 wherein the sloped upper surface is sloped at an angle of approximately 10-13 degrees with respect to a horizontal plane.

47. A method of priming at least a portion of a fluid path set in a fluid delivery system, the method comprising:

placing a tubing section of the fluid path set in fluid connection with a source of a radiopharmaceutical;

placing a portion of the tubing section within a dose calibrator of the fluid delivery system;

pumping a volume of the radiopharmaceutical through the tubing section;

monitoring the dose calibrator to determine if a measured activity level is substantially equal to or above a predetermined activity level; and

if the measured activity level is substantially equal to or above the predetermined activity level, then concluding that the tubing section of the fluid path set has been primed.

48. The method of Claim 47, further comprising:

if the measured activity level is zero or below the predetermined activity level, then concluding that the tubing section of the fluid path has not been primed; and

pumping a second volume of the radiopharmaceutical through the tubing section.

49. The method of Claim 47, further comprising:

placing a second tubing section in fluid connection with a source of medical fluid and the tubing section;

pumping a volume of the medical fluid through the second tubing section and at least a portion of the tubing section to move the volume of the radiopharmaceutical to the portion of the tubing section that is positioned within the dose calibrator.

50. The method of Claim 49, further comprising:

placing the tubing section in fluid connection with a waste receptacle;

pumping a second volume of the medical fluid through the second tubing section and at least a portion of the tubing section to move the volume of the radiopharmaceutical into the waste receptacle.

51. A fluid delivery system, comprising:

a housing having an upper surface defining a plurality of recessed portions for accommodating one or more components of a fluid path set;

a cover movably connected to the housing and adapted to move between a first position that exposes the upper surface and a second position that overlies the upper surface; and.

a locking mechanism associated with the cover and adapted to lock the cover in the second position.

52. The fluid delivery system of Claim 51 wherein the cover is slidably connected to the housing.

53. The fluid delivery system of Claim 51 wherein the first position allows an operator to insert or remove the one or more components of the fluid path set.

54. The fluid delivery system of Claim 51 wherein the plurality of recessed portions includes wells and troughs.

55. The fluid delivery system of Claim 51, further comprising:

one or more handles connected to the housing;

a plurality of wheels or casters connected to the housing; and

a display connected to the housing.

56. The fluid delivery system of Claim 51 wherein the cover and the upper surface comprises or is formed from a radioactive shielding material.

57. The fluid delivery system of Claim 51, further comprising:

a dose calibrator for measuring the radioactivity level of a radiopharmaceutical;

a pumping mechanism for pumping the radiopharmaceutical; and

a controller in communication with the dose calibrator and the pumping mechanism.

58. The fluid delivery system of Claim 51 wherein the locking mechanism comprises a mechanical lock that locks the cover to the housing in the second position.

59. The fluid delivery system of Claim 57 wherein the locking mechanism is a software-implemented lock that is in communication with the controller, the software implemented lock adapted to lock the cover to the housing in the second position.

60. The fluid delivery system of Claim 51, further comprising a printer associated with the housing.

61. A vial shield carrying system for carrying a vial shield containing a pharmaceutical vial, the vial shield carrying system comprising in combination:

a collar unit adapted to removably engage a flange on the vial shield, the collar unit defining two elongated slots formed in a top surface thereof, each of the slots including a pin disposed therein and extending between two opposing walls thereof; and

a handle unit adapted to engage the collar unit, the handle unit comprising a handle connected to a U-shaped cross piece defining two, downwardly extending arms having hook members formed therein, the open ends of the hook members formed on opposite ends of the arms and adapted to engage the pins in the slots of the collar unit through rotation of the handle.

62. The vial shield carrying system of Claim 61, further comprising a plunger connected to the U-shaped cross piece and adapted to mate with a septum cap of the vial shield when the handle unit engages the collar unit on the vial shield.

63. The vial shield carrying system of Claim 62, further comprising a spring disposed between the plunger and the U-shaped cross piece, the spring adapted to bias the plunger into engagement with the septum cap of the vial shield.

64. The vial shield carrying system of Claim 63 wherein the arms are lowered into the slots of the collar unit, the plunger is engaged with the septum cap of the vial shield and the handle is rotated in a clockwise direction to seat the pins of the collar unit in the hook members of the handle unit.

65. The vial shield carrying system of Claim 64 wherein the handle is rotated in a counter-clockwise direction to disengage the hook members of the handle unit from the pins of the collar unit.

66. The vial shield carrying system of Claim 62 wherein the plunger comprises or is formed from a radioactive shielding material.

67. The vial shield carrying system of Claim 61 wherein the collar unit comprises two members that are pivotally connected to allow the collar unit to engage and disengage the flange of the vial shield.

68. A fluid delivery system, comprising:

a syringe comprising a body defining a discharge outlet and a plunger movably disposed within the body;

a connector comprising a valve member and defining first, second and third ports;

a first tubing segment connected between the discharge outlet of the syringe and the first port of the connector;

a cannula defining a fluid port;

a second tubing segment connected between the fluid port of the cannula and the second port of the connector;

a third tubing segment comprising a first end connected to the third port of the connector and a second end comprising a second connector; and

a per-patient tubing set comprising a first end that is adapted to be connected to the second connector on the second end of the third tubing segment and a patient end that is adapted to be connected to venous access device in a patient.

69. The fluid delivery system of Claim 68 wherein the connector comprises a T-connector and the valve member comprises a stopcock.

70. The fluid delivery system of Claim 68 wherein the second connector comprises a swabable valve or a luer connector.

71. The fluid delivery system of Claim 68 wherein the syringe contains a radiopharmaceutical and is disposed within a lead-shielded container.

72. The fluid delivery system of Claim 68 wherein the syringe is a hand-held syringe.

73. The fluid delivery system of Claim 68 wherein the cannula further comprises:

a main hub comprising two opposed lateral sides and defining a vent;

a fluid draw needle in connection with the fluid port and adapted to be placed within a fluid container;

a vent needle in connection with the vent and adapted to be placed within the fluid container; and

two resilient arms connected to the opposed lateral sides of the main hub, each of the two arms comprising a top edge and a hook member formed thereon and extending outwardly therefrom.

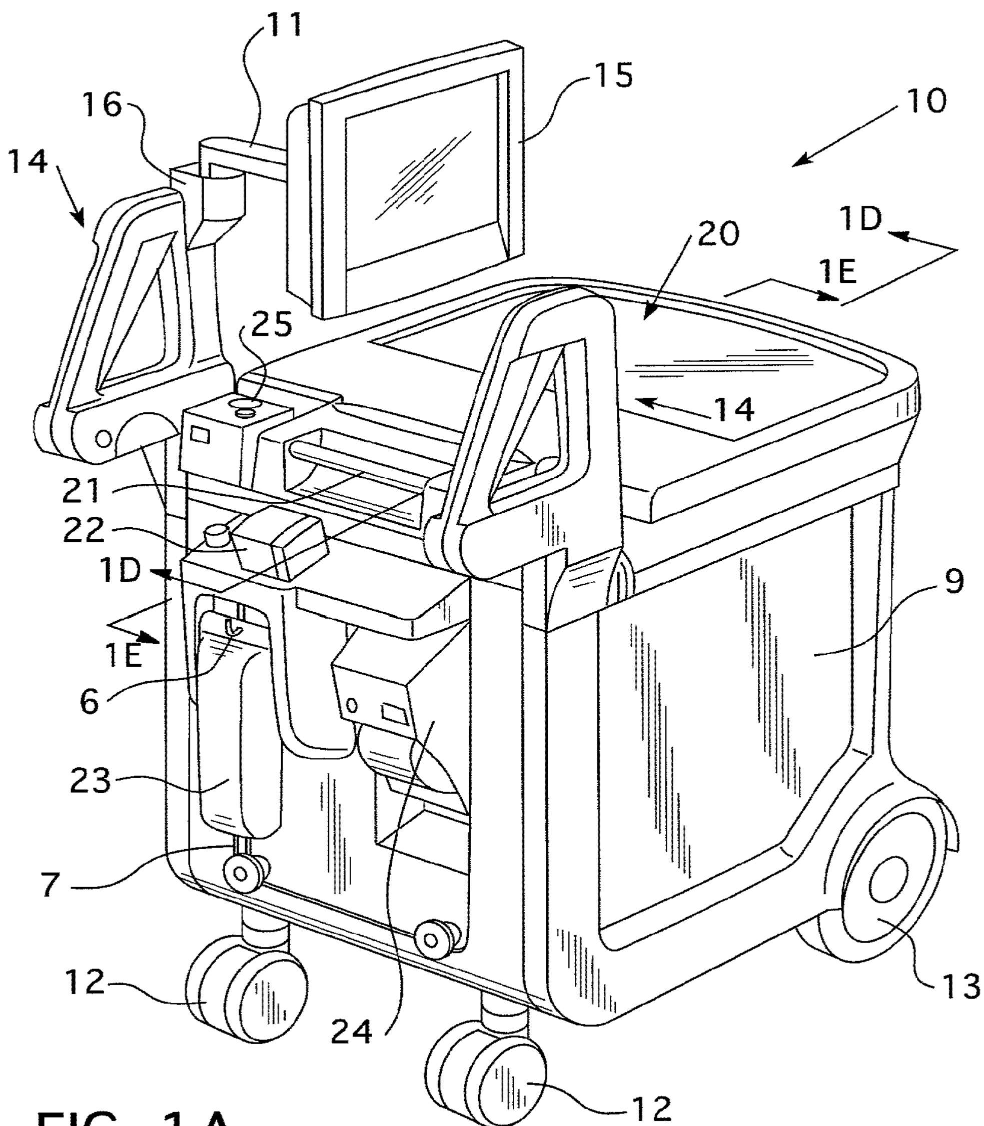


FIG. 1A

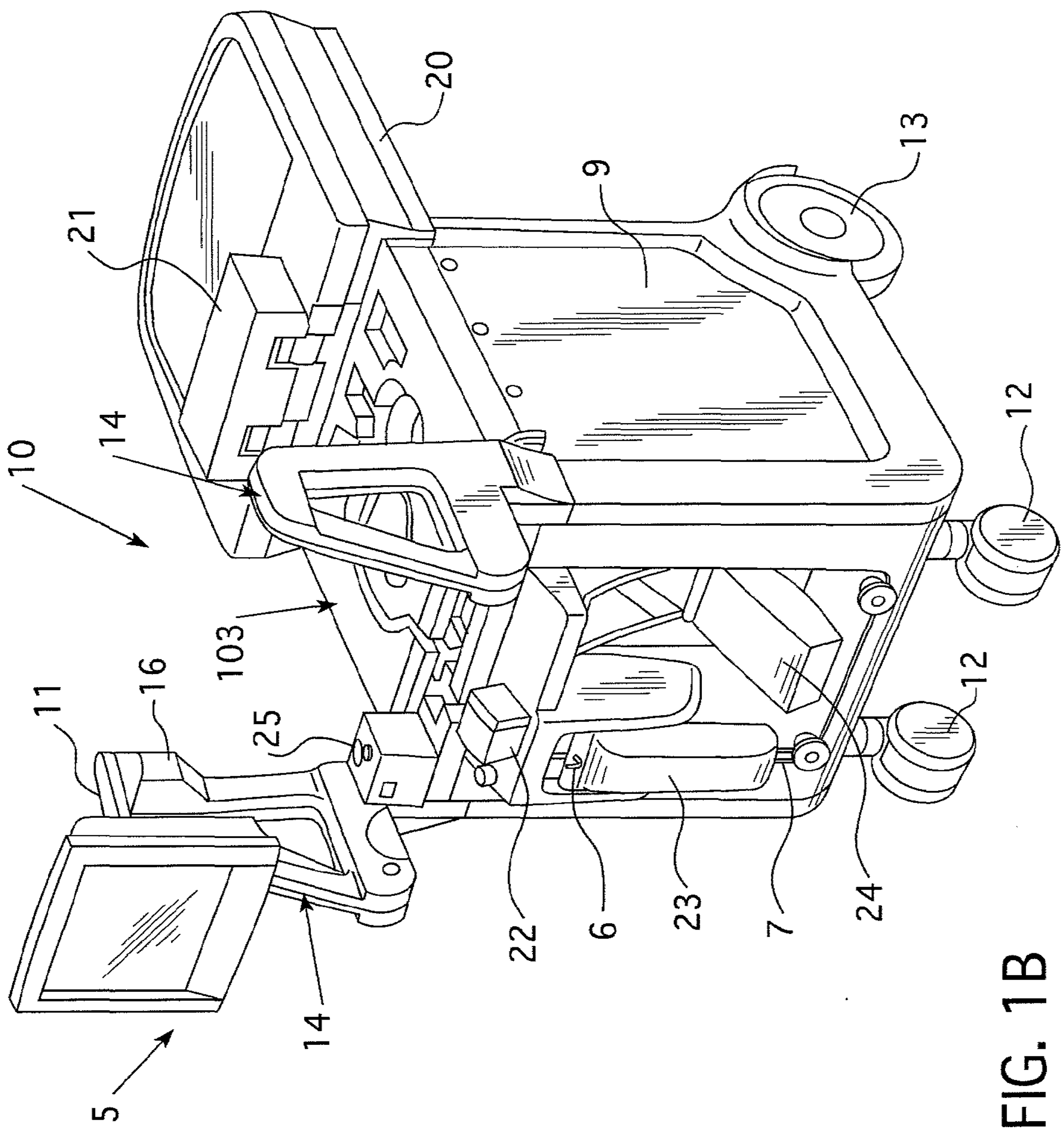
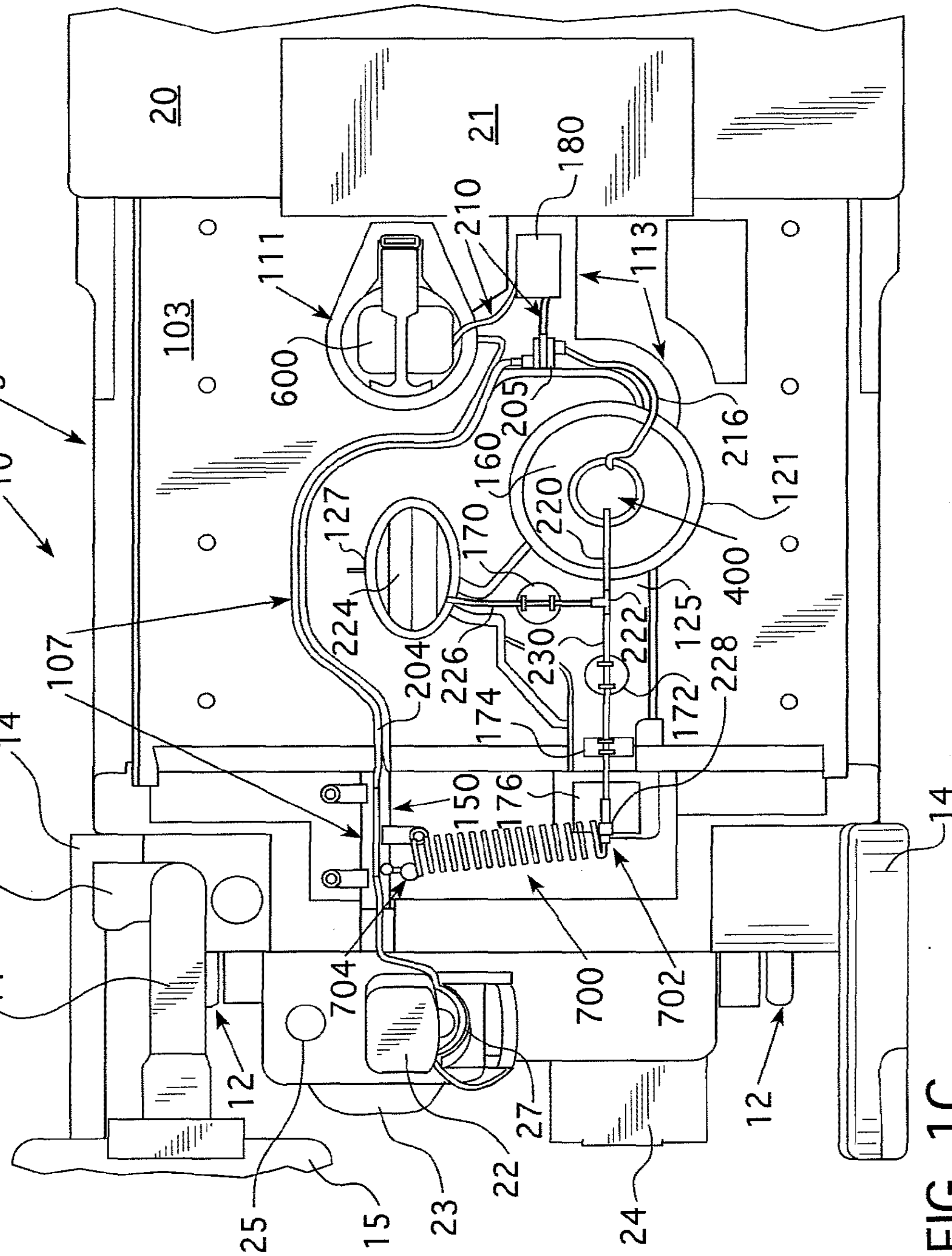


FIG. 1B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222
230
226
204
228
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23
24

FIG. 1C

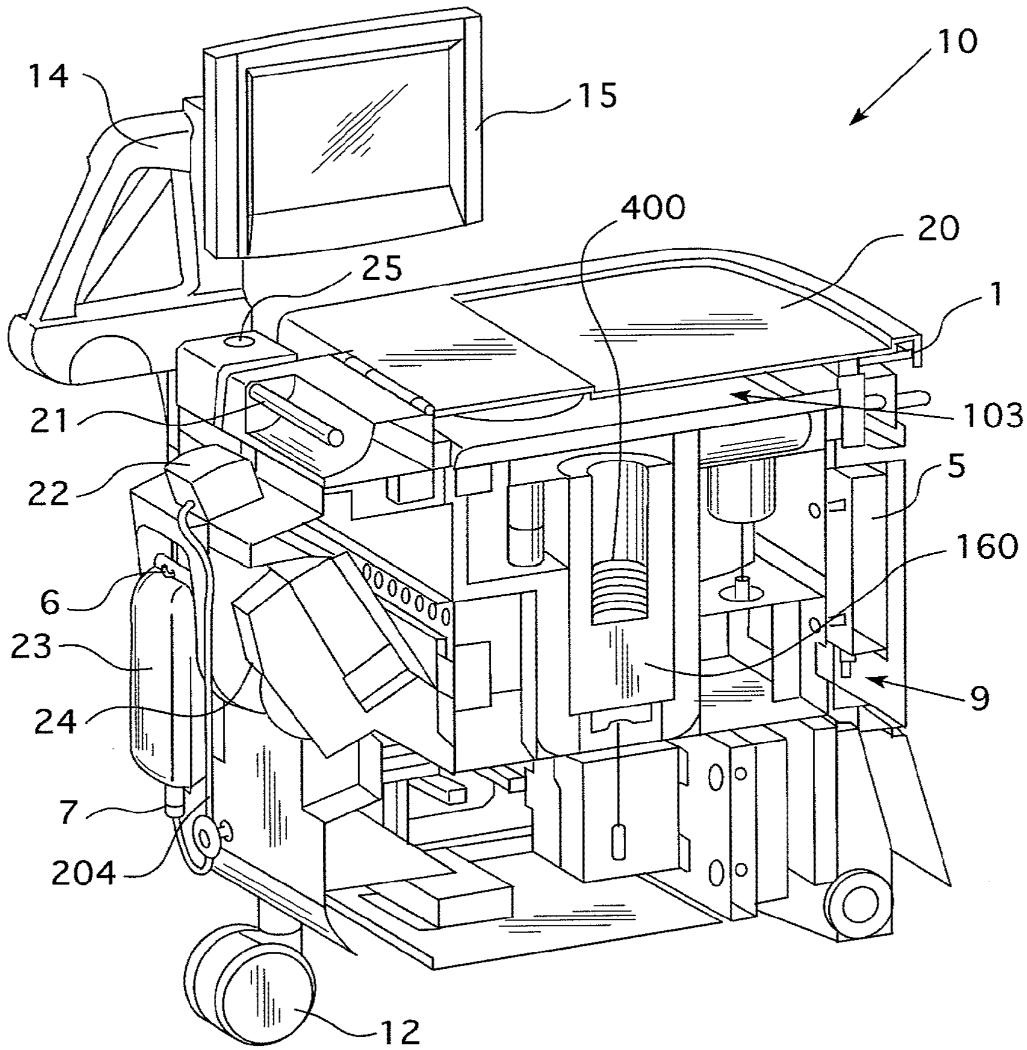


FIG. 1D

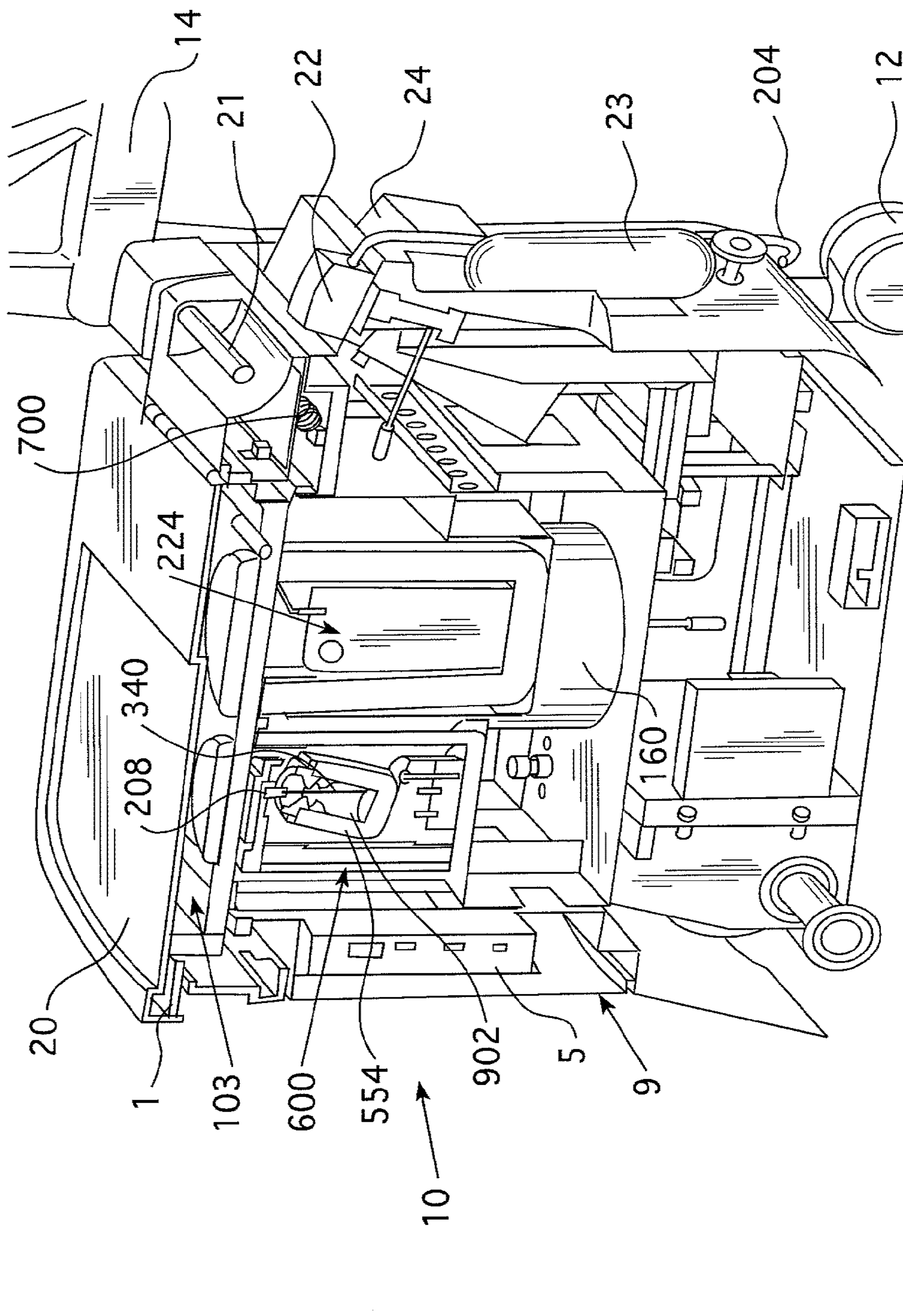
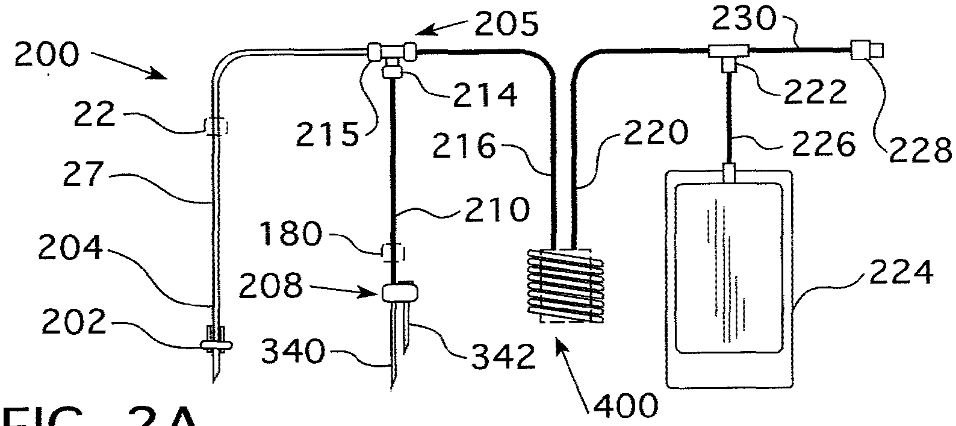


FIG. 1E


200
205
230
22
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216
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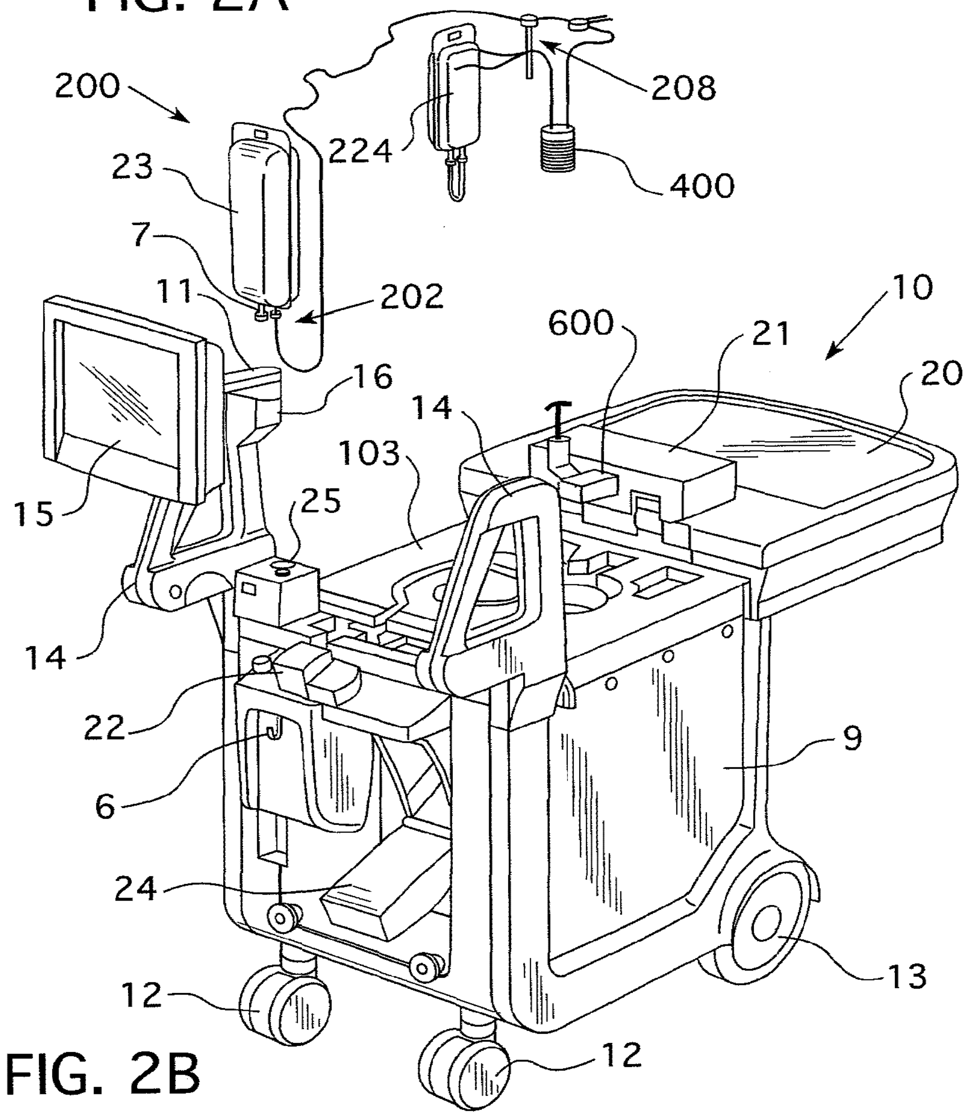
226
228
27
210
180
204
224
208
202
340
342
400

FIG. 2A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200
224
400
23
7
202
11
10
600
21
20
16
14
103
15
25
14
22
9
6
24
13
12
12

FIG. 2B

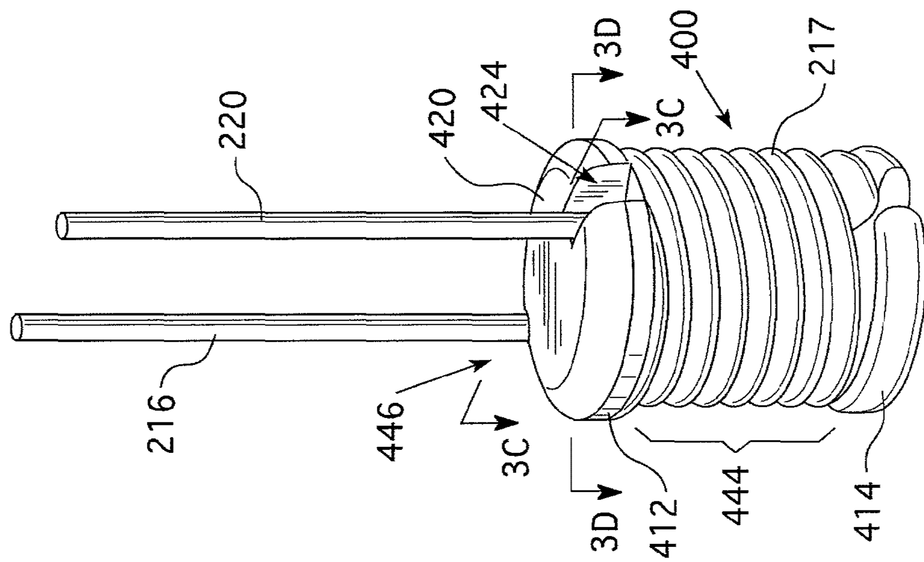

220
216
420
424
3D
3C
400
217
446
3C
3D
412
444
414

FIG. 3A

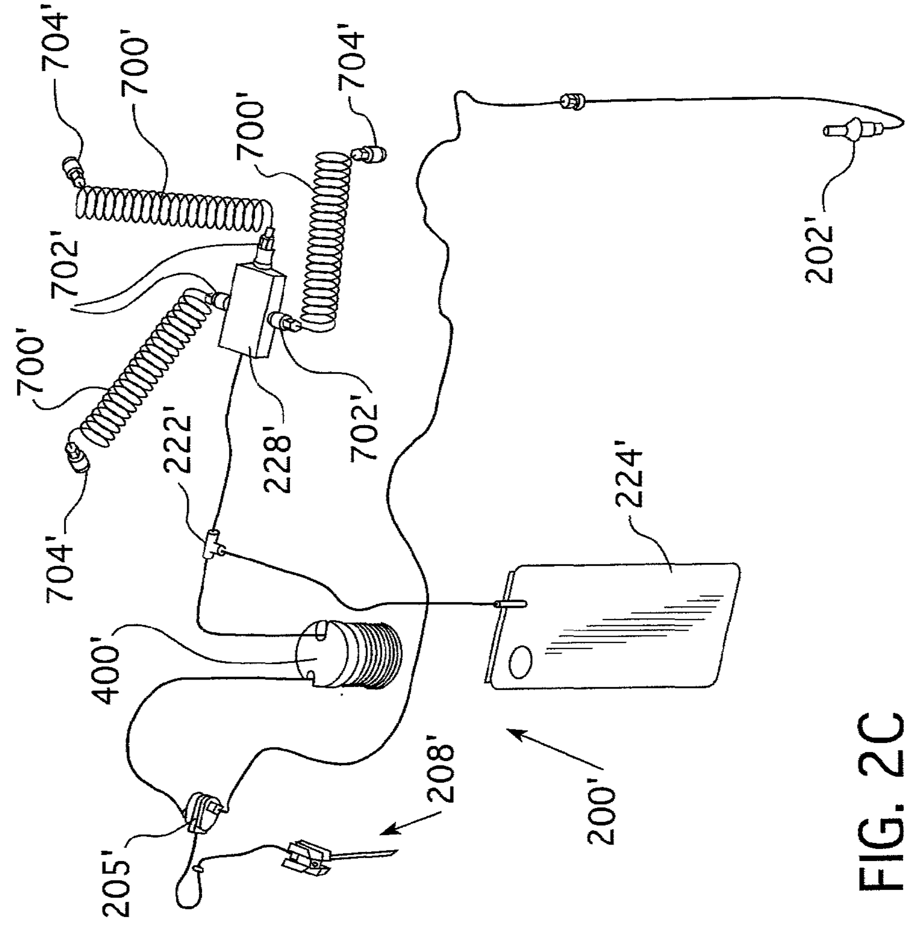

704'
700'
704'
700'
702'
700'
702'
228'
222'
704'
224'
400'
208'
200'
205'
202'

FIG. 2C

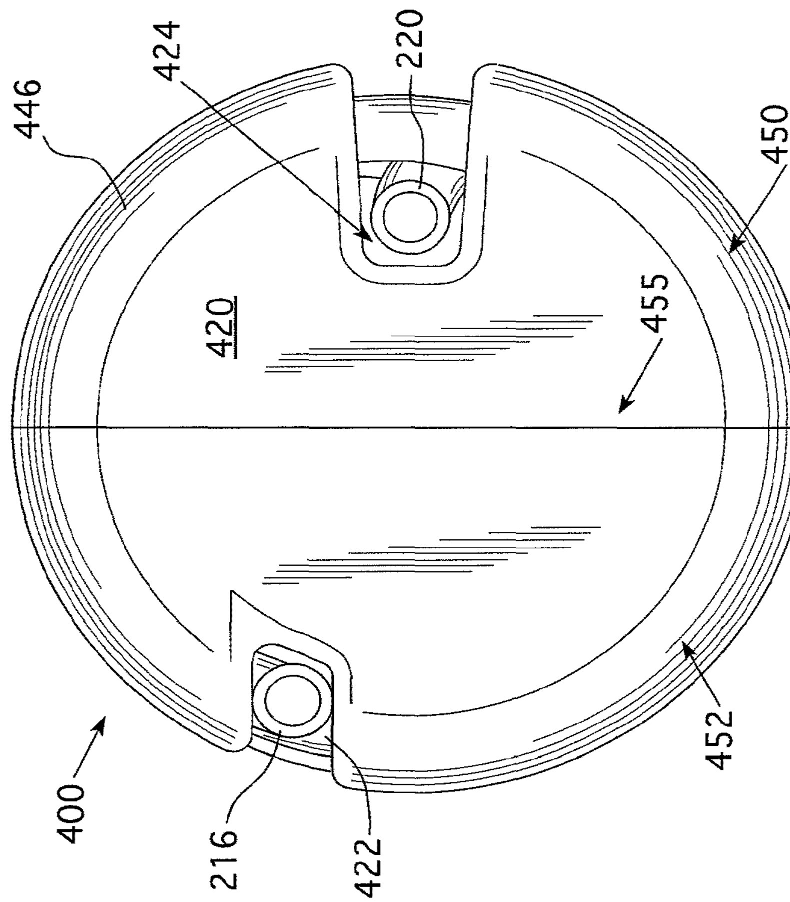

400
446
424
220
450
420
455
216
422
452

FIG. 3C

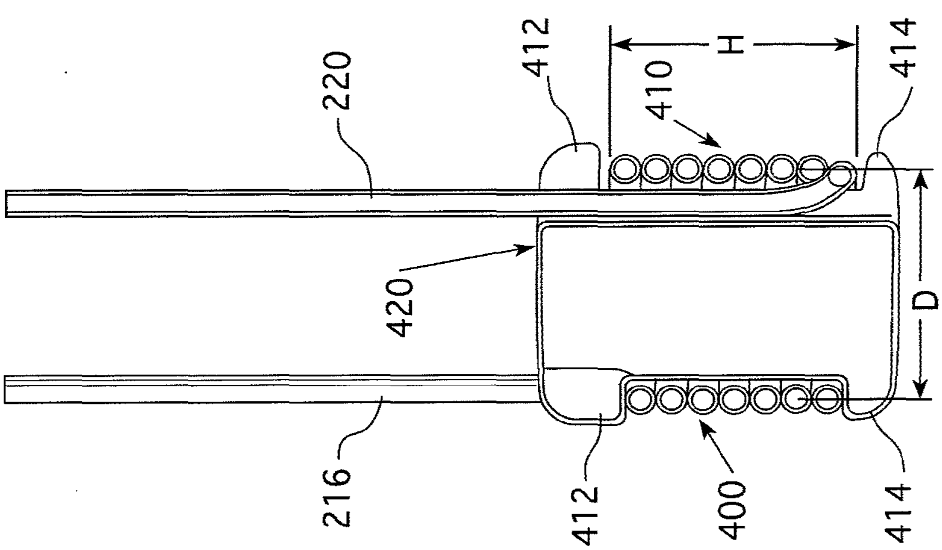

220
412
H
410
414
420
D
216
412
400
414

FIG. 3B

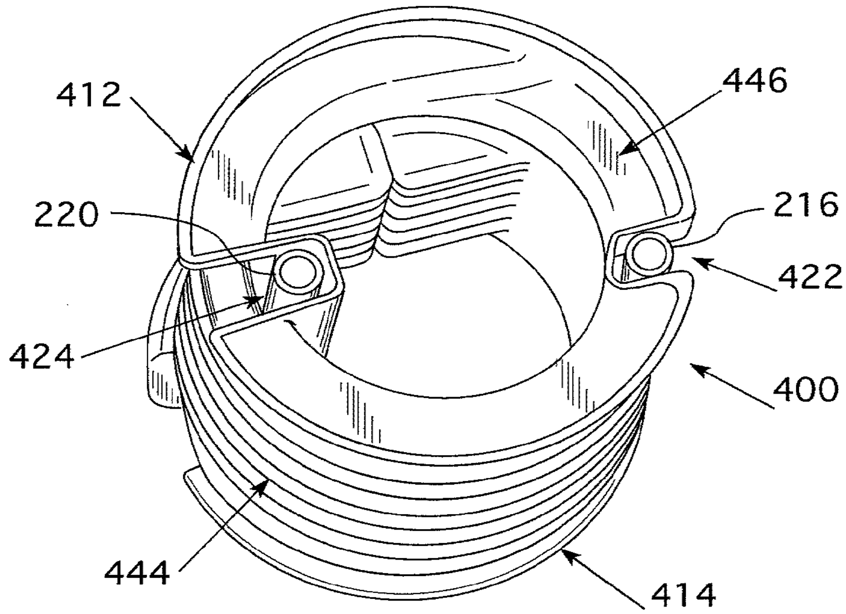

412
446
220
216
422
424
400
444
414

FIG. 3D

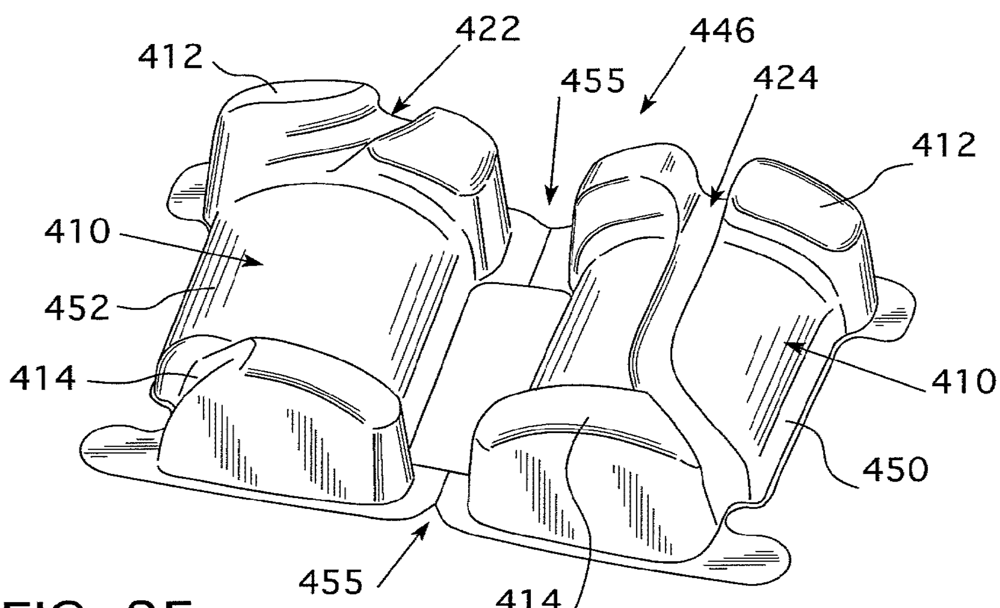

412
422
446
455
424
412
410
452
414
410
450
455
414

FIG. 3E

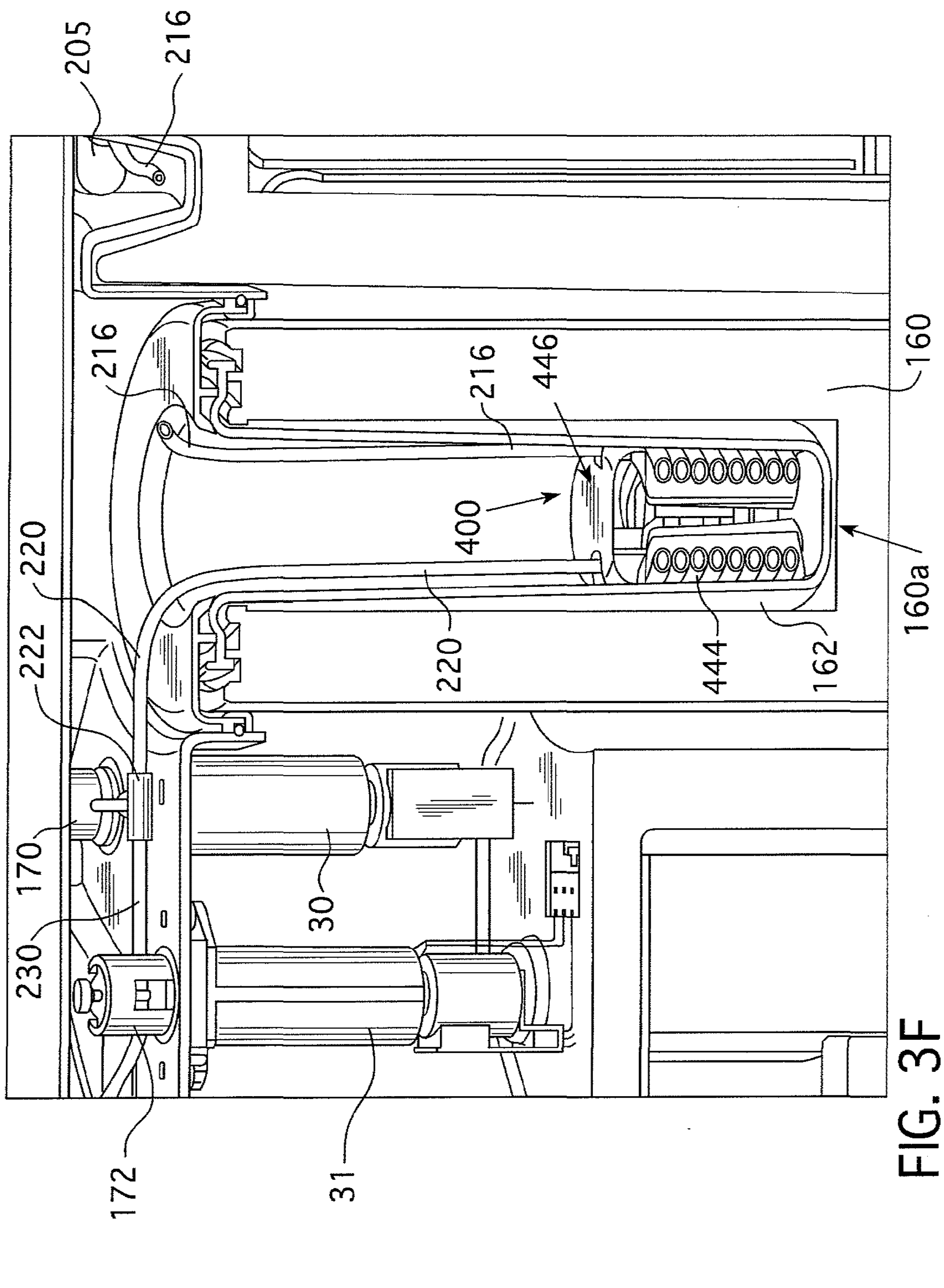

205
216
216
216
446
160
400
220
220
160a
222
444
162
170
30
230
172
31

FIG. 3F

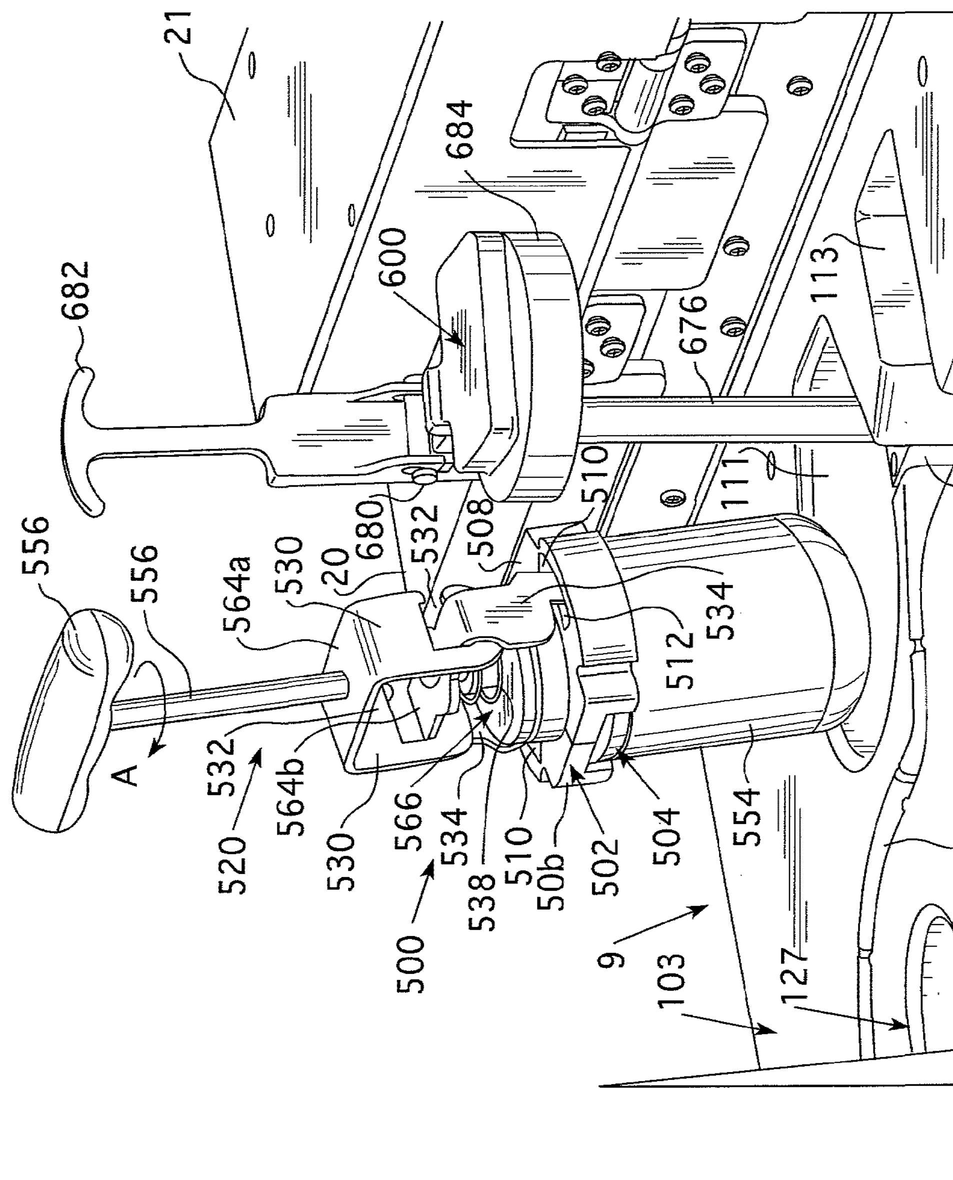

21
682
684
600
676
113
111
678
510
556
556
564a
530
20
680
532
508
534
512
A
532
520
564b
530
566
534
510
538
50b
502
504
554
107
500
9
103
127

FIG. 4A

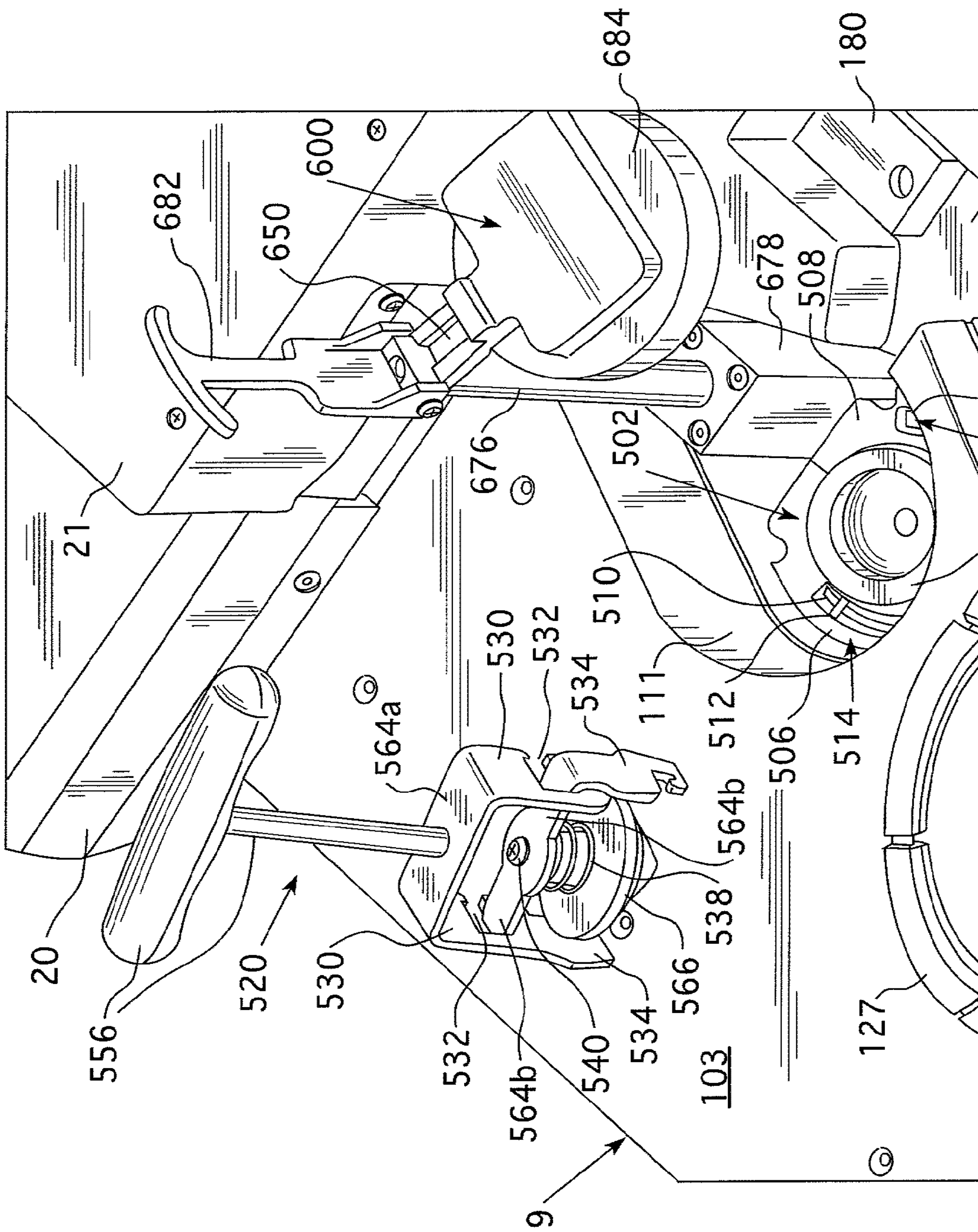

684
180
113
600
682
650
678
508
510
21
676
502
514
510
562
20
556
520
530
564a
530
532
534
111
512
506
514
564b
538
566
534
540
532
564b
103
127
9

FIG. 4B

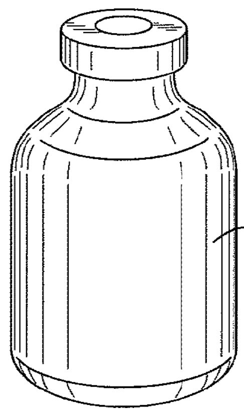


FIG. 4C

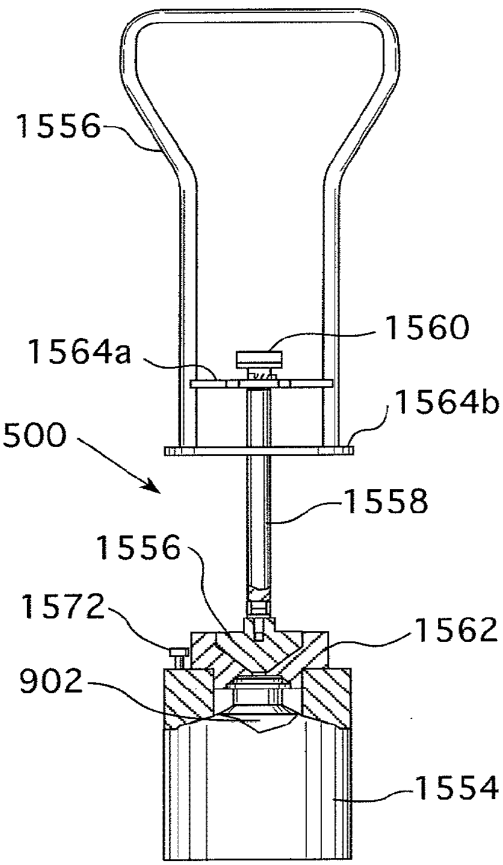


FIG. 5A

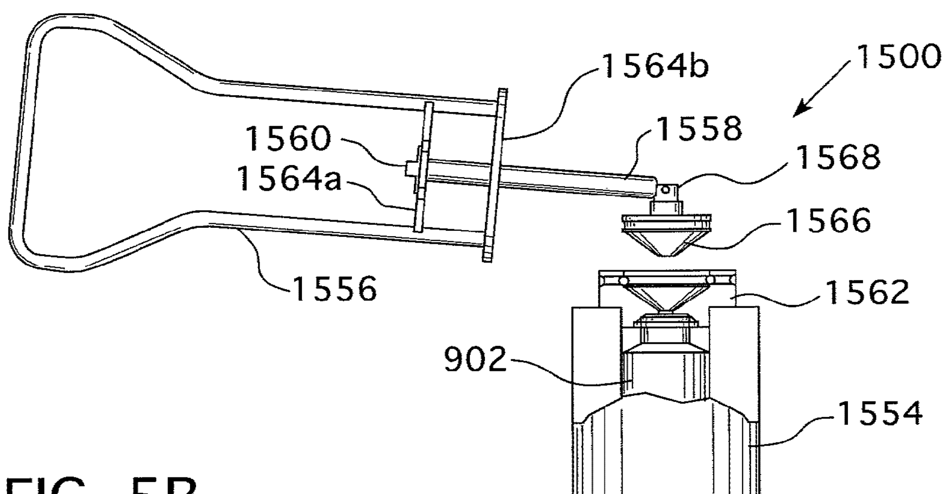


FIG. 5B

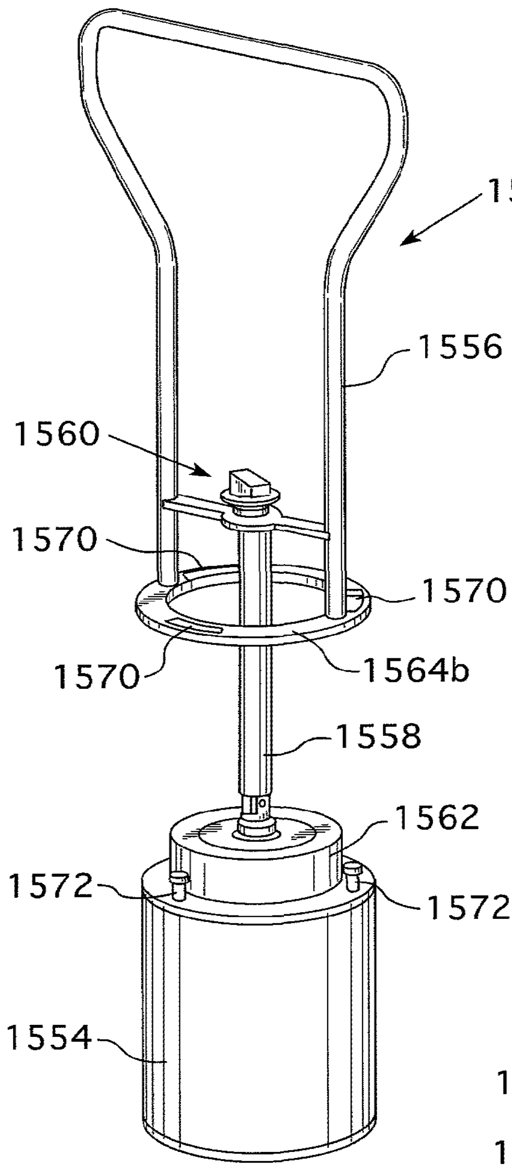

1500
1556
1560
1570
1570
1570
1564b
1558
1562
1572
1572
1554

FIG. 5C

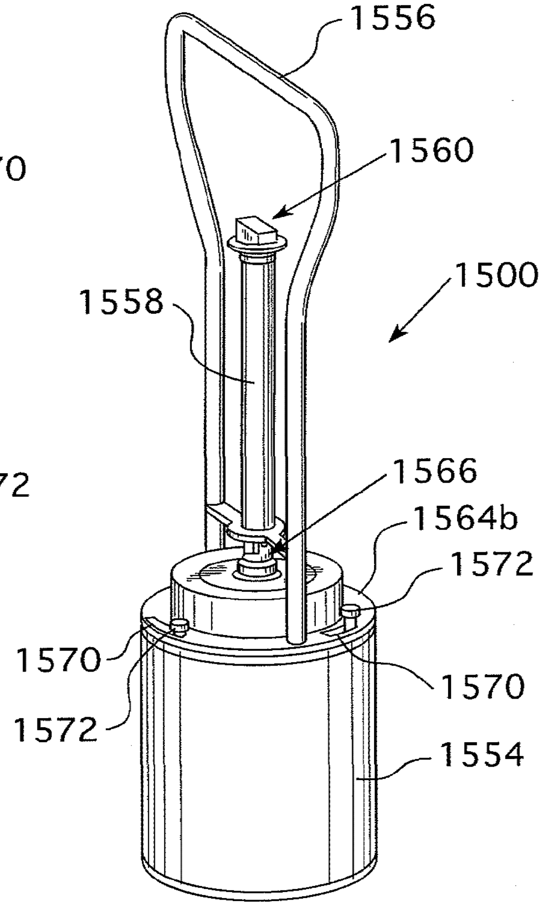

1556
1560
1500
1558
1566
1564b
1572
1570
1570
1572
1554

FIG. 5D

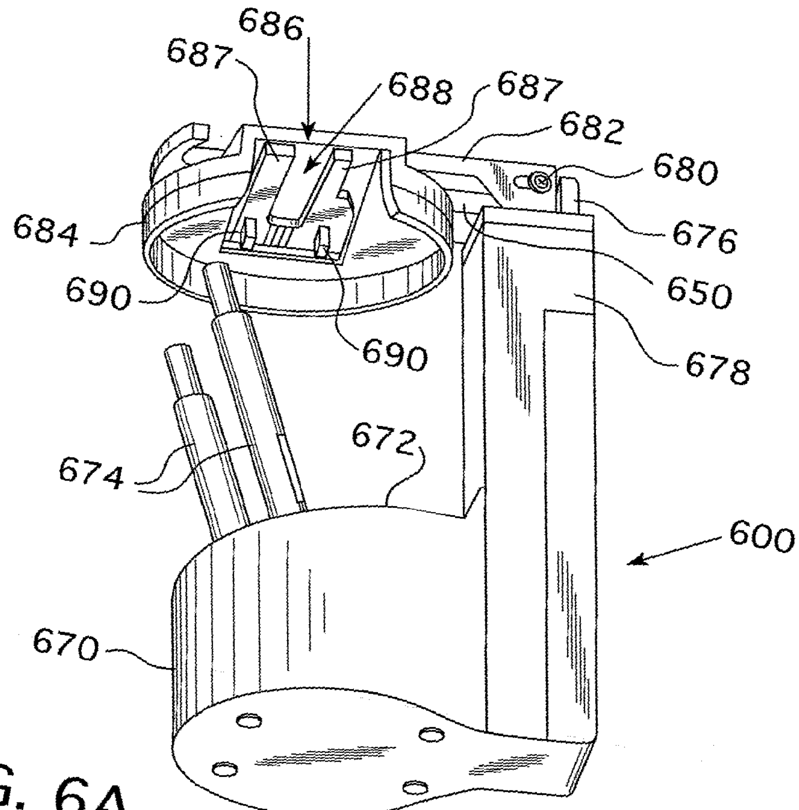

686
687
688
687
682
680
676
650
678
684
690
690
674
672
600
670

FIG. 6A

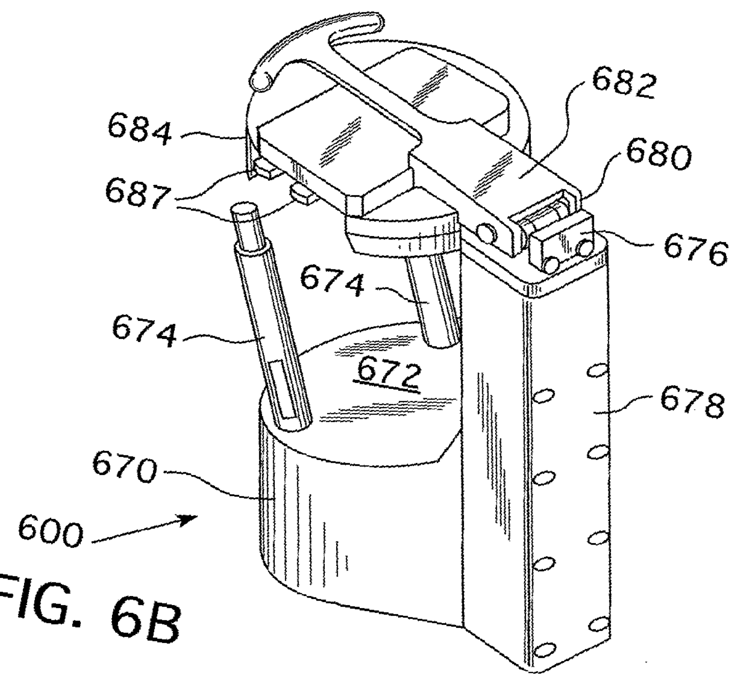

682
684
680
687
676
674
674
672
678
670
600

FIG. 6B

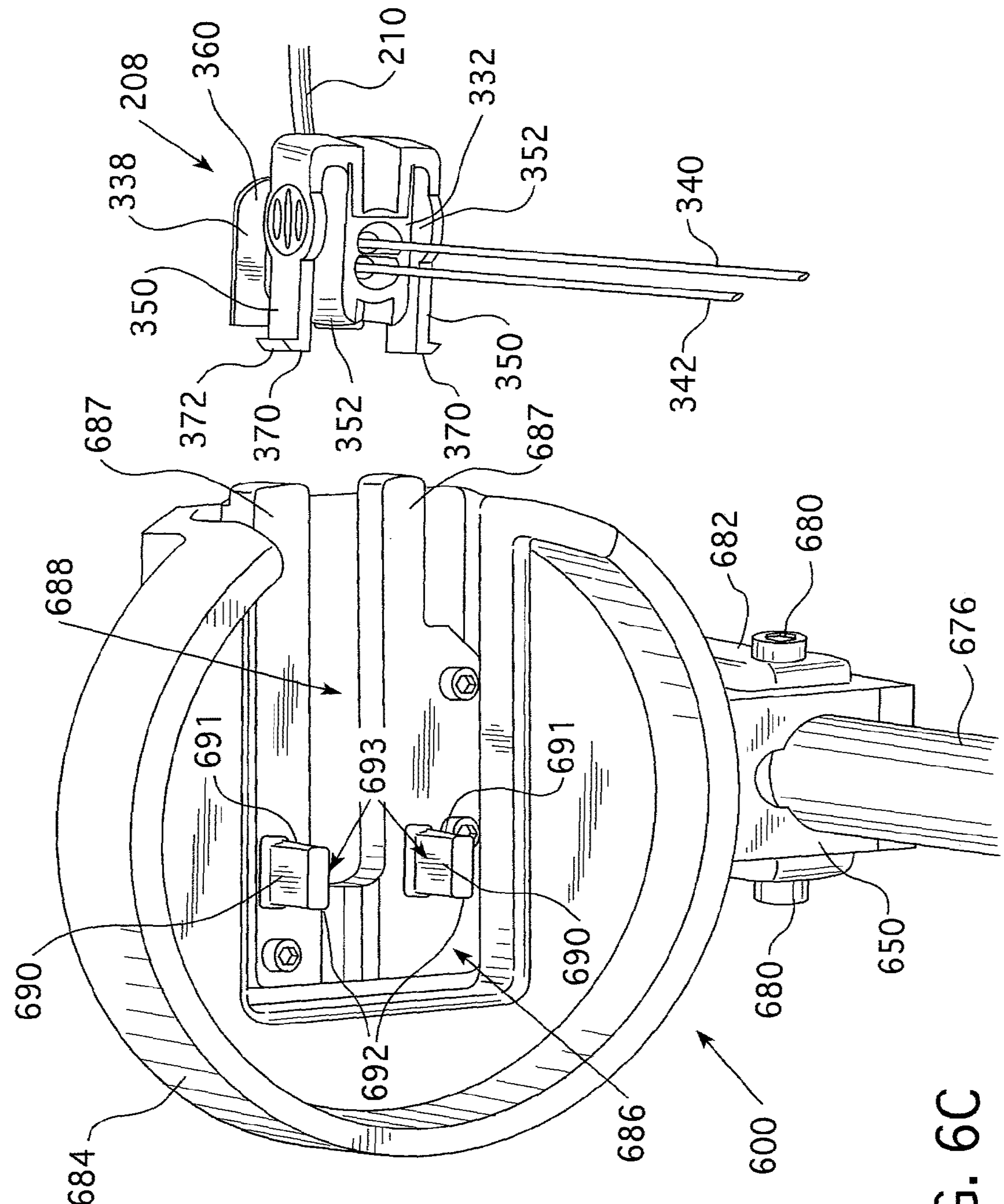

210
208
360
332
338
352
340
350
342
350
372
370
352
370
687
687
688
682
680
676
691
693
691
690
690
650
680
692
686
600
684

FIG. 6C

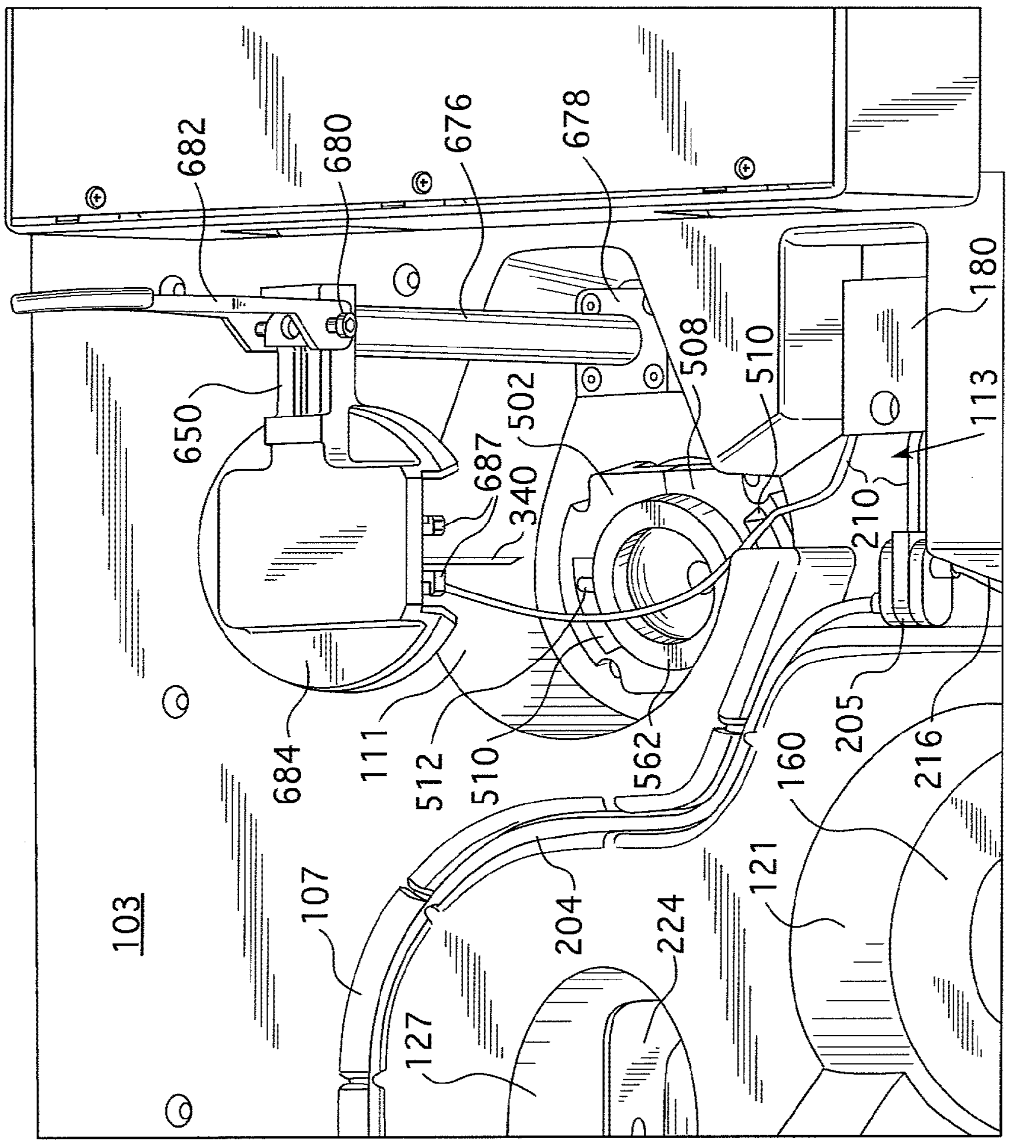

682
680
676
678
650
502
508
510
180
113
687
340
210
684
111
512
510
562
205
216
160
103
107
204
224
121
127

FIG. 6D

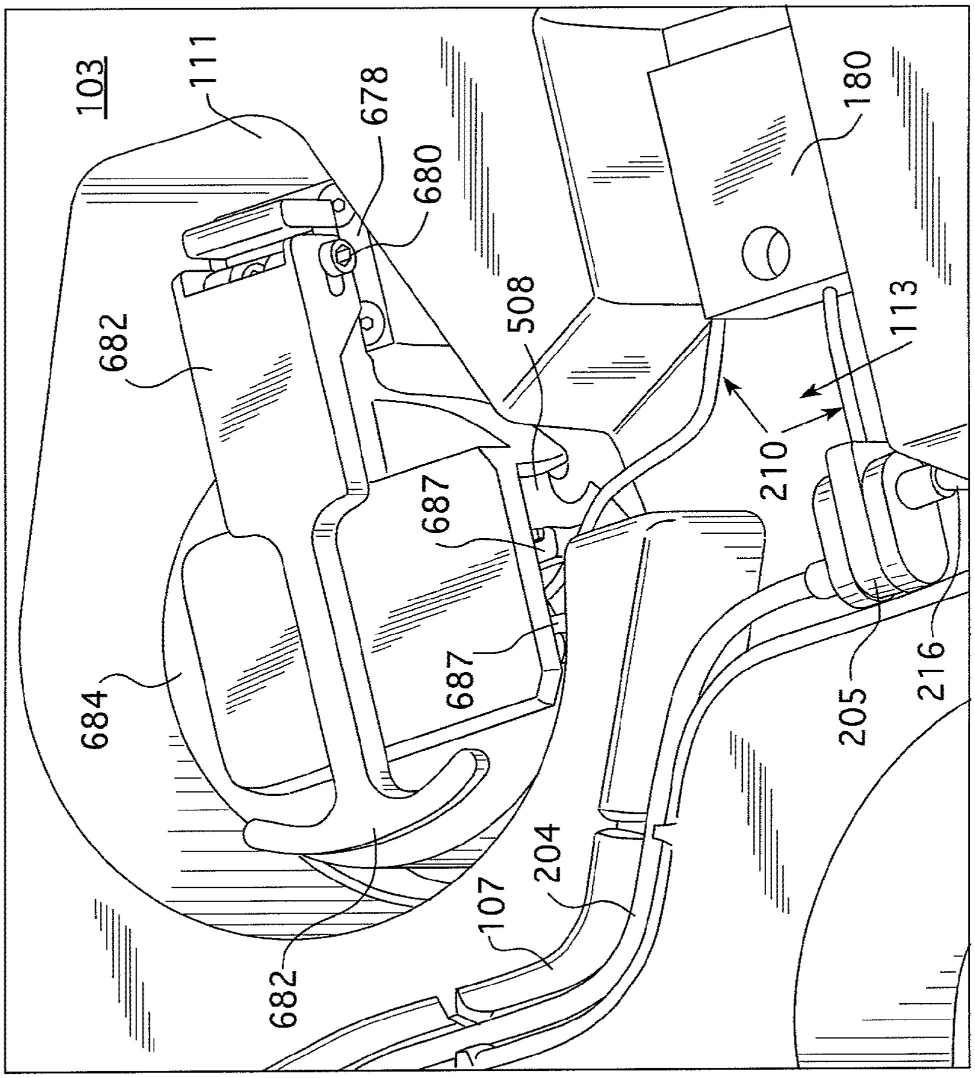

103
111
678
680
180
682
508
113
210
687
687
687
684
205
216
204
107
682

FIG. 6E

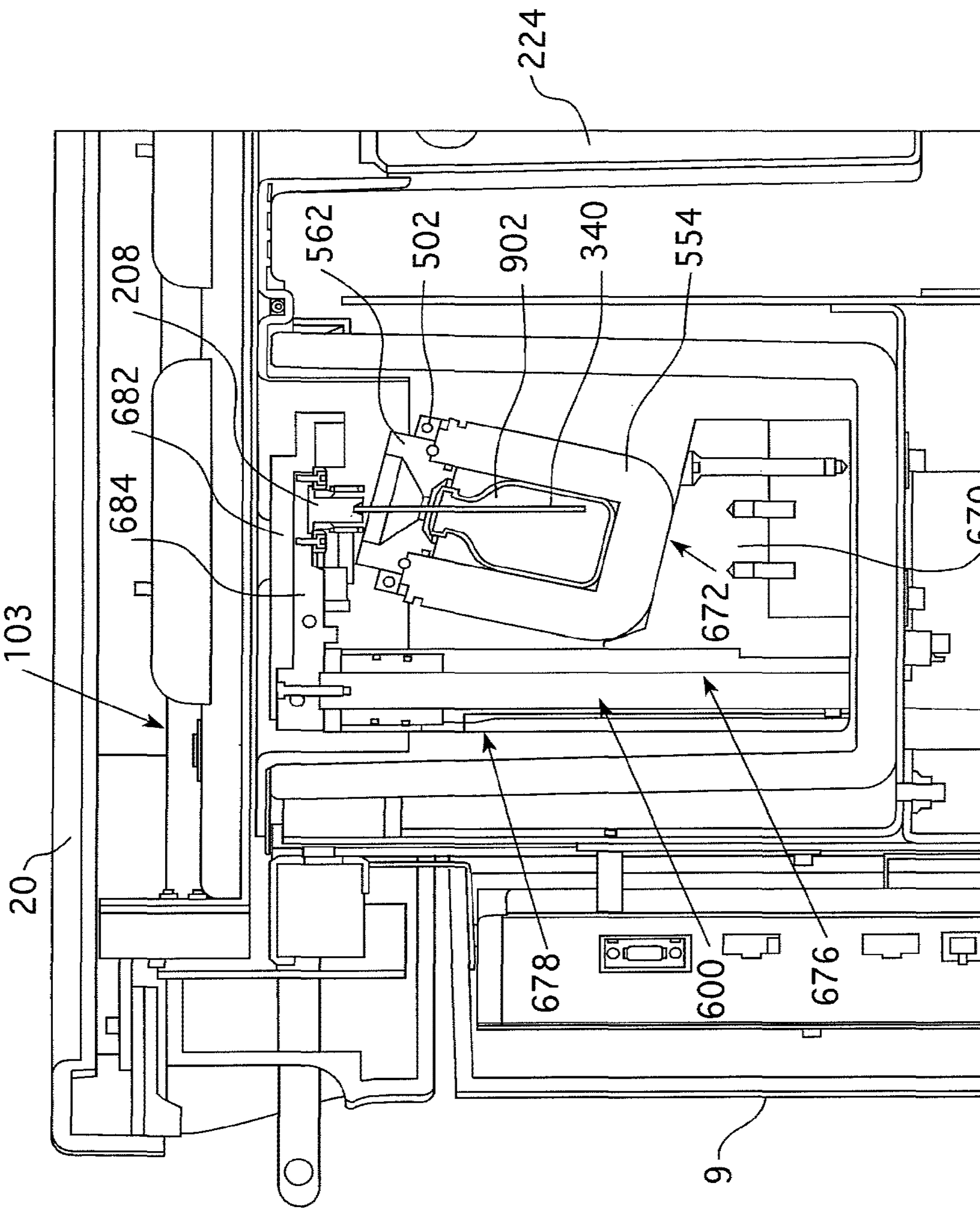


FIG. 6F

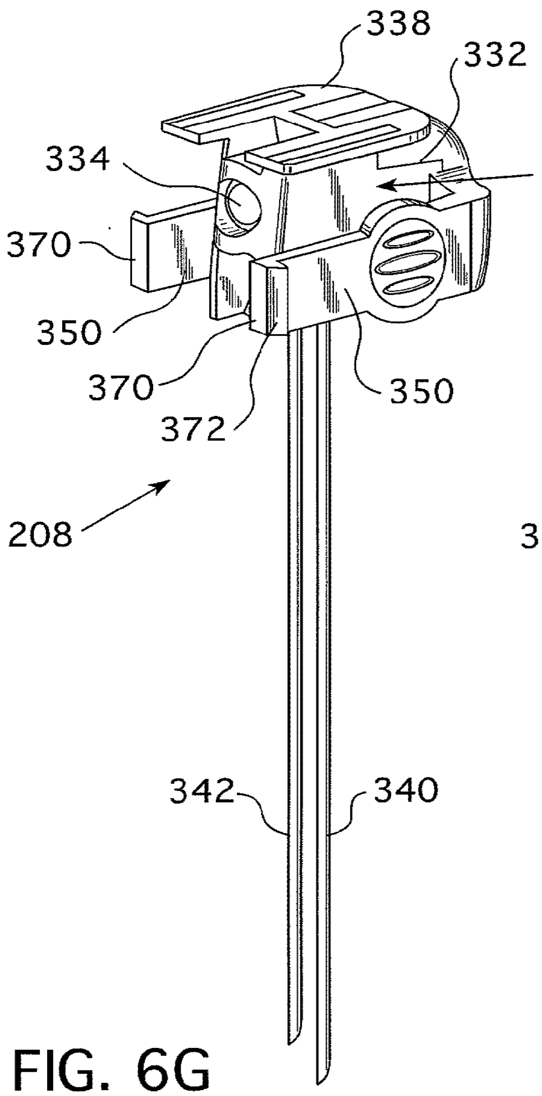

338
332
334
360
370
350
370
350
372
208
342
340

FIG. 6G

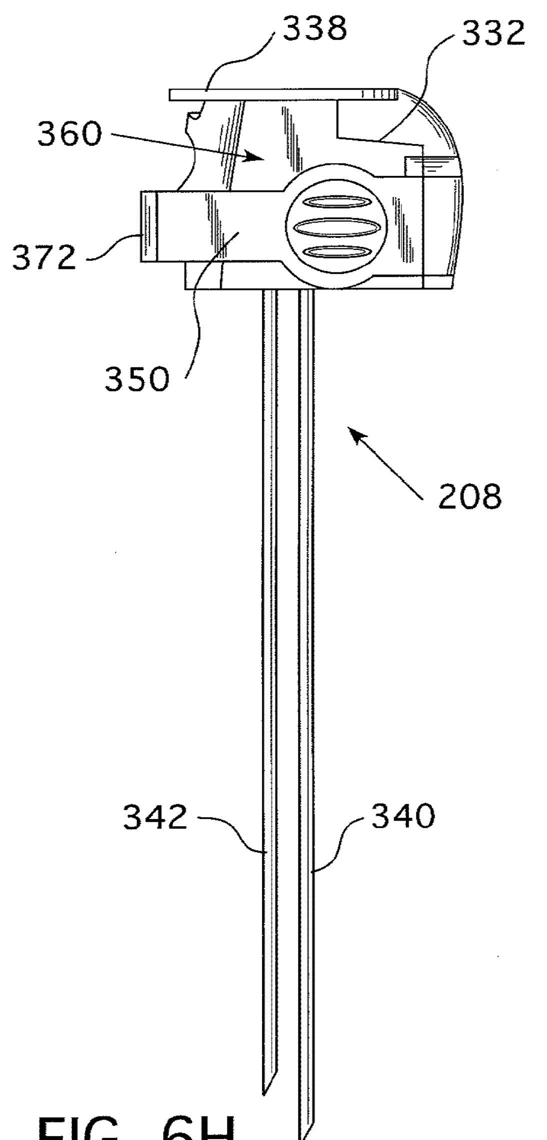

338
332
360
372
350
208
342
340

FIG. 6H

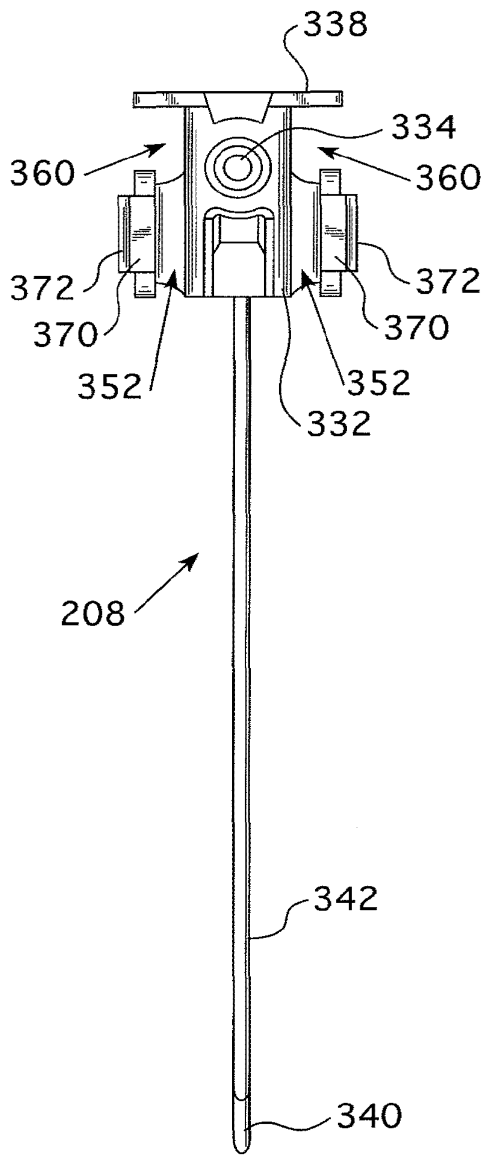

338
334
360
360
372
372
370
370
352
352
332
208
342
340

FIG. 6I

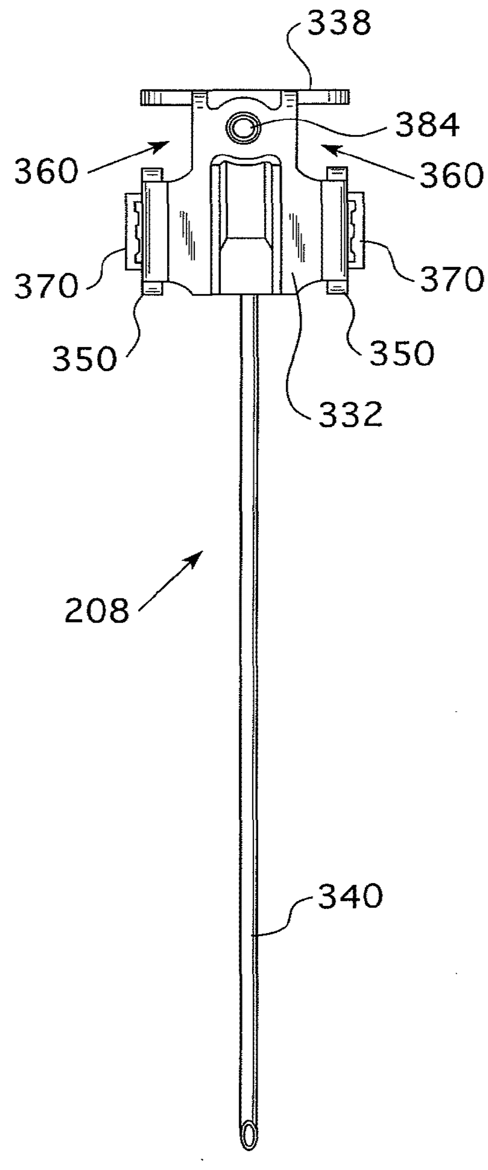

338
384
360
360
370
370
350
350
332
208
340

FIG. 6J

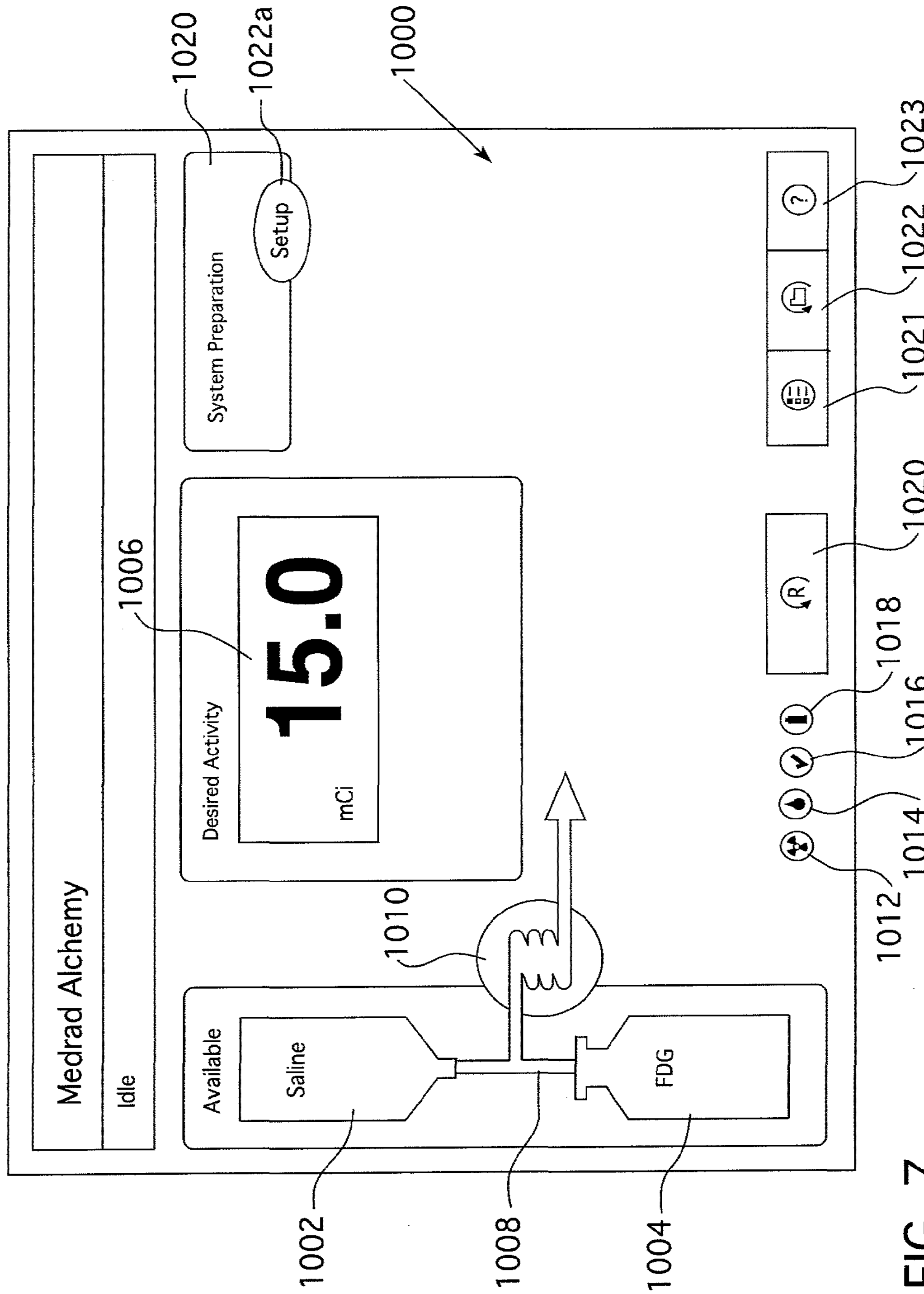

Medrad Alchemy
Idle
System Preparation
Setup
Desired Activity
15.0
mCi
Available
Saline
FDG
1000
1002
1004
1006
1008
1010
1012
1014
1016
1018
1020
1021
1022
1022a
1023

FIG. 7

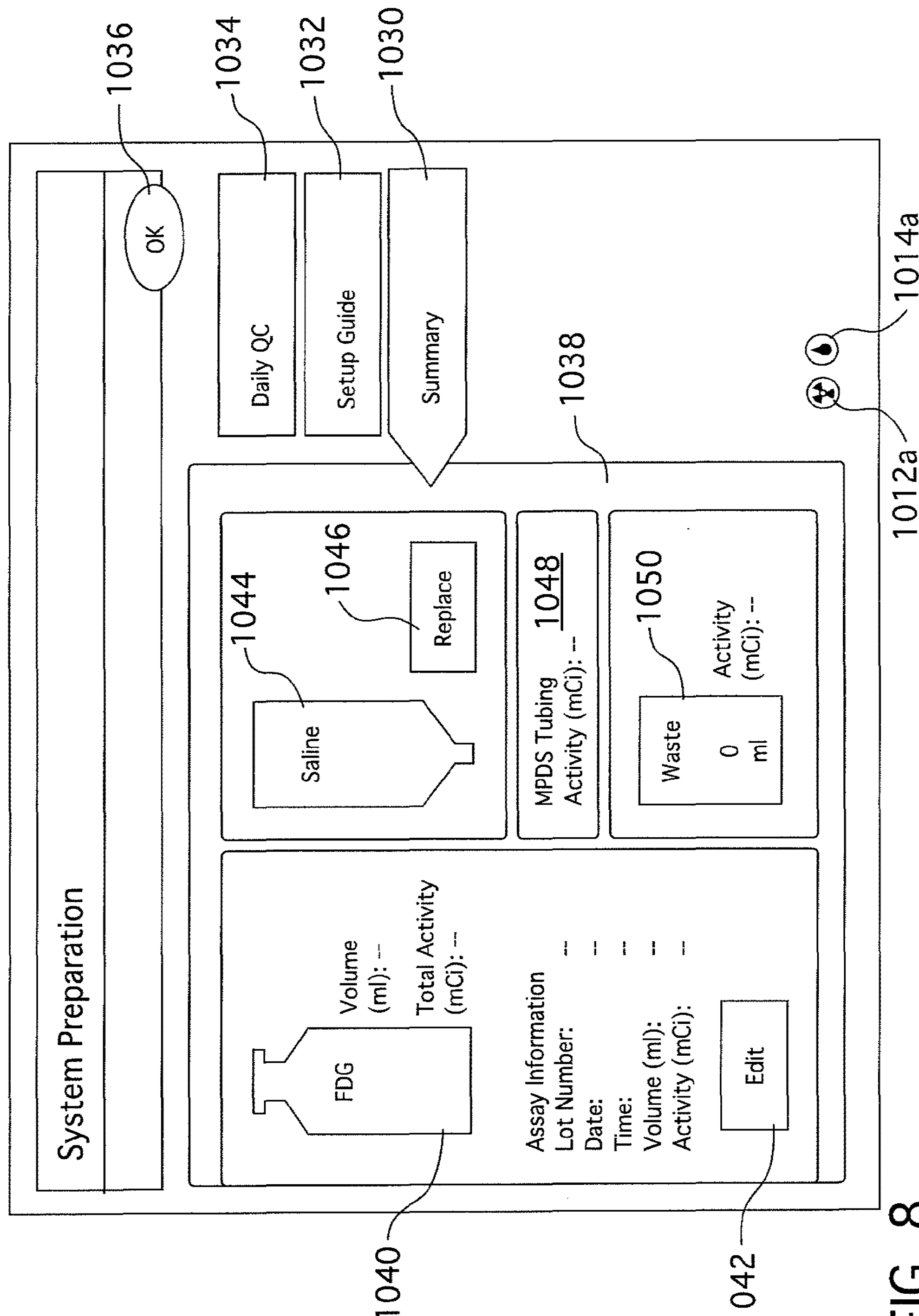

System Preparation
OK
Daily QC
Setup Guide
Summary
FDG
Volume (ml): --
Total Activity (mCi): --
Assay Information
Lot Number: --
Date: --
Time: --
Volume (ml): --
Activity (mCi): --
Edit
Saline
Replace
MPDS Tubing Activity (mCi): --
1048
Waste
0 ml
Activity (mCi): --
1030
1032
1034
1036
1038
1040
1042
1044
1046
1050
1012a
1014a

FIG. 8

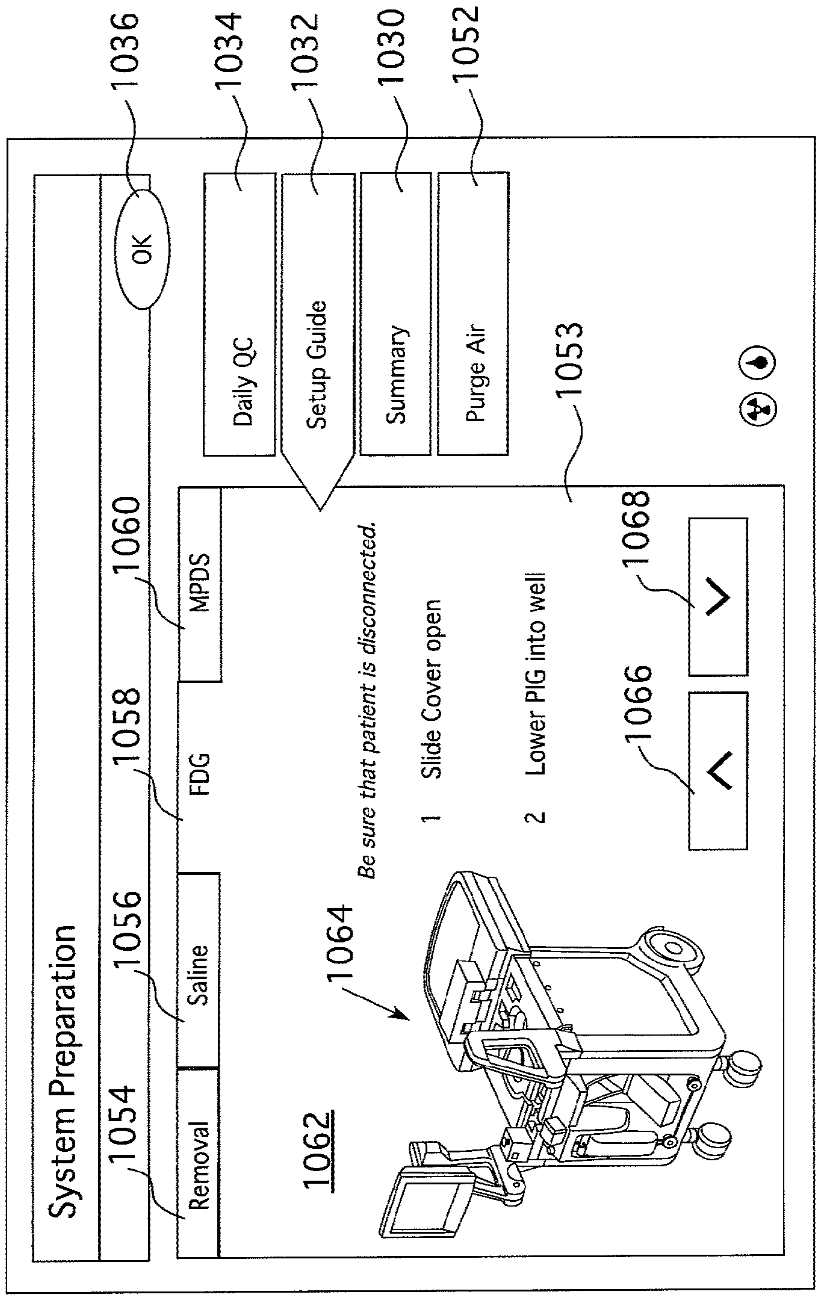

System Preparation
Removal
Saline
FDG
MPDS
OK
Daily QC
Setup Guide
Summary
Purge Air
Be sure that patient is disconnected.
1 Slide Cover open
2 Lower PIG into well
1036
1034
1032
1030
1052
1053
1054
1056
1058
1060
1062
1064
1066
1068

FIG. 9

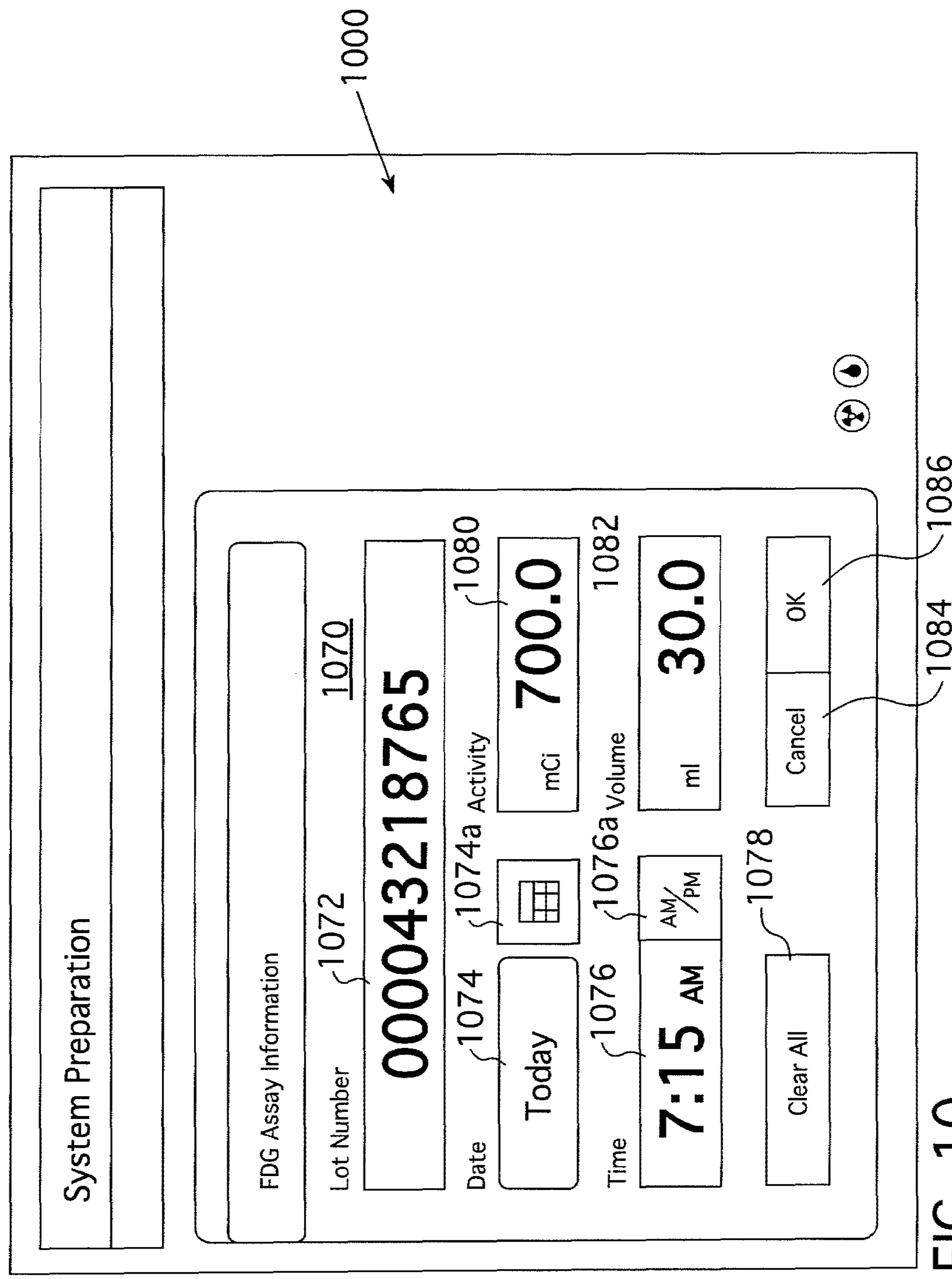

1000
System Preparation
FDG Assay Information
1070
Lot Number
1072
000043218765
Date
1074
Today
1074a
Activity
1080
mCi
700.0
Time
1076
7:15 AM
1076a
AM/PM
Volume
1082
ml
30.0
1078
Clear All
Cancel
1084
OK
1086

FIG. 10

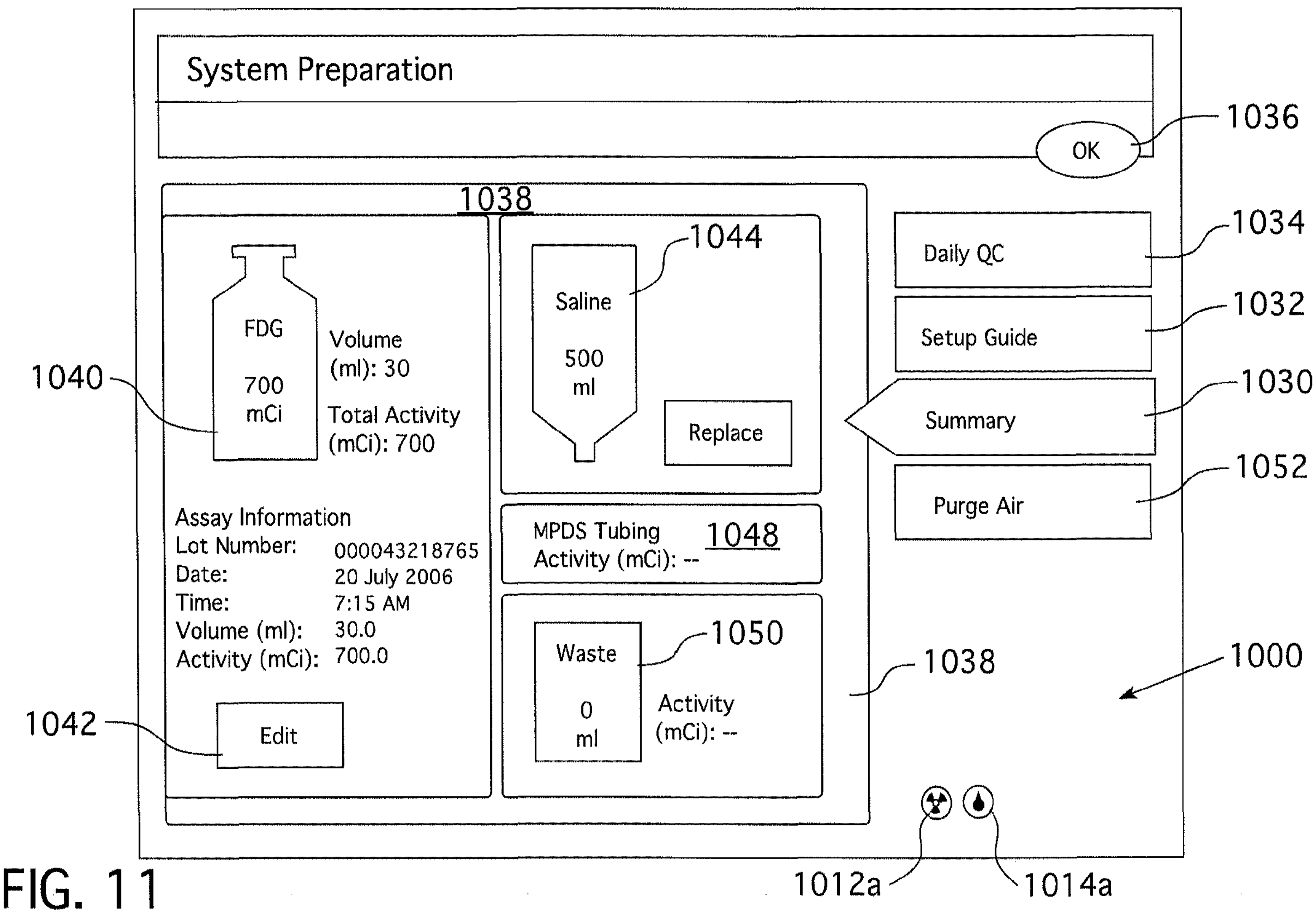

System Preparation
OK
1036
1038
1044
Daily QC
1034
Setup Guide
1032
Summary
1030
Purge Air
1052
1040
FDG
700
mCi
Volume
(ml): 30
Total Activity
(mCi): 700
Saline
500
ml
Replace
Assay Information
Lot Number: 000043218765
Date: 20 July 2006
Time: 7:15 AM
Volume (ml): 30.0
Activity (mCi): 700.0
MPDS Tubing
Activity (mCi): --
1048
Waste
0
ml
1050
Activity
(mCi): --
1038
1000
1042
Edit
1012a
1014a

FIG. 11

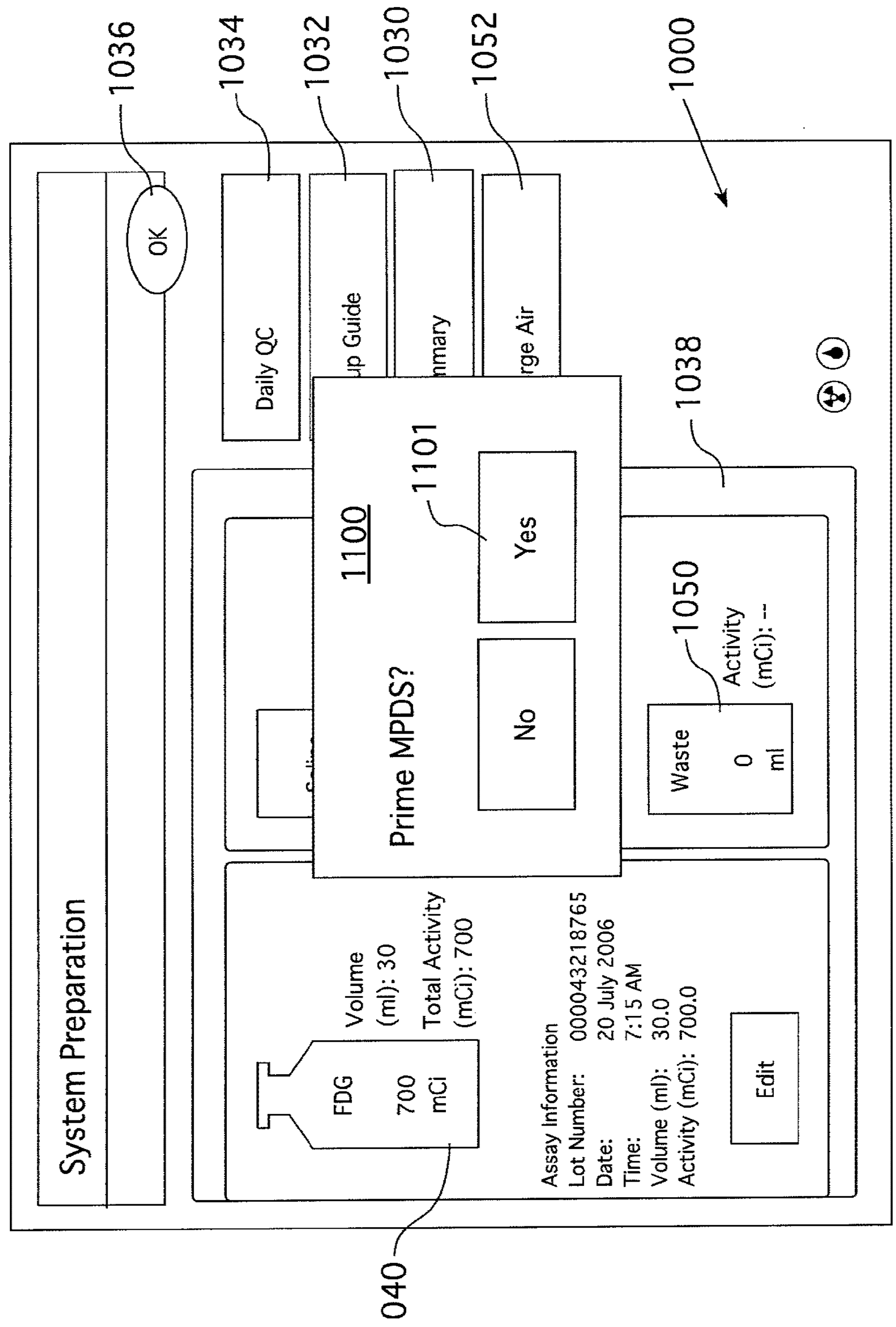

1036
1034
1032
1030
1052
1000
System Preparation
OK
Daily QC
up Guide
mmary
rge Air
1038
1100
Prime MPDS?
1101
Yes
No
1050
Activity
(mCi): --
Waste
0
ml
FDG
700
mCi
Volume
(ml): 30
Total Activity
(mCi): 700
Assay Information
Lot Number: 000043218765
Date: 20 July 2006
Time: 7:15 AM
Volume (ml): 30.0
Activity (mCi): 700.0
Edit
1040

FIG. 12A

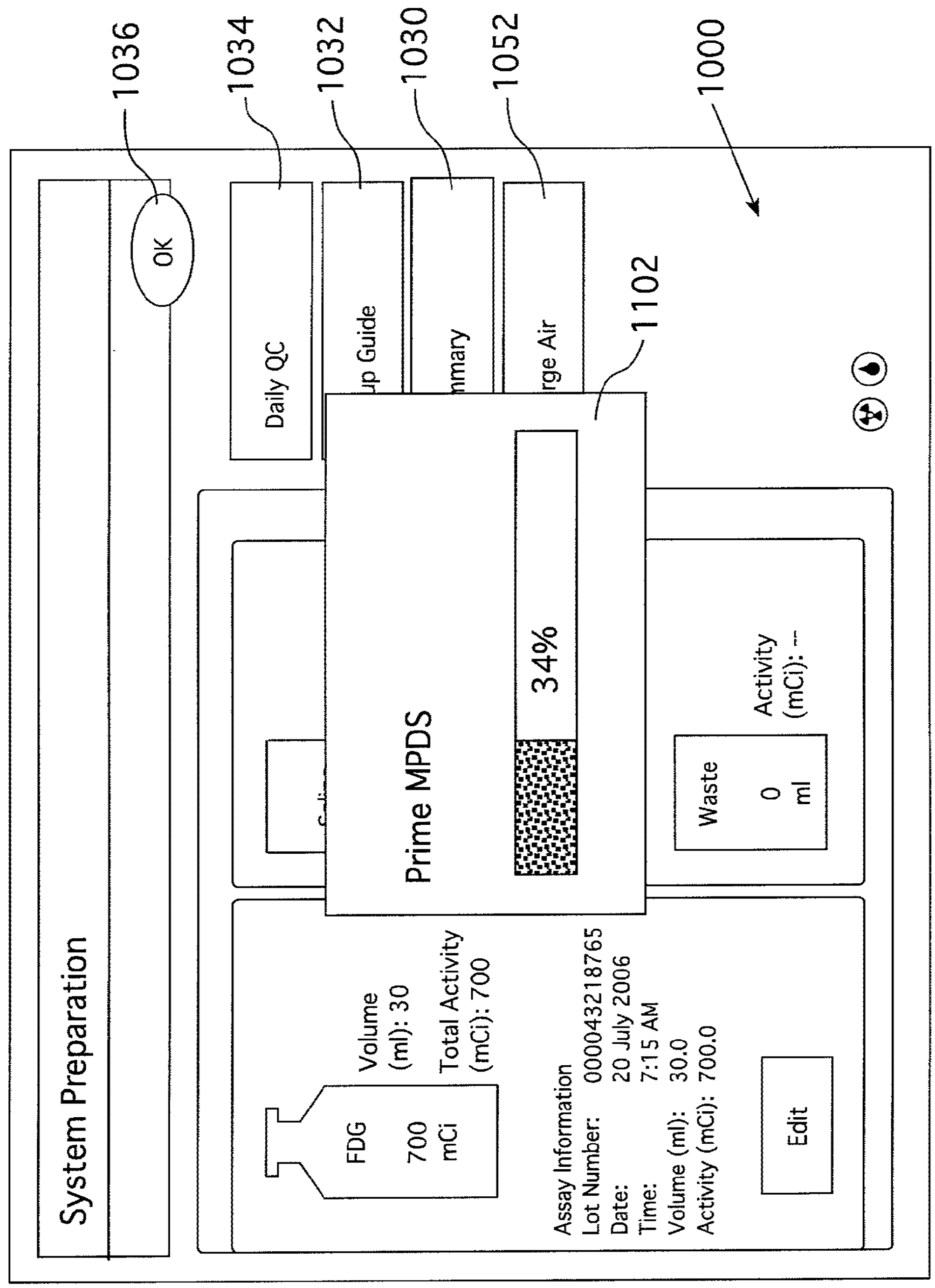

1036
1034
1032
1030
1052
1000
1102
System Preparation
OK
Daily QC
up Guide
mmary
rge Air
Prime MPDS
34%
Waste
0
ml
Activity
(mCi): --
FDG
700
mCi
Volume
(ml): 30
Total Activity
(mCi): 700
Assay Information
Lot Number: 000004321876
Date: 20 July 2006
Time: 7:15 AM
Volume (ml): 30.0
Activity (mCi): 700.0
Edit

FIG. 12B

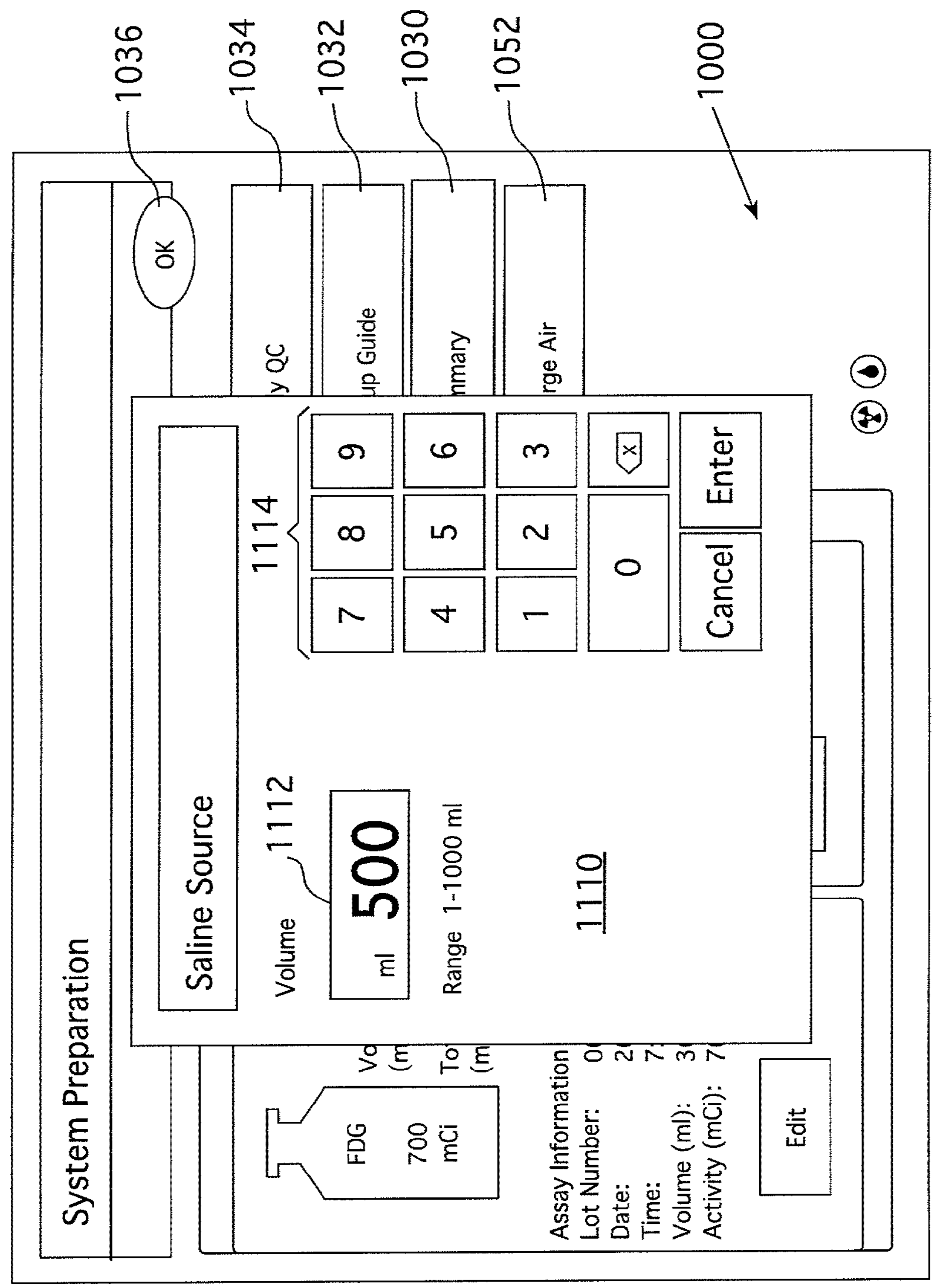

1036
1034
1032
1030
1052
1000
OK
y QC
up Guide
mmary
rge Air
System Preparation
Saline Source
Volume
500
ml
1112
Range 1-1000 ml
1110
1114
7
8
9
4
5
6
1
2
3
0
Cancel
Enter
FDG
700
mCi
Assay Information
Lot Number:
Date:
Time:
Volume (ml):
Activity (mCi):
Edit

FIG. 13

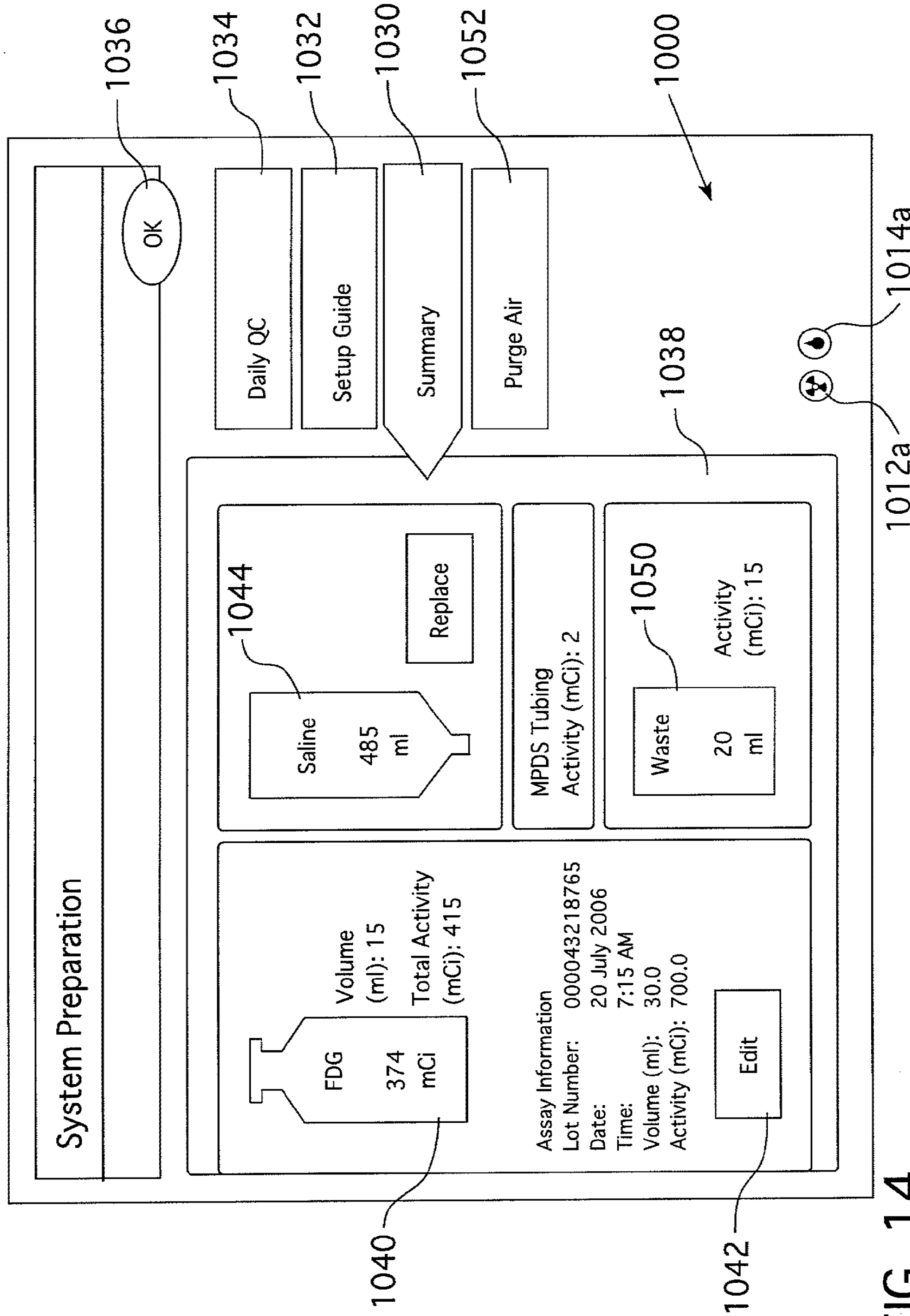

System Preparation
OK
Daily QC
Setup Guide
Summary
Purge Air
FDG
374
mCi
Volume
(ml): 15
Total Activity
(mCi): 415
Assay Information
Lot Number: 000043218765
Date: 20 July 2006
Time: 7:15 AM
Volume (ml): 30.0
Activity (mCi): 700.0
Edit
Saline
485
ml
Replace
MPDS Tubing
Activity (mCi): 2
Waste
20
ml
Activity
(mCi): 15
1000
1012a
1014a
1030
1032
1034
1036
1038
1040
1042
1044
1050
1052

FIG. 14

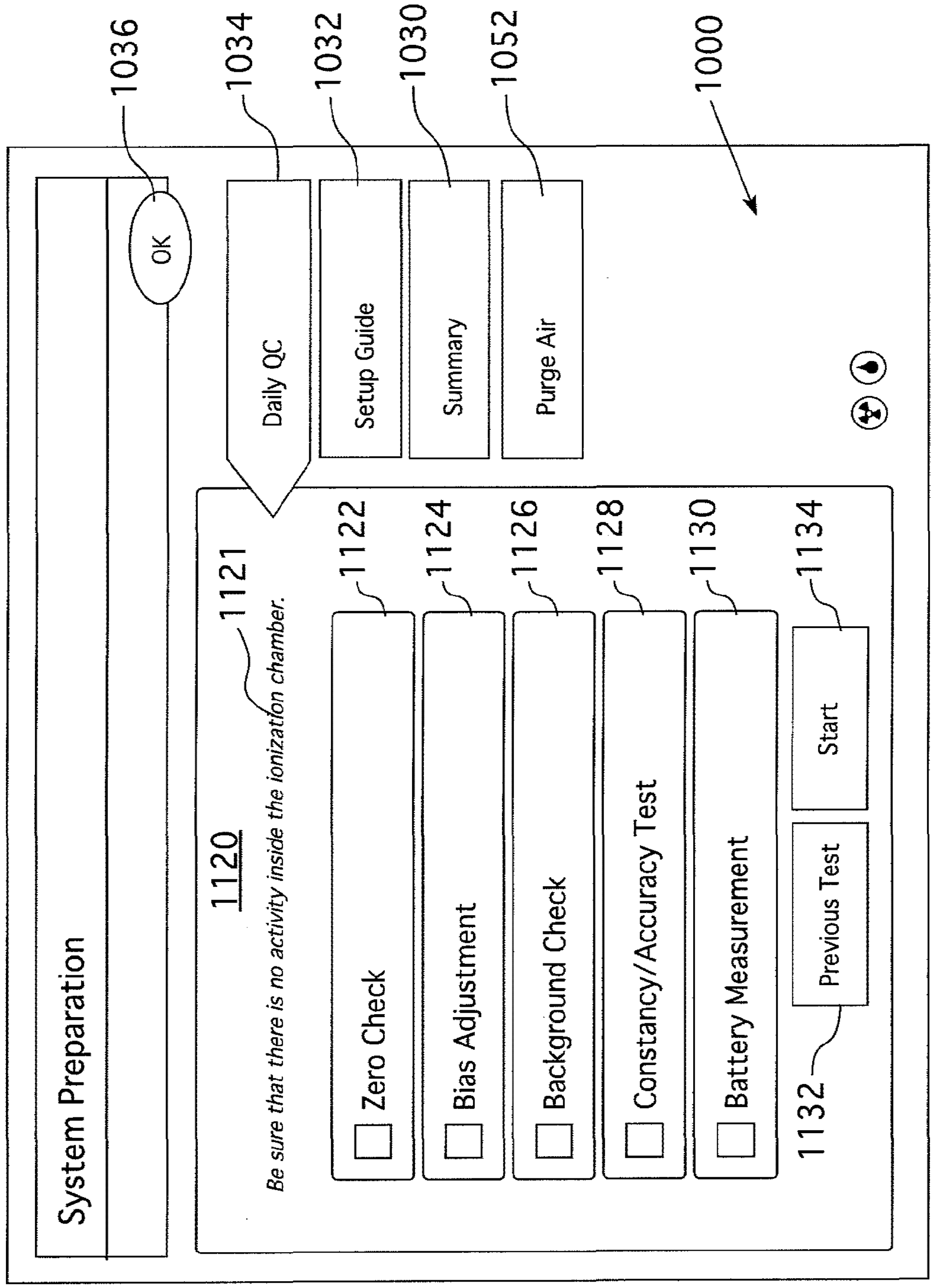

System Preparation
OK
Daily QC
Setup Guide
Summary
Purge Air
1120
Be sure that there is no activity inside the ionization chamber.
Zero Check
Bias Adjustment
Background Check
Constancy/Accuracy Test
Battery Measurement
Previous Test
Start
1036
1034
1032
1030
1052
1000
1121
1122
1124
1126
1128
1130
1134
1132

FIG. 15

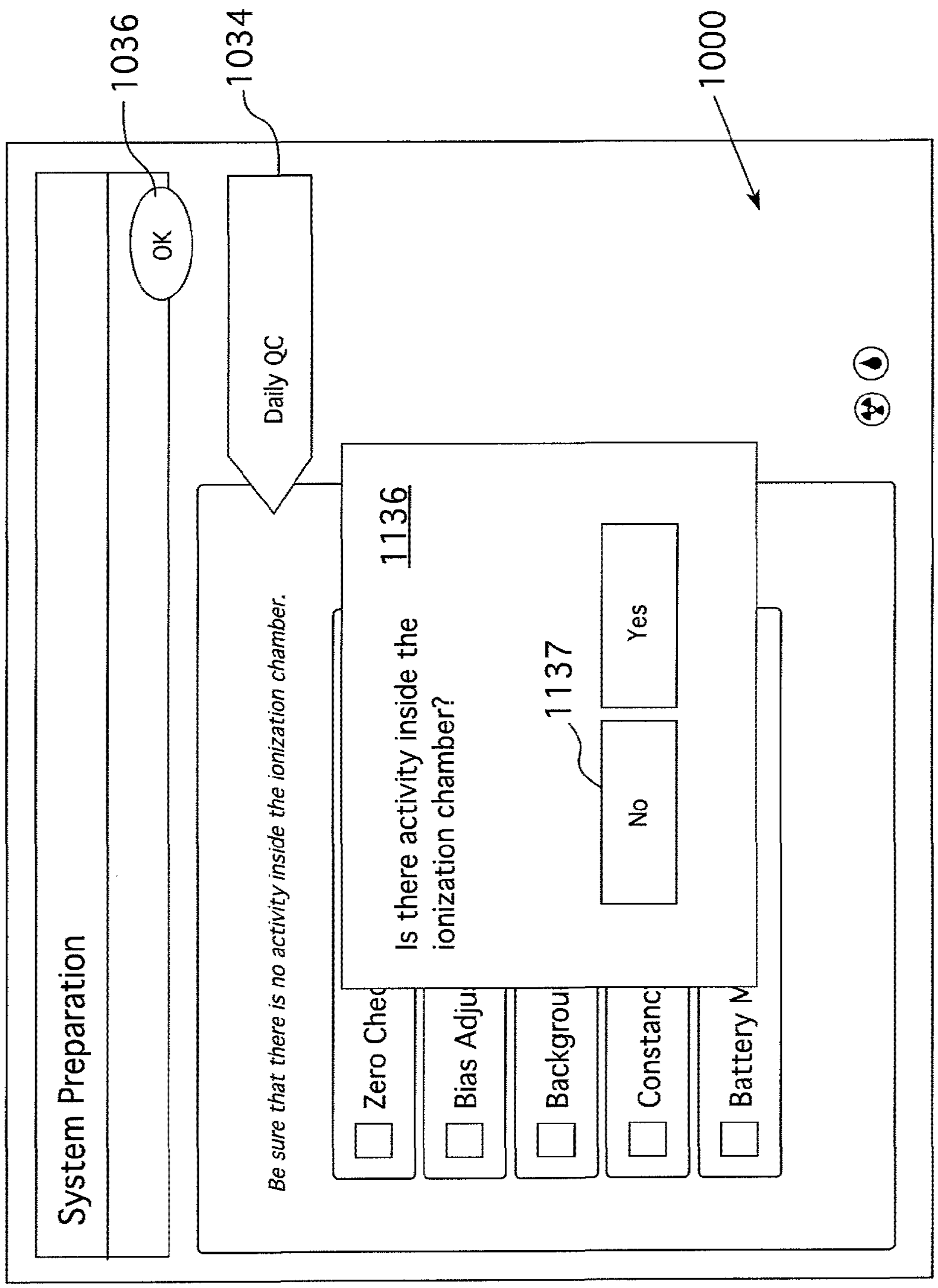

1036
1034
1000
System Preparation
OK
Daily QC
Be sure that there is no activity inside the ionization chamber.
Zero Chec
Bias Adju
Backgrou
Constanc
Battery M
1136
Is there activity inside the ionization chamber?
1137
No
Yes

FIG. 16A

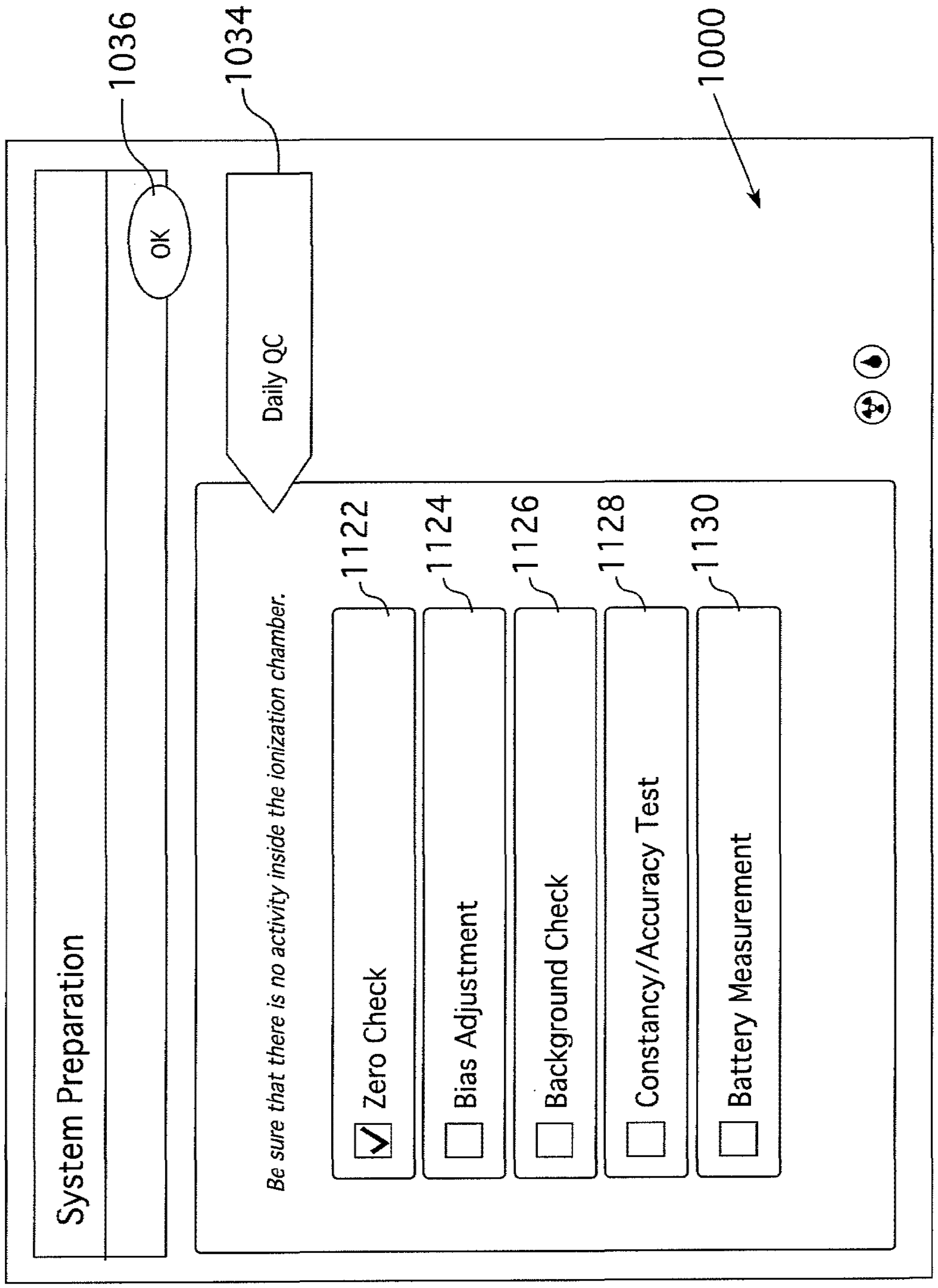

1036
1034
1000
OK
Daily QC
System Preparation
Be sure that there is no activity inside the ionization chamber.
1122
1124
1126
1128
1130
Zero Check
Bias Adjustment
Background Check
Constancy/Accuracy Test
Battery Measurement

FIG. 16B

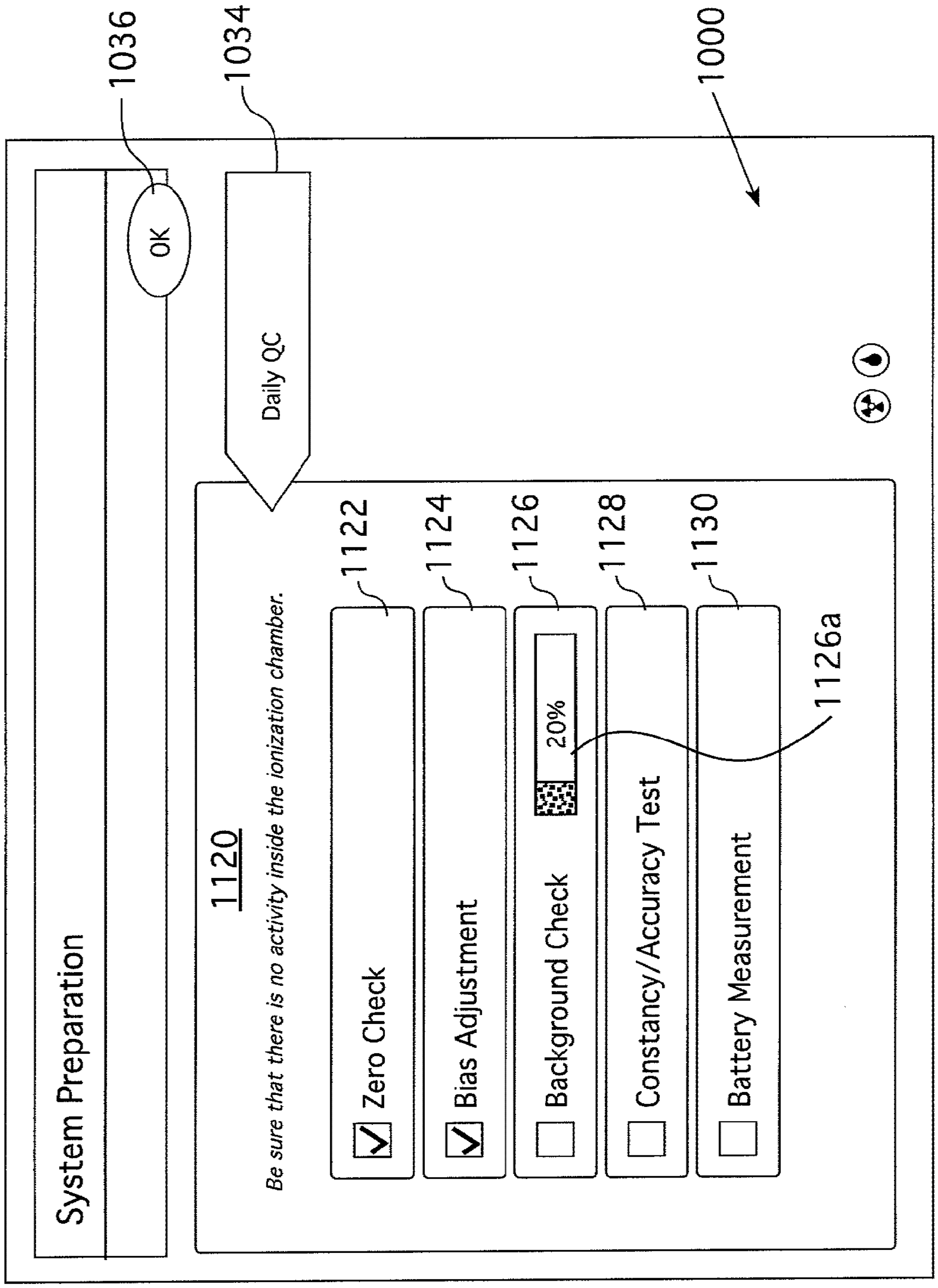

1036
1034
1000
OK
Daily QC
System Preparation
1120
Be sure that there is no activity inside the ionization chamber.
Zero Check
Bias Adjustment
Background Check
20%
Constancy/Accuracy Test
Battery Measurement
1122
1124
1126
1128
1130
1126a

FIG. 17

35/87

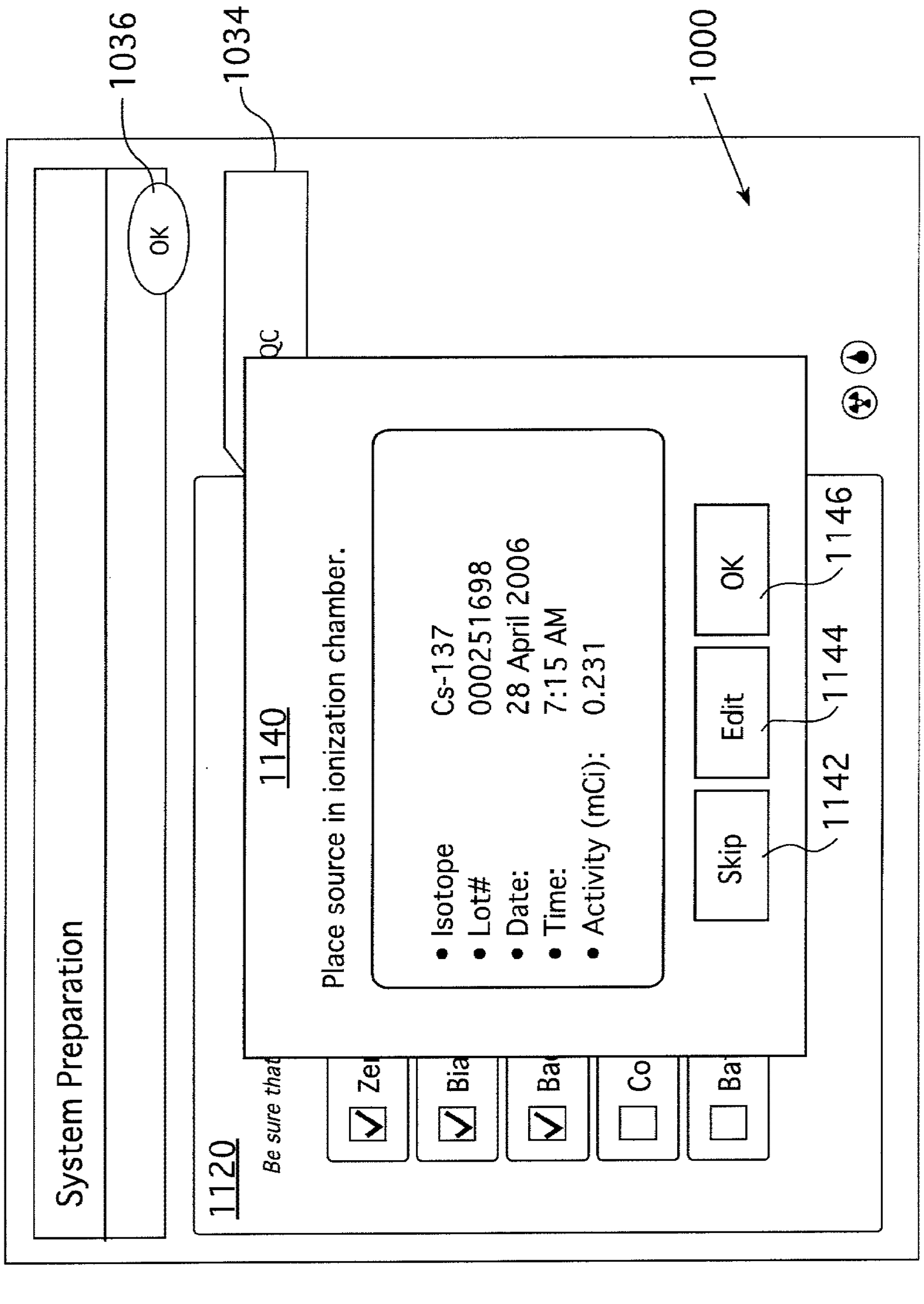

1036
1034
1000
OK
System Preparation
1120
Be sure that
1140
Place source in ionization chamber.
• Isotope Cs-137
• Lot# 000251698
• Date: 28 April 2006
• Time: 7:15 AM
• Activity (mCi): 0.231
Skip
Edit
OK
1142
1144
1146

FIG. 18

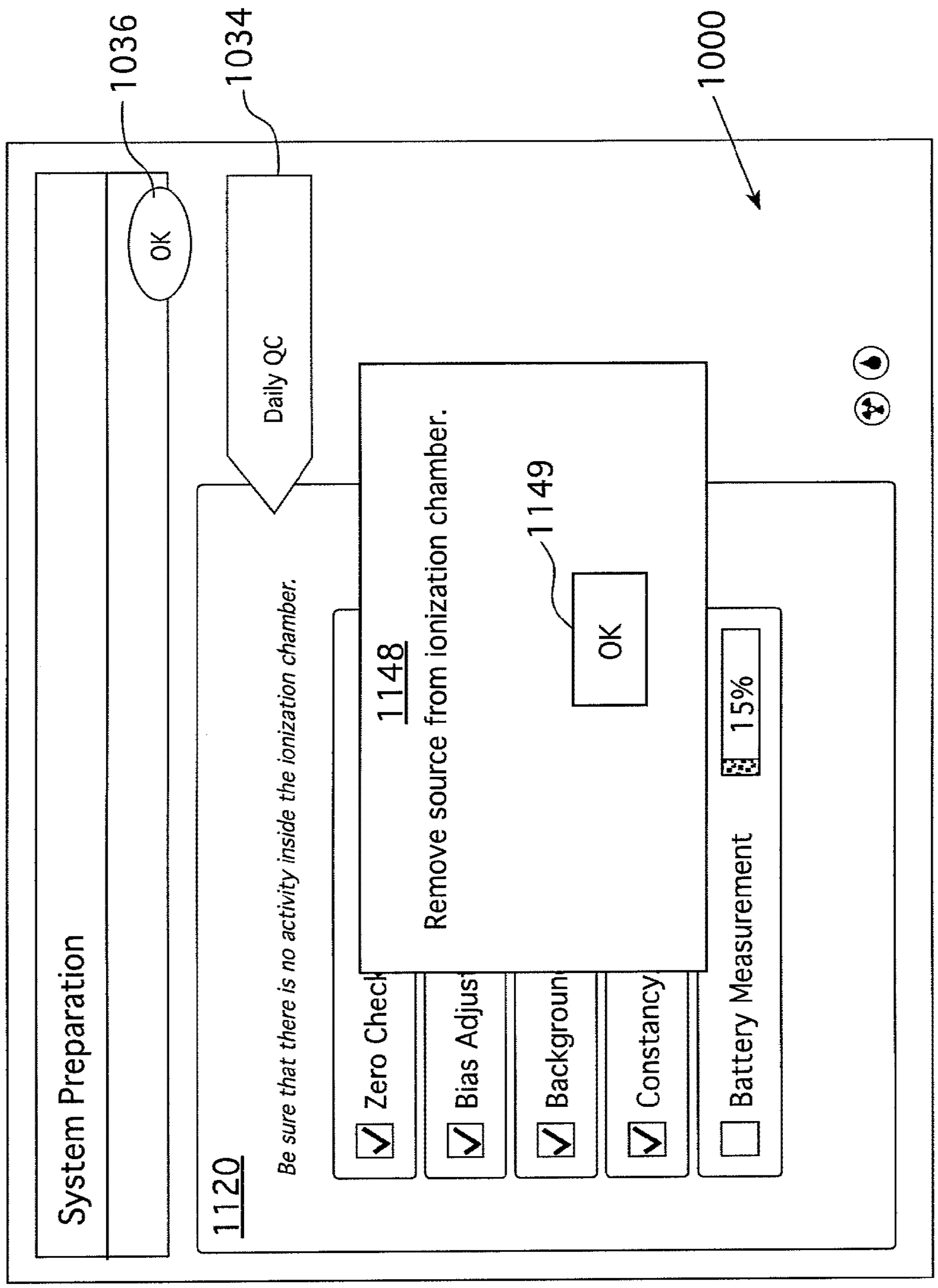

1036
1034
1000
System Preparation
OK
Daily QC
1120
Be sure that there is no activity inside the ionization chamber.
Zero Check
Bias Adjust
Backgroun
Constancy
Battery Measurement
15%
1148
Remove source from ionization chamber.
1149
OK

FIG. 19

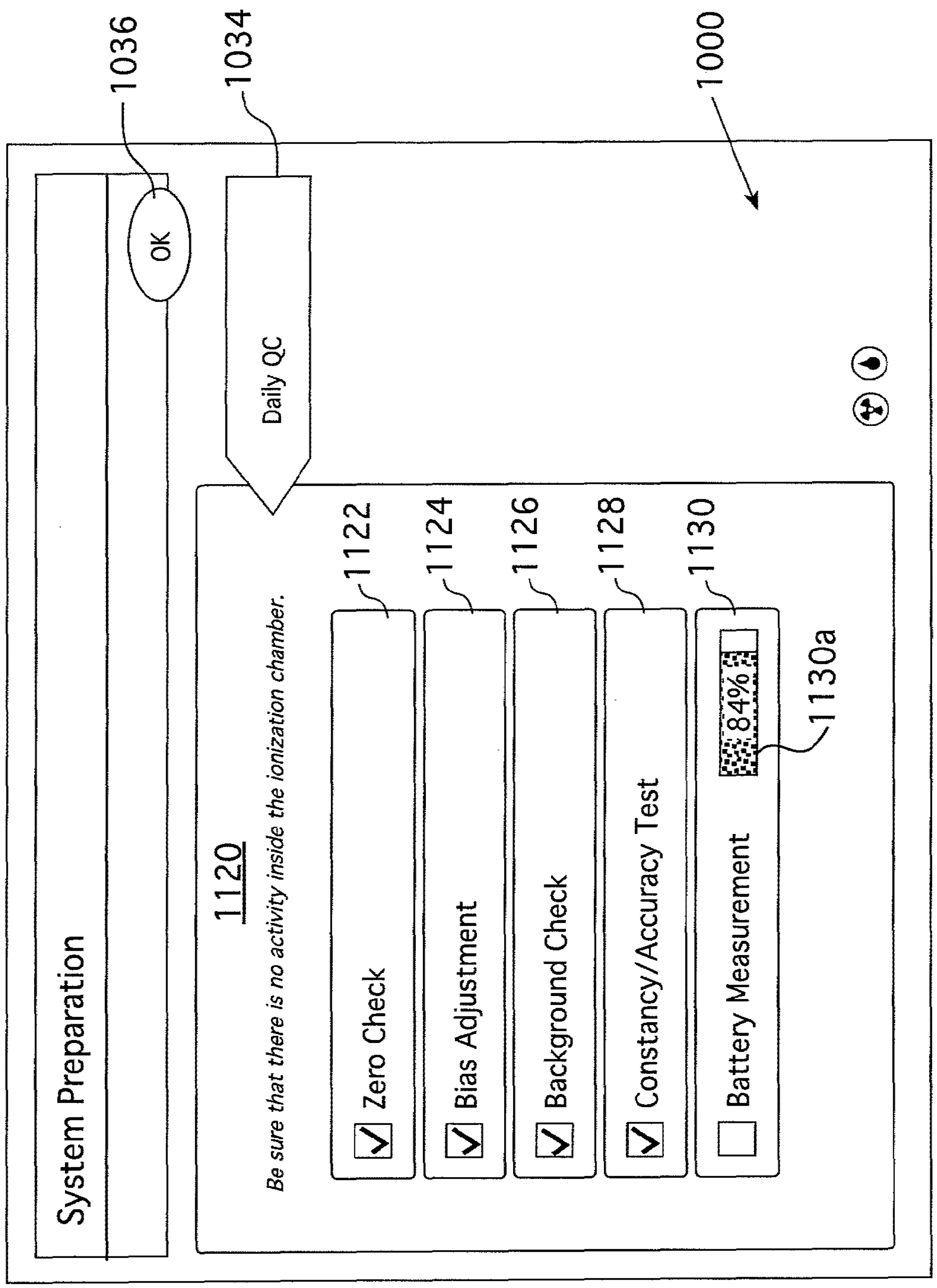

1036
1034
1000
System Preparation
OK
Daily QC
1120
Be sure that there is no activity inside the ionization chamber.
1122
1124
1126
1128
1130
Zero Check
Bias Adjustment
Background Check
Constancy/Accuracy Test
Battery Measurement
84%
1130a

FIG. 20

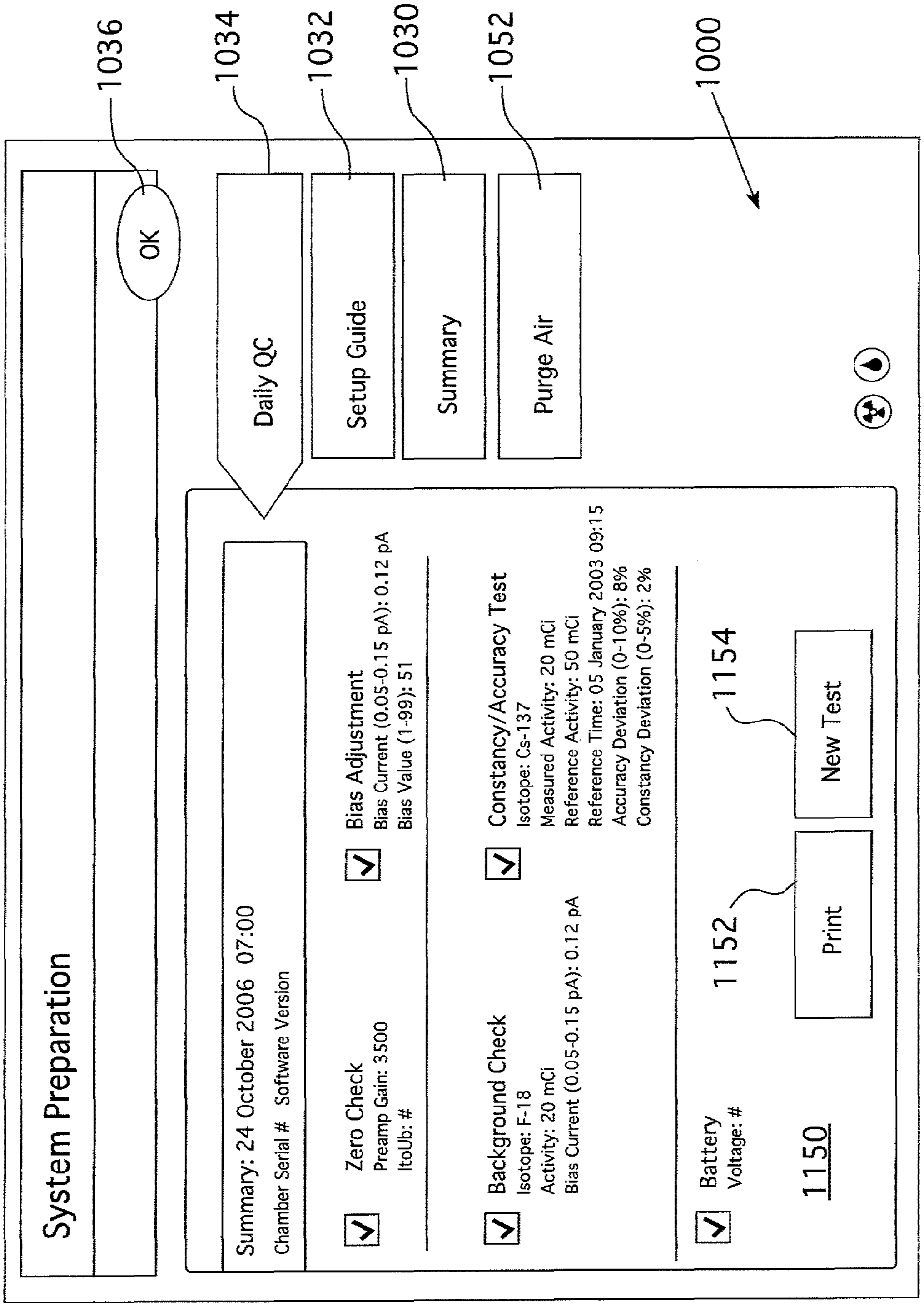

System Preparation
OK
1036
1034
1032
1030
1052
1000
Daily QC
Setup Guide
Summary
Purge Air
Summary: 24 October 2006 07:00
Chamber Serial # Software Version
Zero Check
Preamp Gain: 3500
ItoUb: #
Bias Adjustment
Bias Current (0.05-0.15 pA): 0.12 pA
Bias Value (1-99): 51
Background Check
Isotope: F-18
Activity: 20 mCi
Bias Current (0.05-0.15 pA): 0.12 pA
Constancy/Accuracy Test
Isotope: Cs-137
Measured Activity: 20 mCi
Reference Activity: 50 mCi
Reference Time: 05 January 2003 09:15
Accuracy Deviation (0-10%): 8%
Constancy Deviation (0-5%): 2%
Battery
Voltage: #
1150
1152
Print
1154
New Test

FIG. 21

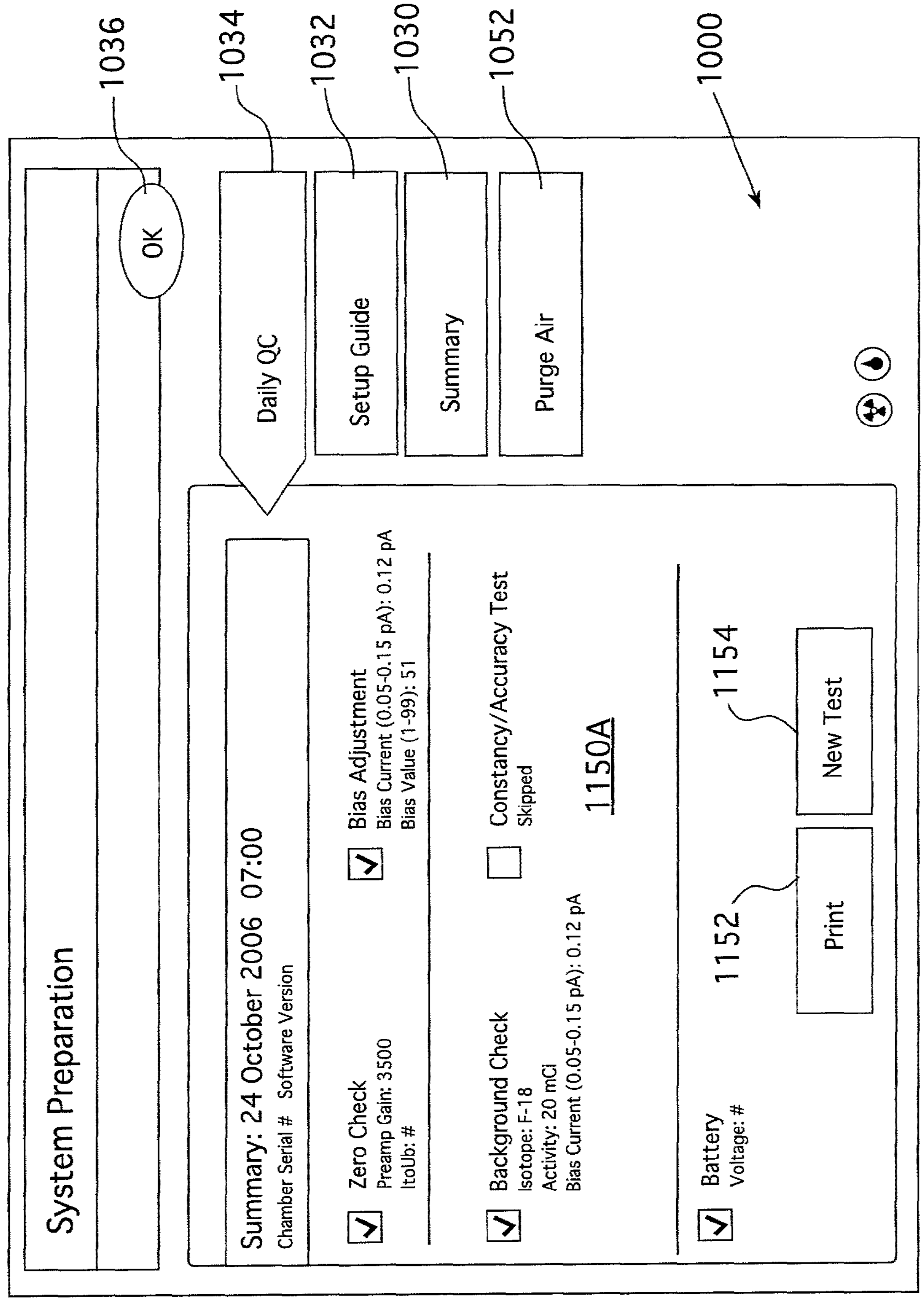

1036
1034
1032
1030
1052
1000
System Preparation
OK
Daily QC
Setup Guide
Summary
Purge Air
Summary: 24 October 2006 07:00
Chamber Serial # Software Version
Zero Check
Preamp Gain: 3500
ItoUb: #
Bias Adjustment
Bias Current (0.05-0.15 pA): 0.12 pA
Bias Value (1-99): 51
Background Check
Isotope: F-18
Activity: 20 mCi
Bias Current (0.05-0.15 pA): 0.12 pA
Constancy/Accuracy Test
Skipped
1150A
Battery
Voltage: #
1152
1154
Print
New Test

FIG. 22

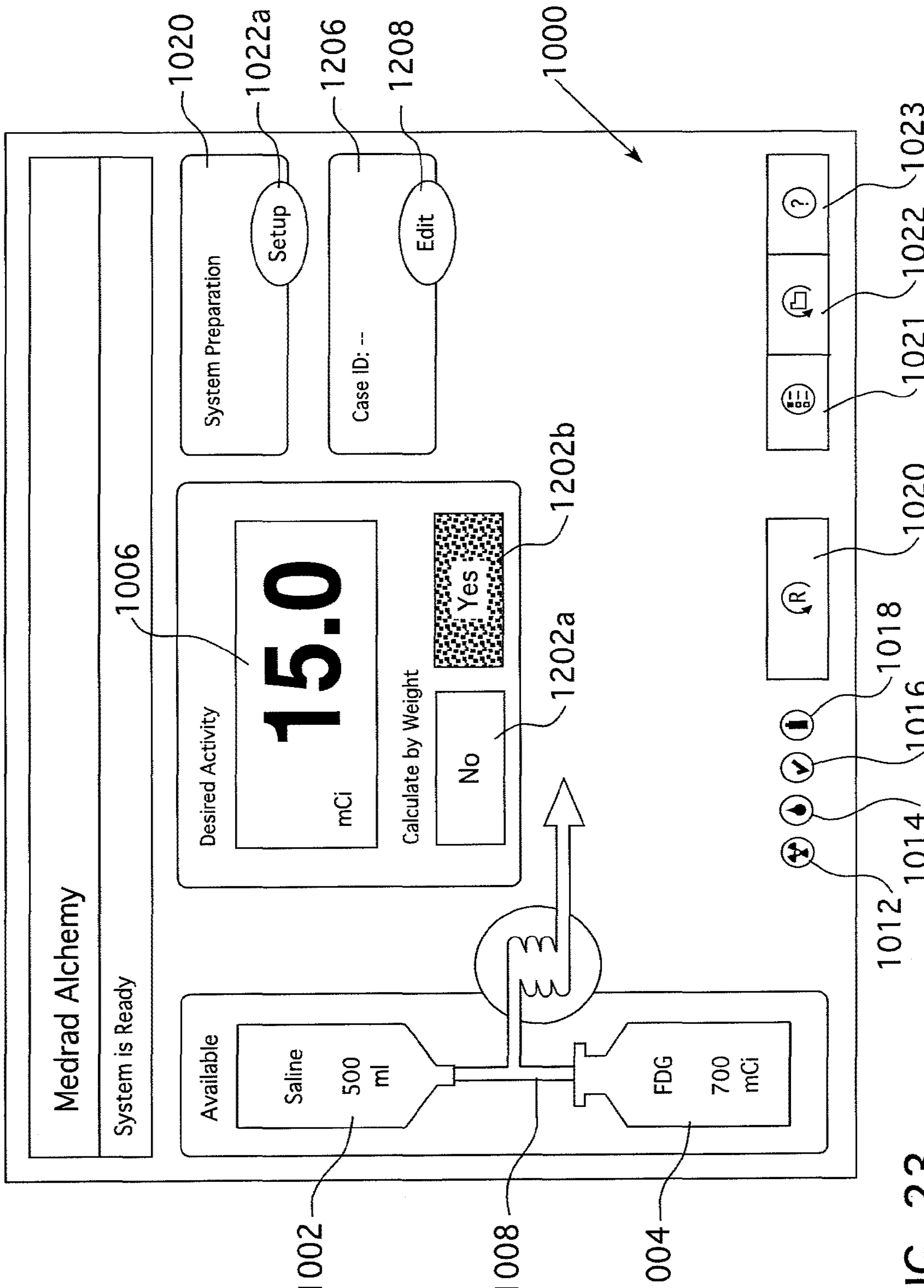

Medrad Alchemy
System is Ready
Available
Saline
500
ml
FDG
700
mCi
Desired Activity
15.0
mCi
Calculate by Weight
No
Yes
System Preparation
Setup
Case ID: --
Edit
1000
1002
1004
1006
1008
1012
1014
1016
1018
1020
1021
1022
1022a
1023
1202a
1202b
1206
1208

FIG. 23

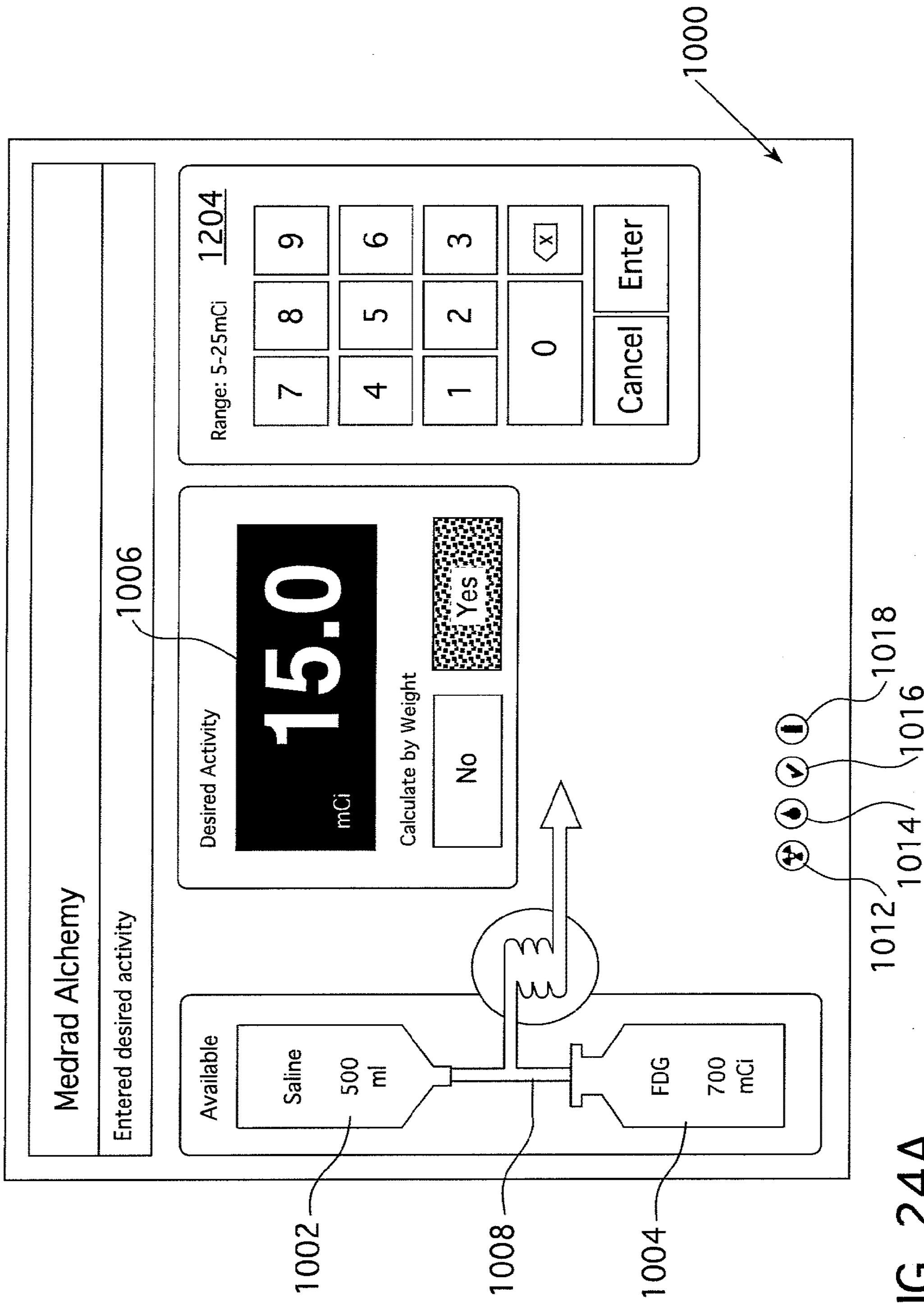
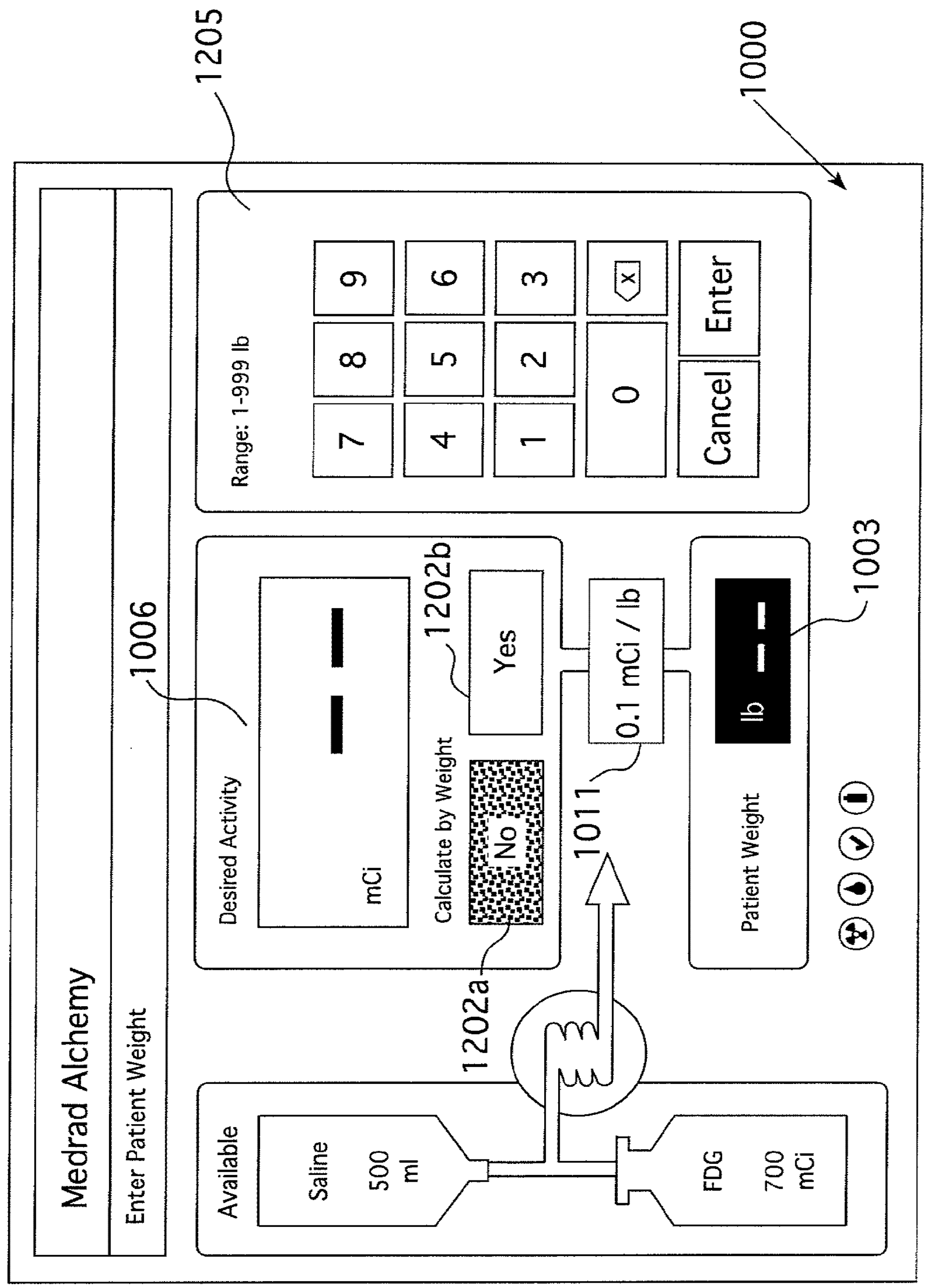

1000
Medrad Alchemy
Entered desired activity
Available
Saline
500
ml
FDG
700
mCi
Desired Activity
15.0
mCi
Calculate by Weight
No
Yes
Range: 5-25mCi
1204
7
8
9
4
5
6
1
2
3
0
Cancel
Enter
1006
1012
1014
1016
1018
1002
1008
1004

FIG. 24A



Medrad Alchemy
Enter Patient Weight
Available
Saline
500
ml
FDG
700
mCi
Desired Activity
mCi
Calculate by Weight
No
Yes
0.1 mCi / lb
Patient Weight
lb
Range: 1-999 lb
7
8
9
4
5
6
1
2
3
0
Cancel
Enter
1205
1000
1006
1202b
1202a
1011
1003

FIG. 24B

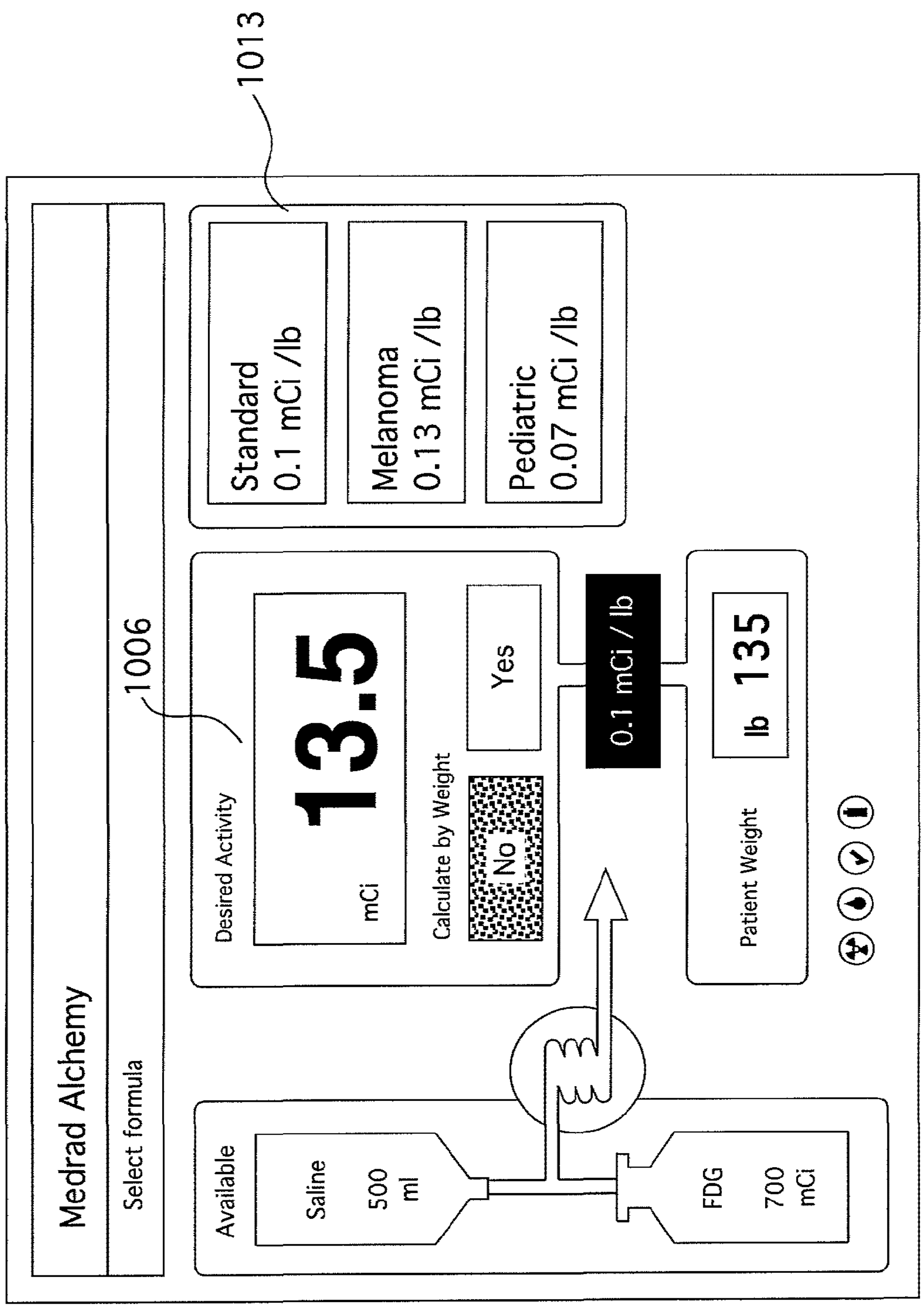
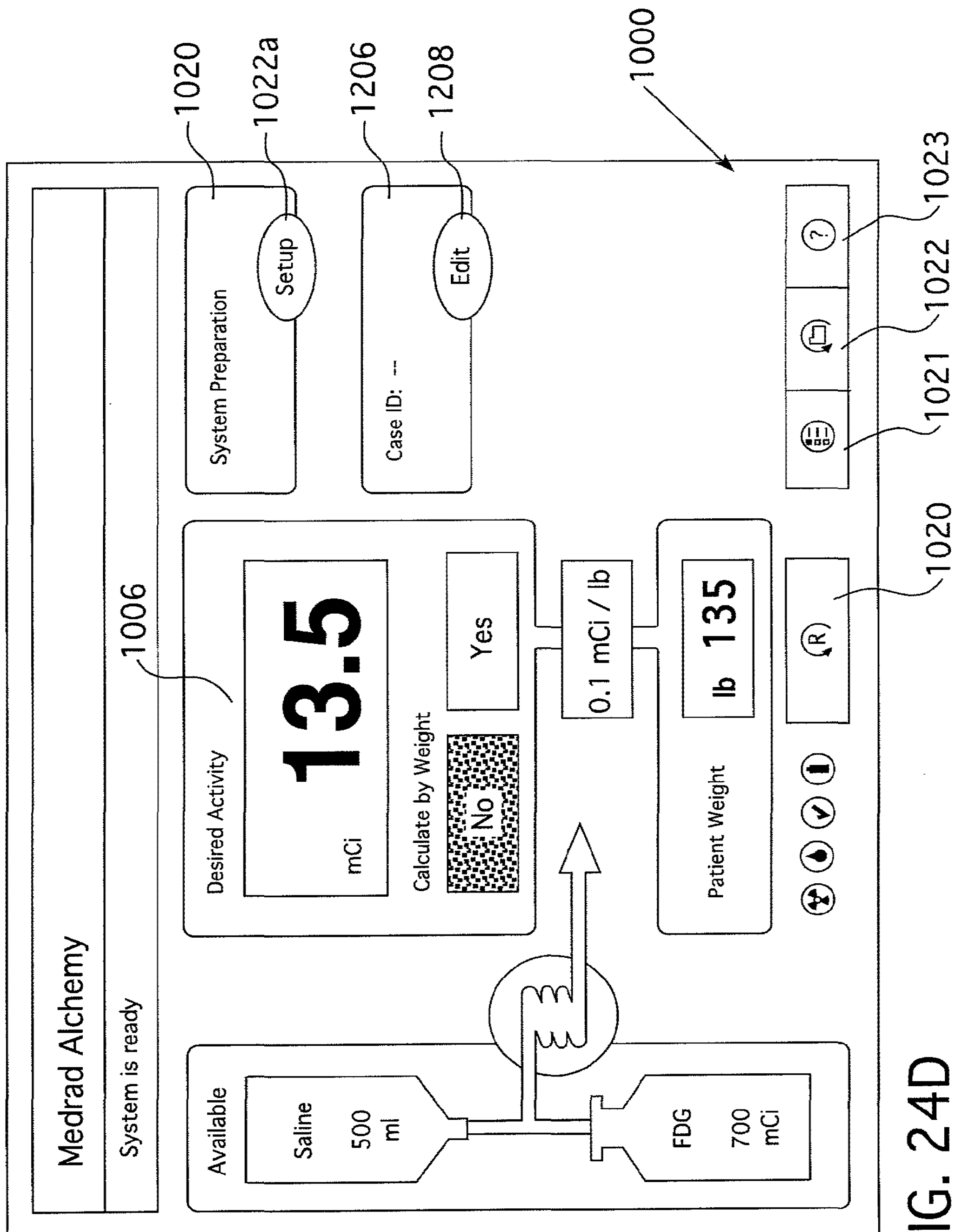

1013
1006
Medrad Alchemy
Select formula
Available
Saline
500
ml
FDG
700
mCi
Desired Activity
13.5
mCi
Calculate by Weight
No
Yes
0.1 mCi / lb
Patient Weight
lb 135
Standard
0.1 mCi /lb
Melanoma
0.13 mCi /lb
Pediatric
0.07 mCi /lb

FIG. 24C



Medrad Alchemy
System is ready
System Preparation
Setup
Case ID: --
Edit
Desired Activity
13.5
mCi
Calculate by Weight
No
Yes
0.1 mCi / lb
Patient Weight
lb 135
Available
Saline
500
ml
FDG
700
mCi
1000
1020
1022a
1206
1208
1006
1021
1022
1023

FIG. 24D

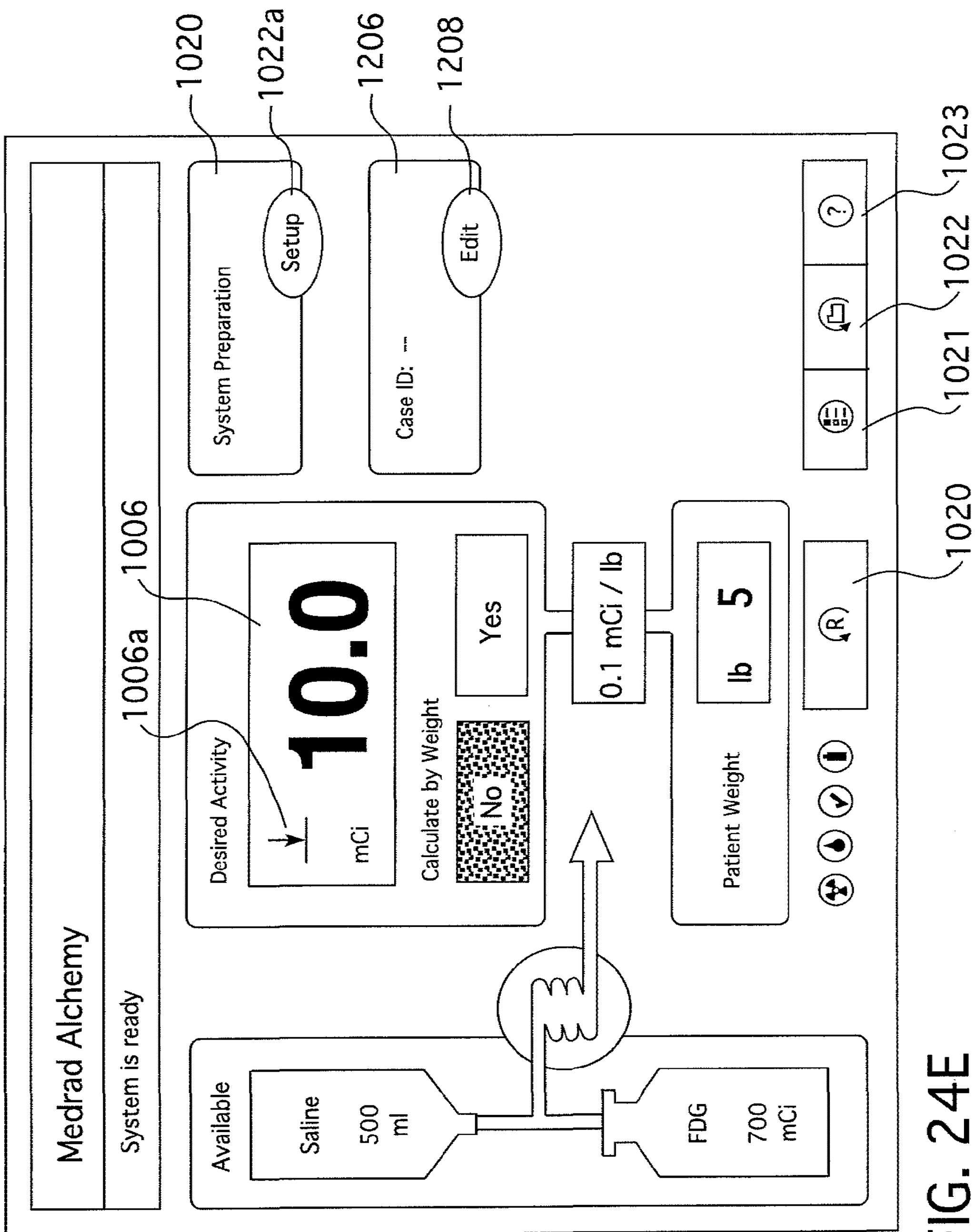

Medrad Alchemy
System is ready
Available
Saline
500
ml
FDG
700
mCi
Desired Activity
10.0
mCi
Calculate by Weight
No
Yes
0.1 mCi / lb
Patient Weight
lb
5
System Preparation
Setup
Case ID: --
Edit
1020
1022a
1206
1208
1006
1006a
1023
1022
1021
1020

FIG. 24E

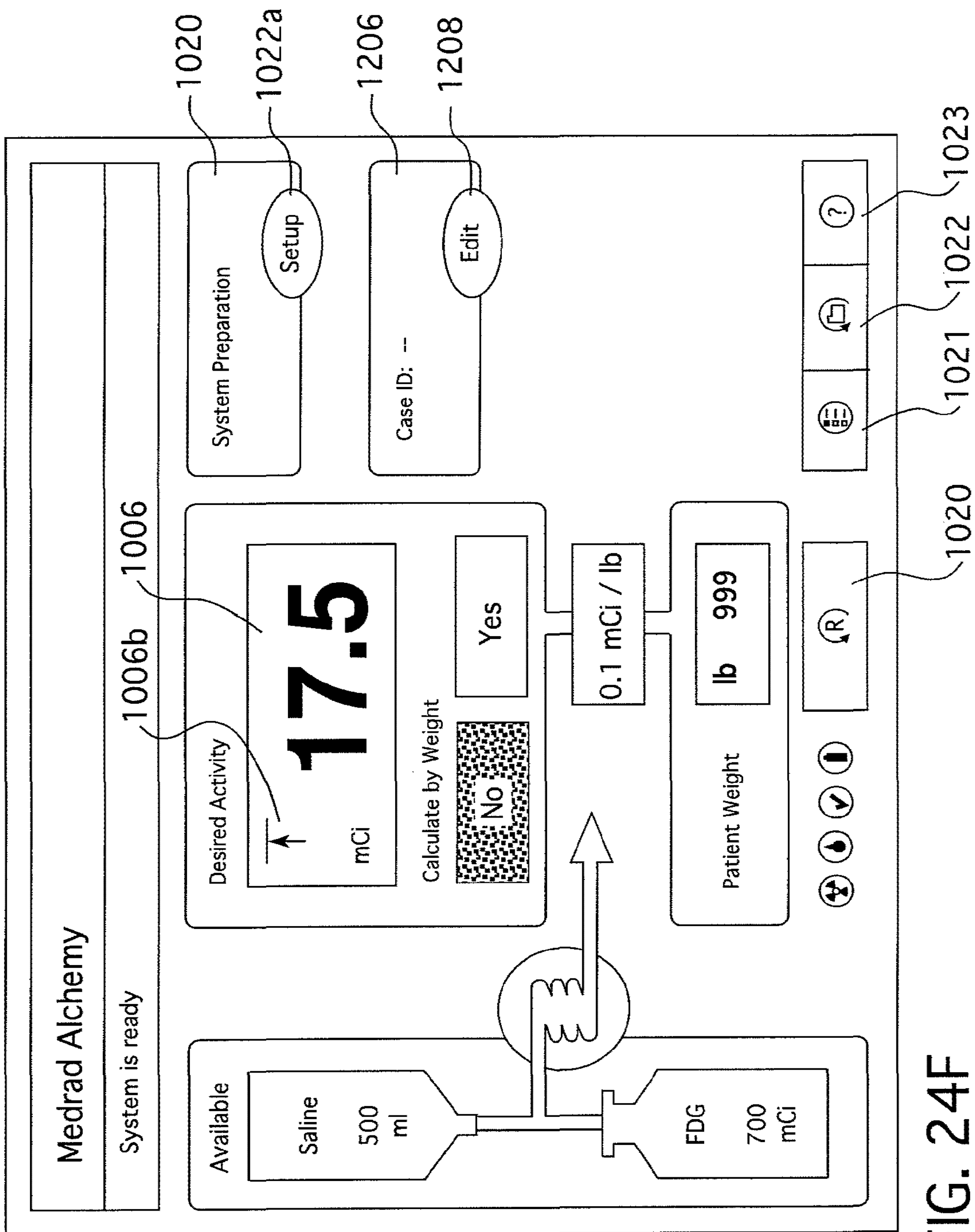
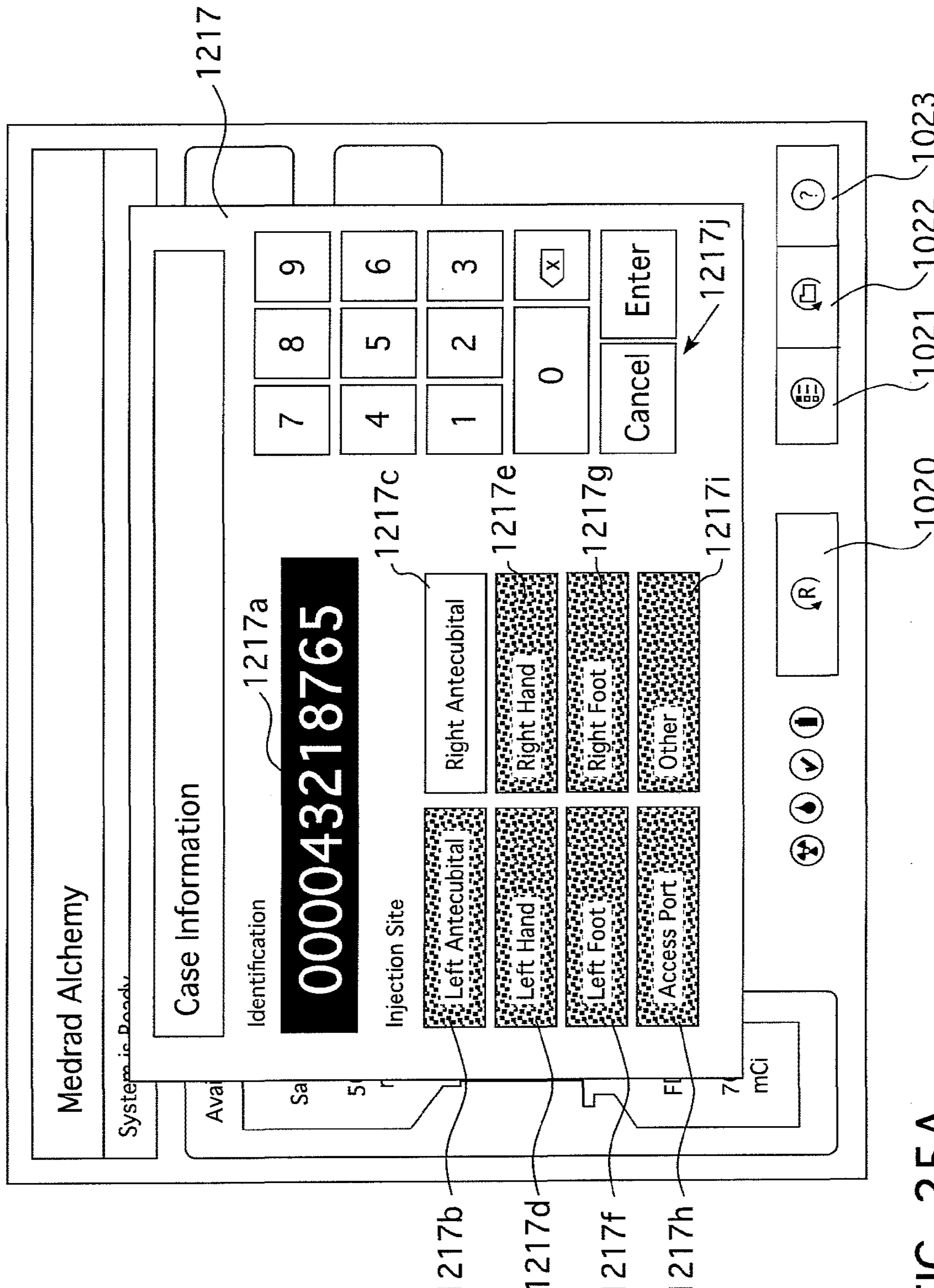

Medrad Alchemy
System is ready
Available
Saline
500 ml
FDG
700 mCi
Desired Activity
17.5
mCi
Calculate by Weight
No
Yes
0.1 mCi / lb
Patient Weight
lb
999
System Preparation
Setup
Case ID: --
Edit
1020
1022a
1206
1208
1006
1006b
1023
1022
1021
1020

FIG. 24F



Medrad Alchemy
Case Information
Identification
000043218765
Injection Site
Left Antecubital
Right Antecubital
Left Hand
Right Hand
Left Foot
Right Foot
Access Port
Other
7
8
9
4
5
6
1
2
3
0
Cancel
Enter
mCi
1217
1217a
1217b
1217c
1217d
1217e
1217f
1217g
1217h
1217i
1217j
1020
1021
1022
1023

FIG. 25A

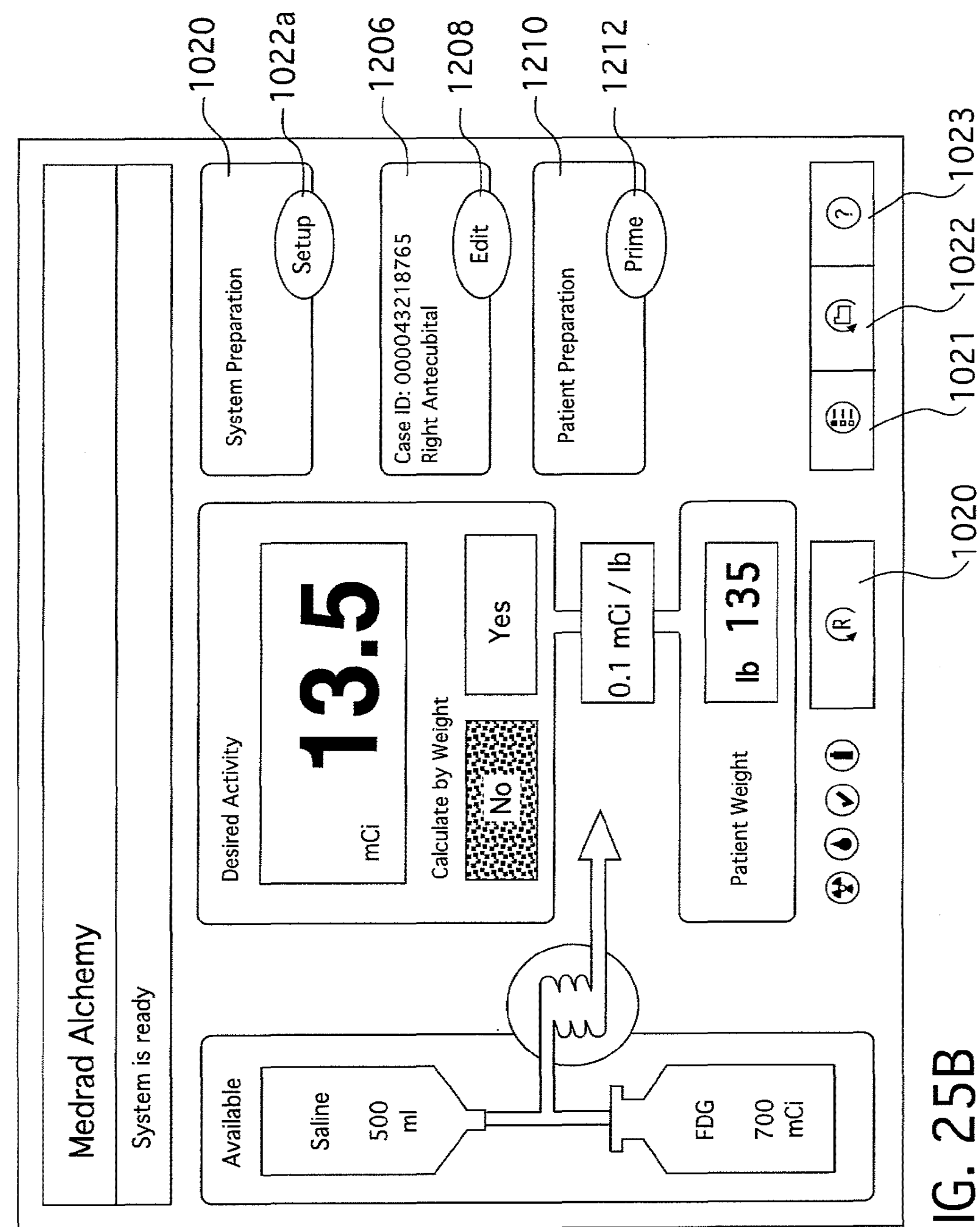
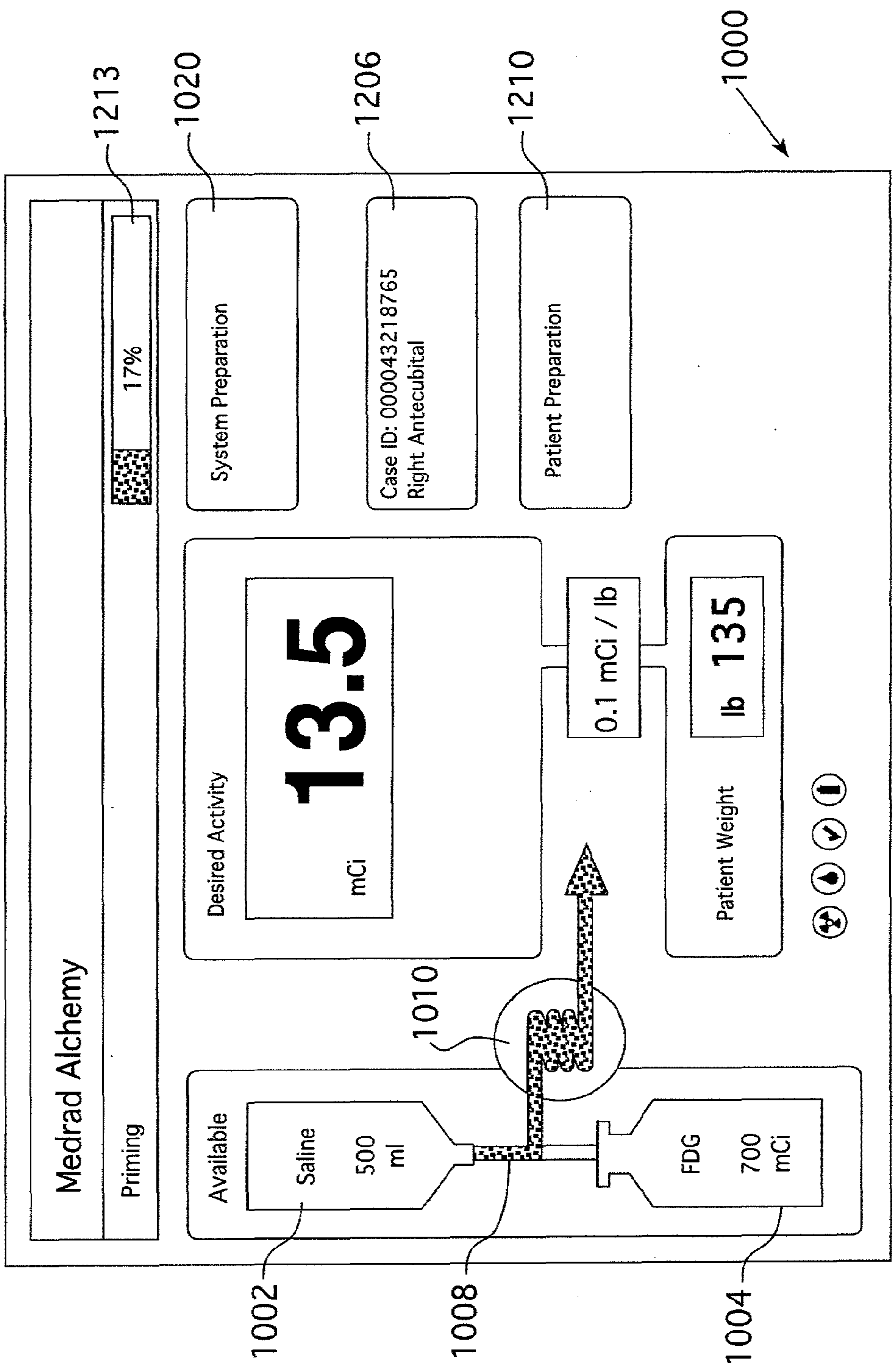

1020
1022a
1206
1208
1210
1212
1023
1022
1021
1020
Medrad Alchemy
System is ready
Available
Saline
500
ml
FDG
700
mCi
Desired Activity
13.5
mCi
Calculate by Weight
No
Yes
0.1 mCi / lb
Patient Weight
lb 135
System Preparation
Setup
Case ID: 000043218765
Right Antecubital
Edit
Patient Preparation
Prime

FIG. 25B



1000
1213
1020
1206
1210
Medrad Alchemy
Priming
17%
System Preparation
Case ID: 000043218765
Right Antecubital
Patient Preparation
Desired Activity
13.5
mCi
0.1 mCi / lb
Patient Weight
lb 135
1010
Available
Saline
500
ml
FDG
700
mCi
1002
1008
1004

FIG. 26A

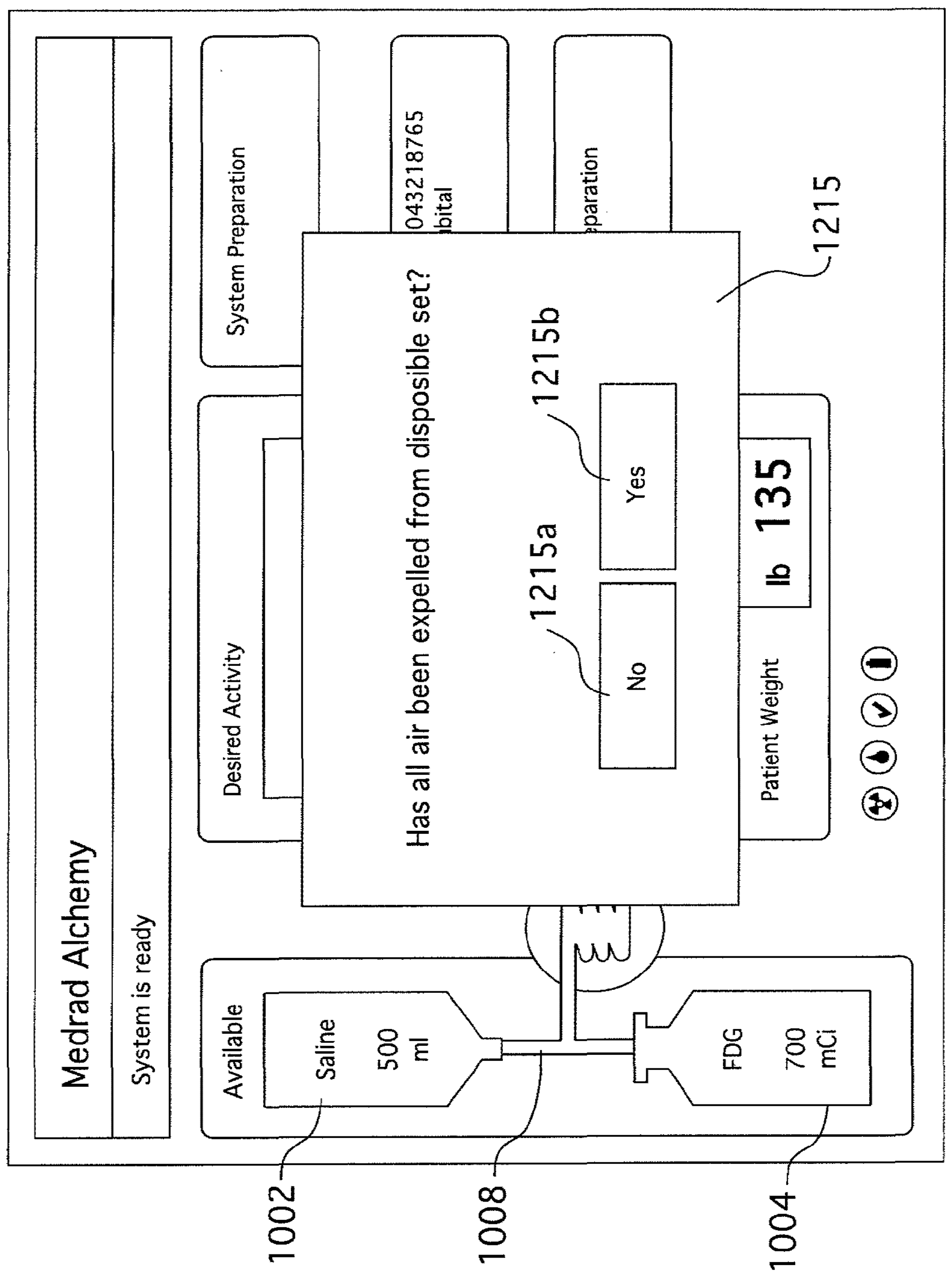

Medrad Alchemy
System is ready
Available
Saline
500
ml
FDG
700
mCi
System Preparation
043218765
bital
eparation
Desired Activity
Patient Weight
lb 135
Has all air been expelled from disposible set?
No
Yes
1215a
1215b
1215
1002
1008
1004

FIG. 26B

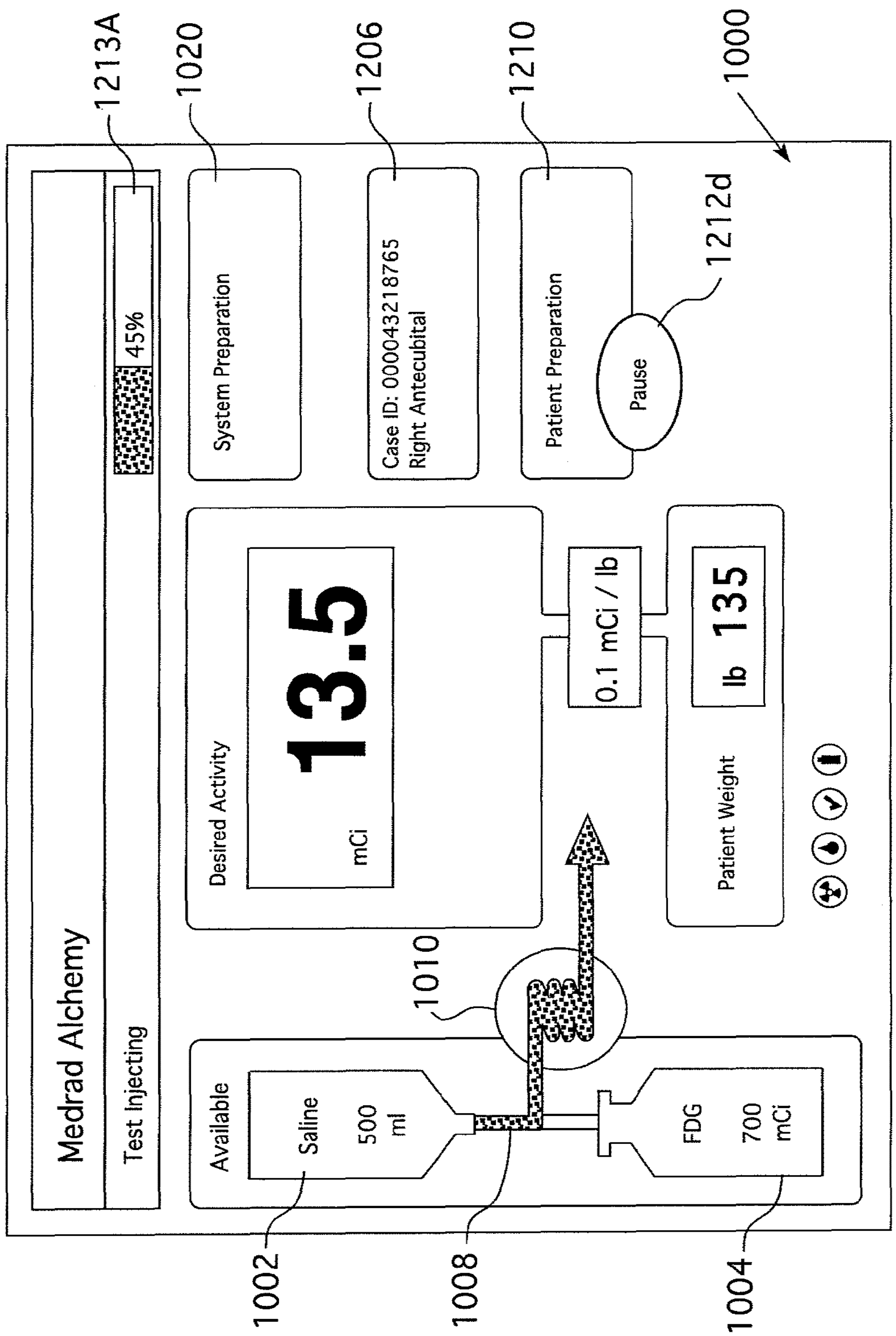

1213A
1020
1206
1210
1000
1212d
Medrad Alchemy
Test Injecting
45%
System Preparation
Case ID: 000043218765
Right Antecubital
Patient Preparation
Pause
Desired Activity
13.5
mCi
0.1 mCi / lb
lb 135
Patient Weight
1010
Available
Saline
500
ml
FDG
700
mCi
1002
1008
1004

FIG. 27A

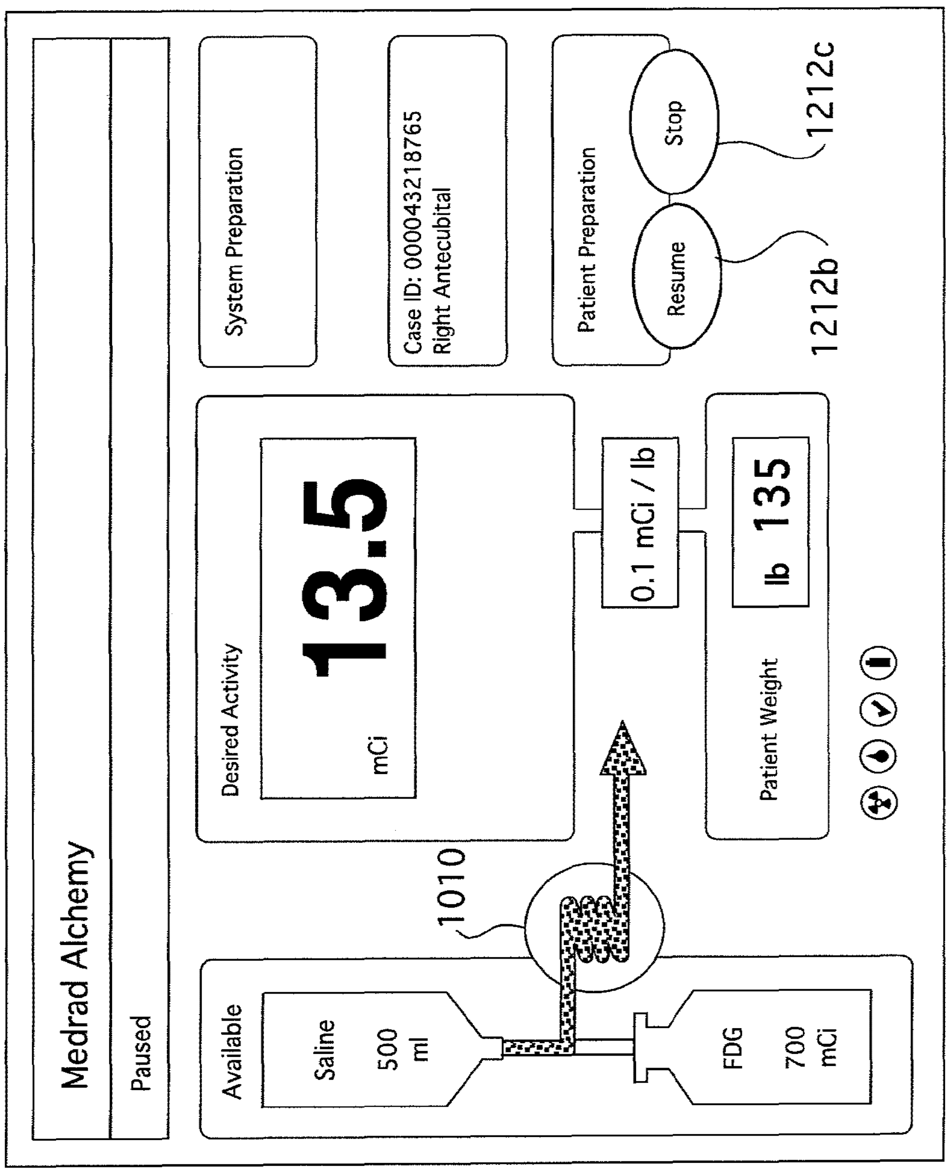

Medrad Alchemy
Paused
Available
Saline
500
ml
FDG
700
mCi
1010
Desired Activity
13.5
mCi
0.1 mCi / lb
Patient Weight
lb 135
System Preparation
Case ID: 000043218765
Right Antecubital
Patient Preparation
Resume
Stop
1212b
1212c

FIG. 27B

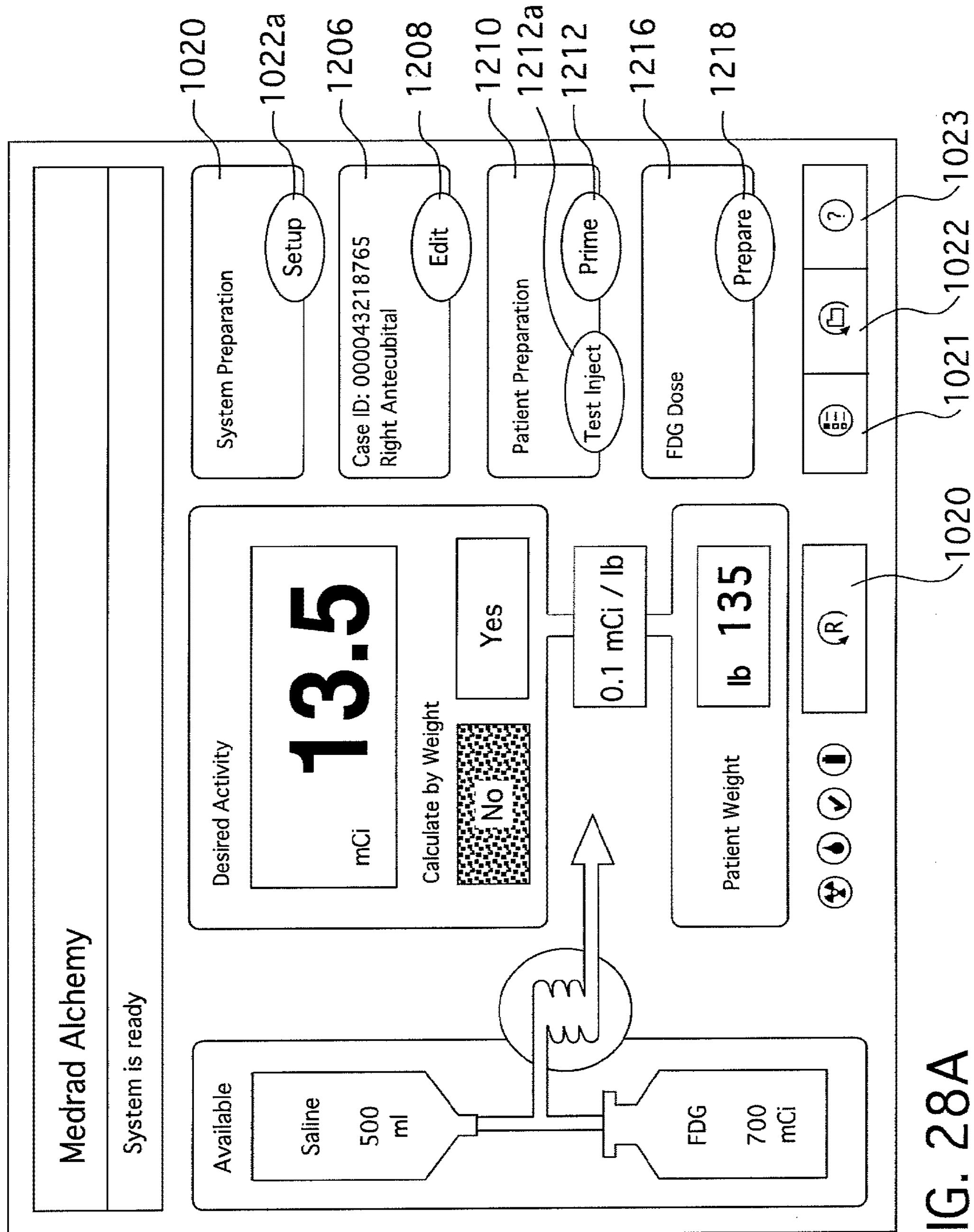

Medrad Alchemy
System is ready
Available
Saline
500
ml
FDG
700
mCi
Desired Activity
13.5
mCi
Calculate by Weight
No
Yes
0.1 mCi / lb
Patient Weight
lb 135
System Preparation
Setup
Case ID: 000043218765
Right Antecubital
Edit
Patient Preparation
Test Inject
Prime
FDG Dose
Prepare
1020
1022a
1206
1208
1210
1212a
1212
1216
1218
1023
1022
1021
1020

FIG. 28A

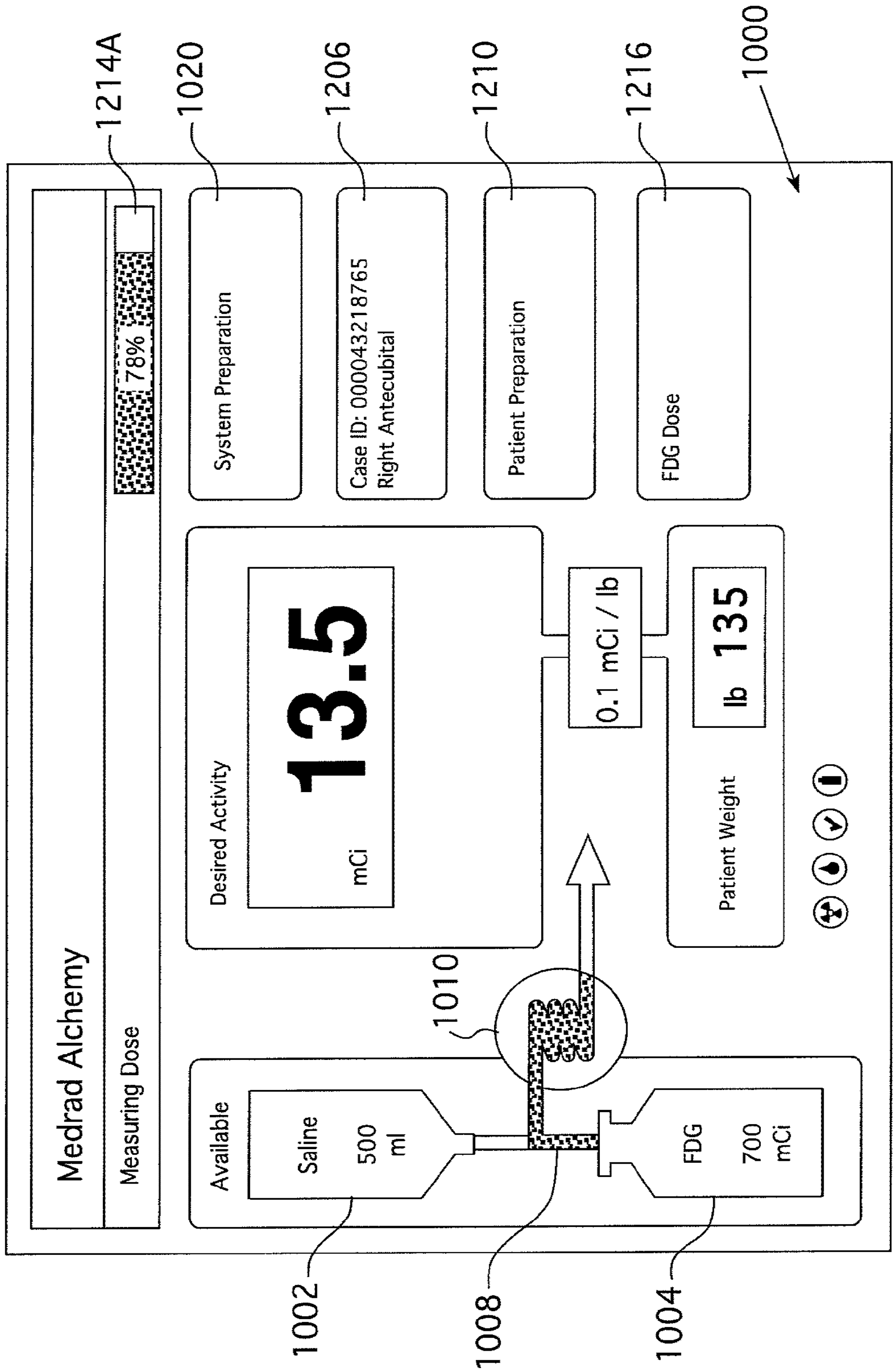

1214A
1020
1206
1210
1216
1000
Medrad Alchemy
Measuring Dose
78%
System Preparation
Case ID: 000043218765
Right Antecubital
Patient Preparation
FDG Dose
Desired Activity
mCi
13.5
0.1 mCi / lb
Patient Weight
lb 135
1010
Available
Saline
500
ml
FDG
700
mCi
1002
1008
1004

FIG. 28B

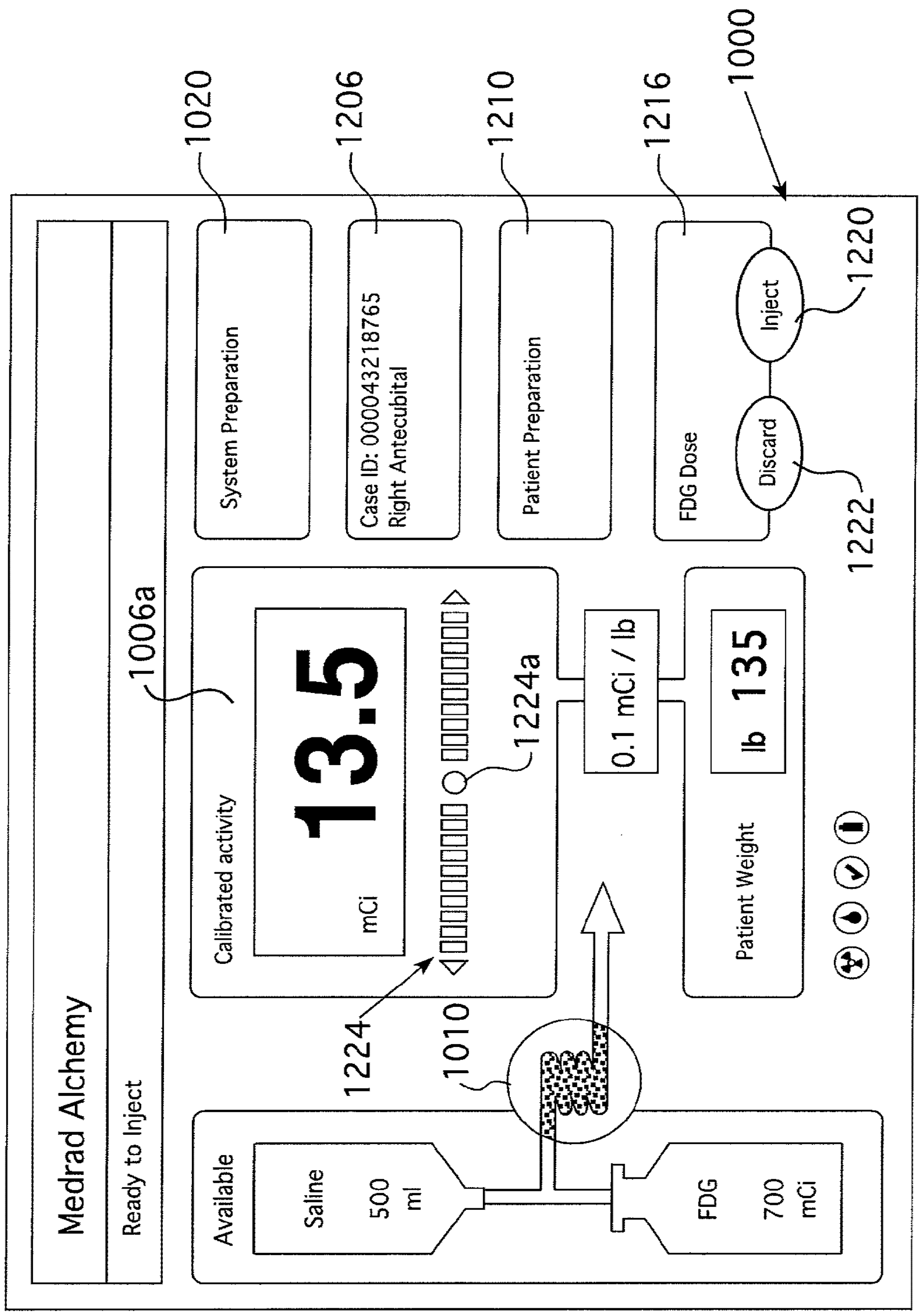

Medrad Alchemy
Ready to Inject
Available
Saline
500
ml
FDG
700
mCi
Calibrated activity
13.5
mCi
0.1 mCi / lb
Patient Weight
lb 135
System Preparation
Case ID: 000043218765
Right Antecubital
Patient Preparation
FDG Dose
Discard
Inject
1000
1020
1206
1210
1216
1220
1222
1006a
1224a
1224
1010

FIG. 29

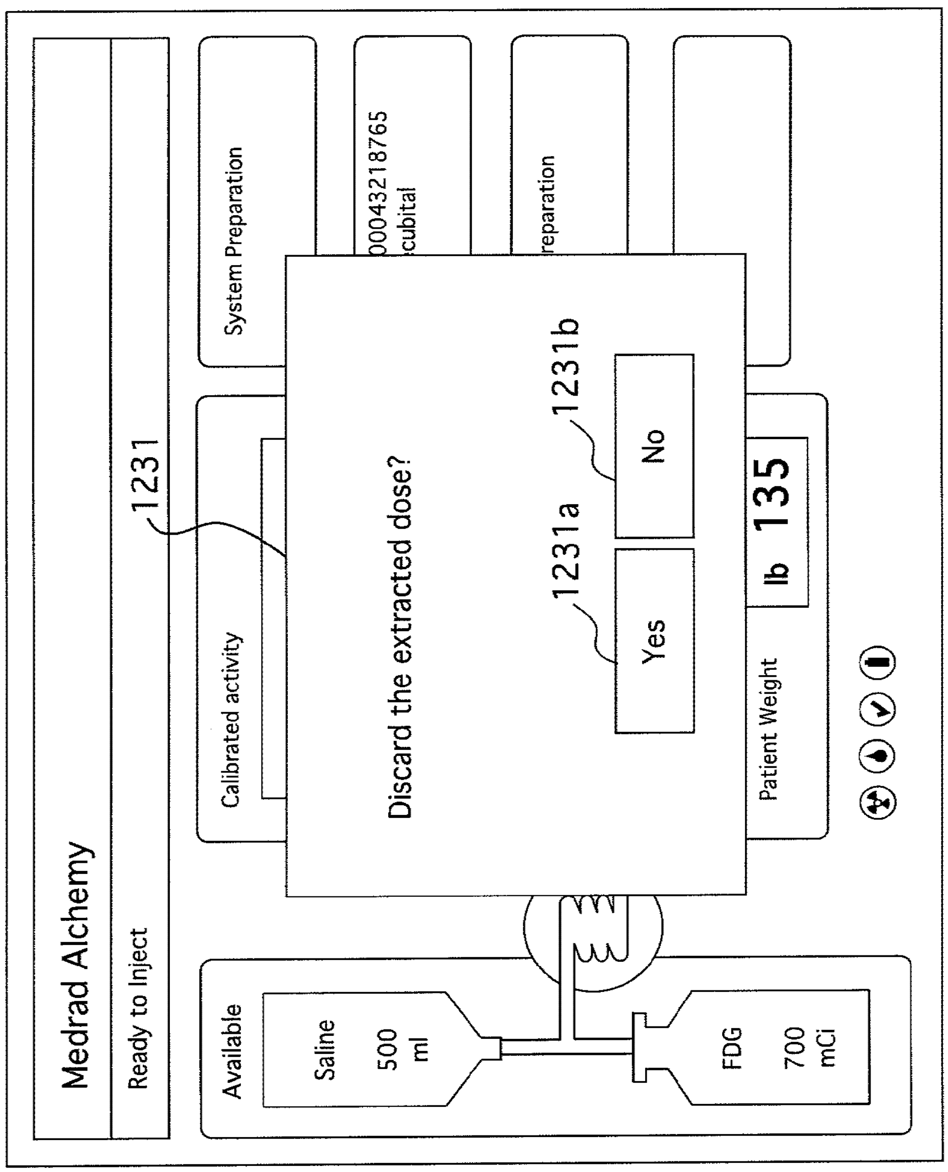

Medrad Alchemy
Ready to Inject
System Preparation
00043218765
cubital
reparation
Calibrated activity
1231
Discard the extracted dose?
1231a
1231b
Yes
No
Patient Weight
lb
135
Available
Saline
500
ml
FDG
700
mCi

FIG. 30A

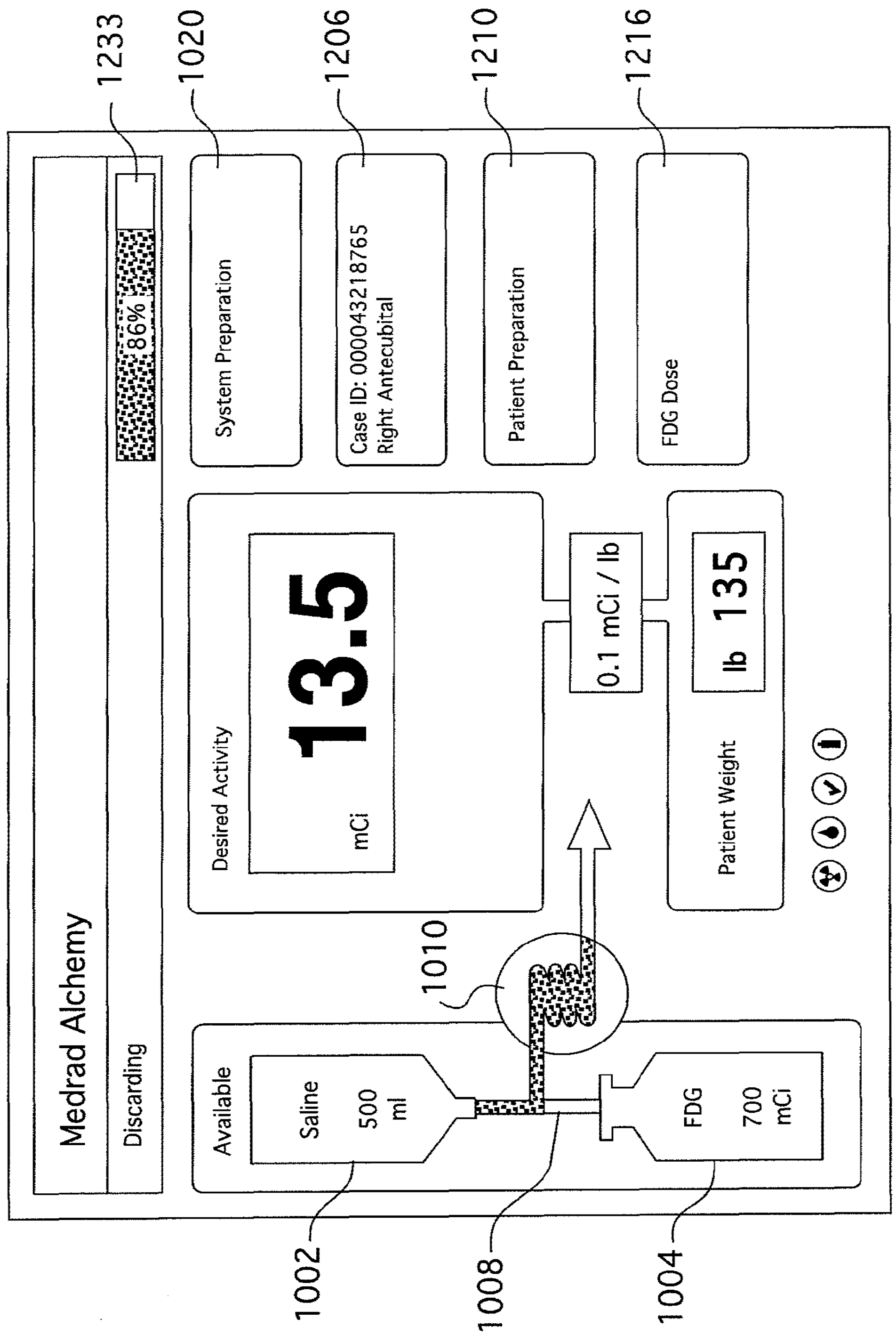

1233
1020
1206
1210
1216
Medrad Alchemy
Discarding
86%
System Preparation
Case ID: 000043218765
Right Antecubital
Patient Preparation
FDG Dose
Desired Activity
13.5
mCi
0.1 mCi / lb
Patient Weight
lb 135
Available
Saline
500
ml
FDG
700
mCi
1010
1002
1008
1004

FIG. 30B

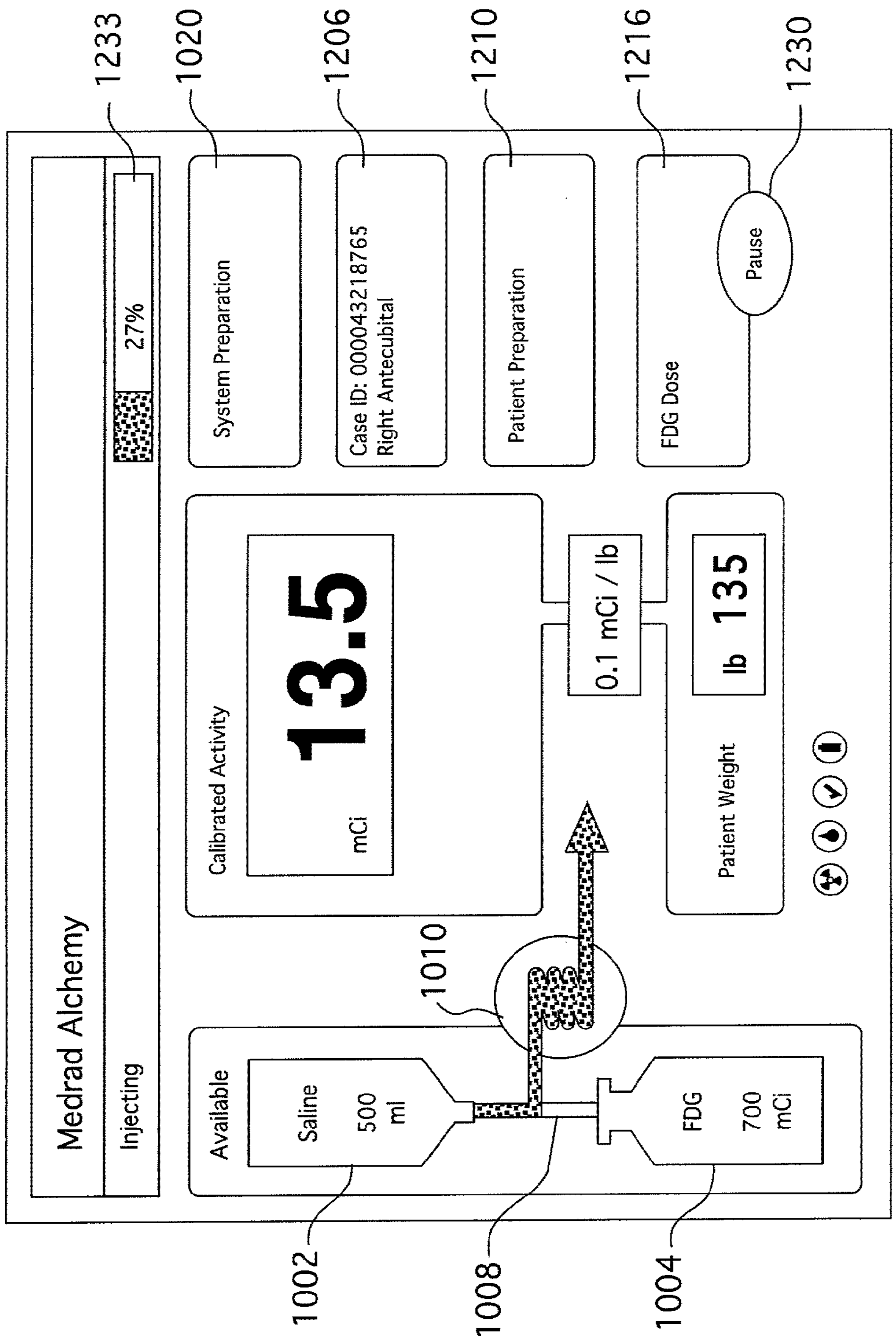
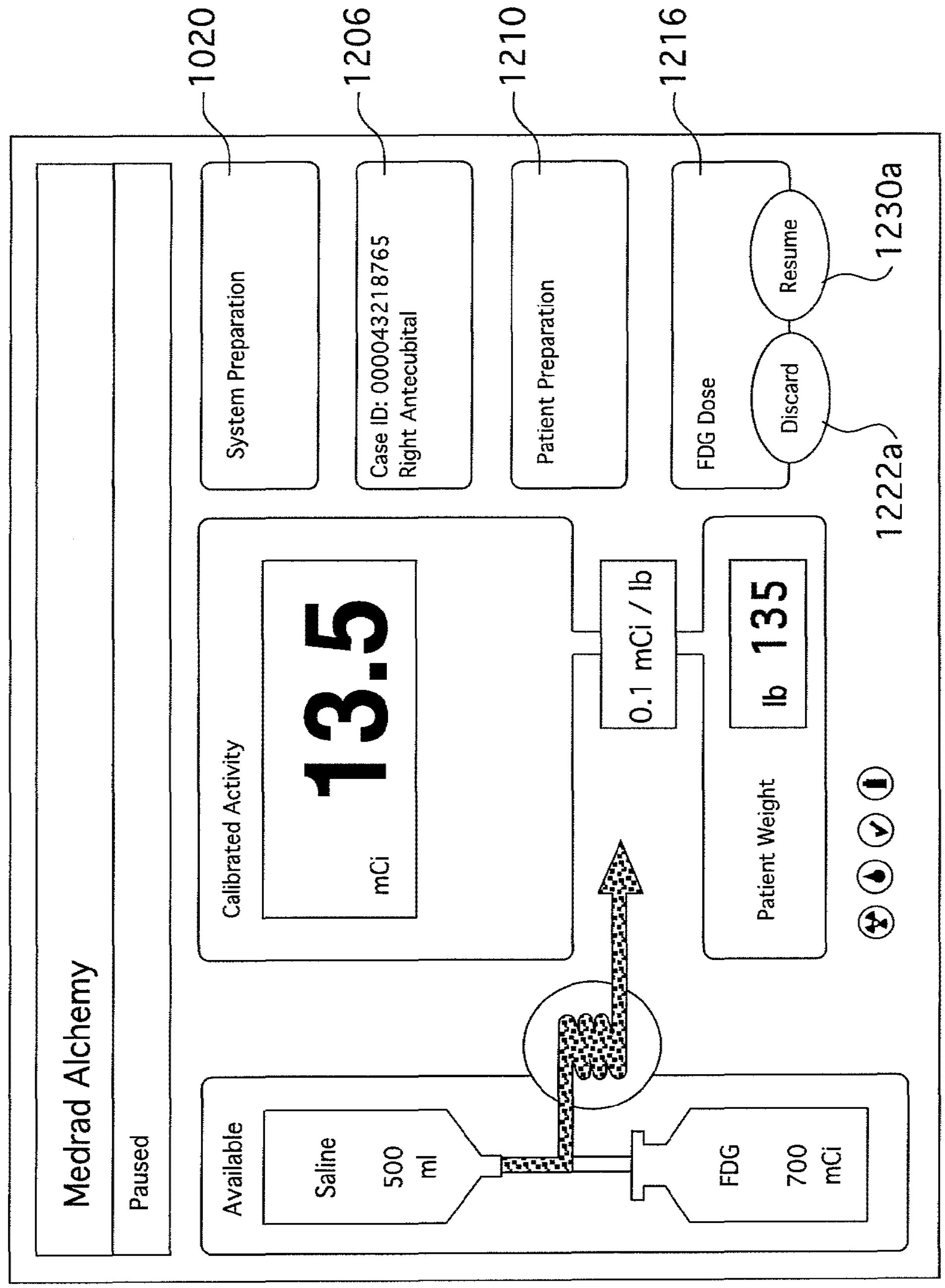

Medrad Alchemy
Injecting
27%
Available
Saline
500
ml
FDG
700
mCi
Calibrated Activity
13.5
mCi
0.1 mCi / lb
Patient Weight
lb 135
System Preparation
Case ID: 000043218765
Right Antecubital
Patient Preparation
FDG Dose
Pause
1233
1020
1206
1210
1216
1230
1010
1002
1008
1004

FIG. 31



1020
1206
1210
1216
Medrad Alchemy
Paused
Available
Saline
500
ml
FDG
700
mCi
System Preparation
Case ID: 000043218765
Right Antecubital
Patient Preparation
FDG Dose
Discard
Resume
1222a
1230a
Calibrated Activity
mCi
13.5
0.1 mCi / lb
Patient Weight
lb 135

FIG. 32A

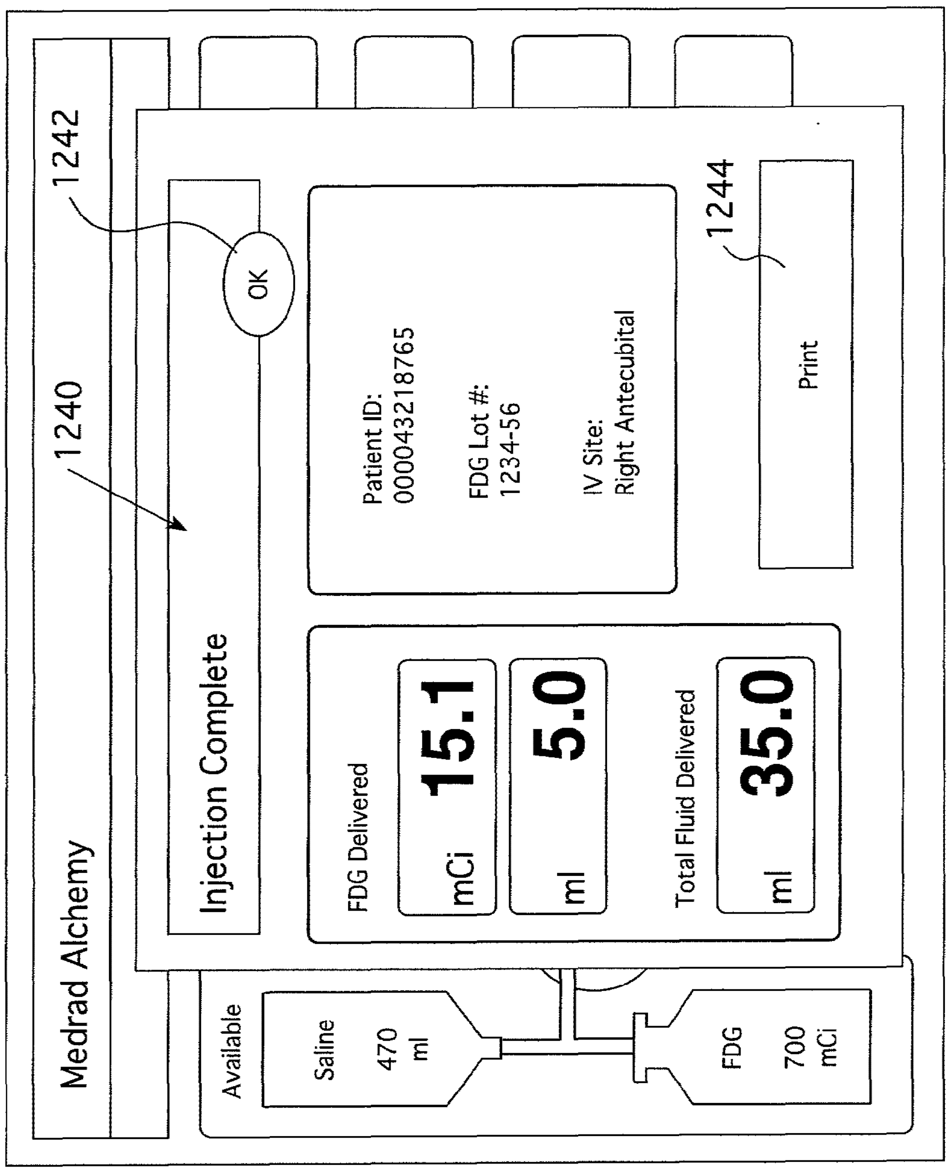
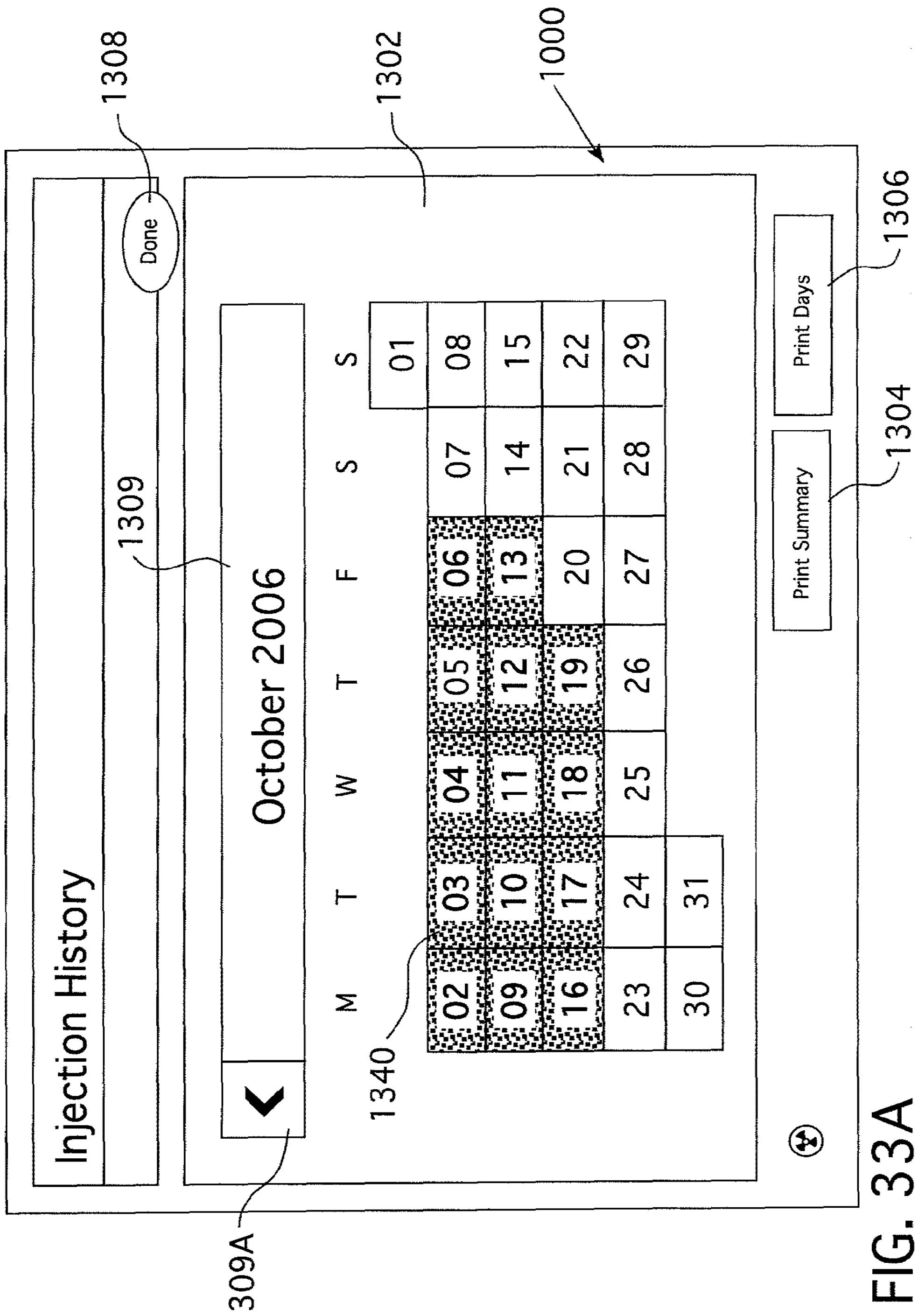

Medrad Alchemy
1242
1240
Injection Complete
OK
Patient ID:
000043218765
FDG Lot #:
1234-56
IV Site:
Right Antecubital
1244
Print
FDG Delivered
mCi
15.1
ml
5.0
Total Fluid Delivered
ml
35.0
Available
Saline
470
ml
FDG
700
mCi

FIG. 32B



1308
1302
1000
1309
1306
1304
1340
1309A
Injection History
Done
October 2006
M
T
W
T
F
S
S
01
02
03
04
05
06
07
08
09
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
Print Summary
Print Days

FIG. 33A

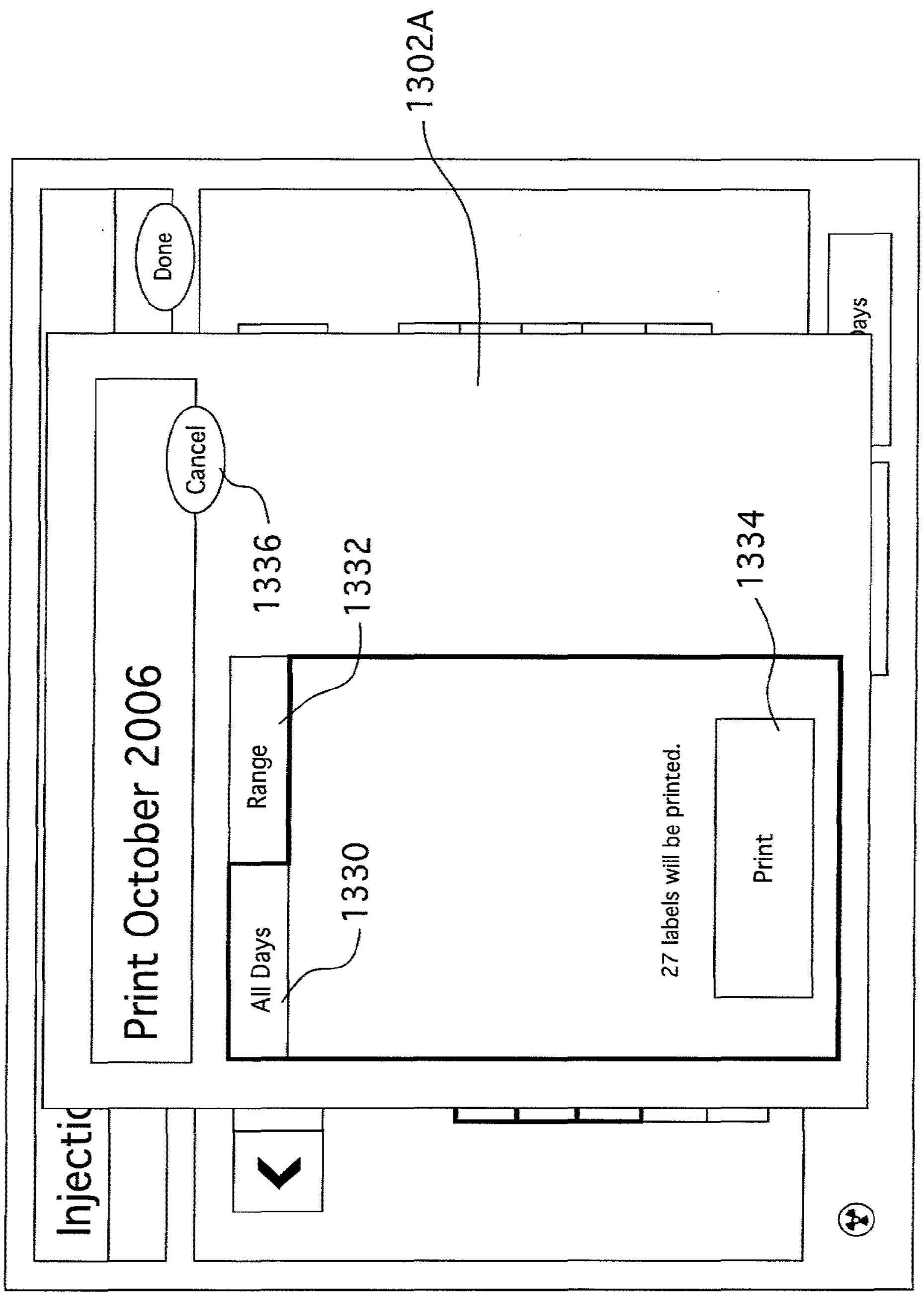

1302A
Done
Cancel
1336
1332
1334
Print October 2006
Range
All Days
1330
27 labels will be printed.
Print
Injectic

FIG. 33B

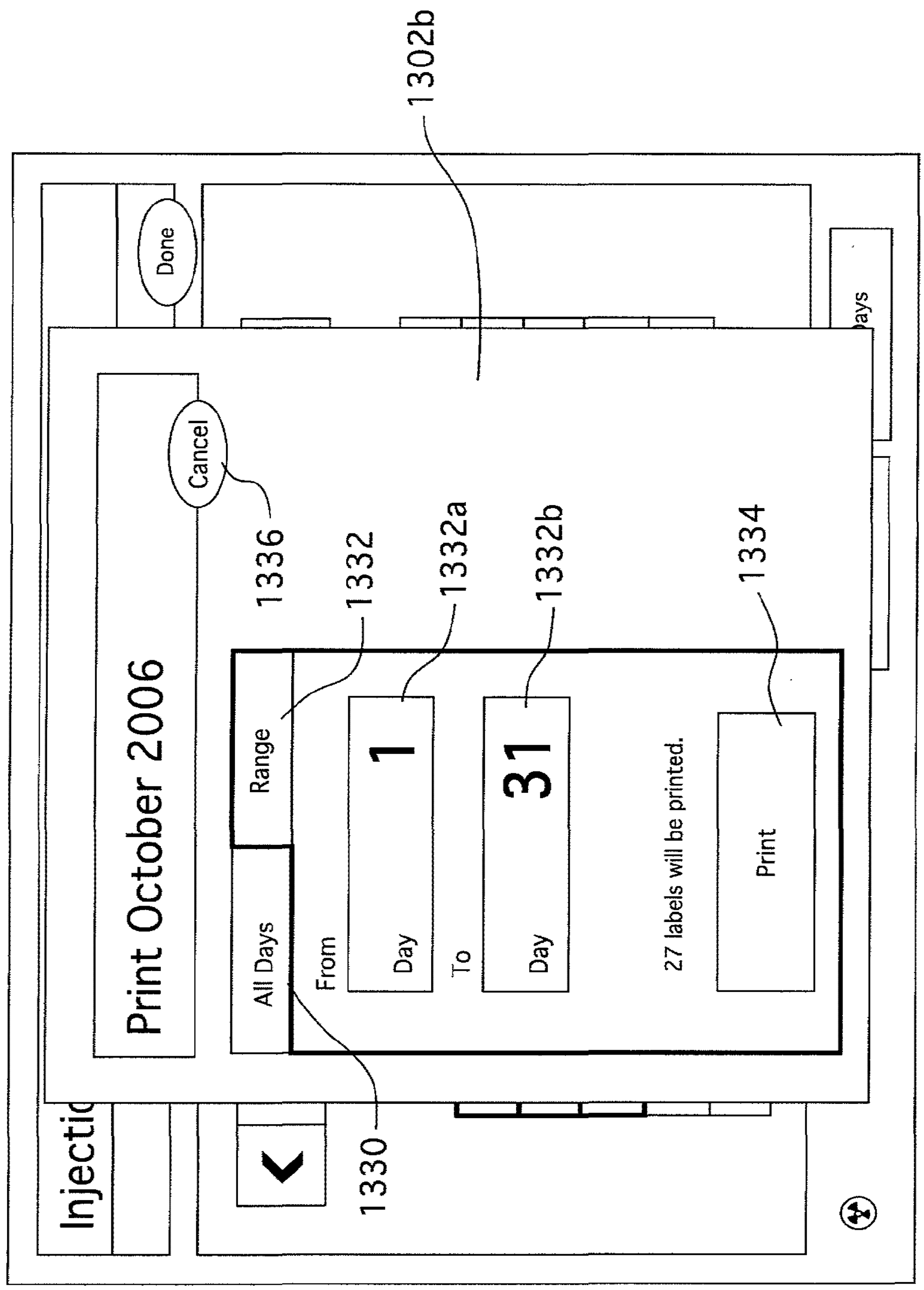

Print October 2006
Cancel
Done
Range
All Days
From
1
Day
To
31
Day
27 labels will be printed.
Print
Injectio
1302b
1336
1332
1332a
1332b
1334
1330

FIG. 33C

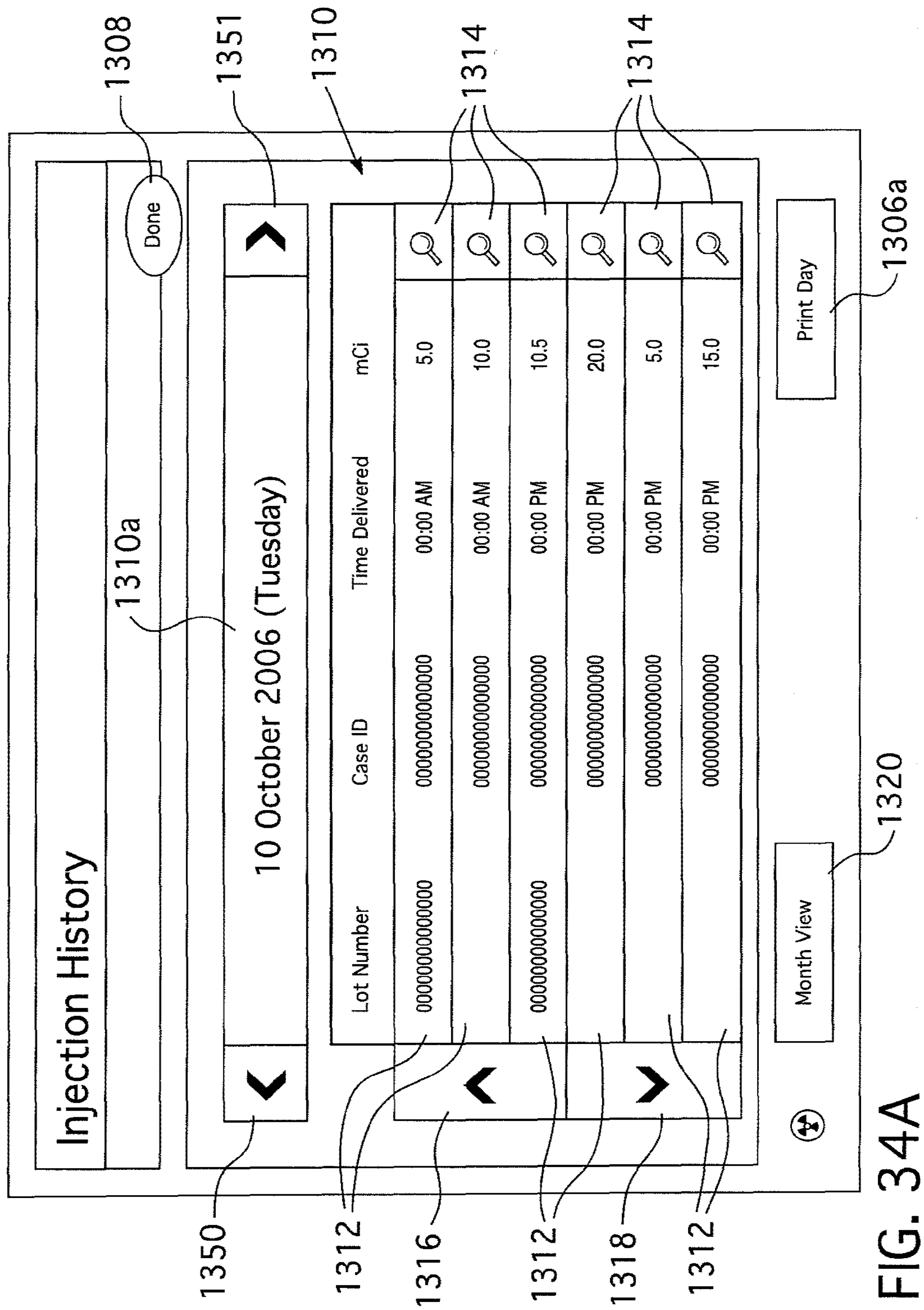

Injection History
Done
10 October 2006 (Tuesday)
Lot Number
Case ID
Time Delivered
mCi
000000000000000
000000000000000
00:00 AM
5.0
000000000000000
00:00 AM
10.0
000000000000000
000000000000000
00:00 PM
10.5
000000000000000
00:00 PM
20.0
000000000000000
00:00 PM
5.0
000000000000000
00:00 PM
15.0
Month View
Print Day
1308
1351
1310
1314
1314
1310a
1306a
1320
1350
1312
1316
1312
1318
1312

FIG. 34A

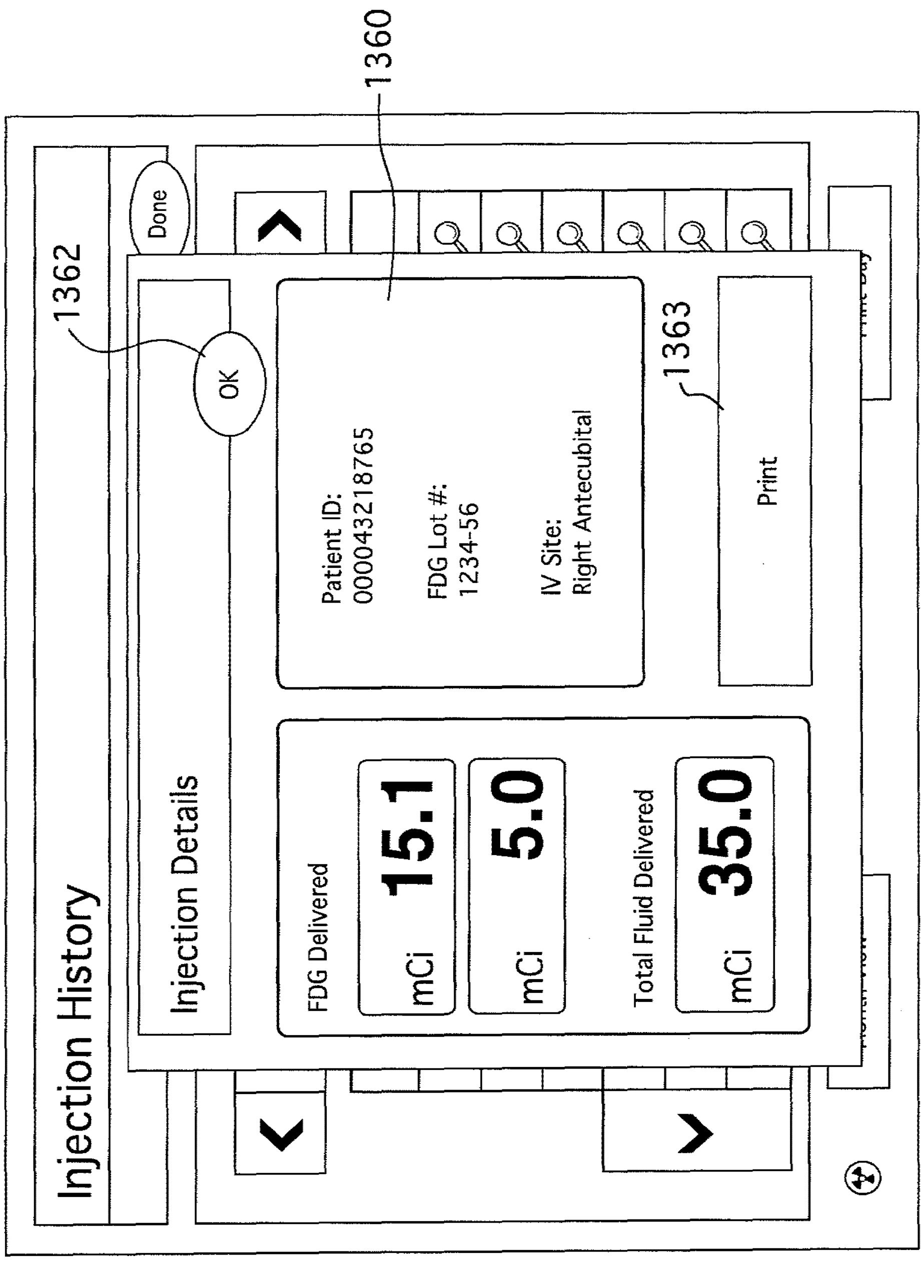

Injection History
Done
1362
1360
OK
Injection Details
Patient ID:
000043218765
FDG Lot #:
1234-56
IV Site:
Right Antecubital
1363
Print
FDG Delivered
mCi
15.1
mCi
5.0
Total Fluid Delivered
mCi
35.0

FIG. 34B

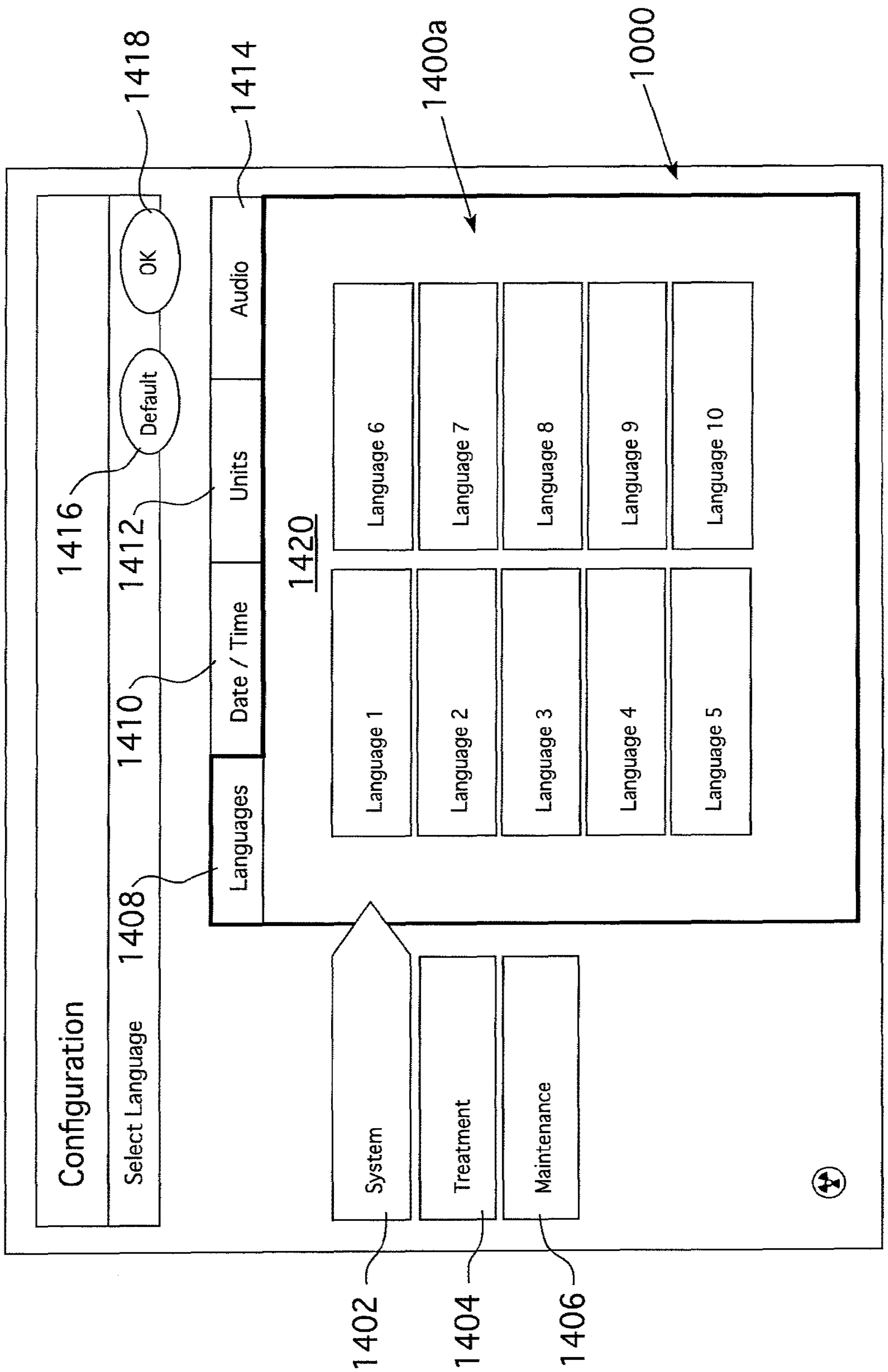

Configuration
Select Language
Default
OK
Languages
Date / Time
Units
Audio
1420
Language 1
Language 2
Language 3
Language 4
Language 5
Language 6
Language 7
Language 8
Language 9
Language 10
System
Treatment
Maintenance
1418
1414
1400a
1000
1416
1412
1410
1408
1402
1404
1406

FIG. 35

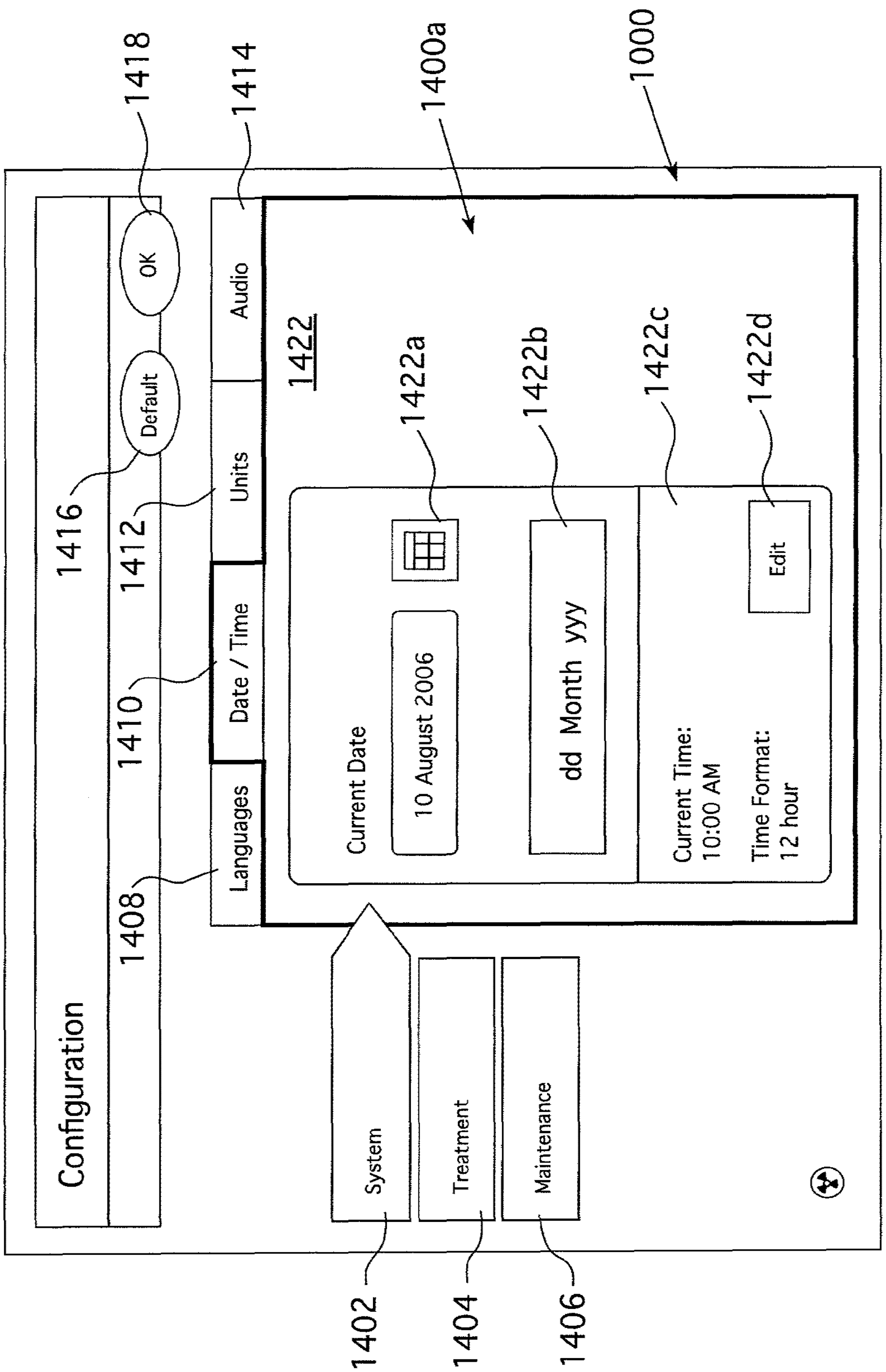
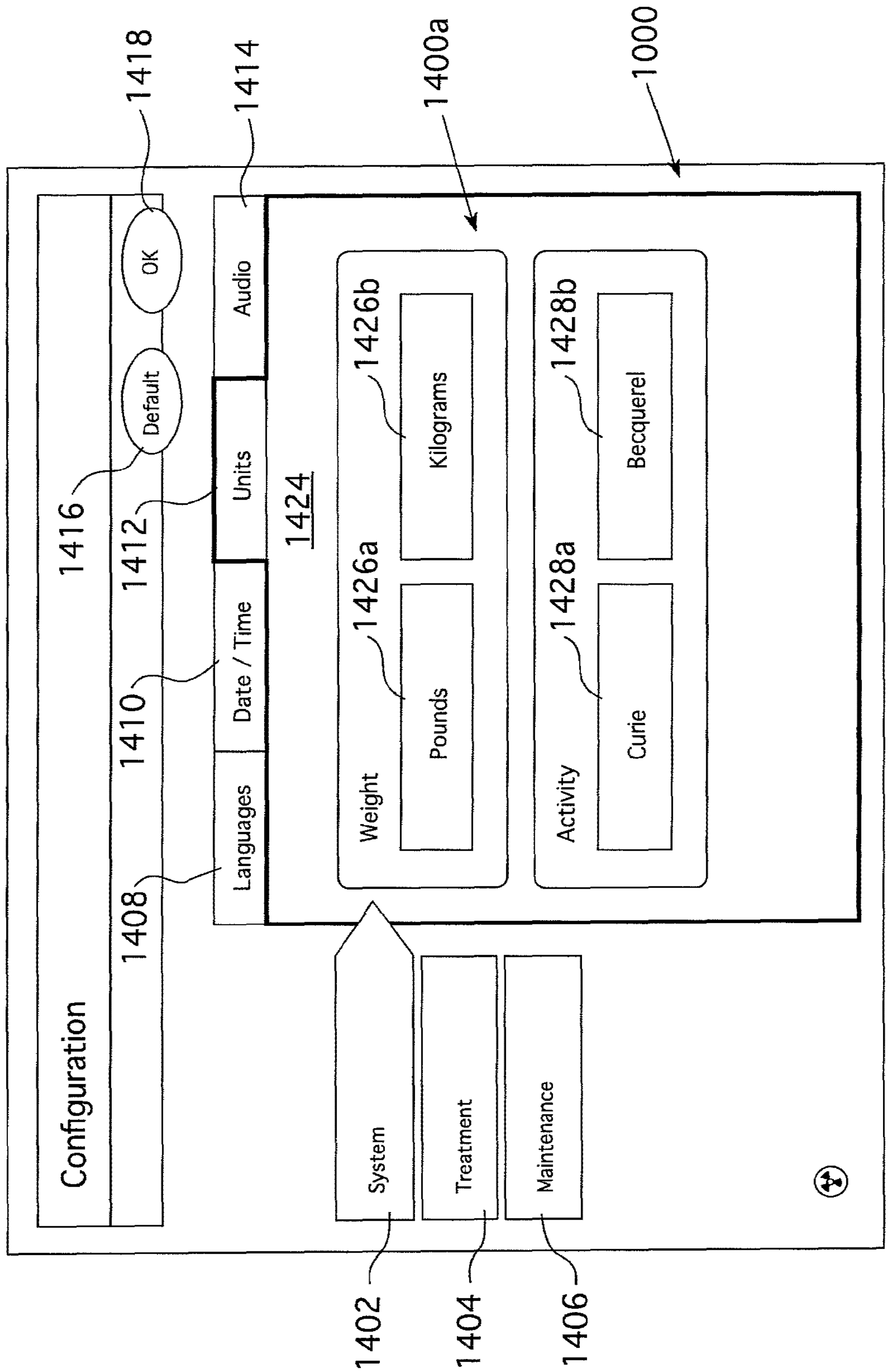

Configuration
Default
OK
Languages
Date / Time
Units
Audio
1422
Current Date
10 August 2006
dd Month yyy
Current Time:
10:00 AM
Time Format:
12 hour
Edit
System
Treatment
Maintenance
1000
1400a
1402
1404
1406
1408
1410
1412
1414
1416
1418
1422a
1422b
1422c
1422d

FIG. 36



Configuration
Languages
Date / Time
Units
Audio
Default
OK
1424
Weight
Pounds
Kilograms
Activity
Curie
Becquerel
System
Treatment
Maintenance
1000
1400a
1402
1404
1406
1408
1410
1412
1414
1416
1418
1426a
1426b
1428a
1428b

FIG. 37

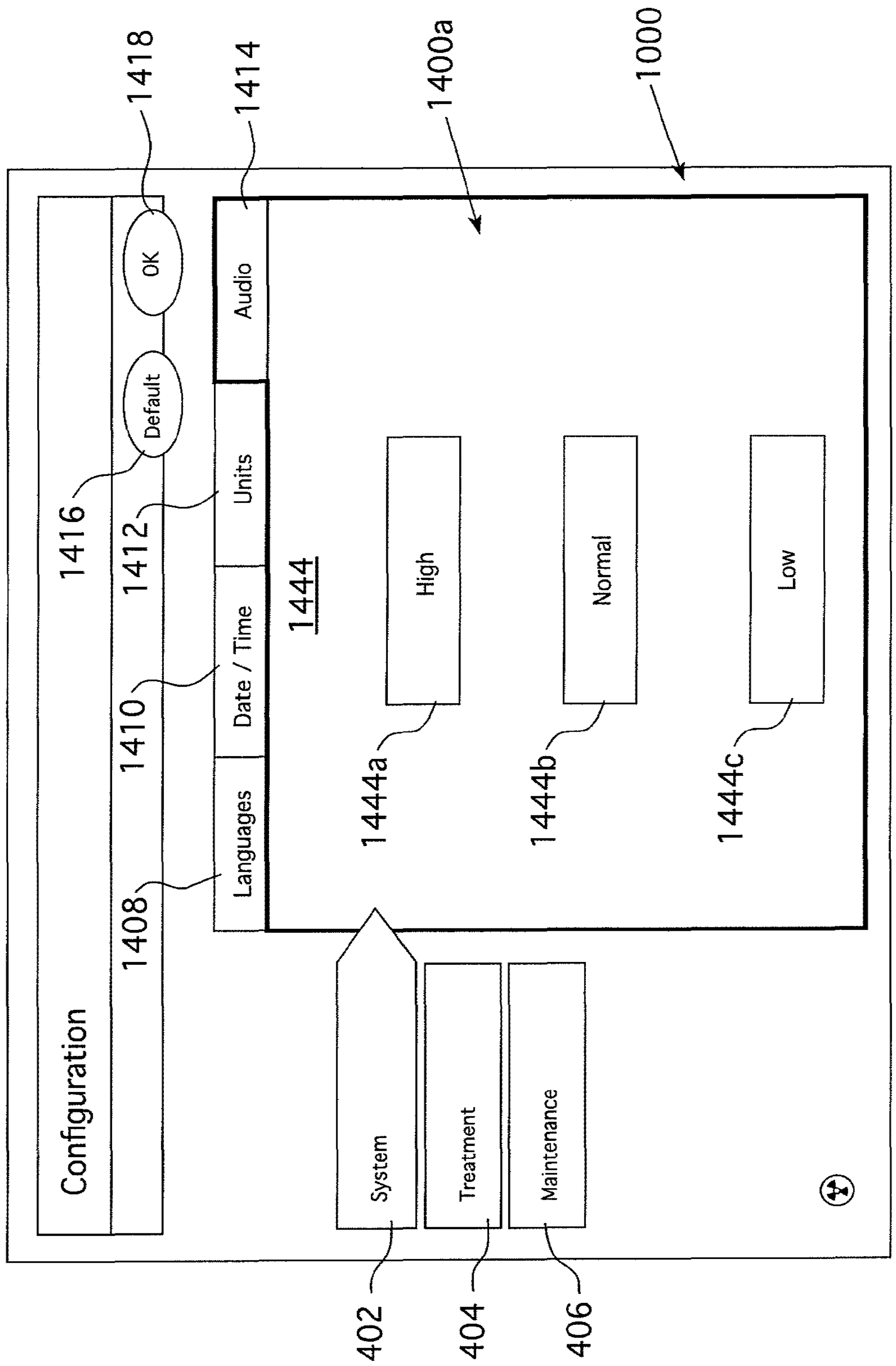

Configuration
Default
OK
Languages
Date / Time
Units
Audio
1444
High
Normal
Low
System
Treatment
Maintenance
1000
1400a
1402
1404
1406
1408
1410
1412
1414
1416
1418
1444a
1444b
1444c

FIG. 38

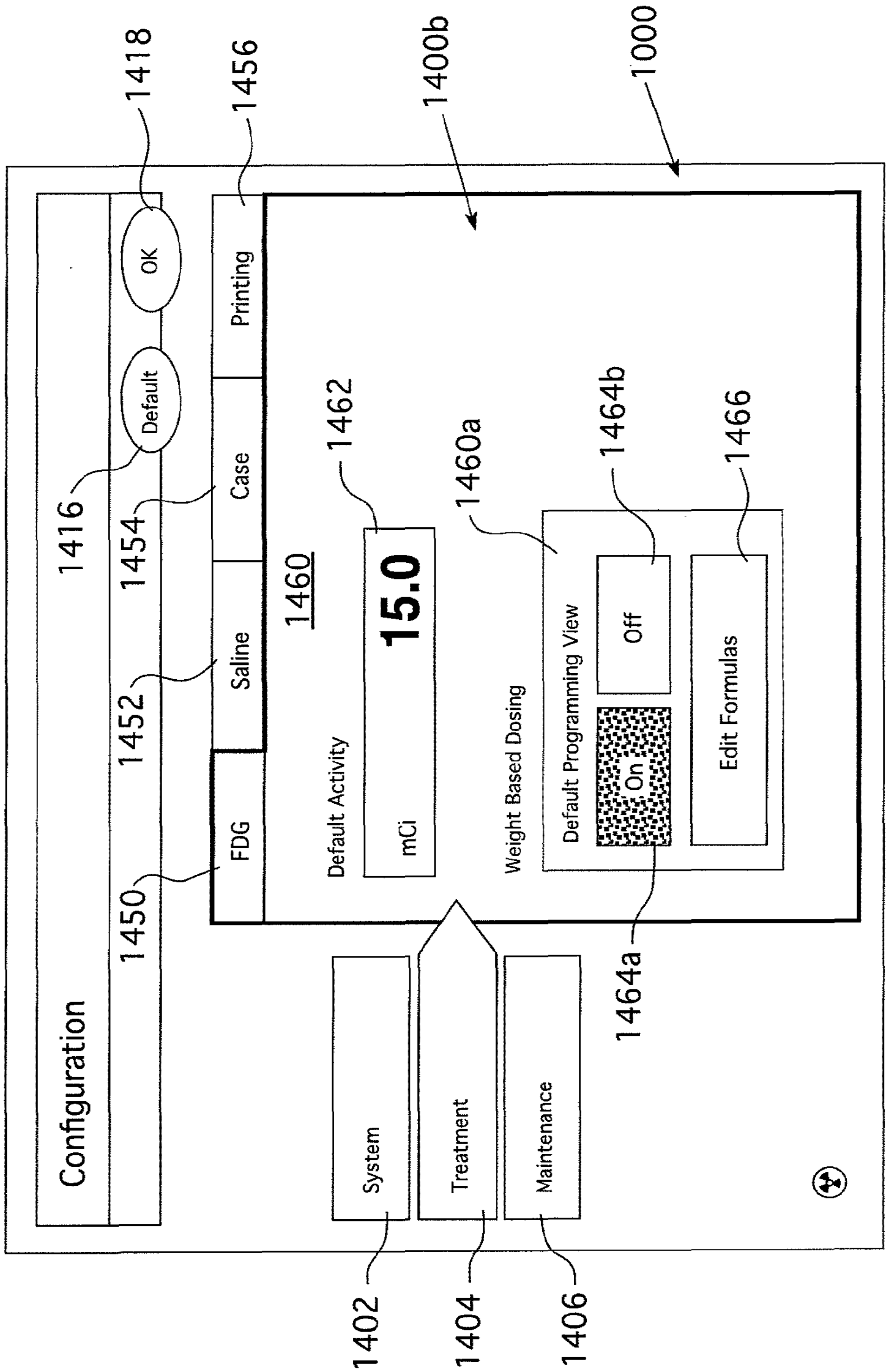

1418
1456
1400b
1000
Configuration
Default
OK
1416
1454
1452
1450
FDG
Saline
Case
Printing
1462
1460a
1464b
1466
1460
Default Activity
15.0
mCi
Weight Based Dosing
Default Programming View
On
Off
Edit Formulas
1464a
System
Treatment
Maintenance
1402
1404
1406

FIG. 39A

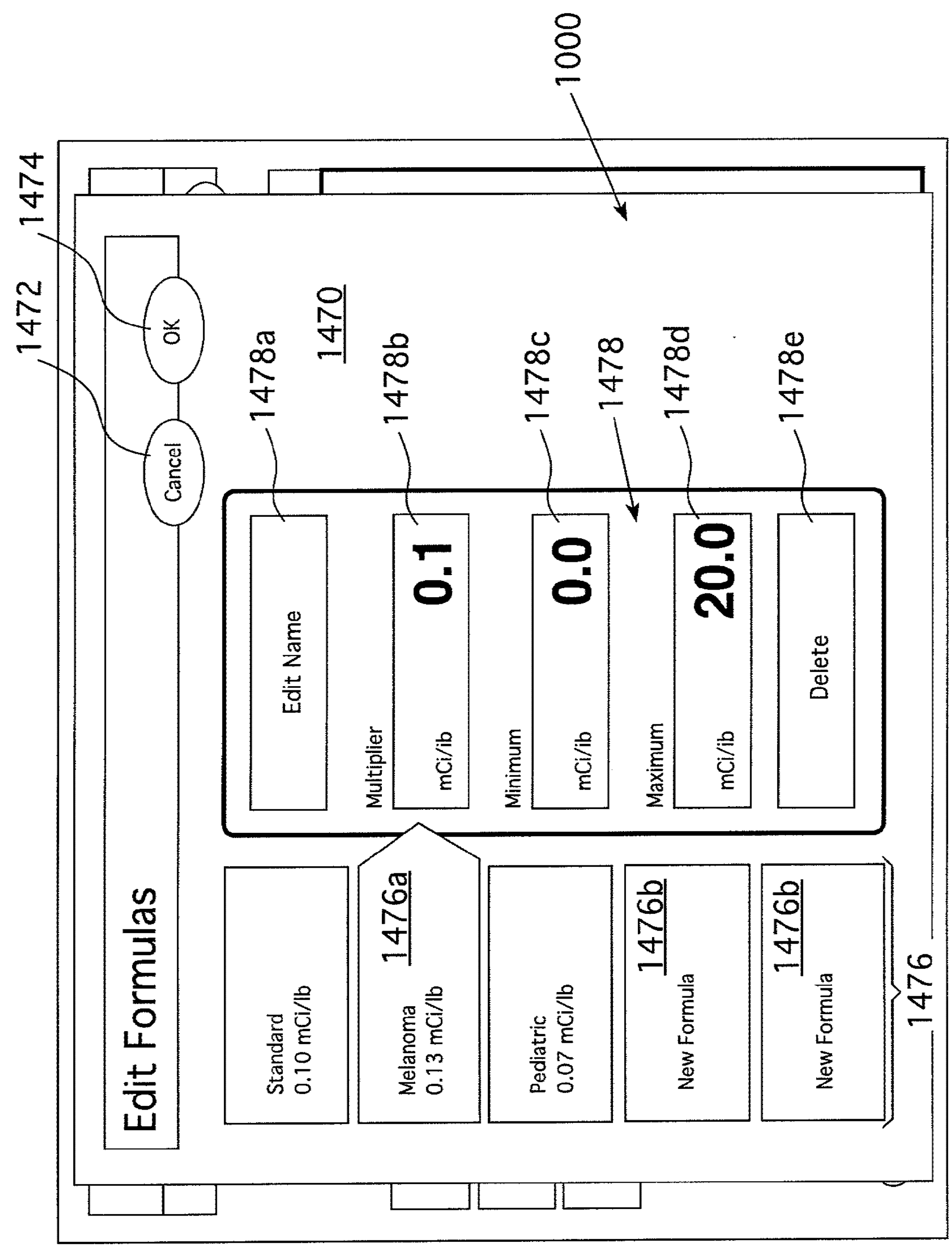

1000
1472
1474
1470
1478a
1478b
1478c
1478
1478d
1478e
OK
Cancel
Edit Formulas
Edit Name
Multiplier
0.1
mCi/ib
Minimum
0.0
mCi/ib
Maximum
20.0
mCi/ib
Delete
Standard
0.10 mCi/lb
1476a
Melanoma
0.13 mCi/lb
Pediatric
0.07 mCi/lb
1476b
New Formula
1476b
New Formula
1476

FIG. 39B

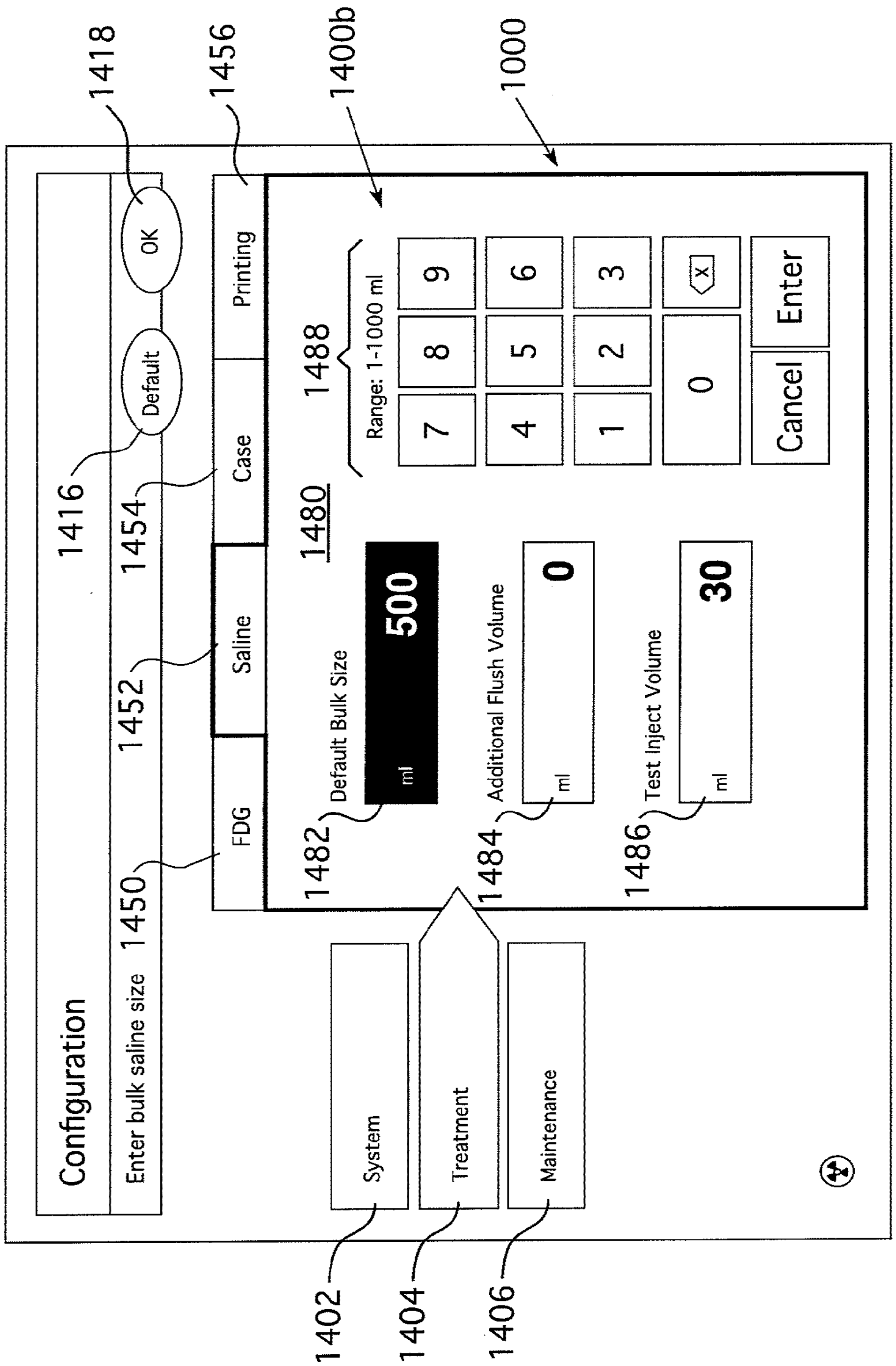

1418
1456
1400b
1000
1416
1454
1452
1450
1488
1480
1482
1484
1486
1402
1404
1406
Configuration
Enter bulk saline size
Default
OK
FDG
Saline
Case
Printing
Range: 1-1000 ml
7
8
9
4
5
6
1
2
3
0
x
Cancel
Enter
Default Bulk Size
500
ml
Additional Flush Volume
0
ml
Test Inject Volume
30
ml
System
Treatment
Maintenance

FIG. 40

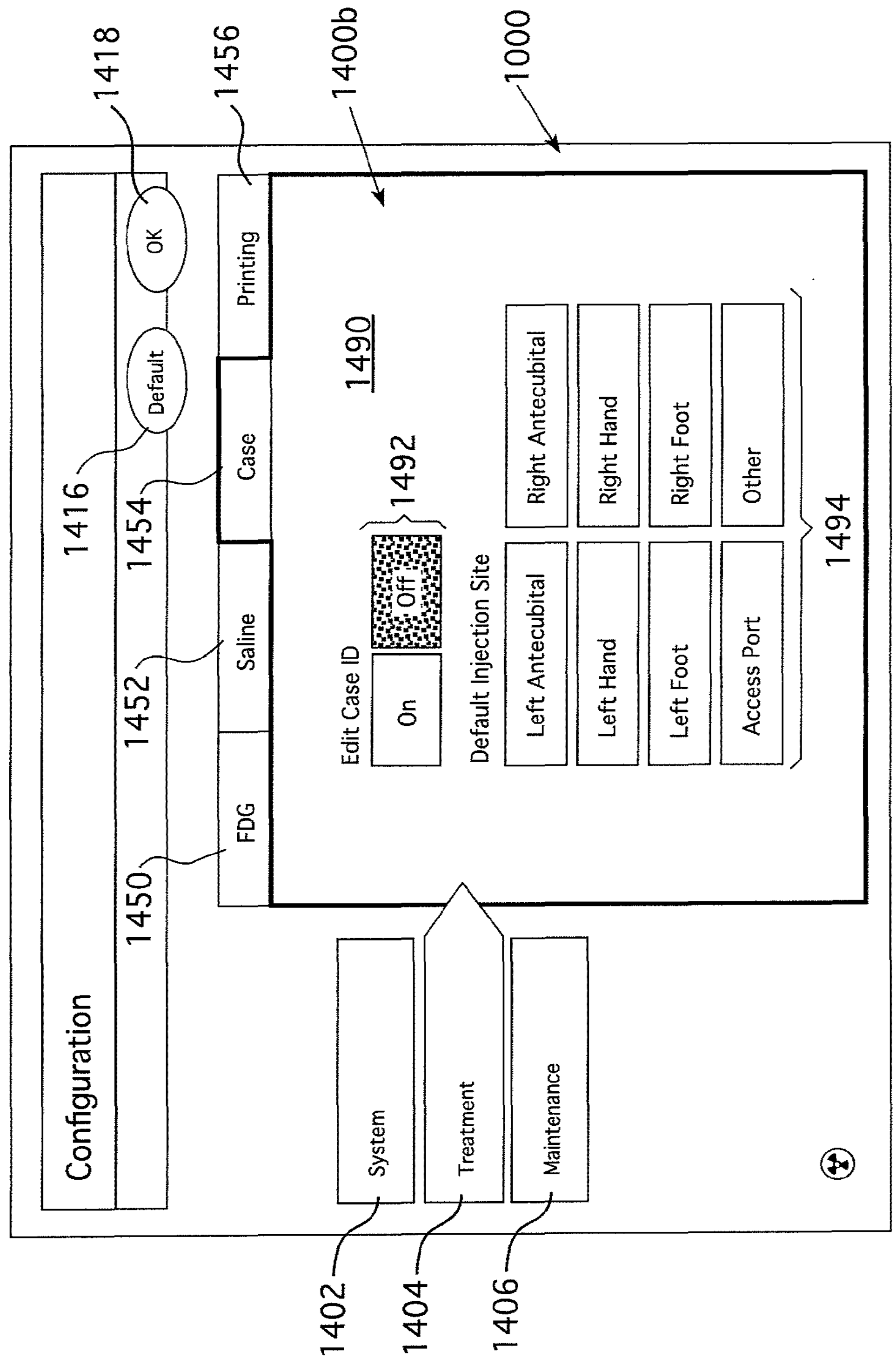

1418
1456
1400b
1000
Configuration
Default
OK
1416
1454
1452
1450
FDG
Saline
Case
Printing
1490
Edit Case ID
On
Off
1492
Default Injection Site
Left Antecubital
Right Antecubital
Left Hand
Right Hand
Left Foot
Right Foot
Access Port
Other
1494
System
Treatment
Maintenance
1402
1404
1406

FIG. 41

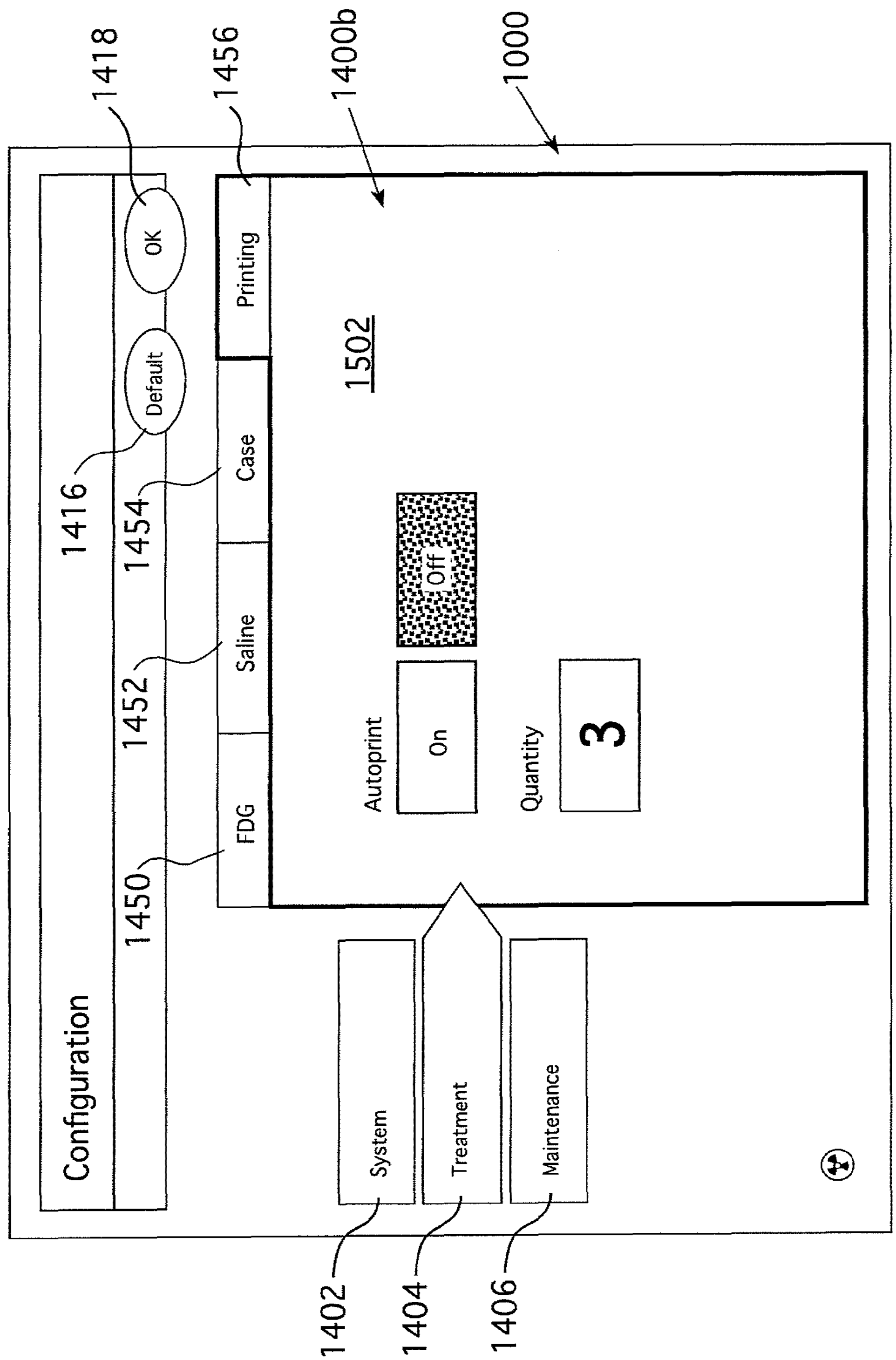

1418
1456
1400b
1000
Configuration
OK
Default
1416
Printing
Case
Saline
FDG
1454
1452
1450
1502
Autoprint
On
Off
Quantity
3
System
Treatment
Maintenance
1402
1404
1406

FIG. 42

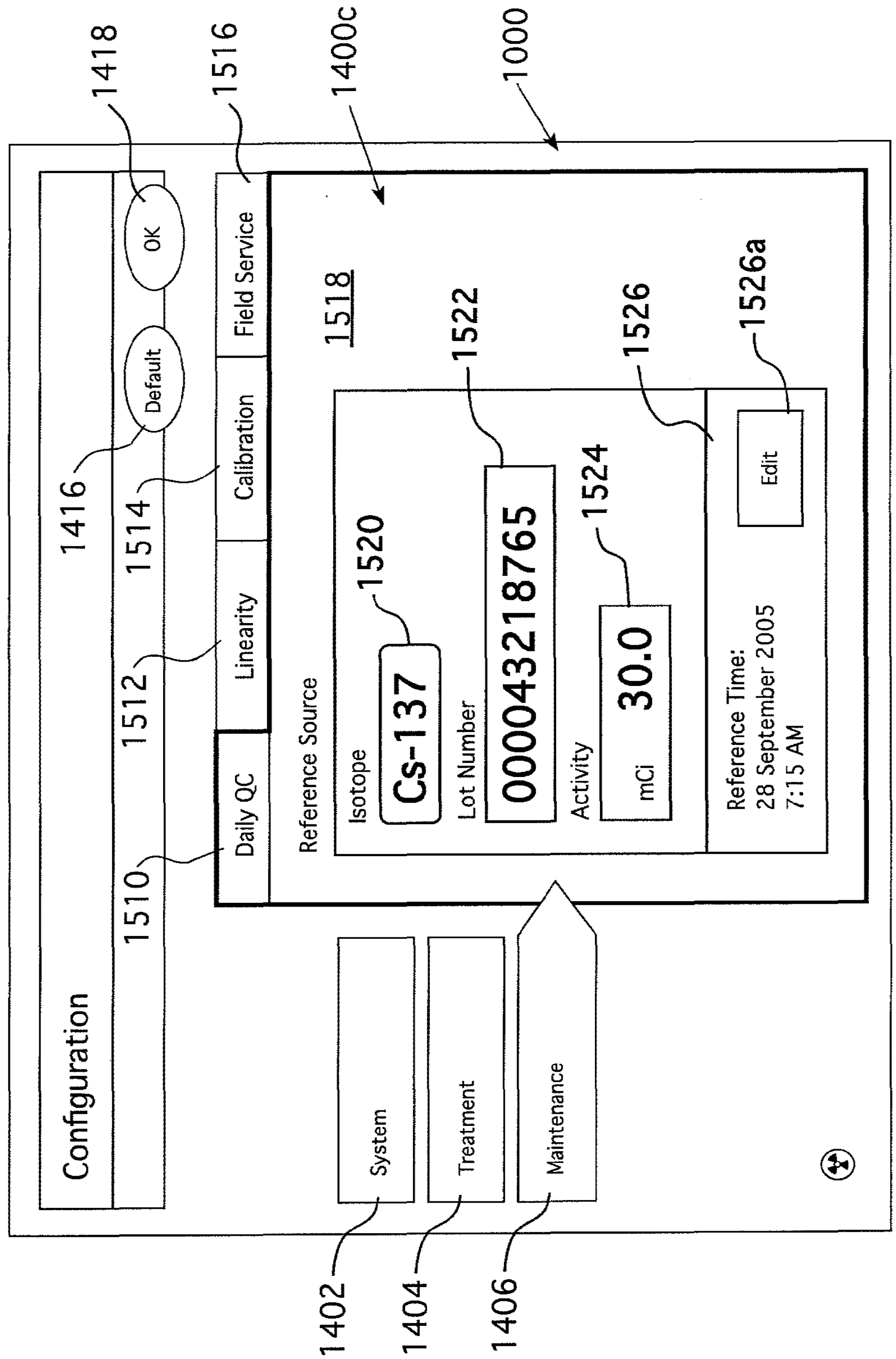

1418
1516
1400c
1000
1416
1514
1512
1510
Configuration
Default
OK
Daily QC
Linearity
Calibration
Field Service
1518
Reference Source
Isotope
Cs-137
1520
Lot Number
000043218765
1522
Activity
mCi
30.0
1524
1526
Reference Time:
28 September 2005
7:15 AM
Edit
1526a
System
Treatment
Maintenance
1402
1404
1406

FIG. 43

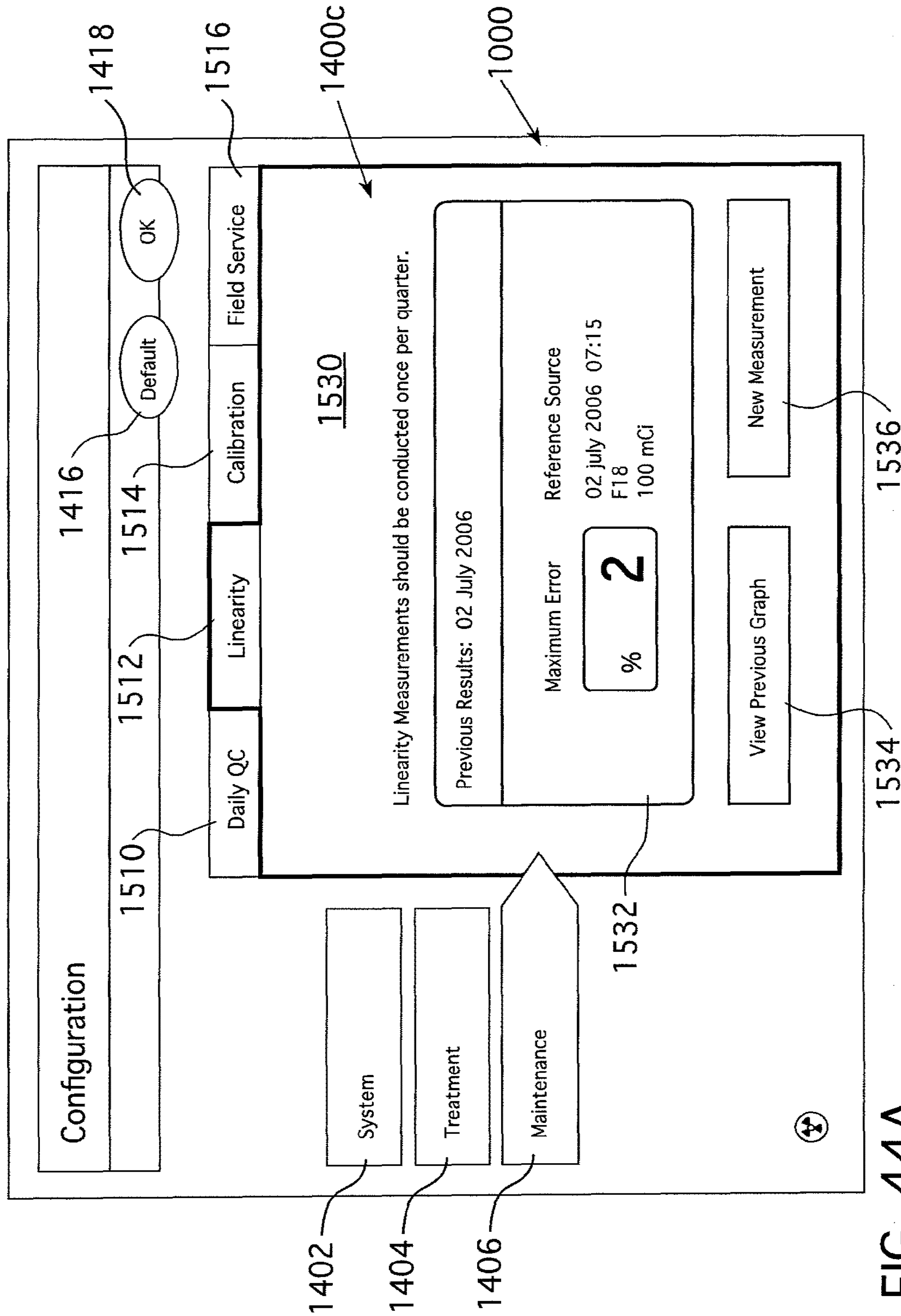

Configuration
Default
OK
Daily QC
Linearity
Calibration
Field Service
1530
Linearity Measurements should be conducted once per quarter.
Previous Results: 02 July 2006
Maximum Error
2
%
Reference Source
02 july 2006 07:15
F18
100 mCi
View Previous Graph
New Measurement
System
Treatment
Maintenance
1418
1516
1400c
1000
1416
1514
1512
1510
1532
1534
1536
1402
1404
1406

FIG. 44A

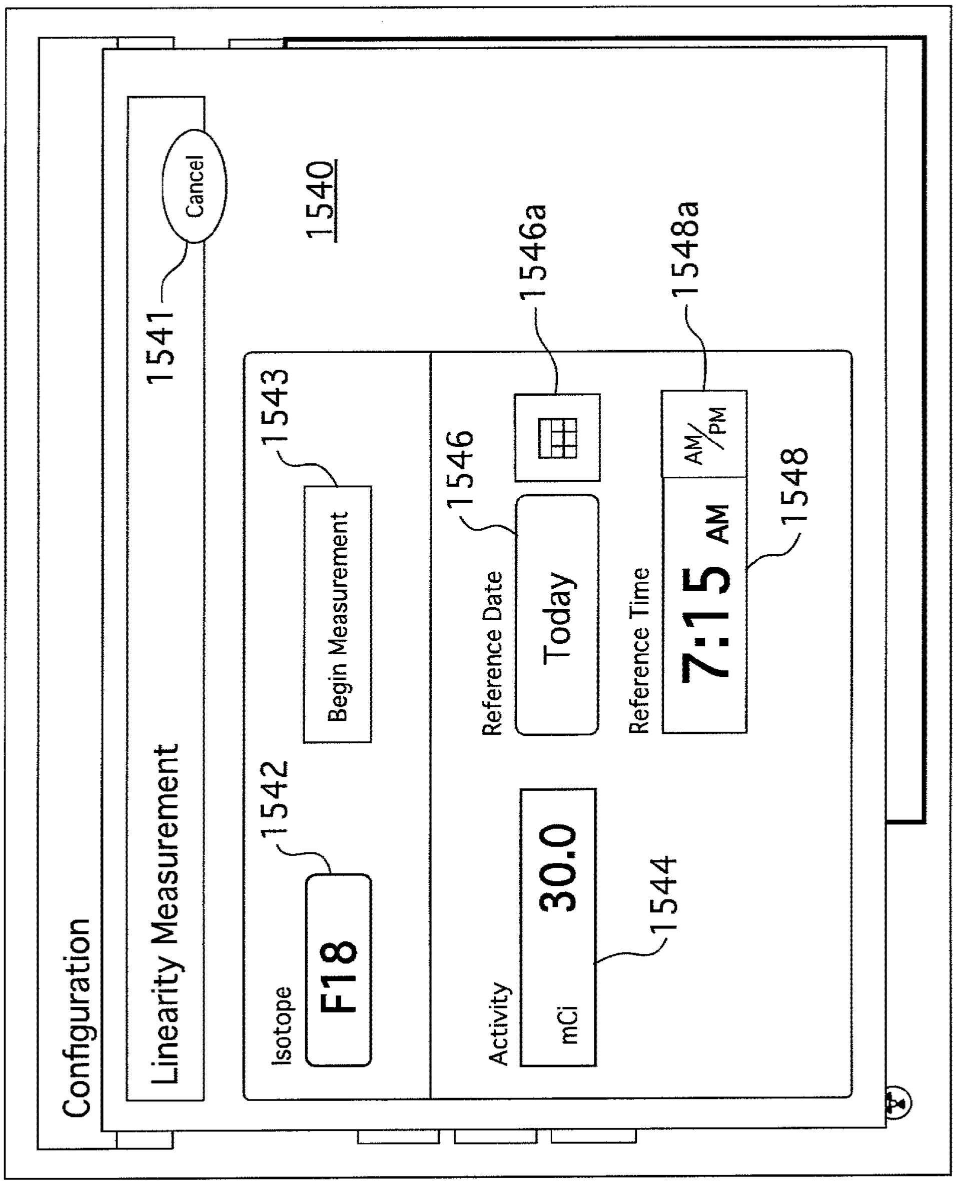

Configuration
Linearity Measurement
Cancel
1541
1540
Isotope
F18
1542
Begin Measurement
1543
Activity
mCi
30.0
1544
Reference Date
Today
1546
1546a
Reference Time
7:15 AM
1548
AM/PM
1548a

FIG. 44B

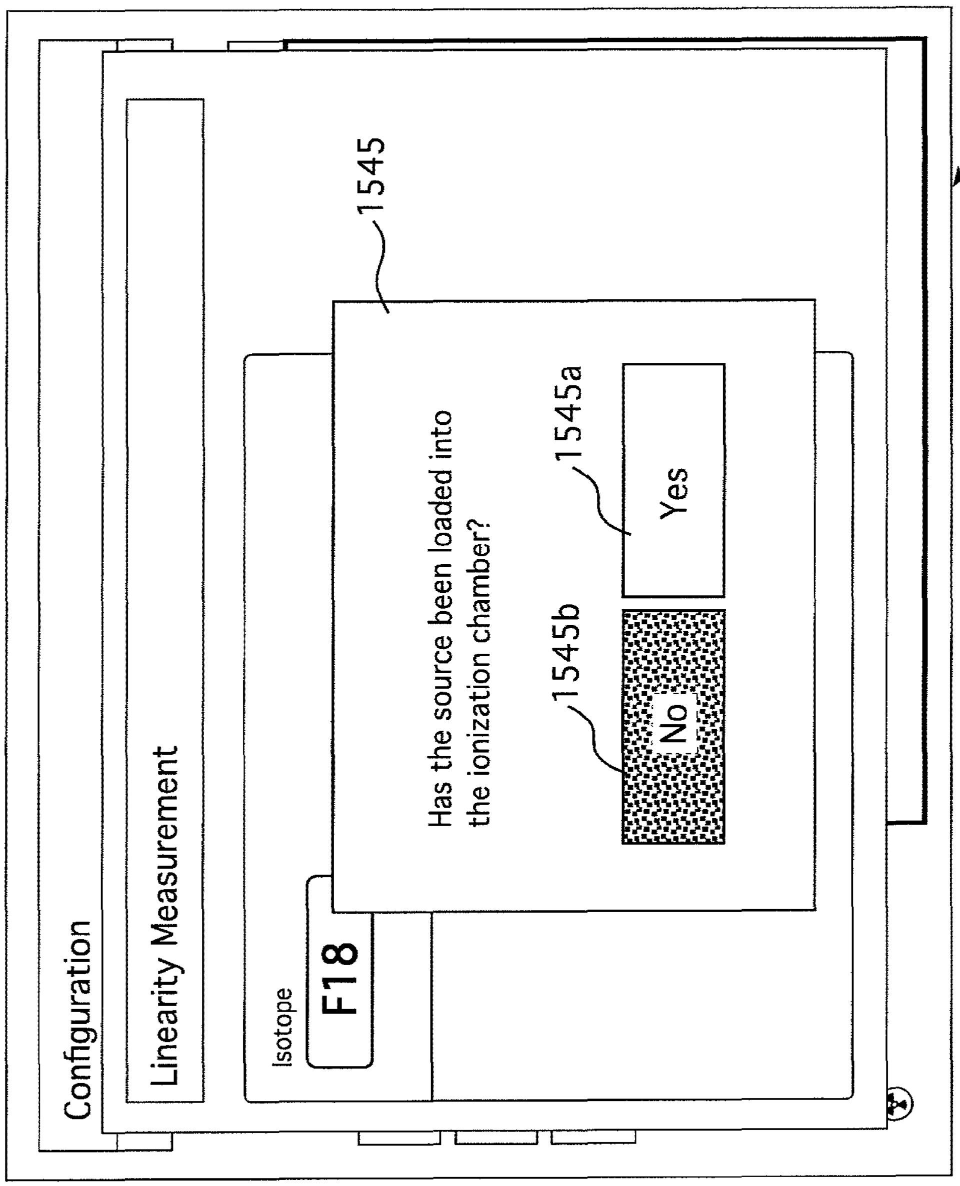

Configuration
Linearity Measurement
Isotope
F18
1545
Has the source been loaded into the ionization chamber?
1545a
Yes
1545b
No
1000

FIG. 44C

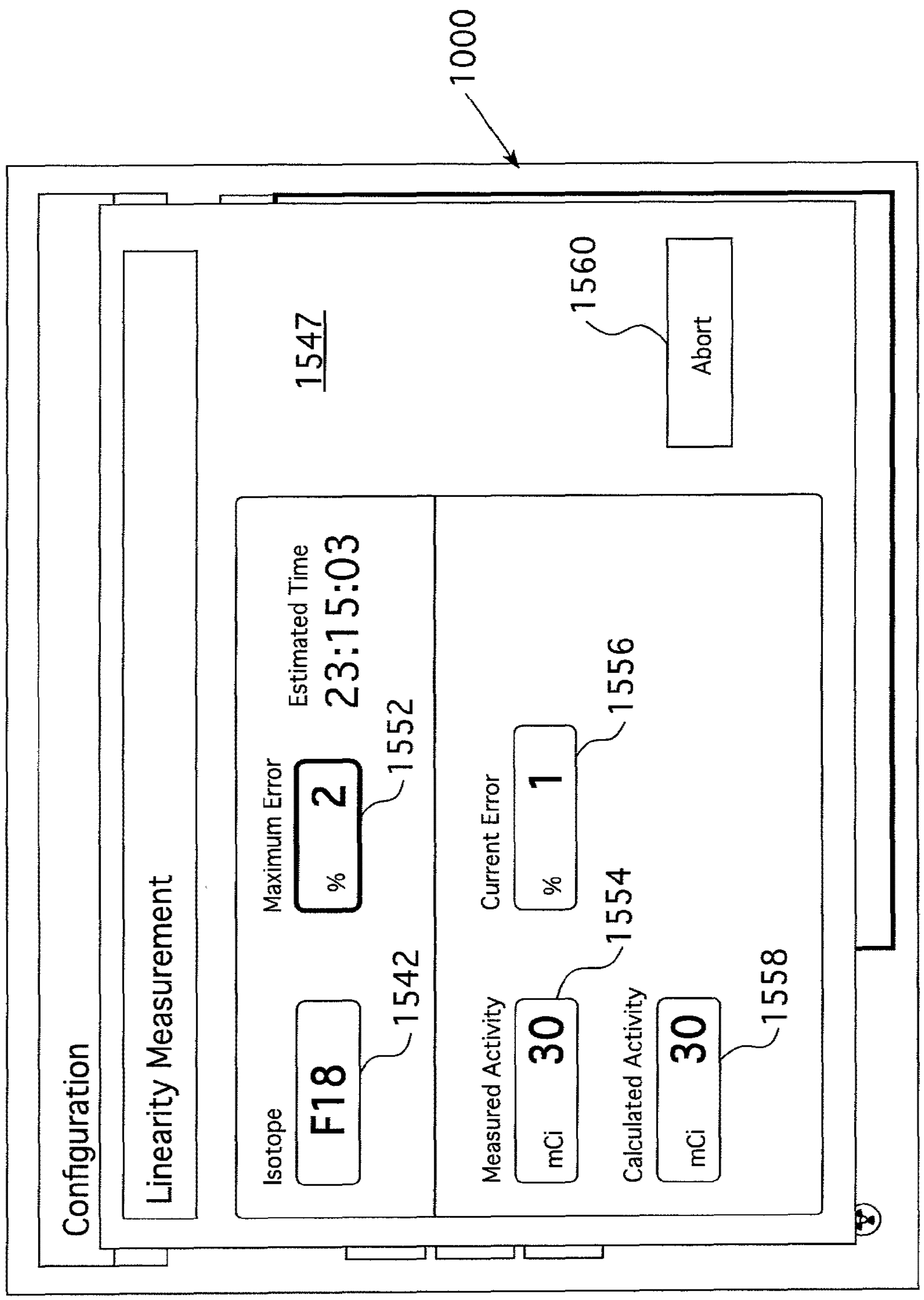

1000
Configuration
Linearity Measurement
1547
1560
Abort
Isotope
F18
1542
Maximum Error
%
2
1552
Estimated Time
23:15:03
Measured Activity
mCi
30
1554
Current Error
%
1
1556
Calculated Activity
mCi
30
1558

FIG. 44D

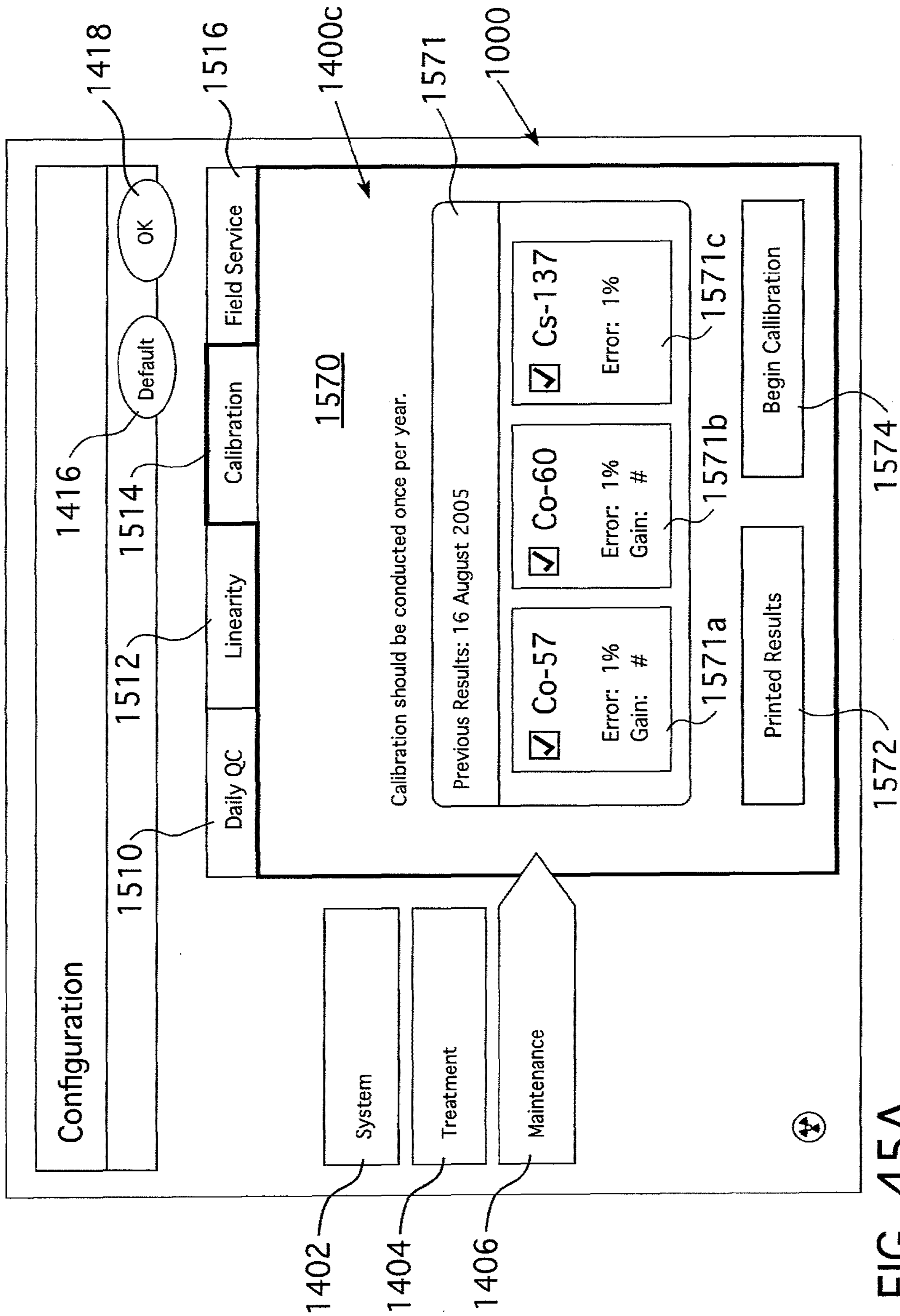

Configuration
Default
OK
Daily QC
Linearity
Calibration
Field Service
1570
Calibration should be conducted once per year.
Previous Results: 16 August 2005
Co-57
Error: 1%
Gain: #
Co-60
Error: 1%
Gain: #
Cs-137
Error: 1%
Printed Results
Begin Callibration
System
Treatment
Maintenance
1418
1416
1516
1514
1512
1510
1400c
1571
1000
1571a
1571b
1571c
1572
1574
1402
1404
1406

FIG. 45A

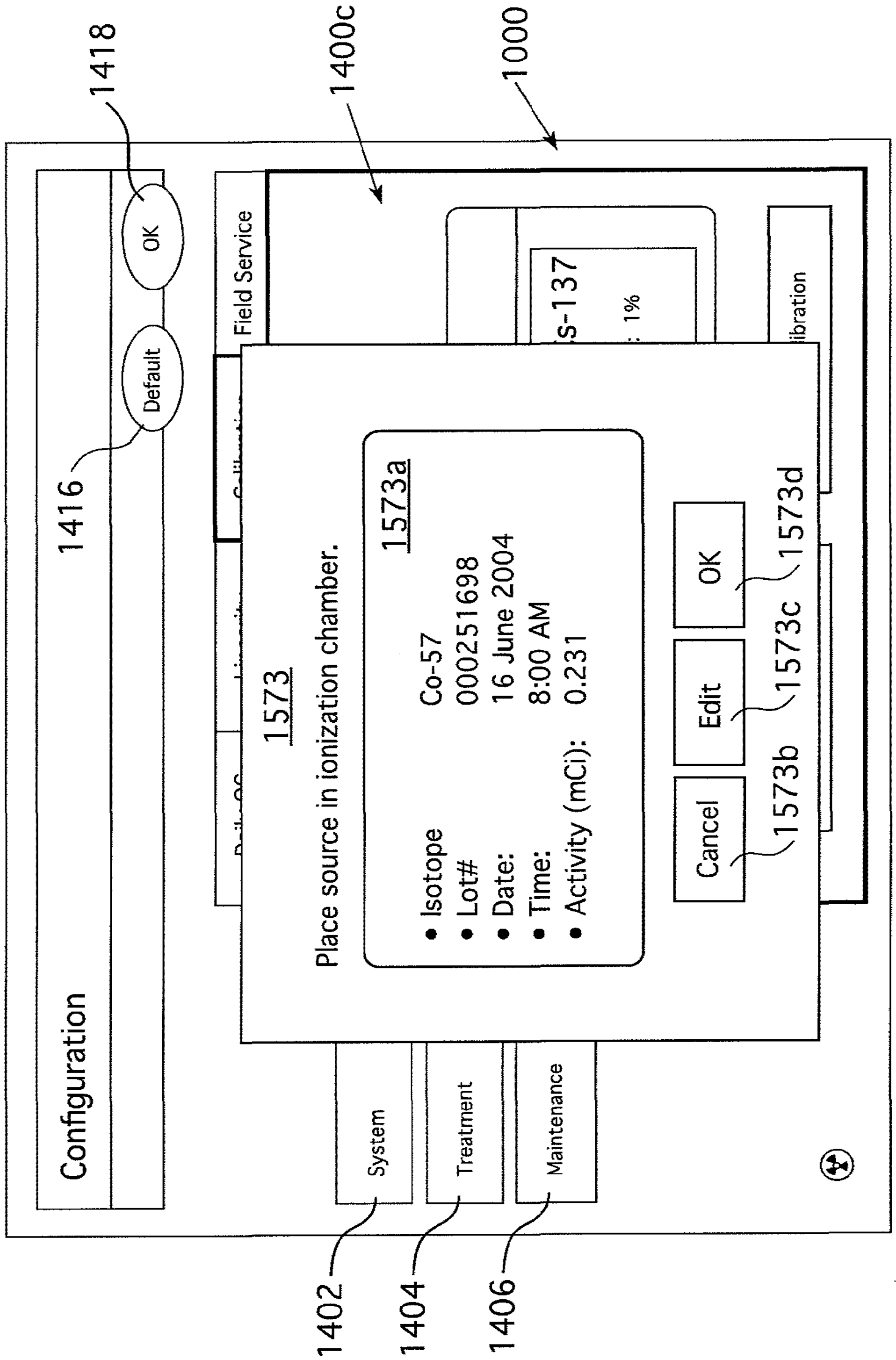

Configuration
OK
Default
Field Service
1418
1416
1400c
1000
s-137
1%
ibration
1573
Place source in ionization chamber.
1573a
• Isotope
• Lot#
• Date:
• Time:
• Activity (mCi):
Co-57
000251698
16 June 2004
8:00 AM
0.231
Cancel
Edit
OK
1573b
1573c
1573d
System
Treatment
Maintenance
1402
1404
1406

FIG. 45B

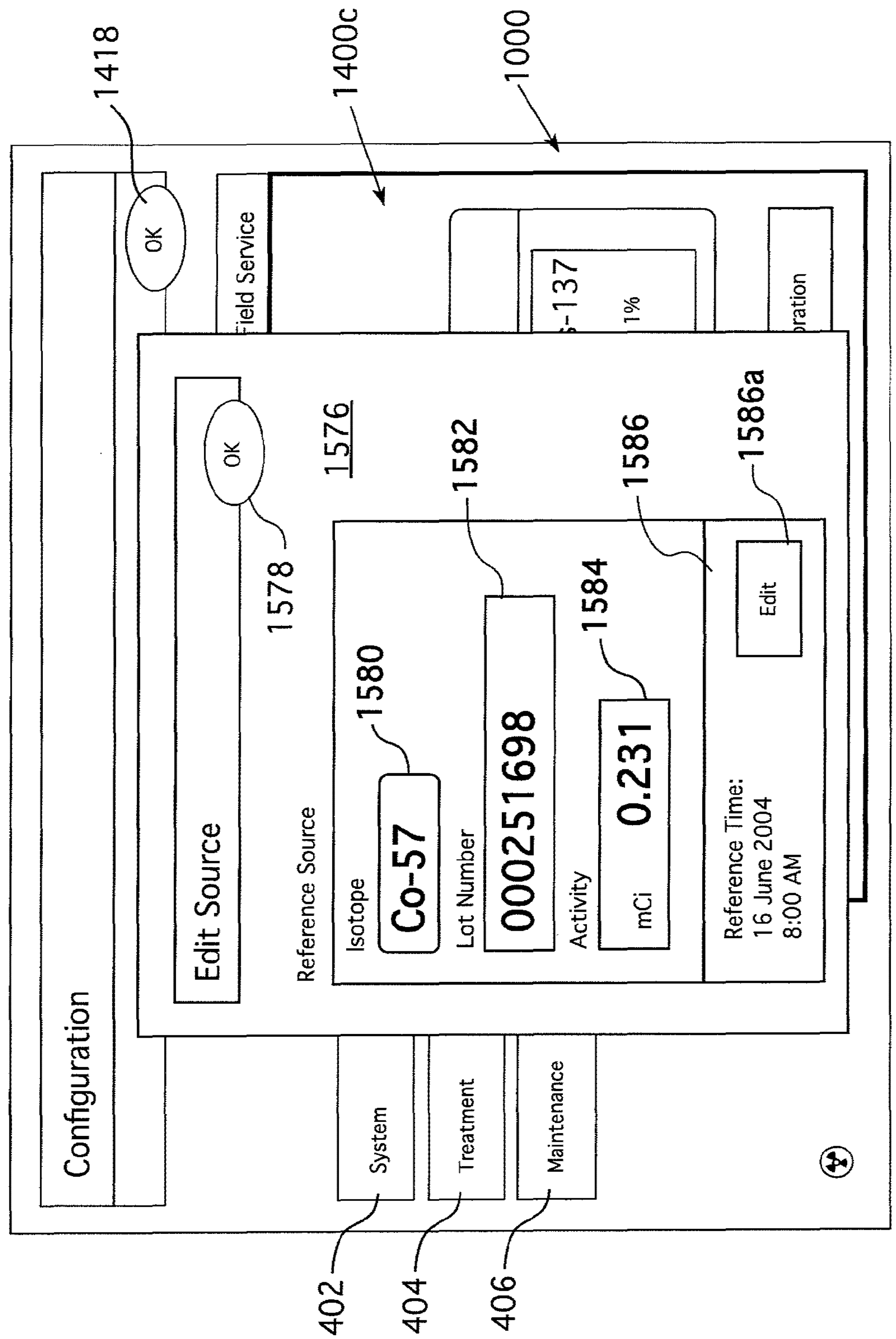

1418
1400c
1000
OK
Field Service
s-137
1%
ration
Configuration
Edit Source
OK
1576
1578
1580
1582
1584
1586
1586a
Reference Source
Isotope
Co-57
Lot Number
000251698
Activity
0.231
mCi
Edit
Reference Time:
16 June 2004
8:00 AM
System
Treatment
Maintenance
1402
1404
1406

FIG. 45C

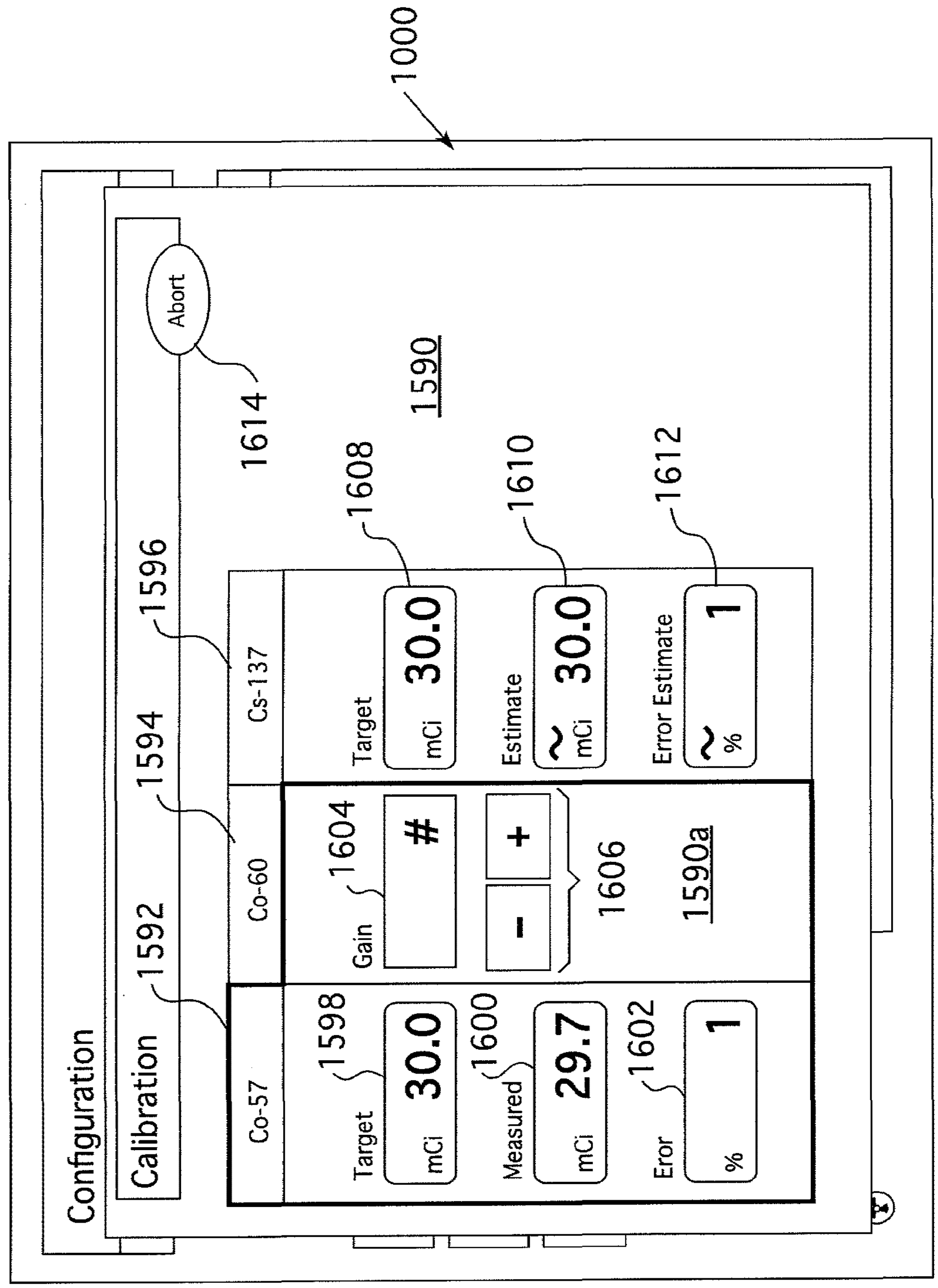

1000
Configuration
Calibration
Abort
1614
1590
Co-57
1592
Co-60
1594
Cs-137
1596
Target
1598
mCi
30.0
Measured
1600
mCi
29.7
Error
1602
%
1
Gain
1604
#
-
+
1606
1590a
Target
1608
mCi
30.0
Estimate
1610
~
mCi
30.0
Error Estimate
1612
~
%
1

FIG. 45D

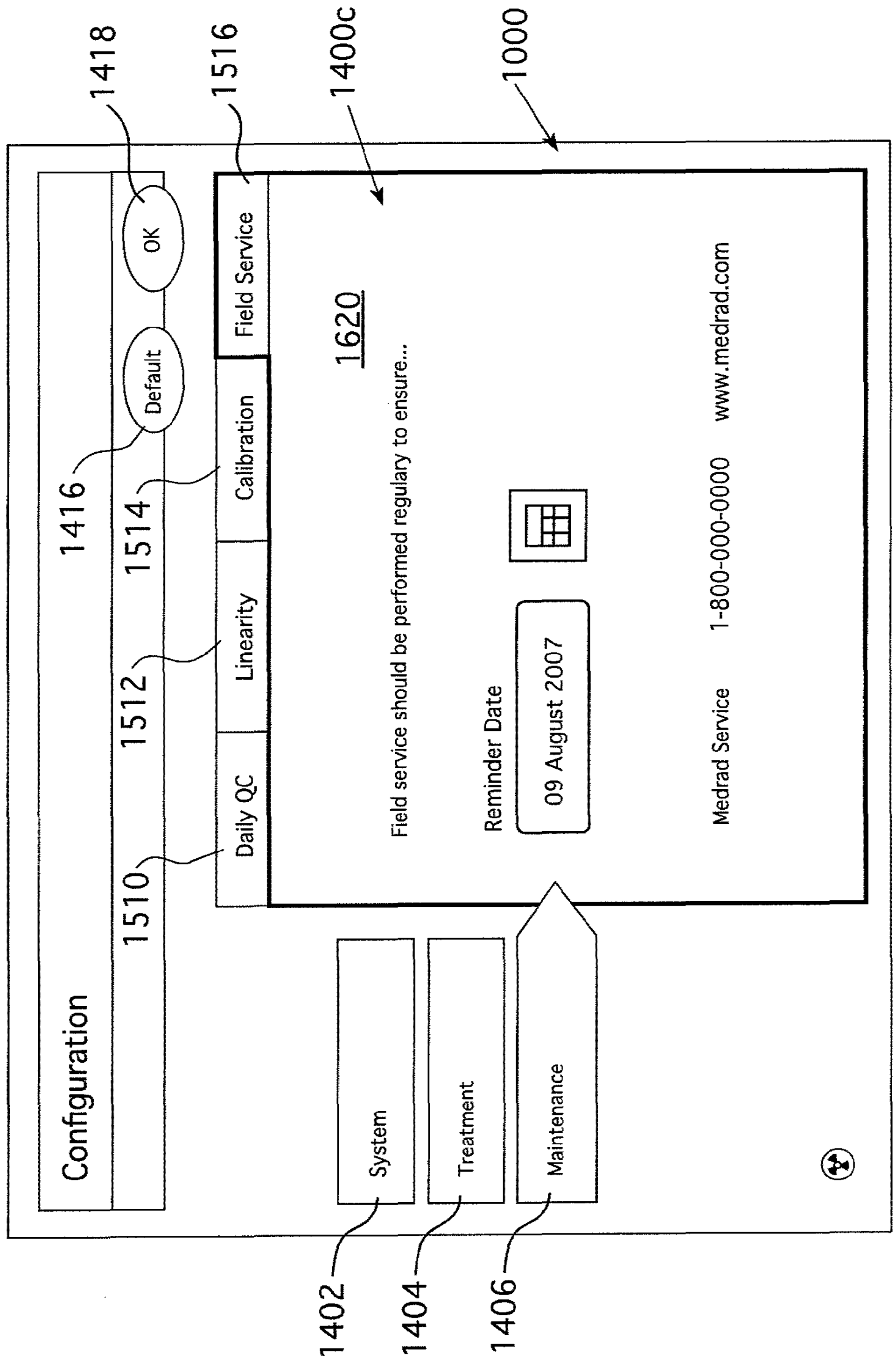

Configuration
OK
Default
Daily QC
Linearity
Calibration
Field Service
1620
Field service should be performed regulary to ensure...
Reminder Date
09 August 2007
Medrad Service
1-800-000-0000
www.medrad.com
System
Treatment
Maintenance
1418
1416
1516
1514
1512
1510
1400c
1000
1402
1404
1406

FIG. 46

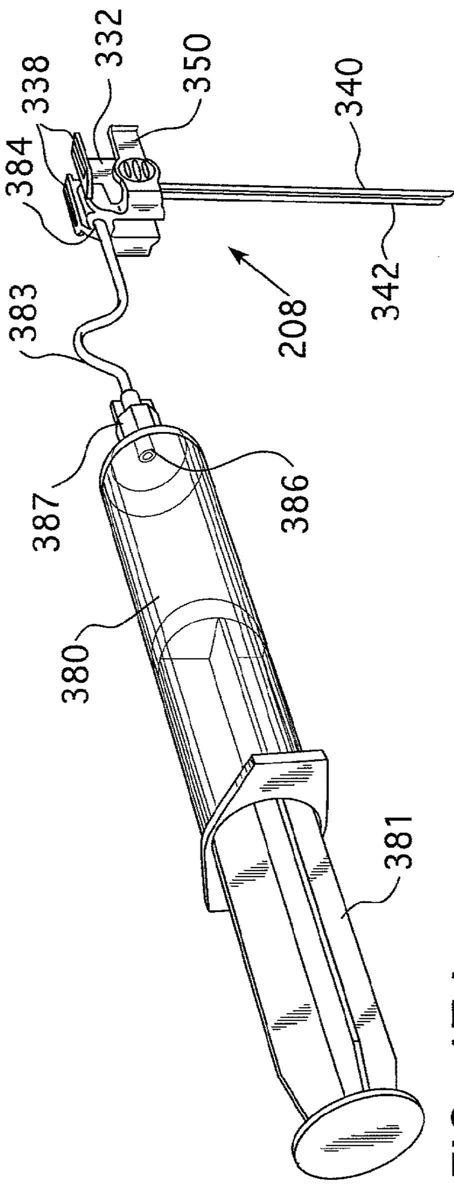


FIG. 47A

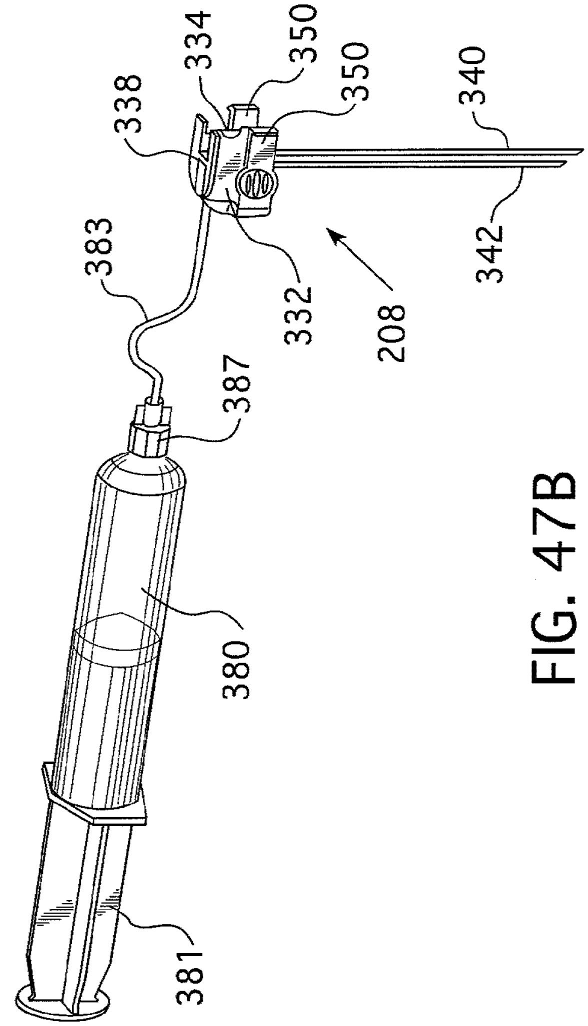


FIG. 47B

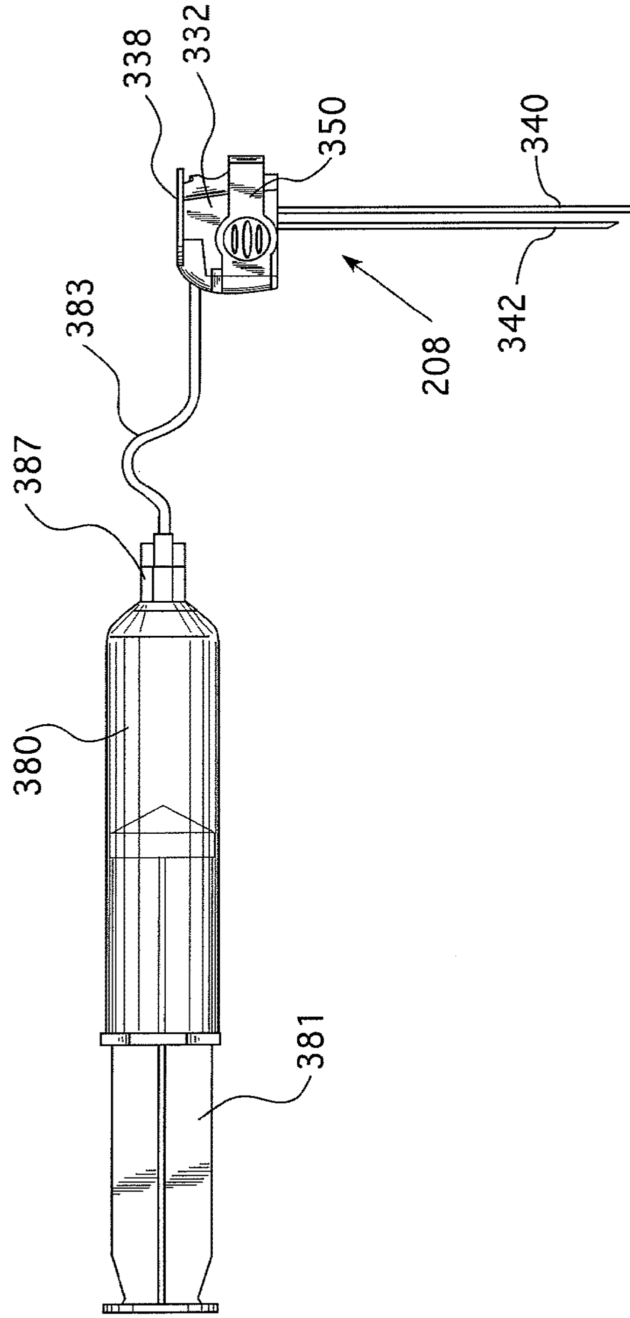


FIG. 47C

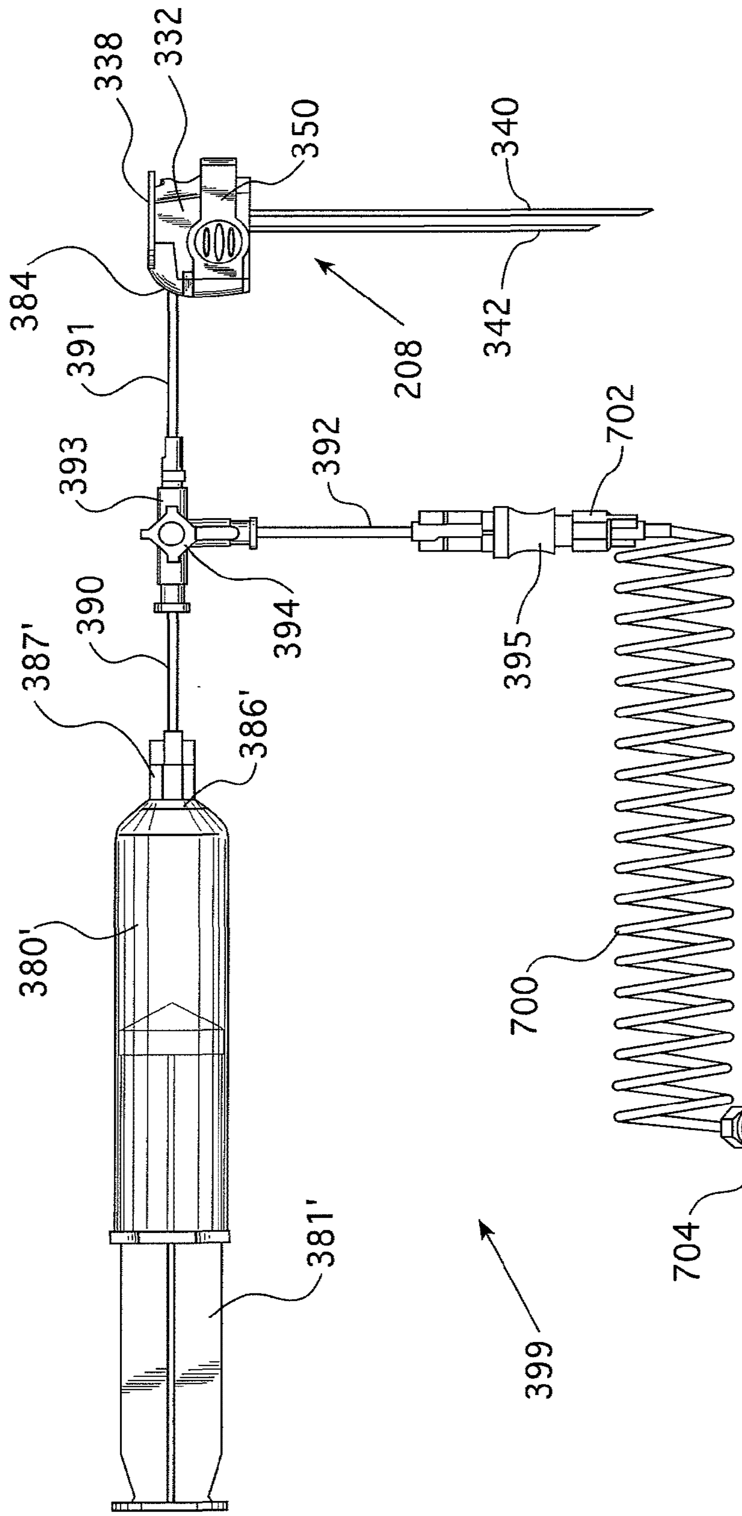

338
332
350
340
342
384
391
208
702
392
393
394
395
390
387'
386'
380'
700
704
381'
399

FIG. 48

(19) Europäisches Patentamt
European Patent Office
Office européen des brevets

(11) Publication number: **0 160 303**
A2

(12) EUROPEAN PATENT APPLICATION

(21) Application number: 85105293.6

(22) Date of filing: 30.04.85

(51) Int. Cl.[4]: **A 61 M 5/14**

(30) Priority: 01.05.84 US 605758

(43) Date of publication of application: 06.11.85 Bulletin 85/45

(84) Designated Contracting States: BE CH DE FR GB IT LI LU NL SE

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(54) Strontium-rubidium infusion system.

(57) This novel strontium-rubidium infusion system includes means for generating a solution containing Rubidium-82, measuring the radioactivity in the solution, and infusing it into a patient in order to perform various studies on the patient's heart. The new system includes a wash syringe which can be used by a physician to manually inject a bolus containing a large amount of radioactivity directly into a patient in order to perform first pass ventriculography studies.

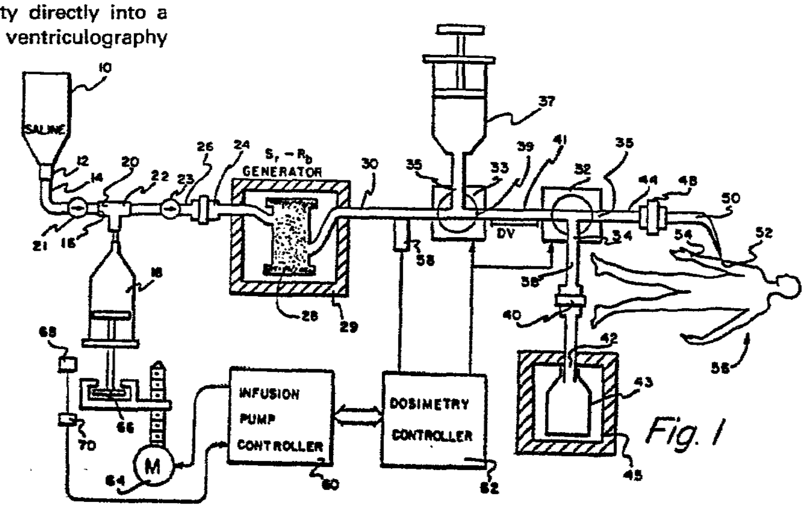


Fig. 1

Croydon Printing Company Ltd.

EP 0 160 303 A2

STRONTIUM-RUBIDIUM INFUSION SYSTEM

The present invention relates to a strontium-rubidium infusion system. More specifically, it relates to a strontium-rubidium infusion system which has an in-line, real time dosimetry system which can be used to infuse patients with Rubidium-82, particularly for first pass ventriculography studies. More precisely, the present invention provides a strontium-rubidium infusion system comprising:

(a) means for generating rubidium-82 in a solution which can be infused into a patient;

(b) means for collecting a predefined volume of solution containing rubidium-82;

(c) means for measuring the radioactivity present in said predefined volume before it is infused into said patient; and

(d) means for quickly infusing said predefined volume of rubidium-82 into said patient as a single bolus.

The present application is related to European Patent Application 84301269.1, entitled DOSIMETRY SYSTEM FOR STRONTIUM-RUBIDIUM INFUSION PUMP, filed February 27, 1984 and published September 5, 1984 under No. EP 0117752 A2.

Current statistics show that approximately one-third of all deaths in the United States are related to coronary artery disease. See, for example, Pohost, G., McKusick, K., and Strauss, W., "Physiologic Basis and Utility of Myocardial Perfusion Imaging", Proceedings of the Second International Symposium on Radiopharmaceuticals, Society of Nuclear Medicine, New York 1979, pp. 465-473. This fact has prompted extensive research to more efficiently diagnose and manage this disease. Recent advances in radiopharmaceutical development and instrument design have established myocardial scintigraphy as an important new approach for evaluating coronary artery disease and myocardial perfusion. See, for example, Pierson, R., Friedman, M., Tansley, W., Castellana, F., Enlander, D., and Huang, P., "Cardiovascular Nuclear Medicine: An Overview", Sem. Nucl. Med., 9, 224-240 (1979); Leppo, J., Scheuer, J., Pohost, G., Freeman, L., and Strauss, H., "The Evaluation of Ischemic Heart Disease Thallium-201 with Comments on Radionuclide Angiography"; Sem. Nucl. Med., 10, 115-126 (1980); Vogel, R., "Quantitative Aspects of Myocardial Perfusion Imaging", Sem. Nucl. Med., 10, 146-156 (1980); Chervu, R., "Radiopharmaceuticals in Cardiovascular Nuclear Medicine", Sem. Nucl. Med., 9, 241-256 (1979); and Pitt, B., and Strauss, H., "Cardiovascular Nuclear Medicine", Sem. Nucl. Med., 7, 3-6 (1977).

Myocardial scintigraphy studies have been performed with several isotopes of potassium, rubidium, cesium, and thallium (Tl-201), although the usefulness of all of these nuclides is limited by their non-optimal physical properties. In spite of its long half-life and low-gamma energy, Tl-201 is currently the most widely used agent for myocardial imaging. See, for example, Poe, N., "Rationale and Radiopharmaceuticals for Myocardial Imaging", Sem. Nucl. Med., 7, 7-14 (1977); Strauss, H. and Pitt, B., "Thallium-201 as a Myocardial Imaging Agent", Sem. Nucl. Med., 7, 49-58 (1977); Botvinick, E., Dunn, R., Hattner, R., and Massie, B., "A Consideration of Factors Affecting the Diagnostic Accuracy of Tl-201 Myocardial Perfusion Scintigraphy in Detecting Coronary Artery Disease", Sem. Nucl. Med., 10, 157-167 (1980); and Wackers, F., "Thallium-201 Myocardial Scintigraphy in Acute Myocardial Infarction and Ischemia", Sem. Nucl. Med., 10, 127-145 (1980).

In diagnostic procedures in which the heart is involved, it is desirable for a diagnostician to be able to view a patient's heart. Heretofore, various radioactive materials have been used together with radiological procedures for viewing internal organs of patients. It has been difficult, however, to view a heart, because the radioactive substances which could be used for viewing the heart have had a very long half-life. Thus, using them with patients has involved an element of danger and each use reduces the number of times that a patient could be infused within any given time period. It would, therefore, be desirable to have a diagnostic apparatus and procedure which could be used with relative safety for viewing the heart.

Rubidium-82 is a potassium analog. That means it acts in a manner similar to potassium when it is infused into a patient. Thus it builds up at a very rapid rate, i.e., within seconds, in the patient's heart. Rubidium-82 also has the advantage of having a very short half-life, approximately 76 seconds. Therefore, it decays after a very short period of time following entry into the body, thereby allowing numerous procedures to be performed within a relatively short time period in a given patient. Rubidium-82 also has the advantage of being observable using a modified gamma camera, such as a gamma camera of the type manufactured by Searle Radiographics, Inc., called the PHO Gamma IV. A problem with using Rubidium-82 in a patient involves measuring the amount of radiation infused into the patient. In view of the very short half-life of Rubidium-82, it has heretofore been impractical to measure the radioactivity of a particular dose and to then infuse it into the patient using conventional means. An accurate method for measuring the amount of radiation being infused into the patient would be highly desirable for this particular application.

The availability of improved instrumentation has stimulated interest in the use of the positron emitter, Rubidium-82, for myocardial imaging. See, for example, Beller G., and Smith, T., "Radionuclide Techniques in the Assessment of Myocardial Ischemia and Infarction", Circulation, 53 (3, Supp. 1) 123-125 (1976); Budinger, T., Yano, Y., Derenzo, S., et al., "Myocardial Uptake of Rubidium-82 Using Positron Emission Tomography", J., Nucl. Med. 20, 603 (1979); Budinger, T., Yano, Y., Derenzo, S., et al., "Infarction Sizing and Myocardial Perfusion Measurements Using Rb-82 and Positron Emission Tomography", Amer. J. Cardiol., 45, 399 (1980). Rubidium-82, an analog of the alkali metal potassium, is rapidly cleared from the blood and concentrated by the myocardium. The short half-life of the Rubidium-82 (76 sec) offers the unique advantage of permitting repeat perfusion and blood flow studies in patients whose clinical status is rapidly changing.

Rubidium-82 is produced by the decay of its parent, strontium-82. E. R. Squibb and Sons, Inc. has developed a Rubidium-82 generator and infusion system which yields an isotonic saline solution of Rubidium-82 at physiological pH for rapid administration. In animal experiments, the safety and myocardial uptake of Rubidium-82 has been demonstrated. Therefore, this agent has been selected as a candidate for clinical trials.

In the European patent application identified above, a system for infusing Rubidium-82 into a patient while measuring the dose going into the patient was described. That system is useful in myocardial scintigraphy studies. In a modification to that system, described herein, a system which permits both myocardial scintigraphy studies, as well as first pass ventriculography studies, is described.

In accordance with the present invention, a strontium-rubidium infusion system is described. The system includes means for generating rubidium-82 in a solution which can be infused into a patient. In particular, the strontium-rubidium generator, described above, is typically used. Generated rubidium-82 is then collected in a piece of tubing having a predefined volume. This tubing is called the "dose volume" tubing, and it contains the dose volume of rubidium-82 solution which is to be infused.

The system also includes means for measuring the radioactivity present in the dose volume before the dose volume is infused into the patient and a wash syringe for quickly infusing the dose volume into the patient as a single bolus.

In the Drawings:

FIG. 1 is an overall schematic diagram of the strontium-rubidium infusion system of the present invention;

FIG. 2 is a front view of the infusion pump control used with the strontium-rubidium infusion system;

FIG. 3 is a front view of the dosimetry control used with the strontium-rubidium infusion system;

FIG. 4 is a graph of radioactivity measured (on the y-axis) by the dosimeter probe versus time (on the x-axis);

FIG. 5 is a perspective view of the dosimetry probe;

FIG. 6 is a schematic diagram of the interface between the dosimetry probe of FIG. 4 and the dosimetry control circuitry;

FIG. 7 is a schematic diagram of the circuit for the Single Channel Analyzer used to convert and shape the raw pulses from the dosimetry probe of FIG. 4;

FIG. 8 is a schematic diagram of the circuit for the Multiply-Divide circuit used to carry out the formula which converts pulses from the Single Channel Analyzer into radioactivity present in front of the dosimetry probe;

FIG. 9 is a schematic diagram of one of the Display Controller circuits used to interface the switches and the displays to the other circuitry;

FIG. 10 is a schematic diagram of the Dose Rate circuit used to provide a display of the amount of radiation present in the eluate;

FIG. 11 is a schematic diagram of the Control Circuit which oversees the operation of the remainder of the circuitry; and

FIG. 12 is a schematic diagram of a valve driver circuit.

Referring now to FIG. 1, a saline bag 10 is connected, through a bullet nose fitting 12 and a piece of tubing 14, to a T-shaped two-way check valve 16 having three arms. A first arm 20 is attached to a one-way valve 21 which permits saline to enter the check valve 16, but does not allow it to exit back into the tubing 14. A second arm 22 includes a check valve 23 which permits saline to exit from the check valve 16 into a filter 24 through a tube 26, but does not allow it to re-enter the check valve 16 from the tube 26. An automatic syringe 18, connected to the check valve 16 fills from the saline bag 10 and pumps out through the tubing 26 into the filter 24. Saline pumped through the filter 24 enters a strontium-rubidium generator 28 which is of the type described more fully in U. S. Patent 4,405,716, issued September 27, 1983, entitled ^{82}RB GENERATING METHOD AND ELUENT. The generator 28 is preferably enclosed in a lead shield 29.

Saline pumped through the strontium-rubidium generator 28 exits the generator 28 through tubing 30 containing Rubidium-82. The tubing 30 is connected to a diverter valve 33 having a first arm 35 which connects to a manually operated wash syringe 37. The remaining arm 39 is connected to a diverter valve 32 through a length of tubing 41 which is called the "dose volume" tubing 41, which has a length, DV. The length, DV, of the dose volume tubing, times its cross-sectional area, gives its volume, hereinafter referred to as the "dose volume".

Diverter valve 32 has a first arm 34 which leads through tubing 38, an antibacterial filter 40, through a tube 42, and ultimately to a waste collection container 43. The waste collection container 43 is preferably enclosed in a lead shield 45. A second arm 35 of the diverter valve 32 is connected through tubing 44, an antibacterial filter 48, additional tubing 50, and into an infusion needle 52. The infusion needle 52 is typically inserted into the arm 54 of a patient 56.

In the preferred embodiment of the invention, the check valve 16 is a dual back check valve of the type made by Beckton Dickenson Inc., and the antibacterial filters 24, 40, 48 are of the type made by Schleicher & Schull as their type FP030/3.

In the operation of the device to perform first pass ventriculography studies, the amount of radioactivity in the saline eluted from the strontium-rubidium generator 28 must be measured. Accordingly, a dosimetry probe 58 is placed adjacent to the tubing 30 where it measures the radioactivity of the rubidium-containing saline as it enters the the diverter valve 33. The diverter valve 33 is a three-part valve which permits flow from either the generator to the diverter valve 32 or from the wash syringe 37 to the diverter valve 32.

The diverter valves 32, 33 are connected to a dosimetry controller 62 for automatic operation. The operation of the dosimetry controller 62 will be further explained hereinafter. Based upon the signal sent by the dosimetry controller 62 to the valves 32, 33, the elution from the generator 28 is directed through the valves 32, 33 and the dose volume tubing 41 into the waste container 43 until such time as the minimum dose rate is met. Once the minimum dose rate for a first pass study has been reached, the dosimetry controller 62 starts integrating patient volume and dose to fill the dose volume tubing 41 with highly radioactive eluate. At that point, the valve 33 is switched to open the valve between the dose volume tubing 41 and the wash syringe 37 and close the valve leading through tubing 30 to the generator 28. Similarly, the diverter valve 32 is switched from the waste position to the patient position, and the physician performing the study quickly injects saline from the wash syringe 37 directly into the patient 56. That operation performs a number of different functions. In particular, it pushes the dose volume of radioactive eluate from the dose volume tubing 41 into the patient as a single highly radioactive bolus. Thereafter, the remaining saline in the wash syringe 37 clears the lines 41, 44, 50, purging them of radioactivity.

An advantage of the wash solution clearing the patient line of radioactivity is that the line does not "glow" in photos taken of the patient. Such a glowing interferes with data from the patient. An advantage of using the manually operated wash syringe 37 is that it allows a high infusion rate, on the order of 300 milliliters per minute, rather than about 50 milliliters per minute which can be obtained through automatic operation. The dose volume line 41 is typically of a length such that, together with its diameter, it holds between 3 and 10 ccs of fluid. Accordingly, it could be 3 to 4 feet long. Because of the length of the dose volume line 41, the dose volume line 41 can be placed within a standard dose calibrator of the type normally used in such studies. Accordingly, while the probe 58 and associated electronics are used to determine when to switch the divertor valves 32, 33 and while the electronics of the present device can also be used to measure the dose which is to be infused into the patient 56, a standard dose calibrator can also be used in first pass ventricularography applications.

As will be explained hereinafter, the

present device can also be used in performing myocardial perfusion studies of the type described in the patent applications referred to earlier.

In order to use the infusion system, various procedures must be performed and controlled. In particular, the syringe 18 must be purged of air, and filled with saline, and the diverter valves 32, 33 must be positioned. These operations are contingent upon a number of factors including the total volume to be infused into the patient 56, the total dosage to be infused into the patient 56, the minimum radioactivity which must be present in the tubing 30 before any eluate is infused into the patient 56, the total volume to be infused (Note: The total volume eluted may differ from the total volume infused into the patient 56 as some volume is likely to be diverted to waste.).

The foregoing parameters may be altered from the front panel of two different controllers shown in FIGS. 2 and 3. These are the infusion pump controller 60 and the dosimetry controller 62, repectively. The infusion pump controller 60 controls the mechanical movement of the syringe's plunger 66 via a stepping motor 64 which is connected to the plunger 66.

In the preferred embodiment of the invention, the syringe 18 is a sterile, disposable plastic syringe of the type made by Sherwood Medical and designated as Part. No. 881-514031. The infusion pump controller 60 limits the movement of the syringe plunger 66 based upon optical limit detectors 68, 70 which limit the fully displaced and fully extended positions of the plunger 66, respectively. The volume control function performed by the infusion pump controller 60 is accomplished by counting the number of pulses sent to the stepping motor 64.

With reference to FIG. 2, the front panel of the infusion pump controller 60 is shown. The infusion pump controller 60 includes an on/off power switch 72 which is used to turn on the power to the unit.

A set of thumbwheel switches 74 is used to select the total volume (ml) to be eluted. An LED display 76 shows the total volume (ml) which has been eluted. A momentary contact push-button switch 78 is used to start and to stop the movement of the plunger 66 in the forward (inject) direction.

A set of push-button potentiometers comprise the Flow Rate Control 80 which is used to determine the volume per unit time which is infused. The Flow Rate Control 80 sets the pulse rate into the stepping motor 64. An LED 82 lights when the end of travel of the plunger 66, as indicated by the optical limit detectors 68, 70 is reached. A pair of momentary contact push-button switches 84, 86 are used to control the purge and refill functions, respectively, of the syringe 18. Thus, if the purge control switch 84 is pushed, and held, the plunger 66 continues to move in the forward direction until it reaches the forward limit detector 68. Similarly, while the refill control switch 84 is pressed and held, the plunger 66 continues to move toward the rear limit detector 70. The speed of movement of the plunger 66 during purge and refill operations are controlled by adjustable screw-type potentiometers 88, 90, respectively.

The infusion pump controller 60 is comprised of a Superior Electric Company STM103 Translator Module which is interfaced to provide signals representative of flow rate, volume eluted, and injection. It is also interfaced to be remotely controlled. A pulse called "INIT" indicates that the Translator Module has been powered. The "INIT" pulse is used to reset the displays on the dosimetry module. An "INJECT" signal indicates that the pump is injecting. Output pulses, corresponding to .1 ml steps of the syringe 18, are provided. An "End of Elution" signal is used to remotely disable the infusion pump controller 60.

With reference now to FIG. 3, the dosimetry controller 62, is comprised of a number of LED displays and thumbwheel switch sets. In addition, the dosimetry controller 62 includes an on/off switch 92 for providing power to the unit.

The first set of thumbwheel switches 94 is used to set the volume (ml) to be infused into the patient 56. The LED display 96, immediately above the thumbwheel switches 94, displays the volume of eluate which has been infused into the patient 56.

The thumbwheel switches 98 are used to set the total dose (mCi) which is to be infused into the patent 56 and the LED display 100 immediately above the total dose thumbwheel switches 98 displays the total dose which has been infused into the patient 56. Similarly, the thumbwheel switches 102 are used to set the dose rate (mCi/sec.) which is to be used to determine when to switch the diverter valve 32 from the waste position to the patient 56 position. The actual dose rate which is present in the eluate within the tube 30 in front of the dosimetry probe 58 is displayed on the LED display 104. The description of the dose present in the eluate at any given time from the start of infusion will be provided hereafter. The dosimetry controller 62 further comprises a pair of LED's 106, 108 which indicate the position of the diverter valves 32, 33. Only one of these two LED's 106, 108, should be on at any given time.

While the normal position of the diverter valves 32, 33 is toward waste from the generator 28, except when eluate is being manually infused into a patient 56, provision must be made to clear the tubing 44, 50 of any air prior to infusing a patient 56. Accordingly, the dosimetry controller 62 includes a toggle switch 110 which is used to hard wire the diverter valve 32 in the patient 56 position.

The present preferred embodiment of the invention also includes a set of thumbwheel switches 112 which are used to set the flow rate which will be used in internal calculations of dosimetry controller 62. It is presently anticipated by the inventor that a future version of the present invention will include automatic means for determining the flow rate based upon the settings used in the infusion pump controller 60.

Referring now to FIG. 4, a graph of the radioactive dosage present in the tubing 30 in front of the dosimetry probe 58, is shown. In the graph, the dosage is measured on the y-axis and time is measured on the x-axis. The time is referenced with zero being the time that the start/stop inject button 78 on the infusion controller 60 is pushed to commence infusion.

For approximately 10 seconds there will be no radioactivity present in the eluate from the strontium-rubidium generator 28. Thereafter, the dose rate rises at a rapid rate up to a maximum, after which the dose rate falls to a level value indicative of the steady state regeneration rate of the Sr-Rb generator 28. Thus, when the infusion starts, there is a delay initially as the dose rate builds up, a reduction in dosage after the generator 28 is partially eluted, and then there is a dosage representative of the steady state regeneration rate of the generator 28.

The setting of the dose rate thumbwheel switches 102 tells the dosimetry controller 62 at what point along the upward slope of the dosage curve to start integrating the patient volume (i.e., the volume in dose volume line 41 which will be infused into the patient 56) and the patient dose. At that point the dose indicated by the LED's 100 will start accumulating from zero, where it had been until that point. Similarly, the patient 56 volume indicated by the LED's 96 will start to accumulate as of that time.

Once highly radioactive eluate is infused into the dose volume line 41 it continues to be infused until one of various stop indications occurs. In particular, when the total patient 56 dose, set by the thumbwheel switches 98, is reached, the diverter valve 32 is opened to the patient position, diverter valve 33 is closed from the generator 28 and opened to the wash syringe 37, and the stepping motor 64 stops, thereby preventing further infusion. Similarly, the diverter valves 32, 33 are switched, and the stepping motor 64 is stopped when the patient volume 96, preset by the thumbwheel switches 94 reaches its preset value or after the total volume to be eluted, set by the volume thumbwheel switches 74 reaches its preset value; or when the purge limit optical stop 68 of the syringe 18 is reached; or if the start/stop inject button 78 is pushed. Any of the foregoing events causes the diverter valves 32, 33 to switch, and causes the stepping motor 64 to stop. Note, however, that the purge and refill switches 84, 86 are disabled as of the time that the start/stop inject button 78 is pushed to commence the infusion.

Quantizing Radioactivity in a Liquid Stream

In order to measure the radioactivity in the saline solution which passes through the line 30 in front of the dosimetry probe 58, it is necessary to count the number of disintigrations which occur in front of the probe 58, while at the same time keeping track of the flow rate of the saline through the tube 30. Given that these quantities are known, it is possible to measure the total activity in milliCuries (mCi) in accordance with the following formula:

$$A = \frac{(C)(F)}{(V)(E)(CM)(Y)}$$

Where, A = total activity (mCi);
C = net counts;
F = flow rate (ml/min);
V = volume in detector view (ml);
E = net efficiency (counts per minute/disintegration per minute);
CM = disintegrations/minute to milliCurie conversion factor; and
Y = net yield of photon.

In the case of the present invention, the above formula can be simplified to:

$$A = \frac{(C)(F)}{K}$$

Where, A = total activity (in milliCuries);
C = net counts (from probe);
F = the flow rate; and
K = the calibration factor.

As noted, the calibration factor, K, takes into account the volume in the detector's view, the net efficiency of the probe, the conversion factor in terms of disintigrations per minute to milliCuries, and the net yield of photons. These factors are substantially constant for any given probe and tubing combination for a reasonable amount of time. Accordingly, provision is made on the circuit board to adjust the calibration factor, K, when the instrument is serviced. However, the calibration factor, K, is not user adjustable in the normal course of operation.

Dosimetry Probe

Referring now to FIG. 5, the dosimetry probe 58 is comprised of a photomultiplier tube 120, such as the RCA C83009E 14 mm diameter 10-stage photomultiplier tube manufactured by the Electro Optics Division of RCA Corporation in Lancaster, Pennsylvania. The photomultiplier tube 120 has a face 122 through which input signals in the form of light are received. On the face 122, a plastic scintillator 124, such as a Nuclear Enterprises Type 102A manufactured in Edinburgh, Scotland, is mounted. In the preferred embodiment of the invention, the plastic scintillator 124 is glued or bonded to the face 122 of the photomultiplier tube 120. After the plastic scintillator 124 has been bonded to the face 122 of the photomultiplier tube 120, an aluminum foil covering (not shown) is placed over the face end of the photomultiplier tube 120, including the plastic scintillator 124. The purpose of the aluminum foil covering is to reflect back into the tube 120 any light which scintillates from the plastic scintillator 124 away from the tube 120. In addition, the aluminum foil covering prevents any stray light which might come into the area of the face 122 from getting into the tube 120. Following the application of the aluminum foil, a light tight material, such as black electrical tape is wrapped over the aluminum foil covered tube 120 in order to further prevent any light from entering into the tube 120. The tape-wrapped tube 120 is then inserted into a mu metal shield 126 which is intended to prevent any electromagnetic radiation effects from affecting the output of the dosimetry probe 58. In the preferred embodiment of the invention, the dosimetry probe 58 is plugged into a standard photomultiplier tube socket base 128 containing a standard resistive biasing network.

Dosimetry Circuitry

Referring now to FIG. 6, the photomultiplier tube socket base 128 includes a resistive network containing biasing resistors for placing appropriate bias voltages on the ten dynodes in the photomultiplier tube 120. Accordingly, the high voltage connection to the photomultiplier tube base 128 is automatically biased to provide appropriate operating voltages to the photomultiplier tube 120. The high voltage supply 130 used in the preferred embodiment of the invention is a 0-1000 volt, adjustable Bertan PMT-10A-P power supply manufactured by Bertan Associates, Inc., Three Aerial Way, Syosset, New York. In the present application, the high voltage supply 130 is adjusted to provide an output voltage of 950 volts. The photomultipler tube socket base 128 is an RCA photomultipler tube socket base, Part No. AJ2273.

An output signal goes from the dosimetry probe 58 on a line 132 to a coupling network comprising a pull up resistor 134, a coupling capacitor 136, and a output resistor 138. Accordingly, an AC signal having a peak to peak maximum of approximately 250 millivolts with negative going pulses, is provided on output line 140.

Single Channel Analyzer

Referring now to FIG. 7, the schematic diagram for a Single Channel Analyzer circuit is shown. The Single Channel Analyzer is used, because the pulses on output line 140 from the Dosimetry circuitry are very sharply defined pulses which may occur at very high frequencies. In view of the fact that it is important to count all the pulses, a very high speed comparator, such as an AM685 voltage comparator 142, manufactured by Advanced Micro Devices, 901 Thompson Place, Sunnyvale, California, with emitter-coupled logic (ECL) output, or other suitable very high speed comparator, must be used.

A biasing network 141 consisting of a series of resistors and capacitors is used as one input to the comparator 142. In view of the fact that the pulses which are handled by the comparator 142 are of very short duration, a one-shot circuit 144, comprised in the preferred embodiment of the invention, of a Motorola Type 1670 master-slave flip-flop integrated circuit, is used to stretch the pulse width up to a uniform pulse width of approximately 50 nanoseconds. The output signal from the one-shot 144 is fed into a programmable divide-by-N circuit 146, which in the preferred embodiment of the invention is comprised of a Motorola Type 10136 universal hexadecimal counter integrated circuit. The divide-by-N circuit 146 is programmable. Accordingly, a very high pulse repetition rate coming into the comparator with very short pulse widths is reformed by the one-shot to have wider, uniform pulses, and the input signal is further reformed by the divide-by-N circuit to bring the pulse repetition rate down into any desirable range. In particular, outputs of the divide-by-N circuit 146 are provided for N equal to 2, 4, 8, and 16.

Up through this point in the circuit, the devices have all been of ECL type in order to be able to handle the very high speed pulses which are detected by the dosimetry probe 58. In view of the fact that it is conventional to use transistor-transistor-logic (TTL) integrated circuits, a type 10125 ECL-to-TTL level converter circuit 150 is hooked to the output of the divide-by-N circuit 146. Thus, the ECL-to-TTL level converter circuit 150 transforms the ECL signal levels into TTL signal levels for further processing. The TTL outputs leave the ECL-to-TTL level converter circuit 150 on four lines 152, 154, 156, 158, which correspond to the TTL level of the counts into the Single Channel Analyzer divided by 2, 4, 8, and 16, respectively. The counts out on the lines 152-158 will be referred to hereafter as the "net counts".

Multiplier-Divider Circuit

Referring now to FIG. 8, there is a Multiplier-Divider circuit 160 which converts the net counts from the Single Channel Analyzer circuit, described above, into a meaningful quantity (milliCuries). The Multiplier-Divider circuit 160 accepts the "net counts" on an input line 162 which is connected to one of the lines 152-158 from the Single Channel Analyzer (i.e., the raw counts converted into TTL levels and then divided by 2, 4, 8, or 16) and multiplies them by the eluate Flow Rate divided by 100. The result is then divided by a constant, K, in order to carry out the formula:

$$A = \frac{(N)(F)}{K}$$

Where, A = total activity (in milliCuries);
N = net counts (from Single Channel Analyzer);
F = Flow Rate; and
K = the calibration factor.

The net counts, N, are first multiplied by a two digit number corresponding to the eluate Flow Rate (entered on the Flow Rate thumbwheel switches 112A, 112B, corresponding to the most significant digit (MSD) and the least significant digit (LSD), respectively, the thumbwheel switches 112A, 112B are on the front panel of the dosimetry controller 62, shown in FIG. 3. The multiplication is accomplished by cascading two TTL Synchronous Decade Rate Multiplier circuits (F74167), and sending their outputs through a NAND gate 168. The resulting output corresponds to F_{out}, where:

$$F_{out} = \frac{(N)(F)}{100}$$

The output pulses are of varying duration, so they are next fed through a pair of one-shots which process them to have a fixed duration. In the preferred embodiment of the invention, the first one-shot is comprised of one-half of an SN74123 integrated circuit 170. The first one-shot is negative edge triggered, and it provides a pulse output of approximately 200 nanoseconds. Its output is double buffered through buffers 172, 174 into a second one-shot which is comprised of one-half of a CD4098BE integrated circuit 176 in order to increase the width of the output pulses, so they will be acceptable to a CMOS divider integrated circuit 178. The second one-shot is configured to be leading edge triggered.

The output of the second one-shot is then divided by the calibration factor, K, which may have a range of between 3 and 9,999. A CD4059A integrated circuit 178 is used as a programmable divide-by-N counter. Programming is accomplished via a series of 16 DIP switches 180 mounted on the printed circuit card. Each set of four switches corresponds to the BCD settings for 1's, 10's, 100's and 1000's. Pull up resistors (not shown) are employed in the standard manner so that when the DIP switches are open the inputs to the divide-by-N circuit 178 are pulled high.

The output of the divider 178 has pulses of random widths, so another one-shot, made up of the second half of the CD4098BE 176 configured for leading edge triggering, is used. This one-shot provides an output pulse duration of approximately 20 microseconds. Before leaving the Multiplier-Divider circuit 160, the output is double buffered through buffers 182, 184 and the output signal on line 186 is sent to the Dose Rate circuit. There will be one dose corrected output pulse on line 186 for each 0.01 milliCurie of activity which passes by the dosimetry probe 58.

Display Controller Circuit

Referring now to FIG. 9, the schematic diagram for a Display Controller Circuit 190 is shown. There are three Display Controller Circuits within the dosimetry controller 62. Each Display Controller 190 is used both to interface a set of thumbwheel switches 192 and to display the quantity associated with the particular set of thumbwheel switches 192. Thus, there is one Display Controller of 190 for Dose Rate (which works with thumbwheel switches 102 and LEDs 104), one for Patient Volume (which works with thumbwheel switches 94 and LEDs 96), and one for Dose (which works with thumbwheel switches 98 and LEDs 100). Each Display Controller Circuit 190 drives four seven-segment displays 194, such as MAN71 displays.

The major component of the Display Controller Circuit 190 of the preferred embodiment of the invention is an Intersil ICM7217IJI integrated circuit 196, which is a device which provides a direct interface to the seven-segment displays 194. Each Display Controller Circuit 190 allows the user to set a level, by programming binary coded decimal (BCD) thumbwheel switches 192. The levels can then be detected. In this way, a preset limit for Dose, for example, will be detected and will be used to shut down the infusion pump. For Dose Rate, the preset level is used to switch the position of the diverter valve 32, through the valve driver circuit which will be explained hereinafter. The Patient Volume can also be preset, and the infusion pump can be stopped at the preset limit.

Dose Rate Circuit

The Dose Rate circuit 200, shown in FIG. 10, provides a visual display of the amount of radiation present in the eluate. The Dose Rate circuit 200 employs a Display Controller Circuit, of the type described above. The Dose Rate display is constantly updated to provide the user with Dose Rate information. The Dose Rate circuit 200, with the Display Controller, is programmed to set a trigger level for switching the eluate from waste to the patient 56.

The Dose Rate circuit 200 uses signals from the Multiplier-Divider circuit 160, described above, and from the Control Board which will be described hereinafter. The dose corrected output pulses on line 186 from the Multiplier-Divider circuit 160 described above (i.e., 1 pulse/.01/mCi) enter the Dose Rate circuit 200, and are double buffered by buffers 202, 204. The buffered pulses are then fed through one-half of a one-shot 206, comprised of a CD4098BE integrated circuit in the preferred embodiment of the invention. The output from the one-shot 206 is gated through NAND gate 207 to the Dose Rate Display 104 since there are three Display Controller Circuits 190, which are used for Dose (circuit "A"), Dose Rate (circuit "B"), and Patient Volume (circuit "C"), the designation "B10" at the output of NAND gate 207 means pin 10 on input connector 197 (see FIG. 9).

The heart of the Dose Rate circuit 200 is an Intersil ICM7207A Oscillator Controller integrated circuit 208. This unit, along with a dual one-shot comprised of a CD4098BE integrated circuit 210, in the preferred embodiment of the invention, provides all of the control necessary for gating, storing, and resetting the display.

The outputs of the Dose Rate Display Controller Circuit provide an easy interface to determine when a predetermined count (corresponding to the dose rate which was set on thumbwheel switches 102) has been reached, and to generate a signal which is used to enable the Dose and Patient Volume Displays, 100, 96, respectively.

In the preferred embodiment of the invention, the signal utilized to enable the Dose and Patient Volume Displays 100, 96, respectively, is derived from one half of a dual D-type flip-flop, such as a CD4013BE integrated circuit 212. The flip-flop 212 is only enabled during an injection. The enabling "INJECT" signal is generated when the pump is injecting. Once an injection is started and a user pre-set Dose Rate limit set on thumbwheel switches 102 is met, the flip-flop 212 latches a positive Q output to enable the Dose Display and the Patient Volume Display.

Control Circuit

Referring now to FIG. 11, the schematic diagram of the Control circuit 220 is shown. The purpose of the Control circuit 220 is to "oversee" all other operations. Specifically, the Control circuit 220 controls the Dose Display and Patient Volume Display. The Control circuit 220 also provides timing for resetting the Multiplier-Divider circuit 160, and it buffers various inputs and outputs to and from the infusion pump control module 60.

The basic function for turning the infusion pump off is the End of Elution signal. The End of Elution signal is derived from either the Dose Display 100 or the Patient Volume Display 96.

These displays 100, 96 are gated to begin counting once the Dose Rate trigger level, the Q output from flip-flop 212, reaches its preset limit, as defined by the Dose Rate thumbwheel switches 102. Then, once the Dose or Patient Volume is met, as defined by the Dose thumbwheel switches 98 and by the Patient Volume thumbwheel switches 94, respectively, the Control circuit 220 signals the pump to stop.

Valve Driver Circuit

The Valve Driver circuit 230, shown schematically in FIG. 12, is used to control the switching of the diverter valves 32, 33 which direct the eluate either to the patient 56 or to waste. The Valve Driver circuit 230 accepts its input from the infusion pump controller or from the Patient Line Purge Switch 110. The Patient Line Purge Switch 110 directly controls the valves 32, 33.

The diverter valves 32, 33 are two position valves which include electrical switches which close individually when the valves 32, 33 are fully in one of their two positions, i.e., either the patient or waste position for valve 32. Movement of the valves 32, 33 from one position to the other is controlled by an AC motor which includes two windings. When the first winding is energized, the motor moves in a clockwise direction. When the second winding is energized, the motor moves in a counterclockwise direction. In the preferred embodiment, one motor controls both diverter valves 32, 33. At each limit of the valves' movement, there is a microswitch 232, 234 which senses when the valve limit has been reached.

When one of the microswitches 232, 234 is open, i.e. switch 232, the input to an associated inverter 236 is essentially at ground. When the switch 232 closes, the input to the inverter 236 increases to approximately five volts. After the switch 232 again opens, it takes some time, due to the RC time constant of the associated resistors and capacitor, before the voltage at the input of the first inverter 236 returns to approximately zero. Accordingly, the combination of inverters and the RC network to which each of the switches 232, 234 are connected acts as a switch debouncer. Thus, the output of inverter 238 will be low when switch 232 is closed and high when switch 232 is opened. Similarly, the output of inverter 240 will be low when switch 234 is closed and high when switch 234 is opened.

NAND gate 242 normally has a high output voltage. Accordingly, as will be obvious to those of ordinary skill in the digital circuitry art, LED 106 will be on when switch 232 is closed. Otherwise, LED 106 will be off. Similarly, LED 108 will be on when switch 234 is closed. Note that these LEDs 106, 108 were previously described with reference to the dosimetry controller 62 (See FIG. 3).

When both switches 232, 234 are opened at the same time, there will be two high signals at the input of NAND gate 254. That will cause NAND gate 256 to trigger a monostable multivibrator comprised of one half of a CD4098BE integrated circuit 258 which provides a low going output pulse having a duration of approximately 700 milliseconds in the preferred embodiment of the invention. The particular time period during which this pulse is low must exceed the time period which it would take for the diverter valves 32, 33 to be moved from one position to the other position. In the preferred embodiment of the invention the movement of the diverter valves 32, 33 takes approximately 600 milliseconds. The outputs from the monostable multivibrator are fed via EXCLUSIVE OR gate 260 into a D-type flip-flop 262 comprised of a CD4013BE integrated circuit. In the event that the diverter valves 32, 33 did not move from one position to the other within the prescribed time period, it is presumed that a fault condition occurred, e.g. one of the diverter valves 32, 33 jammed. Accordingly, the operator is advised of the fault condition by both LEDs 106, 108 flashing simultaneously. The flashing occurs as a result of the output of the flip-flop 262 which is connected on line 264 to NAND gate 242 being kept high, thereby causing NAND gate 242 to act as an astable multivibrator which oscillates between high and low outputs thereby causing the EXCLUSIVE OR gates 248, 250 to change states and to flash the LEDs 106, 108.

At the same time that one output of the flip-flop 262 goes high, the other output, on line 266 goes low. The signal on line 266 is normally high, as it is one input to NAND gate 268. The other input to NAND gate 268 is the "End of Elution" signal previously discussed. When both inputs to NAND gate 268 are high the output on line 270 is high. The output signal on line 270 turns off the infusion pump when it is low. This is the signal which remotely controls the infusion pump, as heretofore described. Thus, in the fault condition, when the signal on line 266 goes low the infusion pump is turned off. When there is no fault condition, the infusion pump will be enabled when the End of Elution signal is high.

The "INJECT" line which indicates when the pump is injecting enters the Valve Controller Circuit 230 on line 252. A series of inverters are used to buffer the INJECT signal in order to obtain an output on line 253. The output on line 253 is used as the input to a pair of solid state relays (not shown) which select between the two windings of the motor which drives the diverter valves 32, 33. Thus, when the INJECT line is low the motor drives the diverter valves 32, 33 into the Patient position, and when the INJECT line is high, the motor drives the diverter valves 32, 33 into the Waste position.

What we claim is:

1. A strontium-rubidium infusion system comprising:

(a) means for generating rubidium-82 in a solution which can be infused into a patient;

(b) means for collecting a predefined volume of solution containing rubidium-82;

(c) means for measuring the radioactivity present in said predefined volume before it is infused into said patient; and

(d) means for quickly infusing said predefined volume of rubidium-82 into said patient as a single bolus.

2. The strontium-rubidium infusion system of Claim 1 wherein said means for generating rubidium-82 in a solution which can be infused into a patient comprises a strontium-rubidium generator.

3. The strontium-rubidium infusion system of Claim 1 or 2 wherein said means for infusing said solution into a patient comprises a syringe.

4. The strontium-rubidium infusion system of Claim 3 wherein said means for infusing said solution into a patient further comprises means for electromechanically operating said syringe.

5. The strontium-rubidium infusion system of Claim 4 wherein said means for electromechanically operating said syringe comprises a stepper motor which drives means for moving the plunger of said syringe.

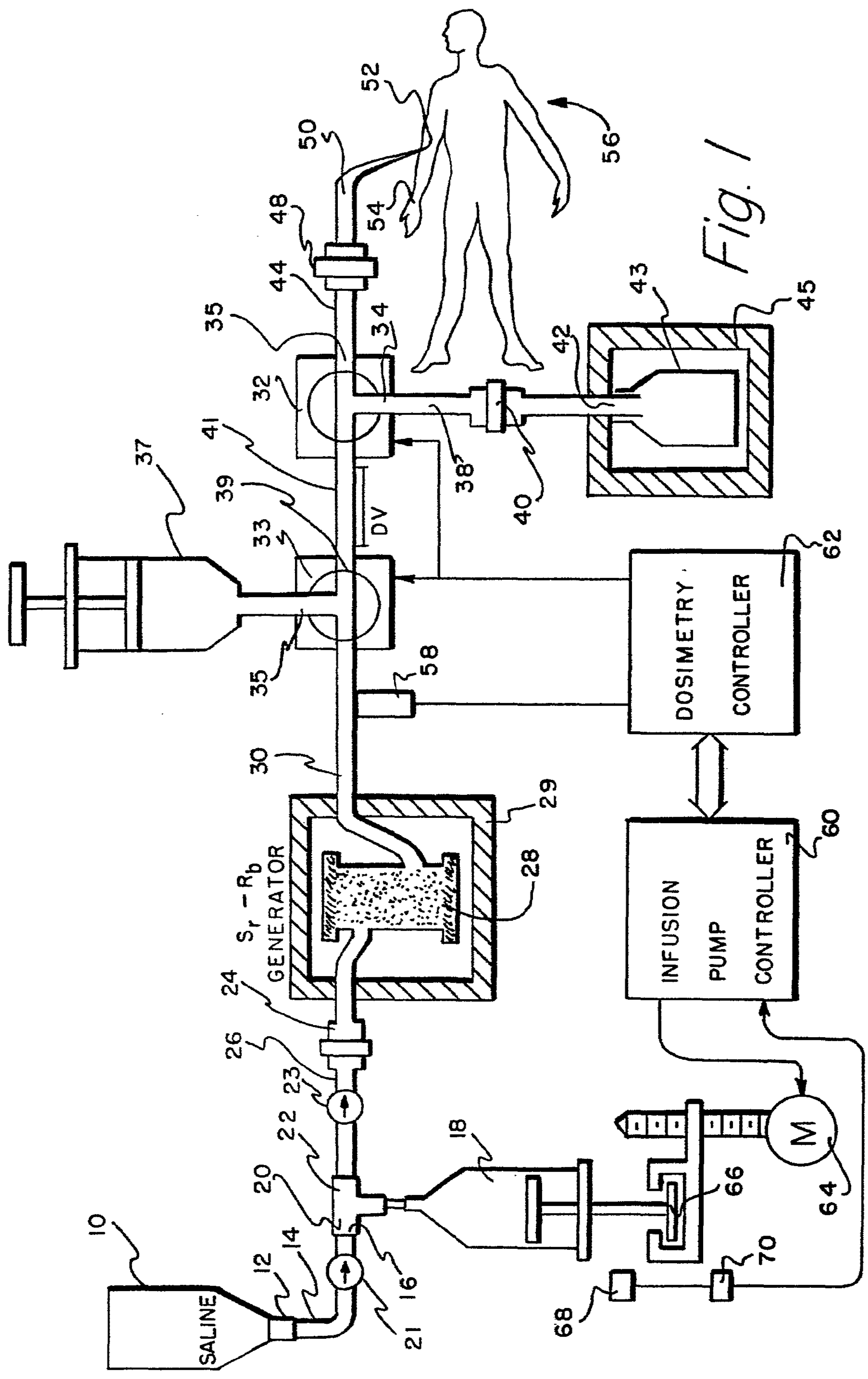
6. The strontium-rubidium infusion system of Claim 5 further comprising electronic means for controlling said stepper motor.

7. The strontium-rubidium infusion system of any one of Claims 1 to 6 wherein said means for measuring the radioactivity present in said solution as it is infused into said patient comprises a dosimetry system.

8. The strontium-rubidium infusion system of Claim 7 wherein said dosimetry system is connected to means for controlling said means for infusing.

9. The strontium-rubidium infusion system of any one of Claims 1 to 8 wherein said means for quickly infusing said predefined volume of rubidium-82 into said patient as a single bolus comprises a manually operated wash syringe.

10. The strontium-rubidium infusion system of Claim 9 wherein said manually operated wash syringe is initially filled with saline solution.


SALINE
$S_r - R_b$ GENERATOR
DV
DOSIMETRY CONTROLLER
INFUSION PUMP CONTROLLER
M
10
12
14
16
18
20
21
22
23
24
26
28
29
30
32
33
34
35
37
38
39
40
41
42
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44
45
48
50
52
54
56
58
60
62
64
66
68
70

Fig. 1

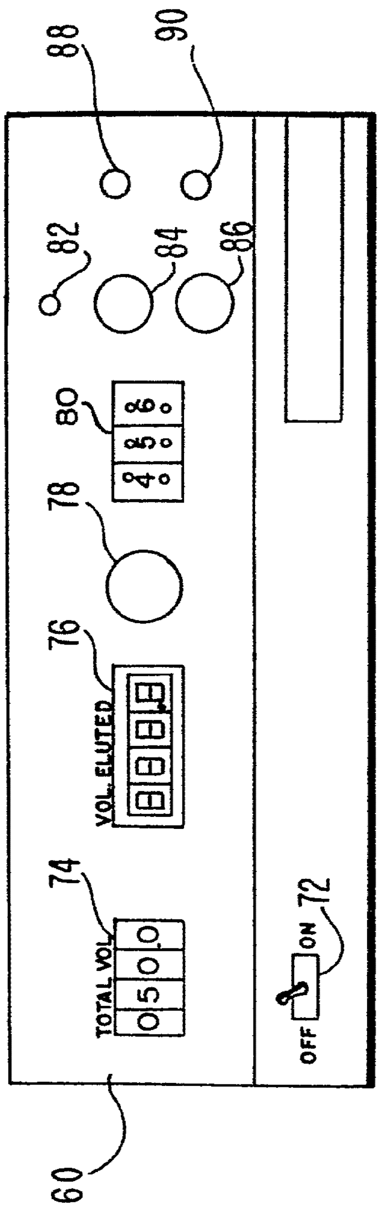
TOTAL VOL
VOL. ELUTED
OFF
ON

Fig. 2

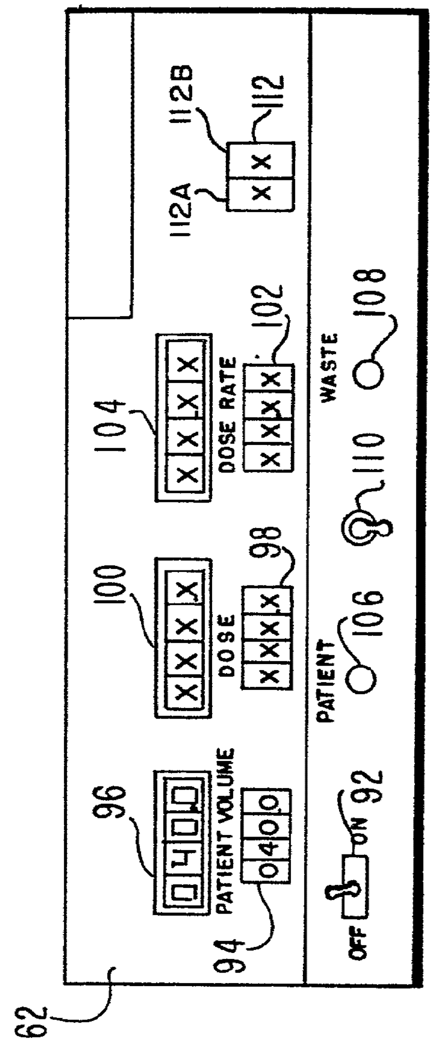
PATIENT VOLUME
DOSE
DOSE RATE
PATIENT
WASTE
OFF
ON

Fig. 3

0160303

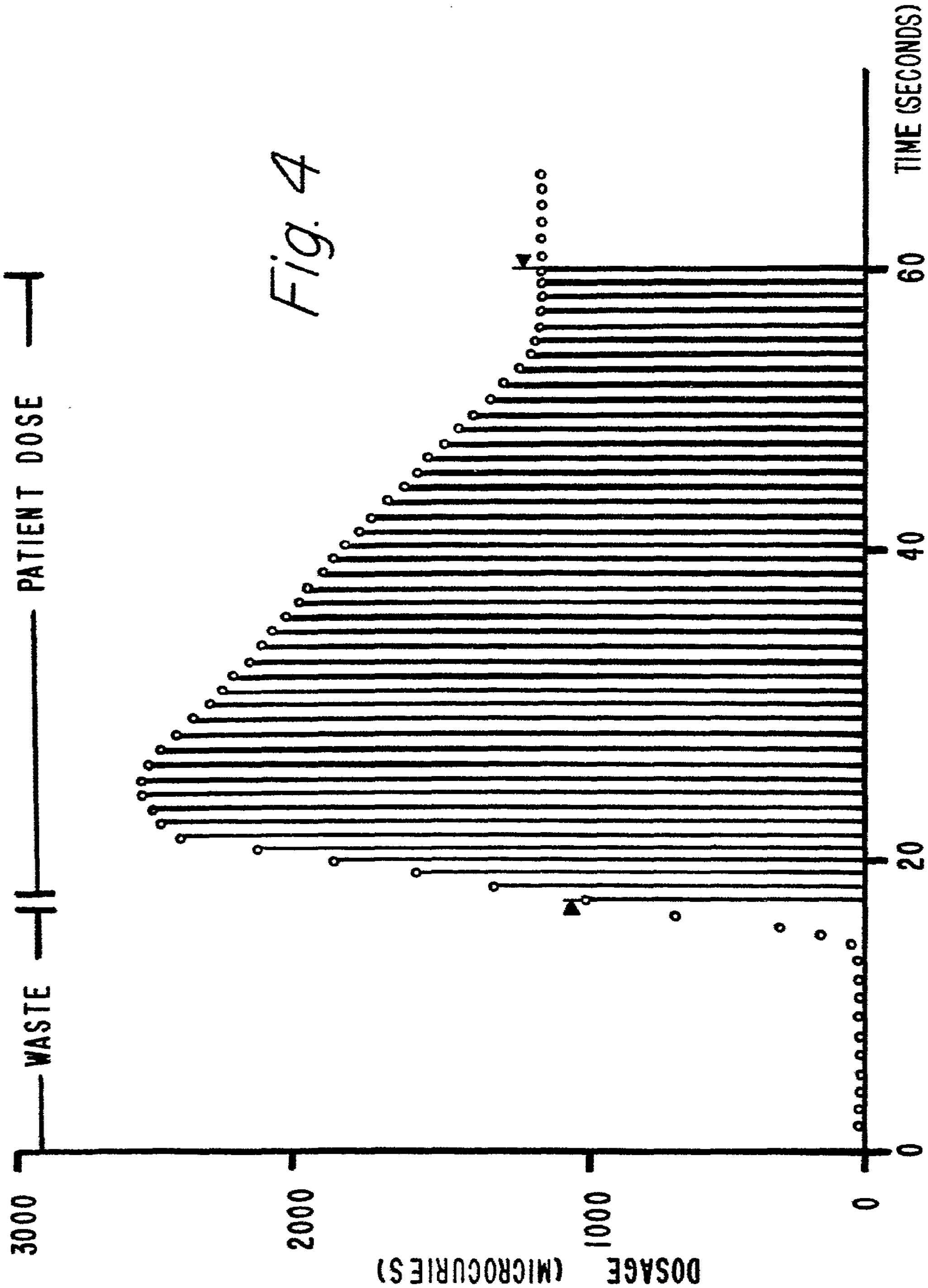

Fig. 4

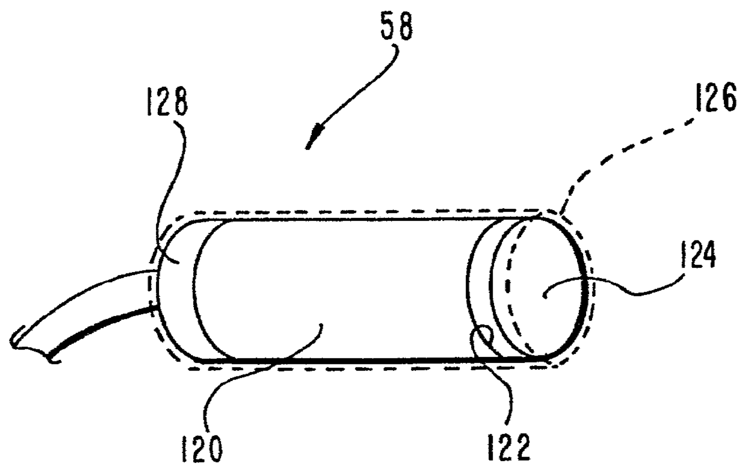
58
128
126
124
120
122

Fig. 5

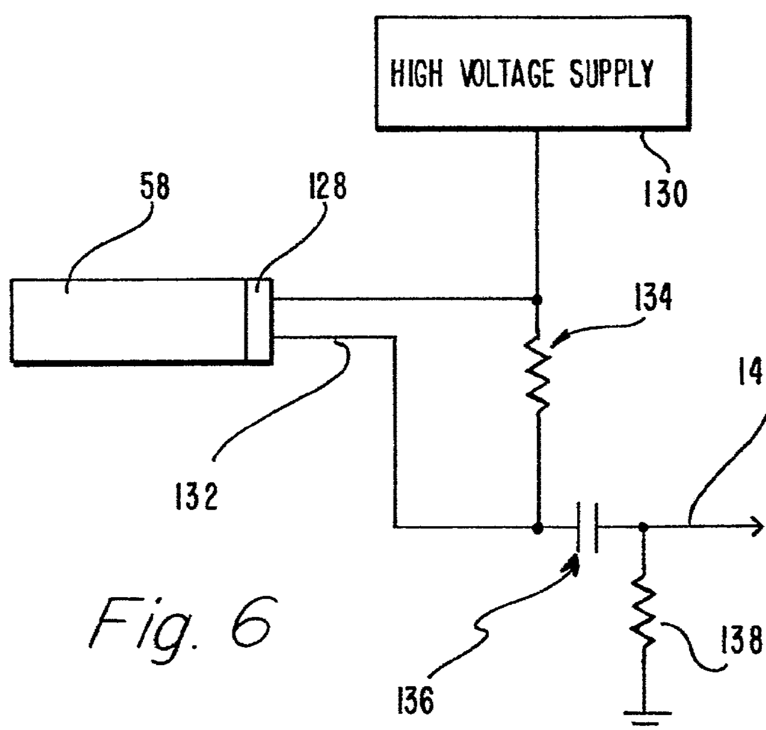
HIGH VOLTAGE SUPPLY
130
58
128
134
140
132
136
138

Fig. 6

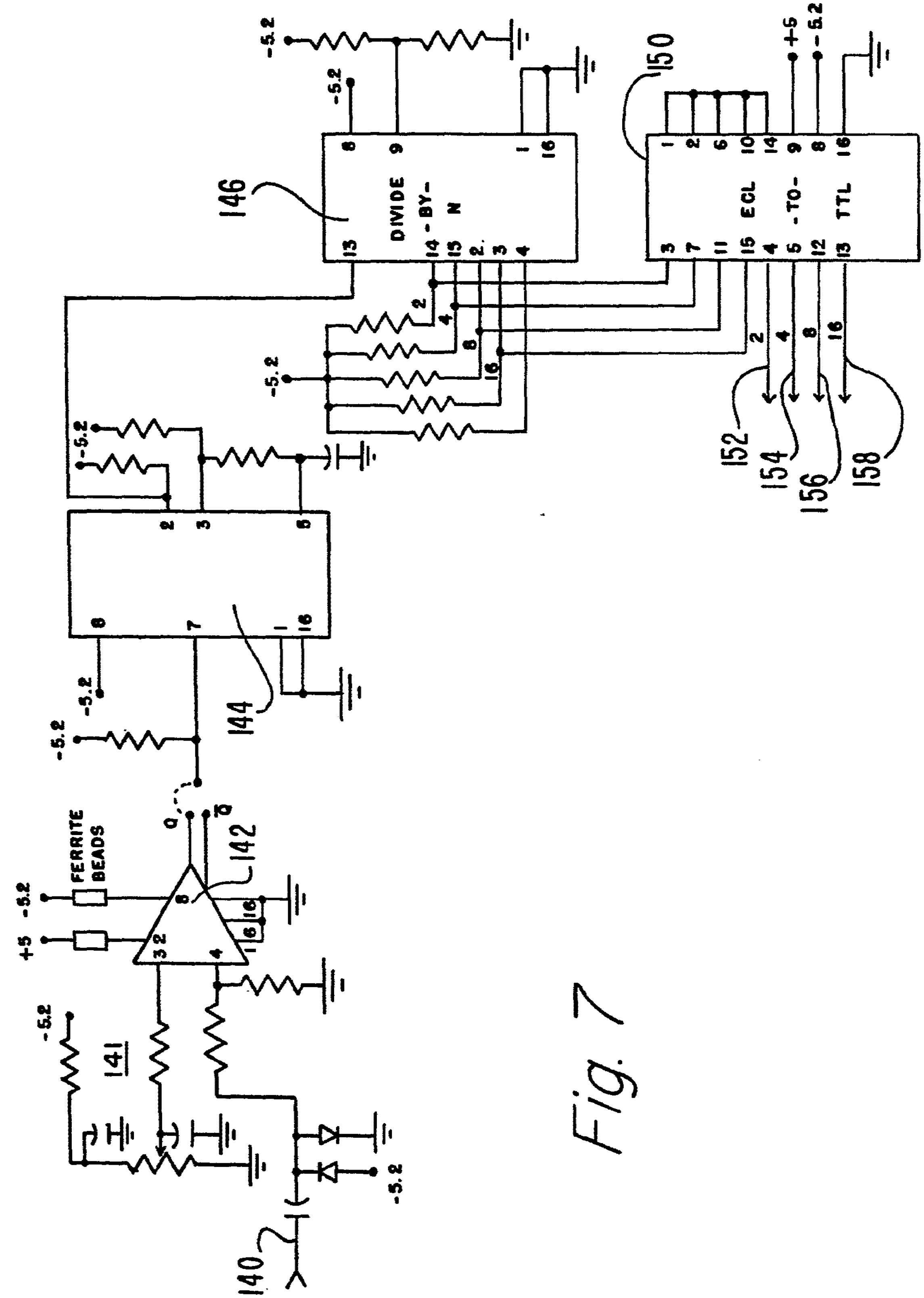
DIVIDE -BY- N
ECL -TO- TTL
FERRITE BEADS
-5.2
+5
140
141
142
144
146
150
152
154
156
158

Fig. 7

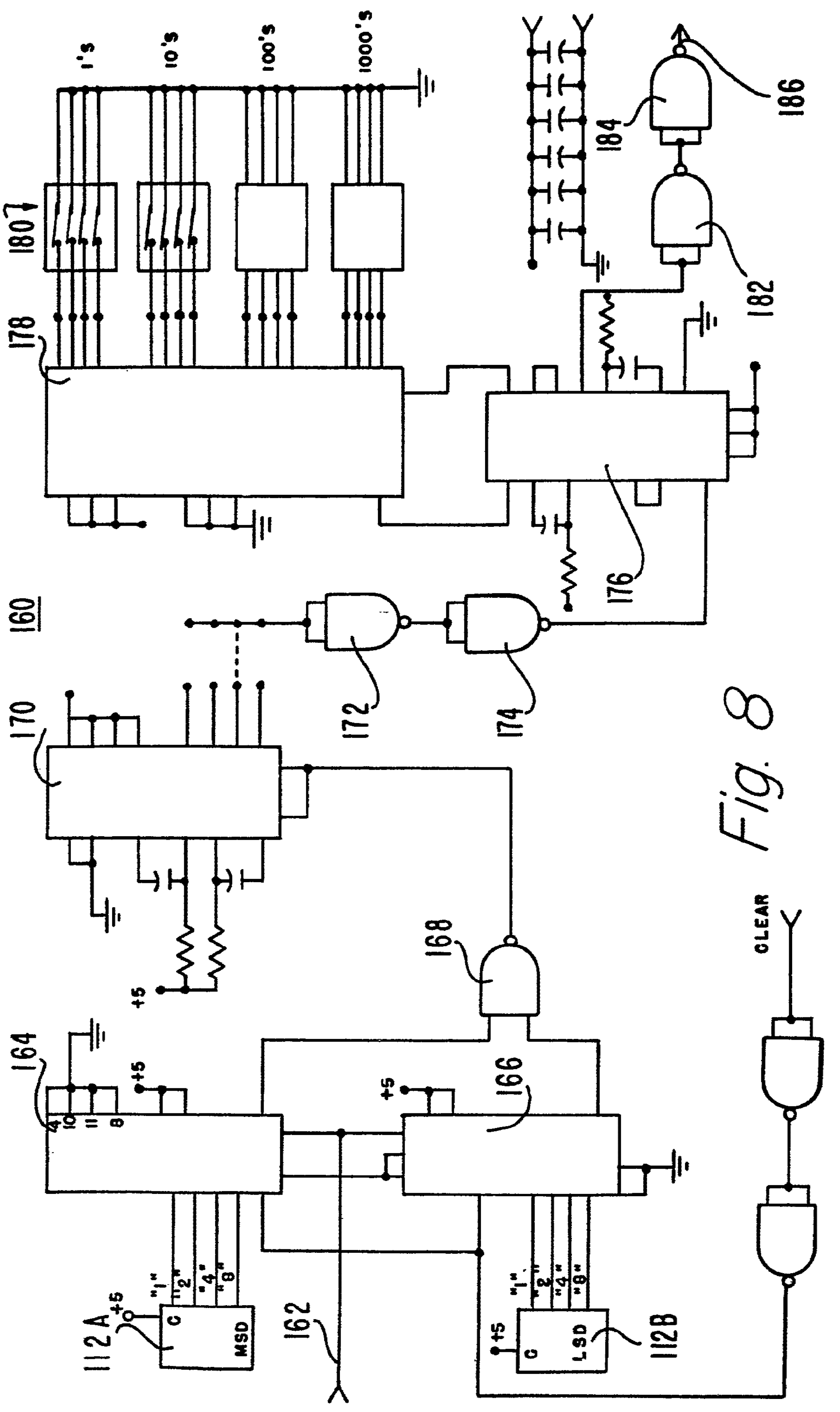
160
178
180
1's
10's
100's
1000's
176
182
184
186
170
172
174
164
166
168
162
112A
MSD
112B
LSD
C
+5
"1"
"2"
"4"
"8"
CLEAR

Fig. 8

0160303

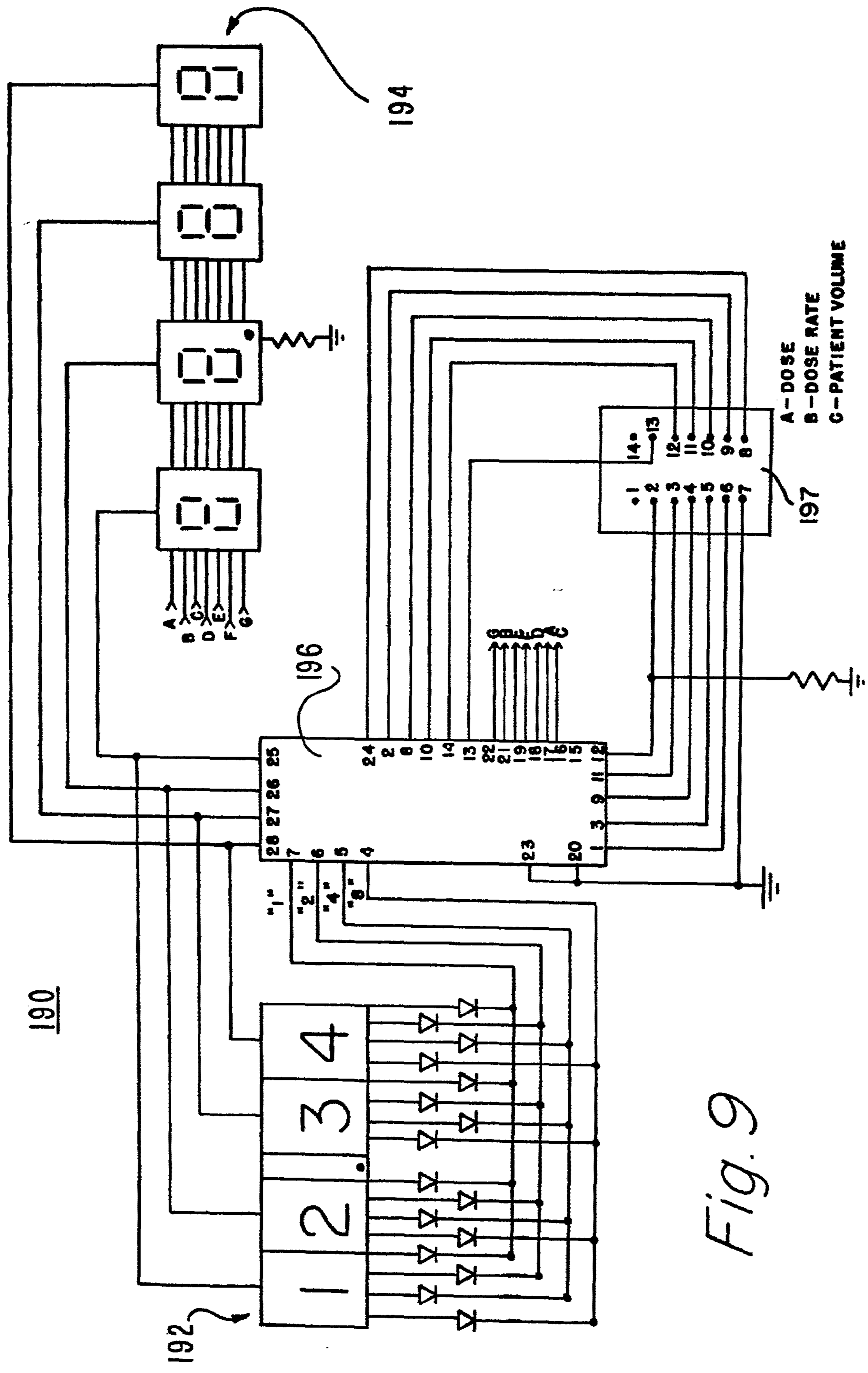

Fig. 9

0160303

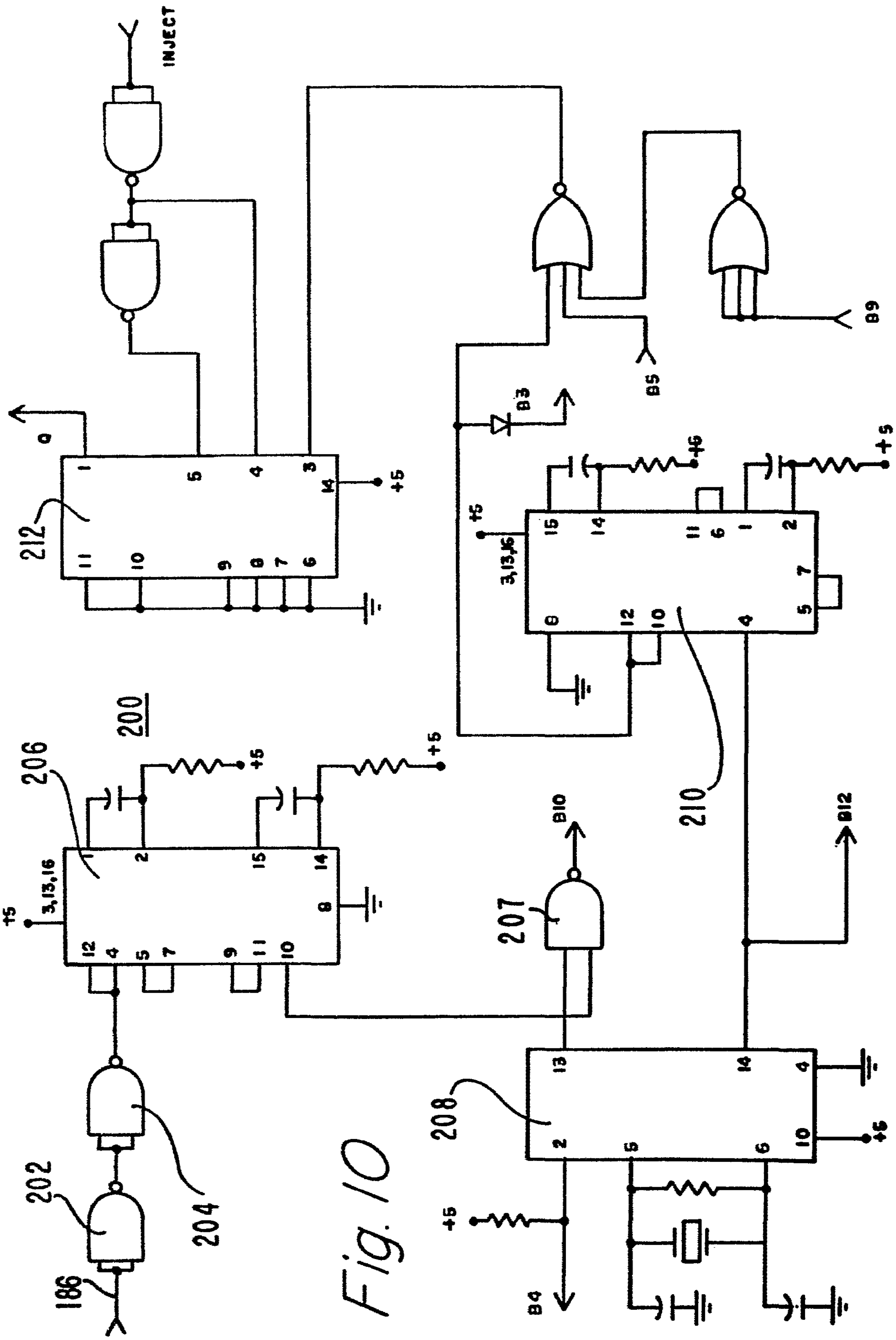

Fig. 10

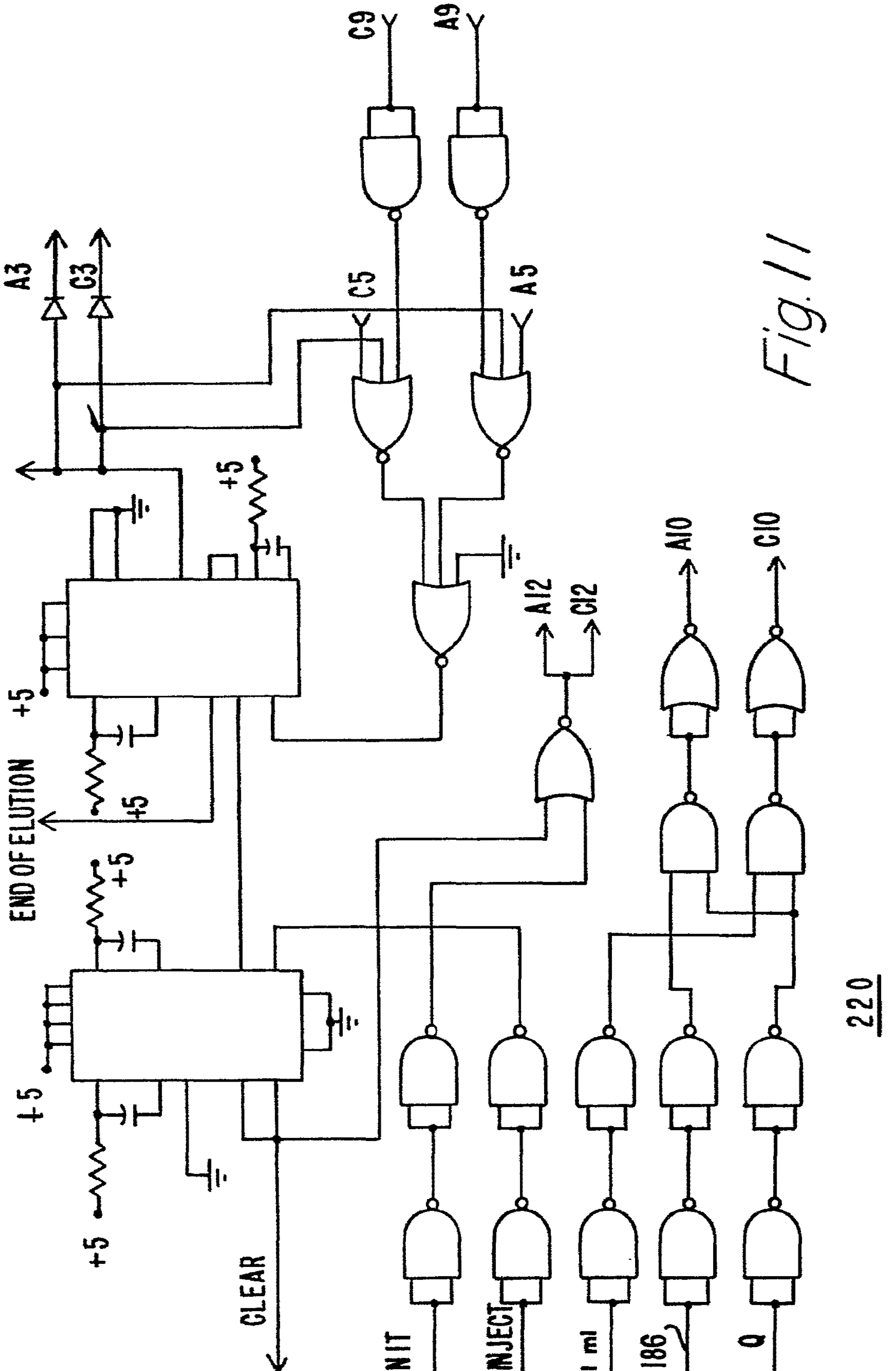
C9
A9
A3
C3
C5
A5
+5
+5
END OF ELUTION
+5
+5
+5
A12
C12
A10
C10
CLEAR
INIT
INJECT
.1 ml
186
Q
220

Fig. 11

0160303

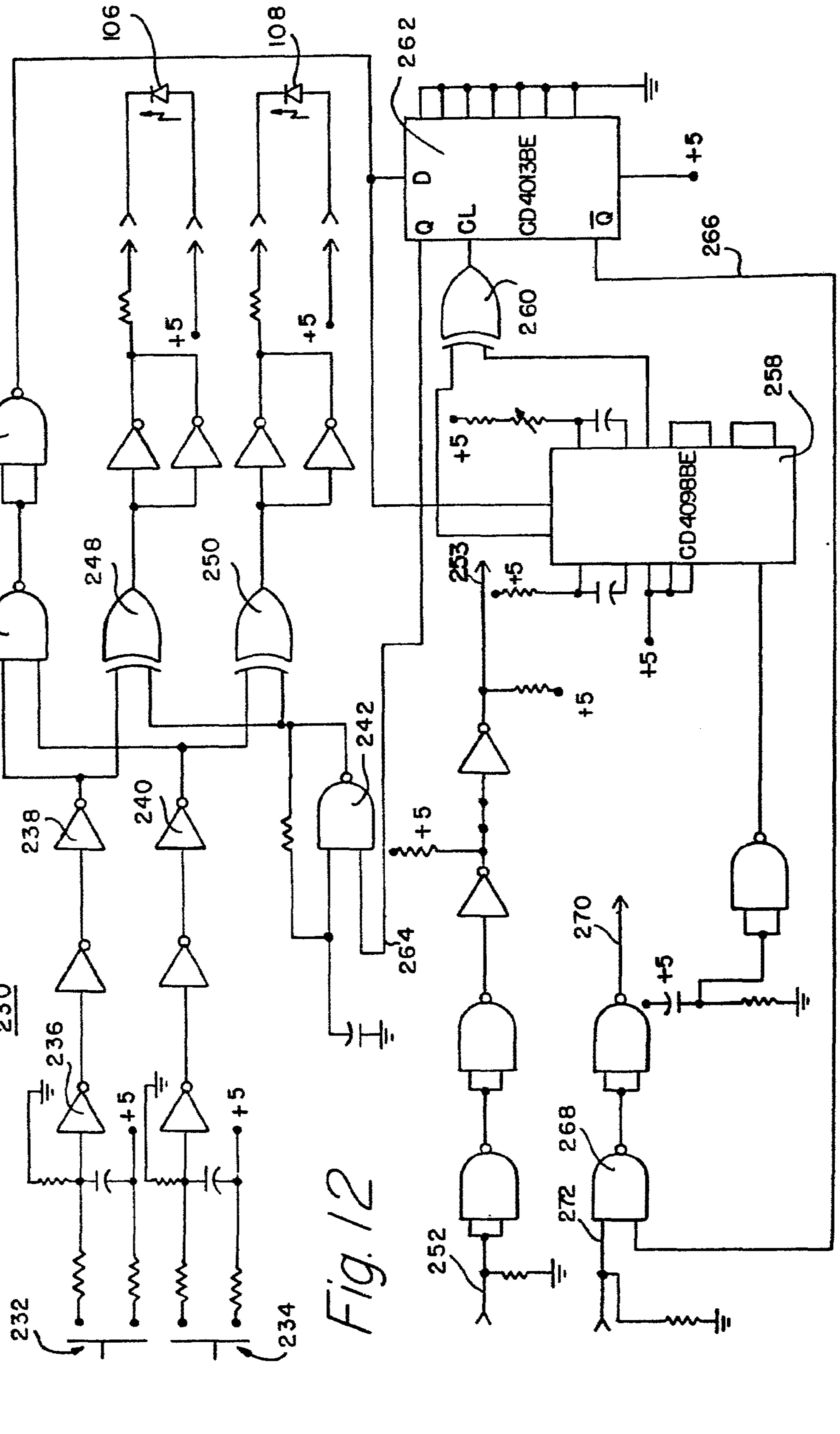

Fig. 12

(19) Europäisches Patentamt
European Patent Office
Office européen des brevets

(11) Publication number: **0 310 148 A2**

(12) **EUROPEAN PATENT APPLICATION**

(21) Application number: **88201030.9**

(51) Int. Cl.4: **G01T 1/203 , A61M 5/14**

(22) Date of filing: **27.02.84**

(30) Priority: **28.02.83 US 470840**
28.02.83 US 470841

(43) Date of publication of application:
05.04.89 Bulletin 89/14

(60) Publication number of the earlier application in accordance with Art.76 EPC: **0 117 752**

(84) Designated Contracting States:
AT BE CH DE FR GB IT LI LU NL SE

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(54) **Dosimetry system for strontium-rubidium infusion pump.**

(57) The dosimetry system used with a strontium-rubidium infusion system is a very high speed circuit capable of measuring the radioactive dosage infused into a patient in real time. The dosimetry system is capable of receiving very short duration input pulses generated by a photomultiplier tube in response to the presence of radioactivity.

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DOSIMETRY SYSTEM FOR STRONTIUM-RUBIDIUM INFUSION PUMP

The present invention relates to a strontium-rubidium infusion system. In particular, it relates to a strontium-rubidium infusion system which has an in-line, real time dosimetry system which can be used to infuse patients with Rubidium-82.

Current statistics show that approximately one-third of all deaths in the United States are related to coronary artery disease. See, for example, Pohost, G., McKusick, K., and Strauss, W., "Physiologic Basis and Utility of Myocardial Perfusion Imaging" Proceedings of the Second International Symposium on Radiopharmaceuticals, Society of Nuclear Medicine, New York 1979, pp. 465-473, and this fact has prompted extensive research to more efficiently diagnose and manage this disease. Recent advances in radiopharmaceutical development and instrument design have established myocardial scintigraphy as an important new approach for evaluating coronary artery disease and myocardial perfusion. See, for example, Pierson, R., Friedman, M., Tansley, W., Castellana, F., Enlander, D., and Huang, P., "Cardiovascular Nuclear Medicine: An Overview", Sem. Nucl. Med., 9, 224-240 (1979); Leppo, J., Scheuer, J., Pohost, G., Freeman, L., and Strauss, H., "The Evaluation of Ischemic Heart Disease Thallium-201 with Comments on Radionuclide Angiography": Sem. Nucl. Med., 10, 115-126 (1980); Vogel, R., "Quantitative Aspects of Myocardial Perfusion Imaging", Sem. Nucl. Med., 10, 146-156 (1980); Chervu, R., "Radiopharmaceuticals in Cardiovascular Nuclear Medicine", Sem. Nucl. Med., 9, 241-256 (1979); and Pitt, B., and Strauss, H., "Cardiovascular Nuclear Medicine", Sem. Nucl. Med., 7, 3-6 (1977).

Myocardial scintigraphy studies have been performed with several isotopes of potassium, rubidium, cesium, and thallium (T1-201), although the usefulness of all of these nuclides is limited by their non-optimal physical properties. In spite of its long half-life and low-gamma energy, T1-201 is currently the most widely used agent for myocardial imaging. See, for example, Poe, N., "Rationale and Radiopharmaceuticals for Myocardial Imaging", Sem. Nucl. Med., 7, 7-14 (1977); Strauss, H. and Pitt, B., "Thallium-201 as a Myocardial Imaging Agent", Sem. Nucl. Med., 7, 49-58 (1977); Botvinick, E., Dunn, R., Hattner, R., and Massie, B., "A Consideration of Factors Affecting the Diagnostic Accuracy of T1-201 Myocardial Perfusion Scintigraphy in Detecting Coronary Artery Disease", Sem. Nucl. Med., 10, 157-167 (1980); and Wackers, F., "Thallium-201 Myocardial Scintigraphy in Acute Myocardial Infarction and Ischemia", Sem. Nucl. Med., 10, 127-145 (1980).

In diagnostic procedures in which the heart is involved, it is desirable for a diagnostician to be able to view a patient's heart. Heretofore, various radioactive materials have been used together with radiological procedures for viewing internal organs of patients. It has been difficult, however, to view a heart because the radioactive substances which could be used for viewing the heart have had a very long half-life. Thus, using them with patients involves an element of danger and also reduces the number of times that a patient could be infused within any given time period. It would therefore be desirable to have a diagnostic apparatus and procedure which could be used with relative safety for viewing the heart.

Rubidium-82 is a potassium analog. That means it acts similar to potassium when it is infused into a patient. Thus it builds up at a very rapid rate, i.e., within seconds, in the patient's heart. Rubidium-82 also has the advantage of having a very short half-life, approximately 76 seconds. Therefore, it decays after a very short period of time following entry into the body, thereby allowing numerous procedures to be performed within a relatively short time period in a given patient. Rubidium-82 also has the advantage of being observable using a modified gamma camera such as a gamma camera of the type manufactured by Searle Radiographics, Inc., called the PHO Gamma IV. A problem with using Rubidium-82 in a patient involves keeping track of the amount of radiation infused into the patient. In view of the very short half-life of Rubidium-82, it is impractical to measure the radioactivity of a particular dose and to then infuse it into the patient using conventional means. An accurate method for measuring the amount of radiation being infused into the patient would be highly desirable for this particular application.

The availability of improved instrumentation has stimulated interest in the use of the positron emitter, Rubidium-82, for myocardial imaging. See for example, Beller G., and Smith, T., "Radionuclide Techniques in the Assessment of Myocardial Ischemia and Infarction," Circulation, 53 (3, Supp. 1) 123-125 (1976); Budinger, T., Yano, Y., Derenzo, S., et al., "Myocardial Uptake of Rubidium-82 Using Positron Emission Tomography," J., Nucl. Med. 20, 603 (1979); Budinger, T., Yano, Y., Derenzo, S., et al., "Infarction Sizing and Myocardial Perfusion Measurements Using Rb-82 and Positron Emission Tomography," Amer. J. Cardiol., 45, 399 (1980). Rubidium-82, an analog of the alkali metal potassium, is rapidly cleared from the blood and concentrated by the myocardium. The short half-life of the Rubidium-82 (76 sec) offers