200

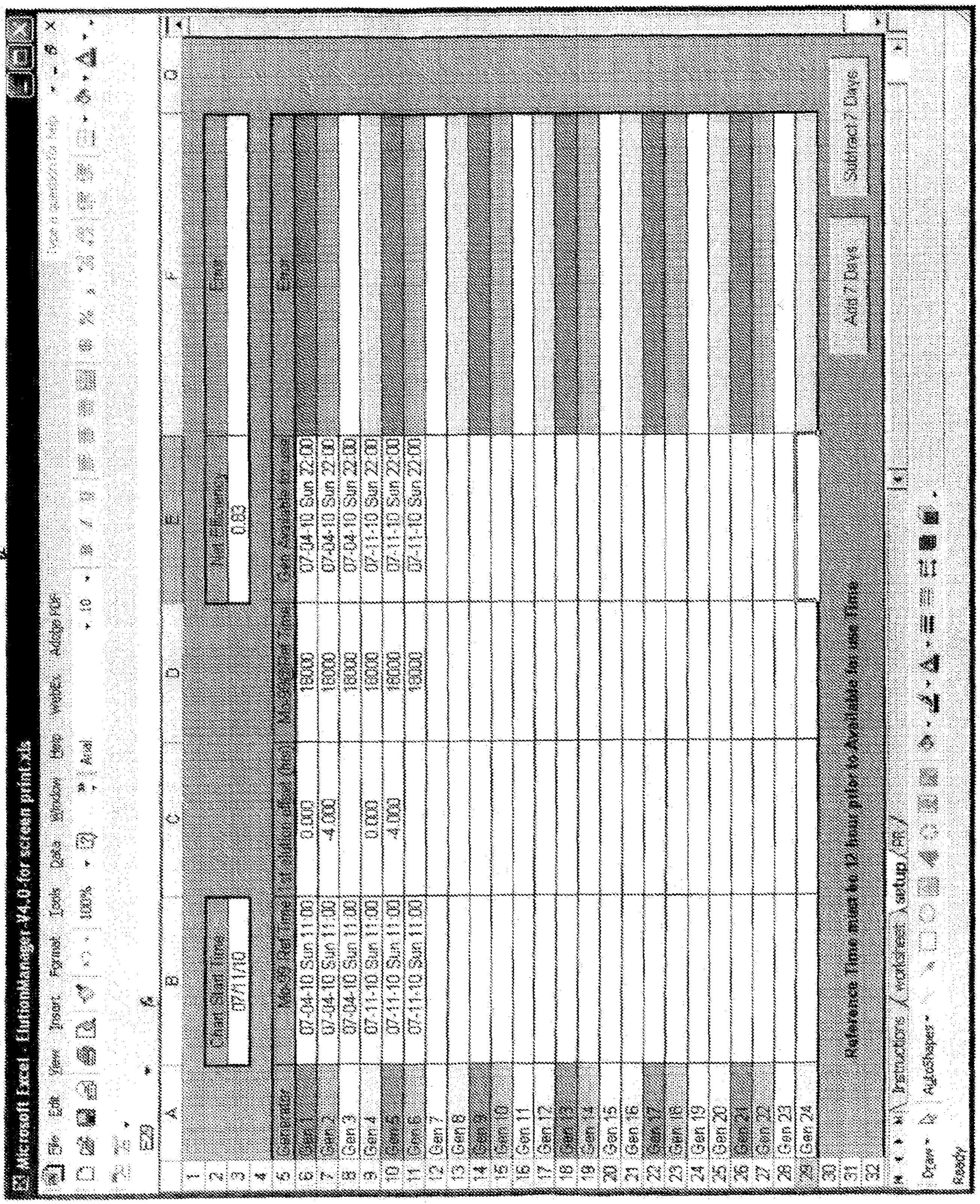
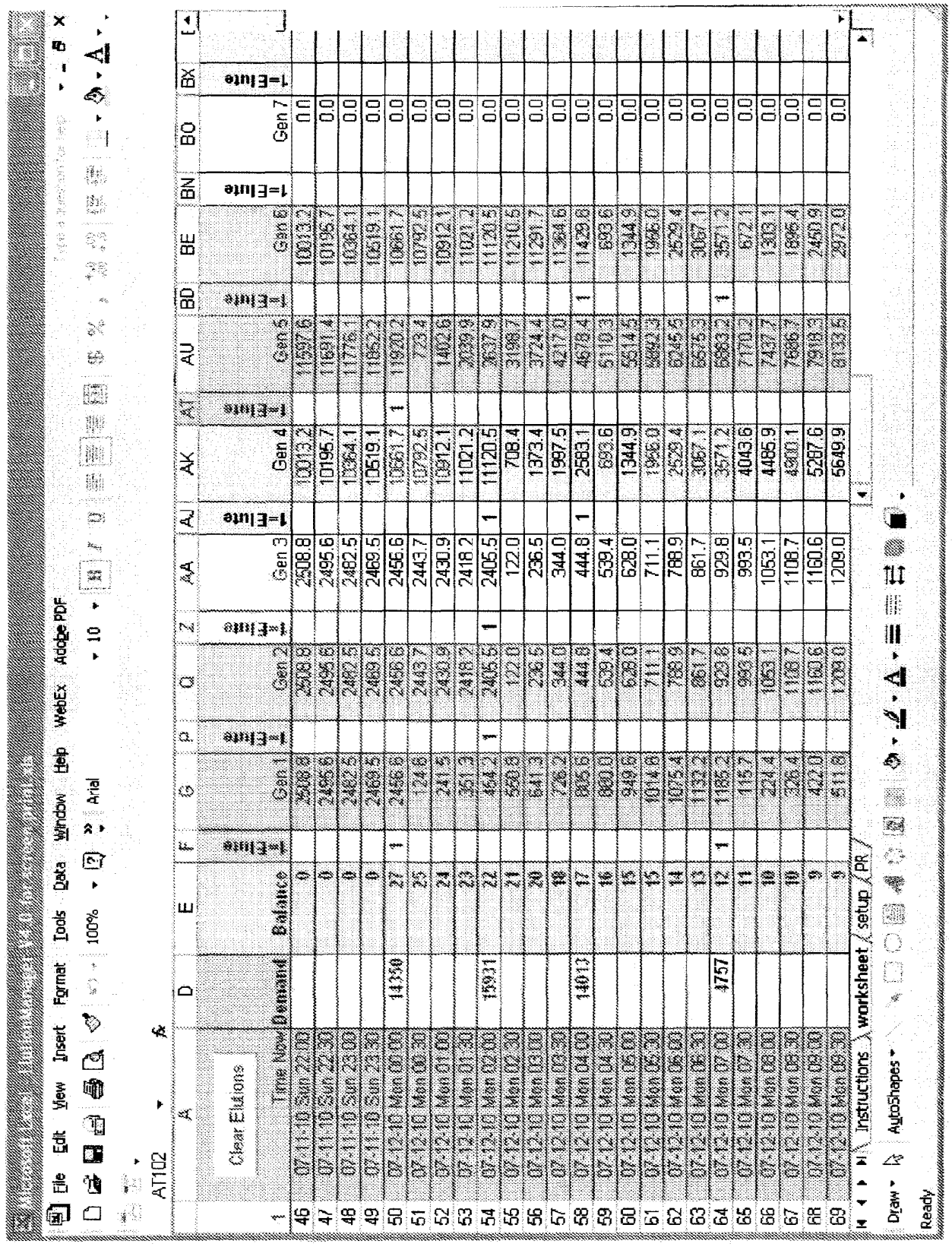

Microsoft Excel - ElutionManager-V4.0-for screen print.xls
Chart Start Time
07/11/10
Generator
Test Efficiency
0.83
Error
Add 7 Days
Subtract 7 Days
Reference Time must be 12 hour prior to Available for use Time
Instructions
worksheet
setup
Ready

FIG 10


File Edit View Insert Format Tools Data Window Help WebEx Adobe PDF
Arial
10
100%
AT102
Clear Elutions
Time Now
Demand
Balance
1=Elute
Gen 1
Gen 2
Gen 3
Gen 4
Gen 5
Gen 6
Gen 7
Instructions
worksheet
setup
PR
Draw
AutoShapes
Ready

8c

Fig 11

Patent Record Full View Thursday, July 25 2013 THOMSON INNOVATION

Patent/Publication: RU2307378C1

Bibliography

DWPI Title

Method for correcting measuring parameters of radioisotope discontinuous threshold detector and device for realization of said method

English Title

METHOD FOR CORRECTING MEASURING PARAMETERS OF RADIOISOTOPE DISCONTINUOUS THRESHOLD DETECTOR AND DEVICE FOR REALIZATION OF SAID METHOD

Assignee/Applicant

Standardized: **OAO SOJUZTSVETMETAVTOMATIKA**

DWPI Assignee/Applicant

SOYUZTSVETMETAVTOMATIKA STOCK CO (SOYU-R)

Inventor

ULITENKO KONSTANTIN JAKOVLEVIC, KARJAKIN JURIJ LEONIDOVICH, DEMIN ALEKSANDR VIKTOROVICH,

DWPI Inventor

DEMIN A V; KARYAKIN YU L; ULITENKO K YA

Publication Date (Kind Code)

2007-09-27 (C1)

DWPI Accession / Update

2007-697597 / 200765

Application Number / Date

RU2006113988A / 2006-04-26

Priority Number / Date / Country

RU2006113988A / 2006-04-26 / RU

Abstract

DWPI Abstract

(RU2307378C1)

Novelty

Suggested radioisotope discontinuous threshold detector contains a source of ionizing radiation, detector of ionizing radiation, threshold frequency generator, comparison device, to addition input of which detector is

connected, and to subtraction input - threshold frequency generator, and also interpolator, threshold cascade and executing mechanism, all serially connected to output of comparison device. Also, device additionally includes transformation time-setting device, launch input of which is connected to output of threshold cascade, and also electronic key, connected by input to detector of ionizing radiations, and by output - to control input of threshold frequency generator, control input of the key is connected to transformation time setting device. Described device realizes corresponding method for correcting measuring parameters of radioisotope discontinuous threshold detector.

Use

Nuclear physics, namely methods and devices for correcting and stabilizing measuring routes of radioisotope devices.

Advantage

Increased precision and increased stability of radioisotope discontinuous threshold detector.2 cl, 3 dwg

Abstract

FIELD: nuclear physics, namely methods and devices for correcting and stabilizing measuring routes of radioisotope devices. ^ SUBSTANCE: suggested radioisotope discontinuous threshold detector contains a source of ionizing radiation, detector of ionizing radiation, threshold frequency generator, comparison device, to addition input of which detector is connected, and to subtraction input - threshold frequency generator, and also interpolator, threshold cascade and executing mechanism, all serially connected to output of comparison device. Also, device additionally includes transformation time-setting device, launch input of which is connected to output of threshold cascade, and also electronic key, connected by input to detector of ionizing radiations, and by output - to control input of threshold frequency generator, control input of the key is connected to transformation time setting device. Described device realizes corresponding method for correcting measuring parameters of radioisotope discontinuous threshold detector. ^ EFFECT: increased precision and increased stability of radioisotope discontinuous threshold detector. ^ 2 cl, 3 dwg

Classes/Indexing

IPC

Current IPC	Invention	Version	Additional	Version
Full	G01T 1/40	20060101	-	-
Main Group	-	-	-	-
Subclass	-	-	-	-

DWPI Class

S03

DWPI Manual Codes

Collapse DWPI Manual Codes

EPI Manual Codes: S03-G02

DWPI Chemistry Resource Numbers

Collapse DWPI Chemistry Resource Numbers

-

DWPI Registry Numbers

Collapse DWPI Registry Numbers

-

Plasdoc Punch Codes

Collapse Plasdoc Punch Codes

-

Plasdoc Key Serial Codes

Collapse Plasdoc Key Serial Codes

-

Enhanced Polymer Indexing

Collapse Enhanced Polymer Indexing

-

Chemical Fragment Codes

Collapse Chemical Fragment Codes

-

Legal Status

INPADOC Legal Status

Get Family Legal Status

Family

Family

Collapse INPADOC Family (1)

	Publication Number	Publication Date	Inventor	Assignee/Applicant	Title
	RU2307378C1	2007-09-27	ULITENKO KONSTANTIN JAKOVLEVIC	OAO SOJUZTSVETMETAVTOMATIKA	METHOD FOR CORRECTING MEASURING PARAMETERS OF RADIOISOTOPE DISCONTINUOUS THRESHOLD DETECTOR AND DEVICE FOR REALIZATION OF SAID METHOD

Collapse DWPI Family (1); Countries (1)

Publication	DWPI Update	Publication Date	IPC Code	Language
RU2307378C1	200765	2007-09-27	G01T000100	Russian

Claims

No Claims exist for this Record

Description

Background/ Summary

Collapse Background/Summary

-

Drawing Description

Collapse Drawing Description

-

Description

Collapse Description

-

Citations

Citation *Record level*

Citing Patents (0)

Cited Patents (0)

Cited Non-patents (0)

Other

DWPI Title Terms

METHOD CORRECT MEASURE PARAMETER RADIOISOTOPE DISCONTINUE THRESHOLD DETECT DEVICE REALISE

DWPI Related Accession Numbers

-

Custom Fields

社内分類

-

Internal Combustion Engine

-

Renewable Energy

-

Review Type

-

コメント

-

Flag Status

-

Tech Support

-

First Tech Class

-

White Field

-

Unified APP name

-

supplier CACC

-

Review Comments

-

大学专利报告

-

patent relevance v2

-

NFC

-

User Interface

-

Mando

-

IMPORTANCE

-

automobile safe

-

Electronic Acknowledgement Receipt

EFS ID:	16717096
Application Number:	12137364
International Application Number:	
Confirmation Number:	7377
Title of Invention:	INFUSION SYSTEMS INCLUDING COMPUTER-FACILITATED MAINTENANCE AND/OR OPERATION AND METHODS OF USE
First Named Inventor/Applicant Name:	Stephen E. Hidem
Customer Number:	22859
Filer:	Paul J. LaVanway Jr.
Filer Authorized By:	
Attorney Docket Number:	56782.1.7
Receipt Date:	29-AUG-2013
Filing Date:	11-JUN-2008
Time Stamp:	14:40:34
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	Information Disclosure Statement (IDS) Form (SB08)	13thSIDS_56782-1-7.pdf	613448 53a5536641d4ac34ba98d8e2e6fa86582f275afd	no	6

Warnings:	
Information:	

2	Foreign Reference	WO2008066586A2.pdf	1272548 8680ae5b7584c393f429ab1b8ea740c09894f890	no	30
Warnings:					
Information:					
3	Foreign Reference	WO2011126522A2.pdf	3863770 03b32ea73aaeb819a89b2b2e2811c298554f32c5	no	60
Warnings:					
Information:					
4	Non Patent Literature	Article_Klein-2004.pdf	802719 7352e689d95ccca91c0c1e377f680c13c74d52ed	no	4
Warnings:					
Information:					
5	Foreign Reference	RU2307378C1_Machine-translation.pdf	155711 3145db7df125c1d6fe7f05ba87b77a67c6db9be9	no	6
Warnings:					
Information:					
			Total Files Size (in bytes):	6708196	

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.

New Applications Under 35 U.S.C. 111

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.

National Stage of an International Application under 35 U.S.C. 371

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.

New International Application Filed with the USPTO as a Receiving Office

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.

PTO/SB/30EFS (07-09)
Approved for use through 07/31/2012. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

REQUEST FOR CONTINUED EXAMINATION(RCE)TRANSMITTAL
(Submitted Only via EFS-Web)

Application Number	12/137,364	Filing Date	2008-06-11	Docket Number (if applicable)	56782.1.7	Art Unit	3763
First Named Inventor	Stephen E. HIDEM			Examiner Name	Jenna ZHANG		

This is a Request for Continued Examination (RCE) under 37 CFR 1.114 of the above-identified application.
Request for Continued Examination (RCE) practice under 37 CFR 1.114 does not apply to any utility or plant application filed prior to June 8, 1995, or to any design application. The Instruction Sheet for this form is located at WWW.USPTO.GOV

SUBMISSION REQUIRED UNDER 37 CFR 1.114

Note: If the RCE is proper, any previously filed unentered amendments and amendments enclosed with the RCE will be entered in the order in which they were filed unless applicant instructs otherwise. If applicant does not wish to have any previously filed unentered amendment(s) entered, applicant must request non-entry of such amendment(s).

☐ Previously submitted. If a final Office action is outstanding, any amendments filed after the final Office action may be considered as a submission even if this box is not checked.

- ☐ Consider the arguments in the Appeal Brief or Reply Brief previously filed on _____
- ☐ Other _____

☒ Enclosed

- ☒ Amendment/Reply
- ☐ Information Disclosure Statement (IDS)
- ☐ Affidavit(s)/ Declaration(s)
- ☐ Other _____

MISCELLANEOUS

☐ Suspension of action on the above-identified application is requested under 37 CFR 1.103(c) for a period of months _____ (Period of suspension shall not exceed 3 months; Fee under 37 CFR 1.17(i) required)

☐ Other _____

FEES

The RCE fee under 37 CFR 1.17(e) is required by 37 CFR 1.114 when the RCE is filed.

☒ The Director is hereby authorized to charge any underpayment of fees, or credit any overpayments, to Deposit Account No 061910

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT REQUIRED

☒ Patent Practitioner Signature

☐ Applicant Signature

PTO/SB/30EFS (07-09)
Approved for use through 07/31/2012. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Signature of Registered U.S. Patent Practitioner			
Signature	/Paul J. LaVanway, Jr./	Date (YYYY-MM-DD)	2013-08-28
Name	Paul J. LaVanway, Jr.	Registration Number	64610

This collection of information is required by 37 CFR 1.114. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.11 and 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450.

If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.

Privacy Act Statement

The Privacy Act of 1974 (P.L. 93-579) requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that: (1) the general authority for the collection of this information is 35 U.S.C. 2(b)(2); (2) furnishing of the information solicited is voluntary; and (3) the principal purpose for which the information is used by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent application or patent. If you do not furnish the requested information, the U.S. Patent and Trademark Office may not be able to process and/or examine your submission, which may result in termination of proceedings or abandonment of the application or expiration of the patent.

The information provided by you in this form will be subject to the following routine uses:

1. The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C. 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether the Freedom of Information Act requires disclosure of these records.

2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.

3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.

4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).

5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent Cooperation Treaty.

6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).

7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (i.e., GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.

8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspections or an issued patent.

9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

22859
Customer Number

PATENT
Attorney Docket No.: 56782.1.7

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

First Named Inventor:	Stephen E. Hidem		
Application No.:	12/137,364	Group Art Unit:	3763
Filed:	June 11, 2008	Examiner:	ZHANG, Jenna
Title:	INFUSION SYSTEMS INCLUDING COMPUTER-FACILITATED MAINTENANCE AND/OR OPERATION AND METHODS OF USE		

Mail Stop FINAL
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

AMENDMENT

Dear Sir:

In response to the Final Office Action mailed May 28, 2013, the period of response for which runs through August 28, 2013, please amend the application as follows. This Amendment is accompanied by a Request for Continued Examination under 37 C.F.R. § 1.114 and constitutes a sufficient submission.

Amendments to the Claims are reflected in the listing of claims which begins on page 2 of this paper.

Remarks begin on page 9 of this paper.

AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions and listings of claims in the application.

Listing of Claims:

1. (Currently Amended) A method for operating an infusion system, the system comprising an eluant reservoir, a pump coupled to the reservoir, an infusion tubing circuit, a radioisotope generator, an activity detector, a waste bottle and a computer including a computer interface, the infusion tubing circuit including an eluant line coupled to the pump and to the generator, a waste line coupled to the generator and to the waste bottle, and a patient line coupled to the generator, the method comprising:

entering, into the computer, via the computer interface, a command to activate the pump in order to generate an eluate from a portion of a volume of eluant pumped through the generator, via an elution within the generator;

receiving an indication that the elution is completed, from the computer, via the computer interface, ~~that the elution is completed,~~ when the pump has completed pumping the portion of the volume of eluant; and

receiving from the computer, via the computer interface, a display of time lapsed since the elution was completed.

2. (Original) The method of claim 1, further comprising:

entering, into the computer, via a computer interface, the volume of eluant contained in the reservoir, prior to the elution; and

receiving, from the computer interface, an indication of a volume of eluant in the reservoir, based upon tracking the portion of the volume of eluant that is pumped from the reservoir.

3. (Previously Presented) The method of claim 1, further comprising:

coupling the patient line of the infusion tubing circuit to a first shielded test vial, in order to collect a first sample of the eluate from the patient line during the elution;

measuring an activity of the first sample; and

entering into the computer, via the computer interface, the measured activity of the first sample and a time between completion of the elution and the measuring of the activity, the computer calculating a breakthrough of the generator.

4. (Original) The method of claim 3, further comprising:

selecting a breakthrough test procedure of the computer, via the computer interface, prior to entering the command to activate the pump; and

wherein coupling the patient line to the first shielded test vial is instructed by the computer interface, after selecting the breakthrough test.

5. (Previously Presented) The method of claim 3, further comprising:

exchanging the patient line of the infusion tubing circuit for a first new patient line, after collecting the first sample;

coupling the first new patient line to a second shielded test vial;

repeating the steps of claim 1, after exchanging the patient line, wherein the pump is activated a second time and a second elution takes place, in order to fill the second vial with a second sample of the eluate from the first new patient line;

measuring an activity of the second sample; and

entering into the computer, via the computer interface, the measured activity of the second sample and a time between completion of the second elution and the measuring of the activity of the second sample, the computer calculating a calibration coefficient for the infusion system based on the measured activity of the second sample and an activity of the eluate detected, during the second elution, by the activity detector of the system.

6. (Original) The method of claim 5, further comprising:

selecting a calibration procedure of the computer, via the computer interface, prior to entering the command to activate the pump for the second time; and

wherein coupling the first new patient line to the second shielded test vial is instructed by the computer interface, after selecting the calibration procedure.

7. (Original) The method of claim 5, further comprising:

exchanging the first new patient line of the infusion tubing circuit for a second new patient line, after the computer calculates the calibration coefficient;

purging air from the second patient line;

coupling the second new patient line to a patient, after purging; and

repeating the steps of claim 1, after exchanging the first new patient line for the second new patient line, wherein the pump is activated a third time and a third elution takes place, in order to inject a dose of the eluate to the patient from the second patient line.

8. (Original) The method of claim 7, further comprising receiving a report from the computer, upon completion of the third elution, the report including a patient identification number and at least one quantification of the dose of the eluate.

9. (Previously Presented) The method of claim 1, further comprising:

coupling the patient line to a shielded test vial in order to collect a sample of the eluate from the patient line during the elution;

measuring an activity of the sample; and

entering into the computer, via the computer interface, the measured activity of the sample and a time between completion of the elution and measuring of the activity, the computer calculating a calibration coefficient for the infusion system based on the measured activity and an activity of the eluate detected, during elution, by the activity detector of the system.

10. (Original) The method of claim 9, further comprising:

selecting a calibration procedure of the computer, via the computer interface, prior to entering the command to activate the pump; and

wherein coupling the patient line to the shielded test vial is instructed by the computer interface, after selecting the calibration procedure.

11. (Original) The method of claim 1, further comprising:

purging air from the patient line;

coupling the patient line to a patient, after purging, in order to inject a dose of the eluate to the patient from the patient line; and

receiving a report from the computer, upon completion of the elution, the report including a patient identification number and at least one quantification of the dose of the eluate.

12. (Original) The method of claim 1, wherein the computer interface comprises a touch-activated display screen.

13. (Original) The method of claim 1, further comprising:

receiving an indication, from the system, that the eluate is being diverted, from the generator, through the waste line of the infusion tubing circuit, when the pump is activated;

receiving an indication, from the system, that the eluate is being diverted from the generator, through the patient line of the infusion tubing circuit, when the pump is activated;

14. (Original) The method of claim 13, wherein:

the system further comprises a light projector;

the indication that the eluate is being diverted through the waste line comprises a flashing light projection from the light projector; and

the indication that the eluate is being diverted through the patient line comprises a solid light projection from the light projector.

15. (Original) The method of claim 13, further comprising receiving an indication from the system that a peak bolus of radioactivity has been detected, in the eluate, by the activity detector.

16. (Original) The method of claim 15, wherein:

the system further comprises a light projector; and

the indication that the peak bolus of radioactivity has been detected comprises a flashing light from the light projector.

17. (Original) The method of claim 1, further comprising:

entering, into the computer, via the computer interface, a command to set a waste bottle level indicator to zero, when the waste bottle is empty and prior to entering the command to activate the pump; and

receiving, from the computer, via the computer interface, an indication that the waste bottle needs to be emptied, based upon the computer tracking a volume of the eluate that is diverted, from the generator, through the waste line of the infusion tubing circuit.

18. (Withdrawn) A computer readable medium having computer executable instructions for executing a method for maintaining an infusion system, the method comprising:

receiving, via a graphical user interface, a volume of eluant contained in a reservoir of the infusion system prior to activating a pump of the infusion system to pump a portion of the volume of eluant through a radioisotope generator of the system in order to generate, via elution, an eluate;

tracking the portion of the volume of eluant that is pumped from the reservoir;

providing an indication of a volume of eluant within the reservoir; and

tracking a volume of the eluate that is diverted from the generator to the waste bottle;

providing an indication that the waste bottle needs to be emptied.

19. (Canceled)

20. (Withdrawn) A computer readable medium having computer executable instructions for executing a method of calibrating an activity detector of an infusion system, the method comprising:

receiving a calibration command;

receiving calibration parameters relating to an elution process;

activating a pump of the infusion system to initiate the elution process, the elution process producing a sample of an eluate;

tracking a time from the end of the elution process;

receiving from the activity detector of the infusion system an activity level detected during the elution process;

receiving a measured activity level of the eluate sample obtained from a dose calibrator;

receiving a time measured from the completion of the elution process to the measurement of the activity level by the dose calibrator;

calculating a calibration coefficient for the infusion system based on the measured activity level of the eluate sample and activity level detected during the elution process; and

providing the calibration coefficient as an output.

21. (Withdrawn) A computer readable medium having computer executable instructions for executing a method of conducting a breakthrough test of a radioisotope generator of an infusion system, the method comprising:

receiving a breakthrough test command;

activating a pump of the infusion system to initiate an elution process, the elution process using the generator to produce a sample of an eluate from a patient line;

tracking a time lapsed from the end of the elution process;

receiving a measured activity level of the eluate sample obtained from a dose calibrator;

receiving a time measured from the completion of the elution process to the measurement of the activity level by the dose calibrator;

calculating a breakthrough of the radioisotope generator based on the measured activity level and the time between completion of the elution process and the measuring of the activity level; and

providing the breakthrough of the generator as an output.

22. (Withdrawn) The computer readable medium of claim 21, further comprising:

receiving a second measured activity level of the eluate sample obtained from a dose calibrator, the second measured activity level being a measurement taken at predetermined time period after the completion of the elution process.

23. (Withdrawn) The computer readable medium of claim 21, wherein the predetermined time period is 60 minutes after completion of the elution process.

24. (Withdrawn) A method for purging a tubing circuit of an infusion system with air, the system comprising a pump coupled to the tubing circuit, a radioisotope generator, a waste bottle and a computer including a computer interface, the method comprising:

receiving instructions from the computer, via the computer interface, to disconnect the pump from an eluant reservoir of the system, and to by-pass the generator by disconnecting an eluant line and an eluate line, of the tubing circuit, from the generator, and connecting the eluant line to the eluate line; and

entering, into the computer, via the computer interface, a command to perform an air purge of the tubing circuit, the air purge being automated, via the computer, to perform purges of individual portions of the tubing circuit, in sequence, via control of the pump and of two divergence valves of the tubing circuit;

wherein a first valve, of the two divergence valves, is located between a first portion of the eluate line and two downstream portions of the eluate line, a first of the two downstream portions extending to a waste bottle of the system and a second of the two downstream portions extending to a vial outside the system;

a second valve, of the two divergence valves, is located between a first portion of the eluant line, extending from the pump, and two downstream portions of the eluant line, a first of the two downstream portions of the eluant line being connected to the first portion of the eluate line, and a second of the two downstream portions of the eluant line being connected to the second of the two downstream portions of the eluate line.

25. (New) The method of claim 1, wherein the display of time lapsed comprises a display of a timer.

REMARKS

This Amendment is responsive to the Final Office Action dated May 28, 2013. Applicant has amended independent claim 1, canceled claim 19, and added new claim 25. No new matter has been added by way of the amendments, and support for the amendments can be found throughout Applicant's original disclosure including, e.g., at paragraph [55]. Claims 1–18 and 20–25 will be pending upon entry of this Amendment with claims 18–24 withdrawn from consideration. Reconsideration of the application is respectfully requested.

Interview Summary

Applicant thanks the Examiner for her time and the courtesies extended during the telephonic interview conducted on August 7, 2013. Examiner Jenna Zhang and Applicant's representative Paul J. LaVanway, Jr. (Reg. No. 64,610) were involved in the telephonic interview. The parties discussed rejected independent claim 1. The parties also discussed Bergner et al. (US 4,585,941, hereinafter "Bergner") and Mozley et al. (US 3,714,429, hereinafter "Mozley"), which were cited in the Final Office Action dated May 28, 2013. No exhibits were introduced or discussed.

Applicant's representative noted distinctions between independent claim 1 and the applied references. For example, Applicant's representative discussed how independent claim 1 specified that "elution is completed, when the pump has completed pumping the portion of the volume of eluant" and how the claim also required "receiving from the computer, via the computer interface, a display of time lapsed since the elution was completed." Applicant's representative submitted that neither Bergner nor Mozley disclosed or suggested the features of independent claim 1.

The Examiner acknowledged the distinctions between independent claim 1 and the Bergner and Mozley references. The Examiner further suggested making clarifying amendments to independent claim 1 consistent with the amendment presented here. Agreement was reached that independent claim 1, particularly as amended herein, was distinguishable from the rejections of record.

Claim Rejections Under 35 U.S.C. § 103(a)

In the Final Office Action, claims 1, 2, 9 and 11 were rejected under 35 U.S.C. § 103(a) as purportedly being unpatentable over Bergner in view of Mozley. In addition, claims 3-8 were rejected under 35 U.S.C. § 103(a) as purportedly being unpatentable over Bergner in view of Mozley and further in view of Gerhart (US 3,774,036); claim 12 was rejected under 35 U.S.C. § 103(a) as purportedly being unpatentable over Bergner in view of Mozley and further in view of Graves et al. (US 7,163,031, hereinafter "Graves"); and claim 17 was rejected under 35 U.S.C. § 103(a) as purportedly being unpatentable over Bergner in view of Mozley and further in view of Agarwal et al. (US 4,096,859, hereinafter "Agarwal").

As discussed and agreed during the telephonic interview, Bergner in view of Mozley does not disclose or suggest all the features of independent claim 1, particularly as independent claim 1 is amended herein. Nothing in the other references cited in the Office Action overcomes the deficiencies in Bergner and Mozley. Accordingly, in view of the agreement reached during the telephonic interview, Applicant requests reconsideration and withdrawal of the outstanding rejection against independent claim 1. Claims 2–17 and 25 depend from independent claim 1 and are therefore patentable at least by virtue of their dependency from the independent claim, as well as in their own right.

CONCLUSION

It is submitted that all claims in this application are in condition for allowance. Applicant respectfully requests reconsideration and prompt allowance of all pending claims.

In view of the differences identified above, Applicant reserves further comment concerning the additional features set forth in the claims. However, Applicant does not acquiesce in the propriety of the Office Action's application or interpretation of the references with respect to the claims, and reserves the right to present additional arguments in any further prosecution of this application.

The Commissioner is authorized to charge any deficiencies and credit any overpayments to Deposit Account No. 06-1910. The Examiner is invited to telephone the undersigned attorney to discuss this application.

Dated: August 28, 2013

Respectfully submitted,

/Paul J. LaVanway, Jr./

FREDRIKSON & BYRON, P.A.
200 South Sixth Street, Suite 4000
Minneapolis, MN 55402-1425 USA
Telephone: (612) 492-7387
Facsimile: (612) 492-7077

Paul J. LaVanway, Jr.
Registration No. 64,610

Please grant any extension of time necessary for entry; charge any fee due to Deposit Account No. 06-1910.

7223790_1.DOC

Electronic Patent Application Fee Transmittal

Application Number:	12137364
Filing Date:	11-Jun-2008
Title of Invention:	INFUSION SYSTEMS INCLUDING COMPUTER-FACILITATED MAINTENANCE AND/OR OPERATION AND METHODS OF USE
First Named Inventor/Applicant Name:	Stephen E. Hidem
Filer:	Paul J. LaVanway Jr.
Attorney Docket Number:	56782.1.7

Filed as Large Entity

Utility under 35 USC 111(a) Filing Fees

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Basic Filing:				
Pages:				
Claims:				
Miscellaneous-Filing:				
Petition:				
Patent-Appeals-and-Interference:				
Post-Allowance-and-Post-Issuance:				
Extension-of-Time:				

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Miscellaneous:				
RCE - 2nd and Subsequent Request	1820	1	1700	1700
		Total in USD ($)		**1700**

Electronic Acknowledgement Receipt

EFS ID:	16712347
Application Number:	12137364
International Application Number:	
Confirmation Number:	7377
Title of Invention:	INFUSION SYSTEMS INCLUDING COMPUTER-FACILITATED MAINTENANCE AND/OR OPERATION AND METHODS OF USE
First Named Inventor/Applicant Name:	Stephen E. Hidem
Customer Number:	22859
Filer:	Paul J. LaVanway Jr.
Filer Authorized By:	
Attorney Docket Number:	56782.1.7
Receipt Date:	28-AUG-2013
Filing Date:	11-JUN-2008
Time Stamp:	17:40:50
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	yes
Payment Type	Credit Card
Payment was successfully received in RAM	$1700
RAM confirmation Number	5325
Deposit Account	
Authorized User	

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)

1	Request for Continued Examination (RCE)	56782_1_7_RCE.pdf	697803 fba1619ca74f882a70dc29a2dcb1d398e93c879d	no	3
Warnings:					
Information:					
2		56782_1_7_Amendment.pdf	128547 fd6d301f3e2b4d8effe5a7c814935a7ca0db363c	yes	11

	Multipart Description/PDF files in .zip description		
	Document Description	**Start**	**End**
	Response After Final Action	1	1
	Amendment Copy Claims/Response to Suggested Claims	2	8
	Applicant Arguments/Remarks Made in an Amendment	9	11

Warnings:					
Information:					
3	Fee Worksheet (SB06)	fee-info.pdf	30344 576d25a48ce2200e740902ddb4951fa5b6c932db	no	2
Warnings:					
Information:					
		Total Files Size (in bytes):	856694		

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.

PTO/SB/06 (09-11)
Approved for use through 1/31/2014. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

PATENT APPLICATION FEE DETERMINATION RECORD Substitute for Form PTO-875	Application or Docket Number 12/137,364	Filing Date 06/11/2008	☐ To be Mailed

ENTITY: ☒ LARGE ☐ SMALL ☐ MICRO

APPLICATION AS FILED – PART I

FOR	(Column 1) NUMBER FILED	(Column 2) NUMBER EXTRA	RATE ($)	FEE ($)
☐ BASIC FEE (37 CFR 1.16(a), (b), or (c))	N/A	N/A	N/A	
☐ SEARCH FEE (37 CFR 1.16(k), (i), or (m))	N/A	N/A	N/A	
☐ EXAMINATION FEE (37 CFR 1.16(o), (p), or (q))	N/A	N/A	N/A	
TOTAL CLAIMS (37 CFR 1.16(i))	minus 20 =	*	X $ =	
INDEPENDENT CLAIMS (37 CFR 1.16(h))	minus 3 =	*	X $ =	
☐ APPLICATION SIZE FEE (37 CFR 1.16(s))	If the specification and drawings exceed 100 sheets of paper, the application size fee due is $310 ($155 for small entity) for each additional 50 sheets or fraction thereof. See 35 U.S.C. 41(a)(1)(G) and 37 CFR 1.16(s).			
☐ MULTIPLE DEPENDENT CLAIM PRESENT (37 CFR 1.16(j))				
* If the difference in column 1 is less than zero, enter "0" in column 2.			TOTAL	

APPLICATION AS AMENDED – PART II

AMENDMENT	08/28/2013	(Column 1) CLAIMS REMAINING AFTER AMENDMENT		(Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR	(Column 3) PRESENT EXTRA	RATE ($)	ADDITIONAL FEE ($)
	Total (37 CFR 1.16(i))	* 24	Minus	** 24	= 0	X $80 =	0
	Independent (37 CFR 1.16(h))	* 5	Minus	***5	= 0	X $420 =	0
	☐ Application Size Fee (37 CFR 1.16(s))						
	☐ FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))						
						TOTAL ADD'L FEE	0

AMENDMENT		(Column 1) CLAIMS REMAINING AFTER AMENDMENT		(Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR	(Column 3) PRESENT EXTRA	RATE ($)	ADDITIONAL FEE ($)
	Total (37 CFR 1.16(i))	*	Minus	**	=	X $ =	
	Independent (37 CFR 1.16(h))	*	Minus	***	=	X $ =	
	☐ Application Size Fee (37 CFR 1.16(s))						
	☐ FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))						
						TOTAL ADD'L FEE	

* If the entry in column 1 is less than the entry in column 2, write "0" in column 3.
** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 20, enter "20".
*** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 3, enter "3".
The "Highest Number Previously Paid For" (Total or Independent) is the highest number found in the appropriate box in column 1.

LIE
/LYNNELL JOHNSON/

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.
12/137,364	06/11/2008	Stephen E. Hidem	56782.1.7	7377

22859 7590 08/15/2013

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

EXAMINER	
ZHANG, JENNA	

ART UNIT	PAPER NUMBER
3763	

NOTIFICATION DATE	DELIVERY MODE
08/15/2013	ELECTRONIC

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.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

IP@FREDLAW.COM

Applicant-Initiated Interview Summary	Application No.	Applicant(s)	
	12/137,364	HIDEM ET AL.	
	Examiner	Art Unit	
	JENNA ZHANG	3763	

All participants (applicant, applicant's representative, PTO personnel):

(1) *JENNA ZHANG*. (3)_____.

(2) *PAUL LAVANWAY*. (4)_____.

Date of Interview: *07 August 2013*.

Type: ☒ Telephonic ☐ Video Conference
☐ Personal [copy given to: ☐ applicant ☐ applicant's representative]

Exhibit shown or demonstration conducted: ☐ Yes ☐ No.
If Yes, brief description: _____.

Issues Discussed ☐101 ☐112 ☐102 ☒103 ☐Others
(For each of the checked box(es) above, please describe below the issue and detailed description of the discussion)

Claim(s) discussed: *1*.

Identification of prior art discussed: *Bergner (US Pat. No. 4,585,941)*.

Substance of Interview
(For each issue discussed, provide a detailed description and indicate if agreement was reached. Some topics may include: identification or clarification of a reference or a portion thereof, claim interpretation, proposed amendments, arguments of any applied references etc...)

Applicant explained how the instant invention is different from Bergner noting in particular how the reference of Bergner does not provide a basis for obviousness for the claimed invention. Examiner explained the interpretation of the claims and further explained how Bergner provides a basis for one of ordinary skills to perform the method steps as claimed. However, Examiner agreed with Applicant the distinction between the instant invention and Bergner and suggested amending the claims to highlight this distinction. Examiner further agrees that the proposed amendments would be sufficient to distinguishing the claimed invention from the current grounds of rejection.

Applicant recordation instructions: The formal written reply to the last Office action must include the substance of the interview. (See MPEP section 713.04). If a reply to the last Office action has already been filed, applicant is given a non-extendable period of the longer of one month or thirty days from this interview date, or the mailing date of this interview summary form, whichever is later, to file a statement of the substance of the interview

Examiner recordation instructions: Examiners must summarize the substance of any interview of record. A complete and proper recordation of the substance of an interview should include the items listed in MPEP 713.04 for complete and proper recordation including the identification of the general thrust of each argument or issue discussed, a general indication of any other pertinent matters discussed regarding patentability and the general results or outcome of the interview, to include an indication as to whether or not agreement was reached on the issues raised.

☐ Attachment

/J. Z./	/Nicholas D Lucchesi/
Examiner, Art Unit 3763	Supervisory Patent Examiner, Art Unit 3763

Summary of Record of Interview Requirements

Manual of Patent Examining Procedure (MPEP), Section 713.04, Substance of Interview Must be Made of Record
A complete written statement as to the substance of any face-to-face, video conference, or telephone interview with regard to an application must be made of record in the application whether or not an agreement with the examiner was reached at the interview.

Title 37 Code of Federal Regulations (CFR) § 1.133 Interviews
Paragraph (b)

In every instance where reconsideration is requested in view of an interview with an examiner, a complete written statement of the reasons presented at the interview as warranting favorable action must be filed by the applicant. An interview does not remove the necessity for reply to Office action as specified in §§ 1.111, 1.135. (35 U.S.C. 132)

37 CFR §1.2 Business to be transacted in writing.
All business with the Patent or Trademark Office should be transacted in writing. The personal attendance of applicants or their attorneys or agents at the Patent and Trademark Office is unnecessary. The action of the Patent and Trademark Office will be based exclusively on the written record in the Office. No attention will be paid to any alleged oral promise, stipulation, or understanding in relation to which there is disagreement or doubt.

The action of the Patent and Trademark Office cannot be based exclusively on the written record in the Office if that record is itself incomplete through the failure to record the substance of interviews.

It is the responsibility of the applicant or the attorney or agent to make the substance of an interview of record in the application file, unless the examiner indicates he or she will do so. It is the examiner's responsibility to see that such a record is made and to correct material inaccuracies which bear directly on the question of patentability.

Examiners must complete an Interview Summary Form for each interview held where a matter of substance has been discussed during the interview by checking the appropriate boxes and filling in the blanks. Discussions regarding only procedural matters, directed solely to restriction requirements for which interview recordation is otherwise provided for in Section 812.01 of the Manual of Patent Examining Procedure, or pointing out typographical errors or unreadable script in Office actions or the like, are excluded from the interview recordation procedures below. Where the substance of an interview is completely recorded in an Examiners Amendment, no separate Interview Summary Record is required.

The Interview Summary Form shall be given an appropriate Paper No., placed in the right hand portion of the file, and listed on the "Contents" section of the file wrapper. In a personal interview, a duplicate of the Form is given to the applicant (or attorney or agent) at the conclusion of the interview. In the case of a telephone or video-conference interview, the copy is mailed to the applicant's correspondence address either with or prior to the next official communication. If additional correspondence from the examiner is not likely before an allowance or if other circumstances dictate, the Form should be mailed promptly after the interview rather than with the next official communication.

The Form provides for recordation of the following information:
- Application Number (Series Code and Serial Number)
- Name of applicant
- Name of examiner
- Date of interview
- Type of interview (telephonic, video-conference, or personal)
- Name of participant(s) (applicant, attorney or agent, examiner, other PTO personnel, etc.)
- An indication whether or not an exhibit was shown or a demonstration conducted
- An identification of the specific prior art discussed
- An indication whether an agreement was reached and if so, a description of the general nature of the agreement (may be by attachment of a copy of amendments or claims agreed as being allowable). Note: Agreement as to allowability is tentative and does not restrict further action by the examiner to the contrary.
- The signature of the examiner who conducted the interview (if Form is not an attachment to a signed Office action)

It is desirable that the examiner orally remind the applicant of his or her obligation to record the substance of the interview of each case. It should be noted, however, that the Interview Summary Form will not normally be considered a complete and proper recordation of the interview unless it includes, or is supplemented by the applicant or the examiner to include, all of the applicable items required below concerning the substance of the interview.

A complete and proper recordation of the substance of any interview should include at least the following applicable items:
1) A brief description of the nature of any exhibit shown or any demonstration conducted,
2) an identification of the claims discussed,
3) an identification of the specific prior art discussed,
4) an identification of the principal proposed amendments of a substantive nature discussed, unless these are already described on the Interview Summary Form completed by the Examiner,
5) a brief identification of the general thrust of the principal arguments presented to the examiner,
   (The identification of arguments need not be lengthy or elaborate. A verbatim or highly detailed description of the arguments is not required. The identification of the arguments is sufficient if the general nature or thrust of the principal arguments made to the examiner can be understood in the context of the application file. Of course, the applicant may desire to emphasize and fully describe those arguments which he or she feels were or might be persuasive to the examiner.)
6) a general indication of any other pertinent matters discussed, and
7) if appropriate, the general results or outcome of the interview unless already described in the Interview Summary Form completed by the examiner.

Examiners are expected to carefully review the applicant's record of the substance of an interview. If the record is not complete and accurate, the examiner will give the applicant an extendable one month time period to correct the record.

Examiner to Check for Accuracy

If the claims are allowable for other reasons of record, the examiner should send a letter setting forth the examiner's version of the statement attributed to him or her. If the record is complete and accurate, the examiner should place the indication, "Interview Record OK" on the paper recording the substance of the interview along with the date and the examiner's initials.

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.
12/137,364	06/11/2008	Stephen E. Hidem	56782.1.7	7377

22859 7590 05/28/2013

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

EXAMINER	
ZHANG, JENNA	

ART UNIT	PAPER NUMBER
3763	

NOTIFICATION DATE	DELIVERY MODE
05/28/2013	ELECTRONIC

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.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

IP@FREDLAW.COM

Office Action Summary	Application No.	Applicant(s)	
	12/137,364	HIDEM 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 *3* 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 *20 April 2012 and 17 May 2012*.

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

3)☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.

4)☐ 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

5)☒ Claim(s) *1-17* is/are pending in the application.

5a) Of the above claim(s) _____ is/are withdrawn from consideration.

6)☐ Claim(s) _____ is/are allowed.

7)☒ Claim(s) *1-17* is/are rejected.

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

9)☐ Claim(s) _____ are subject to restriction and/or election requirement.

* If any claims have been determined allowable, you may be eligible to benefit from the **Patent Prosecution Highway** program at a participating intellectual property office for the corresponding application. For more information, please see http://www.uspto.gov/patents/init_events/pph/index.jsp or send an inquiry to PPHfeedback@uspto.gov.

Application Papers

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

11)☒ The drawing(s) filed on *24 October 2008* 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).

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) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *See Continuation Sheet*.

3) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .

4) ☐ Other: _____.

Continuation of Attachment(s) 2). Information Disclosure Statement(s) (PTO/SB/08), Paper No(s)/Mail Date :5/31/2012; 10/17/2012; 11/7/2012; 1/18/2013; 4/3/2013.

DETAILED ACTION

1. In response to the Responses filed on April 17, 2012 and May 17, 2012, no claims are amended. Currently, claims 1-17 are still pending.

Claim Rejections - 35 USC § 103

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

3. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

4. **Claims 1, 2, 9, and 11** are rejected under 35 U.S.C. 103(a) as being unpatentable over Bergner (US Pat. No. 4,585,941) in view of Mozley et al (US Pat. No. 3,714,429).

Regarding **claim 1**, Bergner teaches a method for operating an infusion system, the system comprising: an eluant reservoir, a pump (64) coupled to the reservoir, an infusion tubing circuit (Fig. 1), a radioisotope generator (28), an activity detector (58), a waste bottle (42) and a computer (60, 62) including a computer interface, the infusion tubing circuit including an eluant line coupled to the pump and to the generator, a waste line coupled to the generator and to the waste bottle, and a patient line coupled to the generator (col. 3, line 23 until col. 4, line 53; Fig. 1), the method comprising:

entering, into the computer, via the computer interface, a command to activate the pump in order to generate an eluate from a portion of a volume of eluant pumped through the generator, via an elution within the generator;

receiving an indication, from the computer, via the computer interface, that the elution is completed, when the pump has completed pumping the portion of the volume of eluant; and

receiving an indication, from the computer, via the computer interface, of time lapsed since the elution was completed (col. 4, line 7 until col. 6, line 19).

Although Bergner discloses that an indication received, Bergner does not teach that a display of time is received form the computer as required by the instant claims. It is noted, however, that Mozley et al teaches that receiving and displaying the time elapsed to show the user the radioactivity distribution of the treatment (col. 7, line 66 until col. 10, line 30). Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to modify the method of operating an infusion system of Bergner with the feature of receiving from the computer, via the computer interface, a display of time lapsed since the elution was completed as taught by Mozley et al such that the radioactivity distribution can be seen by the user.

Regarding **claim 2**, Bergner teaches entering, into the computer (60, 62), via a computer interface, the volume of eluant contained in the reservoir, prior to the elution; and receiving, from the computer interface, an indication of a volume of eluant in the reservoir, based upon tracking the portion of the volume of eluant that is pumped from the reservoir (col. 4, line 4 until col. 5, line 32).

Regarding **claim 9**, Bergner teaches coupling the patient line to a shielded test vial in order to collect a sample of the eluate from the patient line during the elution; measuring an activity of the sample; and entering into the computer, via the computer interface, the measured activity of the sample and a time between completion of the elution and measuring of the activity, so that the computer may calculate a calibration coefficient for the infusion system based on the measured activity and an activity of the eluate detected, during elution, by the activity detector of the system (col. 6, line 21 until col. 9, line 48).

Regarding **claim 10**, Bergner teaches selecting a calibration procedure of the computer, via the computer interface, prior to entering the command to activate the pump (col. 4, line 26 until col. 9, line 48) but does not teach that the step of coupling the patient line to the shielded test vial is instructed by the computer interface, after selecting the calibration procedure. However, it would have been obvious to one of ordinary skill in the art at the time of the invention to modify the device of Bergner so that the controllers 60, 62 would notify the user to perform the step of coupling the patient line to the shielded test vial for an automated reminder to the user to increase the safety of the treatment.

Regarding **claim 11**, Bergner teaches purging air from the patient line; coupling the patient line to a patient, after purging, in order to inject a dose of the eluate to the patient from the patient line; and receiving a report from the computer, upon completion of the elution, the report including a patient identification number and at least one quantification of the dose of the eluate (col. 3, line 63 until col. 4, line 6 and lines 36-53; col. 6, lines 1-19).

Regarding **claims 13-16**, Bergner teaches

> receiving an indication, from the system, that the eluate is being diverted, from the generator, through the waste line of the infusion tubing circuit, when the pump is activated; and receiving an indication, from the system, that the eluate is being diverted from the generator, through the patient line of the infusion tubing circuit, when the pump is activated (col. 5, lines 8-24);

receiving an indication from the system that a peak bolus of radioactivity has been detected, in the eluate, by the activity detector (col. 7, line 1 until col. 9, line 47); and

wherein the system further comprises a light projector (104, 96, 100, 108; col. 9, line 49 until col. 10, line 11);

Although Bergner teaches the use of flashing and solid light projections from the light projector (106, 108) as alerting notifications (col. 11, line 46 until col. 12, line 29), Bergner does not teach that the indication that the eluate is being diverted through the waste line is a flashing light projection, the indication that the eluate is being diverted through the patient line comprises a solid light projection from the light projector, and the indication that the peak bolus of radioactivity has been detected comprises a flashing light from the light projector. However, it would have been obvious to one of ordinary skill in the art at the time of the invention to modify the device of Bergner with the use of flashing and solid light projections as the indication that the eluate is being diverted through the waste line is a flashing light projection, the indication that the eluate is being diverted through the patient line comprises a solid light projection, and the indication that the peak bolus of radioactivity has been detected comprises a flashing light from the light projector, to provide a notification that alerts the user.

5. **Claims 3-8** are rejected under 35 U.S.C. 103(a) as being unpatentable over Bergner (US Pat. No. 4,585,941) in view of Mozley et al (US Pat. No. 3,714,429) further in view of Gerhart (US Pat. No. 3,774,036).

Regarding **claim 3**, Bergner teaches coupling the patient line of the infusion tubing circuit to a first shielded test vial, in order to collect a first sample of the eluate from the patient line during the elution; measuring an activity of the first sample; and entering into the computer, via the computer interface, the measured activity of the first sample and a time between completion of the elution and the measuring of the activity (col. 3, line 55 until col. 5, line 68). However, Bergner does not teach method step of the computer calculating a breakthrough of the generator as required by the amended instant claim. It is noted that Gerhart teaches that breakthrough testing is performed to ensure the safety of a radioactive treatment dosage (col. 2, lines 27-39). Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to modify the method of Bergner with a breakthrough test procedure as taught by Gerhart to ensure the safety level of the treatment. Furthermore, it would have been obvious to one of ordinary skill in the art at the time of the invention to modify the device of Bergner so that the controllers 60, 62 perform the breakthrough test to calculate a breakthrough of the generator since the controllers 60, 62 controls the operations of the device of Bergner.

Regarding **claim 4**, Bergner does not teach selecting a breakthrough test procedure of the computer, via the computer interface, prior to entering the command to activate the pump; and wherein coupling the patient line to the first shielded test vial is instructed by the computer interface, after selecting the breakthrough test. However, as explained for claim 3 above, Bergner in view of Gerhart teaches performing a breakthrough test procedure prior to entering the command to activate the pump to

ensure the safety level of the treatment. Furthermore, it would have been obvious to one of ordinary skill in the art at the time of the invention to modify the device of Bergner so that the controllers 60, 62 would notify the user to perform the step of coupling the patient line to the shielded test vial for an automated reminder to the user to increase the safety of the treatment. Hence, the modified method of Bergner in view of Gerhart discloses selecting a breakthrough test procedure of the computer, via the computer interface, prior to entering the command to activate the pump; and wherein coupling the patient line to the first shielded test vial is instructed by the computer interface, after selecting the breakthrough test.

Regarding **claim 6**, the modified method of Bergner further teaches selecting a calibration procedure of the computer, via the computer interface, prior to entering the command to activate the pump for the second time; and wherein coupling the first new patient line to the second shielded test vial is instructed by the computer interface, after selecting the calibration procedure, as set forth for claim 10 (col. 6, line 21 until col. 9, line 48).

Regarding **claims 5 and 7**, Bergner further teaches repeating the steps of claim 1, wherein the pump is activated a second time and a second elution takes place, in order to fill the second vial with a second sample of the eluate from the first new patient line; measuring an activity of the second sample; and entering into the computer, via the computer interface, the measured activity of the second sample and a time between completion of the second elution and the measuring of the activity of the second sample, so that the computer may calculate a calibration coefficient for the infusion

system based on the measured activity of the second sample and an activity of the eluate detected, during the second elution, by the activity detector of the system. Bergner also teaches purging air from the second patient line; and repeating the steps of claim 1, wherein the pump is activated a third time and a third elution takes place, in order to inject a dose of the eluate to the patient from the second patient line (col. 6, line 21 until col. 9, line 48).

Regarding **claim 8**, Bergner further teaches receiving a report from the computer, upon completion of the third elution, the report including a patient identification number and at least one quantification of the dose of the eluate (col. 5, lines 41-68 and col. 9, line 49 until col. 10, line 11).

6. **Claim 12** is rejected under 35 U.S.C. 103(a) as being unpatentable over Bergner (US Pat. No. 4,585,941) in view of Mozley et al (US Pat. No. 3,714,429) further in view of Graves et al (US Pat. No. 7,163,031 B2).

Regarding **claim 12**, Bergner teaches the use of displays but does not teach a touch-activated display screen. However, it is noted that Graves et al teaches the use of a touch screen electronic display screen for inputting and outputting into a computer for a radiopharmaceutical delivery device (col. 4, line 53 until col. 5, line 2). Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to modify the device of Bergner with using a system that has a touch-activated display screen as disclosed by Graves et al to consolidate the number of components required for inputting and outputting commands and notifications in an infusion device.

7. **Claim 17** is rejected under 35 U.S.C. 103(a) as being unpatentable over Bergner (US Pat. No. 4,585,941) in view of Mozley et al (US Pat. No. 3,714,429) further in view of Agarwal et al (US Pat. No. 4,096,859).

Regarding **claim 17**, Bergner teaches the use of a waste bottle and tracking the waste level to determine the trigger point (col. 10, lines 12-68) but does not explicitly teach entering, into the computer, via the computer interface, a command to set a waste bottle level indicator to zero, when the waste bottle is empty and prior to entering the command to activate the pump; and receiving, from the computer, via the computer interface, an indication that the waste bottle needs to be emptied, based upon the computer tracking a volume of the eluate that is diverted, from the generator, through the waste line of the infusion tubing circuit. However, Agarwal et al teaches a medical delivery device with a waste container in which a controller tracks the waste level to alert the user to empty the waste container (col. 5, line 38 until col. 6, line 36). It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the method of Bergner with the steps of setting initial waste bottle level to zero when the bottle is empty and tracking the waste bottle level so that an alert is given to the user that the waste bottle is full and needs to be emptied as taught by Agarwal et al, to prevent overflowing of waste from the waste bottle.

It is noted that the modified method of Bergner and Agarwal et al teaches entering, into the computer, via the computer interface, a command to set a waste bottle level indicator to zero, when the waste bottle is empty and prior to entering the

command to activate the pump; and receiving, from the computer, via the computer interface, an indication that the waste bottle needs to be emptied, based upon the computer tracking a volume of the eluate that is diverted, from the generator, through the waste line of the infusion tubing circuit

Response to Arguments

8. Applicant's arguments filed on April 20, 2012 and May 17, 2012 have been fully considered but they are not persuasive.

In response to Applicant's argument that Bergner in view of Mozley et al does not disclose a method including a display of time lapsed since an elution was completed, it is noted that Bergner discloses the importance of tracking the time lapsed between elutions because patients can only having a certain amount of radioactive substances within their system for a given time period and quantizing of radioactivity of a liquid stream (col. 1, lines 64-67; col. 3, line 55 until col. 4, line 65; and col. 5, lines 41-67). Although Bergner shows a graph of radioactivity over time, Bergner does not explicitly display of time lapse since elution. However, Mozley et al teaches displaying time lapse of radioactive distribution. Therefore, it would have been obvious to one of ordinary skill in the art that modification of Bergner in view of Mozley et al discloses the step of receiving from the computer, via the computer interface, a display of time lapsed since the elution was completed.

Conclusion

9. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

10. 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
04/23/2013

/Nicholas D Lucchesi/

Supervisory Patent Examiner, Art Unit 3763

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Not for submission under 37 CFR 1.99)

Application Number	12137364
Filing Date	2008-06-11
First Named Inventor	Stephen E. Hidem
Art Unit	3763
Examiner Name	Jenna Zhang
Attorney Docket Number	56782.1.7

U.S.PATENTS Remove

Examiner Initial*	Cite No	Patent Number	Kind Code[1]	Issue Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1	6450936		2002-09-17	Smith, III	

If you wish to add additional U.S. Patent citation information please click the Add button. Add

U.S.PATENT APPLICATION PUBLICATIONS Remove

Examiner Initial*	Cite No	Publication Number	Kind Code[1]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1					

If you wish to add additional U.S. Published Application citation information please click the Add button. Add

FOREIGN PATENT DOCUMENTS Remove

Examiner Initial*	Cite No	Foreign Document Number[3]	Country Code[2] i	Kind Code[4]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear	T[5]
	1							☐

If you wish to add additional Foreign Patent Document citation information please click the Add button Add

NON-PATENT LITERATURE DOCUMENTS Remove

Examiner Initials*	Cite No	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc), date, pages(s), volume-issue number(s), publisher, city and/or country where published.	T[5]

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /J.Z./

Receipt date: 11/07/2012	Application Number	12137364	12137364 - GAU: 3763
INFORMATION DISCLOSURE STATEMENT BY APPLICANT (**Not for submission under 37 CFR 1.99)**	Filing Date	2008-06-11	
	First Named Inventor	Stephen E. Hidem	
	Art Unit	3763	
	Examiner Name	Jenna Zhang	
	Attorney Docket Number	56782.1.7	

	1		☐

If you wish to add additional non-patent literature document citation information please click the Add button **Add**

EXAMINER SIGNATURE

Examiner Signature	/Jenna Zhang/	Date Considered	02/25/2013

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through a citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

[1] See Kind Codes of USPTO Patent Documents at www.USPTO.GOV or MPEP 901.04. [2] Enter office that issued the document, by the two-letter code (WIPO Standard ST.3). [3] For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. [4] Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. [5] Applicant is to place a check mark here if English language translation is attached.

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /J.Z./

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Not for submission under 37 CFR 1.99)

Application Number	12137364
Filing Date	2008-06-11
First Named Inventor	Stephen E. HIDEM
Art Unit	3735
Examiner Name	ZHANG, Jenna
Attorney Docket Number	56782.1.7

U.S.PATENTS Remove

Examiner Initial*	Cite No	Patent Number	Kind Code[1]	Issue Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1					

If you wish to add additional U.S. Patent citation information please click the Add button. Add

U.S.PATENT APPLICATION PUBLICATIONS Remove

Examiner Initial*	Cite No	Publication Number	Kind Code[1]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1					

If you wish to add additional U.S. Published Application citation information please click the Add button. Add

FOREIGN PATENT DOCUMENTS Remove

Examiner Initial*	Cite No	Foreign Document Number[3]	Country Code[2] i	Kind Code[4]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear	T[5]
	1	1968653	CN		2007-05-23	E Z EM INC.		☐

If you wish to add additional Foreign Patent Document citation information please click the Add button Add

NON-PATENT LITERATURE DOCUMENTS Remove

Examiner Initials*	Cite No	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc), date, pages(s), volume-issue number(s), publisher, city and/or country where published.	T[5]

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /J.Z./

Receipt date: 04/03/2013	Application Number	12137364 12137364 - GAU: 3763
INFORMATION DISCLOSURE STATEMENT BY APPLICANT (**Not for submission under 37 CFR 1.99)**	Filing Date	2008-06-11
	First Named Inventor	Stephen E. HIDEM
	Art Unit	3735
	Examiner Name	ZHANG, Jenna
	Attorney Docket Number	56782.1.7

	1		☐

If you wish to add additional non-patent literature document citation information please click the Add button **Add**

EXAMINER SIGNATURE

Examiner Signature	/Jenna Zhang/	Date Considered	04/23/2013

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through a citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

[1] See Kind Codes of USPTO Patent Documents at www.USPTO.GOV or MPEP 901.04. [2] Enter office that issued the document, by the two-letter code (WIPO Standard ST.3). [3] For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. [4] Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. [5] Applicant is to place a check mark here if English language translation is attached.

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /J.Z./

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Not for submission under 37 CFR 1.99)

Application Number	12137364
Filing Date	2008-06-11
First Named Inventor	STEPHEN E. HIDEM
Art Unit	3763
Examiner Name	ZHANG, JENNA
Attorney Docket Number	56782.1.7

U.S.PATENTS Remove

Examiner Initial*	Cite No	Patent Number	Kind Code[1]	Issue Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1					

If you wish to add additional U.S. Patent citation information please click the Add button. Add

U.S.PATENT APPLICATION PUBLICATIONS Remove

Examiner Initial*	Cite No	Publication Number	Kind Code[1]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1	20080177126		2008-07-24	Tate	

If you wish to add additional U.S. Published Application citation information please click the Add button. Add

FOREIGN PATENT DOCUMENTS Remove

Examiner Initial*	Cite No	Foreign Document Number[3]	Country Code[2] i	Kind Code[4]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear	T[5]
	1							☐

If you wish to add additional Foreign Patent Document citation information please click the Add button Add

NON-PATENT LITERATURE DOCUMENTS Remove

Examiner Initials*	Cite No	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc), date, pages(s), volume-issue number(s), publisher, city and/or country where published.	T[5]

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /J.Z./

Receipt date: 05/31/2012	Application Number	12137364 12137364 - GAU: 3763
INFORMATION DISCLOSURE STATEMENT BY APPLICANT (**Not for submission under 37 CFR 1.99)**	Filing Date	2008-06-11
	First Named Inventor	STEPHEN E. HIDEM
	Art Unit	3763
	Examiner Name	ZHANG, JENNA
	Attorney Docket Number	56782.1.7

	1		☐

If you wish to add additional non-patent literature document citation information please click the Add button **Add**

EXAMINER SIGNATURE

Examiner Signature	/Jenna Zhang/	Date Considered	02/25/2013

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through a citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

[1] See Kind Codes of USPTO Patent Documents at www.USPTO.GOV or MPEP 901.04. [2] Enter office that issued the document, by the two-letter code (WIPO Standard ST.3). [3] For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. [4] Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. [5] Applicant is to place a check mark here if English language translation is attached.

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /J.Z./

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Not for submission under 37 CFR 1.99)

Application Number	12137364
Filing Date	2008-06-11
First Named Inventor	Stephen E. Hidem
Art Unit	3763
Examiner Name	Jenna Zhang
Attorney Docket Number	56782.1.7

U.S.PATENTS Remove

Examiner Initial*	Cite No	Patent Number	Kind Code[1]	Issue Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1	5395320		1995-03-07	Padda	

If you wish to add additional U.S. Patent citation information please click the Add button. Add

U.S.PATENT APPLICATION PUBLICATIONS Remove

Examiner Initial*	Cite No	Publication Number	Kind Code[1]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1	20030139640		2003-07-24	Whittacre	
	2	20050187515		2005-08-25	Varrichio	
	3	20050277833		2005-12-15	Williams	

If you wish to add additional U.S. Published Application citation information please click the Add button. Add

FOREIGN PATENT DOCUMENTS Remove

Examiner Initial*	Cite No	Foreign Document Number[3]	Country Code[2] i	Kind Code[4]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear	T[5]
	1							☐

EFS Web 2.1.17

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /J.Z./

Receipt date: 10/17/2012	Application Number	12137364 12137364 - GAU: 3763
INFORMATION DISCLOSURE STATEMENT BY APPLICANT (**Not for submission under 37 CFR 1.99)**	Filing Date	2008-06-11
	First Named Inventor	Stephen E. Hidem
	Art Unit	3763
	Examiner Name	Jenna Zhang
	Attorney Docket Number	56782.1.7

If you wish to add additional Foreign Patent Document citation information please click the Add button			Add
NON-PATENT LITERATURE DOCUMENTS			Remove
Examiner Initials*	Cite No	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc), date, pages(s), volume-issue number(s), publisher, city and/or country where published.	T[5]
	1	LEMER PAX, POSIJET® Integrated FDG dispensing and infusion system, www.lemerpax.com (date unknown).	☐
If you wish to add additional non-patent literature document citation information please click the Add button			Add

EXAMINER SIGNATURE			
Examiner Signature	/Jenna Zhang/	Date Considered	02/25/2013

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through a citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

[1] See Kind Codes of USPTO Patent Documents at www.USPTO.GOV or MPEP 901.04. [2] Enter office that issued the document, by the two-letter code (WIPO Standard ST.3). [3] For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. [4] Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. [5] Applicant is to place a check mark here if English language translation is attached.

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /J.Z./

Search Notes	Application/Control No.	Applicant(s)/Patent Under Reexamination
	12137364	HIDEM ET AL.
	Examiner	Art Unit
	JENNA ZHANG	3763

CPC- SEARCHED		
Symbol	Date	Examiner

CPC COMBINATION SETS - SEARCHED		
Symbol	Date	Examiner

US CLASSIFICATION SEARCHED			
Class	Subclass	Date	Examiner
604	236, and 65-67 with text	9/27/2010	JZ
312	209	9/27/2010	JZ
600	5	9/27/2010	JZ
600	4, and 600/431, 1-8, and 301 with text	9/29/2010	JZ

SEARCH NOTES		
Search Notes	Date	Examiner
Inventor Search	9/27/2010	JZ
Assignee Search	9/27/2010	JZ
Consulted Chris Koharski	9/28/2010	JZ
EAST Search	9/27-29/2010	JZ
Updated EAST Search	1/31/2011	JZ
Updated EAST Search	12/19/2011	JZ
Updated EAST Search	2/25/2013	JZ
Updated EAST Search	4/23/2013	JZ

INTERFERENCE SEARCH			
US Class/ CPC Symbol	US Subclass / CPC Group	Date	Examiner

Index of Claims	Application/Control No.	Applicant(s)/Patent Under Reexamination
	12137364	HIDEM ET AL.
	Examiner	**Art Unit**
	JENNA ZHANG	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	09/27/2010	01/31/2011	12/19/2011	04/23/2013					
	1	✓	✓	✓	✓					
	2	✓	✓	✓	✓					
	3	✓	✓	✓	✓					
	4	✓	✓	✓	✓					
	5	✓	✓	✓	✓					
	6	✓	✓	✓	✓					
	7	✓	✓	✓	✓					
	8	✓	✓	✓	✓					
	9	✓	✓	✓	✓					
	10	✓	✓	✓	✓					
	11	✓	✓	✓	✓					
	12	✓	✓	✓	✓					
	13	✓	✓	✓	✓					
	14	✓	✓	✓	✓					
	15	✓	✓	✓	✓					
	16	✓	✓	✓	✓					
	17	✓	✓	✓	✓					
	18	✓	N	N	N					
	19	✓	N	N	N					
	20	✓	N	N	N					
	21	✓	N	N	N					
	22	✓	N	N	N					
	23	✓	N	N	N					
	24	✓	N	N	N					

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Not for submission under 37 CFR 1.99)

Application Number	12137364
Filing Date	2008-06-11
First Named Inventor	Stephen E. Hidem
Art Unit	3763
Examiner Name	Jenna Zhang
Attorney Docket Number	56782.1.7

U.S.PATENTS Remove

Examiner Initial*	Cite No	Patent Number	Kind Code[1]	Issue Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1	7996068		2011-08-09	Telischak	

If you wish to add additional U.S. Patent citation information please click the Add button. Add

U.S.PATENT APPLICATION PUBLICATIONS Remove

Examiner Initial*	Cite No	Publication Number	Kind Code[1]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1					

If you wish to add additional U.S. Published Application citation information please click the Add button. Add

FOREIGN PATENT DOCUMENTS Remove

Examiner Initial*	Cite No	Foreign Document Number[3]	Country Code[2] i	Kind Code[4]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear	T[5]
	1							☐

If you wish to add additional Foreign Patent Document citation information please click the Add button Add

NON-PATENT LITERATURE DOCUMENTS Remove

Examiner Initials*	Cite No	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc), date, pages(s), volume-issue number(s), publisher, city and/or country where published.	T[5]

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /J.Z./

Receipt date: 01/18/2013	Application Number	12137364 12137364 - GAU: 3763
INFORMATION DISCLOSURE STATEMENT BY APPLICANT (**Not for submission under 37 CFR 1.99)**	Filing Date	2008-06-11
	First Named Inventor	Stephen E. Hidem
	Art Unit	3763
	Examiner Name	Jenna Zhang
	Attorney Docket Number	56782.1.7

	1	R. Klein, "Precise 82RB infusion system for cardiac perfusion measurement using 3D positron emission tomography", Ottawa-Carleton Institute for Electrical and Computer Engineering School of Information Technology and Engineering (Electrical & Computer Engineering), February, 2005, 147 pages	☐
	2	LEMER PAX, POSIJET® Integrated FDG dispensing and infusion system, www.lemerpax.com (copyright date May 2008)	☐

If you wish to add additional non-patent literature document citation information please click the Add button **Add**

EXAMINER SIGNATURE

Examiner Signature	/Jenna Zhang/	Date Considered	02/25/2013

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through a citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

[1] See Kind Codes of USPTO Patent Documents at www.USPTO.GOV or MPEP 901.04. [2] Enter office that issued the document, by the two-letter code (WIPO Standard ST.3). [3] For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. [4] Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. [5] Applicant is to place a check mark here if English language translation is attached.

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /J.Z./

PTO/SB/08a (01-10)
Approved for use through 07/31/2012. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Not for submission under 37 CFR 1.99)

Application Number	12137364
Filing Date	2008-06-11
First Named Inventor	Stephen E. Hidem
Art Unit	3763
Examiner Name	Jenna Zhang
Attorney Docket Number	56782.1.7

U.S.PATENTS Remove

Examiner Initial*	Cite No	Patent Number	Kind Code[1]	Issue Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1					

If you wish to add additional U.S. Patent citation information please click the Add button. Add

U.S.PATENT APPLICATION PUBLICATIONS Remove

Examiner Initial*	Cite No	Publication Number	Kind Code[1]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1					

If you wish to add additional U.S. Published Application citation information please click the Add button. Add

FOREIGN PATENT DOCUMENTS Remove

Examiner Initial*	Cite No	Foreign Document Number[3]	Country Code[2] i	Kind Code[4]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear	T[5]
	1	2492920	EP	A2	2012-08-29	DRAXIMAGE GENERAL PARTNERSHIP		☐
	2	2011126	EP	B1	2012-05-23	DRAXIMAGE GENERAL PARTNERSHIP		☐

If you wish to add additional Foreign Patent Document citation information please click the Add button Add

NON-PATENT LITERATURE DOCUMENTS Remove

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	12137364
	Filing Date	2008-06-11
	First Named Inventor	Stephen E. Hidem
	Art Unit	3763
	Examiner Name	Jenna Zhang
	Attorney Docket Number	56782.1.7

Examiner Initials*	Cite No	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc), date, pages(s), volume-issue number(s), publisher, city and/or country where published.	T[5]
	1		☐

If you wish to add additional non-patent literature document citation information please click the Add button Add

EXAMINER SIGNATURE

Examiner Signature		Date Considered	

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through a citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

[1] See Kind Codes of USPTO Patent Documents at www.USPTO.GOV or MPEP 901.04. [2] Enter office that issued the document, by the two-letter code (WIPO Standard ST.3). [3] For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. [4] Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. [5] Applicant is to place a check mark here if English language translation is attached.

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	12137364
	Filing Date	2008-06-11
	First Named Inventor	Stephen E. Hidem
	Art Unit	3763
	Examiner Name	Jenna Zhang
	Attorney Docket Number	56782.1.7

CERTIFICATION STATEMENT

Please see 37 CFR 1.97 and 1.98 to make the appropriate selection(s):

☐ That each item of information contained in the information disclosure statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(1).

OR

☐ That no item of information contained in the information disclosure statement was cited in a communication from a foreign patent office in a counterpart foreign application, and, to the knowledge of the person signing the certification after making reasonable inquiry, no item of information contained in the information disclosure statement was known to any individual designated in 37 CFR 1.56(c) more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(2).

☐ See attached certification statement.

☒ The fee set forth in 37 CFR 1.17 (p) has been submitted herewith.

☐ A certification statement is not submitted herewith.

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	/Paul J. LaVanway, Jr./	Date (YYYY-MM-DD)	2013-05-22
Name/Print	Paul J. LaVanway, Jr.	Registration Number	64610

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 1 hour to complete, including gathering, preparing and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

Privacy Act Statement

The Privacy Act of 1974 (P.L. 93-579) requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that: (1) the general authority for the collection of this information is 35 U.S.C. 2(b)(2); (2) furnishing of the information solicited is voluntary; and (3) the principal purpose for which the information is used by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent application or patent. If you do not furnish the requested information, the U.S. Patent and Trademark Office may not be able to process and/or examine your submission, which may result in termination of proceedings or abandonment of the application or expiration of the patent.

The information provided by you in this form will be subject to the following routine uses:

1. The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C. 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether the Freedom of Information Act requires disclosure of these record s.

2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.

3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.

4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).

5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent Cooperation Treaty.

6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).

7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (i.e., GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.

8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspections or an issued patent.

9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

(19) Europäisches Patentamt
European Patent Office
Office européen des brevets

(11) EP 2 492 920 A2

(12) EUROPEAN PATENT APPLICATION

(43) Date of publication:
29.08.2012 Bulletin 2012/35

(51) Int Cl.:
G21G 1/02 *(2006.01)*

(21) Application number: **12168843.6**

(22) Date of filing: **16.12.2006**

(84) Designated Contracting States:
AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IS IT LI LT LU LV MC NL PL PT RO SE SI SK TR

(30) Priority: **12.01.2006 US 758419 P**
14.12.2006 US 610574

(62) Document number(s) of the earlier application(s) in accordance with Art. 76 EPC:
06851254.0 / 2 011 126

(71) Applicant: **DRAXIMAGE General Partnership**
Montreal, QC H9H 4J4 (CA)

(72) Inventors:
- **Tartaglia, Daniel**
  St. Leonard, Québec HIR 3Z6 (CA)
- **Coppola, Carlo**
  Pointe-Claire, Québec H9R 5Y2 (CA)
- **Teoli, Vince**
  Montreal, Québec H2N 1W5 (CA)
- **Bournival, Alain Guy**
  St. Lazarre, Québec H2N 1W5 (CA)

(74) Representative: **Holliday, Louise Caroline**
D Young & Co LLP
120 Holborn
London EC1N 2DY (GB)

Remarks:
This application was filed on 22-05-2012 as a divisional application to the application mentioned under INID code 62.

(54) Systems and methods for radioisotope generation

(57) Systems and methods are disclosed for producing customized, predictable, and reproducible supplies of radioisotopes using, for example, a reactor housing that is fabricated from a radioactive shielding material and has both an internal volume and a surface that comprises an entry port and an exit port, a chromatographic column that is positioned within said internal volume such that a first end of said column is in fluid communication with said entry port and a second end of said column is in fluid communication with said exit port, and a changeable filter module that is disposed external to said reactor housing and in fluid communication with said exit port.

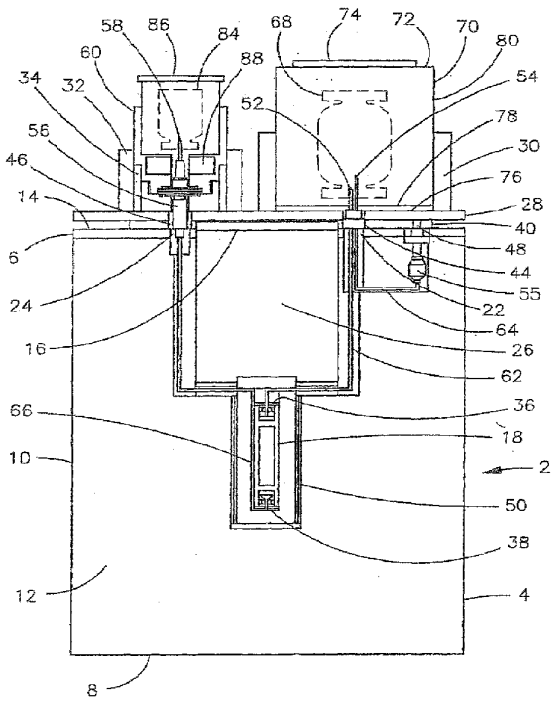


Fig. 1

EP 2 492 920 A2

Description

CROSS REFERENCE TO RELATED APPLICATION

[0001] This application claims the benefit of U.S. Provisional Patent Application Serial Number 60/758,419, filed January 12, 2006, and from U.S. Patent Application Serial No. 11/610,574, filed December 14,2006, the respective contents of which are incorporated herein by reference.

FIELD OF THE INVENTION

[0002] This invention relates generally to systems and methods for radioisotope generation. In one aspect, this invention relates to systems and methods for producing customized, predictable and reproducible supplies of radioisotopes for use in nuclear medicine.

BACKGROUND OF THE INVENTION

[0003] Nuclear medicine is a branch of medicine dealing with the use of radioisotopes as radiopharmaceuticals or radioactive tracers in the diagnosis and treatment of disease. Radioisotopes are natural or artificially created isotopes (isotopes being one of two or more atoms having the same atomic number but different mass numbers) of a chemical element that have an unstable nucleus that decays, emitting alpha, beta, or gamma rays until stability is reached.

[0004] Radioisotopes, such as the meta stable Technetium-99m (Tc-99m), are used in medical tests as radioactive tracers that medical equipment can detect in the body. Other generator-derived radioisotopes that are used as tracers include yttrium-90, rhenium-188, and *gallium*-68. Tc-99m, in particular, emits readily detectable gamma rays, and it has a half-life of 6 hours. A variety of different radiopharmaceuticals based on Tc-99m are used for imaging and functional studies of the brain, myocardium, thyroid, lungs, liver, gallbladder, kidneys, skeleton, blood and tumors. Schwochau, Klaus. Technetium, Wiley-VCH (2000) (ISBN 3-527-29496-1). Scientists continue to find new uses for radioisotopes, such as Tc-99m. For example, doctors recently used Tc-99m to diagnose precisely the infected lymph nodes in breast cancer patients by injecting Tc-99m into the breast around the tumor to allow them to locate the node quickly and precisely before ever making an incision. *Brookhaven National Laboratory site on the history of the technetium cow.* (http://www.bnl.gov/bnJweb/history/Tc-99m.asp).

[0005] A Tc-99m generator, often called a technetium cow, is a device used to extract Tc-99m from decaying molybdenum-99 ("Mo-99"). Mo-99 has a half-life of 66 hours and can be transported over long distances to radiopharmacies and hospitals where its decay product Tc-99m is used for nuclear medicine diagnostic procedures. Removing the Tc-99m from the generator ("milking" the generator) is typically done every 6 hours or, at most, twice daily. Most commercial generators use column chromatography, in which Mo-99 is adsorbed onto alumina. Normal saline solution can be run through a column of immobilized Mo-99 to elute soluble Tc-99m, resulting in a saline solution containing the Tc-99m.

[0006] Today, commercial radiopharmacies typically replace their generators on a biweekly basis, since the useful life of a Tc-99m generator is about 6 half lifes or approximately two weeks. Hence, typical clinical nuclear medicine units purchase at least one such generator every two weeks or order several in a staggered fashion. The lead-lined generators are heavy and bulky and represent significant manipulation and toil for personnel to replace and to dispose of spent generators. Large quantities of lead, molded plastic containers, and packing materials are used only once and discarded after two weeks. Shipping costs and waste are real considerations for end-users. Further, conventional generator systems lack flexibility as they are limited to fixed activity denominations per unit sold, resulting in limited predictability and reproducibility. Typical generators also do not provide activity above 19 Ci.

[0007] It would be desirable therefore to provide systems and methods for producing customized, predictable and reproducible supplies of radioisotopes, including high activity levels, that do not require weekly replacement, handling and transport of heavy shielding materials associated with conventional generators.

SUMMARY OF THE INVENTION

[0008] In one aspect, the present invention provides systems comprising a reactor housing that is fabricated from a radioactive shielding material and has both an internal volume and a surface that comprises an entry port and an exit port; a chromatographic column that is positioned within said internal volume such that a first end of said column is in fluid communication with said entry port and a second end of said column is in fluid communication with said exit port; and a filter module that is disposed external to said reactor housing and in fluid communication with said exit port.

[0009] In another aspect, the present invention provides kits comprising a column, a delivery housing, and a shielded filter module.

[0010] The present invention also provides methods comprising the steps of providing a system that comprises: a reactor housing that is fabricated from a radioactive shielding material and has both an internal volume and a surface that comprises an entry port and an exit port; a first chromatographic column that is positioned within said internal volume such that a first end of said column is in fluid communication with said entry port and a second end of said column is in fluid communication with said exit port; and a first filter module that is disposed external to said reactor housing and in fluid communication with said exit port; and positioning a first delivery vessel comprising a solution of at least one radioisotope

external to said reactor housing and in fluid communication with said entry port for a time and under conditions effective to elute said chromatographic column with at least a portion of said solution.

[0011] In yet another aspect, the present invention provides methods comprising the steps of providing a system that comprises: a reactor housing that is fabricated from a radioactive shielding material and has both an internal volume and a surface that comprises an entry port and an exit port; a first chromatographic column that comprises at least one radioisotope and is positioned within said internal volume such that a first end of said column is in fluid communication with said entry port and a second end of said column is in fluid communication with said exit port; and a filter module that is disposed external to said reactor housing and in fluid communication with said exit port; and removing said first chromatographic column from said reactor housing.

[0012] In still yet another aspect, the present invention provides methods comprising the steps of providing a system that comprises: a reactor housing that is fabricated from a radioactive shielding material and has both an internal volume and a surface that comprises an entry port and an exit port; a first chromatographic column that is positioned within said internal volume such that a first end of said column is in fluid communication with said entry port and a second end of said column is in fluid communication with said exit port; and a first filter module that is disposed external to said reactor housing and in fluid communication with said exit port; and removing said first filter module.

[0013] The present invention also provides methods comprising the steps of: providing a system that comprises: a reactor housing that is fabricated from a radioactive shielding material and has both an internal volume and a surface that comprises an entry port and an exit port; said internal volume being substantially defined by a first end, a second end, and a wall extending between said first end and said second end; a first chromatographic column that is positioned within said internal volume such that a first end of said column is in fluid communication with said entry port and a second end of said column is in fluid communication with said exit port; and a filter module that is disposed external to said reactor housing and in fluid communication with said exit port; positioning a collection vessel external to said reactor housing and in fluid communication with said exit port via said filter module.

[0014] In yet another aspect, the present invention provides methods comprising the steps of: receiving customer information including a target output of a radioisotope; and adding a solution of a parent radioisotope to a delivery vessel in an amount sufficient to produce said target output upon decay of said parent radioisotope.

BRIEF DESCRIPTION OF THE DRAWINGS

[0015] **FIG. 1** is a cutaway side view depicting one generator system according to the invention.

[0016] **FIG. 2** is a cutaway side view depicting one shielded filter module according to the invention.

[0017] **FIG. 3** is an isometric view of one cart according to the invention.

[0018] **FIG. 4** is a cutaway side view of one generator system according to the invention.

[0019] **FIG. 5** is a perspective view of a column assembly being inserted into an internal volume of a reactor housing according to the invention.

[0020] **FIG. 6** is a perspective view of a radioactive shielding plug being inserted into an opening in a reactor housing according to the invention.

[0021] **FIG. 7** is a perspective view of an adapter disk disposed on the surface of a reactor housing according to the invention.

Further aspects of the invention are set out below in the following numbered paragraphs:-

1. A system comprising:

   a reactor housing that is fabricated from a radioactive shielding material and has both an internal volume and a surface that comprises an entry port and an exit port;
   a chromatographic column that is positioned within said internal volume such that a first end of said column is in fluid communication with said entry port and a second end of said column is in fluid communication with said exit port; and
   a filter module that is disposed external to said reactor housing and in fluid communication with said exit port.

2. The system of paragraph 1 wherein said radioactive shielding material is lead, tungsten or depleted uranium.

3. The system of paragraph 1 wherein said reactor housing is substantially rectilinear.

4. The system of paragraph 1 wherein said reactor housing is substantially cylindrical.

5. The system of paragraph 1 wherein said reactor housing includes a first end, a second end, and a wall extending between said first end and said second end.

6. The system of paragraph 5 wherein said entry port and said exit port are positioned at said first end.

7. The system of paragraph 6 further comprising a ridge of radioactive shielding material extending around said entry port at said first end.

8. The system of paragraph 6 further comprising a ridge of radioactive shielding material extending

around said exit port at said first end.

9. The system of paragraph 1 wherein said column comprises aluminum oxide particles from about 50 to about 200 μm in size.

10. The system of paragraph 1 wherein said column comprises silica gel particles from about 20 to about 100 μm in size.

11. The system of paragraph 1 wherein said column comprises one or more layers or polypropylene filter membranes, deactivated fused silica wool, one or more glass filter membranes from about 0.2 to about 10 μm in size and made of polyether sulfone, or stainless steel tubing with needle and filter adaptors.

12. The system of paragraph 11 further comprising two acetal plastic plugs with funnel drains.

13. The system of paragraph 1 wherein said filter module comprises a sterile 13 to 25 mm filter membrane from about 0.1 to about 0.22 μm size.

14. The system of paragraph 1 wherein said filter module is attached to said reactor vessel by a tread type adaptor.

15. The system of paragraph 14 wherein a needle is attached to said filter module.

16. The system of paragraph 1 wherein a collection housing is connected to said reactor housing via said filter module.

17. The system of paragraph 1 wherein said column comprises at least one radioisotope.

18. The system of paragraph 17 wherein said at least one radioisotope is Molybdate Mo- 99.

19. The system of paragraph 17 wherein said at least one radioisotope is Pertechnetate Tc99m.

20. The system of paragraph 1 further comprising a delivery vessel that is disposed external to said reactor housing and in fluid communication with said entry port.

21. The system of paragraph 20 wherein said delivery vessel is contained within a delivery housing that is fabricated from radioactive shielding material, such as lead, tungsten or depleted uranium.

22. The system of paragraph 21 wherein said delivery housing has a first end that includes a first coupling, a second end that includes a second coupling, and a walj extending between said first end and said second end.

23. The system of paragraph 22 wherein said first coupling is threaded.

24. The system of paragraph 22 further comprising a transfer tool that comprises a pick-up and release rod having a handle at a first end thereof and a coupling at a second end thereof that is compatible with said first coupling.

25. The system of paragraph 24 wherein said transfer tool is a T-bar handle.

26. The system of paragraph 20 wherein said delivery vessel comprises a solution of at least one radioisotope.

27. The system of paragraph 26 wherein said at least one radioisotope is Molybdate Mo- 99.

28. The system of paragraph 26 wherein said solution is Sodium Molybdate Mo-99.

29. The system of paragraph 26 wherein said delivery vessel comprises about 1 to about 50 Ci.

30. The system of paragraph 20 wherein said delivery vessel comprises Normal Saline [0.9%] solution.

31. The system of paragraph 21 wherein said delivery housing abuts a ridge of material that is external to said reactor housing and extends around said entry port.

32. The system of paragraph 21 wherein said delivery housing is at least partially contained within a ridge of material that is external to said reactor housing and extends around said entry port.

33. The system of paragraph 20 wherein said delivery vessel is at least partially contained within a ridge of material that is external to said reactor housing and extends around said entry port.

34. The system of paragraph 1 further comprising a collection vessel that is disposed external to said reactor housing and in fluid communication with said exit port via said filter module.

35. The system of paragraph 34 wherein said collection vessel is evacuated.

36. The system of paragraph 34 wherein said collection vessel comprises a solution of at least one radioisotope.

37. The system of paragraph '36 wherein said at least

one radioisotope is Technetium Tc99m.

38. The system of paragraph 36 wherein said solution is Sodium Pertechnetate Tc-99m.

39. The system of paragraph 1 further comprising an adapter disk disposed on said reactor housing, comprising a ridge of material that extends around said entry port and a ridge of material that extends around said exit port.

40. The system of paragraph 39 further comprising an adapter ridge disposed circumferentially internal to said ridge of material that extends around said entry port.

41. The system of paragraph 40 further comprising a saline vessel that is disposed external to said reactor housing and in fluid communication with said entry port.

42. The system of paragraph 41 wherein said saline vessel comprises Normal Saline [0.9%] solution.

43. The system of paragraph 34 wherein said filter module abuts a ridge of radioactive shielding material that is external to said reactor housing and extends around said exit port.

44. The system of paragraph 34 wherein said filter module is at least partially contained within a ridge of radioactive shielding material that is external to said reactor housing and extends around said exit port.

45. The system of paragraph 34 wherein said collection vessel is contained within a collection housing that is fabricated from radioactive shielding material.

46. The system of paragraph 45 wherein said collection housing abuts a ridge of material that is external to said reactor housing and extends around said exit port.

47. The system of paragraph 45 wherein said collection housing is at least partially contained within a ridge of material that is external to said reactor housing and extends around said exit port.

48. The system of paragraph 1 further comprising a cart that includes a plurality of delivery vessels that each independently comprises a reactor vessel.

49. The system of paragraph 1 further comprising a cart that includes a plurality of delivery vessels that each independently comprise a solution of at least one radioisotope and are contained within a delivery housing that is fabricated from radioactive shielding material.

50. The system of paragraph 49 further comprising a conveyor belt for moving said delivery housing.

51. The system of paragraph 49 further comprising a transfer tool for moving said delivery housing.

52. The system of paragraph 49 wherein said at least one radioisotope is Molybdenum-99.

53. The system of paragraph 49 wherein said solution is Sodium Molybdate Mo-99.

54. The system of paragraph 49 wherein said delivery vessels each independently comprise about 1 to about 50 Ci.

55. The system of paragraph 1 further comprising a cart that includes a plurality of evacuated collection vessels.

56. The system of paragraph 1 further comprising a cart that includes a plurality of saline vessels.

57. A kit comprising a column, delivery housing, and a filter module comprising.a radioactive shielding material insert.

58. The kit of paragraph 57 further comprising a transfer tool.

59. The kit of paragraph 57 further comprising a plurality of evacuated collection vessels.

60. The kit of paragraph 57 further comprising a plurality of saline vessels.

61. A method comprising the steps of: providing a system that comprises:

a reactor housing that is fabricated from a radioactive shielding material and has both an internal volume and a surface that comprises an entry port and an exit port;
a first chromatographic column that is positioned within said internal volume such that a first end of said column is in fluid communication with said entry port and a second end of said column is in fluid communication with said exit port; and
a first filter module that is disposed external to said reactor housing and in fluid communication with said exit port; and either:

positioning a first delivery vessel comprising a solution of at least one radioisotope external to said reactor housing and in fluid

communication with said entry port for a time and under conditions effective to elute said chromatographic column with at least a portion of said solution; or
positioning a collection vessel external to said reactor housing and in fluid communication with said exit port via said filter module; or removing said first chromatographic column from said reactor housing; or removing said first filter module.

62. The method of paragraph 61 wherein said first delivery vessel is contained within a delivery housing that is fabricated from radioactive shielding material and has a first end that includes a coupling, a second end that includes a coupling, and a wall extending between said first end and said second end.

63. The method of paragraph 62 wherein positioning said first delivery vessel comprises: mating said coupling at said first end of said delivery housing with a transfer tool comprising a rod having a handle at a first end thereof and a coupling at a second end thereof that is compatible with said coupling at said first end of said delivery housing; and
lifting said delivery housing.

64. The method of paragraph 63 further comprising mating said coupling at said second end of said first delivery housing with a coupling on said reactor housing that is compatible with said coupling at said second end of said first delivery housing.

65. The method of paragraph 61 further comprising removing said first delivery vessel from said position relative to said reactor housing.

66. The method of paragraph 62 wherein said first delivery vessel is contained within a delivery housing that is fabricated from radioactive shielding material and has a first end that includes a coupling, a second end that includes a coupling, and a wall extending between said first end and said second end.

67. The method of paragraph 66 wherein removing said first delivery vessel comprises:

mating said coupling at said first end of said first delivery housing with a transfer tool comprising a rod having a handle at a first end thereof and a coupling at a second end thereof that is compatible with said coupling at said first end of said first delivery housing; and
lifting said delivery housing.

68. The method of paragraph 66 further comprising positioning a second delivery vessel comprising saline external to said reactor housing and in fluid communication with said entry port for a time and under conditions effective to elute said chromatographic column with at least a portion of said saline solution.

69. The method of paragraph 68 further comprising removing said second delivery vessel from said position relative to said reactor housing.

70. The method of paragraph 69 further comprising positioning a subsequent delivery vessel comprising saline external to said reactor housing and in fluid communication with said entry port for a time and under conditions effective to elute said chromatographic column with at least a portion of said saline solution.

71. The method of paragraph 69 further comprising positioning a subsequent delivery vessel comprising a solution of at least one radioisotope external to said reactor housing and in fluid communication with said entry port for a time and under conditions effective to elute said chromatographic column with at least a portion of said solution.

72. The method of paragraph 69 further comprising removing said first chromatographic column from said reactor housing.

73. The method of paragraph 72 further comprising positioning a subsequent chromatographic column in said reactor housing such that a first end of said column is in fluid communication with said entry port and a second end of said column is in fluid communication with said exit port.

74. The method of paragraph 69 further comprising positioning a first collection vessel external to said reactor housing and in fluid communication with said exit port via said filter module.

75. The method of paragraph 74 wherein said collection vessel is contained within a collection housing that is fabricated from radioactive shielding material.

76. The method of paragraph 74 further comprising removing said first collection vessel from said position relative to said reactor housing.

77. The method of paragraph 69 further comprising positioning a subsequent collection vessel external to said reactor housing and in fluid communication with said exit port via said filter module.

78. The method of paragraph 61 further comprising removing said first filter module.

79. The method of paragraph 78 further comprising positioning a subsequent filter module external to

said reactor housing and in fluid communication with said exit port.

80. The method of paragraph 61 comprising the steps of:

providing said system; and
positioning a first delivery vessel comprising a solution of at least one radioisotope external to said reactor housing and in fluid communication with said entry port for a time and under conditions effective to elute said chromatographic column with at least a portion of said solution

81. The method of paragraph 61 comprising the steps of:

providing said system; and removing said first chromatographic column from said reactor housing.

82. The method of paragraph 61 further comprising positioning a subsequent chromatographic column in said reactor housing such that a first end of said column is in fluid communication with said entry port and a second end of said column is in fluid communication with said exit port.

83. The method of paragraph 61 comprising the steps of:

providing said system; and
removing said first filter module.

84. The method of paragraph 61 further comprising positioning a subsequent filter module external to said reactor housing and in fluid communication with said exit port.

85. The method of paragraph 61 comprising the steps of:

providing said system; and
positioning a collection vessel external to said reactor housing and in fluid communication with said exit port via said filter module.

86. A method comprising the steps of;
receiving customer information including a target output of a radioisotope; and adding a solution of a parent radioisotope to a delivery vessel in an amount sufficient to produce said target output upon decay of said parent radioisotope.

87. The method of paragraph 86 wherein said radioisotope is Technetium-99m.

88. The method of paragraph 86 wherein said parent radioisotope is Molybdenum-99.

89. The method of paragraph 86 further comprising shipping said delivery vessel to said customer.

DETAILED DESCRIPTION OF ILLUSTRATIVE EMBODIMENTS

[0022] With reference to the drawings, **FIG. 1** shows one type of generator system **2** according to the invention. The generator system may include a reactor housing **4** fabricated from a radioactive shielding material such as lead, tungsten, or depleted uranium. The reactor housing **4** maybe substantially cylindrical, as shown in **FIG. 1.** In another embodiment, the reactor housing may be substantially rectilinear. The reactor housing **4** may include a first end **6**, a second end **8**, and a wall **10** extending between said first end **6** and said second end **8.** The reactor housing **4** may have both an internal volume **12** and a surface **14** that comprises an opening **16** for inserting a column **18** (said column may be included in a column assembly **20,** shown in more detail in **FIG. 5),** an entry port **22**, and an exit port **24.** The opening **16**, entry port **22** and exit port **24** may be positioned at said first end **6** of said housing **4.** A radioactive shielding plug **26** may be disposed in said opening **16** in said surface **14** above said column **18.** The radioactive shielding plug **26** may be fabricated from a radioactive shield material such as lead, tungsten, or depleted uranium. The reactor housing **4** may have an adapter disk **28** disposed on the surface **14** of said reactor housing **4** that comprises a ridge of guide **material 30** that may extend around said entry port **22** and a ridge of guide material **32** that may extend around said exit port **24.** Preferably, the adapter disk **28** and ridges of guide material **30** and **32** are plastic. A ridge of radioactive shielding material **34** may extend around said exit port **24.**

[0023] A chromatographic column **18** may be positioned within said internal volume **12** such that a first end **36** of said column **18** is in fluid communication with said entry port **22** and a second end **38** of said column **18** is in fluid communication with said exit port **24.** In one embodiment, the column **18** may be included in a column assembly **20.** The column assembly **20**, in turn, may comprise a column adaptor plate **40** having a-radioactive shielding plug opening **42,** an adaptor plate entry port **44** and an adaptor plate exit port **46** corresponding to said entry port **22** and said exit port **24** of said reactor housing, respectively, an adaptor plate vent port **48** (which may include a vent filter), and a column housing **50,** preferably fabricated from radioactive shielding material such as lead, tungsten, or depleted uranium. The column assembly **20** may comprise an entry needle **52** and a vent needle **54** disposed in said adaptor plate entry port **44**, and an exit connection **56**, adapted for fluid communication with a changeable sterile needle **58** of a filter module **60.** An entry pipe **62** may extend from said entry needle **52** to said first end **36** of said column **18.** A vent pipe **64** may

extend from said vent needle **54** to a safety valve **55** (said safety valve **55** protecting said vent filter by preventing back pressure from being released onto said vent filter) and said safety valve **55** may extend to said vent port **48.** An exit pipe 66 may extend from said second end **38** of said column **18** to said exit connection **50.** The column **18** may be inserted into said internal volume **12** of said reactor housing **4** through said opening **16** in said surface **1.4** of said reactor housing **4.** Alternatively, said column assembly **20** maybe positioned such that said column **18** is disposed in said internal volume **12** of said reactor housing **4.** The column **18** may comprise at least one radioisotope, including but not limited to Mo-99, Tc-99m, Y-90, Re-188, or Ga-68. In preferred embodiments, the column **18** is fabricated from glass. The column **18** may contain alumina in the form of aluminum oxide, Al_2O_3 (mp of about 2,000°C and specific gravity of about 4.0). Preferably, the column **18** is a glass column that contains aluminum oxide. The aluminum oxide powder preferably has a particle size of from about 20 to about 200 μm. In addition to the aluminum oxide powder, the column **18** may also include silica gel having a particle size of from about 20 to about 100 μm, The column **18** may also comprise one or more layers or polypropylene filter membranes, deactivated fused silica wool, and/or one or more glass filter membranes, The filter membranes preferably measure from about 0.2 to about 10 μm and may comprise polyether sulfone, Acetal plastic plugs with funnel drains, or stainless steel tubing with needle and filter adaptors. Particularly preferred filter membranes are those fabricated from polyether sulfone at a size of 0.2 μm.

[0024] A delivery vessel **68** may be disposed external to said reactor housing **4** and in fluid communication with said entry port **22.** The delivery vessel **68** may be a 3 to 20 ml (preferably 10 ml) borosilicate glass vessel. The delivery vessel **68** may be contained within a delivery housing **70** that is fabricated from radioactive shielding material such as lead, tungsten, or depleted uranium. The delivery housing **70** preferably is fabricated from radioactive shielding material and has a first end **72** that includes a first coupling **74,** a second end **76** that includes a second coupling **78,** and a wall **80** extending between said first end **72** and said second end **76.** The first coupling **74** and second coupling **78** may be threaded or may form a lure lock. In certain embodiments, delivery vessel **68** comprises a solution of at least one radioisotope, including but not limited Mo-99 or Tc-99m in the form of sodium molybdate Mo-99 or sodium pertechnetate Tc-99m, respectively. In such embodiments, delivery vessel **68** preferably comprises from about 1 to about 50 Ci (1 curie (Ci) is 37 gigabecquerels (GBq) exactly and 1 Bq = 2.7027×10^{-11} Ci). In other embodiments, delivery vessel **68** comprises Normal Saline [0.9%] solution. The delivery housing **70** may abut a ridge of guide material **30** that may be external to said reactor housing **4** and may extend around said entry port **22.** The delivery housing **70** may be at least partially contained within a ridge of guide material **30** that may be external to said reactor housing and may extend around said entry port **22.** In certain embodiments, an adapter guide ridge **81** may be disposed on said adapter disk **28** circumferentially internal to said ridge of guide material **30.** A saline vessel **82** may be disposed external to said reactor housing 4, and in fluid communication with said entry port **22** and may abut said adapter guide ridge **81 (FIG. 4)** that extends around said entry port **22.** The saline vessel **82** may comprise Normal Saline [0.9%] solution.

[0025] The generator system **2** may comprise a collection vessel **84** that is disposed external to said reactor housing **4** and in fluid communication with said exit port **24** via a filter module **60,** discussed below with reference to **FIG. 2.** The collection vessel **84** may be evacuated, and ultimately is used to collect a solution of at least one radioisotope. The collection vessel **84** may be a 10 to 30 ml borosilicate glass vessel. Preferably, the collection vessel **84** is a 20 to 30 ml sterile, evacuated, borosilicate glass vessel. As shown in **FIG. 1,** collection vessel **84** is contained within a collection housing **86** that is fabricated from radioactive shielding material.

[0026] As shown in **FIG. 2,** a filter module **60** may be disposed external to the reactor housing **4** and may be in fluid communication with said exit port **24.** The filter module **60** may include a radioactive shielding material insert **88** that is positioned between said collection vessel **84** and said reactor housing 4. The filter module **60** preferably holds a sterile 13 to 25 mm filter membrane **90** of 0.1 to 0.22 μm size, preferably of 0.2 μm size. The filter module **60** may be attached via a tread type adaptor to join the reactor to a sterile evacuated collection vessel **84.** A changeable sterile needle **58** may be attached to the sterile filter **90** for daily sterile eluting procedures. The filter module **60** may abut a ridge of radioactive shielding material **34** and/or may abut a ridge of guide material **32** that is external to said reactor housing 4 and extends around said exit port **24.** The filter module **60** may be at least partially contained within said ridge of radioactive shielding material **34** and/or said ridge of guide material **32.** The radioactive shielding material may be lead, tungsten, or depleted uranium.

[0027] The generator system may include a cart **92,** as shown in **FIG. 3.** The cart **92** preferably is fabricated from steel and lead. The frame is preferably fabricated from steel. The walls of cart **92** are preferably lead plates or lead brick. The cart **92** may hold a plurality of reactor housings **94, 96, 98, 100, 102, 104,** and **106** that may be fabricated from radioactive shielding material The cart **92** may also comprise a plurality of delivery vessels **68** and/or a plurality of evacuated collection vessels **84** and/or a plurality of saline vessels **82.** The cart **92** may include a transfer tool **108** that comprises a pick-up and release rod **110** having a handle **112** at a first end **114** thereof and a coupling **116** at a second end **118** thereof that is compatible with the first coupling **74** of said delivery housing **70.** The transfer tool **108** preferably is a universal T-bar handle. The cart **92** may also include a conveyor

belt **120**, or other motion enhancing device, to assist a user with moving a delivery housing **70** proximate to a reactor housing (*e.g.*, **94, 96, 98, 100, 102, 104** and **106**).

[0028] Methods of radioisotope generation according to the invention may be described with reference to **FIGS. 1** and **2.** In certain embodiments, such methods involve positioning a first delivery vessel **68** comprising a solution of at least one radioisotope external to said reactor housing **4** and in fluid communication with said entry port **22** for a time and under conditions effective to elute said chromatographic column **18** with at least a portion of said solution. The first delivery vessel **68** maybe positioned by mating said first coupling **74** at said first end **72** of said delivery housing **70** with transfer tool **108** and lifting the delivery housing **70.** The coupling **78** at said second end **76** of said first delivery housing **70** may be mated with a coupling on said reactor housing **4** that is compatible with said coupling **78** at said second end **76** of said first delivery housing **70.** The delivery vessel **68** may be removed from said position relative to said reactor housing **4** by lifting said delivery housing **70.** Subsequent delivery vessels comprising saline solution or a solution of at least one radioisotope may be used to elute said column **18** with at least a portion of said solutions. A collection vessel **84** may be positioned external to said reactor housing **4** and in fluid communication with said exit port **22** via said filter module **60.** The column **18**, column assembly **20**, filter module **60,** filter membrane **90,** sterile needle **58**, delivery vessel **68,** collection vessel **84** and/or saline vessel **82** may be removed from said reactor housing **10** and may be replaced by subsequent columns, column assemblies, filter modules, filter membranes, sterile needles, delivery vessels, collection vessels and/or saline vessels, respectively, as appropriate.

[0029] In certain embodiments, methods of radioisotope generation according to the invention involve the receipt of customer information including a target output of a radioisotope, the addition of a solution of a parent radioisotope to a delivery vessel in an amount sufficient to produce said target output upon decay of said parent radioisotope, and the shipment of said delivery vessel to said customer. The customer's generator system, in turn, may be loaded and re-loaded with varying volumes of said parent radioisotope effective to collect specific target concentrations of the desired radioisotope. The generator systems may be re-loaded more than 2 times, more preferably more than 4 times, and most preferably more than 6 times. Preferably, the customer information received includes a target output of Tc-99m from 1 to 50 Ci, and the solution added to the delivery vessel includes Mo-99 in an amount sufficient to produce said target output upon decay of said Mo-99.

[0030] A kit for radioisotope generation according to the invention is also contemplated and may be described with reference to **FIGs. 1-3.** The kit may include a column **18** or a column assembly **20**, a delivery housing **70** containing a delivery vessel **68** comprising at least one radioisotope, a filter module **60** comprising a radioactive shielding material insert **88**, a transfer tool **108**, a plurality of evacuated collection vessels **84** and a plurality of saline vessels **82.** The kit can be used to replenish existing reactor housings **4** and thereby avoids shipment and disposal thereof.

In addition, exemplary steps for radioisotope generation according to the invention may be described with reference to **FIGs. 1-7.** As shown in **FIG. 5,** a column assembly **20** may be inserted into an internal volume **12** of a reactor housing **4** (said reactor housing having an entry port **22** and an exit port **24),** through an **opening 16** in the surface **14** of the reactor, housing 4. Then, as shown in **FIG. 6,** the opening **16** above the column **18** may be plugged with a radioactive shielding plug **26.** Then, as shown in **FIG. 7,** an adapter disk **28,** comprising a ridge of guide material **30** extending around the entry port **22** and a ridge of guide material **32** extending around the exit port **24,** may be disposed on the surface **14** of the reactor housing **4.** A filter module **60** may then be disposed external to the reactor housing **4** in fluid communication with the exit port **24.** A delivery **vessel 68** containing a radioisotope, contained in a delivery housing **70,** may then be disposed external to the reactor housing **4** and in fluid communication with the entry port **22.** An evacuated collection vessel **84,** contained with a collection housing 86, may then be disposed external to the reactor housing **4** in fluid communication with the exit port **24** via the filter module **60.** After waiting a suitable amount of time (*e.g.*, more than about three minutes), the collection vessel **84** and then the delivery vessel **68** may be removed. An adapter guide ridge **81** may then be disposed on the surface of the adapter disk 28 such that it extends around the entry port **22.** A saline vessel **82** may then be disposed external to the reactor **housing 4** and in fluid communication with the entry port **22.** An evacuated collection vessel 84, contained within a collection housing **86**, may then be disposed external to the reactor housing 4 and in fluid communication with the exit port **24** via the filter module 60. After again waiting a suitable amount of time, said collection housing **86** may be removed. An evacuated collection vessel **84**, contained within a collection housing **86,** may then'be disposed external to the reactor housing **4** and in fluid communication with the exit port **24** via the filter module **60.** The aforementioned exemplary steps may be repeated with subsequent delivery vessels, columns, filter modules and collection vessels as may be appropriate.

[0031] Thus, there have been described systems and methods for producing customized, predictable and reproducible supplies of radioisotopes that do not require weekly replacement, handling and transport of heavy shielding materials associated with conventional generators. It will be appreciated that numerous modifications may be made to the example embodiments described herein, and that such modifications do not depart from the scope of the invention as defined by the following claims.

Claims

1. A system comprising:

   a reactor housing that is fabricated from a radioactive shielding material and has both an internal volume and a surface that comprises an entry port and an exit port;
   a chromatographic column that bears at least one radioisotope and is positioned within said internal volume;
   a filter module that is disposed external to said reactor housing and in fluid communication with said column;
   an adapter disk disposed on said reactor housing, comprising a ridge of material that extended around said entry port and a ridge of material that extends around said exit port, and,
   an adapter ridge disposed circumferentially internal to said ridge of material that extends around said entry port.

2. A system according to claim 1, wherein said reactor house includes a first end, a second end and a wall extending between said first end and said second end.

3. A system according to claim 1, wherein said column comprises aluminum oxide particles from about 50 to 200 μm in size.

4. A system according to claim 1, wherein said column comprises silica gel particles from about 20 to 100 μm in size.

5. A system according to claim 1, wherein a collection housing is connected to said reactor housing via said filter module.

6. A system according to claim 1, including a delivery vessel that is disposed external to said reactor housing in fluid communication with said column.

7. A system according to claim 8, wherein said delivery vessel comprises a solution of about 1 to 50 Ci of at least one radioisotope.

8. A system according to claim 1, including a collection vessel that is disposed external to said reactor housing and in fluid communication with said column via said filter module.

9. A system according to claim 1, wherein said filter module abuts a ridge of radioactive shielding material that is external to said reactor housing and extends around said exit port.

10. A system according to claim 1, wherein said filter module is at least partially contained within a ridge of radioactive shielding material that is external to said reactor housing and extends around said exit port.

11. A system according to claim 1, wherein said collection vessel is contained within a collection housing that is fabricated from radioactive shielding material.

12. A system according to claim 1, including a cart that includes a plurality of delivery vessels that each independently comprises a reactor vessel.

13. A system according to claim 1, including a cart that includes a plurality of delivery vessels that each independently comprise a solution of at least one radioisotope and are contained within a delivery housing that is fabricated from radioactive shielding material.

14. A system according to claim 13, wherein said delivery vessels each independently comprise about 1 to about 50 Ci.

15. A system according to claim 1, wherein said column is configures to be reloaded with radioisotope solution at least one.

16. A system according to claim 1, including a column assembly comprising a further chromatographic column for replacing said chromatographic column after said at least some of said radioisotope has been eluted therefrom.

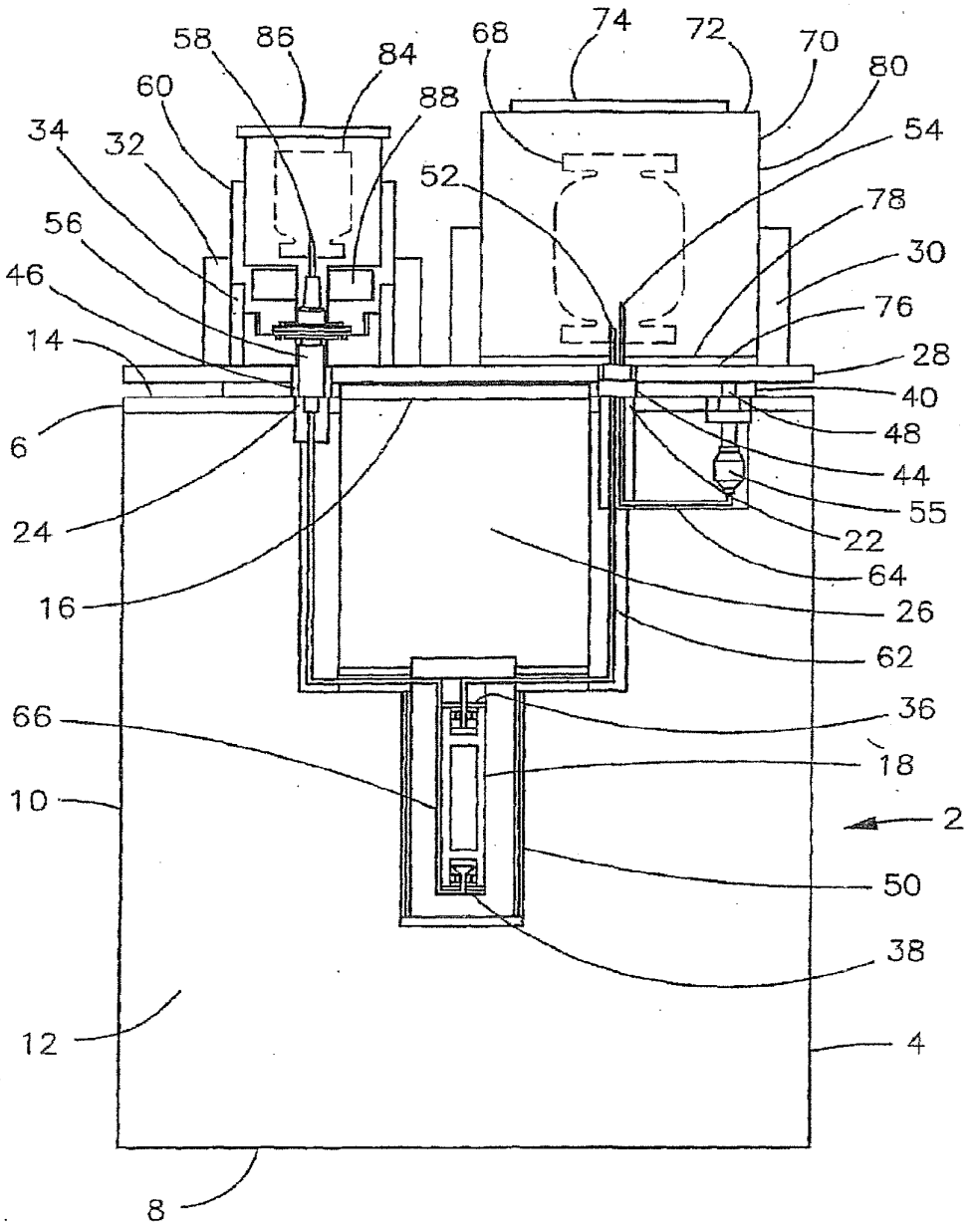

58
86
84
68
74
72
70
80
60
88
54
34
32
52
78
56
30
46
76
14
28
40
48
6
44
55
24
22
64
16
26
62
66
36
18
10
2
50
38
12
4
8

Fig. 1

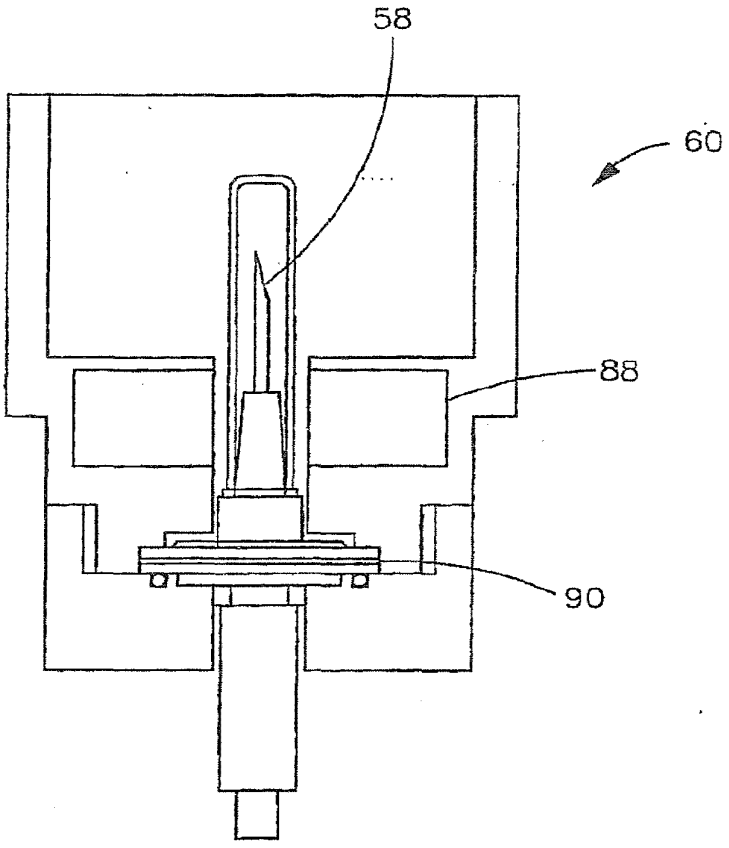


Fig. 2

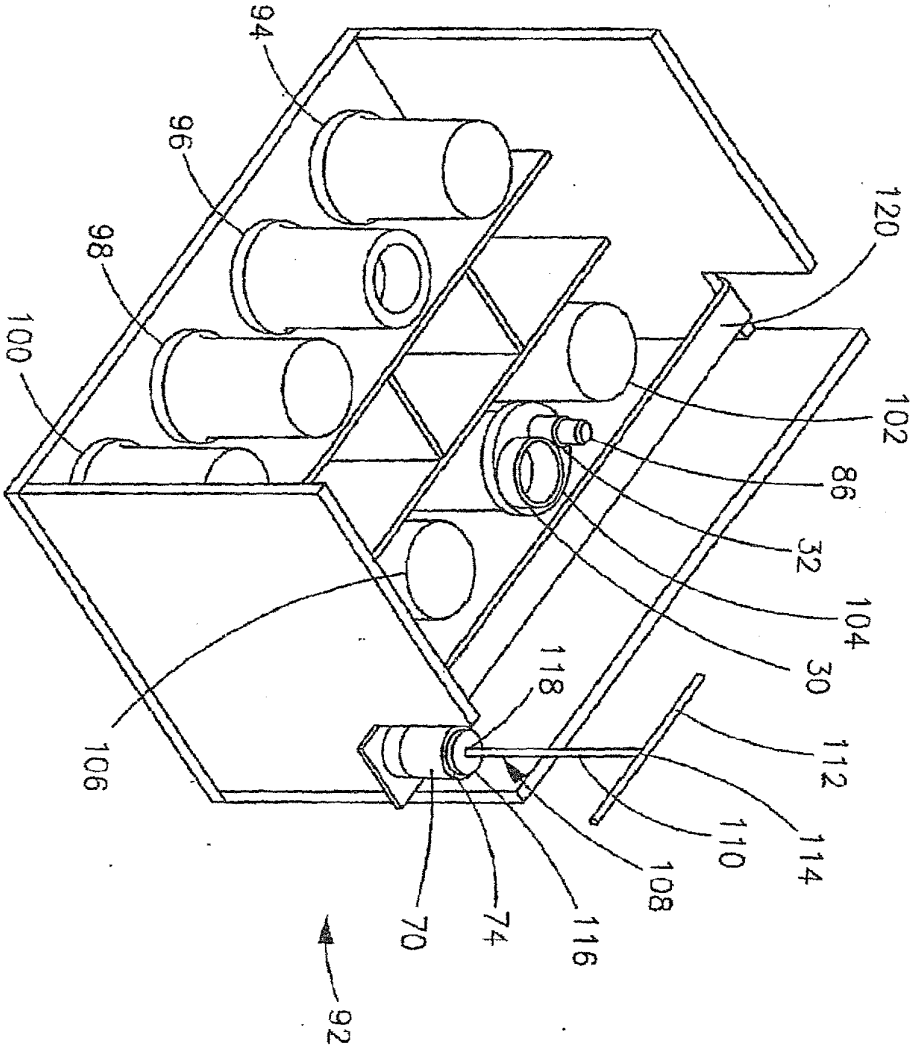

94
96
98
100
106
120
102
86
32
104
30
118
112
114
110
108
116
74
70
92

Fig. 3

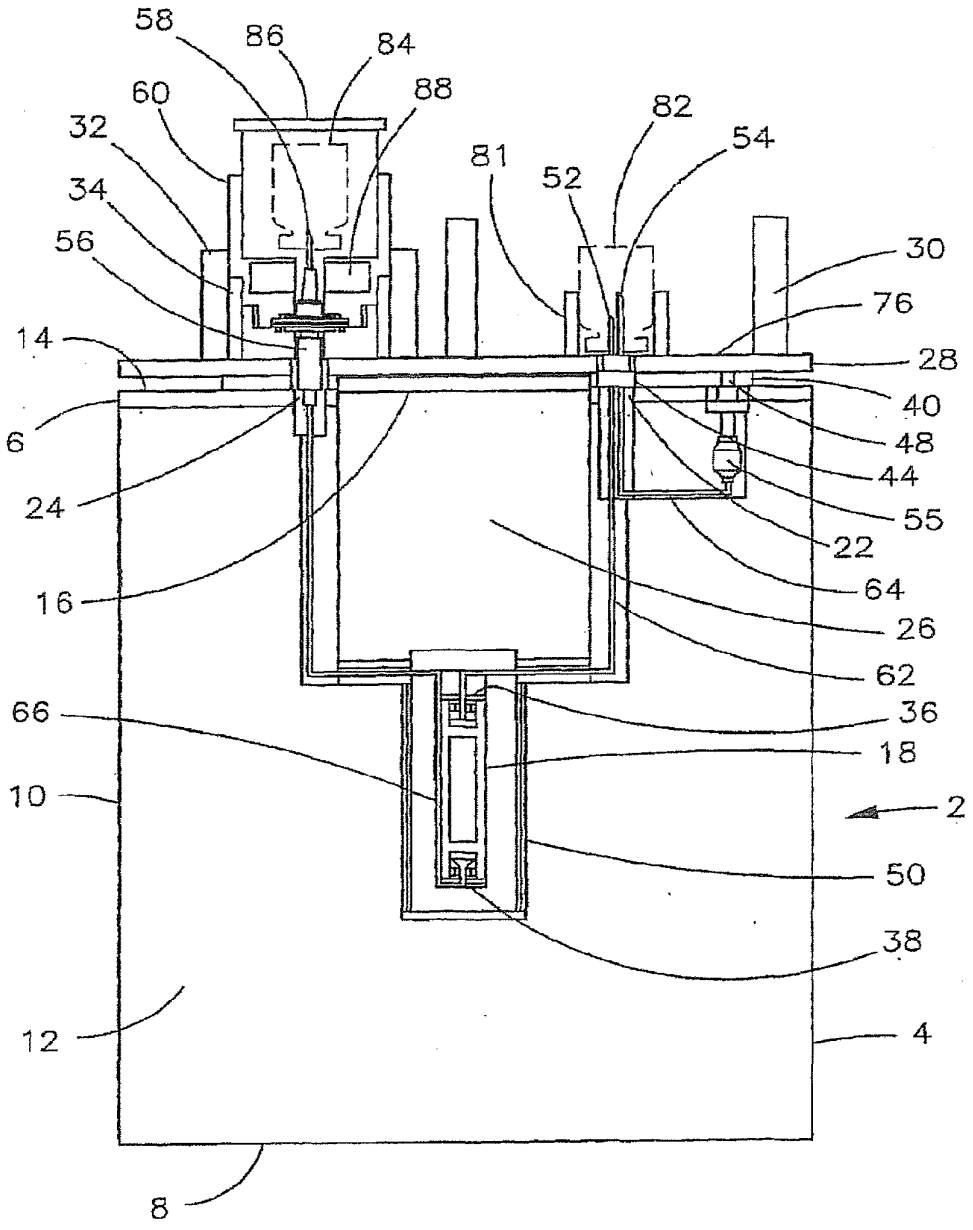

58
86
84
88
60
32
34
56
14
6
24
16
66
10
12
8
81
52
82
54
30
76
28
40
48
44
55
22
64
26
62
36
18
2
50
38
4

Fig. 4

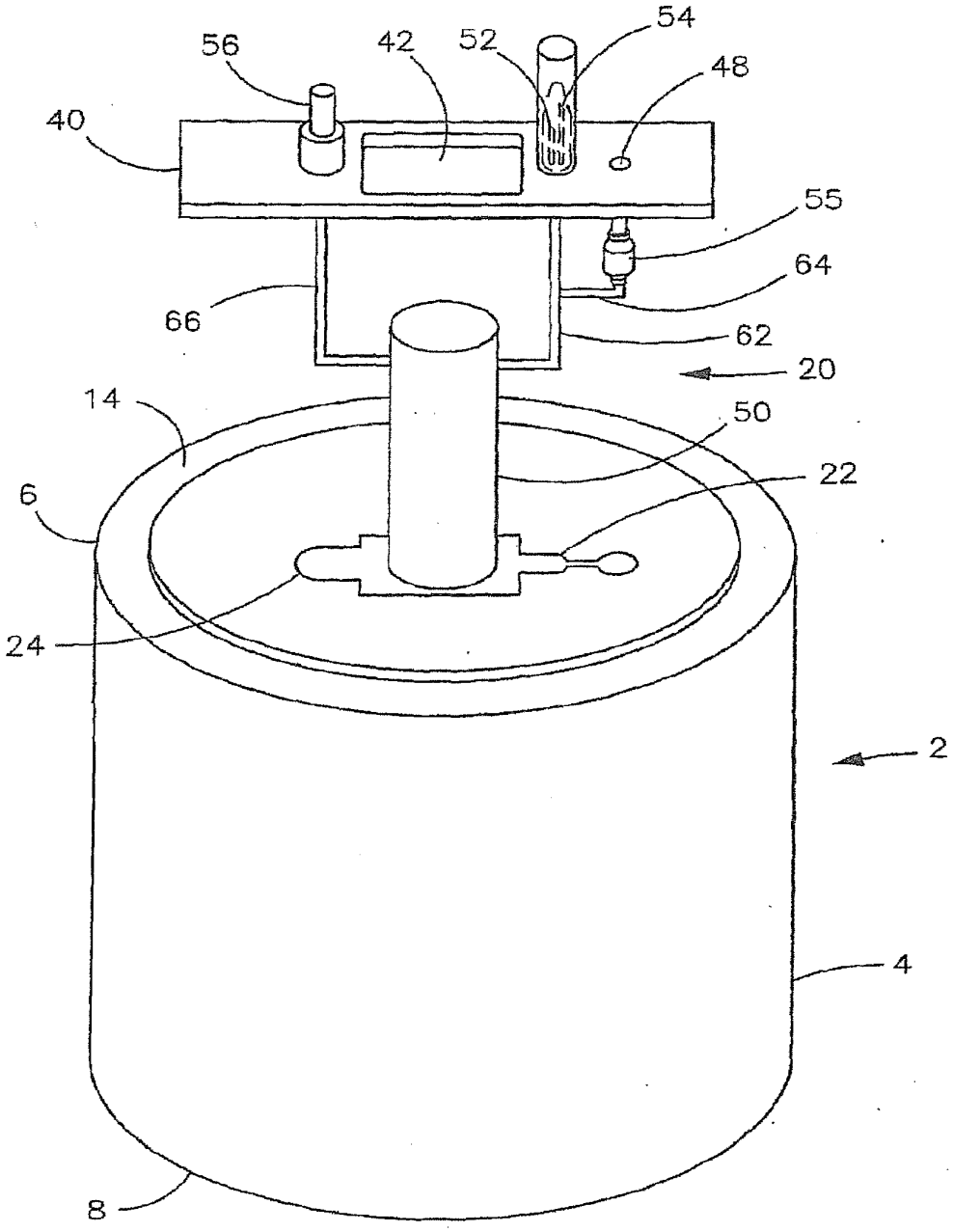


Fig. 5

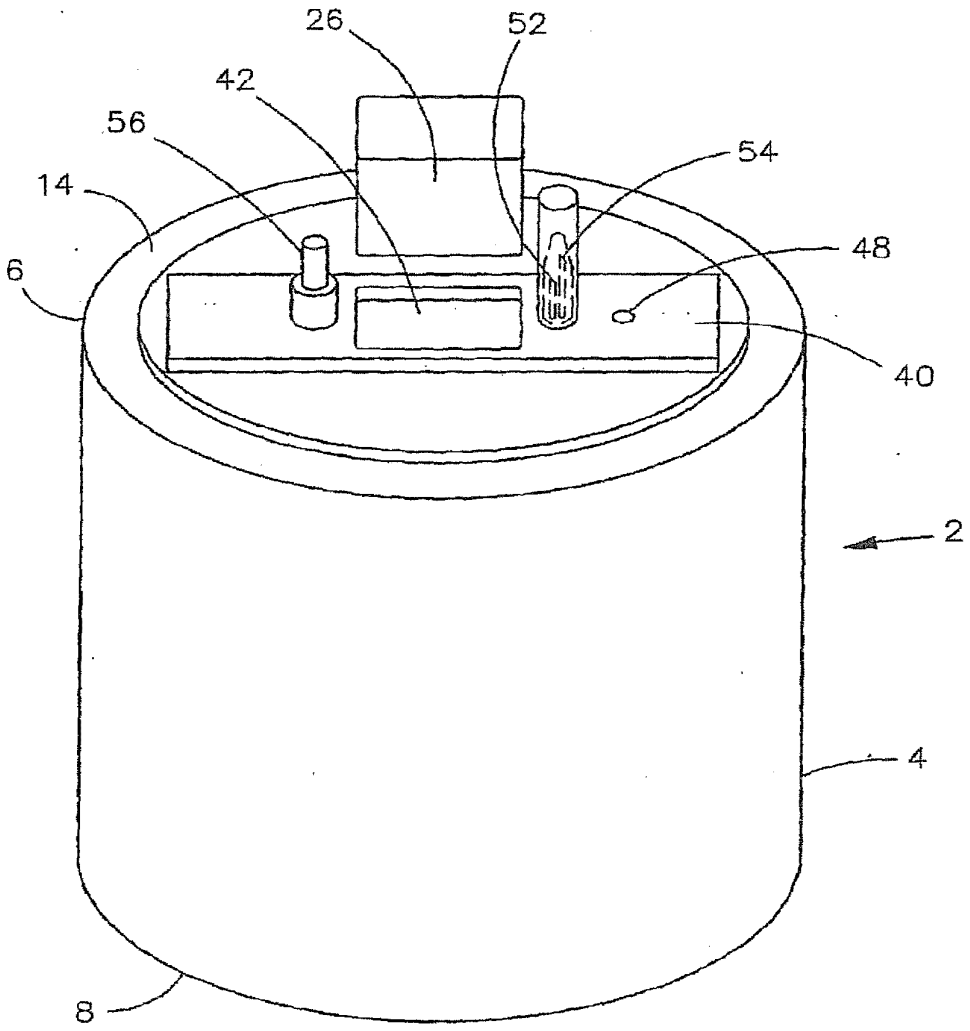


Fig. 6

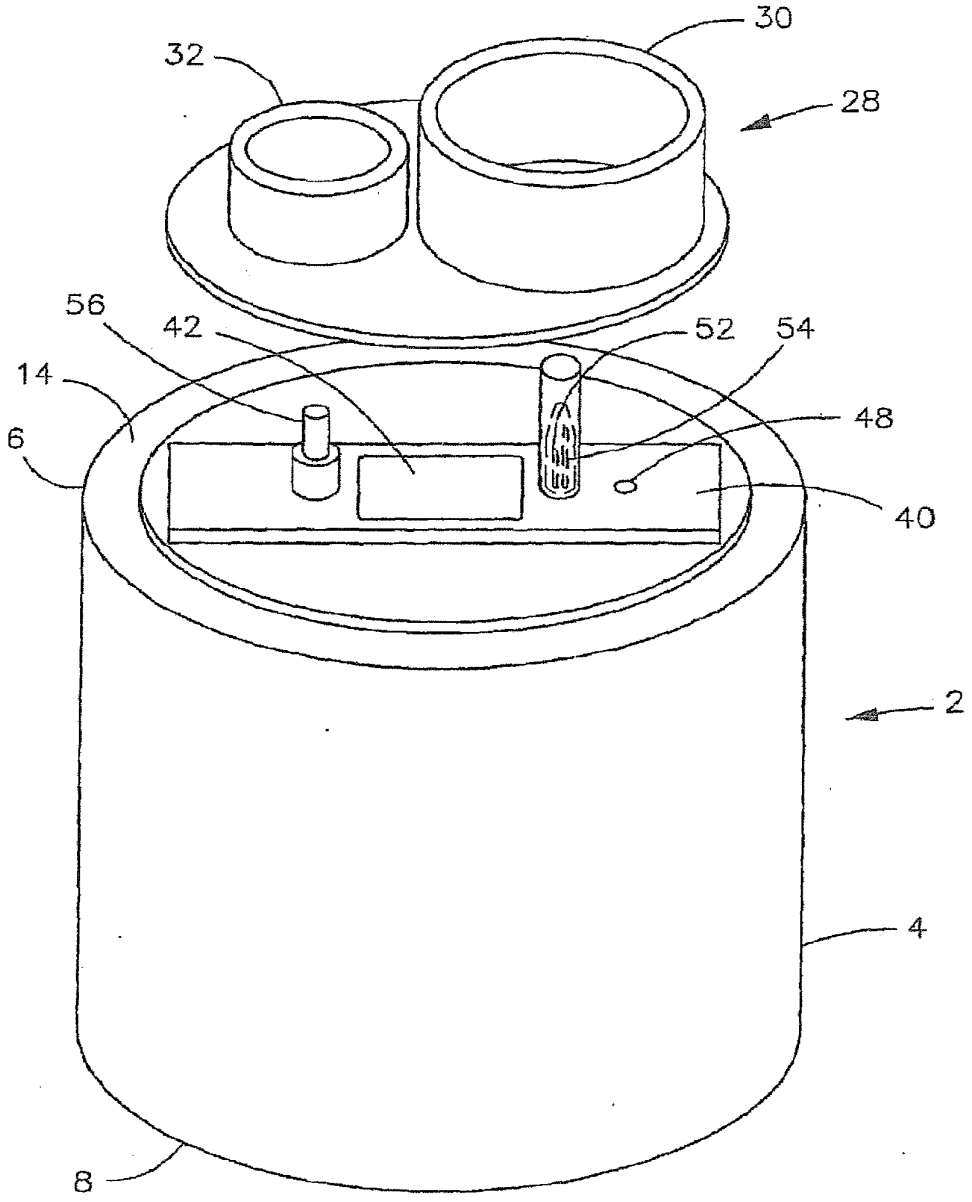


Fig. 7

REFERENCES CITED IN THE DESCRIPTION

This list of references cited by the applicant is for the reader's convenience only. It does not form part of the European patent document. Even though great care has been taken in compiling the references, errors or omissions cannot be excluded and the EPO disclaims all liability in this regard.

Patent documents cited in the description

- US 75841906 P **[0001]**
- US 61057406 A **[0001]**

Non-patent literature cited in the description

- **SCHWOCHAU ; KLAUS.** Technetium. Wiley-VCH, 2000 **[0004]**

(19) Europäisches Patentamt
European Patent Office
Office européen des brevets

(11) EP 2 011 126 B1

(12) **EUROPEAN PATENT SPECIFICATION**

(45) Date of publication and mention of the grant of the patent:
23.05.2012 Bulletin 2012/21

(21) Application number: **06851254.0**

(22) Date of filing: **16.12.2006**

(51) Int Cl.:
G21G 1/00 *(2006.01)* ***B01D 15/10*** *(2006.01)*

(86) International application number:
PCT/IB2006/004294

(87) International publication number:
WO 2008/004028 (10.01.2008 Gazette 2008/02)

(54) **SYSTEMS AND METHODS FOR RADIOISOTOPE GENERATION**

SYSTEM UND VERFAHREN ZUR RADIOISOTOPERZEUGUNG

SYSTÈMES ET PROCÉDÉS POUR LA GÉNÉRATION DE RADIO-ISOTOPES

(84) Designated Contracting States:
AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IS IT LI LT LU LV MC NL PL PT RO SE SI SK TR

(30) Priority: **12.01.2006 US 758419 P**
14.12.2006 US 610574

(43) Date of publication of application:
07.01.2009 Bulletin 2009/02

(73) Proprietor: **DRAXIMAGE General Partnership**
Montreal, QC H9H 4J4 (CA)

(72) Inventors:
- **TARTAGLIA, Daniel**
  St. Leonard, Quebec HIR 3Z6 (CA)
- **COPPOLA, Carlo**
  Pointe-Claire, QC H9R 5Y2 (CA)
- **TEOLI, Vince**
  Montreal, Quebec H2N 1W5 (CA)
- **BOURNIVAL, Alain Guy**
  St. Lazarre, Quebec H2N 1W5 (CA)

(74) Representative: **Holliday, Louise Caroline et al**
D Young & Co LLP
120 Holborn
London EC1N 2DY (GB)

(56) References cited:
WO-A-97/45841
CA-A1- 1 093 223
US-A- 3 462 245
US-A- 3 576 998
US-A- 4 280 053
US-A- 4 286 169
US-A- 4 782 231
US-A- 5 186 913
US-A- 6 157 036
US-B2- 6 998 052

EP 2 011 126 B1

Printed by Jouve, 75001 PARIS (FR)

Description

FIELD OF THE INVENTION

[0001] This invention relates generally to systems and methods for radioisotope generation. In one aspect, this invention relates to systems and methods for producing customized, predictable and reproducible supplies of radioisotopes for use in nuclear medicine.

BACKGROUND OF THE INVENTION

[0002] Nuclear medicine is a branch of medicine dealing with the use of radioisotopes as radiopharmaceuticals or radioactive tracers in the diagnosis and treatment of disease. Radioisotopes are natural or artificially created isotopes (isotopes being one of two or more atoms having the same atomic number but different mass numbers) of a chemical element that have an unstable nucleus that decays, emitting alpha, beta, or gamma rays until stability is reached.

[0003] Radioisotopes, such as the meta stable Technetium-99m (Tc-99m), are used in medical tests as radioactive tracers that medical equipment can detect in the body. Other generator-derived radioisotopes that are used as tracers include yttrium-90, rhenium-188, and gallium-68 . Tc-99m, in particular, emits readily detectable gamma rays, and it has a half-life of 6 hours. A variety of different radiopharmaceuticals based on Tc-99m are used for imaging and functional studies of the brain, myocardium, thyroid, lungs, liver, gallbladder, kidneys, skeleton, blood and tumors. Schwochau, Klaus. Technetium, Wiley-VCH (2000) (ISBN 3-527-29496-1). Scientists continue to find new uses for radioisotopes, such as Tc-99m. For example, doctors recently used Tc-99m to diagnose precisely the infected lymph nodes in breast cancer patients by injecting Tc-99m into the breast around the tumor to allow them to locate the node quickly and precisely before ever making an incision. *Brookhaven National Laboratory site on the history of the technetium cow.* (http://www.bnl.gov/bnlweb/history/Tc-99m.asp).

[0004] A Tc-99m generator, often called a technetium cow, is a device used to extract Tc-99m from decaying molybdenum-99 ("Mo-99"). Mo-99 has a half-life of 66 hours and can be transported over long distances to radiopharmacies and hospitals where its decay product Tc-99m is used for nuclear medicine diagnostic procedures. Removing the Tc-99m from the generator ("milking" the generator) is typically done every 6 hours or, at most, twice daily. Most commercial generators use column chromatography, in which Mo-99 is adsorbed onto alumina. Normal saline solution can be run through a column of immobilized Mo-99 to elute soluble Tc-99m, resulting in a saline solution containing the Tc-99m.

[0005] Today, commercial radiopharmacies typically replace their generators on a biweekly basis, since the useful life of a Tc-99m generator is about 6 half lifes or approximately two weeks. Hence, typical clinical nuclear medicine units purchase at least one such generator every two weeks or order several in a staggered fashion. The lead-lined generators are heavy and bulky and represent significant manipulation and toil for personnel to replace and to dispose of spent generators. Large quantities of lead, molded plastic containers, and packing materials are used only once and discarded after two weeks. Shipping costs and waste are real considerations for end-users. Further, conventional generator systems lack flexibility as they are limited to fixed activity denominations per unit sold, resulting in limited predictability and reproducibility. Typical generators also do not provide activity above 19 Ci.

[0006] It would be desirable therefore to provide systems and methods for producing customized, predictable and reproducible supplies of radioisotopes, including high activity levels, that do not require weekly replacement, handling and transport of heavy shielding materials associated with conventional generators.

SUMMARY OF THE INVENTION

[0007] In one aspect, the present invention provides a system comprising:

a reactor housing that is fabricated from a radioactive shielding material and has both an internal volume and a surface that comprises an entry port and an exit port;

a chromatographic column that is positioned within said internal volume wherein; said first chromatographic column is housed within a column assembly comprising:

a column housing defining an internal space for receiving said first chromatographic column;
a column adaptor plate;
an exit pipe in fluid communication with said first chromatographic column via said column housing and with an exit connection that is mounted on said column adaptor plate; and
an entry pipe in fluid communication with said first chromatographic column via said column housing and with an entry needle that is disposed in an adaptor plate entry port that is mounted on said column adaptor plate;

wherein said column assembly is configured for insertion as a unit into the internal volume of said reactor housing through an opening in an upper portion of said reactor housing; and;

a filter module that is disposed external to said reactor housing and in fluid communication with said column.

[0008] The present invention also provides a method comprising the steps of:

providing a system that comprises:

a reactor housing that is fabricated from a radioactive shielding material and has both an internal volume and a surface that comprises an entry port and an exit port;
a first chromatographic column that is positioned within said internal volume wherein
said first chromatographic column is housed within a column assembly comprising:
a column housing defining an internal space for receiving said first chromatographic column;
a column adaptor plate;
an exit pipe in fluid communication with said first chromatographic column via said column housing and with an exit connection that is mounted on said column adaptor plate; and
an entry pipe in fluid communication with said first chromatographic column via said column housing and with an entry needle that is disposed in an adaptor plate entry port that is mounted on said column adaptor plate;
wherein said column assembly is configured for insertion as a unit into the internal volume of said reactor housing through an opening in an upper portion of said reactor housing; and;
a first filter module that is disposed external to said reactor housing and in fluid communication with said first chromatographic column; and
positioning a first delivery vessel comprising a solution of at least one radioisotope external to said reactor housing and in fluid communication with said first chromatographic column for a time and under conditions effective to elute said first chromatographic column with at least a portion of said solution; and,
positioning a collection vessel external to said reactor housing and in fluid communication with said exit port via said filter module.

[0009] In yet another aspect, the present invention provides a method comprising the steps of:

providing a system that comprises:

a reactor housing that is fabricated from a radioactive shielding material and has both an internal volume and a surface that comprises an entry port and an exit port; and
a first chromatographic column that is positioned within said internal volume, wherein said first chromatographic column is housed within a column assembly comprising
a column housing defining an internal space for receiving said first chromatographic column;
a column adaptor plate;
an exit pipe in fluid communication with said first chromatographic column via said column housing and with an exit connection that is mounted on said column adaptor plate; and
an entry pipe in fluid communication with said first chromatographic column via said column housing and with an entry needle that is disposed in an adaptor plate entry port that is mounted on said column adaptor plate;
wherein said column assembly is configured for insertion as a unit into the internal volume of said reactor housing through an opening in an upper portion of said reactor housing;
removing said first chromatographic column from said internal volume by extracting said column assembly through an opening in an upper portion of said reactor housing;
positioning a second chromatographic column within said internal volume by inserting a second column assembly through said opening in said reactor housing;
positioning a first delivery vessel comprising a solution of at least a first radioisotope external to said reactor housing and in fluid communication with said second chromatographic column for a time and under conditions effective to elute said second chromatographic column with at least a portion of said solution; and,
positioning a first collection vessel external to said reactor housing and in fluid communication with said second chromatographic column.

BRIEF DESCRIPTION OF THE DRAWINGS

[0010] FIG. 1 is a cutaway side view depicting one generator system according to the invention.

[0011] FIG. 2 is a cutaway side view depicting one shielded filter module according to the invention.

[0012] FIG. 3 is an isometric view of one cart according to the invention.

[0013] FIG. 4 is a cutaway side view of one generator system according to the invention.

[0014] FIG. 5 is a perspective view of a column assembly being inserted into an internal volume of a reactor housing according to the invention.

[0015] FIG. 6 is a perspective view of a radioactive shielding plug being inserted into an opening in a reactor housing according to the invention.

[0016] FIG. 7 is a perspective view of an adapter disk disposed on the surface of a reactor housing according to the invention.

DETAILED DESCRIPTION OF ILLUSTRATIVE EMBODIMENTS

[0017] With reference to the drawings, **FIG. 1** shows one type of generator system **2** according to the invention. The generator system may include a reactor housing **4** fabricated from a radioactive shielding material such as lead, tungsten, or depleted uranium. The reactor hous-

ing **4** may be substantially cylindrical, as shown in **FIG. 1**. In another embodiment, the reactor housing may be substantially rectilinear. The reactor housing **4** may include a first end **6**, a second end **8**, and a wall **10** extending between said first end **6** and said second end **8**. The reactor housing **4** may have both an internal volume **12** and a surface **14** that comprises an opening **16** for inserting a column **18** (said column may be included in a column assembly **20**, shown in more detail in **FIG. 5**), an entry port **22**, and an exit port **24**. The opening **16**, entry port **22** and exit port **24** may be positioned at said first end **6** of said housing **4**. A radioactive shielding plug **26** may be disposed in said opening **16** in said surface **14** above said column **18**. The radioactive shielding plug **26** may be fabricated from a radioactive shield material such as lead, tungsten, or depleted uranium. The reactor housing **4** may have an adapter disk **28** disposed on the surface **14** of said reactor housing **4** that comprises a ridge of guide material **30** that may extend around said entry port **22** and a ridge of guide material **32** that may extend around said exit port **24**. Preferably, the adapter disk **28** and ridges of guide material **30** and **32** are plastic. A ridge of radioactive shielding material **34** may extend around said exit port **24**.

[0018] A chromatographic column **18** may be positioned within said internal volume **12** such that a first end **36** of said column **18** is in fluid communication with said entry port **22** and a second end **38** of said column **18** is in fluid communication with said exit port **24**. In one embodiment, the column **18** may be included in a column assembly **20**. The column assembly **20**, in turn, may comprise a column adaptor plate **40** having a radioactive shielding plug opening **42**, an adaptor plate entry port **44** and an adaptor plate exit port **46** corresponding to said entry port **22** and said exit port **24** of said reactor housing, respectively, an adaptor plate vent port **48** (which may include a vent filter), and a column housing **50**, preferably fabricated from radioactive shielding material such as lead, tungsten, or depleted uranium. The column assembly **20** may comprise an entry needle **52** and a vent needle **54** disposed in said adaptor plate entry port **44**, and an exit connection **56**, adapted for fluid communication with a changeable sterile needle **58** of a filter module **60**. An entry pipe **62** may extend from said entry needle **52** to said first end **36** of said column **18**. A vent pipe **64** may extend from said vent needle **54** to a safety valve 55 (said safety valve 55 protecting said vent filter by preventing back pressure from being released onto said vent filter) and said safety valve **55** may extend to said vent port **48**. An exit pipe **66** may extend from said second end **38** of said column **18** to said exit connection **50**. The column **18** may be inserted into said internal volume **12** of said reactor housing **4** through said opening **16** in said surface **14** of said reactor housing **4**. Alternatively, said, column assembly **20** may be positioned such that said column **18** is disposed in said internal volume **12** of said reactor housing **4**. The column **18** may comprise at least one radioisotope, including but not limited to Mo-99, Tc-99m, Y-90, Re-188, or Ga-68. In preferred embodiments, the column **18** is fabricated from glass. The column **18** may contain alumina in the form of aluminum oxide, Al_2O_3 (mp of about 2,000°C and specific gravity of about 4.0). Preferably, the column **18** is a glass column that contains aluminum oxide. The aluminum oxide powder preferably has a particle size of from about 20 to about 200 μm. In addition to the aluminum oxide powder, the column **18** may also include silica gel having a particle size of from about 20 to about 100 μm. The column **18** may also comprise one or more layers or polypropylene filter membranes, deactivated fused silica wool, and/or one or more glass filter membranes. The filter membranes preferably measure from about 0.2 to about 10 μm and may comprise polyether sulfone, Acetal plastic plugs with funnel drains, or stainless steel tubing with needle and filter adaptors. Particularly preferred filter membranes are those fabricated from polyether sulfone at a size of 0.2 μm.

[0019] A delivery vessel **68** may be disposed external to said reactor housing **4** and in fluid communication with said entry port **22**. The delivery vessel **68** may be a 3 to 20 ml (preferably 10 ml) borosilicate glass vessel. The delivery vessel **68** may be contained within a delivery housing **70** that is fabricated from radioactive shielding material such as lead, tungsten, or depleted uranium. The delivery housing **70** preferably is fabricated from radioactive shielding material and has a first end **72** that includes a first coupling **74**, a second end **76** that includes a second coupling **78**, and a **wall 80** extending between said first end **72** and said second end **76**. The first coupling **74** and second coupling **78** may be threaded or may form a lure lock. In certain embodiments, delivery vessel **68** comprises a solution of at least one radioisotope, including but not limited Mo-99 or Tc-99m in the form of sodium molybdate Mo-99 or sodium pertechnetate Tc-99m, respectively. In such embodiments, delivery vessel **68** preferably comprises from about 1 to about 50 Ci (1 curie (Ci) is 37 gigabecquerels (GBq) exactly and 1 Bug $=2.027\times10^{-11}$ Ci). In other embodiments, delivery vessel **68** comprises Normal Saline [0.9%] solution. The delivery housing **70** may abut a ridge of guide material **30** that may be external to said reactor housing **4** and may extend around said entry port **22**. The delivery housing **70** may be at least partially contained within a ridge of guide material **30** that may be external to said reactor housing and may extend around said entry port **22**. In certain embodiments, an adapter guide ridge **81** may be disposed on said adapter disk 28 circumferentially internal to said ridge of guide material **30**. A saline vessel **82** may be disposed external to said reactor housing **4**, and in fluid communication with said entry port **22** and may abut said adapter guide ridge **81 (FIG. 4)** that extends around said entry port **22**. The saline vessel **82** may comprise Normal Saline [0.9%] solution.

[0020] The generator system **2** may comprise a collection vessel **84** that is disposed external to said reactor housing **4** and in fluid communication with said exit port

24 via a filter module 60, discussed below with reference to FIG. 2. The collection vessel 84 may be evacuated, and ultimately is used to collect a solution of at least one radioisotope. The collection vessel 84 may be a 10 to 30 ml borosilicate glass vessel. Preferably, the collection vessel 84 is a 20 to 30 ml sterile, evacuated, borosilicate glass vessel. As shown in FIG. 1, collection vessel 84 is contained within a collection housing 86 that is fabricated from radioactive shielding material.

[0021] As shown in FIG. 2, a filter module 60 may be disposed external to the reactor housing 4 and may be in fluid communication with said exit port 24. The filter module 60 may include a radioactive shielding material insert 88 that is positioned between said collection vessel 84 and said reactor housing 4. The filter module 60 preferably holds a sterile 13 to 25 mm filter membrane 90 of 0.1 to 0.22 μm size, preferably of 0.2 μm size. The filter module 60 may be attached via a tread type adaptor to join the reactor to a sterile evacuated collection vessel 84. A changeable sterile needle 58 may be attached to the sterile filter 90 for daily sterile eluting procedures. The filter module 60 may abut a ridge of radioactive shielding material 34 and/or may abut a ridge of guide material 32 that is external to said reactor housing 4 and extends around said exit port 24. The filter module 60 may be at least partially contained within said ridge of radioactive shielding material 34 and/or said ridge of guide material 32. The radioactive shielding material may be lead, tungsten, or depleted uranium.

[0022] The generator system may include a cart 92, as shown in FIG. 3. The cart 92 preferably is fabricated from steel and lead. The frame is preferably fabricated from steel. The walls of cart 92 are preferably lead plates or lead brick. The cart 92 may hold a plurality of reactor housings 94, 96, 98, 100, 102, 104, and 106 that may be fabricated from radioactive shielding material The cart 92 may also comprise a plurality of delivery vessels 68 and/or a plurality of evacuated collection vessels 84 and/or a plurality of saline vessels 82. The cart 92 may include a transfer tool 108 that comprises a pick-up and release rod 110 having a handle 112 at a first end 114 thereof and a coupling 116 at a second end 118 thereof that is compatible with the first coupling 74 of said delivery housing 70. The transfer tool 108 preferably is a universal T-bar handle. The cart 92 may also include a conveyor belt 120, or other motion enhancing device, to assist a user with moving a delivery housing 70 proximate to a reactor housing (*e.g.*, 94, 96, 98,100, 102, 104, and 106).

[0023] Methods of radioisotope generation according to the invention may be described with reference to FIGs. 1 and 2. In certain embodiments, such methods involve positioning a first delivery vessel 68 comprising a solution of at least one radioisotope external to said reactor housing 4 and in fluid communication with said entry port 22 for a time and under conditions effective to elute said chromatographic column 18 with at least a portion of said solution. The first delivery vessel 68 may be positioned by mating said first coupling 74 at said first end 72 of said delivery housing 70 with transfer tool 108 and lifting the delivery housing 70. The coupling 78 at said second end 76 of said first delivery housing 70 may be mated with a coupling on said reactor housing 4 that is compatible with said coupling 78 at said second end 76 of said first delivery housing 70. The delivery vessel 68 may be removed from said position relative to said reactor housing 4 by lifting said delivery housing 70. Subsequent delivery vessels comprising saline solution or a solution of at least one radioisotope may be used to elute said column 18 with at least a portion of said solutions. A collection vessel 84 may be positioned external to said reactor housing 4 and in fluid communication with said exit port 22 via said filter module 60. The column 18, column assembly 20, filter module 60, filter membrane 90, sterile needle 58, delivery vessel 68, collection vessel 84 and/or saline vessel 82 may be removed from said reactor housing 10 and may be replaced by subsequent columns, column assemblies, filter modules, filter membranes, sterile needles, delivery vessels, collection vessels and/or saline vessels, respectively, as appropriate.

[0024] In certain embodiments, methods of radioisotope generation according to the invention involve the receipt of customer information including a target output of a radioisotope, the addition of a solution of a parent radioisotope to a delivery vessel in an amount sufficient to produce said target output upon decay of said parent radioisotope, and the shipment of said delivery vessel to said customer. The customer's generator system, in turn, may be loaded and re-loaded with varying volumes of said parent radioisotope effective to collect specific target concentrations of the desired radioisotope. The generator systems may be re-loaded more than 2 times, more preferably more than 4 times, and most preferably more than 6 times. Preferably, the customer information received includes a target output of Tc-99m from 1 to 50 Ci, and the solution added to the delivery vessel includes Mo-99 in an amount sufficient to produce said target output upon decay of said Mo-99.

[0025] A kit for radioisotope generation is also contemplated and may be described with reference to FIGs. 1-3. The kit may include a column 18 or a column assembly 20, a delivery housing 70 containing a delivery vessel 68 comprising at least one radioisotope, a filter module 60 comprising a radioactive shielding material insert 88, a transfer tool 108, a plurality of evacuated collection vessels 84 and a plurality of saline vessels 82. The kit can be used to replenish existing reactor housings 4 and thereby avoids shipment and disposal thereof.

In addition, exemplary steps for radioisotope generation according to the invention may be described with reference to FIGs. 1-7. As shown in FIG. 5, a column assembly 20 may be inserted into an internal volume 12 of a reactor housing 4 (said reactor housing having an entry port 22 and an exit port 24), through an opening 16 in the surface 14 of the reactor housing 4. Then, as shown in FIG. 6, the opening 16 above the column 18 may be plugged

with a radioactive shielding plug **26**. Then, as shown in **FIG. 7**, an adapter disk **28**, comprising a ridge of guide material **30** extending around the entry port **22** and a ridge of guide material **32** extending around the exit port **24**, may be disposed on the surface **14** of the reactor housing **4.** A filter module **60** may then be disposed external to the reactor housing **4** in fluid communication with the exit port **24**. A delivery vessel **68** containing a radioisotope, contained in a delivery housing **70**, may then be disposed external to the reactor housing **4** and in fluid communication with the entry port **22.** An evacuated collection vessel **84**, contained with a collection housing **86**, may then be disposed external to the reactor housing **4** in fluid communication with the exit port **24** via the filter module **60.** After waiting a suitable amount of time (*e.g.*, more than about three minutes), the collection vessel **84** and then the delivery vessel **68** may be removed. An adapter guide ridge **81** may then be disposed on the surface of the adapter disk **28** such that it extends around the entry port **22**. A saline vessel **82** may then be disposed external to the reactor housing **4** and in fluid communication with the entry port **22**. An evacuated collection vessel **84**, contained within a collection housing **86**, may then be disposed external to the reactor housing **4** and in fluid communication with the exit port **24** via the filter module **60.** After again waiting a suitable amount of time, said collection housing **86** may be removed. An evacuated collection vessel **84**, contained within a collection housing **86**, may then be disposed external to the reactor housing **4** and in fluid communication with the exit port **24** via the filter module **60**. The aforementioned exemplary steps may be repeated with subsequent delivery vessels, columns, filter modules and collection vessels as may be appropriate.

[0026] Thus, there have been described systems and methods for producing customized, predictable and reproducible supplies of radioisotopes that do not require weekly replacement, handling and transport of heavy shielding materials associated with conventional generators. It will be appreciated that numerous modifications may be made to the example embodiments described herein, and that such modifications do not depart from the scope of the invention as defined by the following claims.

Claims

1. A system comprising:

a reactor housing (4) that is fabricated from a radioactive shielding material and has both an internal volume (12) and a surface (14) that comprises an entry port (22) and an exit port (24);
a first chromatographic column (18) that is positioned within said internal volume (12) wherein;
said first chromatographic column (18) is housed within a column assembly (20) comprising:

a column housing (50) defining an internal space for receiving said first chromatographic column (18);
a column adaptor plate (40);
an exit pipe (66) in fluid communication with said first chromatographic column (18) via said column housing (50) and with an exit connection (46) that is mounted on said column adaptor plate (40); and
an entry pipe (62) in fluid communication with said first chromatographic column (18) via said column housing (50) and with an entry needle (52) that is disposed in an adaptor plate entry port (44) that is mounted on said column

adaptor plate (40);
wherein said column assembly (20) is configured for insertion as a unit into the internal volume (12) of said reactor housing (4) through an opening in an upper portion of said reactor housing (4); and;
a filter module (60) that is disposed external to said reactor housing (4) and in fluid communication with said column (18).

2. The system of claim 1 further comprising one or more of the following:

(i) a delivery vessel (68) that is disposed external to said reactor housing (4) and in fluid communication with said first chromatographic column (18);
(ii) a collection vessel (84) that is disposed external to said reactor housing (4) and in fluid communication with said first chromatographic column (18) via said filter module (60);
(iii) an adapter disk (28) disposed on said reactor housing (4), comprising a ridge of material (30) that extends around said entry port (22) and a ridge of material (34) that extends around said exit port (24); and
(iv) a cart (92) that includes one or more of
a plurality of delivery vessels (68) that each independently comprises a reactor vessel;
a plurality of delivery vessels that each independently comprises a solution of at least one radioisotope and is contained within a delivery housing that is fabricated from radioactive shielding material;
a plurality of evacuated collection vessels (84); and
a plurality of saline vessels (82).

3. A method comprising the steps of:

providing a system that comprises:

a reactor housing (4) that is fabricated from a radioactive shielding material and has both an internal volume (12) and a surface (14) that comprises an entry port (22) and an exit port (24);
a first chromatographic column (18) that is positioned within said internal volume (12) wherein
said first chromatographic column (18) is housed within a column assembly (20) comprising:

a column housing (50) defining an internal space for receiving said first chromatographic column (18);
a column adaptor plate (40);
an exit pipe (66) in fluid communication with said first chromatographic column (18) via said column housing (50) and with an exit connection (46) that is mounted on said column adaptor plate (40); and
an entry pipe (62) in fluid communication with said first chromatographic column (18) via said column housing (50) and with an entry needle (52) that is disposed in an adaptor plate entry port (44) that is mounted on said column adaptor plate (40);

wherein said column assembly (20) is configured for insertion as a unit into the internal volume (12) of said reactor housing (4) through an opening in an upper portion of said reactor housing (4); and;
a first filter module (60) that is disposed external to said reactor housing (4) and in fluid communication with said first chromatographic column (18); and
positioning a first delivery vessel (68) comprising a solution of at least one radioisotope external to said reactor housing (4) and in fluid communication with said first chromatographic column (18) for a time and under conditions effective to elute said first chromatographic column (18) with at least a portion of said solution; and,
positioning a collection vessel (84) external to said reactor housing (4) and in fluid communication with said exit port (24) via said filter module (60).

4. The method of claim 3 further comprising

(i) removing said first delivery vessel (68) from said position relative to said reactor housing (4); and/or
(ii) removing said first filter module (60).

5. The method of claim 3 comprising the steps of:

providing said system; and
positioning a first delivery vessel (68) comprising a solution of at least one radioisotope external to said reactor housing (4) and in fluid communication with said entry port (44) for a time and under conditions effective to elute said chromatographic column (18) with at least a portion of said solution.

6. The method of claim 3 comprising the steps of:

providing said system; and
removing said first chromatographic column (18) from said reactor housing (4).

7. The method of claim 3 further comprising positioning a subsequent chromatographic column in said reactor housing (4) such that a first end of said column is in fluid communication with said entry port (22) and a second end of said column is in fluid communication with said exit port (24).

8. The method of claim 3 comprising the steps of:

providing said system; and
removing said first filter module (60).

9. The method of claim 3 further comprising positioning a subsequent filter module external to said reactor housing (4) and in fluid communication with said exit port (24).

10. The method of claim 3 comprising the steps of:

providing said system; and
positioning a collection vessel (84) external to said reactor housing (4) and in fluid communication with said exit port (24) via said filter module (60).

11. The method according to claim 3 further comprising the steps of:

receiving customer information including a target output of a radioisotope; and
adding a solution of a parent radioisotope to a delivery vessel (68) in an amount sufficient to produce said target output upon decay of said parent radioisotope.

12. The method of claim 11 further comprising shipping said delivery vessel (68) to said customer.

13. A method comprising the steps of:

providing a system that comprises:
a reactor housing (4) that is fabricated from a radioactive shielding material and has both an internal volume (12) and a surface (14) that comprises an entry port (22) and an exit port (24); and
a first chromatographic column (18) that is positioned within said internal volume (12).
wherein said first chromatographic column (18) is housed within a column assembly (20) comprising
a column housing (50) defining an internal space for receiving said first chromatographic column (18);
a column adaptor plate (40);
an exit pipe (66) in fluid communication with said first chromatographic column (18) via said column housing (50) and with an exit connection (46) that is mounted on said column adaptor plate (40); and
an entry pipe (62) in fluid communication with said first chromatographic column (18) via said column housing (50) and with an entry needle (52) that is disposed in an adaptor plate entry port (44) that is mounted on said column adaptor plate (40);
wherein said column assembly (20) is configured for insertion as a unit into the internal volume (12) of said reactor housing (4) through an opening in an upper portion of said reactor housing (4);
removing said first chromatographic column (18) from said internal volume (12) by extracting said column assembly (20) through an opening in an upper portion of said reactor housing (4);
positioning a second chromatographic column within said internal volume (12) by inserting a second column assembly through said opening in said reactor housing (4);
positioning a first delivery vessel (68) comprising a solution of at least a first radioisotope external to said reactor housing (4) and in fluid communication with said second chromatographic column for a time and under conditions effective to elute said second chromatographic column with at least a portion of said solution; and,
positioning a first collection vessel (84) external to said reactor housing (4) and in fluid communication with said second chromatographic column.

14. The method of claim 13 further comprising removing said first delivery vessel (68) from said position relative to said reactor housing (4).

15. The method of claim 13 further comprising positioning a second delivery vessel comprising saline solution external to said reactor housing (4) and in fluid communication with said second chromatographic column for a time and under conditions effective to elute said second chromatographic column with at least a portion of said saline solution.

16. The method of claim 13 further comprising communicating a target output of at least a second radioisotope to a vendor of said solution of at least a first radioisotope.

Patentansprüche

1. System, umfassend:

ein Reaktorgehäuse (4), das aus einem Radioaktivität abschirmenden Material hergestellt ist und das sowohl ein inneres Volumen (12) als auch eine Oberfläche (14) mit einer Eintrittsöffnung (22) und einer Austrittsöffnung (24) aufweist,
eine erste chromatographische Säule (18), die in dem inneren Volumen (12) angeordnet ist, wobei
die erste chromatographische Säule (18) in einer Säulenanordnung (20) angeordnet ist, die:

ein Säulengehäuse (50), das einen inneren Raum zum Aufnehmen der ersten chromatographischen Säule (18) definiert,
eine Säulenanschlussplatte (40),
ein Austrittsröhrchen (66), das in Fluidverbindung steht mit der ersten chromatographischen Säule (18) über das Säulengehäuse (50) und mit einer Austrittsverbindung (46), die auf der Säulenanschlussplatte (40) montiert ist, und
ein Eintrittsröhrchen (62), das in Fluidverbindung steht mit der ersten chromatographischen Säule (18) über das Säulengehäuse (50) und mit einer Eintrittsnadel (52), welche in einer Anschlussplatteneintrittsöffnung (44) angeordnet ist, die auf der Anschlussplatte (40) montiert ist, umfasst,

wobei die Säulenanordnung (20) zum Einführen als eine Einheit in das innere Volumen (12) des Reaktorgehäuses (4) durch eine Öffnung in einem oberen Abschnitt des Reaktorgehäuses (4) ausgestaltet ist, und
ein Filtermodul (60), das außerhalb des Reaktorgehäuses (4) angeordnet ist und in Fluidverbindung mit der Säule (18) steht.

2. System nach Anspruch 1, das weiter eines oder

mehrere der nachfolgenden Merkmale aufweist:

(i) ein Abgabebehälter (68), der außerhalb des Reaktorgehäuses (4) angeordnet ist und der in Fluidverbindung mit der ersten chromatographischen Säule (18) steht,
(ii) ein Sammelbehälter (84), der außerhalb des Reaktorgehäuses (4) angeordnet ist und der über das Filtermodul (60) in Fluidverbindung mit der ersten chromatographischen Säule (18) steht,
(iii) eine Adapterscheibe (28), die auf dem Reaktorgehäuse (4) angeordnet ist und einen Materialwulst (30) aufweist, der sich um die Eintrittsöffnung (22) herum erstreckt, und einen Materialwulst (34), der sich um die Austrittsöffnung (24) herum erstreckt, und
(iv) einen Wagen (92), umfassend einen oder mehrere aus einer Mehrzahl von Abgabebehältern (68), von denen jeder unabhängig voneinander einen Reaktorbehälter aufweist,
einer Mehrzahl von Abgabebehältern, von denen jeder unabhängig voneinander eine Lösung von zumindest einem Radioisotop aufweist und in einem Abgabegehäuse enthalten ist, welches aus einem Radioaktivität abschirmenden Material hergestellt ist,
einer Mehrzahl von evakuierten Sammelbehältern (84) und
einer Mehrzahl von Salzbehältern (82).

3. Verfahren, welches die Schritte aufweist:

Bereitstellen eines Systems, umfassend:

ein Reaktorgehäuse (4), das aus einem Radioaktivität abschirmenden Material hergestellt ist und das sowohl ein inneres Volumen (12) als auch eine Oberfläche (14) mit einer Eintrittsöffnung (22) und einer Austrittsöffnung (24) aufweist,
eine erste chromatographische Säule (18), die in dem inneren Volumen (12) angeordnet ist, wobei
die erste chromatographische Säule (18) in einer Säulenanordnung (20) angeordnet ist, die:

ein Säulengehäuse (50), das einen inneren Raum zum Aufnehmen der ersten chromatographischen Säule (18) definiert,
eine Säulenanschlussplatte (40),
ein Austrittsröhrchen (66), das in Fluidverbindung steht mit der ersten chromatographischen Säule (18) über das Säulengehäuse (50) und mit einer Austrittsverbindung (46), die auf der Säulenanschlussplatte (40) montiert ist, und
ein Eintrittsröhrchen (62), das in Fluidverbindung steht mit der ersten chromatographischen Säule (18) über das Säulengehäuse (50) und mit einer Eintrittsnadel (52), welche in einer Anschlussplatteneintrittsöffnung (44) angeordnet ist, die auf der
Anschlussplatte (40) montiert ist, umfasst,

wobei die Säulenanordnung (20) zum Einführen als eine Einheit in das innere Volumen (12) des Reaktorgehäuses (4) durch eine Öffnung in einem oberen Abschnitt des Reaktorgehäuses (4) ausgestaltet ist, und
ein erstes Filtermodul (60), das außerhalb des Reaktorgehäuses (4)
angeordnet ist und in Fluidverbindung mit der Säule (18) steht, und Anordnen eines ersten Abgabebehälters (68), der eine Lösung von zumindest einem Radioisotop aufweist, außerhalb des Reaktorgehäuses (4) und derart in Fluidverbindung mit der ersten chromatographischen Säule (18) für eine Zeitspanne und unter Bedingungen, die ausreichen, um die erste chromatographischen Säule (18) mit zumindest einem Teil der Lösung zu eluieren, und

Anordnen eines Sammelbehälters (84) außerhalb des Reaktorgehäuses (4) derart, dass der Sammelbehälter über das Filtermodul (60) in Fluidverbindung mit der Austrittsöffnung (24) steht.

4. Verfahren nach Anspruch 3, welches weiter umfasst

(i) Entfernen des ersten Abgabebehälters (68) aus der Anordnung relativ zu dem Reaktorgehäuse (4) und/oder
(ii) Entfernen des Filtermoduls (60).

5. Verfahren nach Anspruch 3, welches die Schritte aufweist:

Bereitstellen des Systems und
Anordnen eines ersten Abgabebehälters (68), der eine Lösung von zumindest einem Radioisotop enthält, außerhalb des Reaktorgehäuses (4) und derart in Fluidverbindung mit der Eintrittsöffnung (44) für eine Zeitspanne und unter Bedingungen, die ausreichen, um die chromatographische Säule (18) mit zumindest einem Teil der Lösung zu eluieren.

6. Verfahren nach Anspruch 3, welches die Schritte

aufweist:

Bereitstellen des Systems und
Entfernen der ersten chromatographischen Säule (18) von dem Reaktorgehäuse (4).

7. Verfahren nach Anspruch 3, welches weiter aufweist: Anordnen einer nachfolgenden chromatographischen Säule in dem Reaktorgehäuse (4) derart, dass ein erstes Ende der Säule in Fluidverbindung mit der Eintrittsöffnung (22) und ein zweites Ende der Säule in Fluidverbindung mit der Austrittsöffnung (24) steht.

8. Verfahren nach Anspruch 3, welches die Schritte aufweist:

Bereitstellen des Systems und
Entfernen des ersten Filtermoduls (60).

9. Verfahren nach Anspruch 3, welches weiter das Anordnen eines nachfolgenden Filtermoduls außerhalb des Reaktorgehäuses (4) und in Fluidverbindung mit der Austrittsöffnung (24) umfasst.

10. Verfahren nach Anspruch 3, welches die Schritte aufweist:

Bereitstellen des Systems und
Anordnen eines Sammelbehälters (84) außerhalb des Reaktorgehäuses (4) derart,
dass der Sammelbehälter über das Filtermodul (60) in Fluidverbindung mit der Austrittsöffnung (24) steht.

11. Verfahren nach Anspruch 3, welches weiter die Schritte aufweist:

Empfangen von Benutzerinformationen einschließlich einer anvisierten Ausgabemenge eines Radioisotops und
Hinzufügen einer Lösung eines Ausgangsradioisotops in einen Abgabebehälter (68) in einer Menge ausreichend zum Herstellen der anvisierten Ausgabemenge aus der Verfallsreihe des Ausgangsradioisotops.

12. Verfahren nach Anspruch 11, welches weiter das Abgeben des Abgabebehälters (68) an den Benutzer umfasst.

13. Verfahren, welches die Schritte aufweist:

Bereitstellen eines Systems, umfassend:

ein Reaktorgehäuse (4), das aus einem Radioaktivität abschirmenden Material hergestellt ist und das sowohl ein inneres Volumen (12) als auch eine Oberfläche (14) mit einer Eintrittsöffnung (22) und einer Austrittsöffnung (24) aufweist, und
eine erste chromatographische Säule (18), die in dem inneren Volumen (12) angeordnet ist, wobei die erste chromatographische Säule (18) in einer Säulenanordnung (20) angeordnet ist, die:

ein Säulengehäuse (50), das einen inneren Raum zum Aufnehmen der ersten chromatographischen Säule (18) definiert,
eine Säulenanschlussplatte (40),
ein Austrittsröhrchen (66), das in Fluidverbindung steht mit der ersten chromatographischen Säule (18) über das Säulengehäuse (50) und mit einer Austrittsverbindung (46), die auf der Säulenanschlussplatte (40) montiert ist, und
ein Eintrittsröhrchen (62), das in Fluidverbindung steht mit der ersten chromatographischen Säule (18) über das Säulengehäuse (50) und mit einer Eintrittsnadel (52), welche in einer Anschlussplattentrittsöffnung (44) angeordnet ist, die auf
der Anschlussplatte (40) montiert ist, umfasst,

wobei die Säulenanordnung (20) zum Einführen als eine Einheit in das innere Volumen (12) des Reaktorgehäuses (4) durch eine Öffnung in einem oberen Abschnitt des Reaktorgehäuses (4) ausgestaltet ist,

Entfernen der ersten chromatographischen Säule (18) aus dem inneren Volumen (12) durch Entnehmen der Säulenanordnung (20) durch eine Öffnung in einem oberen Abschnitt des Reaktorgehäuses (4),
Anordnen einer zweiten chromatographischen Säule innerhalb des inneren Volumens (12) durch Einführen einer zweiten Säulenanordnung durch die Öffnung in dem Reaktorgehäuse (4),
Anordnen eines ersten Abgabebehälters (68), der eine Lösung von zumindest einem ersten Radioisotop enthält, außerhalb des Reaktorgehäuses (4) und derart in Fluidverbindung mit der zweiten Säulenanordnung für eine Zeitspanne und unter Bedingungen, die ausreichen, um die zweite Säulenanordnung mit zumindest einem Teil der Lösung zu eluieren, und
Anordnen eines ersten Sammelbehälters (84) außerhalb des Reaktorgehäuses (4) und in Fluidverbindung mit der zweiten chromatogra-

phischen Säule.

14. Verfahren nach Anspruch 13, welches weiter aufweist: Entfernen des ersten Abgabebehälters (68) aus dessen Anordnung relativ zu dem Reaktorgehäuse (4).

15. Verfahren nach Anspruch 13, welches weiter umfasst: Anordnen eines zweiten Abgabebehälters, der eine Salzlösung enthält, außerhalb des Reaktorgehäuses (4) und derart in Fluidverbindung mit der zweiten chromatographischen Säule für eine Zeitspanne und unter Bedingungen, die ausreichen, um die zweite chromatographische Säule mit zumindest einem Teil der Salzlösung zu eluieren.

16. Verfahren nach Anspruch 13, welches weiter umfasst: Weitergabe der anvisierten Ausgabemenge zumindest eines zweiten Radioisotops an einen Lieferanten der Lösung zumindest eines ersten Radioisotops.

Revendications

1. Système comprenant :

un logement de réacteur (4) qui est fabriqué à partir d'un matériau de blindage radioactif et qui présente à la fois un volume interne (12) et une surface (14) qui comprend un orifice d'entrée (22) et un orifice de sortie (24) ;
une première colonne chromatographique (18) qui est positionnée à l'intérieur dudit volume interne (12) ; dans lequel
ladite première colonne chromatographique (18) est logée à l'intérieur d'un ensemble de colonne (20) comprenant :

un logement de colonne (50) définissant un espace interne pour recevoir ladite première colonne chromatographique (18) ;
une plaque d'adaptation de colonne (40) ;
un tuyau de sortie (66) en communication fluide avec ladite première colonne chromatographique (18) par l'intermédiaire dudit logement de colonne (50) et avec un raccord de sortie (46) qui est monté sur ladite plaque d'adaptation de colonne (40) ; et
un tuyau d'entrée (62) en communication fluide avec ladite première colonne chromatographique (18) par l'intermédiaire dudit logement de colonne (50) et avec une aiguille d'entrée (52) qui est disposée dans un orifice d'entrée de plaque d'adaptation (44) qui est monté sur ladite plaque d'adaptation de colonne (40) ;

dans lequel ledit ensemble de colonne (20) est configuré pour être inséré en tant qu'unité dans le volume interne (12) dudit logement de réacteur (4) à travers une ouverture dans une partie supérieure dudit logement de réacteur (4) ; et
un module de filtre (60) qui est disposé à l'extérieur dudit logement de réacteur (4) et en communication fluide avec ladite colonne (18).

2. Système selon la revendication 1, comprenant en outre un ou plusieurs des éléments suivants :

(i) une cuve de distribution (68) qui est disposée à l'extérieur dudit logement de réacteur (4) et en communication fluide avec ladite première colonne chromatographique (18) ;
(ii) une cuve de collecte (84) qui est disposée à l'extérieur dudit logement de réacteur (4) et en communication fluide avec ladite première colonne chromatographique (18) par le biais dudit module de filtre (60) ;
(iii) un disque d'adaptation (28) disposé sur ledit logement de réacteur (4), comprenant un bourrelet de matière (30) qui s'étend autour dudit orifice d'entrée (22) et un bourrelet de matière (34) qui s'étend autour dudit orifice de sortie (24) ; et
(iv) un chariot (92) qui comprend un ou plusieurs d'une pluralité de cuves de distribution (68) qui comprennent chacune indépendamment une cuve de réacteur ;
d'une pluralité de cuves de distribution qui comprennent chacune indépendamment une solution d'au moins un radio-isotope et sont contenues à l'intérieur d'un logement de distribution qui est fabriqué à partir d'un matériau de blindage radioactif ;
d'une pluralité de cuves de collecte sous vide (84) ; et
d'une pluralité de cuves de solution saline (82).

3. Procédé comprenant les étapes de :

fournir un système qui comprend :

un logement de réacteur (4) qui est fabriqué à partir d'un matériau de blindage radioactif et qui présente à la fois un volume interne (12) et une surface (14) qui comprend un orifice d'entrée (22) et un orifice de sortie (24) ;
une première colonne chromatographique (18) qui est positionnée à l'intérieur dudit volume interne (12) dans lequel
ladite première colonne chromatographique (18) est logée à l'intérieur d'un ensemble de colonne (20) comprenant :
un logement de colonne (50) définissant un espace interne pour recevoir ladite premiè-

re colonne chromatographique (18) ;
une plaque d'adaptation de colonne (40) ;
un tuyau de sortie (66) en communication fluide avec ladite première colonne chromatographique (18) par le biais dudit logement de colonne (50) et avec un raccord de sortie (46) qui est monté sur ladite plaque d'adaptation de colonne (40) ; et
un tuyau d'entrée (62) en communication fluide avec ladite première colonne chromatographique (18) par le biais dudit logement de colonne (50) et avec une aiguille d'entrée (52) qui est disposée dans un orifice d'entrée de plaque d'adaptation (44) qui est monté sur ladite plaque d'adaptation de colonne (40) ;
dans lequel ledit ensemble de colonne (20) est configuré pour être inséré en tant qu'élément dans le volume interne (12) dudit logement de réacteur (4) à travers une ouverture dans une partie supérieure dudit logement du réacteur (4) ; et
un premier module de filtre (60) qui est disposé à l'extérieur dudit logement de réacteur (4) et en communication fluide avec ladite première colonne chromatographique (18) ; et

positionner une première cuve de distribution (68) comprenant une solution d'au moins un radio-isotope à l'extérieur dudit logement de réacteur (4) et en communication fluide avec ladite première colonne chromatographique (18) pendant une durée et dans des conditions efficaces pour éluer ladite première colonne chromatographique (18) avec au moins une partie de ladite solution ; et
positionner une cuve de collecte (84) à l'extérieur dudit logement de réacteur (4) et en communication fluide avec ledit orifice de sortie (24) par le biais dudit module de filtre (60).

4. Procédé selon la revendication 3, comprenant en outre :

(i) retirer ladite première cuve de distribution (68) de ladite position par rapport audit logement de réacteur (4) ; et/ou
(ii) retirer ledit premier module de filtre (60).

5. Procédé selon la revendication 3, comprenant les étapes de :

fournir ledit système ; et
positionner une première cuve de distribution (68) comprenant une solution d'au moins un radio-isotope à l'extérieur dudit logement de réacteur (4) et en communication fluide avec ledit orifice d'entrée (44) pendant une durée et dans des conditions efficaces pour éluer ladite colonne chromatographique (18) avec au moins une partie de ladite solution.

6. Procédé selon la revendication 3, comprenant les étapes de :

fournir ledit système ; et
retirer ladite première colonne chromatographique (18) dudit logement de réacteur (4).

7. Procédé selon la revendication 3, comprenant en outre le positionnement d'une colonne chromatographique subséquente dans ledit logement de réacteur (4) de telle sorte qu'une première extrémité de ladite colonne est en communication fluide avec ledit orifice d'entrée (22) et qu'une seconde extrémité de ladite colonne est en communication fluide avec ledit orifice de sortie (24).

8. Procédé selon la revendication 3, comprenant les étapes de :

fournir ledit système ; et
retirer ledit premier module de filtre (60).

9. Procédé selon la revendication 3, comprenant en outre le positionnement d'un module de filtre subséquent à l'extérieur dudit logement de réacteur (4) et en communication fluide avec ledit orifice de sortie (24).

10. Procédé selon la revendication 3, comprenant les étapes de :

fournir ledit système ; et
positionner une cuve de collecte (84) à l'extérieur dudit logement de réacteur (4) et en communication fluide avec ledit orifice de sortie (24) par le biais dudit module de filtre (60).

11. Procédé selon la revendication 3 comprenant en outre les étapes de :

recevoir des informations de client comprenant une activité cible d'un radio-isotope ; et
ajouter une solution d'un radio-isotope parent dans une cuve de distribution (68) dans une quantité suffisante pour produire ladite activité cible lors de la dégradation dudit radio-isotope parent.

12. Procédé selon la revendication 11, comprenant en outre l'expédition de ladite cuve de distribution (68) audit client.

13. Procédé comprenant les étapes de :

fournir un système qui comprend :

un logement de réacteur (4) qui est fabriqué à partir d'un matériau de blindage radioactif et qui présente à la fois un volume interne (12) et une surface (14) qui comprend un orifice d'entrée (22) et un orifice de sortie (24) ; et
une première colonne chromatographique (18) qui est positionnée à l'intérieur dudit volume interne (12),
dans lequel ladite première colonne chromatographique (18) est logée à l'intérieur d'un ensemble de colonne (20) comprenant :
un logement de colonne (50) définissant un espace interne pour recevoir ladite première colonne chromatographique (18) ;
une plaque d'adaptation de colonne (40) ;
un tuyau de sortie (66) en communication fluide avec ladite première colonne chromatographique (18) par le biais dudit logement de colonne (50) et avec un raccord de sortie (46) qui est monté sur ladite plaque d'adaptation de colonne (40) ; et
un tuyau d'entrée (62) en communication fluide avec ladite première colonne chromatographique (18) par le biais dudit logement de colonne (50) et avec une aiguille d'entrée (52) qui est disposée dans un orifice d'entrée de plaque d'adaptation (44) qui est monté sur ladite plaque d'adaptation de colonne (40) ;
dans lequel ledit ensemble de colonne (20) est configuré pour être inséré en tant qu'élément dans le volume interne (12) dudit logement de réacteur (4) à travers une ouverture dans une partie supérieure dudit logement de réacteur (4) ; et
retirer ladite première colonne chromatographique (18) dudit volume interne (12) en extrayant ledit ensemble de colonne (20) à travers une ouverture dans une partie supérieure dudit logement de réacteur (4) ;
positionner une seconde colonne chromatographique à l'intérieur dudit volume interne (12) en insérant un second ensemble de colonne à travers ladite ouverture dans ledit logement de réacteur (4) ;
positionner une première cuve de distribution (68) comprenant une solution d'au moins un premier radio-isotope à l'extérieur dudit logement de réacteur (4) et en communication fluide avec ladite seconde colonne chromatographique pendant une durée et dans des conditions efficaces pour éluer ladite seconde colonne chromatographique avec au moins une partie de ladite solution ; et
positionner une première cuve de collecte (84) à l'extérieur dudit logement de réacteur (4) et en communication fluide avec ladite seconde colonne chromatographique.

14. Procédé selon la revendication 13, comprenant en outre le retrait de ladite première cuve de distribution (68) de ladite position par rapport audit logement de réacteur (4).

15. Procédé selon la revendication 13, comprenant en outre le positionnement d'une seconde cuve de distribution comprenant une solution saline à l'extérieur dudit logement de réacteur (4) et en communication fluide avec ladite seconde colonne chromatographique pendant une durée et dans des conditions efficaces pour éluer ladite seconde colonne chromatographique avec au moins une partie de ladite solution saline.

16. Procédé selon la revendication 13, comprenant en outre la communication d'une activité cible d'au moins un second radio-isotope à un fournisseur de ladite solution d'au moins un premier radio-isotope.

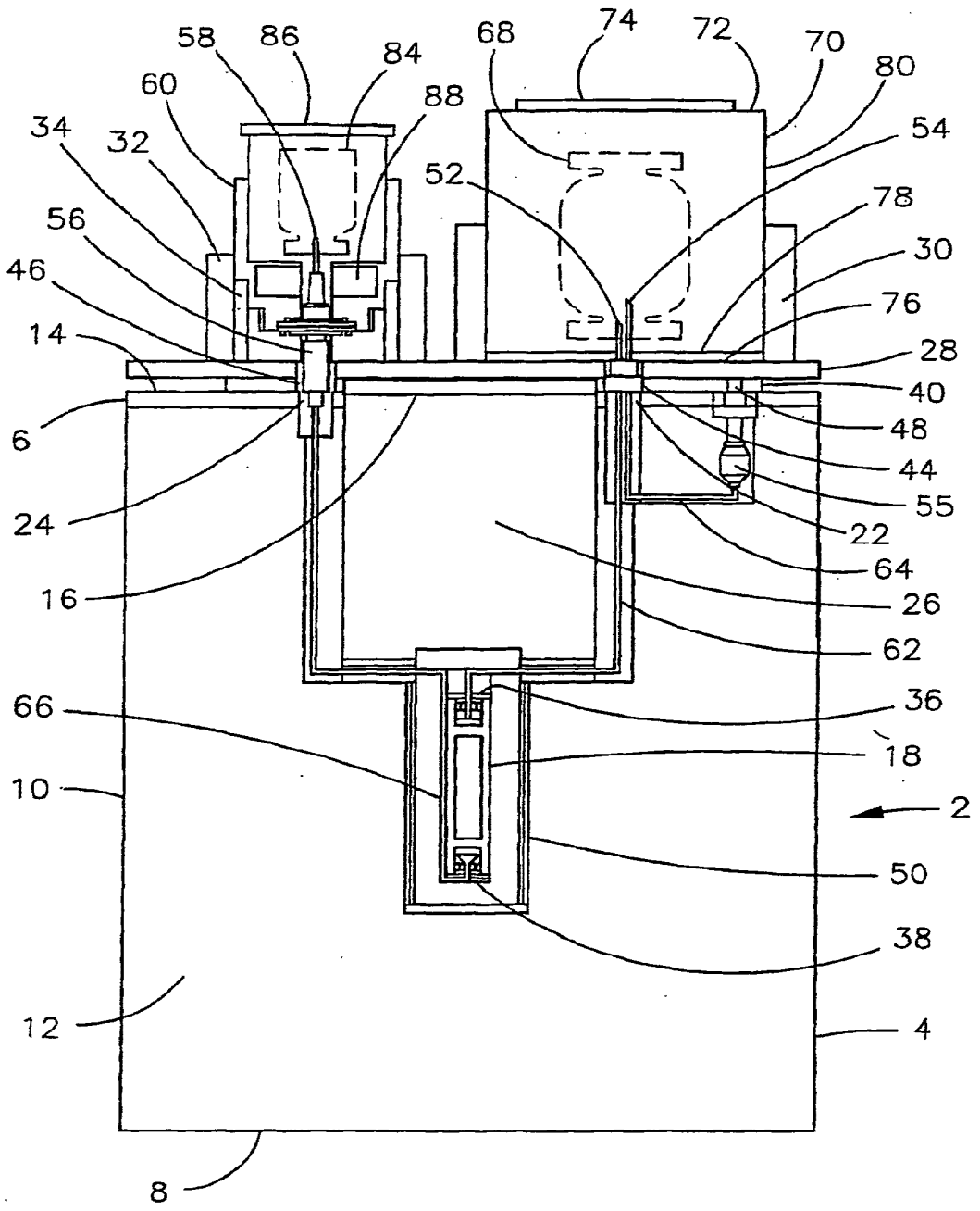

58
86
84
68
74
72
70
80
60
88
34
32
52
54
56
78
46
30
14
76
28
40
6
48
44
24
55
22
64
16
26
62
66
36
18
10
2
50
38
12
4
8

Fig. 1

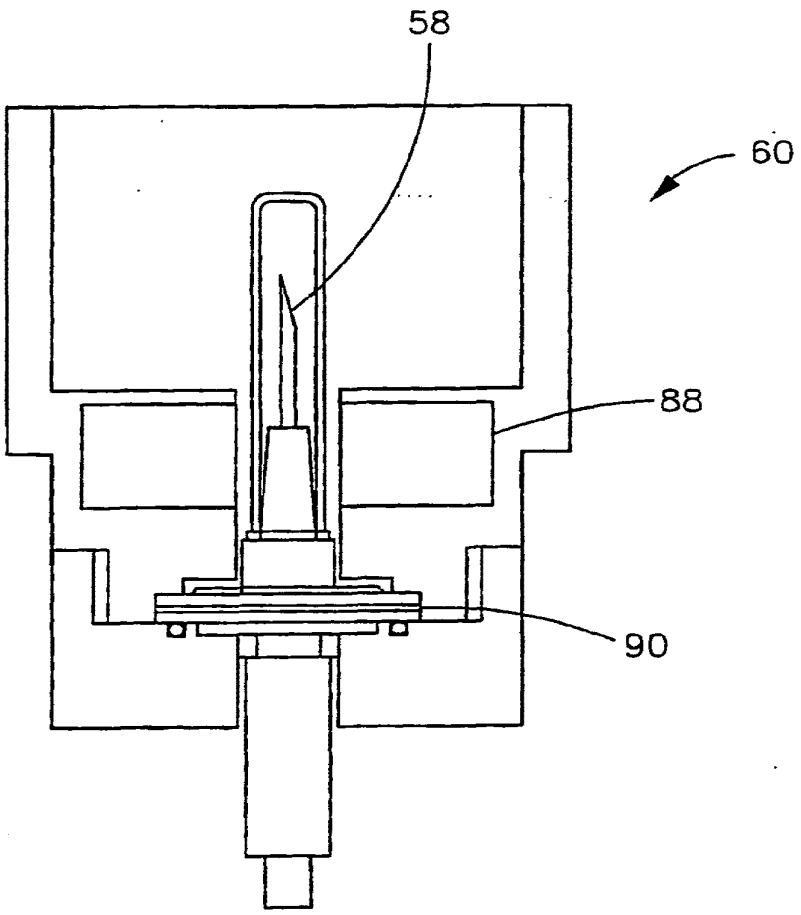


Fig. 2

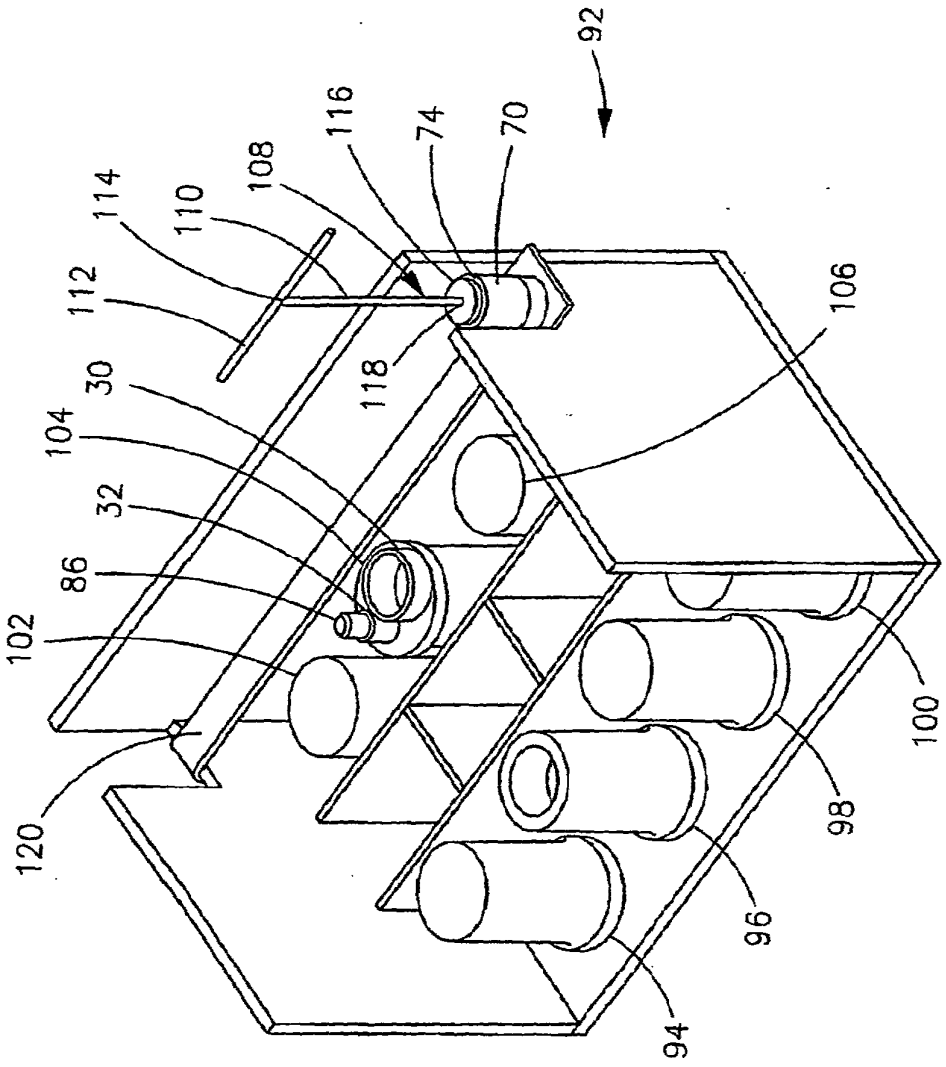

92
116
74
70
108
114
110
112
118
106
30
104
32
86
102
120
100
98
96
94

Fig. 3

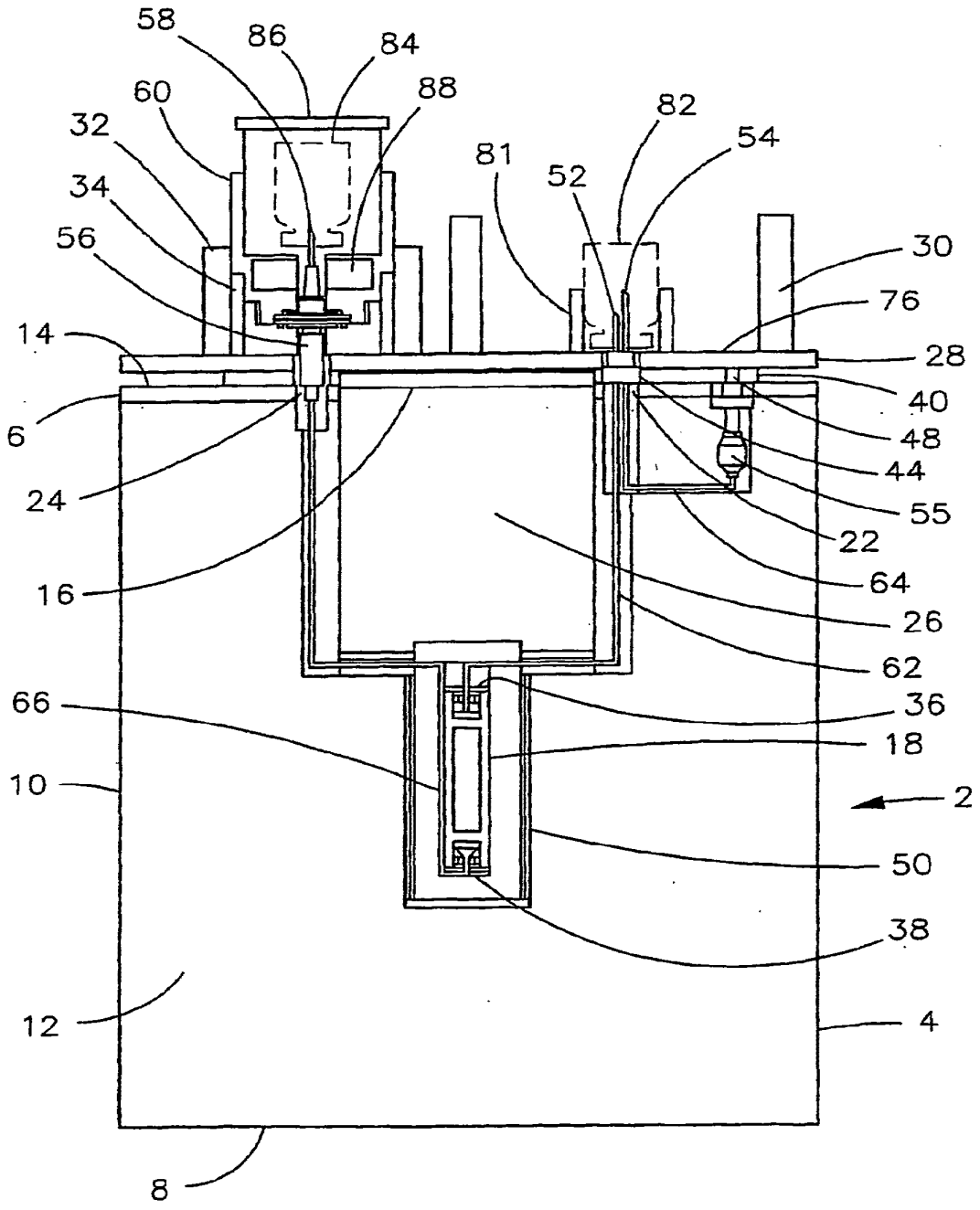

58
86
84
88
60
32
34
56
14
6
24
16
66
10
12
8
81
52
82
54
30
76
28
40
48
44
55
22
64
26
62
36
18
2
50
38
4

Fig. 4

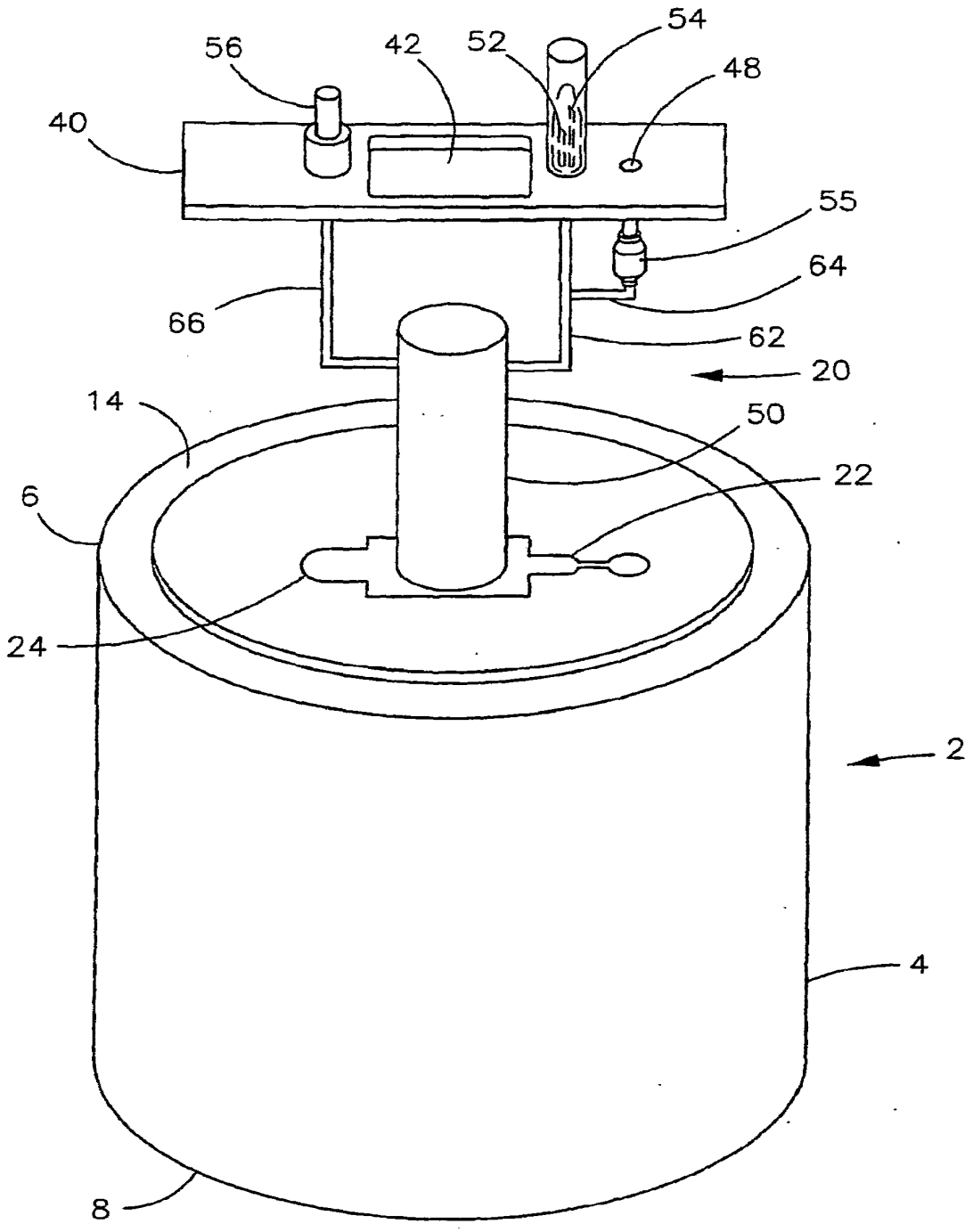


Fig. 5

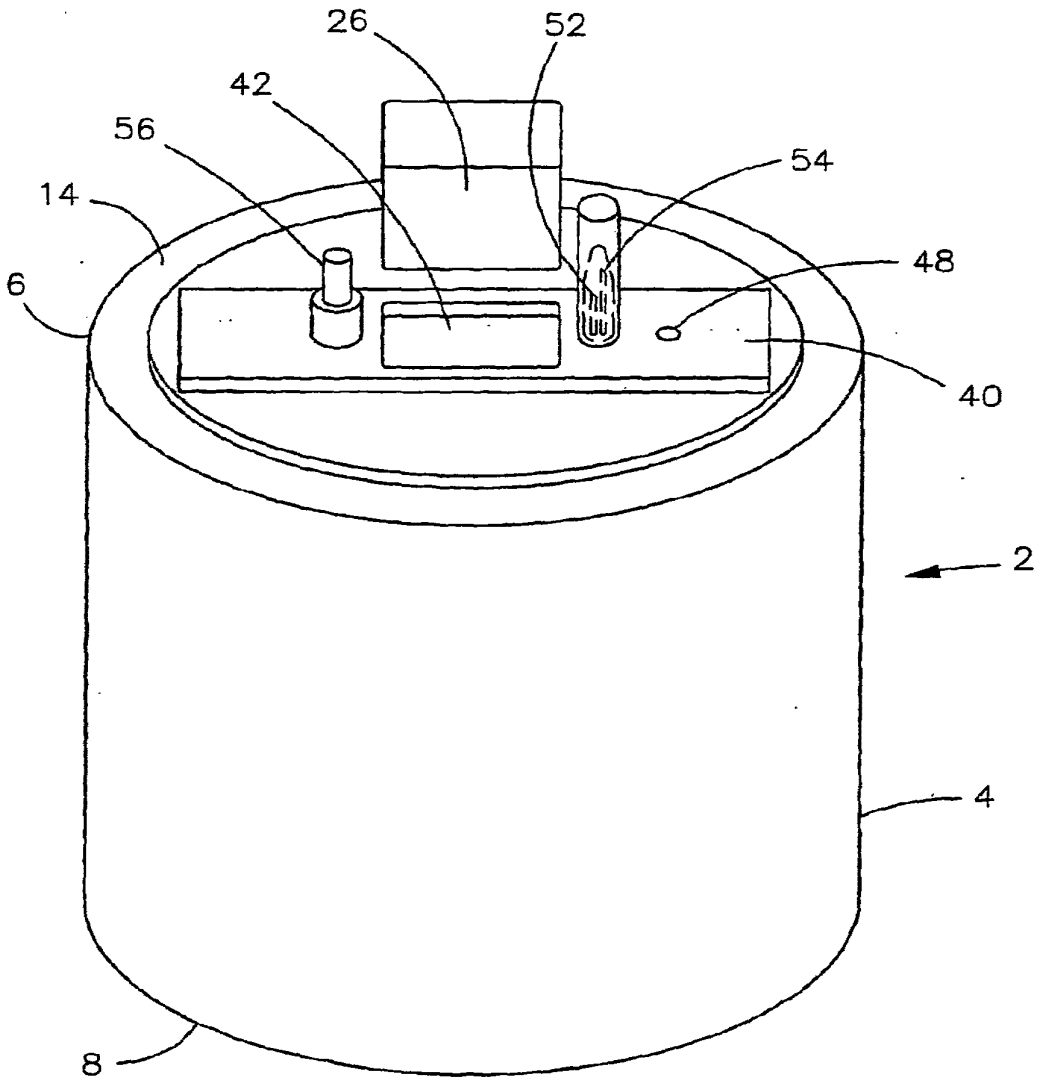


Fig. 6

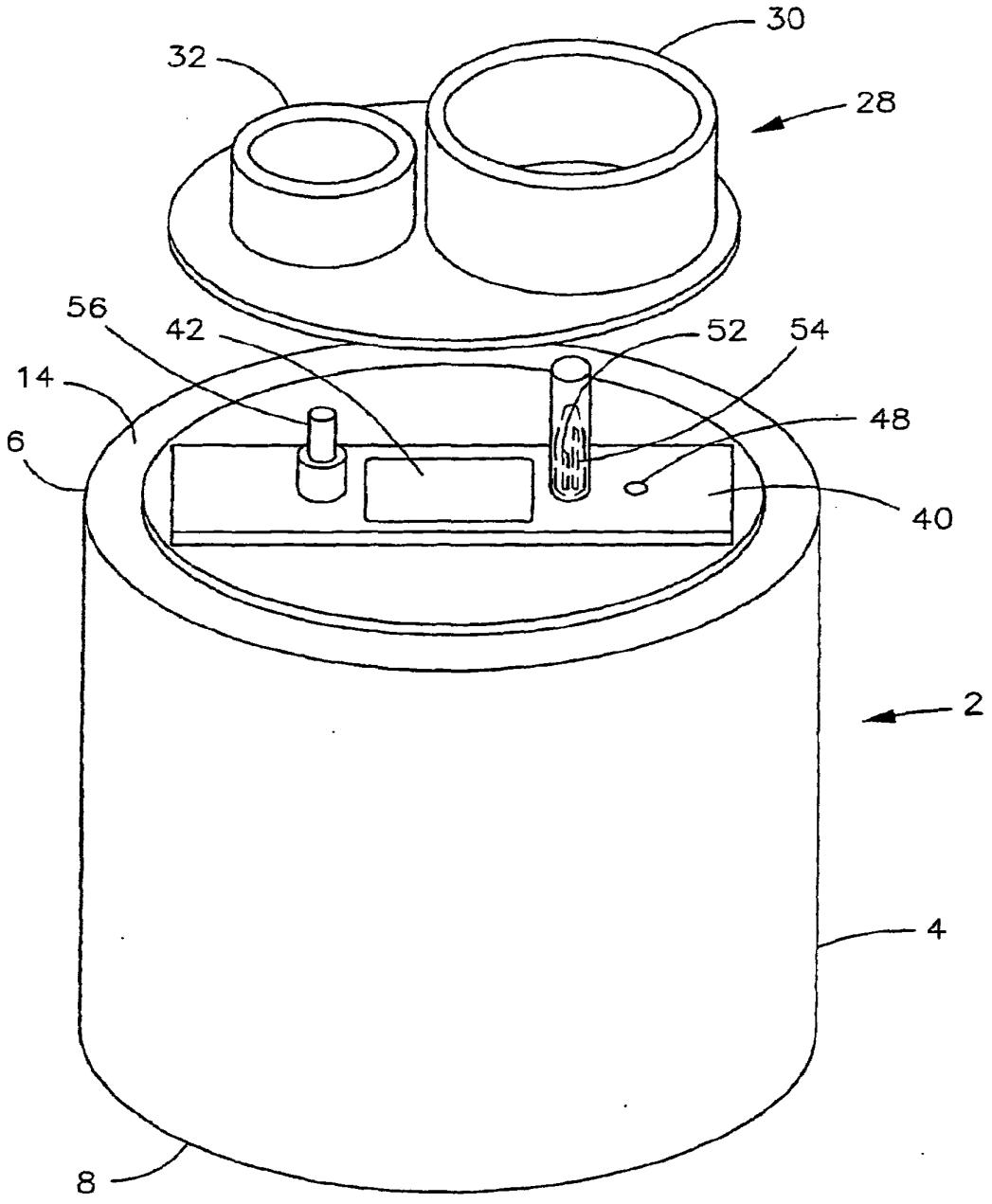


Fig. 7

REFERENCES CITED IN THE DESCRIPTION

This list of references cited by the applicant is for the reader's convenience only. It does not form part of the European patent document. Even though great care has been taken in compiling the references, errors or omissions cannot be excluded and the EPO disclaims all liability in this regard.

Non-patent literature cited in the description

- **SCHWOCHAU.** Klaus. Technetium. Wiley-VCH, 2000 **[0003]**

Electronic Patent Application Fee Transmittal

Application Number:	12137364
Filing Date:	11-Jun-2008
Title of Invention:	INFUSION SYSTEMS INCLUDING COMPUTER-FACILITATED MAINTENANCE AND/OR OPERATION AND METHODS OF USE
First Named Inventor/Applicant Name:	Stephen E. Hidem
Filer:	Paul J. LaVanway Jr.
Attorney Docket Number:	56782.1.7

Filed as Large Entity

Utility under 35 USC 111(a) Filing Fees

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Basic Filing:				
Pages:				
Claims:				
Miscellaneous-Filing:				
Petition:				
Patent-Appeals-and-Interference:				
Post-Allowance-and-Post-Issuance:				
Extension-of-Time:				

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Miscellaneous:				
Submission- Information Disclosure Stmt	1806	1	180	180
		Total in USD ($)		**180**

Electronic Acknowledgement Receipt

EFS ID:	15842613
Application Number:	12137364
International Application Number:	
Confirmation Number:	7377
Title of Invention:	INFUSION SYSTEMS INCLUDING COMPUTER-FACILITATED MAINTENANCE AND/OR OPERATION AND METHODS OF USE
First Named Inventor/Applicant Name:	Stephen E. Hidem
Customer Number:	22859
Filer:	Paul J. LaVanway Jr.
Filer Authorized By:	
Attorney Docket Number:	56782.1.7
Receipt Date:	23-MAY-2013
Filing Date:	11-JUN-2008
Time Stamp:	15:25:50
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	yes
Payment Type	Credit Card
Payment was successfully received in RAM	$180
RAM confirmation Number	2008
Deposit Account	
Authorized User	

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)

1	Information Disclosure Statement (IDS) Form (SB08)	12thSIDS_56782-1-7.pdf	612281 0143602684482b4cb0ceeb56fde42b859b1d7fcb	no	4
Warnings:					
Information:					
A U.S. Patent Number Citation or a U.S. Publication Number Citation is required in the Information Disclosure Statement (IDS) form for autoloading of data into USPTO systems. You may remove the form to add the required data in order to correct the Informational Message if you are citing U.S. References. If you chose not to include U.S. References, the image of the form will be processed and be made available within the Image File Wrapper (IFW) system. However, no data will be extracted from this form. Any additional data such as Foreign Patent Documents or Non Patent Literature will be manually reviewed and keyed into USPTO systems.					
2	Foreign Reference	EP2492920A2.pdf	939755 f392d9dfd6a3af1a57a64bdbb59bb0daa3908ff2	no	18
Warnings:					
Information:					
3	Foreign Reference	EP2011126B1.pdf	1076709 ec5b68efe10ef02ab075d96166c74033b68b06ca	no	21
Warnings:					
Information:					
4	Fee Worksheet (SB06)	fee-info.pdf	30551 b406f6aad4a92445408cbaee43a67d3a2d7e968c	no	2
Warnings:					
Information:					
			Total Files Size (in bytes):	2659296	

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.

New Applications Under 35 U.S.C. 111

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.

National Stage of an International Application under 35 U.S.C. 371

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.

New International Application Filed with the USPTO as a Receiving Office

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.

PTO/SB/08a (01-10)
Approved for use through 07/31/2012. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Not for submission under 37 CFR 1.99)

Application Number	12137364
Filing Date	2008-06-11
First Named Inventor	Stephen E. HIDEM
Art Unit	3735
Examiner Name	ZHANG, Jenna
Attorney Docket Number	56782.1.7

U.S.PATENTS Remove

Examiner Initial*	Cite No	Patent Number	Kind Code[1]	Issue Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1					

If you wish to add additional U.S. Patent citation information please click the Add button. Add

U.S.PATENT APPLICATION PUBLICATIONS Remove

Examiner Initial*	Cite No	Publication Number	Kind Code[1]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1					

If you wish to add additional U.S. Published Application citation information please click the Add button. Add

FOREIGN PATENT DOCUMENTS Remove

Examiner Initial*	Cite No	Foreign Document Number[3]	Country Code[2] i	Kind Code[4]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear	T[5]
	1	1968653	CN		2007-05-23	E Z EM INC.		☐

If you wish to add additional Foreign Patent Document citation information please click the Add button Add

NON-PATENT LITERATURE DOCUMENTS Remove

Examiner Initials*	Cite No	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc), date, pages(s), volume-issue number(s), publisher, city and/or country where published.	T[5]

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	12137364
	Filing Date	2008-06-11
	First Named Inventor	Stephen E. HIDEM
	Art Unit	3735
	Examiner Name	ZHANG, Jenna
	Attorney Docket Number	56782.1.7

	1		☐

If you wish to add additional non-patent literature document citation information please click the Add button Add

EXAMINER SIGNATURE

Examiner Signature		Date Considered	

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through a citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

[1] See Kind Codes of USPTO Patent Documents at www.USPTO.GOV or MPEP 901.04. [2] Enter office that issued the document, by the two-letter code (WIPO Standard ST.3). [3] For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. [4] Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. [5] Applicant is to place a check mark here if English language translation is attached.

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	12137364
	Filing Date	2008-06-11
	First Named Inventor	Stephen E. HIDEM
	Art Unit	3735
	Examiner Name	ZHANG, Jenna
	Attorney Docket Number	56782.1.7

CERTIFICATION STATEMENT

Please see 37 CFR 1.97 and 1.98 to make the appropriate selection(s):

☐ That each item of information contained in the information disclosure statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(1).

OR

☐ That no item of information contained in the information disclosure statement was cited in a communication from a foreign patent office in a counterpart foreign application, and, to the knowledge of the person signing the certification after making reasonable inquiry, no item of information contained in the information disclosure statement was known to any individual designated in 37 CFR 1.56(c) more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(2).

☐ See attached certification statement.

☒ The fee set forth in 37 CFR 1.17 (p) has been submitted herewith.

☐ A certification statement is not submitted herewith.

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	/Paul J. LaVanway, Jr./	Date (YYYY-MM-DD)	2013-04-03
Name/Print	Paul J. LaVanway, Jr.	Registration Number	64610

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 1 hour to complete, including gathering, preparing and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

Privacy Act Statement

The Privacy Act of 1974 (P.L. 93-579) requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that: (1) the general authority for the collection of this information is 35 U.S.C. 2(b)(2); (2) furnishing of the information solicited is voluntary; and (3) the principal purpose for which the information is used by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent application or patent. If you do not furnish the requested information, the U.S. Patent and Trademark Office may not be able to process and/or examine your submission, which may result in termination of proceedings or abandonment of the application or expiration of the patent.

The information provided by you in this form will be subject to the following routine uses:

1. The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C. 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether the Freedom of Information Act requires disclosure of these record s.

2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.

3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.

4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).

5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent Cooperation Treaty.

6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).

7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (i.e., GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.

8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspections or an issued patent.

9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

Electronic Patent Application Fee Transmittal

Application Number:	12137364
Filing Date:	11-Jun-2008
Title of Invention:	INFUSION SYSTEMS INCLUDING COMPUTER-FACILITATED MAINTENANCE AND/OR OPERATION AND METHODS OF USE
First Named Inventor/Applicant Name:	Stephen E. Hidem
Filer:	Paul J. LaVanway Jr.
Attorney Docket Number:	56782.1.7

Filed as Large Entity

Utility under 35 USC 111(a) Filing Fees

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Basic Filing:				
Pages:				
Claims:				
Miscellaneous-Filing:				
Petition:				
Patent-Appeals-and-Interference:				
Post-Allowance-and-Post-Issuance:				
Extension-of-Time:				

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Miscellaneous:				
Submission- Information Disclosure Stmt	1806	1	180	180
		Total in USD ($)		**180**

Electronic Acknowledgement Receipt

EFS ID:	15410418
Application Number:	12137364
International Application Number:	
Confirmation Number:	7377
Title of Invention:	INFUSION SYSTEMS INCLUDING COMPUTER-FACILITATED MAINTENANCE AND/OR OPERATION AND METHODS OF USE
First Named Inventor/Applicant Name:	Stephen E. Hidem
Customer Number:	22859
Filer:	Paul J. LaVanway Jr.
Filer Authorized By:	
Attorney Docket Number:	56782.1.7
Receipt Date:	03-APR-2013
Filing Date:	11-JUN-2008
Time Stamp:	11:47:17
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	yes
Payment Type	Credit Card
Payment was successfully received in RAM	$180
RAM confirmation Number	8959
Deposit Account	
Authorized User	

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)

1	Foreign Reference	CN1968653A.pdf	2476813 666236130d8b55657363291667c2cb2cc4ad146a	no	53
Warnings:					
Information:					
2	Information Disclosure Statement (IDS) Form (SB08)	56782_1_7SIDS.pdf	612150 593b10000f27f017adef3cb71535db78b7a25ae1	no	4
Warnings:					
Information:					

A U.S. Patent Number Citation or a U.S. Publication Number Citation is required in the Information Disclosure Statement (IDS) form for autoloading of data into USPTO systems. You may remove the form to add the required data in order to correct the Informational Message if you are citing U.S. References. If you chose not to include U.S. References, the image of the form will be processed and be made available within the Image File Wrapper (IFW) system. However, no data will be extracted from this form. Any additional data such as Foreign Patent Documents or Non Patent Literature will be manually reviewed and keyed into USPTO systems.

3	Fee Worksheet (SB06)	fee-info.pdf	30551 ac12b9879eb6d0bd0406d76a47fb94f5d73510b5	no	2
Warnings:					
Information:					
		Total Files Size (in bytes):	3119514		

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.

New Applications Under 35 U.S.C. 111

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.

National Stage of an International Application under 35 U.S.C. 371

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.

New International Application Filed with the USPTO as a Receiving Office

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.

No documents available for this priority number.

Espacenet

Bibliographic data: CN1968653 (A) — 2007-05-23

Method system and apparatus for operating a medical injector and diagnostic imaging device

Inventor(s): ROBERT WILLIAMS [US] ± (WILLIAMS ROBERT)

Applicant(s): E Z EM INC [US] ± (E-Z-EM INC, ; ACIST MEDICAL SYSTEMS, INC)

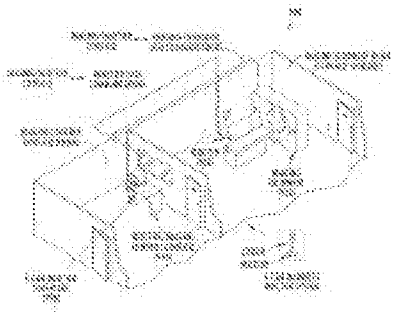
Classification: - international: ***A61B6/00; A61M5/00; A61M5/172;*** *A61B6/03*
- cooperative: **A61B6/463**; **A61B6/481**; **A61B6/504**; **A61M5/007**; **A61M5/172**; A61B6/032; A61B6/4085; A61B6/467; A61B6/468; A61M2205/3561; A61M2205/502

Application number: CN20058010953 20050125

Priority number (s): WO2005US02282 20050125 ; US20040543601P 20040211

Also published as: CN1968653 (B) WO2005076810 (A2) WO2005076810 (A3) US2005203389 (A1) KR20060111719 (A) more

Abstract of CN1968653 (A)



The invention is generally directed, but not limited to, a method system and apparatus that allows an operator to control an injection device and imaging equipement 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. The invention may include an injection system that can be bundled with software and/or hardware that can be 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. Consequently, the efficiency of the test and final quality of the images can be improved.; Additionally, the combined control console will aid in the overall process of caring out the imaging tests.

Last updated: 13.03.2013 Worldwide Database 5.6.6.6; 93p

[19] 中华人民共和国国家知识产权局

[51] Int. Cl.
A61B 6/00 (2006.01)

[12] 发明专利申请公布说明书

[21] 申请号 200580010953.5

[43] 公开日 2007 年 5 月 23 日

[11] 公开号 CN 1968653A

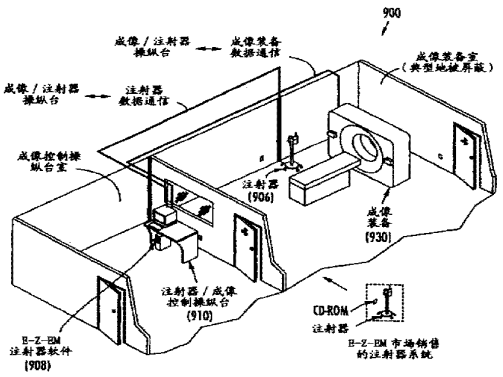
[22] 申请日 2005.1.25
[21] 申请号 200580010953.5
[30] 优先权
[32] 2004. 2.11 [33] US [31] 60/543,601
[86] 国际申请 PCT/US2005/002282 2005.1.25
[87] 国际公布 WO2005/076810 英 2005.8.25
[85] 进入国家阶段日期 2006.10.11
[71] 申请人 E-Z-EM 有限公司
地址 美国纽约
[72] 发明人 罗伯特·威廉斯
[74] 专利代理机构 北京三友知识产权代理有限公司
代理人 李 辉
权利要求书 9 页 说明书 22 页 附图 19 页

[54] 发明名称

用于操作医疗注射器和诊断成像装置的方法系统和设备

[57] 摘要

本发明涉及用于操作医疗注射器和诊断成像装置的方法系统和设备，总体上致力于但不限于允许操作员从公共控制操纵台控制注射装置和成像装置的方法系统和设备。所述注射装置可以被用于向病人施用造影剂，使得成像装置可以获取该病人的内部影像。本发明可以包括注射系统，该注射系统可封包有软件和/或硬件，该软件和/或硬件可用于将现有成像控制操纵台修改成可用于操作注射装置和成像装置两者。在一个实施例中，所述公共控制操纵台可以访问存储的协议，该存储的协议可以包括用于注射装置、成像装置、或这两者的操作参数。因此，可改进检验的效率和影像的最终质量。另外，组合的控制操纵台有助于执行成像检验的整个过程。



1、一种用于将造影剂注入人体并对所述造影剂成像的系统，所述系统包括：

a）注射器装置；

b）成像装置；以及

c）公共控制操纵台，所述公共控制操纵台可操作地连接到所述注射器装置和所述成像装置，所述公共控制操纵台包括显示单元和输入装置，由此，该公共控制操纵台可用于控制所述注射器装置和所述成像装置，并且从所述注射器装置和所述成像装置接收数据。

2、根据权利要求 1 所述的系统，其中，所述公共控制操纵台包括存储介质，所述存储介质用于记录来自所述注射器装置和所述成像装置的数据。

3、根据权利要求 1 所述的系统，其中，所述显示单元是计算机监视器、LCD 显示器、等离子显示器、或者电视监视器。

4、根据权利要求 1 所述的系统，其中，所述公共控制操纵台包括能够同时在单个显示单元上进行显示的注射器装置控制接口和成像装置控制接口。

5、根据权利要求 3 所述的系统，其中，所述注射器装置控制接口显示在所述显示单元上的第一区中，而所述成像装置控制单元显示在所述显示单元上的第二区中。

6、根据权利要求 4 所述的系统，其中，所述公共控制操纵台包括注射器装置应用和单独的成像装置应用，其中，所述注射器装置应用和所述成像装置应用可同时运行。

7、根据权利要求 6 所述的系统，其中，所述注射器装置应用可与所述成像装置应用共享数据和文件。

8、根据权利要求 6 所述的系统，其中，所述成像装置应用可与所述注射器装置应用共享数据和文件。

9、根据权利要求 1 所述的系统，其中，所述公共控制操纵台是计算

机系统。

10、根据权利要求 9 所述的系统，其中，所述计算机系统包括能够操作所述注射器装置和所述成像装置的操作系统。

11、根据权利要求 10 所述的系统，其中，所述操作系统是 Linux、Windows、Mac OS、或者 Unix。

12、根据权利要求 1 所述的系统，其中，所述注射器装置、所述成像装置、以及所述公共控制操纵台通过网络可操作地连接。

13、根据权利要求 12 所述的系统，其中，所述网络是有线网络或无线网络。

14、根据权利要求 1 所述的系统，其中，所述公共控制操纵台包括能够操作所述注射装置和所述成像装置的公共软件应用。

15、根据权利要求 14 所述的系统，其中，所述公共软件应用包括存储的注射装置操作参数和成像装置操作参数。

16、根据权利要求 15 所述的系统，其中，所述注射装置操作参数包括从如下组中选择的操作参数，所述组包括流速、介质、体积、压力、相位、保持静脉通畅、暂停、保持、延迟、开始、以及停止的操作参数。

17、根据权利要求 15 所述的系统，其中，所述成像装置操作参数包括从如下组中选择的操作参数，所述组包括管电流、管电压、准直、节距、检测器配置、转动、暂停、扫描延迟、开始、以及停止的操作参数。

18、根据权利要求 15 所述的系统，其中，所述公共软件应用包括具有可在所述公共控制操纵台上创建、存储、以及调用的多个注射装置协议的数据库，所述注射装置协议包括用于操作所述注射装置的操作参数。

19、根据权利要求 15 所述的系统，其中，所述公共软件应用包括具有可在所述公共控制操纵台上创建、存储、以及调用的多个成像装置协议的数据库，所述成像装置协议包括用于操作所述成像装置的操作参数。

20、根据权利要求 15 所述的系统，其中，所述公共软件应用包括具有可在所述公共控制操纵台上创建、存储、以及调用的多个组合协议的数据库，所述组合协议包括用于操作所述注射装置和所述成像装置的操作参数。

21、一种用于获取主体的多幅内部影像的系统，所述系统包括：

a）注射器装置，其用于将造影剂注入所述主体内；

b）成像装置，其用于获取所述主体的内部影像；

c）处理单元，其可操作地连接到所述注射器装置，用于向所述注射器装置发送数据并从所述注射器装置接收数据；以及

d）公共控制操纵台，其可操作地连接到所述处理单元和所述成像装置，所述公共控制操纵台能够向所述处理单元和所述成像装置发送数据并从所述处理单元和所述成像装置接收数据。

22、根据权利要求 21 所述的系统，其中，所述公共控制操纵台包括显示单元。

23、根据权利要求 22 所述的系统，其中，所述处理单元被设置在所述注射装置中。

24、根据权利要求 21 所述的系统，其中，所述处理单元包括操作系统。

25、根据权利要求 24 所述的系统，其中，所述处理单元还包括在所述操作系统上运行的远程软件。

26、根据权利要求 25 所述的系统，其中，所述远程软件被用于控制所述注射装置，所述远程软件包括：PPREMOTE 软件模块、显示图形软件模块、ODBC 数据库软件模块、PPCOMM 软件模块、PPRESET 软件模块、以及 GINA.DLL 软件模块。

27、根据权利要求 21 所述的系统，其中，公共控制操纵台经由所述处理单元向所述注射器装置发送数据和指令。

28、根据权利要求 27 所述的系统，其中，所述处理单元通过网络连接可操作地连接到所述公共控制操纵台。

29、根据权利要求 28 所述的系统，其中，所述网络连接是有线网络连接或无线网络连接。

30、根据权利要求 29 所述的系统，其中，所述控制操纵台通过因特网连接或 web 浏览器从所述处理单元发送并接收数据。

31、根据权利要求 26 所述的系统，其中，所述远程软件包括多个存

储的协议，所述协议包括用于操作所述注射装置的操作参数。

32、根据权利要求 21 所述的系统，其中，所述公共控制操纵台可以同时控制所述注射装置和所述成像装置。

33、根据权利要求 21 所述的系统，其中，所述控制操纵台包括用于操作所述成像装置的多个存储的协议，并且所述处理单元包括用于操作所述注射装置的多个存储的注射器协议，所述公共控制操纵台能够选择性地检索并运行所述成像协议和所述注射协议，由此，所述公共控制操纵台能够同时操作所述注射装置和所述成像装置。

34、根据权利要求 26 所述的系统，其中，所述 PPREMOTE 软件模块包括具有用于对注射器数据变量进行存储、管理以及数学运算的程序例程的可执行程序。

35、根据权利要求 34 所述的系统，其中，所述 PPREMOTE 软件还包括用于对所述 ODBC 数据文件进行读取和写入的程序例程。

36、一种用于将现有成像控制操纵台修改成公共控制操纵台的设备，由此，该公共控制操纵台能够操作注射器装置和成像装置，所述设备包括：

注射器装置；和

远程软件应用，其用于操作所述注射器装置，其中，所述远程软件能够在成像控制操纵台上运行，由此，所述公共控制操纵台可以远程地操作所述注射器装置。

37、根据权利要求 36 所述的设备，其中，所述远程软件能够在 Windows、Unix、Mac OS、或者 Linux 环境下运行。

38、根据权利要求 36 所述的设备，其中，所述远程软件包括用于操作所述注射器装置的模块。

39、根据权利要求 38 所述的设备，其中，所述用于操作所述注射器装置的模块包括：PPREMOTE 软件模块、显示图形软件模块、ODBC 数据库软件模块、PPCOMM 软件模块、PPRESET 软件模块，以及 GINA.DLL 软件模块。

40、根据权利要求 36 所述的设备，其中，所述远程软件被存储在介

质存储装置上。

41、根据权利要求 40 所述的设备，其中，所述介质存储装置与所述注射器装置一起分布，并且所述设备的特征在于没有单独的注射器控制装置。

42、一种用于操作注射装置和成像装置的设备，该设备包括：

a）注射装置控制接口；

b）成像装置控制接口；以及

c）显示单元，其被配置成显示所述注射装置控制接口和所述成像装置控制接口。

43、根据权利要求 42 所述的设备，其中，所述注射装置控制接口和所述成像装置控制接口同时显示在所述显示单元上。

44、根据权利要求 42 所述的设备，其中，所述显示单元包括：

第一显示区，其被配置成显示所述注射装置控制接口；和

第二显示区，其被配置成显示所述成像装置控制接口。

45、根据权利要求 42 所述的设备，该设备进一步包括：

从所述显示单元到成像装置的第一通信连接部；和

从所述显示单元到注射装置的第二通信连接部。

46、根据权利要求 45 所述的设备，其中，所述第一通信连接部包括：

所述第二通信连接部；和

从所述注射装置到所述成像装置的第三通信连接部。

47、根据权利要求 45 所述的设备，其中，所述第二通信连接部包括：

所述第一通信连接部；和

从所述成像装置到所述注射装置的第三通信连接部。

48、根据权利要求 45 所述的设备，其中，所述第一通信连接部经由网络建立。

49、根据权利要求 48 所述的设备，其中，所述网络的一个链路是无线链路。

50、根据权利要求 45 所述的设备，其中，所述第二通信连接部经由网络建立。

51、根据权利要求 50 所述的设备，其中，所述网络的一个链路是有线链路、无线链路、或有线链路与无线链路的组合。

52、一种适于可操作地连接到成像装置显示器的注射器控制装置，所述注射器控制装置包括：

处理单元，其包括能够操作注射器装置的可执行程序模块；和

多个输入部和多个输出部，其用于向注射器装置发送数据并从注射器装置接收数据，并且用于向成像装置显示器发送数据并从成像装置显示器接收数据。

53、根据权利要求 52 所述的注射器控制装置，其中，在所述注射器控制装置与所述成像装置显示器之间的连接是有线连接、无线连接、或有线连接与无线连接的组合。

54、根据权利要求 52 所述的注射器控制装置，其中，所述成像装置显示器包括公共控制操纵台，该公共控制操纵台被配置成经由所述注射器控制装置远程地操作注射器装置。

55、根据权利要求 52 所述的注射器控制装置，其中，所述可执行程序模块包括从以下组中选择的操作参数，所述组包括流速、介质、体积、压力、相位、保持静脉通畅、暂停、保持、延迟、开始、以及停止的操作参数。

56、根据权利要求 52 所述的注射器控制装置，其中，所述成像装置显示器通过网络连接可操作地连接到所述注射器控制装置。

57、根据权利要求 56 所述的注射器控制装置，其中，所述网络连接包括通过 web 浏览器发送并接收数据。

58、一种用于操作医疗装备的方法，该方法包括以下步骤：

a）与注射装置控制接口交互；

b）与成像装置控制接口交互；以及

c）在公共显示单元上显示所述注射装置控制接口和所述成像装置控制接口。

59、根据权利要求 58 所述的方法，其中，在所述显示单元上同时显示所述注射装置控制接口和所述成像装置控制接口。

60、根据权利要求59所述的方法，其中，所述显示步骤包括以下步骤：

a）在第一显示区中显示所述注射装置控制接口；和

b）在第二显示区中显示所述成像装置控制接口。

61、根据权利要求58所述的方法，该方法进一步包括以下步骤：

a）建立从所述显示单元到成像装置的通信；和

b）建立从所述显示单元到注射装置的通信。

62、根据权利要求61所述的方法，其中，所述建立从所述显示单元到所述成像装置的通信的步骤包括以下步骤：

a）从所述显示单元向所述注射装置发送数据；和

b）从所述注射装置向所述成像装置中继传输所述数据。

63、根据权利要求61所述的方法，其中，所述建立从所述显示单元到所述注射装置的通信的步骤包括以下步骤：

a）从所述显示单元向所述成像装置发送数据；和

b）从所述成像装置向所述注射装置中继传输数据。

64、根据权利要求61所述的方法，其中，所述建立从所述显示单元到所述成像装置的通信的步骤包括以下步骤：

经由网络从所述显示单元向所述成像装置发送数据。

65、根据权利要求64所述的方法，其中，所述网络是有线网络、无线网络、或有线网络与无线网络的组合。

66、根据权利要求61所述的方法，其中，所述建立从所述显示单元到所述注射装置的通信的步骤包括以下步骤：

经由网络从所述显示单元向所述注射装置发送数据。

67、根据权利要求66所述的方法，其中，所述网络的一个链路是无线链路、有线链路、或无线链路与有线链路的组合。

68、一种从公共控制操纵台操作注射器装置和成像装置的方法，该方法包括以下步骤：

a）在显示单元上显示注射器装置控制接口；

b）在所述显示单元上显示成像装置控制接口；

c）从所述公共控制操纵台向所述注射器装置发送操作指令，并且任选地，接收从所述注射器装置到公共控制操纵台的数据；

d）从所述公共控制操纵台向所述成像装置发送操作指令；

e）利用所述注射器装置将造影剂注入主体内；

f）利用所述成像装置扫描所述主体；

g）获取所述主体的多个内部影像；以及

h）从所述成像装置向所述公共控制操纵台发送所述影像。

69、根据权利要求 68 所述的方法，其中，所述显示单元包括用于所述注射器装置控制接口的第一显示区，和用于所述成像装置控制接口的第二显示区。

70、根据权利要求 68 所述的方法，其中，所述注射器装置和所述成像装置共享公共接口。

71、根据权利要求 68 所述的方法，其中，所述公共控制操纵台包括用于存储操作所述注射器装置和所述成像装置的操作参数的数据库。

72、根据权利要求 71 所述的方法，其中，所述数据库包括能够通过所述公共控制操纵台检索的多个协议，所述多个协议包括预先存储的用于操作所述注射器装置、所述成像装置的操作参数，或者包括用于同时操作所述注射器装置和所述成像装置的组合协议。

73、根据权利要求 72 所述的方法，其中，所述向所述注射器装置或所述成像装置发送指令的步骤还包括以下步骤：

从所述数据库中选择并检索协议；

将所述协议加载到所述公共控制操纵台上；以及

开始所述协议，由此，所述协议向所述注射器装置、所述成像装置、或者所述注射器装置和所述成像装置两者发送指令。

74、根据权利要求 68 所述的方法，其中，所述注射器装置控制接口和所述成像装置控制接口同时运行在所述公共控制操纵台上。

75、根据权利要求 68 所述的方法，其中，所述公共控制操纵台通过网络连接与所述注射器装置和所述成像装置之间发送并接收数据。

76、根据权利要求 75 所述的方法，其中，所述网络连接是有线网络

连接或无线网络连接。

77、根据权利要求 68 所述的方法，该方法进一步包括在所述显示单元上显示所述影像的步骤。

用于操作医疗注射器和诊断成像装置的方法系统和设备

技术领域

本发明总体上涉及医疗成像领域，更具体地，涉及用于操作医疗注射器和诊断成像装置的方法和设备。

背景技术

成像装备可与将造影剂引入待检查的主体内的注射装置一起使用。然而，因为成像装备和注射装置是分立的系统，所以各自可具有其自己的接口显示装置。因此，在控制室中，技术员在试图通过分立的接口显示装置同时操作两个系统时可能遇到困难。根据对注射系统的概括评述，可更好地理解所述问题。

例如，与成像装备（例如，CT、MRI、超声波、荧光透视等）一起使用的用于施用造影剂的注射系统，通常具有在机电注射器附近的注射器装置控制接口。在某些情况下，该注射器装置控制接口与一件成像装备相邻。另外，注射系统可以具有远程定位装置控制接口。例如，该注射器装置控制接口可以设置在用于所述诊断放射和/或成像装备的相应成像控制室内。基于成像组（imaging suit）的程序方面或设计功能，多个用户接口可能是必需或有利的。例如，接口可位于病人侧和无电离辐射或其它诊断能量的控制室内。

在这点上，图 1 例示了与成像系统一起使用的现有技术的注射系统。注射器装置 100 通过数据通信线路 120 耦合到注射器装置控制接口 110，并且成像装备 130 通过数据通信线路 150 耦合到成像装置控制接口 140。有线成像组远程控制信号包括数字信号、模拟信号、TTL（晶体管-晶体管逻辑）信号以及/或这些信号类型的混合。

与成像装备在同一房间的针对注射器和/或成像装备的用户接口控制的应用是主要的，但不总是限于在将病人暴露于成像装备的能量之前或

其早期设置的与病人相关联的特征。对于其中病人已被安排好并且位于成像装备室中的诊断成像过程部分，临床医生通过两个不同的接口（即，注射器装置控制接口 110 和成像装置控制接口 140）远程地编程、开始、监视、控制以及终止成像过程。因此，在成像控制室中的临床医生需要同时并且有时要根据临床情况困难地监视用于成像控制单元和注射器控制单元的两个用户接口。

对于不同成像过程，存在这样一种需要，即，将注射的定时与成像能量的暴露定时同步。例如，在 CT 扫描期间，最初，可利用注射器以特定流速（例如，大约 3 cc/sec）对病人静脉施用规定剂量的碘化造影剂（例如，大约 100 cc）。在注射之后的一定最优时段（例如，在大约 10 到 45 秒的范围内）将该病人暴露于成像装备的能量。该最优时段何时出现取决于通过运行注射器施用给病人的造影剂的流体动力特性、病人的具体生理机能，以及要成像的关注组织区域。

当工作在成像组中的临床医生试图实现注射与成像暴露之间的同步时，具有用于注射器和成像装备的两个用户接口给他们带来了负担。为了解决该负担，一些成像装备制造者已经在他们的装备上设置了连接端口，以使注射器装置能够连接到成像装置。这些连接端口典型地提供 TTL 连接，由此实现有限的注射器和成像装备功能。然而，这种连接的功能性仅限于对注射的相应开始与扫描仪的随后开始进行同步。

在这点上，图 2 例示了连接到成像装置的注射装置。注射器装置 200 通过数据通信线路 220 耦合到注射器装置控制接口 210，并且成像装备 230 通过数据通信线路 250 耦合到成像装置控制接口 240。此外，注射器装置 200 还通过信号或数据通信线路 260 耦合到成像装备 230，但是，典型地，数据仅经由信号或数据通信线路 260 单向发送，并且仅用于注射器装置 200 和成像装置 230 的相应开始时间的同步。

由此，存在对一种系统的需求，通过该系统可以从单个接口或显示同时控制注射装置和成像装备的操作参数。

发明内容

在一个可选实施例中，本发明致力于一种从公共控制操纵台控制注射器装置和成像装备的系统和方法。该公共控制操纵台可包括多个接口或单个接口，由此，操作员可以同时控制注射和扫描参数。因此，该系统允许操作员更有效地控制并管理注射和扫描装置及过程。

公共控制操纵台可包括计算机或处理装置，所述计算机或处理装置可操作地与注射装置和成像装置相连接并且相通信。公共控制操纵台可与注射器装置和成像装备/装置之间发送并接收数据。公共控制操纵台可具有显示器或监视器，该显示器或监视器用于查看操作命令并且将操作命令输入至注射器装置和成像装备。公共控制操纵台可采用宽泛的各种不同方式（包括但不限于有线或无线方式）与注射装置通信。注射装置和成像装备可以是网络的一部分，由此，在控制操纵台与注射装置和成像装备之间共享数据。另选地，注射装置或成像装备可以用作彼此与公共控制操纵台之间的中介部（intermediary）。

注射器装置和成像装备可以单独具有处理能力，或者另选地，可由公共处理器控制。在本发明的一个另选实施例中，注射器装置包括数字介质，该数字介质包括可加载到现有成像控制操纵台上以便可远程控制注射装置的软件应用。在本实施例中，所述软件可以允许成像控制操纵台用作同时控制注射器装置和成像装备的公共控制器。所述软件可包括可用于控制并最优化注射器装置的广泛的各种模块。

公共控制操纵台可包括计算机，该计算机在可支持图形用户接口的操作系统下运行。操作系统可包括 Windows、Linux 等及其任意组合。图形用户接口可允许操作员同时管理并运行多个程序。例如，在本发明的一个实施例中，公共控制操纵台可具有同时显示的用于注射装置的接口和用于成像装备的接口。因此，操作员可以同时操作并控制注射装置和成像装备。另外，公共控制操纵台可以存储并检索可以用于操作装置和成像装备的协议。这种协议可包括为进行特定检验（例如，诸如 CT 扫描）而组合在一起的操作参数。可创建包括既用于注射装置也用于成像装备的操作指令的组合协议。所述协议可帮助改进检验的效率和质量。用于注射器的操作参数包括但不限于流速、介质、体积、压力、相位、保持

静脉通畅（KVO）、暂停、保持、延迟、开始，以及停止。用于成像装置的操作参数包括但不限于管电流、管电压、准直、节距、检测器设置、转动、暂停、扫描延迟、开始，以及停止。

在一个另选实施例中，本发明可包括同时控制注射器装置和成像装备的系统和方法。本发明还可提供在公共显示器上监视并控制装备的系统。另外，本发明可提供创建可用于操作注射装置和成像装备的存储协议的系统。在附图和详细描述中阐述了本发明的其它特征。

附图说明

已经概括地描述了本发明，现在对附图进行说明，所述附图不一定是按照比例绘制的，并且其中：

图 1 是在成像组内与成像系统一起使用的现有技术注射系统的例示图；

图 2 是在成像组内连接到成像装置的现有技术注射装置的例示图；

图 3 是示出根据本发明在成像组内共享成像/注射器控制操纵台的成像装置和注射器装置的例示图的对本发明一个另选实施例的非限制性描述；

图 4 是根据本发明至少一个另选实施例的，其中注射器和成像装置由公共控制器控制的系统的非限制性框图；

图 5 是根据本发明至少一个另选实施例的，其中注射器或者成像装备用作中介部的两种系统设计的非限制性框图；

图 6 是根据本发明至少一个另选实施例的，其中注射器和成像装备控制器、注射器、以及成像装备利用网络通信的系统的非限制性框图；

图 7 是根据本发明至少一个另选实施例的，其中各包括至少一个注射器和成像装备的多个成像组被连网在一起的系统的非限制性框图；

图 8 是根据本发明至少一个另选实施例的控制系统架构的非限制性框图；

图 9 是用于根据本发明至少一个另选实施例的包括注射器系统和软件的成像组的市场销售的注射器系统的非限制性例示图；

图 10 是根据本发明至少一个另选实施例的，具有其中存储介质上提供有控制软件的，用于注射器和成像装备的成像组控制的单个计算装置的系统的非限制性框图；

图 11 是根据本发明至少一个另选实施例的，利用网络设备的注射系统的非限制性框图；

图 12 是根据本发明至少一个另选实施例的，如何配置网络设备的示例的非限制性例示图；

图 12A 是根据本发明至少一个另选实施例的，如何将注射器和成像装备视为网络设备的示例的非限制性示意图；

图 13 是根据本发明至少一个另选实施例的，注射器/成像装备操纵台同时显示用于注射器的一专用显示区和用于成像装备的另一专用显示区的非限制性示意图；

图 14 是根据本发明至少一个另选实施例的系统的非限制性框图，其中，注射器控制应用和成像装备控制应用同时运行在一个计算机平台上，该计算机平台具有充足的处理资源、操作系统性能连接端口以及可选专用控制单元，该可选专用控制单元处理仅用于成像装备、仅用于注射器或者用于注射器和成像装备两者的指定控制功能；

图 15 是根据本发明至少一个另选实施例的接口设置的非限制性框图；

图 16 是根据本发明至少一个另选实施例的，其中用户接口应用程序包括注射器属性和成像装备属性的软件架构设置的非限制性框图；

图 17 是根据本发明至少一个另选实施例的，其中单个显示窗口包括注射器和相关联的成像装备两者的用户接口功能的公共注射器/成像装备操纵台的显示区的非限制性例示图；

图 18 是根据本发明至少一个另选实施例的，利用 web 浏览器的注射器系统的非限制性例示图；

图 19 是根据本发明至少一个另选实施例的单个用户接口上的整理存储过程的非限制性图，在该整理存储过程中存在用于注射器和成像装备的单独显示处理；以及

图 20 是根据本发明至少一个另选实施例的，把一个显示处理用于注射器和成像装备两者的单个用户接口上的整理存储过程，和该接口上的包括注射器操作参数和成像装备操作参数的存储过程的非限制性图。

具体实施方式

下面，参照附图对本发明进行描述。可以多种不同形式具体实现本发明，并且在此不应将附图和描述解释为限于在此阐述的实施例。贯穿全文相同标记都指示相同部件。当在此使用时，术语“示例性”指本发明的非限制性另选实施例。

在一个另选实施例中，本发明致力于一种从单个接口或显示部操作医疗注射器和诊断成像装置的方法和系统。所述注射/成像系统可包括注射器系统和成像系统，所述注射系统和成像系统与公共成像控制操纵台或公共接口装置通信并且可操作地受该公共成像控制操纵台或公共接口装置控制。

注射器系统可包括注射器装置和控制接口，该注射器装置可用于施用有效剂量的造影剂，而该控制接口可操作地连接到该注射器装置。该注射器系统可具有一个或更多个控制接口。该控制接口可与注射器装置之间发送并且接收数据。该注射器装置可以是用于将造影剂传递到病人体内或主体内的任何类型的注射器机构（例如，E-Z-EM EMPOWER CT 注射器）。成像系统可包括成像控制操纵台、成像装置或装备，所述成像装置或装备可以用于监视并显示病人体内或主体内的造影剂，获取病人或主体的内部影像，并且将其它诊断数据提供到控制操纵台或存储介质。该成像系统可具有可操作地连接到成像装备的成像接口。

术语“造影剂”包括任何合适的介质，其可被注入到人体或主体内，用于加亮和/或标识人体的选定区域。造影剂可包括但不限于盐介质、冲洗介质等及其任意组合。造影剂可与用于执行诸如 CT 扫描、MRI、超声波等的医疗诊断成像的成像装置一起使用。

参照图 3，示出了描述医学成像组的本发明的另选实施例。如图 3 所示，成像组 300 可包括公共控制操纵台室 304 和成像装备室 302。成像装

备室可包括成像装备装置 330 和注射器装置 306。成像装备装置 330 和注射器装置 306 可与公共控制操纵台 310 通信，并且可操作地受公共控制操纵台 310 控制。公共控制操纵台可以按广泛的各种方式与装置 306、330 通信。如图 3 所示，装置 306、330 可经由通信信道 320、340 分别与控制操纵台通信。在成像装备产生磁场的实施例中，可将装置与控制操纵台和任何附加装置之间的通信信道调整为与本发明的磁场基本上无反应。这种基本上无反应的通信信道包括例如光纤线路、诸如红外线的电磁发送器/接收器等及其任意组合。另外，在成像装备产生磁场的实施例中，成像装备室中的诸如注射器的装置可包括诸如黄铜的材料，该材料基本与磁场无反应。在其它实施例中，成像装备室中的装置可以在室内以基本上不干扰成像装备的方式来取向。

可使用公共控制操纵台从成像控制操纵台室远程地控制注射器装置和成像装置两者。公共控制操纵台可以是已经修改成也可远程操作注射器装置的成像控制操纵台。经修改的控制操纵台可同时控制注射装置和成像装备两者。可通过增加软件和/或硬件来修改成像控制装置。公共控制操纵台可与注射器装置之间发送并接收数据。在此限定的术语“远程”、“远程控制”，以及“远程地”定位，包括彼此没有物理接触的、彼此没有可操作地接合的，以及/或不同位于同一房间中但仍然可通过许多不同的通信技术电子地、机械地以及/或电子机械地进行通信的组件，上述通信技术包括但不限于诸如 Bluetooth®的无线连接装置，即，可将各种控制组件与注射器装置、成像装置、或者可位于医学成像组内部或外部的其它医学装置相连接的计算机网络。

注射器装置和成像装置还可以共享单个处理系统，或者另选地，注射器和成像装置两者可具有独立的处理系统。在本发明一个另选实施例中，如果两个装置具有一个处理系统，则可使用单个系统来控制两个装置。例如，单个系统可具有允许通过其它计算系统远程控制其的软件平台。在该实施例中，例如，操作员可从单个用户接口远程建立并监视注射和成像过程。在一个另选实施例中，该系统可以是专有系统计算架构或者使用市场上可买到的计算平台（例如，运行 Windows 或类似操作系

统的 PC 架构）的开放系统计算架构。在本发明的背景下，开放系统计算架构在其涉及任何注射器或成像装备或任何其它装置（医疗或其它）的控制时，可包括非特定硬件和没有并入预定功能的操作软件。开放系统可包括处理单元和输入-输出装置，诸如例如显示器、键盘，以及诸如鼠标器的定点装置。操作系统可包括现有开放系统计算架构。在另一另选实施例中，操作系统软件可提供限于执行计算平台自身的的基本功能的普通的易于解释的接口，和非专用于任何应用的内部电路的低级软件例程建立功能，如本发明的各个实施例中存在的功能。本发明还可致力于一种在公共显示器上操作注射器和成像装备系统的专用应用。

在一个实施例中，单个计算系统可用于运行多个处理，包括用于成像装备的第一处理，和用于注射器装置的第二处理。本系统可用于通过单个接口同时控制成像装备和注射器装置两者。在这点上，图 4 是例示可以通过公共接口 400 控制注射器装置 410 和成像装置 430 两者的框图。

公共控制操纵台可包括用于提供对成像装备和注射器的装置功能进行操作员控制的操作员接口。操作员接口可包括显示诸如操作控制、装置状态、所获影像等及其任意组合的注射器装置数据和成像装备数据的显示单元。典型地，该显示单元可包括可用于以操作员可读取的格式输出并显示数据、影像、程序等及其任意组合的任何类型的装置。这种装置可包括但不限于计算机和电视监视器、LCD 显示器、等离子显示器、视频显示器等。该显示装置还可包括诸如触摸屏的输入装置。显示单元可以用于观察影像并控制可用于同时操作多个装置的功能。

在另一另选实施例中，公共控制操纵台可包括市场上可买到的诸如 pc 的计算系统。诸如 PDA（个人数字助理）的其它计算系统和装置也可用于控制注射器和成像装置。公共控制操纵台可包括用于与注射器装置和成像装备之间发送并接收数据的多个输入部和多个输出部。这种输入部可包括但不限于键盘、触摸屏、按钮、诸如鼠标的定点控制装置、话音识别软件、专用控制器等及其任意组合。公共控制操纵台还可包括用于存储影像、统计数据、装置操作参数、数据、错误日志、个人备忘等及其任意组合的存储介质（例如，磁介质、光学介质、打印介质，或其

它)。

在另一另选实施例，控制操纵台和注射器及成像装置都可利用有线和无线通信协议可操作地彼此连接并通信。这种通信协议包括但不限于诸如 I2C、ACCESS.bus、RS-232、通用串行总线（USB）、IEE-488（GPIB）的串行通信协议，诸如 TCP/IP 的 LAN/因特网协议，诸如 802.11x 的无线协议；以及蓝牙（Bluetooth）等。通信协议还可包括专有系统。控制操纵台还可利用专用通信信道连接到装置。在这点上，图 4 例示了系统可包括可用于将公共控制操纵台连接到装置的专用通信信道 420、440。另选地，注射器和成像装备可利用不同通信协议与公共控制操纵台通信。例如，串行数据通信信道可以用于在公共控制操纵台与注射器装置之间传递数据，而 TCP/IP 网络可以用于在公共控制操纵台与成像装备之间传递数据。

在本发明另一另选实施例中，注射器装置或成像装备也可用作中介部，使得公共控制操纵台能够通过成像装备与注射器通信，或者相反通过注射器与成像装备通信。在这点上，图 5 例示了其中注射器或成像装备可用作中介部的两种另选系统设计。在系统 500 中，公共控制操纵台 505 经由通信信道 515 与成像装备 510 直接通信。成像装备 510 又经由通信信道 525 与注射器装置 520 直接通信。在系统 530 中，控制操纵台 535 与注射器装置 540 直接通信，注射器装置 540 又与成像装备 550 直接通信。注射器装置和成像装备还可各自独立具有处理能力。这样，每个装置都可以代表另一装置作为通信网络集线器或中介部来处理数据。在本发明的其它另选实施例中，注射器和成像装备都可具有可编程的架构和处理能力，以在向控制操纵台传送应用特定数据之前、期间以及之后对该应用特定数据进行处理。

在本发明的另选实施例中，成像装备、注射器装置、以及公共控制操纵台可通过网络环境可操作地彼此连接并通信。在这种环境下，典型地利用诸如网络集线器、交换机或路由器的独立连网装置互连控制操纵台和装置。在这点上，图 6 例示了其中使用连网装置以便于各个装置与控制操纵台之间的通信的系统。如图 6 所示，公共控制操纵台 606 经由

连网装置 630 与注射器装置 610 和成像装备 620 通信。在例示的实施例中，来自注射器装置和成像装备的数据可以同时显示在单个操作员接口上，并且利用公共通信协议（例如，有线或无线）将该数据传送到网络集线器。

在本发明的另一另选实施例中，用于互连装置和控制操纵台的连网系统可从广泛的各种网络形式中选择。连网形式可包括但不限于 LAN（局域网）、WAN（广域网）、CAN（校域网）、WWW（万维网）等及其组合。装置的网络拓扑还可根据设计者的偏好而改变。网络拓扑图可包括但不限于总线拓扑、环形拓扑、星形拓扑等及其组合。

参照图 7，例示了由多个成像组组成的系统。在成像组 700 中，示出了利用通信连网装置 720 与注射器装置 710 和成像装备 715 互连的公共控制操纵台 705。另选地，可以通过网络或连网装置互连多个成像组。在这点上，图 7 例示了成像组 700 可以可操作地连接到第二成像组 725。如图 7 所示，连网装置 720 与位于独立成像组 725 中的第二连网装置 755 通信。多个成像组可以被连网在一起并且经由任何数量的公共控制操纵台进行控制。在一个实施例中，控制操纵台和成像装备及注射器装置可都连接在公共子网上，该公共子网是共享公共地址部分的网络的一部分。例如，在诸如因特网的 TCP/IP 网络中，子网被限定为其 IP 地址具有相同前缀的全部装置。由此，与控制操纵台和成像/注射器装置的网络连接在同一子网上的操作员可以控制并访问装置。

图 7 还例示了公共控制操纵台可用于控制多个成像装置和/或注射器装置。在这点上，图 7 示出了具有可操作地连接到多个注射器装置 735、740 和多个成像装备装置 745、750 的公共控制操纵台 730 的成像组 725。如图 7 所示，利用诸如网络集线器、路由器或交换机的连网装置将多个装置连网到公共控制操纵台 730。控制操纵台 730 可包括允许操作员同时控制注射器装置和成像装备装置的单个接口。还应当认识到，控制操纵台 730 可以在缺少网络时用于控制多个注射器装置和成像装备装置。在这种系统中，装置可与公共控制操纵台直接通信，或者可通过用作中介部的多个装置之一间接地择路。

本发明还可提供能够执行用于操作注射器和成像装备的各种协议的各种计算机程序产品实施例。在一个另选实施例中，计算机程序产品能够从远程位置控制注射器装置。该计算机程序产品可包括用于接收来自输入装置的用户输入的可执行部分。

在一个实施例中，注射器装置可封包成包括注射器装置和远程计算机程序产品或者可与现有成像控制操纵台一起使用的硬件的封包。该远程计算机程序产品允许成像控制操纵台可操作地连接到成像装备和注射器装置。因此，在本发明的一个另选实施例中，注射器装置可与计算机程序一起分布，而不需要相关注射器控制操纵台。公共控制操纵台可包括可用于控制、显示、分析以及监视各种成像和注射装置的控制系统架构。该控制系统架构还可包括硬件和软件部件。参照在此描述的计算机程序产品，应当认识到，有广泛的各种平台和语言可用于创建执行在此概述的过程的软件。还应当认识到，选择准确平台和语言通常由构造实际系统的特定需要规定。该计算机程序产品典型地包括用于远程控制注射装置的模块和组件。

参照图 8，例示了如建立在 E-Z-EM EmpowerCT™ CT Injector 上的示例性的控制系统架构。如图所示，该控制系统架构可包括多个可执行程序模块，共同用标号 814 表示。该可执行程序模块 814 可位于公共控制操纵台上，或者位于可操作地连接到公共控制操纵台的硬件装置 810 上。在这点上，图 8 例示了可操作地连接到注射器 816 和扫描装置的具有可执行程序模块的远程控制部 810。该远程控制部还可包括多个 I/O 连接部 820，用于与包括扫描仪、成像显示装置、医院网络等及其组合的各种网络和装置通信。在本发明的一些实施例中，公共控制操纵台还可适配成能够与位于过程室（如成像室 302）（参见图 3）内的外渗检测装置（EDA）818 通信，以便能够可操作地与病人从注射器装置 816 接收介质注射的处理相配合。EDA 818 还可以经由有线和/或无线计算机网络与注射器装置 816、远程控制部 810、成像显示器、以及/或其它计算机装置通信。而且，该远程控制部 810 还可被设置成能够发送和/或接收从 EDA 818 设置的外渗数据。尽管图 8 例示了通过 RS-232C 串行通信协议可操作地

连接到注射器装置和 EDA 的远程控制，但是，应当认识到可以利用许多不同协议（包括如 I2C、ACCESS.bus、RS-232、通用串行总线（USB）、IEE-488（GPIB）的串行通信协议，如 TCP/IP 的 LAN/因特网协议，如 802.11x 的无线协议，以及蓝牙等及其任意组合）来连接装置、远程控制部，以及成像控制操纵台。

如图 8 所示，控制系统架构可包括广泛的各种可执行程序模块 814，该可执行程序模块 814 允许公共控制操纵台远程地控制诸如注射器的装置。该可执行程序模块可包括执行特定任务或实现特定数据类型的例程、程序、组件、数据结构等及其任意组合。模块可包括但不限于 PPREMOTE、显示图形、ODBC 数据库、PPCOMM、PPRESET，以及 GINA.DLL 等及其任意组合。下面对这些模块进行讨论。这些模块可以在如 Windows、Unix、Linux、MACOS 等及其任意组合的操作系统层操作。

PPREMOTE 包括可执行程序模块或能够在控制操纵台上执行和运行有关处理的基本应用软件。PPREMOTE 包括关于显示和接收用户输入（例如，键盘、鼠标器、触摸屏等）的用户接口可视组件。该可执行程序还可包括程序例程，该程序例程用于在易失性和非易失性存储器中存储、管理以及算术地操作与注射器的操作有关的数据变量。例程包括这种数据的管理功能以对 ODBC 数据库文件进行读取和写入。该模块也在注射器操作的各种接合的过程中，根据需要与 PPCOMM 模块之间传递数据并且与之共享数据。

显示图形可包括由 PPREMOTE 选择访问和使用以生成用户接口显示的可视组件库。可视组件可包括但不限于文本、触摸板按钮、帮助文件、帮助图形、图标、动画等及其任意组合。该可视组件可包括单个影像文件。

ODBC 数据库文件可以由 PPREMOTE 处理来创建和操作。ODBC 数据库文件可存储例如关于注射器诊断信息、错误状态、使用统计、EDA 性能、EDA 生物阻抗配置、用户保存的注射协议、外语消息等或其任何组合的归档数据。这种文件可以存储在诸如包括例如硬盘驱动器的磁存储装置的可读写介质上，或者存储在诸如 CD-ROM 或 DVD 驱动器的光

学存储装置上。另选地，这种文件还可存储在诸如闪速存储装置的数字介质上。

PPCOMM 包括能够在控制操纵台上执行和运行有关处理的通信软件模块。PPCOMM 可用于建立注射器装置的控制并维持与注射器的数据通信。该模块可以组织基于预定周期向注射器发送的数据序列和消息。该 PPCOMM 模块还可以基于预定周期接收并解析来自注射器的附赠（complimentary）数据序列或消息。PPCOMM 还可以具有逻辑以识别何时和是否发生了数据传输问题。基于编程到该模块中的逻辑，该模块可以具有在双向通信应当保持完好时干涉并试图改正问题的能力。另选地，该模块的编程的逻辑可以通知 PPREMOTE 应用发生了通信故障状况，由此，迫使注射器操作自动中止，直到问题可以解决为止。

PPREST 可包括能够在控制操纵台上执行和运行有关处理的软件模块。PPRESET 可以提供用于控制操纵台的故障处理和重置能力。

GINA.DLL 可包括动态链接库，该动态链接库针对运行在操作系统（诸如 Windows、Unix、Linux、MACOS 等及其任意组合）下的控制操纵台软件部件或模块提供系统功能性。

在一个另选实施例中，上述模块都可以封装并制备成可以设置在可移动数字介质（例如，CD-ROM、闪速卡等）上的软件包。该软件可以并入远程控制注射器所需的模块。在一个另选实施例中，预想软件可以与注射器一起销售，使得可升级现有成像控制操纵台，以便可以将现有成像控制操纵台可操作地与注射器装置和成像装备相连接。在这点上，图 9 例示了已设置有注射器 906 和用于利用控制操纵台 910 远程控制注射器的软件 908 的成像组 900。因此，可以从注射器/成像控制操纵台 910 监视并控制成像装备 930 和注射器装置 906。图 10 还例示了远程控制软件可以设置在存储介质上，并且可以安装在用于控制注射器装置和成像装备两者的单个计算装置中。

另选地，注射器远程软件可以结合具有网络能力的计算机或处理单元（也称为网络或 PC 模块）来使用。例如，在本发明的一个另选实施例中，处理单元可包括在注射器装置中，或者可以包含在独立封装中。在

其它现有实施例中，处理单元可以与成像控制操纵台通信并由成像控制操纵台控制。成像控制操纵台可以经由网络连接和协议与处理单元通信。在这点上，图 11 例示了通过与公共控制操纵台通信的示例性处理单元（可连网 PC 模块）将注射装置连网。在该非另选实施例中，注射器装置可与处理单元/可连网 PC 模块通信，该处理单元/可连网 PC 模块又与公共控制操纵台通信。如图 11 所示，处理单元可以通过网络连接与公共控制操纵台通信。在另一非另选实施例中，公共控制操纵台接口可利用诸如浏览器的网络应用或其它应用来控制注射器。在该实施例中，处理单元可包括远程软件，该远程软件可包括控制注射器并且与公共控制操纵台之间发送数据的模块或部件。该模块和部件都运行在如 Windows、Linux、Mac OS、Unix 等或其任意组合的操作系统上。

另选地，注射器控制部可被配置成网络客户端或服务器。在本发明的一个另选实施例中，如果注射器控制部被配置成客户端，则可直接从成像控制单元、或者经由另一服务器装置、代理，或根据本发明的其它方面提供控制注射器操作的相关操作数据。如果注射器控制部被配置成服务器，则可连网 PC 模块（参见图 12）可以从注射器向成像控制操纵台提供相关数据。因此，成像控制操纵台可用作注射器装置和成像装备的公共控制操纵台。

另外，在本发明的另一另选实施例中，注射器处理单元还可与检验设施内部网络（诸如例如本地医院网络）相连接并与其通信。在该实施例中，处理单元/可连网 PC 模块可连接到本地网络，而注射系统可以被配置成网络内的网络设备。在此配置中，注射器可通过成像组中的可用网络空间间接地与成像控制站通信。处理单元到网络的连接可以是有线网络或无线的。图 12 还例示了通过本地网络将注射系统作为网络设备进行控制。在该另选实施例中，利用网络连接的成像控制操纵台可以用作注射器装置和成像装备的公共控操纵台。

在图 12A 例示的另一实施例中，注射器装置和成像装备可作为网络设备通过网络空间共享操作参数。在该设置中，例如，公共控制操纵台可同时从注射器和成像装备中获得操作参数和控制信息。成像装备、注

射装置、以及控制操纵台共享公共网络。

在本发明的另一另选实施例中，成像装备接口和注射器接口可包括在利用多任务操作系统的计算机系统内运行的独立处理。在这点上，图13和14例示了同时显示用于注射器的专用显示区，和用于成像装备的专用显示区的公共控制操纵台。在此实施例中，该显示器可用于同时显示分别与注射器装置或者成像装备独立通信的应用。

应当认识到，本发明中可以使用各种不同的计算机平台和系统。该计算机平台可包括但不限于基于诸如例如 Windows 或 Linux 的操作系统运行图形用户接口（GUI）的 PC 或其它工作站。用户接口设计可以允许用户在注射器控制应用与成像控制应用之间自由地切换。注射器装置和成像装备两者的全部用户接口可经由单个显示器、键盘、定点装置或其它公用用户接口硬件装置来显示并管理。控制操纵台和图形接口还可包括可用于使注射器装置和成像装备执行特定命令的专用控制操纵台。对于成像装备来说，这种特定命令是已知的，并且包括频繁使用的专用按钮或键，或者与安全相关的操作功能。这种操作功能包括但不限于开始、暂停、以及停止影像装备，影像恢复，影像装备相互通信等及其任意组合。图 13 和 14 例示了也包括一个或更多个专用控制装置的公共控制操纵台。如图 13 和 14 所示，专用控制装置可包括可用于与影像装备和 GUI 接口连接的接口装置。所述系统还包括频繁使用的专用控制操纵台或关于注射系统的安全的操作功能。类似地，频繁使用或与安全相关的操作功能可以并入用于注射器装置和成像装备两者的单个专用控制部中。如图 14 所示，专用控制操纵台可包括用于注射器装置的专用控制部、用于成像装备的专用控制部，或者用于注射器装置和成像装备两者的专用控制部。

专用控制操纵台可采用广泛的各种方法与注射器装置和成像装备通信，所述各种方法包括但不限于直接连接到成像装备和注射器装置的专用通信信道、经由逻辑互连到公共成像装备/注射器操纵台的间接连接及其组合和交换。

图 13 和 14 中例示的接口设计可以是在公共控制操纵台上执行的独

立处理。该公共控制操纵台可包括计算机平台 CPU、存储器、I/O、键盘、显示器、定点装置等及其任意组合。公共控制操纵台与通过其可操作地连接注射器装置和成像装备的输入/输出装置相关联。注射器装置和成像装备可以共享公共显示接口，并且它们也可在功能上彼此独立。在本发明的一个实施例中，成像装备应用可以访问运行在公共控制操纵台上的注射器数据文件。例如，公共控操纵台可包括诸如可从 E-Z-EM 得到的 EMPOWERCT 的软件应用，所述软件应用允许成像装备用户接口访问注射器数据、统计，以及来自数据库或类似文件（诸如与注射器装置相关联的 ODBC 数据库文件）的其它相关数据。

类似地，在本发明的另一另选实施例中，如果成像装备用户接口也包括允许其对成像装备数据和统计进行创建、存取，以及归档到可比较数据库文件的软件应用，则注射器接口应用也可访问这些文件。这是一种另选方法，通过该方法独立的注射器和成像装备应用可在它们中间共享数据，以增强它们各自的显示，或者取代它们中之一。在这点上，图 15 例示了其中注射器接口应用可以访问与成像装备应用相关联的文件的公共控制操纵台。在该另选非限制实施例中，成像装备应用也可存取与注射器装置接口相关联的文件。

另选地，公共控制操纵台可包括组合的接口应用、程序、或处理，该组合的接口应用、程序、或处理包括注射器和成像装备属性并且可以用于控制并管理该两个装置。在这点上，图 16 例示了具有能够控制注射器装置和成像装备两者的组合接口应用的公共控制操纵台。如图 16 所示，公共应用程序典型地包括与注射器接口和成像装备接口相关联的模块和程序部件。这种模块可包括例如数据库文件、显示图形、库、装置驱动程序、装置专用通信驱动程序等或其任意组合。

在本发明的另一另选实施例中，用户接口包括可具体实现注射器和成像装备功能的在关键处聚合设置的单个公共用户接口。因此，在该公共控制操纵台上可以例行地自动运行需要同步或任何其它操作上的相互依赖的远程控制的注射器和成像装备的功能。在这点上，图 17 例示了根据本发明一个非限制实施例的公共注射器/成像装备操纵台的显示区，在

该显示区中，单个显示窗包括注射器和相关联的成像装备的用户接口功能。

另选地，注射器装置和/或成像装备接口可被配置成 web 或网络端口。在该另选的非限制性实施例中，在公共控制操纵台上可使用基于普通 web 浏览器或专用网络的应用，以显示注射器装置和成像装备接口。可以广泛的各种方式使用 web 浏览器。例如，可与图 11 中例示的网络模块设置一起来使用网页浏览器。另选地，成像装备、CPU、以及注射器都是可以通过网络协议互连的网络设备装置。这些连接例如可以是例如点对点、LAN、WAN、以及/或因特网。另外，这些连接可以是有线连接或无线连接。在建立连接之后，注射器用户接口显示可显示在采用支持诸如 HTML、XML、JAVA、.NET 等或其任意组合的标准的 web 浏览器的成像装备操纵台上。

图 18 例示了利用 web 浏览器的注射装置。如图所示，注射器用户接口与成像装备应用一起同时显示在 web 浏览器上。成像装备接口也可以与注射器应用一起同时显示在公共用户接口上的 web 浏览器上。另选地，在具有显示器和输入装置的公共处理装置上，注射器和成像装备接口可提供到两个 web 浏览器窗口。这种混合接口设计可适于在被提供在 web 浏览器上的注射器接口与直接在公共显示接口 CPU 上运行处理的成像装备接口之间的预编程数据传送，或者可适于在被提供在 web 浏览器上的成像装备接口与直接在公共显示接口 CPU 上运行处理的注射器接口之间的预编程数据的传送。

在本发明的一个有利形式中，系统可包括诸如 CT 注射器的注射器、成像装备，以及公共控制操纵台。在该实施例中，注射器操作参数可以存储并显示在用户接口处。可对操作参数进行处理以最优化成像和检测数据。特定的参数取决于被注射的特定介质、待成像的主体的区域等及其任意组合。介质典型地包括造影剂、盐介质等及其任意组合。这种操作参数包括但不限于针对 x 射线曝光的相位、流速、体积、压力、定时暂停、保持，以及延迟。可为了特定检验而将操纵参数分组在一起并且将其存储以便稍后调用。这种参数也可以置于各个组中。操作参数的这

些组一般最常称为协议。在本发明一个实施例中，存储的协议允许操作员快速调用可用于后续检验的最优化参数。因此，可改进检验效率和成像质量。

类似地，也可将用于成像装备的操作参数分组到协议中以便用于后续检验。对于 CT 扫描仪的情况，这种参数典型地包括但不限于 kV（施加到 x 射线管的电压）、mA（x 射线管电流）、检测器准直、节距（pitch）（工作台速度）、起重台（gantry）转速、检测器配置（检测器片数、合成尺寸数）、自动控制参数（剂量）、定时暂停、保持、以及/或延迟等及其任意组合。成像参数可以显示在用户接口上。

参照图 19，例示了可以同时显示用于注射器装置和成像装备两者的操作参数的用户接口。如图 19 所示，该用户接口可用于访问包括用于注射器装置和成像装备两者的各种协议的数据库文件。该用户接口可以用于允许操作员易于调用用于注射器和成像装备的协议。上述和图 19 中例示的操作参数包括用于 CT 注射和扫描的参数。应当明白，本发明不限于 CT 扫描和成像，并且在本发明的具体实践中还可使用用于广泛的各种其它检验的操作参数和协议。

例如，在现有 CT 或计算 x 线体层照相术（tomography）成像实践中，由于使用两个显示操纵台，所以执行例如心脏 CT 血管造影术（angiography）过程的临床医生将一方面在设置处理中访问成像操纵台，而另一方面及时地访问与成像操纵台彼此独立的注射器远程控制部。在成像操纵台上，临床医生将手动输入 CT 扫描参数或调用预存储的 CT 扫描参数。对于心脏 CT 血管造影术过程来说，在下面的表 1 中呈现了现今的 16 片多检测器行 CT 扫描仪的典型过程变量。

表 1：CT 扫描仪参数

CT 扫描仪参数	在成像操纵台处输入/存储/调用的值
管电流	150 mAs
管电压	120 Kvp
准直	16 片×0.625 mm 片厚度

节距	1.0
起重台转动	0.5 秒每转
扫描触发	制造者指定

上面列出的CT扫描仪控制参数对于各种CT扫描仪制造者平台和工业领域一般通用。然而，各制造者都可具有若干辅助或专用参数作为他们的CT扫描仪设计的一部分，所以上面列表不应视为详尽的，而且将任何其它辅助参数包括到用于输入、存储或调用这种参数的成像操纵台接口设计中是非常容易的。例如，可在用户命名的协议标识符下电子地保存并且检索上述分组的CT扫描仪参数。在此情况下，可以使用“心脏”来命名有关CT操纵台的协议。

类似地，对于独立于并且远离成像操纵台的注射器远程控制部，临床医生将手动输入CT注射参数或调用预存储的CT注射参数。针对心脏CT血管造影术过程，在下面的表2中呈现了用于现今的两相位对比注射盐冲洗介质的典型过程变量。

表2：CT注射器参数

CT注射器参数	在注射器远程控制部输入/存储/调用的值
相位1对比流速	4 ml/sec
相位1对比体积	100 ml
相位2盐介质流速	4 ml/sec
相位2盐介质体积	30 ml
压力	300 psi
扫描延迟	15 秒

上面列出的CT注射器控制参数对于各种CT注射器制造者平台和工业领域一般通用。然而，各制造者可具有若干辅助或专用参数，作为他

们的 CT 注射器设计的一部分，所以上面列表不应视为详尽的，而且将任何其它辅助参数包括到用于输入、存储或调用这种参数的注射器远程接口设计中是非常容易的。例如，可在用户命名的协议标识符下电子地保存和检索上面分组的 CT 扫描仪参数。在此情况下，可使用相同名字，即，用于命名关于 CT 操纵台的协议的“心脏”。

对于所建议的利用满足 CT 扫描仪和 CT 注射器两者需求的公共操纵台来获取心脏 CT 影像的实践，理想的是在一个唯一标识符下对用于 CT 扫描仪和 CT 注射器两者的过程变量进行调用。例如，本发明有利于在用户特定的名称下单个组合的装置协议的设计和形式。例如，用于 CT 扫描仪和 CT 注射器的公共操纵台可具有命名“心脏”的协议，该协议“心脏”具有如下的前述参数：

表 3：组合的 CT 成像和扫描协议

用于扫描和对比注射的 CT 过程参数	在同时提供 CT 扫描仪和 CT 注射器的操作台处输入/存储/调用的值
管电流	150 mAs
管电势	120 Kvp
准直	16 片×0.625 mm 片厚度
节距	1.0
起重台转动	0.5 秒每转
相位 1 对比流速	4 ml/sec
相位 1 对比体积	100 ml
相位 2 盐介质流速	4 ml/sec
相位 2 盐介质体积	30 ml
压力	300 psi
扫描触发/扫描延迟	制造者指定

在具有此能力的用于成像和注射器装置的公共操纵台的接口内的过程参数存储和调用的设计提供协议组织，从而提供益于临床医生的便利

性以及生产率。

另选地，可将用于注射装置和成像装备的操作参数合并到单个协议中。在这点上，图 20 示出了包括用于注射器装置和成像装备两者的操作参数的各种协议。如图 20 所示，可在单个显示器上显示组合的协议。操作员可以使用组合的协议来操作注射器装置和成像装备。这些组合的协议将允许操作员有效地调用已针对特定检验被最优化的用于注射器装置和成像装备的操作参数。因此，可以改进检验的效率和影像的质量。在图 20 中，仅出于示例的目的而给出 CT 扫描和注射参数，而不应视为对本发明的限制。

注射/成像系统可特别用于从病人或主体内部获得一个或更多个内部影像。为了获取多个影像，可将病人安置在注射器装置和成像装备附近的诸如床的表面上。公共控制操纵台典型地用于从存储器中选择并检索用于将造影剂注射到病人体内的所需操作参数。操作员可在接口处改变该参数，或者另选地，该参数可被包括在包含操作参数分组的存储协议中。典型地，用于图像装备的操作参数可由操作员检索或者加载到系统上。这些参数也可由操作员在接口处单个改变并控制，或者可被分组到可从存储器或另一装置检索的存储协议中。用于成像装备和注射装置的协议被同步，使得注射/成像系统协调且同时地运行，从而有效地执行检验。另选地，可以创建并且从存储器检索包括用于注射器装置和成像装备的操作指令的组合协议。

当病人准备好时，可使用公共控制操纵台向注射装置和成像装置传送指令。注射装置可根据其从公共控制操纵台接收到的指令将有效量的造影剂注射到病人体内。成像装备可以扫描病人以获取内部影像。在扫描期间，成像装备可将扫描影像数据传送到可对该数据进行存储、分析、打印等的公共控制操纵台。如果希望，则操作员典型地可以采用广泛的各种方式来控制扫描仪以获得所希望的影像。

本发明所属领域的技术人员容易想到具有在前文说明和相关附图中呈现的教导的益处的，在此阐述的本发明的其它修改例和其它实施例。因此，应当明白，本发明不限于公开的特定实施例，而是旨在将修改例

和其他实施例包括在所附权利要求中。尽管在此采用了特定的术语，但是它们仅用于一般和描述的意义，而不是用于限制的目的。

此外，在整个说明书中，在构成被描述为具有、包括、或包含特定组件，或者处理或方法被描述为具有、包括、或包含特定步骤的情况下，认为本发明的构成也基本上由所述组件组成或者由所述组件组成，而且认为本发明的处理和方法也基本上由所述步骤组成或者由所述步骤组成。此外，应当理解，步骤的顺序和执行特定动作的顺序并不重要，只要本发明保持可操作性即可。此外，关于在此公开的本发明，可以同时进行两个或更多个步骤或动作。

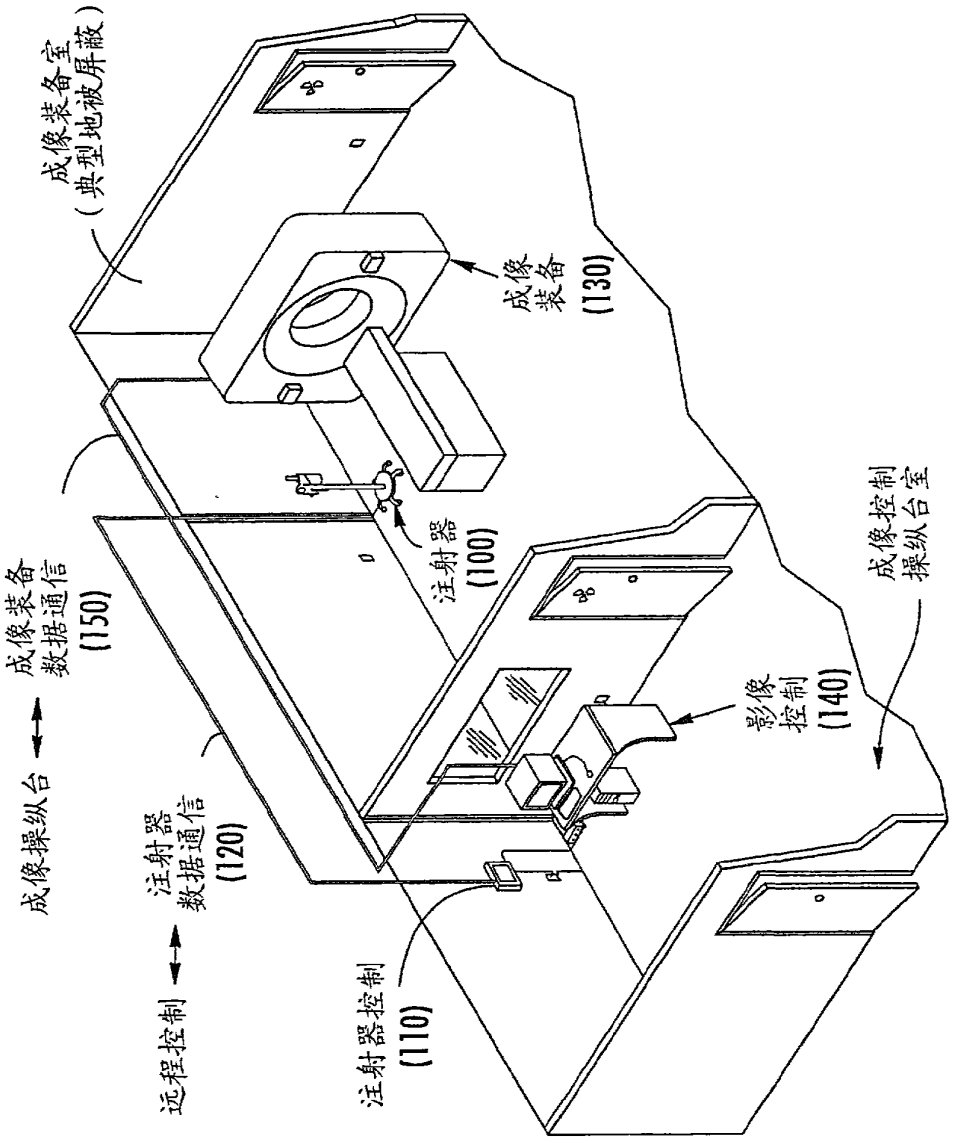

成像装备室
（典型地被屏蔽）
成像装备
(130)
注射器
(100)
成像装备
数据通信
(150)
成像操纵台
注射器
数据通信
(120)
远程控制
注射器控制
(110)
影像
控制
(140)
成像控制
操纵台室

图 1

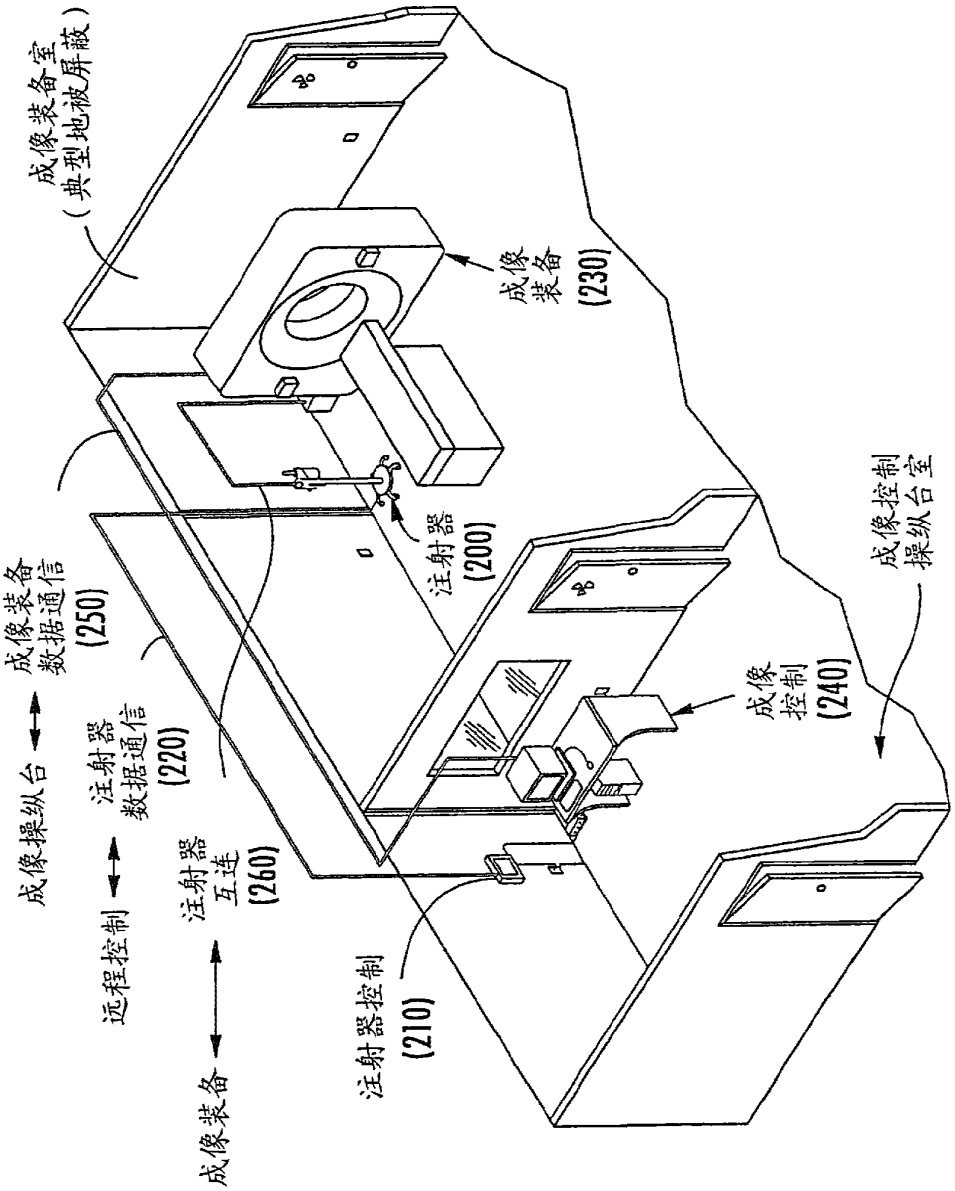

成像装备室
（典型地被屏蔽）
成像装备
(230)
注射器
(200)
成像控制
(240)
成像控制
操纵台室
注射器控制
(210)
成像操纵台
远程控制
成像装备
成像装备
数据通信
(250)
注射器
数据通信
(220)
注射器
互连
(260)

图 2

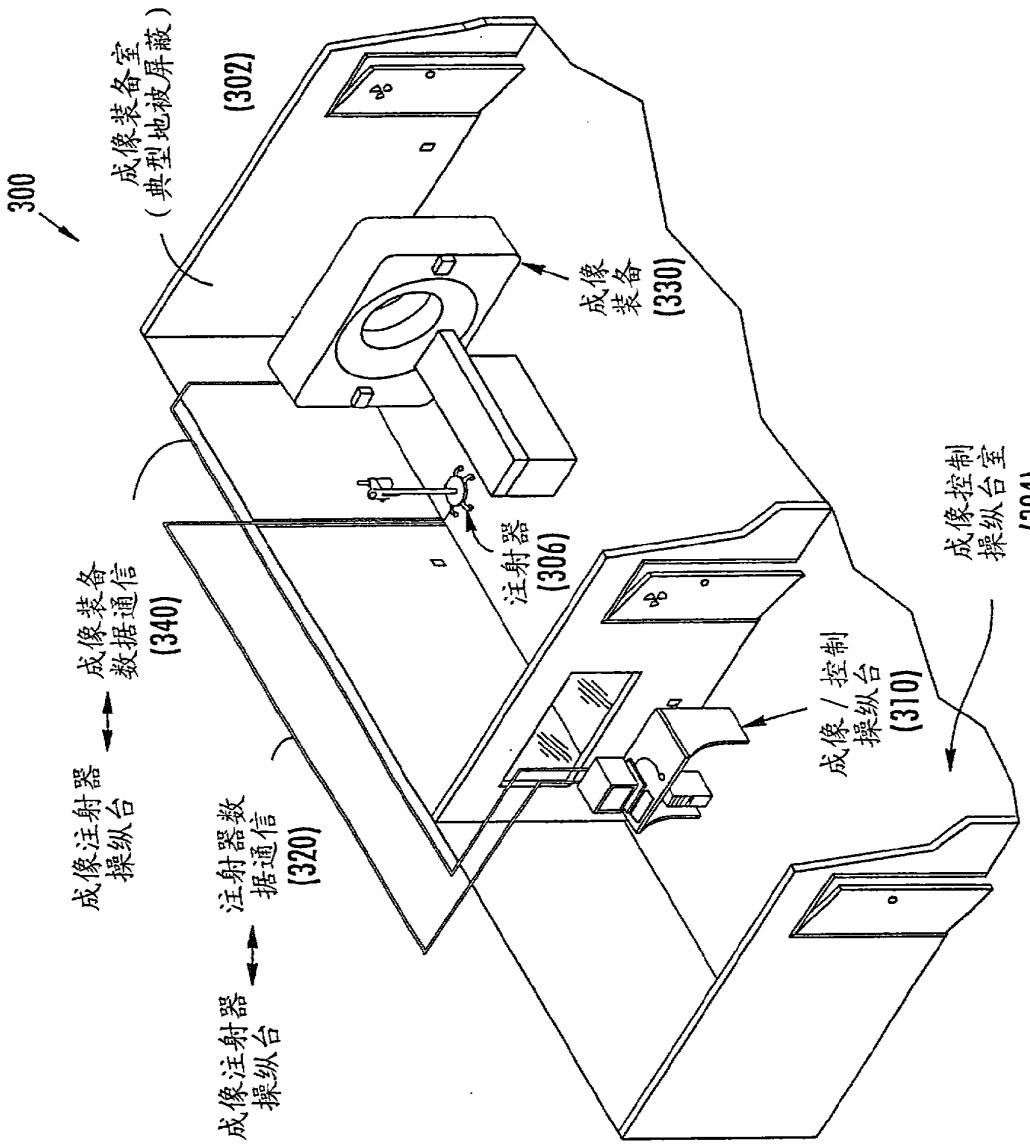

300
成像装备室
（典型地被屏蔽）
(302)
成像装备
(330)
注射器
(306)
成像装备
数据通信
(340)
成像注射器
操纵台
注射器数
据通信
(320)
成像注射器
操纵台
成像/控制
操纵台
(310)
成像控制
操纵台室
(304)

图 3

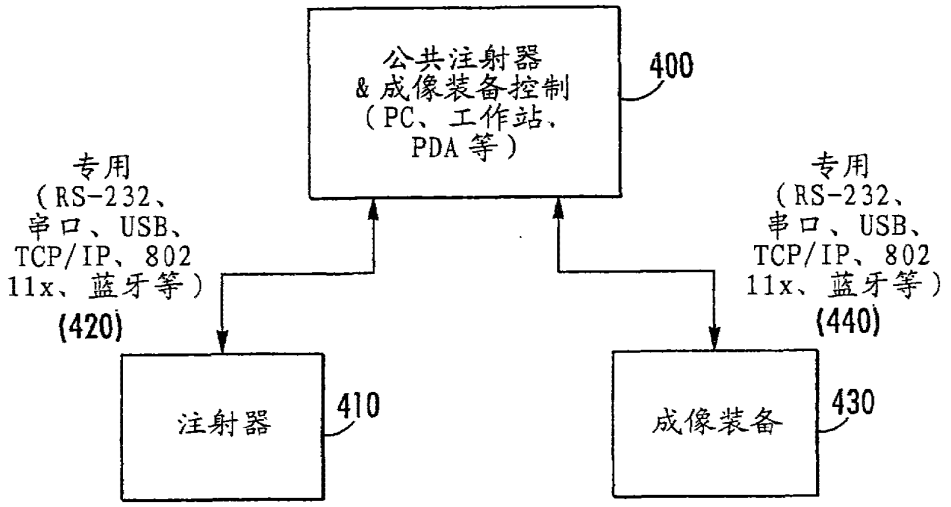

公共注射器
& 成像装备控制
（PC、工作站、
PDA 等）
400
专用
（RS-232、
串口、USB、
TCP/IP、802
11x、蓝牙等）
(420)
专用
（RS-232、
串口、USB、
TCP/IP、802
11x、蓝牙等）
(440)
注射器
410
成像装备
430

图 4

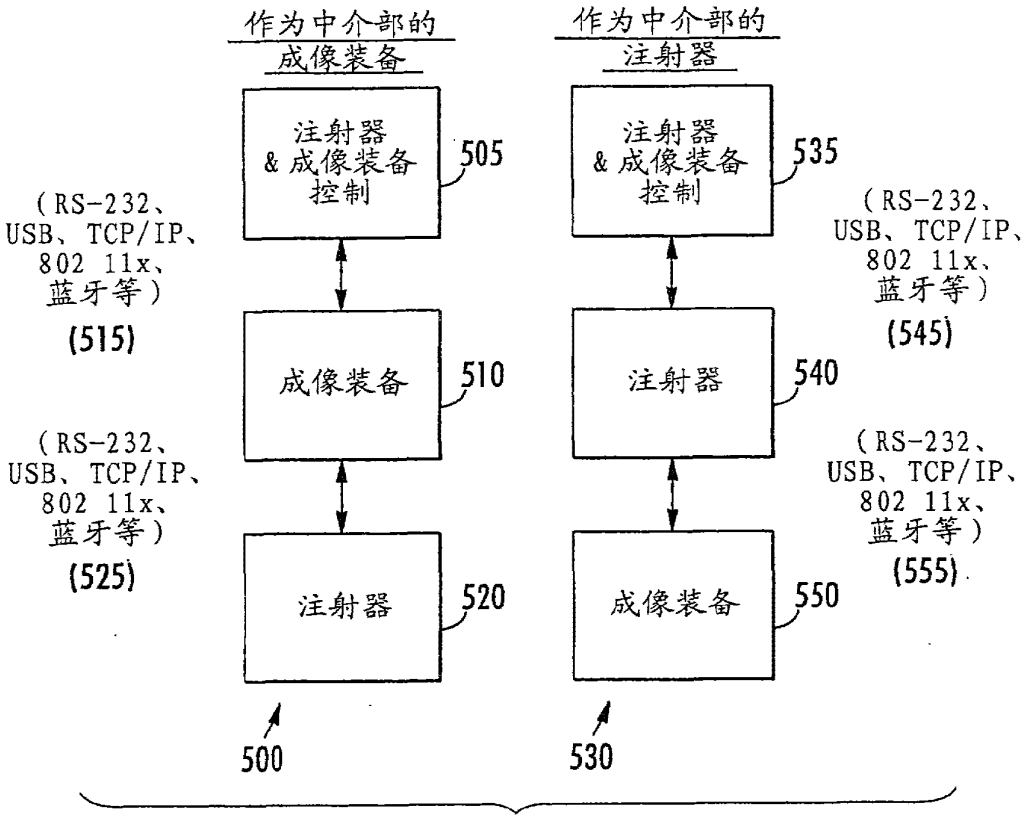

作为中介部的
成像装备
作为中介部的
注射器
注射器
& 成像装备
控制
505
注射器
& 成像装备
控制
535
（RS-232、
USB、TCP/IP、
802 11x、
蓝牙等）
(515)
（RS-232、
USB、TCP/IP、
802 11x、
蓝牙等）
(545)
成像装备
510
注射器
540
（RS-232、
USB、TCP/IP、
802 11x、
蓝牙等）
(525)
（RS-232、
USB、TCP/IP、
802 11x、
蓝牙等）
(555)
注射器
520
成像装备
550
500
530

图 5

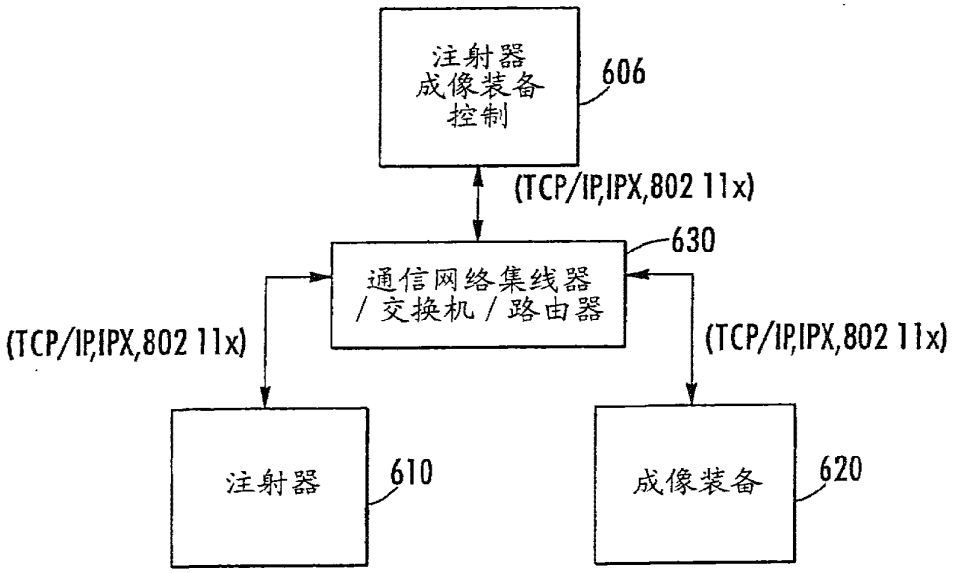

注射器
成像装备
控制
606
(TCP/IP,IPX,802 11x)
630
通信网络集线器
/ 交换机 / 路由器
(TCP/IP,IPX,802 11x)
(TCP/IP,IPX,802 11x)
注射器
610
成像装备
620

图 6

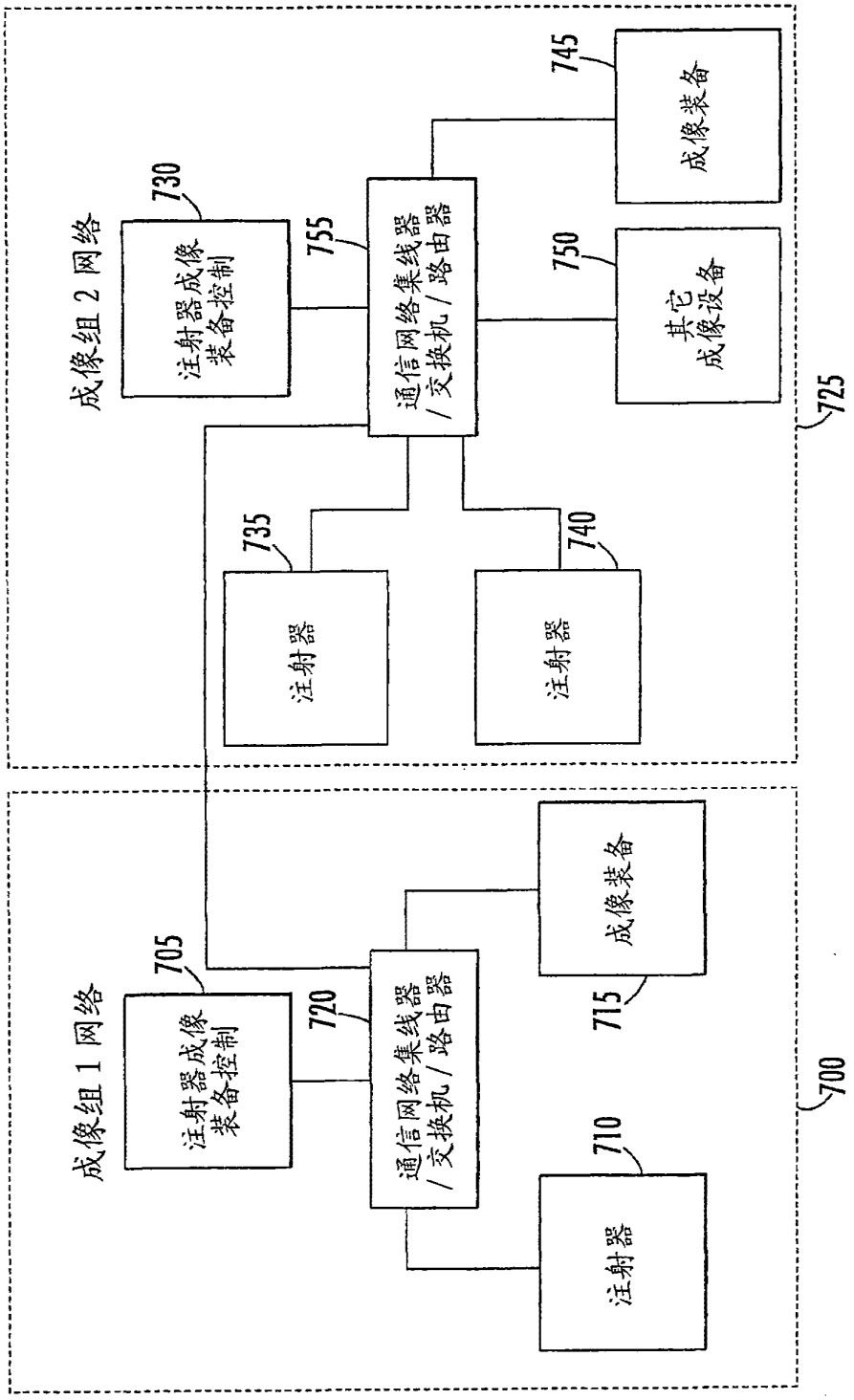


图 7

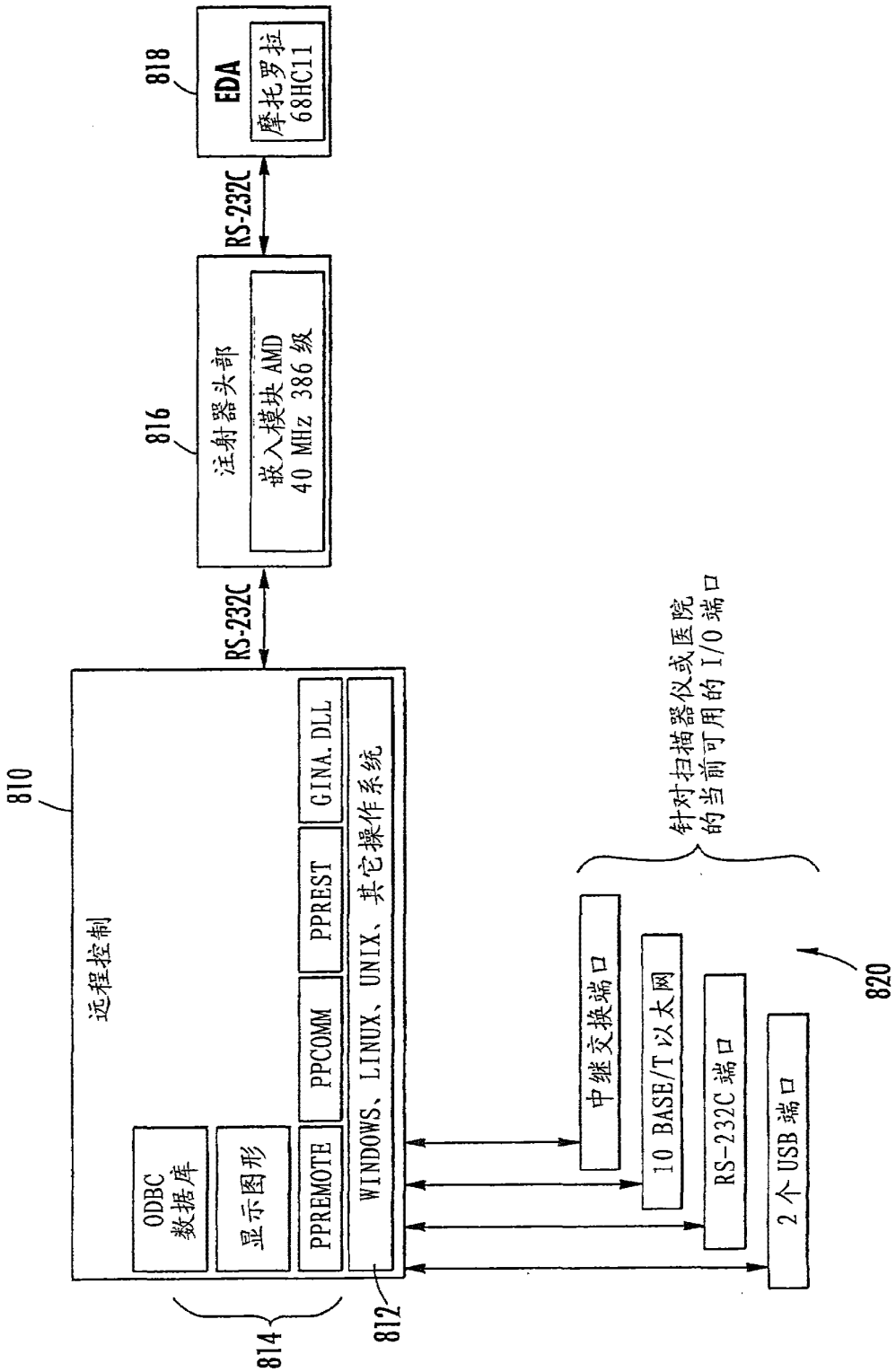

818
EDA
摩托罗拉
68HC11
RS-232C
816
注射器头部
嵌入模块 AMD
40 MHz 386 级
RS-232C
810
远程控制
ODBC
数据库
显示图形
PPREMOTE
PPCOMM
PPREST
GINA.DLL
WINDOWS、LINUX、UNIX、其它操作系统
814
812
中继交换端口
10 BASE/T以太网
RS-232C 端口
2 个 USB 端口
针对扫描器仪或医院
的当前可用的 I/O 端口
820

图 8

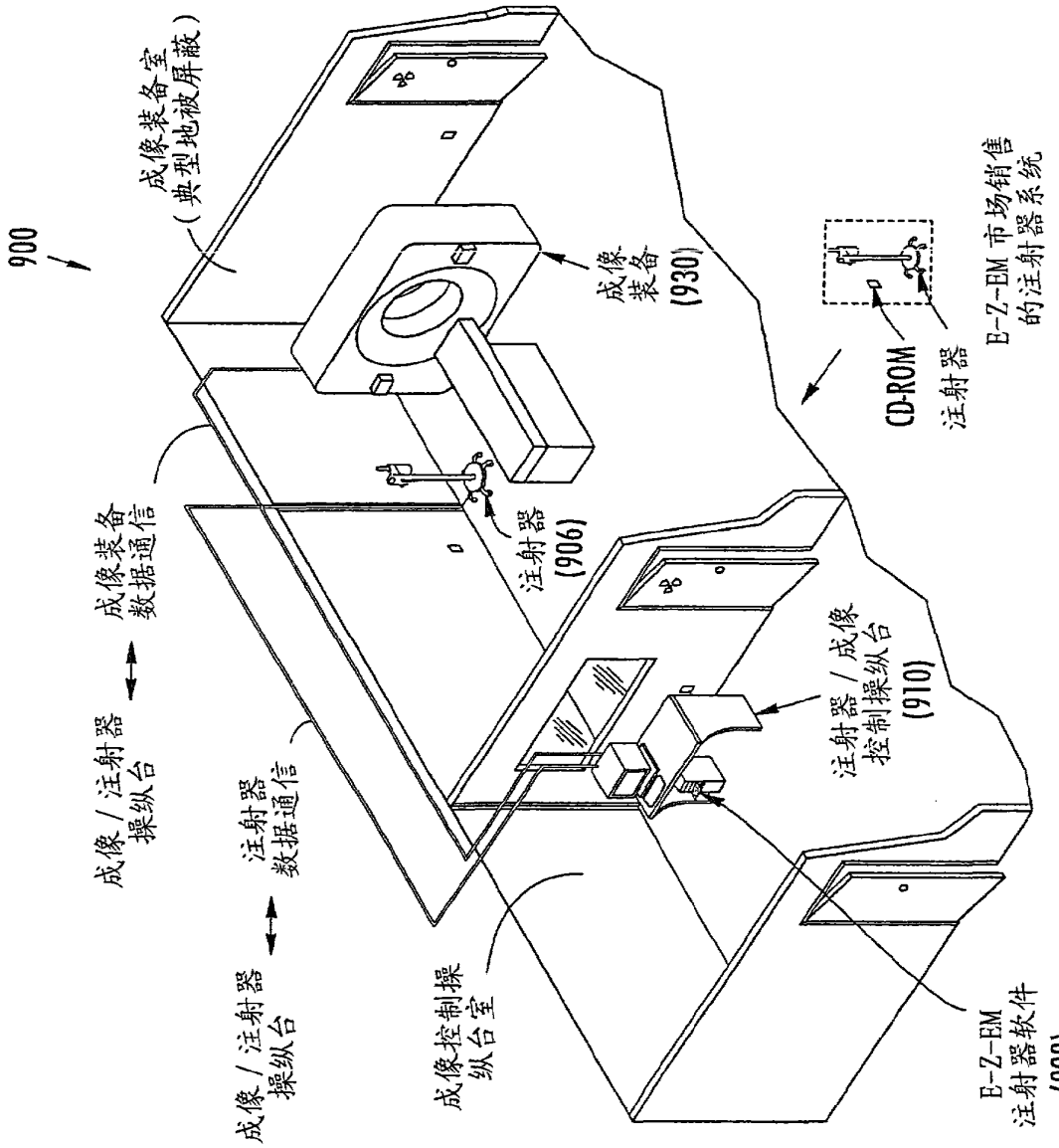

900
成像装备室
(典型地被屏蔽)
成像装备
(930)
注射器
(906)
成像装备
数据通信
成像/注射器
操纵台
注射器
数据通信
成像/注射器
操纵台
成像控制操
纵台室
注射器/成像
控制操纵台
(910)
CD-ROM
注射器
E-Z-EM 市场销售
的注射器系统
E-Z-EM
注射器软件
(908)

图 9

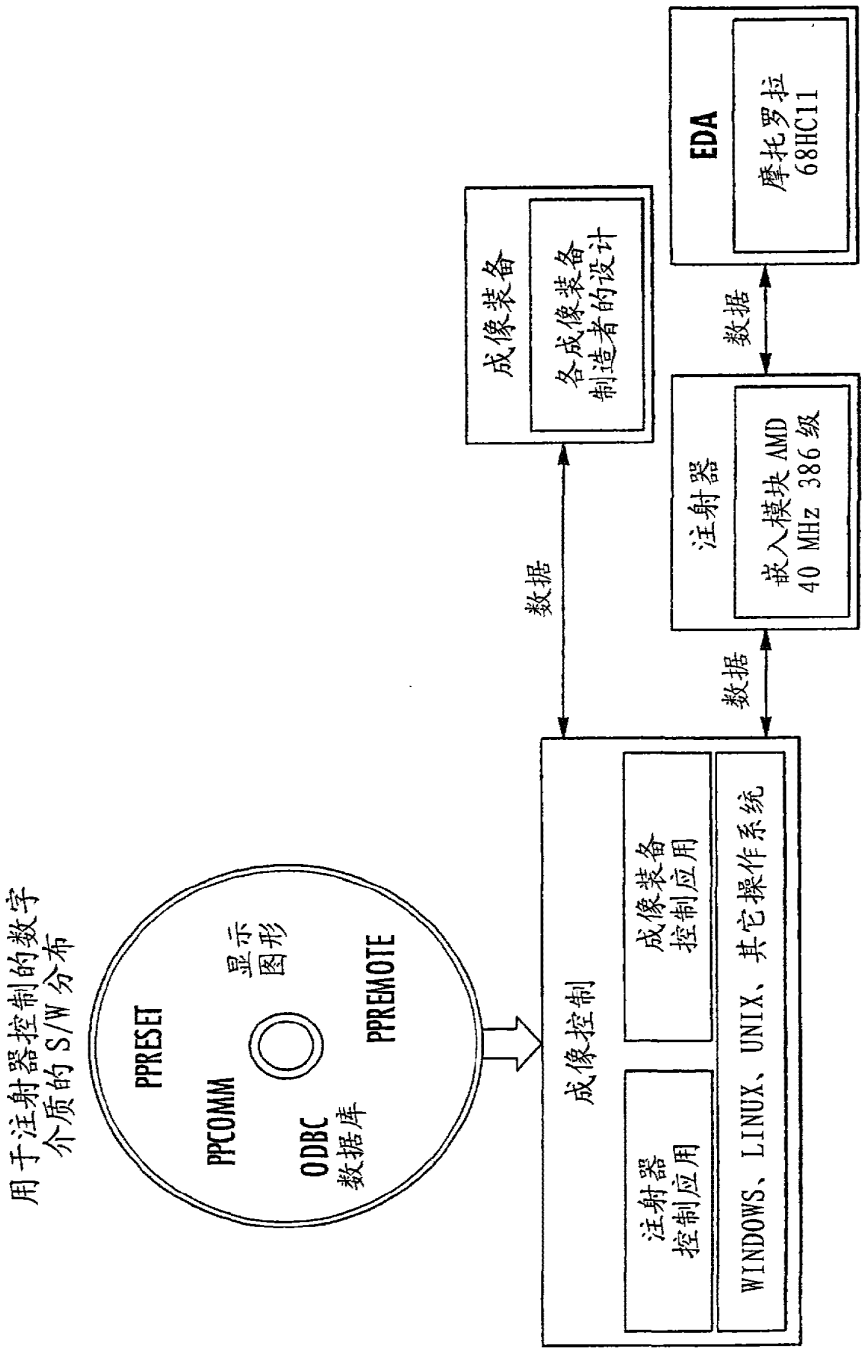


图 10

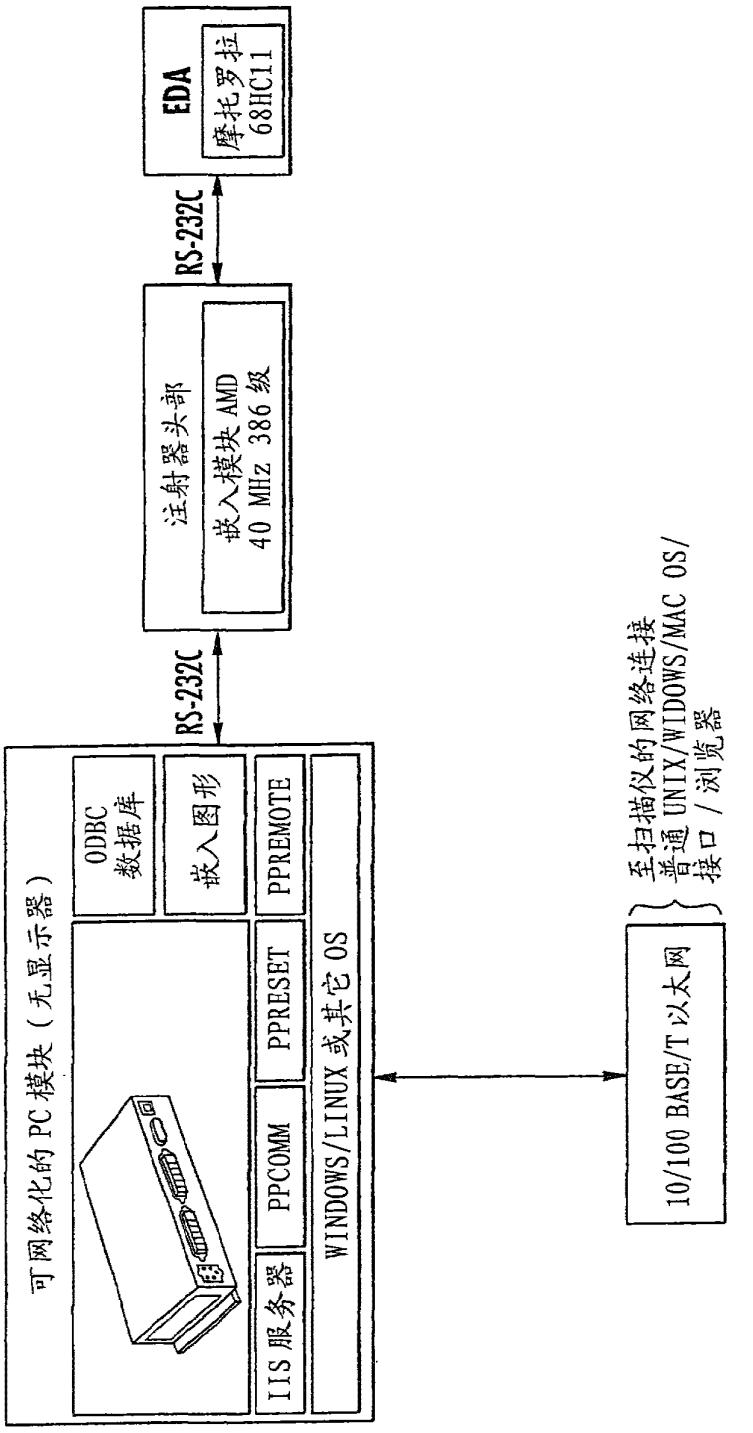

可网络化的 PC 模块（无显示器）
ODBC 数据库
嵌入图形
IIS 服务器
PPCOMM
PPRESET
PPREMOTE
WINDOWS/LINUX 或其它 OS
RS-232C
注射器头部
嵌入模块 AMD 40 MHz 386 级
RS-232C
EDA
摩托罗拉 68HC11
10/100 BASE/T 以太网
至扫描仪的网络连接
普通 UNIX/WIDOWS/MAC OS/ 接口 / 浏览器

图 11

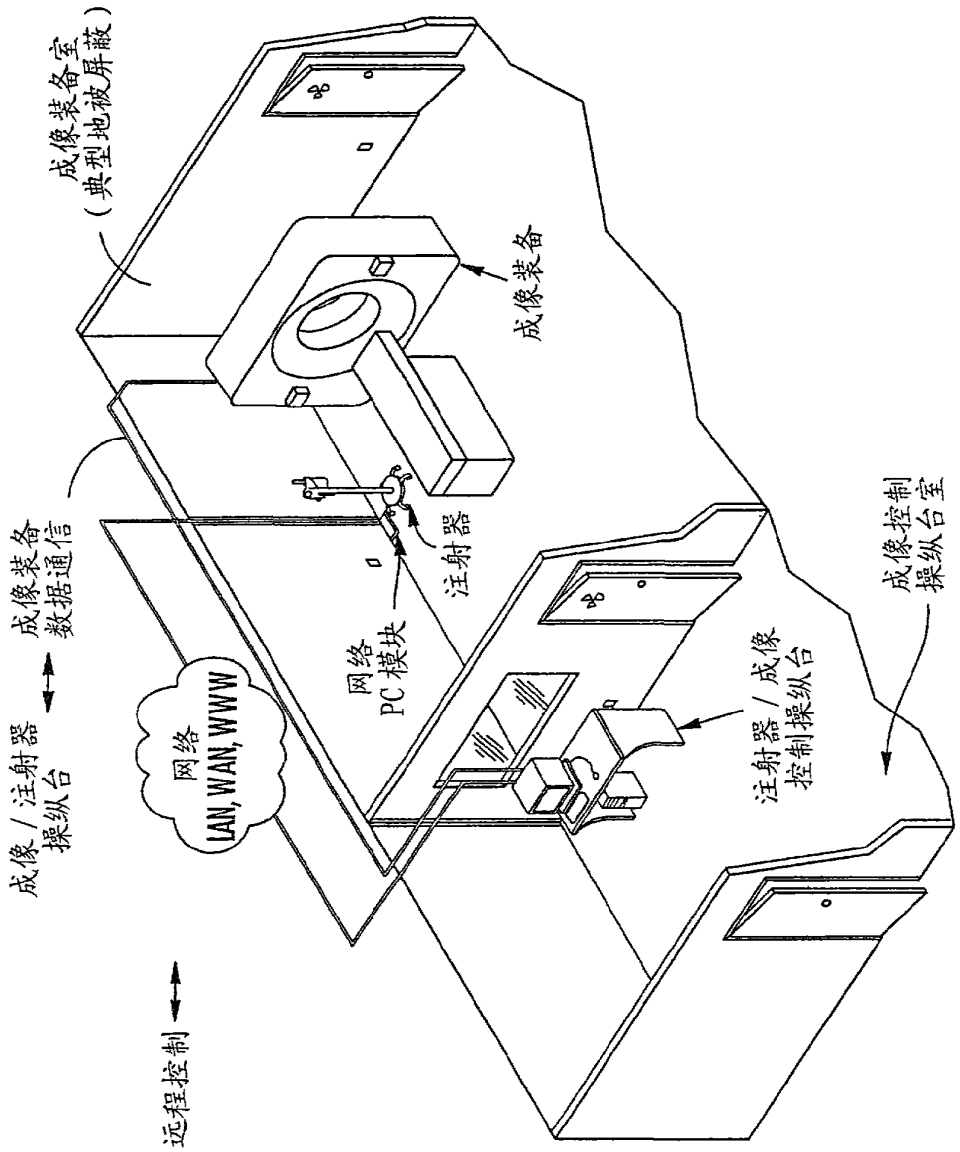

成像装备室
(典型地被屏蔽)
成像装备
网络
PC 模块
注射器
成像装备
数据通信
成像 / 注射器
操纵台
网络
LAN, WAN, WWW
远程控制
注射器 / 成像
控制操纵台
成像控制
操纵台室

图 12

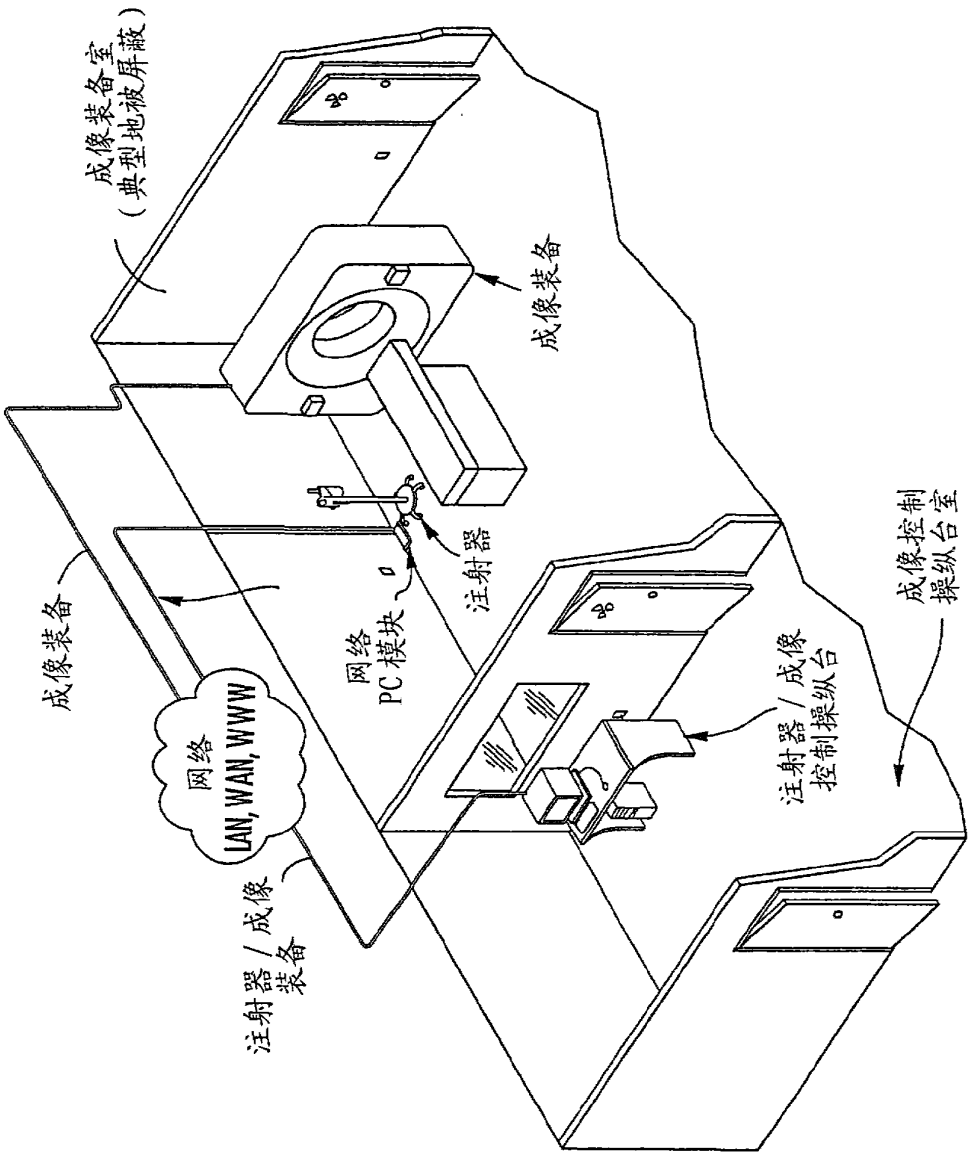

成像装备室
（典型地被屏蔽）
成像装备
网络
PC模块
注射器
成像装备
网络
LAN, WAN, WWW
注射器 / 成像
装备
注射器 / 成像
控制操纵台
成像控制
操纵台室

图 12A

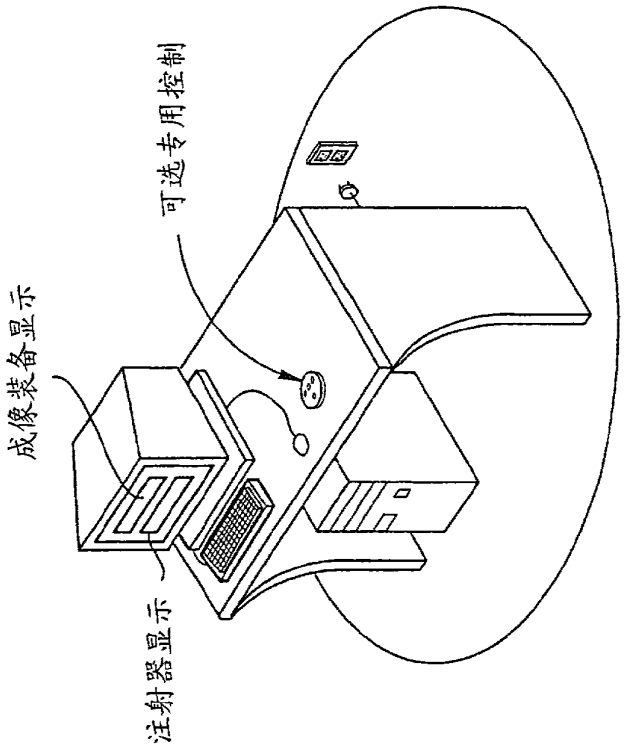


图 13

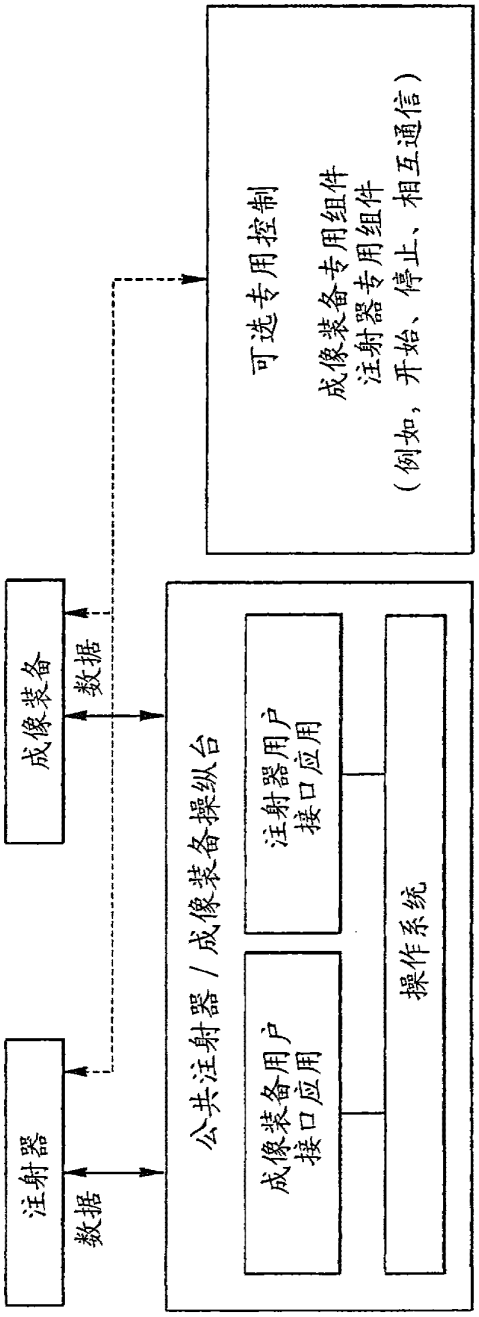

可选专用控制
成像装备专用组件
注射器专用组件
（例如，开始、停止、相互通信）
成像装备
数据
注射器
数据
公共注射器 / 成像装备操纵台
成像装备用户
接口应用
注射器用户
接口应用
操作系统

图 14

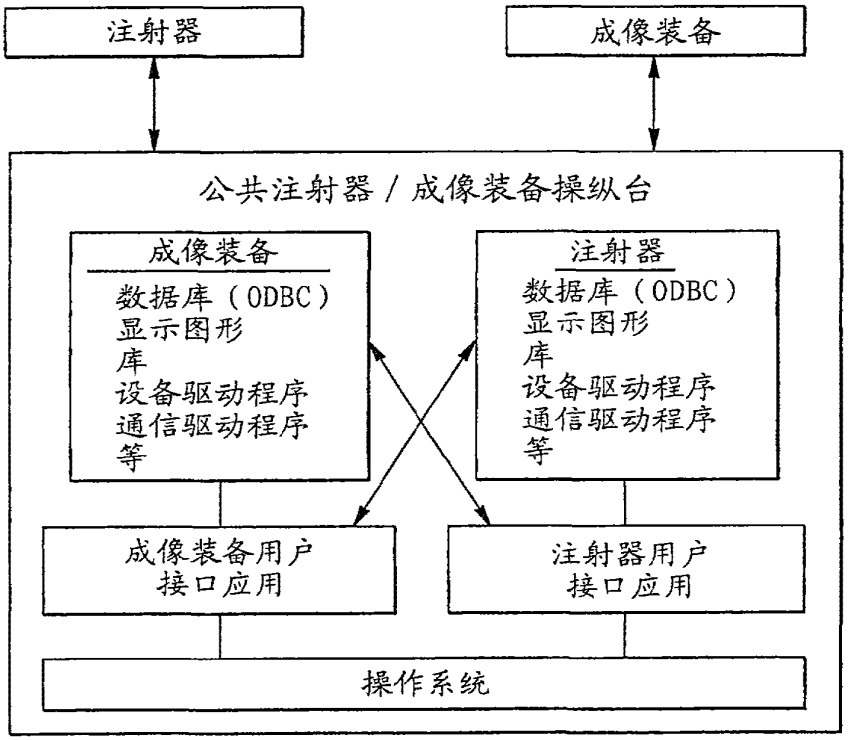

注射器
成像装备
公共注射器 / 成像装备操纵台
成像装备
数据库（ODBC）
显示图形
库
设备驱动程序
通信驱动程序
等
注射器
数据库（ODBC）
显示图形
库
设备驱动程序
通信驱动程序
等
成像装备用户
接口应用
注射器用户
接口应用
操作系统

图 15

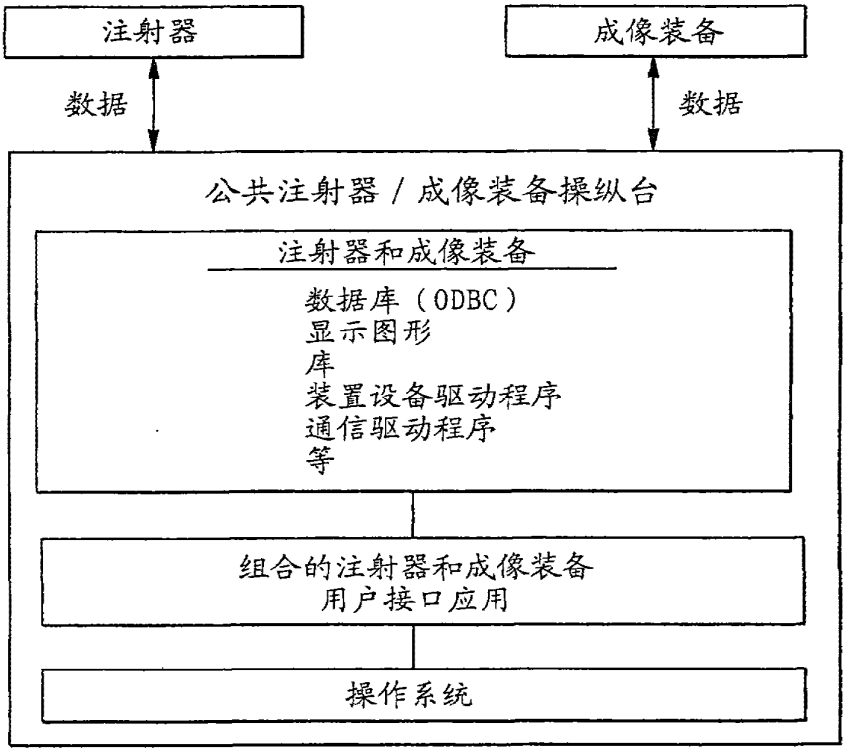

注射器
成像装备
数据
数据
公共注射器 / 成像装备操纵台
注射器和成像装备
数据库（ODBC）
显示图形
库
装置设备驱动程序
通信驱动程序
等
组合的注射器和成像装备
用户接口应用
操作系统

图 16

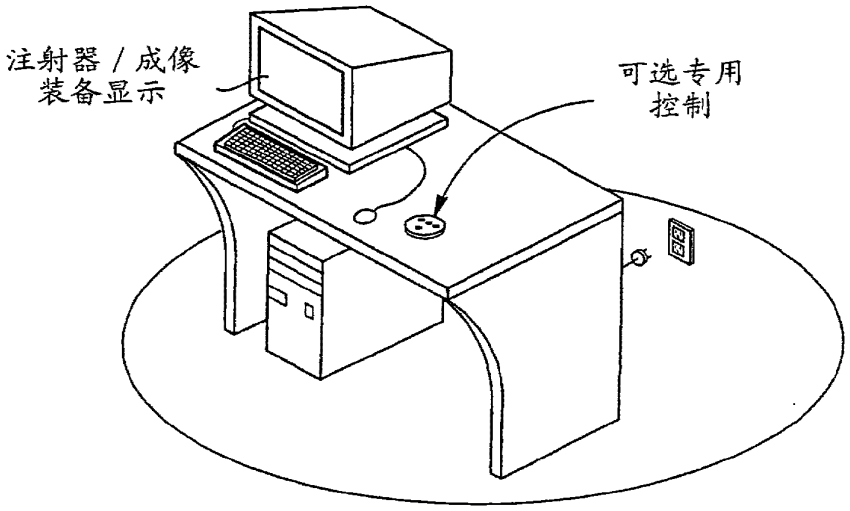


图 17

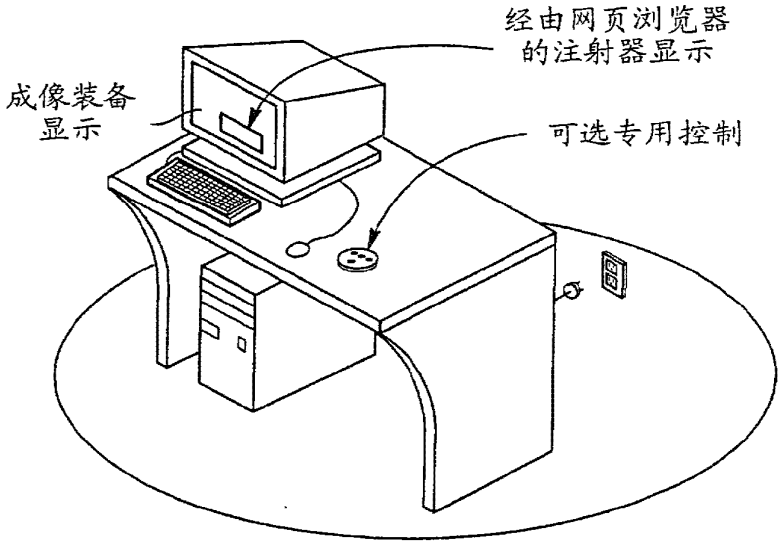


图 18

可选择扫描协议 1 到 n 的数据库
协议 1: kV、mA、准直、节距、转动、检测器设置、AEC、暂停等
协议 2: kV、mA、准直、节距、转动、检测器设置、AEC、暂停等
协议 3: kV、mA、准直、节距、转动、检测器设置、AEC、暂停等
协议 n: kV、mA、准直、节距、转动、检测器设置、AEC、暂停等
成像装备用户界面接口和显示操纵台（例如，CT）
可选择注射协议 1 到 m 的数据库
协议 1: 相位 1、(介质、流速、容积、暂停、延迟)、相位 2、相位 3 等
协议 2: 相位 1、(介质、流速、容积、暂停、延迟)、相位 2、相位 3 等
协议 3: 相位 1、(介质、流速、容积、暂停、延迟)、相位 2、相位 3 等
协议 m: 相位 1、(介质、流速、容积、暂停、延迟)、相位 2、相位 3 等
注射器用户接口和显示操纵台（例如，CT）
当前实践（2 个单独的用户接口）

图 19

可选择程序协议（扫描和注射）1到n的数据库
协议1：kV、mA、准直、节距、转动、检测器设置、AEC、暂停等
相位1、（介质、流速、容积、暂停、延迟）、相位2、相位3等
协议2：kV、mA、准直、节距、转动、检测器设置、AEC、暂停等
相位1、（介质、流速、容积、暂停、延迟）、相位2、相位3等
协议3：kV、mA、准直、节距、转动、检测器设置、AEC、暂停等
相位1、（介质、流速、容积、暂停、延迟）、相位2、相位3等
协议n：kV、mA、准直、节距、转动、检测器设置、AEC、暂停等
相位1、（介质、流速、容积、暂停、延迟）、相位2、相位3等
注射器成像装备公共用户接口和显示操纵台（例如，CT）
建议的实践应用（公共用户接口）

图 20

PTO/SB/08a (01-10)
Approved for use through 07/31/2012. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Not for submission under 37 CFR 1.99)

Application Number	12137364
Filing Date	2008-06-11
First Named Inventor	Stephen E. Hidem
Art Unit	3763
Examiner Name	Jenna Zhang
Attorney Docket Number	56782.1.7

U.S.PATENTS Remove

Examiner Initial*	Cite No	Patent Number	Kind Code[1]	Issue Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1	7996068		2011-08-09	Telischak	

If you wish to add additional U.S. Patent citation information please click the Add button. Add

U.S.PATENT APPLICATION PUBLICATIONS Remove

Examiner Initial*	Cite No	Publication Number	Kind Code[1]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1					

If you wish to add additional U.S. Published Application citation information please click the Add button. Add

FOREIGN PATENT DOCUMENTS Remove

Examiner Initial*	Cite No	Foreign Document Number[3]	Country Code[2] i	Kind Code[4]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear	T[5]
	1							☐

If you wish to add additional Foreign Patent Document citation information please click the Add button Add

NON-PATENT LITERATURE DOCUMENTS Remove

Examiner Initials*	Cite No	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc), date, pages(s), volume-issue number(s), publisher, city and/or country where published.	T[5]

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	12137364
	Filing Date	2008-06-11
	First Named Inventor	Stephen E. Hidem
	Art Unit	3763
	Examiner Name	Jenna Zhang
	Attorney Docket Number	56782.1.7

	1	R. Klein, "Precise 82RB infusion system for cardiac perfusion measurement using 3D positron emission tomography", Ottawa-Carleton Institute for Electrical and Computer Engineering School of Information Technology and Engineering (Electrical & Computer Engineering), February, 2005, 147 pages	☐
	2	LEMER PAX, POSIJET® Integrated FDG dispensing and infusion system, www.lemerpax.com (copyright date May 2008)	☐

If you wish to add additional non-patent literature document citation information please click the Add button Add

EXAMINER SIGNATURE

Examiner Signature		Date Considered	

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through a citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

[1] See Kind Codes of USPTO Patent Documents at www.USPTO.GOV or MPEP 901.04. [2] Enter office that issued the document, by the two-letter code (WIPO Standard ST.3). [3] For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. [4] Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. [5] Applicant is to place a check mark here if English language translation is attached.

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	12137364
	Filing Date	2008-06-11
	First Named Inventor	Stephen E. Hidem
	Art Unit	3763
	Examiner Name	Jenna Zhang
	Attorney Docket Number	56782.1.7

CERTIFICATION STATEMENT

Please see 37 CFR 1.97 and 1.98 to make the appropriate selection(s):

☐ That each item of information contained in the information disclosure statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(1).

OR

☐ That no item of information contained in the information disclosure statement was cited in a communication from a foreign patent office in a counterpart foreign application, and, to the knowledge of the person signing the certification after making reasonable inquiry, no item of information contained in the information disclosure statement was known to any individual designated in 37 CFR 1.56(c) more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(2).

☐ See attached certification statement.

☒ The fee set forth in 37 CFR 1.17 (p) has been submitted herewith.

☐ A certification statement is not submitted herewith.

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	/Paul J. LaVanway, Jr./	Date (YYYY-MM-DD)	2013-01-17
Name/Print	Paul J. LaVanway, Jr.	Registration Number	64610

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 1 hour to complete, including gathering, preparing and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

Privacy Act Statement

The Privacy Act of 1974 (P.L. 93-579) requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that: (1) the general authority for the collection of this information is 35 U.S.C. 2(b)(2); (2) furnishing of the information solicited is voluntary; and (3) the principal purpose for which the information is used by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent application or patent. If you do not furnish the requested information, the U.S. Patent and Trademark Office may not be able to process and/or examine your submission, which may result in termination of proceedings or abandonment of the application or expiration of the patent.

The information provided by you in this form will be subject to the following routine uses:

1. The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C. 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether the Freedom of Information Act requires disclosure of these record s.

2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.

3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.

4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).

5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent Cooperation Treaty.

6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).

7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (i.e., GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.

8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspections or an issued patent.

9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

Electronic Patent Application Fee Transmittal

Application Number:	12137364
Filing Date:	11-Jun-2008
Title of Invention:	INFUSION SYSTEMS INCLUDING COMPUTER-FACILITATED MAINTENANCE AND/OR OPERATION AND METHODS OF USE
First Named Inventor/Applicant Name:	Stephen E. Hidem
Filer:	Paul J. LaVanway Jr.
Attorney Docket Number:	56782.1.7

Filed as Large Entity

Utility under 35 USC 111(a) Filing Fees

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Basic Filing:				
Pages:				
Claims:				
Miscellaneous-Filing:				
Petition:				
Patent-Appeals-and-Interference:				
Post-Allowance-and-Post-Issuance:				
Extension-of-Time:				

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Miscellaneous:				
Submission- Information Disclosure Stmt	1806	1	180	180
		Total in USD ($)		**180**

Electronic Acknowledgement Receipt

EFS ID:	14701105
Application Number:	12137364
International Application Number:	
Confirmation Number:	7377
Title of Invention:	INFUSION SYSTEMS INCLUDING COMPUTER-FACILITATED MAINTENANCE AND/OR OPERATION AND METHODS OF USE
First Named Inventor/Applicant Name:	Stephen E. Hidem
Customer Number:	22859
Filer:	Paul J. LaVanway Jr.
Filer Authorized By:	
Attorney Docket Number:	56782.1.7
Receipt Date:	18-JAN-2013
Filing Date:	11-JUN-2008
Time Stamp:	15:03:43
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	yes
Payment Type	Credit Card
Payment was successfully received in RAM	$180
RAM confirmation Number	1667
Deposit Account	
Authorized User	

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)

1	Non Patent Literature	RKlein-MASc-thesis-2005.pdf	2226047 5199c027c97cd1df37f9296f66665c3d7029ed98	no	147
Warnings:					
Information:					
2	Non Patent Literature	Posijet.pdf	4244122 f4131e1134a2c00962cd96c7bfa6d81d41d39b39	no	4
Warnings:					
Information:					
3	Information Disclosure Statement (IDS) Form (SB08)	11thSIDS_56782-1-7.pdf	612416 7f48ba07ac9ec7dde613d167baaa471207c61236	no	4
Warnings:					
Information:					
4	Fee Worksheet (SB06)	fee-info.pdf	30548 cdc67eb3fe6ebaad456bf9b2e95a34b47927f378	no	2
Warnings:					
Information:					
		Total Files Size (in bytes):	7113133		

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.

New Applications Under 35 U.S.C. 111

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.

National Stage of an International Application under 35 U.S.C. 371

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.

New International Application Filed with the USPTO as a Receiving Office

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.

PTO/SB/08a (01-10)
Approved for use through 07/31/2012. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Not for submission under 37 CFR 1.99)

Application Number	12137364
Filing Date	2008-06-11
First Named Inventor	Stephen E. Hidem
Art Unit	3763
Examiner Name	Jenna Zhang
Attorney Docket Number	56782.1.7

U.S.PATENTS Remove

Examiner Initial*	Cite No	Patent Number	Kind Code[1]	Issue Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1	6450936		2002-09-17	Smith, III	

If you wish to add additional U.S. Patent citation information please click the Add button. Add

U.S.PATENT APPLICATION PUBLICATIONS Remove

Examiner Initial*	Cite No	Publication Number	Kind Code[1]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1					

If you wish to add additional U.S. Published Application citation information please click the Add button. Add

FOREIGN PATENT DOCUMENTS Remove

Examiner Initial*	Cite No	Foreign Document Number[3]	Country Code[2] i	Kind Code[4]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear	T[5]
	1							☐

If you wish to add additional Foreign Patent Document citation information please click the Add button Add

NON-PATENT LITERATURE DOCUMENTS Remove

Examiner Initials*	Cite No	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc), date, pages(s), volume-issue number(s), publisher, city and/or country where published.	T[5]

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	12137364
	Filing Date	2008-06-11
	First Named Inventor	Stephen E. Hidem
	Art Unit	3763
	Examiner Name	Jenna Zhang
	Attorney Docket Number	56782.1.7

	1		☐

If you wish to add additional non-patent literature document citation information please click the Add button Add

EXAMINER SIGNATURE

Examiner Signature		Date Considered	

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through a citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

[1] See Kind Codes of USPTO Patent Documents at www.USPTO.GOV or MPEP 901.04. [2] Enter office that issued the document, by the two-letter code (WIPO Standard ST.3). [3] For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. [4] Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. [5] Applicant is to place a check mark here if English language translation is attached.

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	12137364
	Filing Date	2008-06-11
	First Named Inventor	Stephen E. Hidem
	Art Unit	3763
	Examiner Name	Jenna Zhang
	Attorney Docket Number	56782.1.7

CERTIFICATION STATEMENT

Please see 37 CFR 1.97 and 1.98 to make the appropriate selection(s):

☐ That each item of information contained in the information disclosure statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(1).

OR

☐ That no item of information contained in the information disclosure statement was cited in a communication from a foreign patent office in a counterpart foreign application, and, to the knowledge of the person signing the certification after making reasonable inquiry, no item of information contained in the information disclosure statement was known to any individual designated in 37 CFR 1.56(c) more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(2).

☐ See attached certification statement.

☒ The fee set forth in 37 CFR 1.17 (p) has been submitted herewith.

☐ A certification statement is not submitted herewith.

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	/Paul J. LaVanway, Jr./	Date (YYYY-MM-DD)	2012-10-31
Name/Print	Paul J. LaVanway, Jr.	Registration Number	64610

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 1 hour to complete, including gathering, preparing and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

Privacy Act Statement

The Privacy Act of 1974 (P.L. 93-579) requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that: (1) the general authority for the collection of this information is 35 U.S.C. 2(b)(2); (2) furnishing of the information solicited is voluntary; and (3) the principal purpose for which the information is used by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent application or patent. If you do not furnish the requested information, the U.S. Patent and Trademark Office may not be able to process and/or examine your submission, which may result in termination of proceedings or abandonment of the application or expiration of the patent.

The information provided by you in this form will be subject to the following routine uses:

1. The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C. 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether the Freedom of Information Act requires disclosure of these record s.

2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.

3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.

4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).

5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent Cooperation Treaty.

6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).

7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (i.e., GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.

8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspections or an issued patent.

9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

Electronic Patent Application Fee Transmittal

Application Number:	12137364
Filing Date:	11-Jun-2008
Title of Invention:	INFUSION SYSTEMS INCLUDING COMPUTER-FACILITATED MAINTENANCE AND/OR OPERATION AND METHODS OF USE
First Named Inventor/Applicant Name:	Stephen E. Hidem
Filer:	Paul J. LaVanway Jr.
Attorney Docket Number:	56782.1.7

Filed as Large Entity

Utility under 35 USC 111(a) Filing Fees

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Basic Filing:				
Pages:				
Claims:				
Miscellaneous-Filing:				
Petition:				
Patent-Appeals-and-Interference:				
Post-Allowance-and-Post-Issuance:				
Extension-of-Time:				

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Miscellaneous:				
Submission- Information Disclosure Stmt	1806	1	180	180
		Total in USD ($)		**180**

Electronic Acknowledgement Receipt

EFS ID:	14109899
Application Number:	12137364
International Application Number:	
Confirmation Number:	7377
Title of Invention:	INFUSION SYSTEMS INCLUDING COMPUTER-FACILITATED MAINTENANCE AND/OR OPERATION AND METHODS OF USE
First Named Inventor/Applicant Name:	Stephen E. Hidem
Customer Number:	22859
Filer:	Paul J. LaVanway Jr.
Filer Authorized By:	
Attorney Docket Number:	56782.1.7
Receipt Date:	07-NOV-2012
Filing Date:	11-JUN-2008
Time Stamp:	10:45:26
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	yes
Payment Type	Credit Card
Payment was successfully received in RAM	$180
RAM confirmation Number	20506
Deposit Account	
Authorized User	

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)

1	Information Disclosure Statement (IDS) Form (SB08)	10thSIDS_56782-1-7.pdf	612181 40d0ef157217c37c131f2dab498f3e572f74e6cd	no	4
Warnings:					
Information:					
2	Fee Worksheet (SB06)	fee-info.pdf	30540 7ec7642e58a08a708024b88e493e645b3686146b	no	2
Warnings:					
Information:					
			Total Files Size (in bytes):	642721	

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.

New Applications Under 35 U.S.C. 111

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.

National Stage of an International Application under 35 U.S.C. 371

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.

New International Application Filed with the USPTO as a Receiving Office

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.

PTO/SB/08a (01-10)
Approved for use through 07/31/2012. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Not for submission under 37 CFR 1.99)

Application Number	12137364
Filing Date	2008-06-11
First Named Inventor	Stephen E. Hidem
Art Unit	3763
Examiner Name	Jenna Zhang
Attorney Docket Number	56782.1.7

U.S.PATENTS Remove

Examiner Initial*	Cite No	Patent Number	Kind Code[1]	Issue Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1	5395320		1995-03-07	Padda	

If you wish to add additional U.S. Patent citation information please click the Add button. Add

U.S.PATENT APPLICATION PUBLICATIONS Remove

Examiner Initial*	Cite No	Publication Number	Kind Code[1]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1	20030139640		2003-07-24	Whittacre	
	2	20050187515		2005-08-25	Varrichio	
	3	20050277833		2005-12-15	Williams	

If you wish to add additional U.S. Published Application citation information please click the Add button. Add

FOREIGN PATENT DOCUMENTS Remove

Examiner Initial*	Cite No	Foreign Document Number[3]	Country Code[2] ¡	Kind Code[4]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear	T[5]
	1							☐

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	12137364
	Filing Date	2008-06-11
	First Named Inventor	Stephen E. Hidem
	Art Unit	3763
	Examiner Name	Jenna Zhang
	Attorney Docket Number	56782.1.7

If you wish to add additional Foreign Patent Document citation information please click the Add button			Add
NON-PATENT LITERATURE DOCUMENTS			Remove
Examiner Initials*	Cite No	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc), date, pages(s), volume-issue number(s), publisher, city and/or country where published.	T[5]
	1	LEMER PAX, POSIJET® Integrated FDG dispensing and infusion system, www.lemerpax.com (date unknown).	☐
If you wish to add additional non-patent literature document citation information please click the Add button			Add

EXAMINER SIGNATURE			
Examiner Signature		Date Considered	

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through a citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

[1] See Kind Codes of USPTO Patent Documents at www.USPTO.GOV or MPEP 901.04. [2] Enter office that issued the document, by the two-letter code (WIPO Standard ST.3). [3] For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. [4] Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. [5] Applicant is to place a check mark here if English language translation is attached.

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	12137364
	Filing Date	2008-06-11
	First Named Inventor	Stephen E. Hidem
	Art Unit	3763
	Examiner Name	Jenna Zhang
	Attorney Docket Number	56782.1.7

CERTIFICATION STATEMENT

Please see 37 CFR 1.97 and 1.98 to make the appropriate selection(s):

☐ That each item of information contained in the information disclosure statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(1).

OR

☐ That no item of information contained in the information disclosure statement was cited in a communication from a foreign patent office in a counterpart foreign application, and, to the knowledge of the person signing the certification after making reasonable inquiry, no item of information contained in the information disclosure statement was known to any individual designated in 37 CFR 1.56(c) more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(2).

☐ See attached certification statement.

☒ The fee set forth in 37 CFR 1.17 (p) has been submitted herewith.

☐ A certification statement is not submitted herewith.

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	/Paul J. LaVanway, Jr./	Date (YYYY-MM-DD)	2012-10-17
Name/Print	Paul J. LaVanway, Jr.	Registration Number	64610

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 1 hour to complete, including gathering, preparing and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

Privacy Act Statement

The Privacy Act of 1974 (P.L. 93-579) requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that: (1) the general authority for the collection of this information is 35 U.S.C. 2(b)(2); (2) furnishing of the information solicited is voluntary; and (3) the principal purpose for which the information is used by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent application or patent. If you do not furnish the requested information, the U.S. Patent and Trademark Office may not be able to process and/or examine your submission, which may result in termination of proceedings or abandonment of the application or expiration of the patent.

The information provided by you in this form will be subject to the following routine uses:

1. The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C. 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether the Freedom of Information Act requires disclosure of these record s.

2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.

3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.

4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).

5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent Cooperation Treaty.

6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).

7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (i.e., GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.

8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspections or an issued patent.

9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

Electronic Patent Application Fee Transmittal

Application Number:	12137364
Filing Date:	11-Jun-2008
Title of Invention:	INFUSION SYSTEMS INCLUDING COMPUTER-FACILITATED MAINTENANCE AND/OR OPERATION AND METHODS OF USE
First Named Inventor/Applicant Name:	Stephen E. Hidem
Filer:	Paul J. LaVanway Jr.
Attorney Docket Number:	56782.1.7

Filed as Large Entity

Utility under 35 USC 111(a) Filing Fees

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Basic Filing:				
Pages:				
Claims:				
Miscellaneous-Filing:				
Petition:				
Patent-Appeals-and-Interference:				
Post-Allowance-and-Post-Issuance:				
Extension-of-Time:				

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Miscellaneous:				
Submission- Information Disclosure Stmt	1806	1	180	180
		Total in USD ($)		**180**

Electronic Acknowledgement Receipt

EFS ID:	13946975
Application Number:	12137364
International Application Number:	
Confirmation Number:	7377
Title of Invention:	INFUSION SYSTEMS INCLUDING COMPUTER-FACILITATED MAINTENANCE AND/OR OPERATION AND METHODS OF USE
First Named Inventor/Applicant Name:	Stephen E. Hidem
Customer Number:	22859
Filer:	Paul J. LaVanway Jr.
Filer Authorized By:	
Attorney Docket Number:	56782.1.7
Receipt Date:	17-OCT-2012
Filing Date:	11-JUN-2008
Time Stamp:	12:09:25
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	yes
Payment Type	Credit Card
Payment was successfully received in RAM	$180
RAM confirmation Number	9671
Deposit Account	
Authorized User	

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)

1	Non Patent Literature	Posijet.pdf	4244122 f4131e1134a2c00962cd96c7bfa6d81d41d39b39	no	4
Warnings:					
Information:					
2	Information Disclosure Statement (IDS) Form (SB08)	9thSIDS_56782-1-7.pdf	612375 074e2688c66b8d9f5564fd3983dceb34095a673b	no	4
Warnings:					
Information:					
3	Fee Worksheet (SB06)	fee-info.pdf	30547 46b4ac40fc217a511c8736598bafa8656c506378	no	2
Warnings:					
Information:					
			Total Files Size (in bytes):	4887044	

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.

New Applications Under 35 U.S.C. 111
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.

National Stage of an International Application under 35 U.S.C. 371
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.

New International Application Filed with the USPTO as a Receiving Office
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.

PTO/SB/08a (01-10)
Approved for use through 07/31/2012. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Not for submission under 37 CFR 1.99)

Application Number	12137364
Filing Date	2008-06-11
First Named Inventor	STEPHEN E. HIDEM
Art Unit	3763
Examiner Name	ZHANG, JENNA
Attorney Docket Number	56782.1.7

U.S.PATENTS Remove

Examiner Initial*	Cite No	Patent Number	Kind Code[1]	Issue Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1					

If you wish to add additional U.S. Patent citation information please click the Add button. Add

U.S.PATENT APPLICATION PUBLICATIONS Remove

Examiner Initial*	Cite No	Publication Number	Kind Code[1]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1	20080177126		2008-07-24	Tate	

If you wish to add additional U.S. Published Application citation information please click the Add button. Add

FOREIGN PATENT DOCUMENTS Remove

Examiner Initial*	Cite No	Foreign Document Number[3]	Country Code[2] i	Kind Code[4]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear	T[5]
	1							☐

If you wish to add additional Foreign Patent Document citation information please click the Add button Add

NON-PATENT LITERATURE DOCUMENTS Remove

Examiner Initials*	Cite No	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc), date, pages(s), volume-issue number(s), publisher, city and/or country where published.	T[5]

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	12137364
	Filing Date	2008-06-11
	First Named Inventor	STEPHEN E. HIDEM
	Art Unit	3763
	Examiner Name	ZHANG, JENNA
	Attorney Docket Number	56782.1.7

	1		☐

If you wish to add additional non-patent literature document citation information please click the Add button Add

EXAMINER SIGNATURE

Examiner Signature		Date Considered	

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through a citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

[1] See Kind Codes of USPTO Patent Documents at www.USPTO.GOV or MPEP 901.04. [2] Enter office that issued the document, by the two-letter code (WIPO Standard ST.3). [3] For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. [4] Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. [5] Applicant is to place a check mark here if English language translation is attached.

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	12137364
	Filing Date	2008-06-11
	First Named Inventor	STEPHEN E. HIDEM
	Art Unit	3763
	Examiner Name	ZHANG, JENNA
	Attorney Docket Number	56782.1.7

CERTIFICATION STATEMENT

Please see 37 CFR 1.97 and 1.98 to make the appropriate selection(s):

☐ That each item of information contained in the information disclosure statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(1).

OR

☐ That no item of information contained in the information disclosure statement was cited in a communication from a foreign patent office in a counterpart foreign application, and, to the knowledge of the person signing the certification after making reasonable inquiry, no item of information contained in the information disclosure statement was known to any individual designated in 37 CFR 1.56(c) more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(2).

☐ See attached certification statement.

☒ The fee set forth in 37 CFR 1.17 (p) has been submitted herewith.

☐ A certification statement is not submitted herewith.

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	/Paul J. LaVanway, Jr./	Date (YYYY-MM-DD)	2012-05-31
Name/Print	Paul J. LaVanway, Jr.	Registration Number	64,610

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 1 hour to complete, including gathering, preparing and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

Privacy Act Statement

The Privacy Act of 1974 (P.L. 93-579) requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that: (1) the general authority for the collection of this information is 35 U.S.C. 2(b)(2); (2) furnishing of the information solicited is voluntary; and (3) the principal purpose for which the information is used by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent application or patent. If you do not furnish the requested information, the U.S. Patent and Trademark Office may not be able to process and/or examine your submission, which may result in termination of proceedings or abandonment of the application or expiration of the patent.

The information provided by you in this form will be subject to the following routine uses:

1. The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C. 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether the Freedom of Information Act requires disclosure of these record s.

2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.

3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.

4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).

5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent Cooperation Treaty.

6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).

7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (i.e., GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.

8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspections or an issued patent.

9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

Electronic Patent Application Fee Transmittal

Application Number:	12137364
Filing Date:	11-Jun-2008
Title of Invention:	INFUSION SYSTEMS INCLUDING COMPUTER-FACILITATED MAINTENANCE AND/OR OPERATION AND METHODS OF USE
First Named Inventor/Applicant Name:	Stephen E. Hidem
Filer:	Paul J. LaVanway Jr.
Attorney Docket Number:	56782.1.7

Filed as Large Entity

Utility under 35 USC 111(a) Filing Fees

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Basic Filing:				
Pages:				
Claims:				
Miscellaneous-Filing:				
Petition:				
Patent-Appeals-and-Interference:				
Post-Allowance-and-Post-Issuance:				
Extension-of-Time:				

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Miscellaneous:				
Submission- Information Disclosure Stmt	1806	1	180	180
		Total in USD ($)		**180**

Electronic Acknowledgement Receipt

EFS ID:	12904076
Application Number:	12137364
International Application Number:	
Confirmation Number:	7377
Title of Invention:	INFUSION SYSTEMS INCLUDING COMPUTER-FACILITATED MAINTENANCE AND/OR OPERATION AND METHODS OF USE
First Named Inventor/Applicant Name:	Stephen E. Hidem
Customer Number:	22859
Filer:	Paul J. LaVanway Jr.
Filer Authorized By:	
Attorney Docket Number:	56782.1.7
Receipt Date:	31-MAY-2012
Filing Date:	11-JUN-2008
Time Stamp:	15:55:24
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	yes
Payment Type	Credit Card
Payment was successfully received in RAM	$180
RAM confirmation Number	2811
Deposit Account	
Authorized User	

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)

1	Information Disclosure Statement (IDS) Form (SB08)	8thSIDS_56782-1-7.pdf	757881 fc67818663152007bf9c2c3db1a7a59b545e403b	no	4
Warnings:					
Information:					
2	Fee Worksheet (SB06)	fee-info.pdf	30548 c07fcd05aaddb8fbe04291d80d40a12e4e9e10b5	no	2
Warnings:					
Information:					
			Total Files Size (in bytes):	788429	

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.

New Applications Under 35 U.S.C. 111
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.

National Stage of an International Application under 35 U.S.C. 371
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.

New International Application Filed with the USPTO as a Receiving Office
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.

22859
Customer Number

Patent Case No.: 56782.1.7

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

First Named Inventor:	STEPHEN E. HIDEM		
Application No.:	12/137,364	Group Art Unit:	3763
Filed:	June 11, 2008	Examiner:	Jenna ZHANG
Title:	INFUSION SYSTEMS INCLUDING COMPUTER-FACILITATED MAINTENANCE AND/OR OPERATION AND METHODS OF USE		

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

INTERVIEW SUMMARY

Applicant thanks the Examiner for her time and the courtesies extended during the telephonic interview conducted on April 26, 2012, and the follow-up interview conducted on May 03, 2012. Examiner Janna Zhang and Applicant's representative Paul J. LaVanway, Jr. (Reg. No. 64,610) were involved in the telephonic interviews. The parties discussed rejected independent claim 1. The parties also discussed Bergner (U.S. Patent No. 4,585,941) and Mozley et al. (U.S. Patent No. 3,714,429), which were previously cited by the Patent Office. No exhibits were introduced or discussed.

Applicant's representative noted distinctions between the independent claim and the previously applied references. For example, Applicant's representative discussed how neither Bergner nor Mozley, whether taken alone or in combination, disclose or suggest a method that includes receiving a display of time lapsed since an elution was completed.

During the course of discussion, the Examiner suggested that Bergner appears to provide a basis for determining a time lapsed since elution was completed and that Mozley appears to teach a display of time lapsed. Applicant's representative respectfully disagreed with the characterization of both Bergner and Mozley advanced by the Examiner. Applicant's representative noted that Bergner does not discuss determining a time lapsed since elution was completed or in any way indicate that such a parameter could be useful. In particular, Applicant's representative noted that even with the data displayed in cited FIGS. 2 and 3 of Bergner and knowledge of the radioactive decay of Rubidium-82, it would not be possible to

determine a time lapsed since elution was completed because the data in FIGS. 2 and 3 of Bergner do not provide any indication how much time has passed since an elution was completed. This is contrary to the characterization of Bergner previously advanced by the Examiner.[1] Moreover, Applicant's representative pointed out that Mozley does not display a time lapsed but rather a time lapse summation picture of radioactivity distribution in a selected plane of a patient.[2]

The Examiner agreed that the pending claims appeared distinguishable over the cited references, although the Examiner indicated that further search and examination of the claims would be required. The Examiner is invited to telephone the undersigned attorney to discuss this application further.

Dated: May 17, 2012

Respectfully submitted,

/Paul J. LaVanway, Jr./

FREDRIKSON & BYRON, P.A.
200 South Sixth Street, Suite 4000
Minneapolis, MN 55402-1425 USA
Telephone: (612) 492-7387
Facsimile: (612) 492-7077

Paul J. LaVanway, Jr.
Registration No. 64,610

Please grant any extension of time necessary for entry; charge any fee due to Deposit Account No. 06-1910.

5138351_1.DOC

[1] *See* Final Office Action dated February 04, 2011, at page 11.
[2] *See* Mozley at col. 10, ll. 10–12.

Electronic Acknowledgement Receipt

EFS ID:	12801747
Application Number:	12137364
International Application Number:	
Confirmation Number:	7377
Title of Invention:	INFUSION SYSTEMS INCLUDING COMPUTER-FACILITATED MAINTENANCE AND/OR OPERATION AND METHODS OF USE
First Named Inventor/Applicant Name:	Stephen E. Hidem
Customer Number:	22859
Filer:	Paul J. LaVanway Jr.
Filer Authorized By:	
Attorney Docket Number:	56782.1.7
Receipt Date:	17-MAY-2012
Filing Date:	11-JUN-2008
Time Stamp:	12:50:27
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	Applicant summary of interview with examiner	56782_1_7IS.pdf	97038 5b4cb373f93953ded765fdfe4518fd1922b5b701	no	2

Warnings:	
Information:	

Total Files Size (in bytes):	97038

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.

New Applications Under 35 U.S.C. 111
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.

National Stage of an International Application under 35 U.S.C. 371
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.

New International Application Filed with the USPTO as a Receiving Office
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.
12/137,364	06/11/2008	Stephen E. Hidem	56782.1.7	7377

22859 7590 05/15/2012

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

EXAMINER	
ZHANG, JENNA	
ART UNIT	PAPER NUMBER
3763	

NOTIFICATION DATE	DELIVERY MODE
05/15/2012	ELECTRONIC

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.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

IP@FREDLAW.COM

Applicant-Initiated Interview Summary	Application No.	Applicant(s)	
	12/137,364	HIDEM ET AL.	
	Examiner	Art Unit	
	JENNA ZHANG	3763	

All participants (applicant, applicant's representative, PTO personnel):

(1) *JENNA ZHANG*. (3)_____.

(2) *PAUL LAVANWAY, JR*. (4)_____.

Date of Interview: *03 May 2012*.

Type: ☒ Telephonic ☐ Video Conference
☐ Personal [copy given to: ☐ applicant ☐ applicant's representative]

Exhibit shown or demonstration conducted: ☐ Yes ☐ No.
If Yes, brief description: _____.

Issues Discussed ☐101 ☐112 ☒102 ☐103 ☐Others
(For each of the checked box(es) above, please describe below the issue and detailed description of the discussion)

Claim(s) discussed: *1*.

Identification of prior art discussed: *Bergner (US Pat. No. 4,585,941)*.

Substance of Interview
(For each issue discussed, provide a detailed description and indicate if agreement was reached. Some topics may include: identification or clarification of a reference or a portion thereof, claim interpretation, proposed amendments, arguments of any applied references etc...)

Discuss the claim limitation of "time lapsed since the elution was completed" and Examiner's interpretation and rejection for this limitation. Applicant's explanation of the prior art and upon further review of Bergner, Examiner agrees that Bergner does not explicitly disclose the step of "receiving from the computer, via the computer intervace a display of time lapsed since the elution was completed" as claimed; however, the Examiner continues to note that Bergner appears to provide the importance of determining time lapsed since elution was completed since Bergner discloses the importance of monitoring radioactivity level in the patient during a treatment period to ensure that repeated dosing or treatment sessions is maintained at a safe level of radioactivity.

Applicant recordation instructions: The formal written reply to the last Office action must include the substance of the interview. (See MPEP section 713.04). If a reply to the last Office action has already been filed, applicant is given a non-extendable period of the longer of one month or thirty days from this interview date, or the mailing date of this interview summary form, whichever is later, to file a statement of the substance of the interview

Examiner recordation instructions: Examiners must summarize the substance of any interview of record. A complete and proper recordation of the substance of an interview should include the items listed in MPEP 713.04 for complete and proper recordation including the identification of the general thrust of each argument or issue discussed, a general indication of any other pertinent matters discussed regarding patentability and the general results or outcome of the interview, to include an indication as to whether or not agreement was reached on the issues raised.

☐ Attachment

/J. Z./	/Nicholas D Lucchesi/
Examiner, Art Unit 3763	Supervisory Patent Examiner, Art Unit 3763

Summary of Record of Interview Requirements

Manual of Patent Examining Procedure (MPEP), Section 713.04, Substance of Interview Must be Made of Record
A complete written statement as to the substance of any face-to-face, video conference, or telephone interview with regard to an application must be made of record in the application whether or not an agreement with the examiner was reached at the interview.

Title 37 Code of Federal Regulations (CFR) § 1.133 Interviews
Paragraph (b)

In every instance where reconsideration is requested in view of an interview with an examiner, a complete written statement of the reasons presented at the interview as warranting favorable action must be filed by the applicant. An interview does not remove the necessity for reply to Office action as specified in §§ 1.111, 1.135. (35 U.S.C. 132)

37 CFR §1.2 Business to be transacted in writing.
All business with the Patent or Trademark Office should be transacted in writing. The personal attendance of applicants or their attorneys or agents at the Patent and Trademark Office is unnecessary. The action of the Patent and Trademark Office will be based exclusively on the written record in the Office. No attention will be paid to any alleged oral promise, stipulation, or understanding in relation to which there is disagreement or doubt.

The action of the Patent and Trademark Office cannot be based exclusively on the written record in the Office if that record is itself incomplete through the failure to record the substance of interviews.

It is the responsibility of the applicant or the attorney or agent to make the substance of an interview of record in the application file, unless the examiner indicates he or she will do so. It is the examiner's responsibility to see that such a record is made and to correct material inaccuracies which bear directly on the question of patentability.

Examiners must complete an Interview Summary Form for each interview held where a matter of substance has been discussed during the interview by checking the appropriate boxes and filling in the blanks. Discussions regarding only procedural matters, directed solely to restriction requirements for which interview recordation is otherwise provided for in Section 812.01 of the Manual of Patent Examining Procedure, or pointing out typographical errors or unreadable script in Office actions or the like, are excluded from the interview recordation procedures below. Where the substance of an interview is completely recorded in an Examiners Amendment, no separate Interview Summary Record is required.

The Interview Summary Form shall be given an appropriate Paper No., placed in the right hand portion of the file, and listed on the "Contents" section of the file wrapper. In a personal interview, a duplicate of the Form is given to the applicant (or attorney or agent) at the conclusion of the interview. In the case of a telephone or video-conference interview, the copy is mailed to the applicant's correspondence address either with or prior to the next official communication. If additional correspondence from the examiner is not likely before an allowance or if other circumstances dictate, the Form should be mailed promptly after the interview rather than with the next official communication.

The Form provides for recordation of the following information:
- Application Number (Series Code and Serial Number)
- Name of applicant
- Name of examiner
- Date of interview
- Type of interview (telephonic, video-conference, or personal)
- Name of participant(s) (applicant, attorney or agent, examiner, other PTO personnel, etc.)
- An indication whether or not an exhibit was shown or a demonstration conducted
- An identification of the specific prior art discussed
- An indication whether an agreement was reached and if so, a description of the general nature of the agreement (may be by attachment of a copy of amendments or claims agreed as being allowable). Note: Agreement as to allowability is tentative and does not restrict further action by the examiner to the contrary.
- The signature of the examiner who conducted the interview (if Form is not an attachment to a signed Office action)

It is desirable that the examiner orally remind the applicant of his or her obligation to record the substance of the interview of each case. It should be noted, however, that the Interview Summary Form will not normally be considered a complete and proper recordation of the interview unless it includes, or is supplemented by the applicant or the examiner to include, all of the applicable items required below concerning the substance of the interview.

A complete and proper recordation of the substance of any interview should include at least the following applicable items:
1) A brief description of the nature of any exhibit shown or any demonstration conducted,
2) an identification of the claims discussed,
3) an identification of the specific prior art discussed,
4) an identification of the principal proposed amendments of a substantive nature discussed, unless these are already described on the Interview Summary Form completed by the Examiner,
5) a brief identification of the general thrust of the principal arguments presented to the examiner,
   (The identification of arguments need not be lengthy or elaborate. A verbatim or highly detailed description of the arguments is not required. The identification of the arguments is sufficient if the general nature or thrust of the principal arguments made to the examiner can be understood in the context of the application file. Of course, the applicant may desire to emphasize and fully describe those arguments which he or she feels were or might be persuasive to the examiner.)
6) a general indication of any other pertinent matters discussed, and
7) if appropriate, the general results or outcome of the interview unless already described in the Interview Summary Form completed by the examiner.

Examiners are expected to carefully review the applicant's record of the substance of an interview. If the record is not complete and accurate, the examiner will give the applicant an extendable one month time period to correct the record.

Examiner to Check for Accuracy

If the claims are allowable for other reasons of record, the examiner should send a letter setting forth the examiner's version of the statement attributed to him or her. If the record is complete and accurate, the examiner should place the indication, "Interview Record OK" on the paper recording the substance of the interview along with the date and the examiner's initials.

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.
12/137,364	06/11/2008	Stephen E. Hidem	56782.1.7	7377

22859 7590 05/11/2012

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

EXAMINER	
ZHANG, JENNA	

ART UNIT	PAPER NUMBER
3763	

NOTIFICATION DATE	DELIVERY MODE
05/11/2012	ELECTRONIC

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.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

IP@FREDLAW.COM

Applicant-Initiated Interview Summary	Application No.	Applicant(s)	
	12/137,364	HIDEM ET AL.	
	Examiner	Art Unit	
	JENNA ZHANG	3763	

All participants (applicant, applicant's representative, PTO personnel):

(1) *JENNA ZHANG*. (3)_____.

(2) *PAUL LAVANWAY, JR.*. (4)_____.

Date of Interview: *26 April 2012*.

Type: ☒ Telephonic ☐ Video Conference
☐ Personal [copy given to: ☐ applicant ☐ applicant's representative]

Exhibit shown or demonstration conducted: ☐ Yes ☐ No.
If Yes, brief description: _____.

Issues Discussed ☐101 ☐112 ☐102 ☒103 ☐Others
(For each of the checked box(es) above, please describe below the issue and detailed description of the discussion)

Claim(s) discussed: *1*.

Identification of prior art discussed: *Bergner (US Pat. No. 4,585,941) and Mozley et al (US Pat. No. 3,714,429)*.

Substance of Interview
(For each issue discussed, provide a detailed description and indicate if agreement was reached. Some topics may include: identification or clarification of a reference or a portion thereof, claim interpretation, proposed amendments, arguments of any applied references etc...)

Discuss the claim limitation of "a display of time lapsed since the elution was completed" and Examiner's interpretation and rejection for this limitation. Discuss the computed time lapse summation picture as taught by Mozley et al with respect to "a display of time lapsed" required by the claims. Applicant noted the difference between the two and further noted that Bergner et al does not teach of "time lapsed since the elution was completed" as required by the claim. Examiner notes that Bergner appears to provide a basis for determining time lapsed since elution was completed. Although applicant's arguments appears to distinguish the instant claims from the current grounds of rejection, further consideration of the Bergner and the art is required.

Applicant recordation instructions: The formal written reply to the last Office action must include the substance of the interview. (See MPEP section 713.04). If a reply to the last Office action has already been filed, applicant is given a non-extendable period of the longer of one month or thirty days from this interview date, or the mailing date of this interview summary form, whichever is later, to file a statement of the substance of the interview

Examiner recordation instructions: Examiners must summarize the substance of any interview of record. A complete and proper recordation of the substance of an interview should include the items listed in MPEP 713.04 for complete and proper recordation including the identification of the general thrust of each argument or issue discussed, a general indication of any other pertinent matters discussed regarding patentability and the general results or outcome of the interview, to include an indication as to whether or not agreement was reached on the issues raised.

☐ Attachment

/J. Z./	/Nicholas D Lucchesi/
Examiner, Art Unit 3763	Supervisory Patent Examiner, Art Unit 3763

Summary of Record of Interview Requirements

Manual of Patent Examining Procedure (MPEP), Section 713.04, Substance of Interview Must be Made of Record
A complete written statement as to the substance of any face-to-face, video conference, or telephone interview with regard to an application must be made of record in the application whether or not an agreement with the examiner was reached at the interview.

Title 37 Code of Federal Regulations (CFR) § 1.133 Interviews
Paragraph (b)

In every instance where reconsideration is requested in view of an interview with an examiner, a complete written statement of the reasons presented at the interview as warranting favorable action must be filed by the applicant. An interview does not remove the necessity for reply to Office action as specified in §§ 1.111, 1.135. (35 U.S.C. 132)

37 CFR §1.2 Business to be transacted in writing.
All business with the Patent or Trademark Office should be transacted in writing. The personal attendance of applicants or their attorneys or agents at the Patent and Trademark Office is unnecessary. The action of the Patent and Trademark Office will be based exclusively on the written record in the Office. No attention will be paid to any alleged oral promise, stipulation, or understanding in relation to which there is disagreement or doubt.

The action of the Patent and Trademark Office cannot be based exclusively on the written record in the Office if that record is itself incomplete through the failure to record the substance of interviews.

It is the responsibility of the applicant or the attorney or agent to make the substance of an interview of record in the application file, unless the examiner indicates he or she will do so. It is the examiner's responsibility to see that such a record is made and to correct material inaccuracies which bear directly on the question of patentability.

Examiners must complete an Interview Summary Form for each interview held where a matter of substance has been discussed during the interview by checking the appropriate boxes and filling in the blanks. Discussions regarding only procedural matters, directed solely to restriction requirements for which interview recordation is otherwise provided for in Section 812.01 of the Manual of Patent Examining Procedure, or pointing out typographical errors or unreadable script in Office actions or the like, are excluded from the interview recordation procedures below. Where the substance of an interview is completely recorded in an Examiners Amendment, no separate Interview Summary Record is required.

The Interview Summary Form shall be given an appropriate Paper No., placed in the right hand portion of the file, and listed on the "Contents" section of the file wrapper. In a personal interview, a duplicate of the Form is given to the applicant (or attorney or agent) at the conclusion of the interview. In the case of a telephone or video-conference interview, the copy is mailed to the applicant's correspondence address either with or prior to the next official communication. If additional correspondence from the examiner is not likely before an allowance or if other circumstances dictate, the Form should be mailed promptly after the interview rather than with the next official communication.

The Form provides for recordation of the following information:
- Application Number (Series Code and Serial Number)
- Name of applicant
- Name of examiner
- Date of interview
- Type of interview (telephonic, video-conference, or personal)
- Name of participant(s) (applicant, attorney or agent, examiner, other PTO personnel, etc.)
- An indication whether or not an exhibit was shown or a demonstration conducted
- An identification of the specific prior art discussed
- An indication whether an agreement was reached and if so, a description of the general nature of the agreement (may be by attachment of a copy of amendments or claims agreed as being allowable). Note: Agreement as to allowability is tentative and does not restrict further action by the examiner to the contrary.
- The signature of the examiner who conducted the interview (if Form is not an attachment to a signed Office action)

It is desirable that the examiner orally remind the applicant of his or her obligation to record the substance of the interview of each case. It should be noted, however, that the Interview Summary Form will not normally be considered a complete and proper recordation of the interview unless it includes, or is supplemented by the applicant or the examiner to include, all of the applicable items required below concerning the substance of the interview.

A complete and proper recordation of the substance of any interview should include at least the following applicable items:
1) A brief description of the nature of any exhibit shown or any demonstration conducted,
2) an identification of the claims discussed,
3) an identification of the specific prior art discussed,
4) an identification of the principal proposed amendments of a substantive nature discussed, unless these are already described on the Interview Summary Form completed by the Examiner,
5) a brief identification of the general thrust of the principal arguments presented to the examiner,
   (The identification of arguments need not be lengthy or elaborate. A verbatim or highly detailed description of the arguments is not required. The identification of the arguments is sufficient if the general nature or thrust of the principal arguments made to the examiner can be understood in the context of the application file. Of course, the applicant may desire to emphasize and fully describe those arguments which he or she feels were or might be persuasive to the examiner.)
6) a general indication of any other pertinent matters discussed, and
7) if appropriate, the general results or outcome of the interview unless already described in the Interview Summary Form completed by the examiner.

Examiners are expected to carefully review the applicant's record of the substance of an interview. If the record is not complete and accurate, the examiner will give the applicant an extendable one month time period to correct the record.

Examiner to Check for Accuracy

If the claims are allowable for other reasons of record, the examiner should send a letter setting forth the examiner's version of the statement attributed to him or her. If the record is complete and accurate, the examiner should place the indication, "Interview Record OK" on the paper recording the substance of the interview along with the date and the examiner's initials.

22859
Customer Number

Patent Case No.: 56782.1.7

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

First Named Inventor:	STEPHEN E. HIDEM		
Application No.:	12/137,364	Group Art Unit:	3763
Filed:	June 11, 2008	Examiner:	Jenna ZHANG
Title:	INFUSION SYSTEMS INCLUDING COMPUTER-FACILITATED MAINTENANCE AND/OR OPERATION AND METHODS OF USE		

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

RESPONSE

Dear Sir:

In response to the Office Action mailed January 20, 2012, the period of response for which runs through April 20, 2012, reconsideration of the application is respectfully requested in view of the following remarks.

Remarks begin on page 2 of this paper.

REMARKS

These Remarks are responsive to the Office Action dated January 20, 2012. Claims 1–24 remain pending, with claims 18–24 withdrawn from consideration. Reconsideration of the application is respectfully requested.

Claim Rejections Under 35 U.S.C. § 103(a)

In the Office Action, claims 1, 2, 9, and 11 were rejected under 35 U.S.C. § 103(a) as purportedly being unpatentable over Bergner (US 4,585,941) in view of Mozley et al. (US 3,714,429, hereinafter "Mozley"). In addition, claims 3–8 were rejected under 35 U.S.C. § 103(a) as purportedly being unpatentable over Bergner and Mozley in further view of Gerhart (US 3,774,036), claim 12 was rejected under 35 U.S.C. § 103(a) as purportedly being unpatentable over Bergner and Mozley in further view of Graves et al. (US 7,163,031, hereinafter "Graves"), and claim 17 was rejected under 35 U.S.C. § 103(a) as purportedly being unpatentable over Bergner and Mozley in further view of Argarwal et al. (US 4,096,859, hereinafter "Argarwal").

Applicant respectfully traverses the rejections. The applied references fail to disclose or suggest the features defined by the claims, and there would have been no apparent reason for modification to arrive at the claimed features.

Independent Claim 1

Independent claim 1 is directed to a method for operating an infusion system. The method includes entering, into a computer, via a computer interface, a command to activate a pump in order to generate an eluate and receiving an indication, from the computer, via the computer interface, that an elution is completed. The method of independent claim 1 also requires receiving from the computer, via the computer interface, a display of time lapsed since the elution was completed.

In support of the rejection of independent claim 1, the Office Action acknowledged that Bergner does not disclose a method that includes receiving from a computer, via a computer interface, a display of time lapsed since an elution was completed.[1] The Office Action then cited

[1] *See* Office Action dated January 20, 2012, at page 3.

Mozley in an attempt to overcome this deficiency.[2] The Office Action alleged that column 7, line 66 through column 10, line 30 of Mozley discloses "receiving and displaying the time elapsed to show the user the radioactivity distribution of the treatment," and that it would have been obvious to modify the technique of Bergner in view of Mozley "such that the radioactivity distribution can be seen by the user."[3] However, the cited portion of Mozley only describes a "time lapse summation picture of radioactivity distribution."[4] The cited passage does not disclose receiving a display of time lapsed since an elution was completed, as per claim 1. Accordingly, the Office Action did not establish that Bergner in view of Mozley discloses each and every feature of claim 1, as required to support a rejection under 35 U.S.C. § 103.

Mozley is directed to a method for tomographic imaging that uses a radioisotopic detector.[5] Mozley explains that the radioisotopic detector includes a scintillation camera with collimator that moves back and forth in a linear motion during operation.[6] Mozley also describes that accumulated radioactive count information can be computed, stored, retrieved, and selectively integrated to produce a tomographic image of radioactive distribution in any selected plane in a field scanned.[7]

Mozley does not, however, disclose or suggest a technique that receives a display of time lapsed since an elution was completed, as per claim 1. The only discussion of time lapse within the cited portion of Mozley is time-lapse summation of radioactive count rate information.[8] For example, Mozley describes that a "computer 70 may be programmed to permit time-lapsed summation of the information obtained in the respective passes during the scanning operation."[9] Mozley further describes that "computing means may then accomplish, by a time lapse summation, the accentuation of the radioactive distribution in any plane located in the scanned field below the surface of the crystal."[10] In particular, Mozley describes the use of time-lapse summation as follows:

> [T]he location of radioactive source in the field may be precisely located and complete tomographic imaging of the radioactivity distribution in the total field

---

[2] *See id.*
[3] *Id.* at page 4.
[4] Mozley at col. 10, ll. 10–12.
[5] *See id.* at Abstract.
[6] *See id.*
[7] *See id.*
[8] *See id.* at Abstract, col. 9, ll. 42–45.
[9] *Id.* at col. 9, ll. 42–45.
[10] *Id.* at col. 7, ll. 56–59.

> may be obtained by suitable summing of count rate information collected by each of the collimator holes during the entire scan.[11]

The cited portion of Mozley concludes that "a computed time lapse summation picture of radioactivity distribution in [a] selected plane may thus be presented on the face of the cathode ray tube 101. In the computed picture, radiation actually originating from the selected plane which will be located a distance corresponding to the chosen 1 value below the camera will be displayed in its true position."[12]

Thus, unlike claim 1 which requires receiving a display of time lapsed since an elution was completed, the time lapse in Mozley is not since an elution was completed. Rather, the time lapse in Mozley is time lapsed during passes in a scanning operation.[13] Mozley does not in anyway disclose or suggest that the time lapse described in the reference is since an elution was completed. Indeed, Mozley does not even describe generating an eluant or completing an elution.

Nor is the time lapse described by Mozley in anyway displayed. As indicated above, Mozley uses time lapse summation information to generate a picture of radioactivity distribution. While Mozley explains that this radioactivty distribution picture can be presented, the cited portion of Mozley does not disclose or suggest displaying the time lapse itself. This is contrary to claim 1, which recites "receiving a display of time lapsed since an elution was completed."

Accordingly, because Mozley does not disclose receiving a display of time lapsed since an elution was completed, and because the Office Action conceded that Bergner does not disclose this feature of independent claim 1, Bergner in view of Mozley likewise does not disclose receiving a display of time lapsed since an elution was completed. For at least this reason, the Office Action failed to establish a *prima facie* case of obviousness of independent claim 1.

Dependent Claims

Claims 2–17 depend from independent claim 1 and are patentable for at least the reasons given above with respect to the independent claim, as well as upon additional patentable features and elements claimed in the dependent claims but not explicitly discussed herein. None of the

[11] *Id.* at col. 7, ll. 59–65.
[12] Mozley at col. 10, ll. 10–17.
[13] *See, e.g.*, *id.* at col. 9, ll. 42–45.

other references cited in the Office Action overcome the deficiencies evident in Bergner and Mozley, as set for above with respect to independent claim 1.

For example, Bergner in view of Mozley does not disclose or suggest a method that includes entering, into a computer, via a computer interface, a volume of eluant contained in a reservoir, prior to the elution, as per claim 2. In support of the rejection of claim 2, the Office Action cited column 4, line 4 through column 5, line 32 of Bergner as allegedly disclosing this feature of claim 2.[14] This portion of Bergner generally describes different switches for an infusion pump controller 60 and dosimetry controller 62. For example, Bergner describes that the infusion pump controller 60 includes switches 74 to select the total volume to be eluted and a flow rate control 80 to set the pulse rate of a stepping motor.[15] Bergner continues to describe that the dosimetry controller 62 has a first set of thumbwheel switches 94 used to set the volume to be infused into the patient and thumbwheel switches 98 used to set the total dose (mCi) which is to be infused into the patient.[16] The cited portion of Bergner does not describe entering a volume of eluant contained in a reservoir, as per claim 2.

Applicant notes that Bergner is a complex reference and the Office Action cited a large portion of the reference as allegedly disclosing the features of claim 2—features Applicant did not locate in the cited passage. Applicant respectfully requests that if any rejection of claim 2 based on Bergner is maintained that the Examiner provide a subsequent Non-Final Office Action designating the particular portion of the reference relied upon to support the rejection.[17]

CONCLUSION

It is submitted that all claims in this application are in condition for allowance. Applicant respectfully requests reconsideration and prompt allowance of all pending claims.

In view of the fundamental differences identified above, Applicant reserves further comment concerning the additional features set forth in the claims. However, Applicant does not acquiesce in the propriety of the Office Action's application or interpretation of the references

[14] *See* Office Action dated January 20, 2012, at page 4.
[15] *See* Bergner at col. 4, ll. 30–40.
[16] *See id.* at col. 5, ll. 3–12.
[17] 37 C.F.R. § 1.104(c)(2) ("When a reference is complex or shows or describes inventions other than that claimed by the applicant, the particular part relied on must be designated as nearly as practicable. The pertinence of each reference, if not apparent, must be clearly explained and each rejected claim specified.").

with respect to the claims, and reserves the right to present additional arguments in any further prosecution of this application.

The Commissioner is authorized to charge any deficiencies and credit any overpayments to Deposit Account No. 06-1910. The Examiner is invited to telephone the undersigned attorney to discuss this application.

Dated: April 20, 2012

Respectfully submitted,

/Paul J. LaVanway, Jr./

FREDRIKSON & BYRON, P.A.
200 South Sixth Street, Suite 4000
Minneapolis, MN 55402-1425 USA
Telephone: (612) 492-7387
Facsimile: (612) 492-7077

Paul J. LaVanway, Jr.
Registration No. 64,610

Please grant any extension of time necessary for entry; charge any fee due to Deposit Account No. 06-1910.

5094135_1.DOC

Electronic Acknowledgement Receipt

EFS ID:	12591365
Application Number:	12137364
International Application Number:	
Confirmation Number:	7377
Title of Invention:	INFUSION SYSTEMS INCLUDING COMPUTER-FACILITATED MAINTENANCE AND/OR OPERATION AND METHODS OF USE
First Named Inventor/Applicant Name:	Stephen E. Hidem
Customer Number:	22859
Filer:	Paul J. LaVanway Jr.
Filer Authorized By:	
Attorney Docket Number:	56782.1.7
Receipt Date:	20-APR-2012
Filing Date:	11-JUN-2008
Time Stamp:	14:39:46
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	Applicant Arguments/Remarks Made in an Amendment	56782_1_7RESPONSE.pdf	136384 1bf4051dca912e68395d02c32ba9362e3eb2c350	no	6

Warnings:	
Information:	

Total Files Size (in bytes):	136384

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.

New Applications Under 35 U.S.C. 111

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.

National Stage of an International Application under 35 U.S.C. 371

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.

New International Application Filed with the USPTO as a Receiving Office

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.
12/137,364	06/11/2008	Stephen E. Hidem	56782.1.7	7377

22859 7590 01/20/2012

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

EXAMINER	
ZHANG, JENNA	

ART UNIT	PAPER NUMBER
3763	

NOTIFICATION DATE	DELIVERY MODE
01/20/2012	ELECTRONIC

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.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

IP@FREDLAW.COM

Office Action Summary	Application No.	Applicant(s)	
	12/137,364	HIDEM 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 *3* 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 *28 April 2011*.

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

3)☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.

4)☐ 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

5)☒ Claim(s) *1-17* is/are pending in the application.

5a) Of the above claim(s) _____ is/are withdrawn from consideration.

6)☐ Claim(s) _____ is/are allowed.

7)☒ Claim(s) *1-17* is/are rejected.

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

9)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

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

11)☐ 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).

12)☐ 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

13)☐ 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 *12/16/2011*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. In response to the Amendments filed on April 28, 2011, claim 1 is amended. Currently, claims 1-17 are still pending.

Continued Examination Under 37 CFR 1.114

2. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on April 1, 2011 has been entered.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.

4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

4. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

5. **Claims 1, 2, 9, and 11** are rejected under 35 U.S.C. 103(a) as being unpatentable over Bergner (US Pat. No. 4,585,941) in view of Mozley et al (US Pat. No. 3,714,429).

Regarding **claim 1**, Bergner teaches a method for operating an infusion system, the system comprising: an eluant reservoir, a pump (64) coupled to the reservoir, an infusion tubing circuit (Fig. 1), a radioisotope generator (28), an activity detector (58), a waste bottle (42) and a computer (60, 62) including a computer interface, the infusion tubing circuit including an eluant line coupled to the pump and to the generator, a waste line coupled to the generator and to the waste bottle, and a patient line coupled to the generator (col. 3, line 23 until col. 4, line 53; Fig. 1), the method comprising:

entering, into the computer, via the computer interface, a command to activate the pump in order to generate an eluate from a portion of a volume of eluant pumped through the generator, via an elution within the generator;

receiving an indication, from the computer, via the computer interface, that the elution is completed, when the pump has completed pumping the portion of the volume of eluant; and

receiving an indication, from the computer, via the computer interface, of time lapsed since the elution was completed (col. 4, line 7 until col. 6, line 19).

Although Bergner discloses that an indication received, Bergner does not teach that a display of time is received form the computer as required by the instant claims. It is noted, however, that Mozley et al teaches that receiving and displaying the time elapsed to show the user the radioactivity distribution of the treatment (col. 7, line 66 until col. 10, line 30). Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to modify the method of operating an infusion system of Bergner with the feature of receiving from the computer, via the computer interface, a display of time lapsed since the elution was completed as taught by Mozley et al such that the radioactivity distribution can be seen by the user.

Regarding **claim 2**, Bergner teaches entering, into the computer (60, 62), via a computer interface, the volume of eluant contained in the reservoir, prior to the elution; and receiving, from the computer interface, an indication of a volume of eluant in the reservoir, based upon tracking the portion of the volume of eluant that is pumped from the reservoir (col. 4, line 4 until col. 5, line 32).

Regarding **claim 9**, Bergner teaches coupling the patient line to a shielded test vial in order to collect a sample of the eluate from the patient line during the elution; measuring an activity of the sample; and entering into the computer, via the computer interface, the measured activity of the sample and a time between completion of the elution and measuring of the activity, so that the computer may calculate a calibration coefficient for the infusion system based on the measured activity and an activity of the eluate detected, during elution, by the activity detector of the system (col. 6, line 21 until col. 9, line 48).

Regarding **claim 10**, Bergner teaches selecting a calibration procedure of the computer, via the computer interface, prior to entering the command to activate the pump (col. 4, line 26 until col. 9, line 48) but does not teach that the step of coupling the patient line to the shielded test vial is instructed by the computer interface, after selecting the calibration procedure. However, it would have been obvious to one of ordinary skill in the art at the time of the invention to modify the device of Bergner so that the controllers 60, 62 would notify the user to perform the step of coupling the patient line to the shielded test vial for an automated reminder to the user to increase the safety of the treatment.

Regarding **claim 11**, Bergner teaches purging air from the patient line; coupling the patient line to a patient, after purging, in order to inject a dose of the eluate to the patient from the patient line; and receiving a report from the computer, upon completion of the elution, the report including a patient identification number and at least one

quantification of the dose of the eluate (col. 3, line 63 until col. 4, line 6 and lines 36-53; col. 6, lines 1-19).

Regarding **claims 13-16**, Bergner teaches

receiving an indication, from the system, that the eluate is being diverted, from the generator, through the waste line of the infusion tubing circuit, when the pump is activated; and receiving an indication, from the system, that the eluate is being diverted from the generator, through the patient line of the infusion tubing circuit, when the pump is activated (col. 5, lines 8-24);

receiving an indication from the system that a peak bolus of radioactivity has been detected, in the eluate, by the activity detector (col. 7, line 1 until col. 9, line 47); and

wherein the system further comprises a light projector (104, 96, 100, 108; col. 9, line 49 until col. 10, line 11);

Although Bergner teaches the use of flashing and solid light projections from the light projector (106, 108) as alerting notifications (col. 11, line 46 until col. 12, line 29), Bergner does not teach that the indication that the eluate is being diverted through the waste line is a flashing light projection, the indication that the eluate is being diverted through the patient line comprises a solid light projection from the light projector, and the indication that the peak bolus of radioactivity has been detected comprises a flashing light from the light projector. However, it would have been obvious to one of ordinary skill in the art at the time of the invention to modify the device of Bergner with the use of flashing and solid light projections as the indication that the eluate is being

diverted through the waste line is a flashing light projection, the indication that the eluate is being diverted through the patient line comprises a solid light projection, and the indication that the peak bolus of radioactivity has been detected comprises a flashing light from the light projector, to provide a notification that alerts the user.

6. **Claims 3-8** are rejected under 35 U.S.C. 103(a) as being unpatentable over Bergner (US Pat. No. 4,585,941) in view of Mozley et al (US Pat. No. 3,714,429) further in view of Gerhart (US Pat. No. 3,774,036).

Regarding **claim 3**, Bergner teaches coupling the patient line of the infusion tubing circuit to a first shielded test vial, in order to collect a first sample of the eluate from the patient line during the elution; measuring an activity of the first sample; and entering into the computer, via the computer interface, the measured activity of the first sample and a time between completion of the elution and the measuring of the activity (col. 3, line 55 until col. 5, line 68). However, Bergner does not teach method step of the computer calculating a breakthrough of the generator as required by the amended instant claim. It is noted that Gerhart teaches that breakthrough testing is performed to ensure the safety of a radioactive treatment dosage (col. 2, lines 27-39). Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to modify the method of Bergner with a breakthrough test procedure as taught by Gerhart to ensure the safety level of the treatment. Furthermore, it would have been obvious to one of ordinary skill in the art at the time of the invention to modify the device of Bergner so that the controllers 60, 62 perform the breakthrough test to calculate a breakthrough

of the generator since the controllers 60, 62 controls the operations of the device of Bergner.

Regarding **claim 4**, Bergner does not teach selecting a breakthrough test procedure of the computer, via the computer interface, prior to entering the command to activate the pump; and wherein coupling the patient line to the first shielded test vial is instructed by the computer interface, after selecting the breakthrough test. However, as explained for claim 3 above, Bergner in view of Gerhart teaches performing a breakthrough test procedure prior to entering the command to activate the pump to ensure the safety level of the treatment. Furthermore, it would have been obvious to one of ordinary skill in the art at the time of the invention to modify the device of Bergner so that the controllers 60, 62 would notify the user to perform the step of coupling the patient line to the shielded test vial for an automated reminder to the user to increase the safety of the treatment. Hence, the modified method of Bergner in view of Gerhart discloses selecting a breakthrough test procedure of the computer, via the computer interface, prior to entering the command to activate the pump; and wherein coupling the patient line to the first shielded test vial is instructed by the computer interface, after selecting the breakthrough test.

Regarding **claim 6**, the modified method of Bergner further teaches selecting a calibration procedure of the computer, via the computer interface, prior to entering the command to activate the pump for the second time; and wherein coupling the first new patient line to the second shielded test vial is instructed by the computer interface, after

selecting the calibration procedure, as set forth for claim 10 (col. 6, line 21 until col. 9, line 48).

Regarding **claims 5 and 7**, Bergner further teaches repeating the steps of claim 1, wherein the pump is activated a second time and a second elution takes place, in order to fill the second vial with a second sample of the eluate from the first new patient line; measuring an activity of the second sample; and entering into the computer, via the computer interface, the measured activity of the second sample and a time between completion of the second elution and the measuring of the activity of the second sample, so that the computer may calculate a calibration coefficient for the infusion system based on the measured activity of the second sample and an activity of the eluate detected, during the second elution, by the activity detector of the system. Bergner also teaches purging air from the second patient line; and repeating the steps of claim 1, wherein the pump is activated a third time and a third elution takes place, in order to inject a dose of the eluate to the patient from the second patient line (col. 6, line 21 until col. 9, line 48).

Regarding **claim 8**, Bergner further teaches receiving a report from the computer, upon completion of the third elution, the report including a patient identification number and at least one quantification of the dose of the eluate (col. 5, lines 41-68 and col. 9, line 49 until col. 10, line 11).

7. **Claim 12** is rejected under 35 U.S.C. 103(a) as being unpatentable over Bergner (US Pat. No. 4,585,941) in view of Mozley et al (US Pat. No. 3,714,429) further in view of Graves et al (US Pat. No. 7,163,031 B2).

Regarding **claim 12**, Bergner teaches the use of displays but does not teach a touch-activated display screen. However, it is noted that Graves et al teaches the use of a touch screen electronic display screen for inputting and outputting into a computer for a radiopharmaceutical delivery device (col. 4, line 53 until col. 5, line 2). Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to modify the device of Bergner with using a system that has a touch-activated display screen as disclosed by Graves et al to consolidate the number of components required for inputting and outputting commands and notifications in an infusion device.

8. **Claim 17** is rejected under 35 U.S.C. 103(a) as being unpatentable over Bergner (US Pat. No. 4,585,941) in view of Mozley et al (US Pat. No. 3,714,429) further in view of Agarwal et al (US Pat. No. 4,096,859).

Regarding **claim 17**, Bergner teaches the use of a waste bottle and tracking the waste level to determine the trigger point (col. 10, lines 12-68) but does not explicitly teach entering, into the computer, via the computer interface, a command to set a waste bottle level indicator to zero, when the waste bottle is empty and prior to entering the command to activate the pump; and receiving, from the computer, via the computer interface, an indication that the waste bottle needs to be emptied, based upon the computer tracking a volume of the eluate that is diverted, from the generator, through

the waste line of the infusion tubing circuit. However, Agarwal et al teaches a medical delivery device with a waste container in which a controller tracks the waste level to alert the user to empty the waste container (col. 5, line 38 until col. 6, line 36). It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the method of Bergner with the steps of setting initial waste bottle level to zero when the bottle is empty and tracking the waste bottle level so that an alert is given to the user that the waste bottle is full and needs to be emptied as taught by Agarwal et al, to prevent overflowing of waste from the waste bottle.

It is noted that the modified method of Bergner and Agarwal et al teaches entering, into the computer, via the computer interface, a command to set a waste bottle level indicator to zero, when the waste bottle is empty and prior to entering the command to activate the pump; and receiving, from the computer, via the computer interface, an indication that the waste bottle needs to be emptied, based upon the computer tracking a volume of the eluate that is diverted, from the generator, through the waste line of the infusion tubing circuit

Response to Arguments

9. Applicant's arguments filed April 28, 2011 have been fully considered but are moot in view of the new ground(s) of rejection.

Conclusion

10. 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
12/19/11

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

Notice of References Cited	Application/Control No. 12/137,364	Applicant(s)/Patent Under Reexamination HIDEM ET AL.	
	Examiner JENNA ZHANG	Art Unit 3763	Page 1 of 1

U.S. PATENT DOCUMENTS

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Name	Classification
*	A	US-4,585,941	04-1986	Bergner, Brian C.	250/363.02
*	B	US-3,774,036	11-1973	Gerhart, James M.	252/645
*	C	US-4,096,859	06-1978	Agarwal et al.	604/28
*	D	US-7,163,031 B2	01-2007	Graves et al.	141/9
*	E	US-3,714,429	01-1973	Mozley et al.	250/363.04
	F	US-			
	G	US-			
	H	US-			
	I	US-			
	J	US-			
	K	US-			
	L	US-			
	M	US-			

FOREIGN PATENT DOCUMENTS

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Country	Name	Classification
	N					
	O					
	P					
	Q					
	R					
	S					
	T					

NON-PATENT DOCUMENTS

*		Include as applicable: Author, Title Date, Publisher, Edition or Volume, Pertinent Pages)
	U	
	V	
	W	
	X	

*A copy of this reference is not being furnished with this Office action. (See MPEP § 707.05(a).)
Dates in MM-YYYY format are publication dates. Classifications may be US or foreign.

Search Notes	Application/Control No.	Applicant(s)/Patent Under Reexamination
	12137364	HIDEM ET AL.
	Examiner	Art Unit
	JENNA ZHANG	3763

SEARCHED

Class	Subclass	Date	Examiner
604	236, and 65-67 with text	9/27/2010	JZ
312	209	9/27/2010	JZ
600	5	9/27/2010	JZ
600	4, and 600/431, 1-8, and 301 with text	9/29/2010	JZ

SEARCH NOTES

Search Notes	Date	Examiner
Inventor Search	9/27/2010	JZ
Assignee Search	9/27/2010	JZ
Consulted Chris Koharski	9/28/2010	JZ
EAST Search	9/27-29/2010	JZ
Updated EAST Search	1/31/2011	JZ
Updated EAST Search	12/19/2011	JZ

INTERFERENCE SEARCH

Class	Subclass	Date	Examiner

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Not for submission under 37 CFR 1.99)

Application Number	12137364
Filing Date	2008-06-11
First Named Inventor	STEPHEN E. HIDEM
Art Unit	3763
Examiner Name	ZHANG, JENNA
Attorney Docket Number	56782.1.7

U.S.PATENTS Remove

Examiner Initial*	Cite No	Patent Number	Kind Code[1]	Issue Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1	3483867		1969-12-16	Markovitz	
	2	4336036		1982-06-22	Leeke	
	3	4466888		1984-08-21	Verkaart	
	4	4623102		1986-11-18	Hough, Jr.	
	5	4769008		1988-09-06	Hessel	
	6	4994056		1991-02-19	Ikeda	
	7	5702115		1997-12-30	Pool	
	8	5765842		1998-06-16	Phaneuf	

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /J.Z./

Receipt date: 12/16/2011	Application Number	12137364	12137364 - GAU: 3763
INFORMATION DISCLOSURE STATEMENT BY APPLICANT (**Not for submission under 37 CFR 1.99)**	Filing Date	2008-06-11	
	First Named Inventor	STEPHEN E. HIDEM	
	Art Unit	3763	
	Examiner Name	ZHANG, JENNA	
	Attorney Docket Number	56782.1.7	

	9	5827429		1998-10-27	Ruschke	
	10	6347711		2002-02-19	Goebel	
	11	6558125		2003-05-06	Futterknecht	
	12	7612999		2009-11-03	Clark	
	13	7862534		2011-01-04	Quirico	

If you wish to add additional U.S. Patent citation information please click the Add button. Add

U.S.PATENT APPLICATION PUBLICATIONS Remove

Examiner Initial*	Cite No	Publication Number	Kind Code[1]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1	20040104160		2004-06-03	Scagliarini	
	2	20060015056		2006-01-19	Ellingboe	
	3	20090309466		2009-12-17	Quirico	
	4	20090318745		2009-12-24	Quirico	

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /J.Z./

Receipt date: 12/16/2011	Application Number	12137364	12137364 - GAU: 3763
INFORMATION DISCLOSURE STATEMENT BY APPLICANT (**Not for submission under 37 CFR 1.99)**	Filing Date	2008-06-11	
	First Named Inventor	STEPHEN E. HIDEM	
	Art Unit	3763	
	Examiner Name	ZHANG, JENNA	
	Attorney Docket Number	56782.1.7	

	5	20100125243		2010-05-20	Balestracci	
	6	20100270226		2010-10-28	Balestracci	
	7	20100312039		2010-12-09	Quirico	
	8	20110071392		2011-03-24	Quirico	
	9	20110172524		2011-07-14	Hidem	
	10	20060151048		2005-12-27	Tochon-Danguy	

If you wish to add additional U.S. Published Application citation information please click the Add button. Add

FOREIGN PATENT DOCUMENTS Remove

Examiner Initial*	Cite No	Foreign Document Number[3]	Country Code[2] i	Kind Code[4]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear	T[5]
	1	0919249	EP		1999-06-02	NISSHO KK		☐
	2	1421960	EP		2004-05-26	GVS S P A		☐
	3	2009152320	WO		2009-12-17	BRACCO DIAGNOSTICS INC		☐

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /J.Z./

Receipt date: 12/16/2011	Application Number	12137364	12137364 - GAU: 3763
INFORMATION DISCLOSURE STATEMENT BY APPLICANT (**Not for submission under 37 CFR 1.99)**	Filing Date	2008-06-11	
	First Named Inventor	STEPHEN E. HIDEM	
	Art Unit	3763	
	Examiner Name	ZHANG, JENNA	
	Attorney Docket Number	56782.1.7	

	4	2004059661	WO		2004-07-15	LYNNTECH INC		☐

If you wish to add additional Foreign Patent Document citation information please click the Add button Add

NON-PATENT LITERATURE DOCUMENTS Remove

Examiner Initials*	Cite No	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc), date, pages(s), volume-issue number(s), publisher, city and/or country where published.	T[5]
	1	Brochure, "IV and Liquid Filters: Speedflow Adult 0.2 um Positive", http://www.gvs.it/flex/FixedPages/UK/LiquidFilters.php/L/UK/ID/Speedflow%20Adjust%.... taken off of web on 11/11/2008	☐
	2	International Search Report and Written Opinion, dated 01-04-2010 for PCT Application No. PCT/US2009/063788, 13 pages	☐

If you wish to add additional non-patent literature document citation information please click the Add button Add

EXAMINER SIGNATURE

Examiner Signature	/Jenna Zhang/	Date Considered	12/19/2011

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through a citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

[1] See Kind Codes of USPTO Patent Documents at www.USPTO.GOV or MPEP 901.04. [2] Enter office that issued the document, by the two-letter code (WIPO Standard ST.3). [3] For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. [4] Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. [5] Applicant is to place a check mark here if English language translation is attached.

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /J.Z./

EAST Search History

EAST Search History (Prior Art)

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
S35	22	("4401108" | "4409966" | "4472403" | "4562829" | "4585009" | "4883459" | "5383858" | "5472403" | "5514071" | "5520653" | "5918443" | "5927351" | "5947890" | "6267717" | "6450936" | "6471674" | "6520930").PN. OR ("6767319").URPN.	US-PGPUB; USPAT; USOCR	OR	ON	2010/05/06 15:44
S36	23	("3866608" | "3918453" | "4781707" | "5055198" | "5378227" | "5407425"). PN. OR ("5656027"). URPN.	US-PGPUB; USPAT; USOCR	OR	ON	2010/05/06 15:54
S37	91	("2804075" | "3896733" | "3965896" | "3993067" | "4006745" | "4014329" | "4033345" | "4047526" | "4631050" | "4744785" | "4772256" | "4796644" | "4798578" | "4867738" | "4874359" | "4886487" | "4898572" | "4976682"). PN. OR ("5055198"). URPN.	US-PGPUB; USPAT; USOCR	OR	ON	2010/05/06 15:57
S50	10	("3996017" | "4911807" | "5193990" | "5260028" | "5372695" | "5989423" | "6325775" | "6582386" | "6605223" | "6712963"). PN. OR ("7001513"). URPN.	US-PGPUB; USPAT; USOCR	OR	ON	2010/05/06 17:31
S78	2	(stephen near3 hidem). in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2010/09/27 19:21
S79	1	(aaron near3 fontaine). in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2010/09/27 19:21

S80	1	(janet near3 gelbach).in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2010/09/27 19:21
S81	74	(patrick near3 mcdonald).in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2010/09/27 19:21
S82	1	(kathryn near3 hunter).in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2010/09/27 19:22
S83	75	(S78 S79 S80 S81 S82)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2010/09/27 19:22
S84	1	(S78 S79 S80 S81 S82) and (radioisotope radioactive PET (positron adj emission adj tomography) radiation rubidium strontium)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2010/09/27 19:23
S85	46	("20030004463" | "20050278066" | "20070213848" | "20070140958" | "20070232980" | "20070282263" | "20080093564" | "20080242915" | "20080071219" | "20080166292" | "20090312635" | "3710118" | "3774036" | "3997784" | "4286169" | "4562829" | "4585009" | "4585941" | "4625118" | "4679142" | "4755679" | "4853546" | "5590648" | "5039863" | "5258906" | "5274239" | "5475232" | "5485831" | "5739508" | "5840026" | "5885216" | "6157036" | "6442418" | "6626862" | "6767319" | "6870175" | "6901283" | "6908598" | "7163031" |	US-PGPUB; USPAT; USOCR	OR	ON	2010/09/27 19:35

		"7169135" | "7204797" | "7256888" | "7413123" | "7476377" | "7504646").PN.				
S86	128	(BRACCO near3 DIAGNOSTICS).as.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2010/09/27 19:37
S87	33	S86 and (radioisotope radioactive PET (positron adj emission adj tomography) radiation rubidium strontium)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2010/09/27 19:37
S88	68	(S87 S85) and (command $3 activat$3 enter$3 receiv$3 indicat$3 tim$3 select$3 measur$4 test$3 purg$3 calibrat$3)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2010/09/27 19:41
S89	147150	("128" "600" "604" "606" "607" "623" "312" "345" "700" "702" "705" "715" "417" "514").clas. and (radioisotope radioactive PET (positron adj emission adj tomography) radiation rubidium strontium)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2010/09/27 19:44
S90	145900	S89 and (command$3 activat$3 enter$3 receiv $3 indicat$3 tim$3 select $3 measur$4 test$3 purg $3 calibrat$3)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2010/09/27 19:44
S91	149	S89 and (command$3 activat$3 enter$3 receiv $3 indicat$3 tim$3 select $3 measur$4 test$3 purg $3 calibrat$3)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	AND	ON	2010/09/27 19:44
S92	282	S89 and (command$3 activat$3 enter$3 receiv $3 indicat$3 tim$3 select $3 measur$4 test$3 purg $3 (calibrat$3 or initial$3 or initiat$3))	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	AND	ON	2010/09/27 19:45

S93	73	S89 and (command$3 enter$3 receiv$3 indicat $3 tim$3 (select$3 or choos$3) measur$4 test $3 ((purg$3 or remov$3 or releas$3) near3 (air gas)) (calibrat$3 or initial $3 or activat$3 or initiat $3))	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	AND	ON	2010/09/27 19:46
S94	961	312/209.ccls.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2010/09/27 19:54
S95	300	604/236.ccls.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2010/09/27 19:54
S96	301	604/65,66,67.ccls. and (radioisotope radioactive PET (positron adj emission adj tomography) radiation rubidium strontium)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2010/09/27 19:54
S97	87	600/5.ccls.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2010/09/27 19:55
S98	174	(radio$1pharmaceutical $1) and "604".clas.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2010/09/27 19:56
S99	11522	"604".clas. and (radioisotope radioactive PET (positron adj emission adj tomography) radiation rubidium strontium radio $1pharmaceutic$4)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2010/09/28 10:38

S101	23	S99 and (command$3 enter$3 receiv$3 indicat $3 tim$3 (select$3 or choos$3) measur$4 test $3 ((purg$3 or remov$3 or releas$3) near3 (air gas)) (calibrat$3 or initial $3 or activat$3 or initiat $3))	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	AND	ON	2010/09/28 10:39
S103	23	S99 and (command$3 enter$3 receiv$3 (indicat $3 or flash$3 or blink$3 or light) tim$3 (select$3 or choos$3) measur$4 test$3 ((purg$3 or remov $3 or releas$3) near3 (air gas)) (calibrat$3 or initial $3 or activat$3 or initiat $3))	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	AND	ON	2010/09/28 12:28
S104	1786	"604".clas. and (radioisotope radioactive radio$1pharmaceutic$4)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2010/09/28 12:29
S105	0	S104 and (command$3 enter$3 receiv$3 (indicat $3 or flash$3 or blink$3 or light) tim$3 (select$3 or choos$3) measur$4 test$3 ((purg$3 or remov $3 or releas$3) near3 (air gas)) (calibrat$3 or initial $3 or activat$3 or initiat $3))	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	AND	ON	2010/09/28 12:29
S106	133999	(radioisotope radioactive radio$1pharmaceutic$4) and (medica$4 medicin$2 therapy therapeutic$5 diagnos$4 drug)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2010/09/28 12:31
S110	5	("20060151048" "20030216609" "20030004463" "20050238576" "2010030009" "20080177126").pn.	US-PGPUB; USPAT; USOCR	OR	ON	2010/09/28 12:47
S111	8	("20080242915" "6773673" "4562829" "20080093564" "20080224065" "20030216609" "20030004463" "20050238576").pn.	US-PGPUB; USPAT; USOCR	OR	ON	2010/09/28 12:50

S112	4	("4585941" "4585009" "20070140958" "20070213848").pn.	US-PGPUB; USPAT; USOCR	OR	ON	2010/09/28 12:52
S113	14	S110 S111 S112	US-PGPUB; USPAT; USOCR	OR	ON	2010/09/28 12:53
S114	6	("5168901" | "5223434" | "5326532" | "5468355" | "5482865" | "5514071").PN. OR ("6773673").URPN.	US-PGPUB; USPAT; USOCR	OR	ON	2010/09/28 13:12
S115	42	("3528407" | "3827427" | "4091287").PN. OR ("4585941").URPN.	US-PGPUB; USPAT; USOCR	OR	ON	2010/09/28 13:12
S116	30	("4006736").PN. OR ("4585009").URPN.	US-PGPUB; USPAT; USOCR	OR	ON	2010/09/28 13:12
S117	14	("4202345").PN. OR ("4562829").URPN.	US-PGPUB; USPAT; USOCR	OR	ON	2010/09/28 13:12
S118	77	S114 S115 S116 S117	US-PGPUB; USPAT; USOCR	OR	ON	2010/09/28 13:12
S120	5	("20060151048" "20030216609" "20030004463" "20050238576" "2010030009" "20080177126").pn.	US-PGPUB; USPAT; USOCR	OR	ON	2010/09/28 17:24
S121	8	("20080242915" "6773673" "4562829" "20080093564" "20080224065" "20030216609" "20030004463" "20050238576").pn.	US-PGPUB; USPAT; USOCR	OR	ON	2010/09/28 17:24
S122	4	("4585941" "4585009" "20070140958" "20070213848").pn.	US-PGPUB; USPAT; USOCR	OR	ON	2010/09/28 17:24
S123	14	S120 S121 S122	US-PGPUB; USPAT; USOCR	OR	ON	2010/09/28 17:24
S125	14	S123 and (command$3 enter$3 receiv$3 (indicat $3 flash$3 blink$3 light) tim$3 (select$3 or choos $3) measur$4 test$3 ((purg$3 remov$3 releas $3) near3 (air gas)) (calibrat$3 initial$3 activat $3 initiat$3))	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2010/09/28 17:26
S127	6	("5168901" | "5223434" | "5326532" | "5468355" | "5482865" | "5514071").PN. OR ("6773673").URPN.	US-PGPUB; USPAT; USOCR	OR	ON	2010/09/28 17:49

S128	42	("3528407" | "3827427" | "4091287").PN. OR ("4585941").URPN.	US-PGPUB; USPAT; USOCR	OR	ON	2010/09/28 17:49
S129	30	("4006736").PN. OR ("4585009").URPN.	US-PGPUB; USPAT; USOCR	OR	ON	2010/09/28 17:49
S130	14	("4202345").PN. OR ("4562829").URPN.	US-PGPUB; USPAT; USOCR	OR	ON	2010/09/28 17:49
S131	77	S127 S128 S129 S130	US-PGPUB; USPAT; USOCR	OR	ON	2010/09/28 17:49
S133	76	S131 and (command$3 enter$3 receiv$3 (indicat $3 flash$3 blink$3 light) tim$3 (select$3 or choos $3) measur$4 test$3 ((purg$3 remov$3 releas $3) near3 (air gas)) (calibrat$3 initial$3 activat $3 initiat$3))	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2010/09/28 17:50
S134	54	S133 and (radioisotope radioactive PET (positron adj emission adj tomography) radiation rubidium strontium)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2010/09/28 17:50
S135	11	(S131 S123) and (elution eluate eluant)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2010/09/28 17:52
S136	1272	600/431.ccls.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2010/09/28 18:16
S137	772	S136 and (radioisotope radioactive PET (positron adj emission adj tomography) radiation rubidium strontium)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2010/09/28 18:16
S138	141	600/4.ccls.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2010/09/29 19:06

S139	3552	600/1-8,301.ccls. and (command$3 enter$3 receiv$3 (indicat$3 flash $3 blink$3 light) tim$3 (select$3 or choos$3) measur$4 test$3 ((purg $3 remov$3 releas$3) near3 (air gas)) (calibrat $3 initial$3 activat$3 initiat$3))	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2010/09/29 19:08
S140	2	600/1-8,301.ccls. (command$3 enter$3 receiv$3 (indicat$3 or flash$3 or blink$3 or light) tim$3 (select$3 or choos$3) measur$4 test $3 ((purg$3 or remov$3 or releas$3) near3 (air gas)) (calibrat$3 or initial $3 or activat$3 or initiat $3))	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	AND	ON	2010/09/29 19:12
S141	86	600/1-8,301.ccls. and (eluant elution eluate)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2010/09/29 19:13
S142	71	600/1-8,301.ccls. and (eluant elution eluate) and (computer processor control$4)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2010/09/29 19:13
S143	66	600/1-8,301.ccls. and (eluant elution eluate) and (computer processor control$4) and (radioisotope radioactive PET (positron adj emission adj tomography) radiation rubidium strontium)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2010/09/29 19:14

EAST Search History (Interference)

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
S64	476	604/30.ccls.	US-PGPUB; USPAT; UPAD	OR	ON	2010/08/10 09:49
S65	12	(charles near3 quirico).in.	US-PGPUB; USPAT; UPAD	OR	ON	2010/08/10 09:55

S66	37	(ernest near3 balestracci).in.	US-PGPUB; USPAT; UPAD	OR	ON	2010/08/10 09:56
S67	12	(daniel near3 darst).in.	US-PGPUB; USPAT; UPAD	OR	ON	2010/08/10 09:56
S68	19	(eric near3 krause).in.	US-PGPUB; USPAT; UPAD	OR	ON	2010/08/10 09:56
S69	5	(vishal near3 lokhande).in.	US-PGPUB; USPAT; UPAD	OR	ON	2010/08/10 09:56
S70	5	(jacob near3 childs).in.	US-PGPUB; USPAT; UPAD	OR	ON	2010/08/10 09:56
S71	70	S65 S66 S67 S68 S69 S70	US-PGPUB; USPAT; UPAD	OR	ON	2010/08/10 09:57
S72	75	(BRACCO near3 DIAGNOSTICS).as.	US-PGPUB; USPAT; UPAD	OR	ON	2010/08/10 09:59
S73	183	604/236-238,30-34,65-67,4.01-6.16.ccls. and valve and (activity same (detect$3 monitor$3))	US-PGPUB; USPAT; UPAD	OR	ON	2010/08/10 09:59
S74	195	604/236-238,30-34,65-67,4.01-6.16.ccls. and valve and ((eluate radioactiv$5 activity) same (detect$3 monitor$3))	US-PGPUB; USPAT; UPAD	OR	ON	2010/08/10 10:03
S75	2	312/209.ccls. and valve and ((eluate radioactiv$5 activity) same (detect$3 monitor$3))	US-PGPUB; USPAT; UPAD	OR	ON	2010/08/10 10:04
S76	116	600/1-8,436.ccls. and valve and ((eluate radioactiv$5 activity) same (detect$3 monitor$3))	US-PGPUB; USPAT; UPAD	OR	ON	2010/08/10 10:04
S77	311	S74 S75 S76	US-PGPUB; USPAT; UPAD	OR	ON	2010/08/10 10:04

9/30/2010 4:46:45 PM
C:\Documents and Settings\jzhang1\My Documents\EAST\Workspaces\12137364.wsp

Index of Claims	Application/Control No.	Applicant(s)/Patent Under Reexamination
	12137364	HIDEM ET AL.
	Examiner	**Art Unit**
	JENNA ZHANG	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	09/27/2010	01/31/2011	12/19/2011						
	1	✓	✓	✓						
	2	✓	✓	✓						
	3	✓	✓	✓						
	4	✓	✓	✓						
	5	✓	✓	✓						
	6	✓	✓	✓						
	7	✓	✓	✓						
	8	✓	✓	✓						
	9	✓	✓	✓						
	10	✓	✓	✓						
	11	✓	✓	✓						
	12	✓	✓	✓						
	13	✓	✓	✓						
	14	✓	✓	✓						
	15	✓	✓	✓						
	16	✓	✓	✓						
	17	✓	✓	✓						
	18	✓	N	N						
	19	✓	N	N						
	20	✓	N	N						
	21	✓	N	N						
	22	✓	N	N						
	23	✓	N	N						
	24	✓	N	N						

PTO/SB/08a (01-10)
Approved for use through 07/31/2012. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Not for submission under 37 CFR 1.99)

Application Number	12137364
Filing Date	2008-06-11
First Named Inventor	STEPHEN E. HIDEM
Art Unit	3763
Examiner Name	ZHANG, JENNA
Attorney Docket Number	56782.1.7

U.S.PATENTS Remove

Examiner Initial*	Cite No	Patent Number	Kind Code[1]	Issue Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1	3483867		1969-12-16	Markovitz	
	2	4336036		1982-06-22	Leeke	
	3	4466888		1984-08-21	Verkaart	
	4	4623102		1986-11-18	Hough, Jr.	
	5	4769008		1988-09-06	Hessel	
	6	4994056		1991-02-19	Ikeda	
	7	5702115		1997-12-30	Pool	
	8	5765842		1998-06-16	Phaneuf	

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	12137364
	Filing Date	2008-06-11
	First Named Inventor	STEPHEN E. HIDEM
	Art Unit	3763
	Examiner Name	ZHANG, JENNA
	Attorney Docket Number	56782.1.7

	9	5827429		1998-10-27	Ruschke	
	10	6347711		2002-02-19	Goebel	
	11	6558125		2003-05-06	Futterknecht	
	12	7612999		2009-11-03	Clark	
	13	7862534		2011-01-04	Quirico	

If you wish to add additional U.S. Patent citation information please click the Add button. Add

U.S.PATENT APPLICATION PUBLICATIONS Remove

Examiner Initial*	Cite No	Publication Number	Kind Code[1]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1	20040104160		2004-06-03	Scagliarini	
	2	20060015056		2006-01-19	Ellingboe	
	3	20090309466		2009-12-17	Quirico	
	4	20090318745		2009-12-24	Quirico	

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	12137364
	Filing Date	2008-06-11
	First Named Inventor	STEPHEN E. HIDEM
	Art Unit	3763
	Examiner Name	ZHANG, JENNA
	Attorney Docket Number	56782.1.7

	5	20100125243		2010-05-20	Balestracci	
	6	20100270226		2010-10-28	Balestracci	
	7	20100312039		2010-12-09	Quirico	
	8	20110071392		2011-03-24	Quirico	
	9	20110172524		2011-07-14	Hidem	
	10	20060151048		2005-12-27	Tochon-Danguy	

If you wish to add additional U.S. Published Application citation information please click the Add button. Add

FOREIGN PATENT DOCUMENTS Remove

Examiner Initial*	Cite No	Foreign Document Number[3]	Country Code[2] i	Kind Code[4]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear	T[5]
	1	0919249	EP		1999-06-02	NISSHO KK		☐
	2	1421960	EP		2004-05-26	GVS S P A		☐
	3	2009152320	WO		2009-12-17	BRACCO DIAGNOSTICS INC		☐

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	12137364
	Filing Date	2008-06-11
	First Named Inventor	STEPHEN E. HIDEM
	Art Unit	3763
	Examiner Name	ZHANG, JENNA
	Attorney Docket Number	56782.1.7

	4	2004059661	WO		2004-07-15	LYNNTECH INC		☐

If you wish to add additional Foreign Patent Document citation information please click the Add button Add

NON-PATENT LITERATURE DOCUMENTS Remove

Examiner Initials*	Cite No	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc), date, pages(s), volume-issue number(s), publisher, city and/or country where published.	T[5]
	1	Brochure, "IV and Liquid Filters: Speedflow Adult 0.2 um Positive", http://www.gvs.it/flex/FixedPages/UK/LiquidFilters.php/L/UK/ID/Speedflow%20Adjust%.... taken off of web on 11/11/2008	☐
	2	International Search Report and Written Opinion, dated 01-04-2010 for PCT Application No. PCT/US2009/063788, 13 pages	☐

If you wish to add additional non-patent literature document citation information please click the Add button Add

EXAMINER SIGNATURE

Examiner Signature		Date Considered	

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through a citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

[1] See Kind Codes of USPTO Patent Documents at www.USPTO.GOV or MPEP 901.04. [2] Enter office that issued the document, by the two-letter code (WIPO Standard ST.3). [3] For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. [4] Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. [5] Applicant is to place a check mark here if English language translation is attached.

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	12137364
	Filing Date	2008-06-11
	First Named Inventor	STEPHEN E. HIDEM
	Art Unit	3763
	Examiner Name	ZHANG, JENNA
	Attorney Docket Number	56782.1.7

CERTIFICATION STATEMENT

Please see 37 CFR 1.97 and 1.98 to make the appropriate selection(s):

☐ That each item of information contained in the information disclosure statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(1).

OR

☐ That no item of information contained in the information disclosure statement was cited in a communication from a foreign patent office in a counterpart foreign application, and, to the knowledge of the person signing the certification after making reasonable inquiry, no item of information contained in the information disclosure statement was known to any individual designated in 37 CFR 1.56(c) more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(2).

☐ See attached certification statement.

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

☒ A certification statement is not submitted herewith.

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	/Paul J. LaVanway, Jr./	Date (YYYY-MM-DD)	2011-12-16
Name/Print	Paul J. LaVanway, Jr.	Registration Number	64,610

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 1 hour to complete, including gathering, preparing and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

Privacy Act Statement

The Privacy Act of 1974 (P.L. 93-579) requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that: (1) the general authority for the collection of this information is 35 U.S.C. 2(b)(2); (2) furnishing of the information solicited is voluntary; and (3) the principal purpose for which the information is used by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent application or patent. If you do not furnish the requested information, the U.S. Patent and Trademark Office may not be able to process and/or examine your submission, which may result in termination of proceedings or abandonment of the application or expiration of the patent.

The information provided by you in this form will be subject to the following routine uses:

1. The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C. 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether the Freedom of Information Act requires disclosure of these record s.

2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.

3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.

4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).

5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent Cooperation Treaty.

6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).

7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (i.e., GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.

8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspections or an issued patent.

9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

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

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
15 July 2004 (15.07.2004)

PCT

(10) International Publication Number
WO 2004/059661 A1

(51) International Patent Classification[7]: G21G 4/08

(21) International Application Number:
PCT/US2002/041676

(22) International Filing Date:
30 December 2002 (30.12.2002)

(25) Filing Language: English

(26) Publication Language: English

(71) Applicant: **LYNNTECH, INC.** [US/US]; 7610 Eastmark Drive, College Station, TX 77845 (US).

(72) Inventor: **SYLVESTER, Paul**; 80 N. Warren, Apt.16, Woburn, MA 01801 (US).

(74) Agent: **STREETS, Jeffrey, L.**; Streets & Steele, 13831 Northwest Freeway, Suite 355, Houston, TX 77040 (US).

(81) Designated States *(national)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, 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, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW.

(84) Designated States *(regional)*: ARIPO patent (GH, GM, KE, LS, MW, MZ, 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, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

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.

WO 2004/059661 A1

(54) Title: RUBIDIUM-82 GENERATOR BASED ON SODIUM NONATITANATE SUPPORT, AND SEPARATION METHODS FOR THE RECOVERY OF THE RECOVERY OF STRONTIUM-82 FROM IRRADIATED TARGETS

(57) Abstract: Sodium nonatitanate compositions, a method using the composition for recovery of 82Sr from irradiated targets, and a method using the composition for generating 82Rb. The sodium nonatitanate materials of the invention are highly selective at separating strontium from solutions derived from the dissolution of irradiated target materials, thus reducing target processing times. The compositions also have a very low affinity for rubidium, making it an ideal material for use as a 82Rb generator. Sodium nonatitanate materials of this type both improve the recovery of 82Sr and provide a safer, more effective 82Rb generator system.

RUBIDIUM-82 GENERATOR BASED ON SODIUM NONATITANATE SUPPORT, AND SEPARATION METHODS FOR THE RECOVERY OF STRONTIUM-82 FROM IRRADIATED TARGETS

BACKGROUND OF THE INVENTION

Field of the Invention

This invention relates to the selective separation of strontium-82 from other radioisotopes, such as those resulting from an irradiated molybdenum target, and in the manufacture of a rubidium-82 generator.

Background of the Related Art

The use of radioisotopes as diagnostic and imaging agents in medicine has expanded rapidly in recent years. Positron (β+) emitters are particularly useful in the study of metabolic processes because the positron-electron annihilation reaction produces a pair of gamma rays with an energy level of 511 keV travelling in opposite directions. By placing a series of detectors around a patient who has been administered a positron emitter, both the location and amount of radioactivity can be accurately determined. This property is utilized in Positron Emission Tomography (PET) to image metabolic processes *in vivo*. Rubidium-82 (82Rb) is a short-lived positron-emitting isotope ($T_{1/2}$ = 75 seconds) that is increasingly being used to study blood flow through the heart and brain. Physiologically, rubidium is an analogue of potassium, and consequently enters the body's large potassium pool, which has a comparatively slow turnover. Thus, after 82Rb is injected intravenously, the tracer's uptake in tissue reflects the rate of delivery, i.e. blood flow, and thus 82Rb rapidly builds up in the heart. This can be used, for example, to study blood-brain barrier leakage and heart muscle perfusion.

The short half-life of 82Rb means that it must be supplied to physicians in the form of a generator, where the parent 82Sr ($T_{1/2}$ = 25 days) is immobilized on a solid substrate or support and 82Rb eluted as required. The generators that are currently available use hydrous tin oxide to immobilize the 82Sr and allow the elution of 82Rb by saline or other appropriate eluant. The 82Sr ($T_{1/2}$ = 25 days) is accompanied by unwanted 85Sr ($T_{1/2}$ = 64 days), generated as a by-product during the manufacture of 82Sr, wherein both isotopes have a relatively long half-life and a high radiotoxicity due to their tendency to accumulate in bone. Thus, it is essential to minimize or eliminate the introduction of 82Sr and 85Sr into a patient during the administration of 82Rb. Although hydrous tin oxide has proved acceptable to date

for use in generators, new materials exhibiting far higher strontium affinities, improved strontium/rubidium separation factors and greater radiolytic stability are needed in order to lower the amount of 82Sr and 85Sr released during elution of the 82Rb.

The parent 82Sr is generated by the proton irradiation of rubidium, rubidium chloride or molybdenum targets followed by dissolution and processing to isolate the 82Sr. The demand for 82Rb generators has grown so great that there is a need to reduce processing times and to increase the yield of 82Sr from processed targets. One method of improving the supply of 82Sr is to improve the processes used to extract 82Sr from irradiated targets. Current methods utilize organic ion exchange or chelating resins to extract very low levels of strontium from dissolved targets containing molar concentrations of inert ions. However, a satisfactory separation of 82Sr from the target materials and other radioisotopes generated during the irradiation procedure requires multiple treatment steps due to the relatively low affinity and low selectivity of the organic ion exchange resins for 82Sr.

82Sr is produced by the proton irradiation of molybdenum metal, rubidium metal and rubidium chloride targets. The irradiation process also produces a range of other radioactive isotopes (e.g. 88Y, 88Zr, 85Sr) and as a consequence, a series of carefully designed separation procedures have been designed to separate the desired 82Sr from other radioisotopes and inactive species present. The primary method used to separate 82Sr is by a series of ion exchange and selective elution steps. Typically, AG 50 W-X8 ion exchange resin is used to separate 82Sr from dissolved targets. However, this resin is relatively non-selective and will absorb numerous polyvalent cations (e.g., 88Y) in addition to the desired 82Sr. Consequently, multiple separation steps are required to isolate 82Sr from the other isotopes present.

82Rb can be conveniently supplied to physicians in the form of a generator in which the parent 82Sr is immobilized on an ion exchange material and the 82Rb eluted when required. This means that 82Rb PET can be performed at clinical facilities where a typical generator may last several months before the yield of 82Rb diminishes below a usable level.

To be suitable for use in a 82Rb generator, an ion exchange material must exhibit a high affinity for strontium but a low affinity for rubidium, allowing the 82Rb daughter to be eluted from a column containing immobilized 82Sr. Generators have been proposed that were based on a number of separation media including Chelex 100, Al_2O_3, Sb(V) hexacyanoferrate, polyantimonic acid, titanium vanadate and hydrated tin(IV) oxide, with the hydrated tin(IV) oxide being the most widely used.

However, the crucial component of any system is the actual ion exchange material containing the immobilized 82Sr parent. Current systems using hydrous tin

oxide have a limited life due to the breakdown of the hydrous tin dioxide, necessitating frequent replacement.

Therefore, there is a need for a highly strontium selective ion exchange material in place of ion exchange resins and hydrated tin(IV) oxide, so that the separation and recovery of 82Sr from Rb, RbCl and Mo targets is greatly facilitated. This will lead to a reduction in processing steps, a decrease in target processing times and thus a decrease in the cost of the 82Sr product. There is also a need for an ion exchange material suitable for use as a 82Rb generator having a very high selectivity for 82Sr and a very low selectivity for 82Rb to allow elution of the 82Rb by isotonic saline or other solutions.

SUMMARY OF THE INVENTION

The present invention provides a method of chemically isolating strontium-82 from proton-irradiated molybdenum targets. This comprises dissolving the molybdenum metal target containing the strontium-82, adjusting the pH of the dissolved molybdenum target solution to an alkaline pH, removing precipitates from the solution, and then absorbing the strontium-82 from the solution onto a support comprising sodium nonatitanate. Sodium nonatitanate can also be applied to the efficient recovery of strontium-82 from alkaline RbCl solutions produced during the processing of proton-irradiated rubidium metal and rubidium chloride targets.

The present invention also provides a rubidium-82 generator, comprising a strontium-82 support medium comprising sodium nonatitanate. Preferably, the sodium nonatitanate is characterized by a strontium selectivity greater than 250,000 mL/g at an alkaline pH, and/or the sodium nonatitanate is characterized by a rubidium selectivity less than 100 mL/g at an alkaline pH. More preferably, the sodium nonatitanate is characterized by a strontium/rubidium separation factor greater than 1,000, and even more preferably greater than 100,000.

The rubidium-82 generator is prepared by a process comprising: preparing sodium nonatitanate from titanium isopropoxide and aqueous sodium hydroxide; heating the sodium nonatitanate at a temperature between 100°C and 250°C for a period between 12 hours and 2 weeks; and absorbing strontium-82 on the sodium nonatitanate from an aqueous solution comprising strontium-82 and a soluble sodium salt, wherein the sodium salt concentration is between 0.1 and 1 molar. It is also preferred that the titanium isopropoxide and the aqueous sodium hydroxide solution are provided at a sodium hydroxide to titanium isopropoxide molar ratio of greater than 0.44, but preferably providing a large molar excess of sodium

hydroxide. The sodium hydroxide to titanium isopropoxide molar ratio is preferably between 1 and 10, more preferably between 2 and 6, and most preferably about 4.

Furthermore, the invention provides a process for preparing a solution containing rubidium-82. The process comprises providing a solution containing strontium-82 at a pH between 10 and 14, absorbing the strontium-82 from the solution onto a sodium nonatitanate support medium, and eluting rubidium-82 from the sodium nonatitanate support medium with a solvent. The solvent is preferably selected from the group consisting of water and saline solutions. More particularly, the solvent may be an aqueous solution having a sodium chloride concentration between 0.001 molar and 1 molar, preferably between 0.2 molar and 1 molar. The solvent may also be a pharmaceutical grade isotonic saline and buffer solution.

DETAILED DESCRIPTION OF THE INVENTION

The present invention provides improved sodium nonatitanate compositions, a method using the composition for recovery of 82Sr from irradiated targets, and a method using the composition for generating 82Rb. The sodium nonatitanate materials of the invention are far more selective at separating strontium from solutions derived from the dissolution of irradiated target materials than current ion exchange resins used in the production of 82Sr. The present invention reduces the number of processing steps required, and thus leads to a decrease in target processing times and a reduction in the cost of the 82Sr product. Waste generation and disposal are also decreased.

According to the present invention, synthetic conditions are adjusted to produce a material with improved properties more applicable to 82Sr processing. The sodium nonatitanate of the present invention has been found to have a very low affinity for rubidium in addition to an exceptionally high affinity for strontium, making it ideal for use as a replacement for the hydrous tin dioxide used in current 82Rb generators. Sodium nonatitanate materials of this type will both improve the recovery of 82Sr and lead to a safer, more effective 82Rb generator system for clinical applications.

Sodium nonatitanate, $Na_4Ti_9O_{20}.xH_2O$, is an inorganic ion exchange material that has been used for the removal of 90Sr from neutral and alkaline nuclear wastes. The sodium nonatitanate of the present invention has a number of advantages over conventional organic ion exchange resins (e.g., Chelex 100) that include: very high selectivity for trace levels of strontium in the presence of molar concentrations of other ions at alkaline pH; very low affinity for rubidium; excellent radiation, chemical and thermal stability so that there is no release of contaminants (e.g. Ti) into the 82Rb product; rapid reaction kinetics; high cation exchange capacity; absorbed ions readily stripped by treatment with dilute mineral acid allowing the sodium nonatitanate to be recycled, if desired; scale up of similar synthesis has

already been demonstrated; and the sodium nonatitanate powder can be manufactured into pellets appropriate for column operations. Other chemically related sodium titanate materials suitable for use in the same manner as the aforementioned sodium nonatitanate ($Na_4Ti_9O_{20}.xH_2O$) include other titanate materials exhibiting high Sr affinity and low Rb affinity, including Sr-Treat (available from Selion Oy) and monosodium titanate (available from Boulder Scientific) It is also anticipated that analogous zirconates may exhibit similar properties.

The invention also provides important improvements in the processing of irradiated targets to recover 82Sr. Sodium nonatitanate has a much greater affinity for 82Sr than currently used ion exchange resins, and a low affinity for other radioactive isotopes. Consequently, the use of sodium nonatitanate greatly simplifies the extraction process by reducing the number of separation steps that are required to produce chemically pure 82Sr. Thus, targets can be processed more rapidly and the recovery of 82Sr improved. Improved isotope selectivity may also facilitate the isolation of other useful isotopes from the targets, leading to greater payback from target processing operations.

Furthermore, less than 1g of sodium nonatitanate material is needed in a 82Rb generator and 1 kg of this material is expected to be sufficient to process a large number of targets, even if the sodium nonatitanate material is not recycled and is disposed of after one use. Consequently, the additional cost incurred by the use of sodium nonatitanate will be negligible in comparison with the cost savings achieved in the 82Sr production.

It has been determined that replacing hydrous tin dioxide with sodium nonatitanate reduces the amount of 82Sr released during the operation of the 82Rb generator, thereby reducing the exposure of the patient to 82Sr. Sodium nonatitanate is also more chemically stable and less likely to leach non-radioactive contaminants into solution during operation of the generator. The sodium nonatitanate is also more amenable to recycling since the 82Sr can readily be stripped with mineral acid without producing additional impurities. Recycling of 82Sr generators is already being used as a source of additional 82Sr, and improvements to the recycling procedure (obtained by using a superior ion exchange material) will facilitate the recovery of 82Sr from this source.

Although the sodium nonatitanate may be used as a direct replacement for hydrous tin dioxide in the 82Rb generator, it is also possible to use sodium nonatitanate in the form of a disposable add-on filter that could be used to trap any 82Sr that is leached from the generator during the production of 82Rb.

The first step in preparing a 82Rb generator is to load the parent 82Sr onto the sodium nonatitanate material and place the ion exchange material into a suitable column. It is essential that sufficient time be allowed for the 82Sr to be absorbed by the sodium

nonatitanate material in order to maximize the loading of the parent radioisotope per gram of ion exchange material.

Sodium nonatitanate should be loaded with 82Sr before being placed in an ion exchange column, to avoid preferential loading of the 82Sr on the top of the ion exchange column rather than uniformly throughout the material. This high concentration of radioactivity on a very small volume may result in undesirable radiolytic problems. Although sodium nonatitanate has been shown to be highly resistant to radiation damage, it is considered prudent to avoid any potential problems.

EXAMPLES

These Examples investigated the suitability of sodium nonatitanate for the use in separating 82Sr from irradiated targets and in the construction of a 82Sr/82Rb generator. Initial batch experiments compared the rubidium and strontium selectivities of a number of different sodium nonatitanate samples with commercially available ion exchange materials (e.g. AW 500, Chelex 100) and some experimental materials that had also exhibited high strontium selectivities (e.g. sodium titanosilicate). Column experiments were then performed using target simulants and generator simulants on materials that exhibited favorable selectivity characteristics. Some work was also performed to investigate the likely interference from other isotopes present in irradiated targets on the production of 82Sr.

Example 1 - Preparation of Sodium Nonatitanate

Sodium nonatitanate (NaTi) was synthesized hydrothermally as follows. 77.5 g of titanium isopropoxide was added to 84.35 g of a 50 wt.% solution of NaOH with vigorous stirring and 60 mL of deionized water was added. The resultant gel was heated at approximately 108°C for 3 hours, transferred to a hydrothermal pressure vessel with an additional 90 mL of deionized water, and heated at either 170°C or 200°C for times ranging from 21 hours to 1 week. After the allotted time, the materials were filtered, washed with ethanol to remove residual base and dried at 60°C. The mass of sodium nonatitanate produced was approximately 31 g. Each sample was characterized using x-ray powder diffraction (XRD). The reaction is outlined in Equation 1.

$$9\ Ti(OC_3H_7)_4 + 4\ NaOH(aq) \text{ ----> } Na_4Ti_9O_{20}.xH_2O + 9\ C_3H_7OH \quad (1)$$

The crystallinity of the material was shown to be dependent upon the reaction time and temperature, with the most crystalline materials being produced after 1 week of hydrothermal treatment (200°C for 7 days). Samples that received no hydrothermal treatment,

or only a few days, were virtually amorphous with only a few very broad reflections visible on the XRD pattern.

The theoretical cation exchange capacity (CEC) of sodium nonatitanate is quite high and has a value of 4.74 meq/g, which compares favorably with organic ion exchange resins.

Alternative titanium salts that could be used to manufacture sodium nonatitanate include titanium tetrachloride, $TiCl_4$, and titanium sulfate, $TiOSO_4.xH_2SO_4.yH_2O$. However, hydrolysis of these salts leads to the generation of hydrochloric acid and sulfuric acid, respectively, and thus additional base is required during the hydrothermal process. The final product also needed to be exhaustively washed to remove residual sodium chloride or sodium sulfate. Consequently, titanium isopropoxide (which hydrolyzes to form propanol) is the preferred starting material because the final product is free from additional sodium salts.

Example 2 - Determination of Strontium Selectivity

Sodium nonatitanate and a variety of other ion exchange materials were obtained and evaluated for use in the separation of 82Sr from targets and in a 82Rb generator. These materials are described below in Table 1.

Table 1. Characteristics of ion exchange materials evaluated in this study.

Material	Source	Sample Preparation
Na-Clinoptilolite	GSA Resources, AZ	Ground to powder.
AW500	Aldrich (1.6 mm Pellets)	Ground to powder.
Hydrous SnO_2	Synthesized in house	NaOH + $SnCl_4$. Washed with acetic acid/sodium acetate buffer.
K+ Pharmacosiderite ($K_3H(TiO)_4(SiO_4)_3.4H_2O$)	Synthesized according to literature method.	None. Used as synthesized.
Sodium Titanosilicate ($Na_2Ti_2O_3SiO_4.2H_2O$)	Synthesized according to literature method.	None. Used as synthesized.
AG 50W-X8 (Na+) (25 - 50 Mesh)	BioRad. Strong acid ion exchange resin.	Converted to Na+ form (for alkaline solutions only)
Chelex 100 (Na+) (50 - 100 Mesh)	BioRad. Chelating resin with iminodiacetic acid functionality.	None. Used as received.
Sodium Nonatitanate	Honeywell, IL	None. Used as received.
Hydrous SiO_2	Synthesized in house	Acetic acid hydrolysis of tetraethyl orthosilicate. Washed with H_2O

Hydrous TiO_2	Synthesized in house	Hydrolysis of titanium isopropoxide. Washed with H_2O
Hydrous ZrO_2	Synthesized in house	$ZrOCl_2$ + NaOH. Washed with deionized water.

The strontium selectivity of the ion exchange materials of Table 1 was evaluated in sodium chloride and rubidium chloride solutions using radiotracer techniques. Samples were evaluated using a simple batch technique to allow the rapid screening of a large number of materials over a range of ionic strengths. Blanks were run for each matrix to check for any loss of strontium during filtration or absorption of strontium onto the scintillation vials. In all solutions evaluated, strontium absorption was negligible.

0.05g of each of the ion exchange materials was contacted with 10 mL of a solution, spiked with 89Sr, in a capped scintillation vial. (The total strontium content was approximately 1.6 ppm, thus preventing any loss of strontium in solution due to precipitation of sparingly soluble $Sr(OH)_2$ at alkaline pH values.) The mixtures were shaken for 6 hours, filtered through a 0.2 μm syringe filter and the residual activity determined using liquid scintillation counting (LSC). Distribution Coefficients (K_d values) were then determined according to Equation 2:

$$K_d = (A_i - A_f) / A_f * v/m \qquad (2)$$

where: A_i = initial activity in solution (counts per minute (cpm)/mL)

A_f = final activity in solution (cpm/mL)

v = volume of solution (mL)

m = mass of exchanger (g)

The final pH of the solution was also noted. The period of 6 hours was chosen to allow equilibrium to be reached for each of the ion exchange materials. However, previous work on the titanosilicates and titanates had shown the reaction rates to be rapid with the majority of the uptake occurring in only a few minutes. The concentration of the chloride solutions was varied from 1M to 0.001M to evaluate the effect of increasing Rb+ and Na+ concentrations on the uptake of Sr^{2+}. All experiments were performed in duplicate, and if significant variations between duplicate samples occurred, the experiments were repeated until good agreements on the K_d values were obtained. The results are shown in Tables 2 and 3 and represented the average K_d obtained, quoted to 3 significant figures.

Table 2. Strontium selectivity data from unbuffered sodium chloride solutions.

Ion Exchange Material	K_d mL/g 1M NaCl	0.1M NaCl	0.01M NaCl	0.001M
NaCl				
Na-Clinoptilolite	8	124	3,260	36,900
AW500	1,860	88,300	1,270,000	1,210,000
Hydrous SnO_2	767	43,000	124,000	51,800
K+ Pharmacosiderite	18,300	251,000	594,000	281,000
Sodium Titanosilicate	556,000	273,000	119,000	42,900
AG 50W (Na+)	32	3,380	365,000	2,510,000
Chelex 100 (Na+)	610	26,400	726,000	1,300,000
NaTi (Honeywell)	80,600	1,030,000	258,000	166,000
NaTi (No hydrothermal)	1,530,000	2,570,000	739,000	372,000
NaTi (170°C, 21hr)	1,030,000	1,240,000	272,000	172,000
NaTi (170°C, 3d)	959,000	633,000	218,000	93,100
NaTi (170°C, 7d)	167,000	834,000	264,000	90,400
NaTi (200°C, 21hr)	439,000	1,390,000	197,000	120,000
NaTi (200°C, 3 d)	261,000	898,000	251,000	158,000
NaTi (200°C, 7d)	195,000	955,000	265,000	214,000
ZrO_2	3,360	52,200	213,000	232,000

Table 3. *Strontium* selectivity data from unbuffered rubidium chloride solutions

Material	K_d mL/g 1M RbCl	0.1M RbCl	0.01M RbCl	0.001M
RbCl				
Na-Clinoptilolite	19	3	88	11,000
AW500	9,750	107,000	1,020,000	1,280,000
Hydrous SnO_2	766	66,100	104,000	51,800
K+ Pharmacosiderite	1,950	40,800	419,000	427,000
Sodium Titanosilicate	12,600	94,700	164,000	179,000
AG-50W (Na+)	44	3,870	237,000	800,000
Chelex 100 (Na+)	1,580	38,400	555,000	977,000
NaTi (Honeywell)	13,900	108,000	279,000	324,000
NaTi (No hydrothermal)	14,220	116,000	345,000	429,000
NaTi (170°C, 21hr)	10,500	71,700	193,000	205,000
NaTi (170°C, 3d)	15,100	39,500	68,000	95,200
NaTi (170°C, 7d)	23,000	55,800	31,200	110,000
NaTi (200°C, 21hr)	11,000	66,400	110,000	103,000
NaTi (200°C, 3 d)	10,600	56,800	146,000	158,000
NaTi (200°C, 7d)	10,500	57,400	146,000	158,000
ZrO_2	3,000	42,400	184,000	221,000

Comparing the selectivity data from sodium and rubidium solutions, it is evident that rubidium ions cause a reduction in affinity for the strontium ion for all of the exchangers indicating that the affinity of these materials for rubidium is significantly higher than the affinity for sodium ions. The pH of the final solutions was generally alkaline for the nonatitanates (NaTi) and titanosilicates, with pH values as high as 12 being measured. This was due to hydrolysis of the exchangers resulting in the absorption of protons and the release

of sodium ions, thus increasing the pH of the aqueous phase. This effect can be overcome, if desired, by buffering the solution.

The most distinct trend was observed in 1M NaCl solutions for the sodium nonatitanate samples. The highest K_d was observed for the non-hydrothermal material and the K_d values decreased with increasing reaction time for both the 200°C and 170°C materials. Clearly, strontium uptake is facilitated by having a low-crystallinity material. This suggests that as the crystallinity increases and the size of the nonatitanate crystallites also increases, it becomes thermodynamically less favorable for exchange of the sodium ions by strontium. It is also interesting to note that the majority of the sodium nonatitanates exhibit a higher selectivity for strontium in 1M NaCl than in 0.001M NaCl. This indicates that the higher ionic strength facilitates the Na^+/Sr^{2+} exchange reaction and more than compensates for the increased competition for the ion exchange sites from the additional Na+ ions.

This data shows that sodium nonatitanate is an ideal material for the recovery of 82-Sr from irradiated rubidium and rubidium chloride targets and in the manufacture of a 82-Rb generator.

Example 3 - Rubidium Selectivity from NaCl Solutions

For an ion exchange material to be suitable for use in a 82Rb generator, it must have a very high selectivity for strontium to prevent any loss of 82Sr from the ion exchange column and release to the patient undergoing a PET scan. This property was clearly demonstrated in Example 2. It must also have a very low selectivity towards rubidium, thus allowing 82Rb to be released into solution as saline is passed through the 82Rb generator. Consequently, the rubidium selectivity of the ion exchange materials was evaluated in sodium chloride media following the procedure described in Example 2. The same procedure was followed using 86Rb to spike the solutions to give an activity of approximately 200,000 cpm/mL. Total rubidium in solution was < 0.05 ppm. The selectivities of the materials are shown below in Table 4.

Table 4. Rubidium selectivity data from unbuffered sodium chloride solutions.

Material	86Rb K_d mL/g			
	1M NaCl	0.1M NaCl	0.01M NaCl	0.001M
NaCl				
AW500	116	620	4,920	21,900
Hydrous SnO_2	1	6	36	290
K+ Pharmacosiderite	148	475	2,030	4,020
Sodium Titanosilicate	8,010	194,000	114,000	75,800
AG 50W (Na+)	7	75	688	6,680
Chelex 100 (Na+)	3	8	43	256
NaTi (Honeywell)	9	102	488	817

NaTi (No hydrothermal)	4	59	280	446
NaTi (170°C, 21hr)	9	56	209	297
NaTi (170_oC, 3d)	7	46	198	311
NaTi (170°C, 7d)	3	15	47	71
NaTi (200°C, 21hr)	8	79	334	502
NaTi (200°C, 3d)	8	52	207	307
NaTi (200°C, 7d)	4	25	111	178
ZrO_2	1	12	60	154

From the data in Table 4, it is clear that the all of the sodium nonatitanate materials have a very low affinity for rubidium, particularly in the presence of relatively high amounts of sodium ions. In general, the rubidium selectivity decreased with increasing reaction time for both series of nonatitanates (170°C and 200°C) with the lowest affinity being demonstrated by the sample that was heated hydrothermally at 170°C for 1 week. Uptake was negligible in 1M NaCl and the very low reduction in activity that was noted could be accounted for by absorption of rubidium during filtration and by pipetting errors during the counting procedure. Consequently, samples with K_d values that were below 10 mL/g can be considered to have no affinity at all for 86Rb. Some rubidium uptake was evident in very dilute sodium solutions, but the K_d values were low for all of the titanate samples. This suggests that the uptake of rubidium was more likely due to the materials having an exceptionally low affinity for sodium rather than any real affinity for rubidium. All of the sodium nonatitanate materials performed better than the commercially available sample obtained from Honeywell Inc. The materials are clearly ideal for use in a 82-Rb generator.

Hydrous tin dioxide exhibited some of the lowest rubidium affinities and was comparable with Chelex 100, the best of the nonatitanates and the hydrous zirconium dioxide. However, hydrous tin dioxide exhibited much lower strontium K_d values than the nonatitanates. Therefore, nonatitanate materials are preferred because they have higher strontium/rubidium separation factors. Hydrous tin dioxide also has a limited pH stability range and significant dissolution and release of absorbed strontium is likely to occur should any significant pH perturbations occur outside the range of pH 4 to pH 9. Radiation stability of hydrous tin dioxide is also limited, with particle breakdown causing current 82-Rb generators to be replaced before decay has reduced the 82-Rb below useable levels.

The rubidium selectivity data also indicates that AW500, potassium Pharmacosiderite and the sodium titanosilicate have a strong affinity for rubidium in a range of saline solutions. Consequently, these materials will be unsuitable for use in a 82Rb generator and have only limited applications in the processing of irradiated target materials.

Example 4 - Sr and Rb Selectivity in 0.1M Sodium Acetate/Acetic Acid Buffer

In order to prevent hydrolysis reactions from raising the pH as described above, some strontium and rubidium selectivity experiments were performed in a 0.1M sodium acetate / acetic acid buffer solution. In these tests, the final pH remained between 5.2 and 6.3, which is a more clinically acceptable pH for an 82Rb infusion. Rubidium K_d values remained low, as expected, following the trend observed in Table 5. Strontium K_d values were considerably lower, with a maximum K_d value of 80,000 mL/g being obtained for the sodium nonatitanate sample that was heated hydrothermally at 170°C for 21 hours. This is considerably lower than the K_d value of over 1,200,00 mL/g that was obtained in unbuffered 0.1M NaCl. The K_d values obtained for the other ion exchange materials were also considerably lower. However, the Sr/Rb separation factors remained high and the sodium nonatitanates still outperformed hydrous tin dioxide and the organic ion exchange resins. The affinity of sodium nonatitanate for strontium is greatest at higher pH values.

Example 5 - Molybdenum Targets

The basic steps of a proposed process to obtain 82Sr from irradiated molybdenum targets are as follows:

1. Dissolve the irradiated molybdenum target in 30% hydrogen peroxide, ensuring excess hydrogen peroxide is destroyed.
2. Add sodium hydroxide to bring the pH to approximately 12.
3. Filter the solution to remove any precipitate. It is predicted that the majority of 88Zr and 59Fe will be found in the precipitate, and experiments already performed have confirmed that 99% or more of the 88Y precipitated out of solution on the addition of NaOH.
4. Pass the solution through a column of sodium nonatitanate and wash the column with two bed volumes of 0.1M NaCl, adjusted to pH 12 with NaOH. 82Sr and 85Sr will be absorbed. 82Rb and other Rb isotopes will remain in the aqueous phase. Molybdate anions will also pass through the column.
5. The column can then be stripped using dilute mineral acid to recover the 82Sr and the sodium nonatitanate reused or discarded.

There is a range of other isotopes present in addition to 82Sr, including 75Se, 73As, 74As, 7Be, 68Ge, 48V, 60Co (and other Co isotopes), 54Mn, 51Cr and 95mTc. In the alkaline target solution, Se, As, V, Ge, Cr, Mn and Tc are expected to be present as anions and thus will not be absorbed onto the sodium nonatitanate. Significant amounts of Co would be expected to precipitate when the target solution is neutralized, and thus little is expected to be available under alkaline conditions to absorb onto the sodium nonatitanate. The most

likely isotope to be absorbed is beryllium, because it is a Group II metal with a similar aqueous chemistry to strontium. However, the affinity of sodium nonatitanate for Group II metals decreases in the order Sr > Ca > Mg. No data is available for beryllium, but if the trend continues, the affinity would be expected to be low. Thus, any absorbed 7Be would be readily removed by an alkaline sodium chloride (or similar) wash.

The current process for recovering 82Sr from irradiated rubidium metal and rubidium chloride targets requires minimal modification to facilitate the use of sodium nonatitanate. Both targets are processed following standard processing procedures to generate rubidium chloride solutions in an ammonia/ammonium chloride buffer solution. These solutions are then passed through a sodium nonatitanate column and washed with additional buffer to remove any weakly held rubidium cations. Strontium and possibly some other cationic species present will be absorbed onto the nonatitanate column, whereas rubidium cations, ammonium cations and anions will rapidly pass through the column. If additional cations are absorbed onto the sodium nonatitanate, they can be selectively removed by washing with an appropriate eluant (e.g. citrate, nitrilotriacetate.) The strontium selectivity of sodium nonatitanate has been shown to be unaffected by a number of common complexants and as a consequence, it should be a relatively simple manner to elute any undesirable cations from the column, leaving pure 82/85Sr.

Figure 1 clearly shows the exceptionally high affinity of the sodium nonatitanate materials in comparison with the currently utilized organic resin Chelex 100. All of the sodium nonatitanates performed equally well in the buffered rubidium target solutions indicating that the synthetic conditions are not too important when the material is being used in solutions containing high concentrations of rubidium ions. Thus, by replacing the Chelex 100 with sodium nonatitanate, a more efficient 82Sr isolation can be achieved.

It has also been shown that it is possible to tailor the selectivity of the sodium nonatitanate to achieve the optimum Sr/Rb separation by manipulating the reaction conditions. The differing selectivities were most obvious in sodium solutions, with the less crystalline materials exhibiting the highest strontium distribution coefficients. However, the series of nonatitanates showed little difference in behavior when the predominant cation in solution was Rb+. The materials synthesized clearly demonstrated superior characteristics to the commercially available sample in almost all matrices evaluated. The majority of the sodium nonatitanate samples also exhibited greater strontium selectivities than hydrous tin dioxide in a range of sodium chloride solutions, from 1M to 0.001M. Rubidium selectivities were low, making the sodium nonatitanate ideal as a replacement for hydrous tin dioxide in a 82Rb generator.

Commercially, one method of 82-Sr production is via the proton spallation reaction with natural molybdenum metal targets. A simulated molybdate target solution was prepared as follows. 12.5 g of molybdenum powder was carefully dissolved in 30% H_2O_2 solution and made up to a total volume of 500 mL to produce a clear yellow solution of molybdic acid, H_2MoO_4. Solid sodium hydroxide granules totaling 10.9 g were then carefully added to neutralize the solution and bring the pH to approximately 12.3. The colorless solution was then filtered to remove any precipitate. This alkaline molybdate solution was spiked with either 86Rb or 89Sr and K_d values determined as described previously. Separation factors for the strontium/rubidium selectivity were also calculated by dividing the strontium K_d by the rubidium K_d, thus allowing the relative affinities of the ion exchange materials to be directly compared. The results are illustrated below in Table 5.

Table 5. Strontium and rubidium absorption from simulated molybdate target solutions

Material	Sr K_d mL/g	Rb K_d mL/g	Separation Factor
AW500	7,070	194	36.4
K+ Pharmacosiderite	187,000	142	1320
Sodium Titanosilicate	547,000	6500	84.2
Chelex 100 (Na+)	3,120	5	624
AG 50W-X8 (Na+)	69	18	3.83
NaTi (Honeywell)	337,000	27	12,500
NaTi (No hydrothermal)	1,690,000	12	141,000
NaTi (170°C, 21hr)	1,000,000	12	83,300
NaTi (170°C, 3d)	829,000	14	59,200
NaTi (170°C, 7d)	324,000	3	108,000
NaTi (200°C, 21hr)	954,000	12	79,500
NaTi (200°C, 3 d)	687,000	11	62,500
NaTi (200°C, 7d)	772,000	9	85,800
ZrO_2	168,000	8	21,000

From this data, it is clear that the sodium nonatitanate materials are far superior to Chelex 100 and AG 50W-X8 ion exchange resins for the recovery of 82Sr from irradiated molybdenum targets. High K_d values in excess of 500,000 mL/g indicate that almost 100% strontium removal was achieved by some of the nonatitanate samples, with the residual strontium in solution approaching background levels. In the alkaline conditions used in this test, the Chelex 100 resin had the lowest affinity for strontium of all of the materials evaluated. The selectivity of the sodium nonatitanate for rubidium was lowest for the sodium nonatitanate material that was prepared by heating for 1 week at 170°C to obtain a relatively crystalline product. However, strontium selectivity also decreased with increasing reaction time.

The best overall strontium/rubidium separation factor was obtained for the material that had not undergone any hydrothermal treatment. All of the materials performed better than the commercially available nonatitanate materials. Thus, it is possible to alter the selectivity of the material by controlling the reaction conditions to produce an improved sodium nonatitanate material for use in 82Sr separations. Rubidium selectivities were very low for all of the nonatitanates, indicating minimal rubidium absorption would occur in a column process and that any rubidium absorbed would be readily removed by a dilute saline wash.

The sodium titanosilicate, potassium Pharmacosiderite and AW500 exhibit selectivities for rubidium that are too high to allow their use in the selective removal of 82Sr from irradiated molybdenum targets. This high selectivity would result in some rubidium being retained on the column that would not be readily removed by a simple saline wash, thus leading to contamination of the 82Sr product with both radioactive and stable rubidium isotopes. Hydrous tin oxide was not evaluated because, due to the amphoteric nature of tin, significant dissolution would be expected at a pH in excess of 12.

Example 6 - Acid Molybdate Target Solutions

Sodium nonatitanate has a relatively low affinity for strontium at pH values less than 6, and was not expected to exhibit any affinity for strontium from the acidic molybdate target solutions prior to the addition of sodium hydroxide. K_d values were determined to confirm this and to compare it with the K_d values for both Chelex 100 and AG 50W-X8 under identical conditions. The data obtained is shown below in Table 6.

Table 6. The affinity of selected ion exchange materials for strontium in acidic molybdate target solutions

Ion Exchange Material	Sr K_d mL/g	Final pH of Solution
Chelex 100	25	1.43
AG 50W-X8	18,300	1.42
Sodium Nonatitanate (Honeywell)	1,260	1.53

These data clearly indicate that for the processing of acid molybdate solutions, the strong acid ion exchange resin AG 50W-X8 is the preferred medium. However, the Sr K_d value of 18,300 mL/g in the acidic media is nearly two orders of magnitude lower than the K_d value of 1,690,000 mL/g that was obtained for the best of the sodium nonatitanate materials in alkaline molybdate solutions. Consequently, it is evident that 82Sr can be recovered more effectively from alkaline solution using sodium nonatitanate than is currently achieved using AG 50W-X8 from acidic media.

Example 7 - Rubidium and Rubidium Chloride Target Solutions

The processing of either rubidium chloride or rubidium metal targets follows a similar procedure once the target has been successfully dissolved. In essence, 82Sr needs to be selectively extracted from a solution of RbCl in a 0.1 M NH_3 / 0.1M NH_4Cl buffer adjusted to a pH of between 9 and 10. Batch experiments were performed in simulated buffer solutions to determine the strontium selectivity in the presence of high concentrations of rubidium ions. Only the ion exchange materials that exhibited high strontium selectivities in the initial scoping studies with NaCl solutions were evaluated. K_d values were obtained as described previously. Two rubidium chloride solutions were selected which represent typical rubidium concentrations obtained during the processing of rubidium metal (1.95 M Rb+) and rubidium chloride targets (0.68 M Rb+). In both cases, Chelex 100 is used in the preliminary step to remove the 82Sr from the buffered rubidium solutions. The K_d values for the ion exchange materials are shown in Figure 1.

In the buffered rubidium solutions, there is little difference between the different nonatitanates evaluated. This is in stark contrast to the sodium molybdate solutions where a large variation in the performance of the titanates was observed. The nonatitanates were clearly the most effective materials at removing strontium from the buffered solutions with strontium K_d values of around 15,000 mL/g in 0.68 M Rb+ solutions and approximately 5,000 mL/g in 1.96 M Rb+ solutions. By contrast, Chelex 100 ion exchange resin gave K_d values of less than 1,000 mL/g in both solutions. Hydrous titanium oxide and hydrous tin oxide also exhibited appreciable K_d values, but they performed less efficiently than the nonatitanates in both solutions. Consequently, this data demonstrates that using sodium nonatitanate in place of Chelex 100 ion exchange resin will greatly increase the amount of strontium extracted from the target solutions.

The ion exchange materials were also evaluated for their rubidium selectivity from 0.1 M NH_3 / 0.1M NH_4Cl buffer solution. The buffer was prepared, spiked with 86Rb and the pH adjusted to approximately 9.25 with concentrated ammonia. 86Rb K_d values were then determined following the method described earlier. All of the sodium nonatitanates had a K_d < 20 mL/g. The very low rubidium selectivity in the pure buffer is almost certainly due to competition from NH_4+ ions for the available ion exchange sites. Consequently, absorption of rubidium during the processing of rubidium and rubidium chloride targets will be minimal, and any rubidium absorbed will be readily removed by washing with additional 0.1 M NH_3 / 0.1M NH_4Cl buffer solution. Thus, a clean separation of 82Sr from these targets can be obtained using sodium nonatitanate.

The performance could also be improved by removing the buffer and increasing the pH to improve the amounts of strontium absorbed. (Buffers were initially utilized to maximize the performance of the organic ion exchange resins currently used and are not essential to the 82Sr recovery process.)

Example 9 - Kinetic Experiments

In order for the sodium nonatitanate materials to find applications in the processing of irradiated target solutions, they must exhibit fast ion exchange kinetics allowing solutions to be passed through an ion exchange column at an acceptable rate. The kinetics of strontium absorption from alkaline molybdate target solutions was evaluated using a simple batch procedure. Ion exchange material, in the amount of 0.05 g, was shaken with 10 mL of molybdate solution spiked with 89Sr to give a total activity of approximately 155,000 cpm/mL. After an allotted time, the material was filtered through a 0.2 m syringe filter and the activity in the aqueous phase determined by LSC. The results are shown below in Figure 2.

From the data in Figure 2, it is clear that the reaction kinetics for the sodium nonatitanate powder is extremely rapid, with over 99 % of the 89Sr removed in only 1 minute. By contrast, the reaction kinetics of the organic ion exchanged resins was much slower and the total amount of 89Sr removed after 1 hour was much less.

The exceedingly rapid kinetics can partly be explained by the fact that the nonatitanate was in the form of a fine powder, whereas the two resins were in the form of beads (see Table 1). As a consequence, a relatively slow reaction rate would be expected for the beads because the uptake of 82Sr will be dependent upon the rate of diffusion of the 82Sr to the internal functional groups. The rate of uptake of a sample of sodium nonatitanate pellets (using hydrous titanium dioxide as a binder) was significantly slower than the powdered form, but the kinetics and amount of 82Sr absorbed was still significantly better than for either of the two organic resins. As the pelletization process is improved, it is expected that the kinetics and selectivity of the pelletized sodium nonatitanate will improve substantially. Other sodium nonatitanate powders of varying crystallinities also showed rapid kinetics. Other potentially suitable binders for forming suitable pellets include titanium isopropoxide or tetraethyl orthosilicate (TEOS) as a binder precursor.

Example 10 - 82Sr Removal from Irradiated Targets Using Pelletized Sodium Nonatitanate

A sample of sodium nonatitanate was mixed with titanium isopropoxide as a binder and the resulting paste dried at 105°C for 12 hours. The material was gently broken up using a mortar and pestle and then sieved to produce particles in the range 40 to 60 mesh. The binder content was approximately 20%. These particles were then used to assess the extraction of 89Sr from simulated target solutions.

1 mL of pelletized sodium nonatitanate was slurried into a column and the target simulant that had been spiked with 89Sr to give an activity of approximately 200,000 cpm/mL was passed through the column at a flow rate of 15 mL per hour. The amount of activity removed from solution was then determined. The results are given below in Table 1.

Table 1. Removal of 82Sr From Irradiated Target Solutions

Target (%)	Solution Composition	Volume (mL)	82Sr Removed
Rubidium Metal	1.95M RbCl in 0.1M NH_3/NH_4Cl Buffer, pH10	20	97.3
Rubidium Chloride	0.68M RbCl in 0.1M NH_3/NH_4Cl Buffer, pH 10	20	98.8
Molybdenum Metal	0.26M Na_2MoO_4, pH 12	20	99.9

This data clearly shows the effectiveness of sodium nonatitanate at removing strontium isotopes from 82Sr target materials. Rubidium absorption under these conditions is minimal.

Example 11 - Elution of Strontium

Strontium was quantitatively eluted from the sodium nonatitanate column of Example 10 using 6M nitric acid. Hydrochloric acid was found to be much less effective and also resulted in breakdown of the sodium nonatitanate particles and blocked the ion exchange column.

While the foregoing is directed to the preferred embodiment of the present invention, other and further embodiments of the invention may be devised without

departing from the basic scope thereof, and the scope thereof is determined by the claims that follow.

What is claimed is:

1. A rubidium-82 generator, comprising:

(a) a strontium-82 support medium comprising sodium nonatitanate.

2. The rubidium-82 generator of claim 1, wherein the sodium nonatitanate is characterized by a strontium selectivity greater than 250,000 mL/g at an alkaline pH.

3. The rubidium-82 generator of claim 1, wherein the sodium nonatitanate is characterized by a rubidium selectivity less than 100 mL/g at an alkaline pH.

4. The rubidium-82 generator of claim 1, wherein the sodium nonatitanate is characterized by a strontium/rubidium separation factor greater than 1,000.

5. The rubidium-82 generator of claim 1, wherein the sodium nonatitanate is characterized by a strontium/rubidium separation factor greater than 100,000.

6. A process for preparing a rubidium-82 generator, comprising:

(a) preparing sodium nonatitanate from titanium isopropoxide and aqueous sodium hydroxide;

(b) heating the sodium nonatitanate at a temperature between 100°C and 250°C for a period between 12 hours and 2 weeks; and

(c) absorbing strontium-82 on the sodium nonatitanate from an aqueous solution comprising strontium-82 and sodium chloride, wherein the sodium chloride concentration is between 0.1 and 1 molar.

7. The process of claim 6, wherein the molar ratio of aqueous sodium hydroxide to titanium isopropoxide is in excess of 0.44.

8. The process of claim 6, wherein the molar ratio of aqueous sodium hydroxide to titanium isopropoxide is between 2 and 6.

9. A method of chemically isolating strontium-82 from a proton-irradiated molybdenum target, comprising:

(a) dissolving the molybdenum metal target containing the strontium-82;

(b) adjusting the pH of the dissolved molybdenum target solution to an alkaline pH;

(c) removing precipitates from the solution; and then

(d) absorbing the strontium-82 from the solution onto a support comprising sodium nonatitanate.

10. A process for preparing a solution containing rubidium-82, comprising:

(a) providing a solution containing strontium-82 at a pH between 10 and 14;

(b) absorbing strontium-82 onto a sodium nonatitanate support medium; and

(c) eluting rubidium-82 from the sodium nonatitanate support medium with a solvent.

11. The process of claim 10, wherein the solvent is selected from the group consisting of water and saline solutions.

12. The process of claim 10, wherein the solvent is an aqueous solution having a sodium chloride concentration between 0.001 molar and 1 molar.

13. The process of claim 10, wherein the solvent is an aqueous solution having a sodium chloride concentration between 0.2 molar and 1 molar.

14. The process of claim 10, wherein the solvent is a pharmaceutical-grade saline and buffer solution.

15. A method of chemically isolating strontium-82 from a proton-irradiated rubidium or rubidium chloride target, comprising:

(a) dissolving the target containing the strontium-82;

(b) adjusting the pH of the dissolved target solution to an alkaline pH;

(c) removing precipitates from the solution; and then

(d) absorbing the strontium-82 from the solution onto a support comprising sodium nonatitanate without absorbing rubidium.

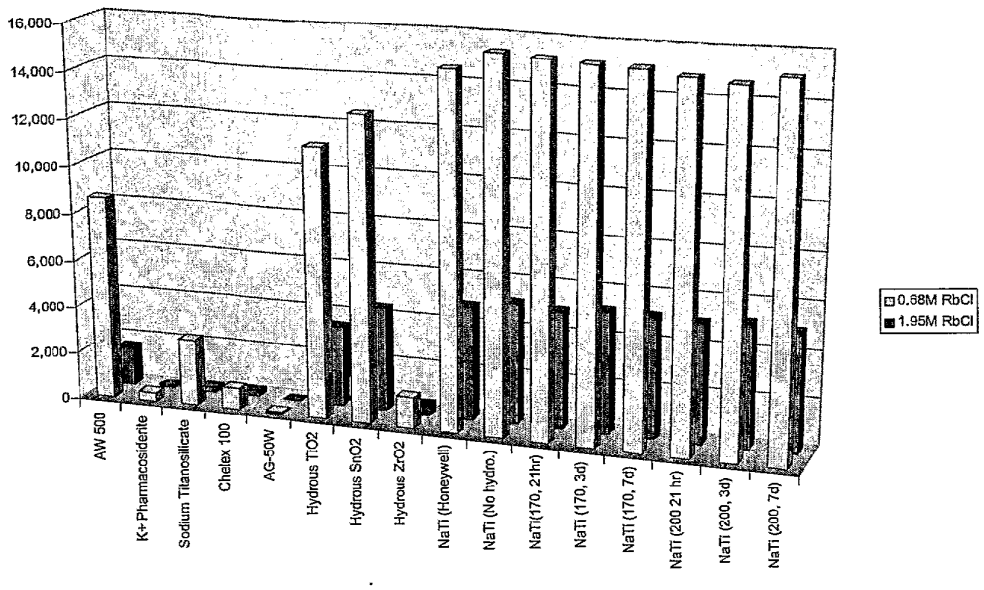


Figure 1. 82Sr K_d Values for the ion exchange materials from simulated rubidium and rubidium chloride target solutions

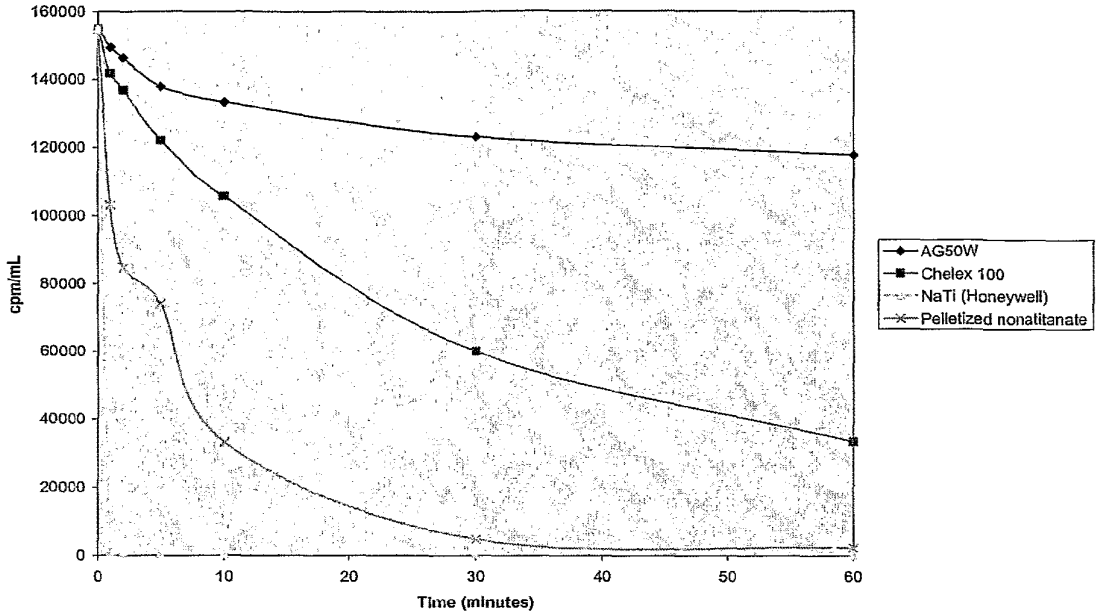


Figure 2. The reduction of 82Sr activity with increasing time.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 02/41676

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 G21G4/08

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)
IPC 7 G21G

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, COMPENDEX

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	EP 0 043 650 A (SQUIBB & SONS INC) 13 January 1982 (1982-01-13) the whole document	1-15
A	US 3 953 567 A (GRANT PATRICK M ET AL) 27 April 1976 (1976-04-27) the whole document	1-15
A	US 4 406 877 A (NEIRINCKX RUDI D ET AL) 27 September 1983 (1983-09-27) the whole document	1-15
A	US 3 957 945 A (GRANT PATRICK M ET AL) 18 May 1976 (1976-05-18) the whole document	9

-/--

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

[X] Patent family members are listed in 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
15 September 2003	25/09/2003

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, Tx. 31 651 epo nl, Fax: (+31–70) 340–3016	Ludi, M

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

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication,where appropriate, of the relevant passages	Relevant to claim No.
A	SYLVESTER P ET AL: "AN ASSESSMENT OF INORGANIC ION-EXCHANGE MATERIALS FOR THE REMOVAL OF STRONTIUM FROM SIMULATED HANFORD TANK WASTES" SEPARATION SCIENCE AND TECHNOLOGY, DEKKER,,NEW YORK,NY,, US, vol. 34, no. 10, 1999, pages 1981-1992, XP009013438 ISSN: 0149-6395 the whole document ---	1-15
A	SAHA G B ET AL: "USE OF THE 82SR/82RB GENERATOR IN CLINICAL PET STUDIES" INTERNATIONAL JOURNAL OF RADIATION APPLICATIONS AND INSTRUMENTATION PART B: NUCLEAR MEDICINE AND BIOLOGY, ELSEVIER SCIENCE PUBLISHERS, NEW YORK, NY, US, vol. 17, no. 8, 1990, pages 763-768, XP000166064 ISSN: 0883-2897 the whole document -----	1

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/US 02/41676

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
EP 0043650 A	13-01-1982	US 4400358 A	23-08-1983
		AT 22188 T	15-09-1986
		AU 548918 B2	09-01-1986
		AU 7135281 A	07-01-1982
		CA 1176618 A1	23-10-1984
		DE 3175292 D1	16-10-1986
		EP 0043650 A2	13-01-1982
		IE 51449 B1	24-12-1986
		JP 1662587 C	19-05-1992
		JP 3025760 B	08-04-1991
		JP 57030545 A	18-02-1982
		ZA 8103677 A	30-06-1982
US 3953567 A	27-04-1976	CA 1057946 A1	10-07-1979
		CH 591750 A5	30-09-1977
		DE 2542415 A1	15-04-1976
		FR 2286480 A1	23-04-1976
		JP 51060900 A	27-05-1976
US 4406877 A	27-09-1983	AU 7068681 A	10-12-1981
		CA 1171354 A1	24-07-1984
		EP 0041356 A1	09-12-1981
		JP 57031624 A	20-02-1982
		ZA 8103320 A	26-05-1982
US 3957945 A	18-05-1976	NONE	

Form PCT/ISA/210 (patent family annex) (July 1992)

Electronic Acknowledgement Receipt

EFS ID:	11635565
Application Number:	12137364
International Application Number:	
Confirmation Number:	7377
Title of Invention:	INFUSION SYSTEMS INCLUDING COMPUTER-FACILITATED MAINTENANCE AND/OR OPERATION AND METHODS OF USE
First Named Inventor/Applicant Name:	Stephen E. Hidem
Customer Number:	22859
Filer:	Paul J. LaVanway Jr.
Filer Authorized By:	
Attorney Docket Number:	56782.1.7
Receipt Date:	16-DEC-2011
Filing Date:	11-JUN-2008
Time Stamp:	14:37:11
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	Foreign Reference	EP0919249A1.pdf	1041653 120cd7eac47e368daa3cf979f03c445e82efafc6	no	25

Warnings:	
Information:	

2	Foreign Reference	EP1421960A1.pdf	602979 df441eea183dc8af25823419d1535d4e3da6f32c	no	11
Warnings:					
Information:					
3	Foreign Reference	WO2009152320A2.pdf	3029042 50db57966273fb4a35de35c1a630c2a1c081c822	no	71
Warnings:					
Information:					
4	Non Patent Literature	Brochure-IV-Liquid-Filters.pdf	88247 79b0e5e0fee23e68fcfae6694762ca1c596bd35a	no	2
Warnings:					
Information:					
5	Non Patent Literature	ISR-56782-1-9-1.pdf	1532421 b210207372ffa5795892305aa08527a8279c5d05	no	13
Warnings:					
Information:					
6	Information Disclosure Statement (IDS) Form (SB08)	7thSIDS_56782-1-7.pdf	982438 658d32a759518ad45239910d20bd0cc5f52ec76d	no	6
Warnings:					
Information:					
7	Foreign Reference	WO2004059661A1.pdf	1378510 90312f92d7372cc3550f43aebce82c4c3bd9cd9d	no	27
Warnings:					
Information:					
			Total Files Size (in bytes):	8655290	

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.

New Applications Under 35 U.S.C. 111

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.

National Stage of an International Application under 35 U.S.C. 371

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.

New International Application Filed with the USPTO as a Receiving Office

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.

(19) Europäisches Patentamt
European Patent Office
Office européen des brevets

(11) EP 0 919 249 A1

(12) EUROPEAN PATENT APPLICATION

(43) Date of publication:
02.06.1999 Bulletin 1999/22

(51) Int. Cl.[6]: **A61M 1/36**

(21) Application number: **98121181.6**

(22) Date of filing: **13.11.1998**

(84) Designated Contracting States:
AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
Designated Extension States:
AL LT LV MK RO SI

(30) Priority: **20.11.1997 JP 320194/97**
19.12.1997 JP 350381/97
19.06.1998 JP 172805/98

(71) Applicant: **Nissho Corporation**
Osaka-shi, Osaka-fu, 531-8510 (JP)

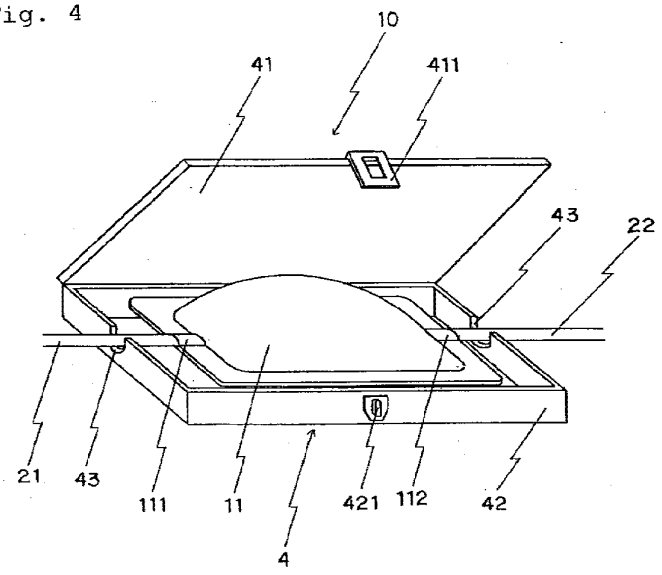
(72) Inventors:
- **Sasayama, Norihisa**
  Osaka-shi, Osaka-fu 531-8510 (JP)
- **Kikuchi, Toshihiro**
  Osaka-shi, Osaka-fu 531-8510 (JP)
- **Harada, Shinichiro**
  Osaka-shi, Osaka-fu 531-8510 (JP)
- **Takagi, Nobuo**
  Osaka-shi, Osaka-fu 531-8510 (JP)
- **Wakabayashi, Takahito**
  Osaka-shi, Osaka-fu 531-8510 (JP)

(74) Representative:
Weisert, Annekäte, Dipl.-Ing. Dr.-Ing. et al
Patentanwälte
Kraus Weisert & Partner
Thomas-Wimmer-Ring 15
80539 München (DE)

(54) A blood filter set and a method of recovering blood components by use of the same

(57) This invention relates to a blood filter set comprising a bag body having a blood flow inlet and a blood flow outlet and charged with a filter material, and an accommodation vessel for accommodating said bag body and a method of recovering blood components by use of the filter set.

Fig. 4



EP 0 919 249 A1

Description

Field of the Invention

[0001] The present invention relates to a filter set for recovering desired blood components from human blood and a method of recovering blood components by use of the filter set.

Background of the Invention

[0002] It is known that hematopoietic malady occurs as side effects of chemotherapy for hematopoietic organ tumors such as leukemia etc., and solid tumors, and bone marrow transplant and peripheral blood stem cell transplant are applied as therapies for the hematopoietic malady. These therapies are methods of recovering from hematopoietic malady, in which hematopoietic stem cells and/or hematopoietic precursor cells contained in bone marrow and peripheral blood are transplanted into human body. By establishing these transplant therapies, chemotherapy for tumors such as leukemia and solid tumors was made feasible. Further, it was found in recent years that hematopoietic stem cells and/or hematopoietic precursor cells are also contained in umbilical cord blood, and a therapy by transplanting hematopoietic cells and/or hematopoietic precursor cells from umbilical cord blood is also expected to be a promising method.

[0003] Usually, blood used for these transplant therapies is cryopreserved after collecting till transplanting. If cryopreserved blood is contaminated with erythrocytes, the erythrocytes are lyzed to cause side effects after thawing, therefore, before thawing the blood to be transplanted erythrocytes should be removed from the blood.

[0004] Known methods of removing erythrocytes from blood to be transplanted include a centrifugation method and a filter method. A centrifugation method utilizes the difference in specific gravity between erythrocytes and leukocytes derived from hematopoietic stem cells and/or hematopoietic precursor cells. A filter method of recovering leukocytes utilizes a filter for passing erythrocytes but capturing leukocytes derived from hematopoietic stem cells and/or hematopoietic precursor cells and the leukocytes captured therein is recovered with a washing solution.

[0005] However, the centrifugation method requires such skills as not to cause disturbance of the interfaces among separated blood components, while the filter method has the disadvantage of low yield because the density of the filter material is so high as to capture hematopoietic stem cell- and/or hematopoietic precursor cell-derived leukocytes at high concentration, thus making it difficult to remove leukocytes which have adhered to the filter material even if a washing solution is used.

[0006] The present invention is to solve these problems, and the object of the present invention is to provide a filter set for efficiently recovering desired blood components from blood and a method of recovering blood components by use of the filter set.

[0007] As a result of their eager study for achieving the above object, the present inventors found that desired blood components can be efficiently recovered from blood with a blood filter set which comprises a bag body charged with a filter material and an accommodation vessel for accommodating said bag body. Further, they found that a filter set comprises preferably a bag body consisting of a flexible sheet charged inside with a filter material and a rigid accommodation vessel for accommodating the bag body in a compressed condition or in a freely expansive and compressive condition. Additionally, they found that mainly leukocytes could be efficiently recovered from blood by a bag body charged inside with a filter material and a flexible tube body accommodating the bag body in a compressed condition in the thickness direction.

Summary of the Invention

[0008] That is, the present invention relates to a filter set comprising a bag body having a blood flow inlet and a blood flow outlet and charged with a filter material, and an accommodation vessel for accommodating said bag body.

[0009] One embodiment of this invention is a filter set comprising a bag body having a blood flow inlet and a blood flow outlet and consisting of a flexible sheet charged inside with a filter material, and a rigid accommodation vessel for accommodating said bag body which is freely removed therefrom and for accommodating said bag body in a compressed condition at the time of accommodation.

[0010] The rigid accommodation vessel is a rectangular parallelepiped vessel provided with a takeout port from which the bag body can be removed or a vessel provided with a lid which can be opened and closed or the like.

[0011] Another embodiment of this invention is a filter set comprising a bag body having a blood flow inlet and a blood flow outlet and consisting of a flexible sheet charged inside with a filter material, and a rigid accommodation vessel for accommodating said bag body, wherein said bag body is compressed by filling with compressed gas, and after blood is passed through said bag body in a compressed condition, the compressed gas is exhausted to relieve the compression of said bag body through which a washing solution is then passed.

[0012] The rigid accommodation vessel includes a vessel compressing said bag body by filling with compressed gas

and relieving the compression of the bag body by exhausting the compressed gas. Otherwise, the vessel is capable of further expanding the bag body by evacuating the inside of the vessel after relieving the compression condition.

[0013] Another embodiment is a filter set comprising a bag body having a blood flow inlet and a blood flow outlet and being charged inside with a filter material and a flexible tube body accommodating the bag body in a compressed condition in the thickness direction, wherein said bag body can be removed from said tube body.

[0014] The tube body is a heat-shrinkable tube or possesses a similar length to that of the bag body and a smaller volume than that of the bag body. If the tube body is heat-shrinkable, the tube body is preferably provided with a ruptured portion. And if the tube body possesses a similar length to that of the bag body and a smaller volume than that of the bag body, the tube body is preferably provided at least one end with a grasping portion for removing the tube body from the bag body.

[0015] The present invention relates to a method of recovering blood components comprises accommodating a bag body into an accommodation vessel, wherein the bag body has a blood flow inlet and a blood flow outlet and is charged inside with a filter material, passing blood flow through said bag body in a condition compressed by said accommodation vessel to adhere blood components to the filter material, removing the bag body from said accommodation vessel, passing a washing solution through the inside of said bag body in an expanded condition so as to wash off the blood components adhered to said filter material, and recovering the blood components.

[0016] One embodiment of the present invention relates to a method of recovering blood components comprises filling a bag body with compressed gas to compress said bag body, wherein the bag body has a blood flow inlet and a blood flow outlet, consists of a flexible sheet and is charged inside with a filter material and accommodated in a rigid accommodation vessel, passing blood flow through said bag body in a compressed condition to adhere blood component to the filter material, exhausting the compressed gas to relieve the compression condition of said bag body, passing a washing solution through the inside of said bag body so as to wash off the blood components adhered to said filter material and recovering the blood components.

[0017] After the compressed gas is exhausted, the inside of the vessel may be evacuated to further expand said bag body through which the washing solution is then passed to wash and recover blood components having adhered to said filter.

[0018] Another embodiment is a method of recovering blood components comprising passing blood through a bag body in a compressed condition, wherein the bag body has a blood flow inlet and a blood flow outlet, consists of a flexible sheet and is charged with a filter material and accommodated in a flexible tubular body in a compressed condition in the thickness direction, removing the bag body from the flexible tubular body to relieve the compression of the bag body, passing a washing solution through the inside of said bag body so as to wash off the blood components adhered to the filter material, and recovering the blood components.

Brief Description of the Drawings

[0019]

Fig. 1 is a drawing showing one example of the filter set of the present invention.
Fig. 2 is a longitudinal section of the filter set shown in Fig. 1.
Fig. 3 is a drawing illustrating the filter set shown in Fig. 1.
Fig. 4 is a drawing showing another example of the filter set of the present invention.
Fig. 5 is a drawing showing the method of recovering blood components according to the present invention.
Fig. 6 is a drawing showing another example of the blood filter set of the present invention.
Fig. 7 is a longitudinal section of the bag body compressed by filling the blood filter set in Fig. 6 with compressed gas.
Fig. 8 is a longitudinal section showing the condition under which the bag body whose compression was relieved by exhausting the compressed gas from the blood filter set shown in Fig. 6.
Fig. 9 shows one example of the filter set of the present invention.
Fig. 10 is a longitudinal section of the filter set shown in Fig. 9.
Fig.11 shows another example of the filter of the present invention.

Description of Preferred Embodiments

[0020] Examples of the present invention are described with reference to the drawings.

[0021] As shown in Figs. 1, 2 and 3, the filter set 1 is composed of bag body 11 charged inside with filter material 12, tube 21 connected to blood flow inlet 111 and tube 22 connected to blood flow outlet 112 for the bag body 11, and an accommodation vessel 3 for accommodating the bag body 11 in a compressed condition. Figs. 1 and 2 show that the bag body 11 has been removed from the accommodation vessel 3 and Fig. 3 shows that the bag body 11 has been

accommodated in the accommodation vessel 3.

[0022] The bag body 11 consists of two flexible sheets welded along the edge thereof. The material of the bag body 11 includes soft polyvinyl chloride, ethylene-vinyl acetate copolymers, styrene-butadiene-styrene copolymers, polyurethane, polyamide, polyester, polyethylene, polypropylene etc. The welding method is preferably thermal welding, high frequency welding, ultrasonic welding, solvent welding or the like.

[0023] The bag body 11 has been charged inside with the filter material 12, and the filter material 12 is sealed along the edge to the weld of the bag body 11. The filter material 12 is to capture desired blood components (mainly leukocytes) from blood, and it is composed preferably of synthetic fibers such as polyester, polypropylene, polyethylene, polymethyl methacrylate, polyamide etc., natural fibers such as cotton etc.

[0024] The diameter of the fiber is preferably in the range of 0.1 to 40 μm, preferably 0.5 to 25 μm, more preferably 0.5 to 10 μm, and most preferably 0.5 to 3 μm, and in the case of a diameter of less than 0.1 μm, spaces between the fibers per unit area tend to become small thus increasing filtration resistance, while in the case of a diameter of more than 40 μm, the volume of the fibers tends to become large thus increasing absorption of undesired blood components.

[0025] The bulk density of fiber agglomerate in compressed bag body 11 is 0.05 to 0.50 g/cm^3, preferably 0.08 to 0.30 g/cm^3, and more preferably 0.10 to 0.20 g/cm^3. If the bulk density is less than 0.05 g/cm^3, the yield of leukocytes recovered in the filter tends to decrease, and if the bulk density exceeds 0.50 g/cm^3, the flow rate of blood passing through the filter tends to decrease.

[0026] The amount of the filter material 12 charged may be any amount enough to achieve degrees of capture possessed by a conventional leukocyte-removing filter in a compressed condition.

[0027] This filter material 12 may be formed of two or more materials or may comprise layers of different substances or different mesh sizes laminated therein. If the filter material 12 is composed of a multi-layer fiber agglomerate, at least one layer has a fiber diameter of 25 μm or less and a bulk density of 0.05 to 0.50 g/cm^3 in a compressed condition. The multi-layer structure is composed of 2 to 6 layers, where a layer near the blood flow inlet consisting of fiber agglomerate having a large fiber diameter and a high bulk density and a layer near the blood flow outlet consisting of a fiber agglomerate having a small fiber diameter and a low bulk density are preferably arranged so that leukocytes can be captured in the order of a decreasing diameter through the layers.

[0028] For example, if the filter material 12 in compressed bag body 11 is a multi-layer fiber agglomerate consisting of a fiber agglomerate with a fiber diameter of 10 μm and a bulk density of 0.23 g/cm^3 as a first layer, a fiber agglomerate with a fiber diameter of 3.5 μm and a bulk density of 0.11 g/cm^3 as a second layer and a fiber agglomerate with a fiber diameter of 1.8 μm and a bulk density of 0.12 g/cm^3 as a third layer, then blood components with large diameters will be captured by the first layer, monocytes and granulocytes by the second layer and lymphocytes by the third layer.

[0029] This filter material 12 may be formed of two or more materials or may comprise layers of different substances or different mesh sizes laminated therein. Further, the filter material 12 is not limited to the structure in which it is sealed along the edge to the weld of the bag body 11, and as shown in e.g. Japanese Laid-Open Patent Publication No. 67952/1995, the filter material may be formed into a hanging-bell form, and its edge is sealed by welding from a lower part to the side while an upper part is open and the end of the upper part is welded with a bag body.

[0030] In the bag body 11, the blood flow inlet 111 and the blood flow outlet 112 are arranged in the opposite side to each other relative to the filter material 12, and blood introduced from the blood flow inlet 111 is passed through the filter material 12 and discharged from the blood flow outlet 112. Similarly, a washing solution introduced from the blood flow inlet 111 or the blood flow outlet 112 is passed through the filter material 12 and discharged from the blood flow outlet 112 or the blood flow inlet 111. The bag body 11 made of a flexible sheet charged with the filter material 12 is freely expansive and compressive, and spaces between the fibers in the filter material 12 are variable, therefore, spaces between the fibers are made small when blood is passed, while spaces between the fibers is made large when a washing solution is passed. Here, the washing solution is to wash away the blood components having adhered to filter material 12 and recover them, and it is preferably physiological saline, Hank's solution, Dulbecco phosphate buffer, dextran etc. which may optionally contain human serum albumin or an anti-coagulation agent.

[0031] Tube 21 is connected to the blood flow inlet 111, and tube 22 is connected to the blood flow outlet 112. The connection method includes welding, adhesion, connection by a connector, etc. In the case of connection by a connector, usually the tube 21 has been connected to the bag body 11, but the tube 21 may be aseptically connected to the bag body 11 just before use. When the filter set of the present invention is used, one end of tubes 21 and 22 is attached to the bag body 11, and a blood bag (not shown) is attached to the other end of tubes 21 and 22, but in place of tubes 21 and 22, syringes etc. may be connected to the blood flow inlet 111 and the blood flow outlet 112.

[0032] The accommodation vessel 3 is a rectangular parallelepiped vessel which is formed of a rigid material so as to accommodate the bag body 11 in a compressed condition and which is provided with the bag body-removing port 31 from which the bag body 11 can be removed. The vessel is attached so as to slide freely in the longitudinal direction on tube 21 attached to the side of the blood flow inlet 111. The material includes synthetic resin such as polycarbonate, polystyrene, rigid polyvinyl chloride, polypropylene etc. or metals. The accommodation vessel 3 preferably has a size enough to compress the bag body 11 to achieve degrees of capture possessed by a conventional leukocyte-removing

filter. However, the accommodation vessel 3 in the present invention is not limited to the shape shown in Figs. 1, 2 and 3, and the accommodation vessel 3 may have any shape by which the bag body 11 is accommodated in a compressed condition so as to capture desired blood components and from which the bag body 11 can be removed so as to efficiently recover blood components captured in the filter material 12.

[0033] The filter set of the present invention may be constituted as shown in Fig. 4. The accommodation vessel 4 has a lid 41, which can be opened and closed freely, the bag body accommodated therein is compressed by closing the lid 41 in Fig.4. A groove 43 in which a tube connected with a bag body 11 is inserted and a connecting means to close a lid 41 are provided with the accommodation vessel 4. The connecting means may be such that can not put out the connection by the resiliency of the compressed bag body when the lid is closed. For instance, they are constituted with an arm 411 provided with the lid 41 and a protuberance 421 connected with said arm 411 and provided with the vessel body 42. In this example this filter set has advantages that there is no risk for damaging the bag body 11 and it may be possible to relieve a compression of the bag body 11 more rapidly because the bag body is not necessarily operated directly and the lid of the accommodation vessel is to be opened simply.

[0034] The method of recovering hematopoietic stem cell- and/or hematopoietic precursor cell-derived leukocytes from umbilical cord blood by use of the filter set 1 shown in Figs. 1, 2 and 3 is described.

[0035] First, the bag body 11 is accommodated in the accommodation vessel 3, and umbilical cord blood is passed from the blood flow inlet 111, through the bag body 11 in a compressed condition, to the blood flow outlet 112. In this step, the filter material 12 is compressed and spaces between the fibers are made small, so leukocytes derived from hematopoietic stem cells and/or hematopoietic precursor cells can be accurately captured.

[0036] Then, the bag body 11 is removed from the accommodation vessel 3, and a washing solution is passed from the blood flow outlet 112 to the blood flow inlet 111. In this step, the compression of the filter material 12 is relieved and spaces between the fibers are made large, so hematopoietic stem cell-and/or hematopoietic precursor cell-derived leukocytes having adhered to the filter material 12 can be easily removed and easily washed away with the washing solution for recovery. Because spaces between the fibers are made large, the washing solution can be easily passed therethrough to reduce the time necessary for passing the solution. Here, the washing solution may be introduced from the blood flow inlet 111 or blood flow outlet 112.

[0037] The washing solution containing leukocytes derived from hematopoietic stem cells and/or hematopoietic precursor cells is once recovered in a vessel and then separated by centrifugation or passage through a filter, whereby hematopoietic stem cells and/or hematopoietic precursor cells are recovered. At this step, a filter capturing granulocytes and monocytes but passing hematopoietic stem cells and/or hematopoietic precursor cells is preferably used.

[0038] The blood filter set of the present invention is described with reference to Figs. 6, 7 and 8. The blood filter set 1 is composed of the bag body 11 charged inside with the filter material 12, tube 21 connected to blood flow inlet 111 and tube 22 connected to blood flow outlet 112 for the bag body 11, and the rigid accommodation vessel 3 for accommodating the bag body 11. The accommodation vessel 3 includes ports 31, 32 provided on regions where tubes 21, 22 connected to the bag body 11 penetrate the accommodation vessel 3, in order to maintain the airtightness of the vessel. Introduction and discharge of gas is conducted through the 2-directional stopcock 33.

[0039] The accommodation vessel 3 is a rectangular parallelepiped vessel which is formed of a rigid material so as to accommodate the bag body 11 in a compressed condition by filling the vessel with compressed gas and which is provided with ports 31, 32 for maintaining the airtightness of the tube-connecting portions and with the 2-directional stopcock 33 for introducing and discharging gas. O-rings (not shown) are inserted into between ports 31, 32 and tubes 21, 22 to maintain the airtightness of the accommodation vessel 3. If the accommodation vessel 3 is formed of synthetic resin, the port and the tube may be welded by ultrasonic wave. The compressed gas used includes inert gases such as air, nitrogen, argon etc.

[0040] Because the bag body 11 is compressed to achieve degrees of capture possessed by a conventional leukocyte-removing filter; the accommodation vessel 3 should be formed of a material capable of enduring the compression. The material includes synthetic resin such as polycarbonate, polystyrene, rigid polyvinyl chloride etc. and metals such as stainless steel, aluminum etc. The accommodation vessel 3 is preferably in such a size that it can accommodate the bag body 11 expanded to increase spaces between the fibers in the filter material 12.

[0041] However, the accommodation vessel 3 in the present invention is not limited to the shape shown in the drawings and may have any shape by which the bag body 11 can be accommodated in a compressed condition so as to capture desired blood components and the bag body 11 can be expanded so as to efficiently recover blood components captured in the filter material 12.

[0042] Fig. 5 is a drawing showing the method of collecting blood components by use of the blood filter set in Fig. 6. Blood components collecting apparatus 50 in Fig. 5 includes a filter set of this invention.

[0043] From the blood bag 51 in which whole blood was accommodated, the whole blood is passed through the 3-directional stopcock 55, then tube 21, and introduced from the blood flow inlet 111 into the inside of the bag body 11 in a compressed condition. Leukocytes in the filter material 12 have been captured for example in spaces between the fibers therein, while erythrocytes are passed through the filter material 12, then through the blood flow outlet 112, tube 22

and 3-directional stopcock 56 and are recovered in the erythrocyte-recovering bag 53. The erythrocyte-recovering bag 53 can also accommodate platelets in addition to erythrocytes, depending on the type of the filter material 12. Thereafter, a washing solution in the wash bag 52 is passed through the 3-directional stopcock 55, tube 21, and blood flow inlet 111, thus washing away leukocytes from the filter material 12 having spaces increased between the fibers, whereby the leukocytes are passed through the blood flow outlet 112, tube 22, and 3-directional stopcock 56 and recovered in the leukocyte-recovering bag 54.

[0044] The method of recovering hematopoietic stem cell- and/or hematopoietic precursor cell-derived leukocytes from umbilical cord blood by use of the filter set 1 in Fig.6 is described.

[0045] First, umbilical cord blood is passed from the blood flow inlet 111, through the bag body 11 compressed in the accommodation vessel 3 by filling the vessel with compressed gas, to the blood flow outlet 112. In this step, the filter material 12 is also compressed, and leukocytes derived from hematopoietic stem cells and/or hematopoietic precursor cells are captured in spaces between the fibers. The compressed gas may be filled by a pump or may be injected by a syringe that was directly connected to the 2-directional stopcock 33.

[0046] Then, the 2-directional stopcock 33 is opened, and the compressed gas is exhausted from the accommodation vessel 3 to relieve the compressed condition of the bag body 11, thus expanding the bag body 11 through which the washing solution is then passed from the blood flow inlet 111 to blood flow outlet 112. During this step, the compression of the filter material 12 is also relieved and spaces between the fibers are made large, so leukocytes derived from hematopoietic stem cells and/or hematopoietic precursor cells having adhered to the filter material 12 are easily removed, easily washed away with the washing solution, and recovered in the leukocyte-recovering bag 54 in Fig. 6. Here, the washing solution may be introduced from the blood flow inlet 111 or blood flow outlet 112.

[0047] The washing solution containing leukocytes derived from hematopoietic stem cells and/or hematopoietic precursor cells is once recovered in a blood-recovery vessel and then separated by centrifugation or passage through a filter, whereby hematopoietic stem cells and/or hematopoietic precursor cells are recovered. As the filter used, a filter capturing granulocytes and monocytes but passing hematopoietic stem cells and/or hematopoietic precursor cells is preferably used.

[0048] In this case, the inside of the vessel is further evacuated by exhausting the compressed gas followed by evacuation by a vacuum pump, or by reducing the pressure in the vessel by use of the syringe connected to the 2-directional stopcock 33, whereby the bag body 11 is further expanded and spaces between the fibers in the filter are further enlarged thus facilitating recovery and reducing the time required for recovery.

[0049] As described above, because the filter set of the present invention can relieve the compressed condition by merely opening the 2-directional stopcock 33, its operation is easier than in the prior art. Further, the washing solution can be easily passed by increasing spaces between the fibers to reduce the time necessary for passing the solution.

[0050] As shown in Figs. 9,10 and 11, the filter set is composed of bag body 11 charged inside with filter material 12, tube 21 connected to blood flow inlet 111 and tube 22 connected to blood flow outlet 112 for the bag body 11, and flexible tube body 6 or 7 for accommodating the bag body 11 in a compressed state in the thickness direction.

[0051] The bag body 11 consists of two flexible sheets which were welded along the edge thereof by thermal welding, high-frequency welding, ultrasonic welding, solvent welding or the like. The material of the bag body 11 is preferably synthetic resin such as soft polyvinyl chloride, ethylene-vinyl acetate copolymers, styrene-butadiene-styrene copolymers, polyurethane, polyamide, polyester, polyethylene, polypropylene etc.

[0052] As shown in Fig. 10, the bag body 1 has been charged inside with the filter material 12. The filter material 12 is to capture mainly leukocytes from blood, and it is composed preferably of synthetic fibers such as polyester, polypropylene, polyethylene, polymethyl methacrylate, polyamide etc., natural fibers such as cotton, etc. The diameter of the fiber is preferably in the range of 0.1 to 40 μm, and in the case of a diameter of less than 0.1 μm, spaces between the fibers per unit area tend to become small thus increasing filtration resistance, while in the case of a diameter of more than 40 μm, the volume of the fibers tends to become large thus increasing absorption of excess blood components. The amount of the filter material 12 charged may be any amount enough to achieve degrees of capture possessed by a conventional leukocyte-removing filter in a compressed condition.

[0053] The tube body 6 shown in Fig. 9 consists of a heat-shrinkable tube formed of one or more layers of synthetic resin such as polyvinyl chloride, polyester, polypropylene, polyethylene, polystyrene etc., and after the bag body 11 is accommodated therein, the tube body 3 is heat-shrunk to compress the bag body 11 in a desired shrinkage condition. The tube body 6 may be provided at one end (in the side of tube 22) with a ruptured portion such as V-shaped cutting 61, and a perforation may be provided along the longitudinal direction from the cutting 61 so that after blood is passed through the bag body 11, the tube body 6 can be easily ruptured along the perforation 62. The tube body 6 is not particularly limited, but usually formed to have a thickness of about 10 to 100 μm.

[0054] As shown in Fig. 11, the tube body possessing a similar length to that of the bag body 1 and a smaller volume than that of the bag body 11 can be used to accommodate the bag body 11 in a desired compressed condition. The tube body 7 may be provided at one end (in the side of tube 22) with a grasping portion 63 for removing the tube body 7 from the bag body 11. After blood is passed through the bag body 11, the tube body 7 easily slides so that it can be

removed from the bag body 11. That is, it can easily slide for removal from the bag body 11 by supporting the bag body 11 with one hand and pulling the grasping portion 63 with the other hand. The material of the tube body 7 is preferably synthetic resin such as polyvinyl chloride, polyethylene, polypropylene etc. The grasping portion 63 may be formed of synthetic resin such as polypropylene, polyethylene etc., but the grasping portion 63, if provided in a rib form along the edge of the tube body 7 as shown in this example, is formed preferably into one body using the same material as the tube body 7.

[0055] The tube body may be in any shape enough to compress the bag body 11 to achieve degrees of capture possessed by a conventional leukocyte-removing filter, and the shape is not limited to the shapes shown in Figs. 9 and 11.

[0056] The method of recovering hematopoietic stem cell- and/or hematopoietic precursor cell-derived leukocytes from umbilical cord blood is described with reference to Fig. 9.

[0057] First, umbilical cord blood is passed from the blood flow inlet 111, through the bag body 11 accommodated in the tube body 6, to the blood flow outlet 112. In this step, the filter material 12 is compressed to attain suitable spaces between the fibers, therefore, leukocytes derived from hematopoietic stem cells and/or hematopoietic precursor cells can be accurately captured.

[0058] Then, the tube body 6 is ruptured along the perforation 62 from the ruptured portion 61 to remove the bag body 11 from the tube body 6, and a washing solution is passed from the blood flow outlet 112 to the blood flow inlet 111. During this step, the compression of the filter material 12 is relieved and spaces between the fibers are made large, therefore, leukocytes derived from hematopoietic stem cells and/or hematopoietic precursor cells having adhered to the filter material 11 are easily removed and easily washed away with the washing solution for recovery. Because spaces between the fibers are made large, the washing solution can be easily passed therethrough to reduce the time necessary for passing the solution. Here, the washing solution may be introduced from the blood flow inlet 111 or blood flow outlet 112.

Example 1

[0059] The filter set 1 shown in Fig. 1 is used. The filter material 12 charged in the bag body 11 consists of a 3-layer nonwoven fabric (filtration area 12.6 cm^2) using polyethylene terephthalate fibers. The structure of the three layers in the bag body 11 compressed in the accommodation vessel 3 consists of a nonwoven fabric with a fiber diameter of 10 μm and a bulk density of 0.23 g/cm^3 in an upper layer as a first layer, a nonwoven fabric with a fiber diameter of 3.5 μm and a bulk density of 0.09 g/cm^3 in an interlayer as a second layer and a nonwoven fabric with a fiber diameter of 1.8 μm and a bulk density of 0.12 g/cm^3 in a sublayer as a third layer. The weight ratio thereof was 52: 21: 27, and the total thickness was 7.4 mm.

[0060] As shown in Fig. 3, the bag body 11 was accommodated in the accommodation vessel and 100 ml bovine blood containing ACD solution as an anti-coagulation agent was passed therethrough under a compressed condition at a flow rate of 5 ml/min. whereby leukocytes were captured in the inside of the bag body 11 while erythrocytes were passed through the bag body 11 and recovered in the erythrocyte-recovering bag 53 shown in Fig. 5.

[0061] The yield of erythrocytes recovered in the erythrocyte-recovering bag 53 was 92 %, and the yield of platelets therein was 15 %.

[0062] Then, the 3-directional stopcock 56 was closed and then the accommodation vessel was removed as shown in Fig. 1 and the compressed condition of the bag body 11 was relieved. And after the bag body 11 was filled with dextran to widen spaces between the fibers, 150 ml dextran solution was poured out at a flow rate of 15 ml/min. and accommodated into the leukocyte accommodation bag 54. The ratio of enlargement of the filter material 12 due to removing of the bag body 11 from the accommodation vessel 3 and the recovery of leukocytes recovered in the leukocyte-recovering bag 54 are shown in Table 1.

[0063] The volume expansion ratio is the ratio of the inner volume of the bag body 11 in which the compression of the filter material 12 was relieved by removing the accommodation vessel versus the inner volume of the bag body 11 in which the filter material 12 was compressed by accommodating the bag body in the accommodation vessel. The leukocyte recovery ratio is the ratio of the number of leukocytes in the dextran solution recovered in the leukocyte-recovering bag 54 versus the number of leukocytes in blood accommodated in the blood bag 51.

Example 2

[0064] The filter set 1 shown in Fig. 1 is used. A nonwoven fabric with a fiber diameter of 10 μm and a nonwoven fabric with a fiber diameter of 1.83 μm were immersed in 0.25 % 2-hydroxyethyl methacrylate/diethylaminoethyl methacrylate copolymer in ethanol to make a 2-layer laminate. A filter material 12 having a 2-layer structure consisting of said nonwoven fabric having a fiber diameter of 10 μm and a bulk density of 0.32 g/cm^3 as an upper layer (first layer) and said nonwoven fabric with a fiber diameter of 1.8 3 μm and a bulk density of 0.12 g/cm^3 as a sublayer (second layer) in a compressed condition (volume ratio 72.7 : 27.3) was accommodated in a bag body 11 (filtration area 12.6 cm^2).

[0065] The bag body 11 was accommodated in the accommodation vessel 3, and 50 ml umbilical cord blood using a heparin solution as an anti-coagulation agent was passed therethrough at a flow rate of 5 ml/min. whereby leukocytes derived from hematopoietic stem cells and/or hematopoietic precursor cells were captured in the filter material 12 in the inside of the bag body 11. Erythrocytes and platelets were passed through the bag body 11 and recovered in the erythrocyte-recovering bag 53. The yield of erythrocytes recovered in the erythrocyte-recovering bag 53 was 85 % and the yield of platelets therein was 81 %. Then, after closing the 3-directional stopcock 56, removing the accommodation vessel and relieving the compression of the bag body, dextran solution was passed into the bag body 11 so that leukocytes derived from hematopoietic stem cells and/or hematopoietic precursor cells were recovered in the leukocyte-recovering bag 54.

[0066] The volume expansion ratio of the bag body 11 and the yield of leukocytes recovered in the leukocyte-recovering bag 54, as determined in the_same manner as in Example 1, are shown in Table 1.

Example 3

[0067] The similar experiment to Example 1 was done by using the filter set 10 shown in Fig. 4. The bag body 11 and the filter material 12 are same as in Example 1.

[0068] The ratio of enlargement of the bag body 11 due to opening the lid and the recovery of leukocytes recovered in the leukocyte-recovering bag 54 are shown in Table 1.

[0069] The volume expansion ratio is the ratio of the inner volume of the bag body 11 in which the compression of the filter material 12 was relieved by opening the lid versus the inner volume of the bag body 11 in which the filter material 12 was compressed by closing the lid. The leukocyte recovery ratio is the ratio of the number of leukocytes in the dextran solution recovered in the leukocyte-recovering bag 54 versus the number of leukocytes in blood accommodated in the blood bag 51.

Example 4

[0070] The similar experiment to Example 2 was done by using the filter set 10 shown in Fig. 4. The bag body 11 and the filter material 12 are same as in Example 2.

[0071] The ratio of enlargement of the bag body 11 due to opening the lid and the recovery of leukocytes recovered in the leukocyte-recovering bag 54 are shown in Table 1.

Table 1

	Volume expansion ratio (fold)	Leukocyte recovery ratio (%)
Example 1	1.00	42.6
	1.51	78.2
Example 2	1.01	41.5
	1.46	76.5
Example 3	1.00	49.6
	1.48	83.2
Example 4	1.00	41.5
	1.51	80.6

Example 5

[0072] The filter set 1 shown in Fig. 6 is used. The filter material 12 charged in the bag body 11 consists of a 3-layer nonwoven fabric (filtration area 12.6 cm^2) using polyethylene terephthalate fibers. The structure of the three layers in the bag body 11 compressed in the accommodation vessel 3 consists of a nonwoven fabric with a fiber diameter of 10 μm and a bulk density of 0.19 g/cm^3 in an upper layer as a first layer, a nonwoven fabric with a fiber diameter of 3.5 μm and a bulk density of 0.05 g/cm^3 in an interlayer as a second layer and a nonwoven fabric with a fiber diameter of 1.8 μm and a bulk density of 0.14 g/cm^3 in a sublayer as a third layer. The weight ratio thereof was 52: 21: 27, and the total thickness was 6.0 mm.

[0073] As shown in Fig. 7, the bag body 11 was compressed by injecting compressed air into the accommodation vessel 3 by use of a syringe, and 100 ml bovine blood containing ACD solution as an anti-coagulation agent was passed therethrough under a compressed condition at a flow rate of 5 ml/min. whereby leukocytes were captured in the inside of the bag body 11 while erythrocytes were passed through the bag body 11 and recovered in the erythrocyte-recovering bag 53 shown in Fig. 5.

[0074] The yield of erythrocytes recovered in the erythrocyte-recovering bag 53 was 90 %, and the yield of platelets therein was 13 %.

[0075] Then, the 3-directional stopcock 56 was closed and then the 2-directional stopcock 33 was opened to exhaust the compressed air from the accommodation vessel 3 so that as shown in Fig. 8, the bag body 11 was expanded due to relieved compression. Thereafter, the bag body 11 was filled with dextran solution to widen spaces between the fibers. After shifting the direction of the 3-directional stopcock 56 to the leukocyte-recovering bag 54, 150 ml dextran solution was passed at a flow rate of 15 ml/min. and recovered in the leukocyte-recovering bag 54. The compressed air was exhausted from the accommodation vessel 3. The ratio of enlargement of the filter material 12 due to the relieved compression of the bag body 11 and the recovery of leukocytes recovered in the leukocyte-recovering bag 54 are shown in Table 2.

[0076] The volume expansion ratio is the ratio of the inner volume of the bag body 11 in which the compression of the filter material 12 was relieved by exhausting the compressed air versus the inner volume of the bag body 11 in which the filter material 12 was compressed by filling the accommodation vessel 3 with the compressed air. The leukocyte recovery ratio is the ratio of the number of leukocytes in the dextran recovered in the leukocyte-recovering bag 54 versus the number of leukocytes in blood recovered in the blood bag 51.

Table 2

Volume expansion ratio (fold)	1.00	1.05	1.20	1.40	1.60	1.80	2.00
Leukocyte recovery ratio (%)	32.0	52.0	75.0	84.0	85.0	84.0	83.0

[0077] As is evident from Table 2, the yield of leukocyte increases with an increasing volume expansion ratio, but when the volume expansion ratio is 1.4 or more, the yield becomes nearly constant.

Example 6

[0078] The filter set 1 shown in Fig. 6 is used. A nonwoven fabric with a fiber diameter of 10 μm and a nonwoven fabric with a fiber diameter of 1.8 μm were immersed in 0.25 % 2-hydroxyethyl methacrylate/diethylaminoethyl methacrylate copolymer in ethanol to make a 2-layer laminate. A filter material 12 having a 2-layer structure consisting of said nonwoven fabric having a fiber diameter of 10 μm and a bulk density of 0.3 g/cm^3 as an upper layer (first layer) and said nonwoven fabric with a fiber diameter of 1.8 μm and a bulk density of 0.14 g/cm^3 as a sublayer (second layer) in a compressed condition (volume ratio 72.7 : 27.3) was accommodated in a bag body 11 (filtration area 12.6 cm^2).

[0079] The bag body 11 was compressed by injecting compressed air into the accommodation vessel 3 by use of a syringe, and 50 ml umbilical cord blood using a heparin solution as an anti-coagulation agent was passed therethrough at a flow rate of 5 ml/min. whereby leukocytes derived from hematopoietic stem cells and/or hematopoietic precursor cells were captured in the filter material 12 in the inside of the bag body 11.

[0080] Erythrocytes and platelets were passed through the bag body 11 and recovered in the erythrocyte-recovering bag 53. The yield of erythrocytes recovered in the erythrocyte-recovering bag 53 was 87 % and the yield of platelets therein was 91 %. Then, the 3-directional stopcock 56 was closed and then the 2-directional stopcock 33 was opened to exhaust the compressed air thus relieving the compressed condition of the bag body 11, and dextran solution was passed into the bag body 11 so that leukocytes derived from hematopoietic stem cells and/or hematopoietic precursor cells were recovered in the leukocyte-recovering bag 54.

[0081] The volume expansion ratio of the bag body 11 and the yield of leukocytes recovered in the leukocyte-recovering bag 54, as determined in the same manner as in Example 1, are shown in Table 3.

Table 3

Volume expansion ratio (fold)	1.00	1.05	1.20	1.40	1.60	1.80	2.00
Leukocyte recovery ratio (%)	41.0	48.0	78.0	85.0	87.0	87.0	85.0

[0082] As is evident from Table 3, the yield of leukocyte increases with an increasing volume expansion ratio, but when

the volume expansion ratio is 1.4 or more, the yield becomes nearly constant.

Effects of the Invention

[0083] As is evident from the foregoing description, blood components having adhered to the filter material can be efficiently recovered by the blood filter set of the present invention. Further, the time required for passing the washing solution can be reduced. The filter set of the present invention can relieve the compression of the filter material in simple operation.

Explanation of the Reference signs

[0084]

1,10	filter set,
11	bag body,
12	filter material,
111	blood flow inlet,
112	blood flow outlet,
21,22	tube,
3,4	accommodation vessel
31,32	bag body-removing port
33	2-directinal stopcock
41	lid
411	arm
42	vessel body
421	protuberance
43	groove
50	blood components collecting apparatus
51	blood bag
52	washing solution bag
53	erythrocyte-recovering bag
54	leukocyte-recovering bag
55,56	3-directional stopcock
61	ruptured portion
62	perforation
63	grasping portion

Claims

1. A blood filter set comprising a bag body having a blood flow inlet and a blood flow outlet and charged with a filter material, and an accommodation vessel for accommodating said bag body.

2. The blood filter set of claim 1 wherein the accommodation vessel is for accommodating said bag body which is freely removed therefrom and for accommodating said bag body in a compressed condition at the time of accommodation.

3. The blood filter set of claim 1 wherein the accommodation vessel has a lid, which can be opened and closed easily.

4. The blood filter set of claim 1 wherein said bag body is compressed by filling with compressed gas, and after blood is passed through said bag body in a compressed condition, the compressed gas is exhausted to relieve the compression of said bag body and then a washing solution is passed through the bag body.

5. The blood filter set of claim 4 wherein the accommodation vessel further expands said bag body by evacuating the inside of the accommodation vessel.

6. The blood filter set of claim 1 wherein the bag body consists of a flexible sheet.

7. The blood filter set of claim 1 wherein the accommodation vessel is rigid.

8. The blood filter set of claim 1 wherein the accommodation vessel is a flexible tubular body.

9. The blood filter set of claim 1 wherein the filter material is a fiber.

10. The blood filter set of claim 9 wherein the diameter of the fiber is in the range of 0.1 to 40 μm.

11. The blood filter set of claim 9 wherein the bulk density of fiber agglomerates in compressed bag body is 0.05 to 0.50 g/cm^3.

12. A blood filter set comprising a bag body having a blood flow inlet and a blood flow outlet and consisting of a flexible sheet charged inside with a filter material, and a rigid accommodation vessels for accommodating said bag body which is freely removed therefrom and for accommodating said bag body in a compressed condition at the time of accommodation.

13. A blood filter set comprising a bag body having a blood flow inlet and a blood flow outlet and consisting of a flexible sheet charged inside with a filter material, and a rigid accommodation vessel for accommodating said bag body, wherein said bag body is compressed by filling with compressed gas, and after blood is passed through said bag body in a compressed condition, the compressed gas is exhausted to relieve the compression of said bag body through which a washing solution is then passed.

14. The blood filter set of claim 12 or 13 wherein said accommodation vessel further expands said bag body by evacuating the inside of the vessel.

15. A blood filter set comprising a bag body having a blood flow inlet and a blood flow outlet and being charged with a filter material, and a flexible tube body accommodating the bag body in a compressed condition in the thickness direction, wherein said body can be removed from said tube body.

16. The blood filter set of claim 15 wherein the tube body is heat-shrinkable.

17. The blood filter set of claim 15 wherein the tube is provided with a ruptured portion.

18. The blood filter set of claim 15 wherein the tube body possesses a similar length to that of the bag body and a smaller volume than that of the bag body.

19. The blood filter set of claim 15 wherein the tube body is provided at least one end thereof, with a grasping portion for removing the tube body from the bag body.

20. A method of recovering blood components comprises

accommodating a bag body into an accommodation vessel, wherein the bag body has a blood flow inlet and a blood flow outlet and is charged inside with a filter material,
passing blood flow through said bag body in the condition compressed by said accommodation vessel to adhere blood components to the filter material,
removing the bag body from said accommodation vessel,
passing a washing solution through the inside of said bag body in an expanded condition so as to wash off the blood components adhered to said filter material, and
recovering the blood components.

21. The method of claim 20 wherein the bag body consists of a flexible sheet.

22. The method of claim 20 wherein the accommodation vessel is rigid.

23. The method of claim 20 wherein the filter material is a fiber.

24. The method of claim 20 wherein the blood component is leukocyte.

25. A method of recovering blood components comprises

filling a bag body with compressed gas to compress said bag body, wherein the bag body has a blood flow inlet and a blood flow outlet, consists of a flexible sheet and is charged inside with a filter material and accommodated in a rigid accommodation vessel,

passing blood flow through said bag body in a compressed condition to adhere blood components to the filter material, exhausting the compressed gas to relieve the compression condition of said bag body,

passing a washing solution through the inside of said bag body so as to wash off the blood components adhered to said filter material, and

recovering blood components.

26. The methods of recovering blood components of claim 25 wherein further evacuating the inside of vessel to expand said bag body after the compressed gas is exhausted.

27. A method of recovering blood components comprising

passing blood through a bag body in a compressed condition, wherein the bag body has a blood flow inlet and a blood flow outlet, consists of a flexible sheet and is charged with a filter material and accommodated in a flexible tubular body in a compressed condition in the thickness direction,

removing the bag body from the flexible tubular body to relieve the compression of the bag body,

passing a washing solution through the inside of said bag body so as to wash off the blood components adhered to the filter material, and

recovering the blood components.

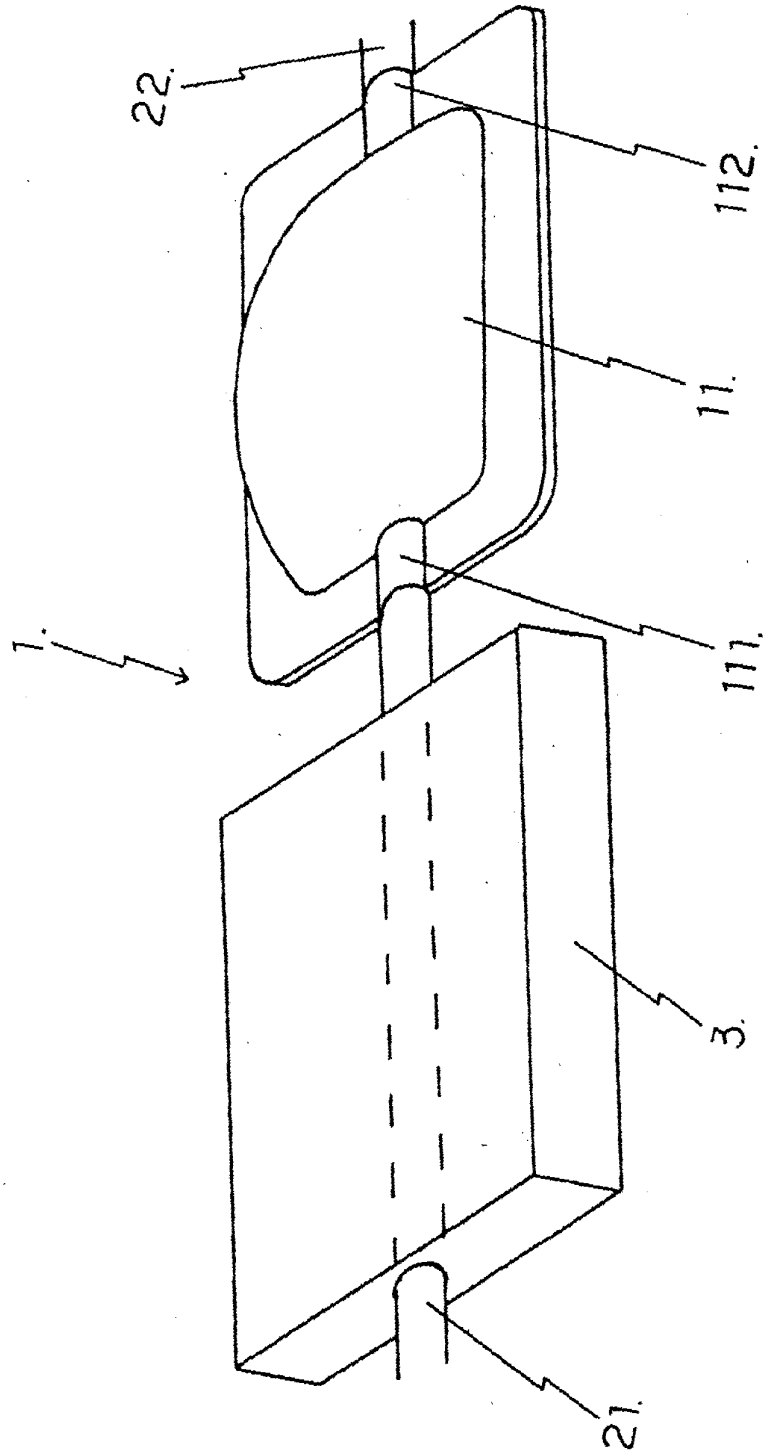


Fig. 1

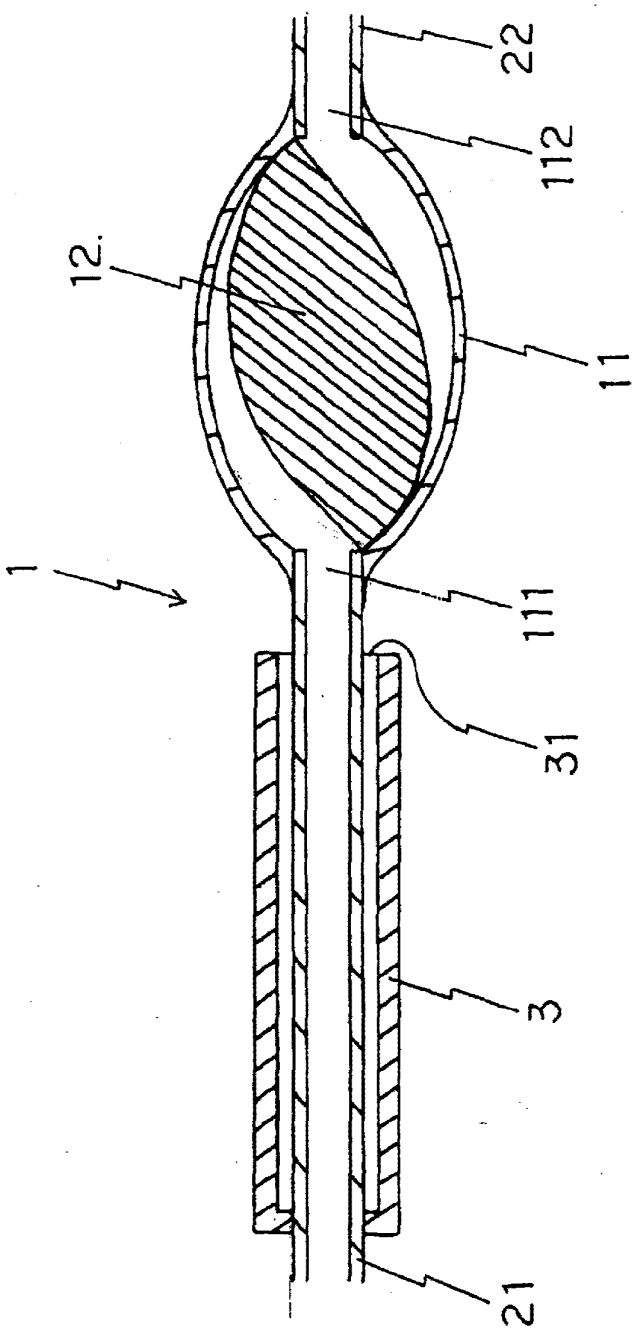


Fig. 2

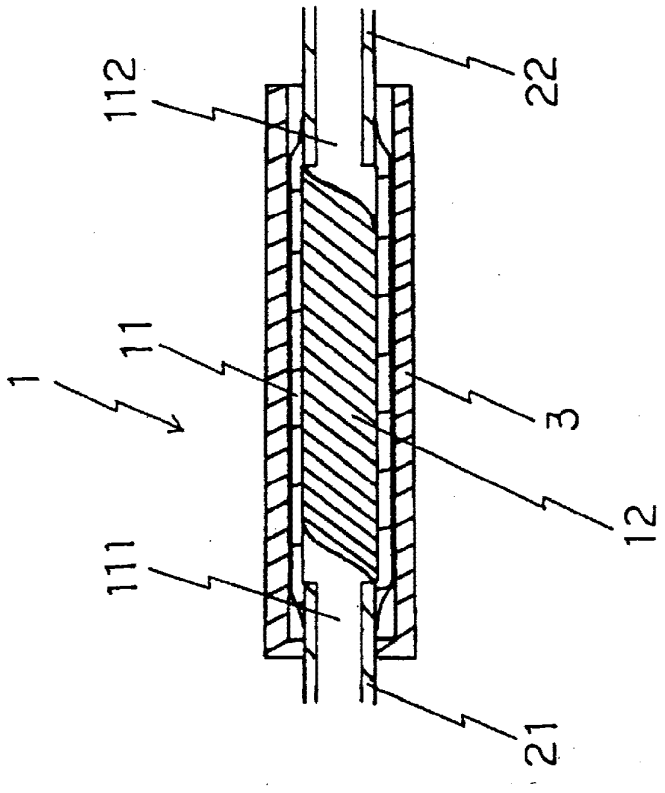


Fig. 3

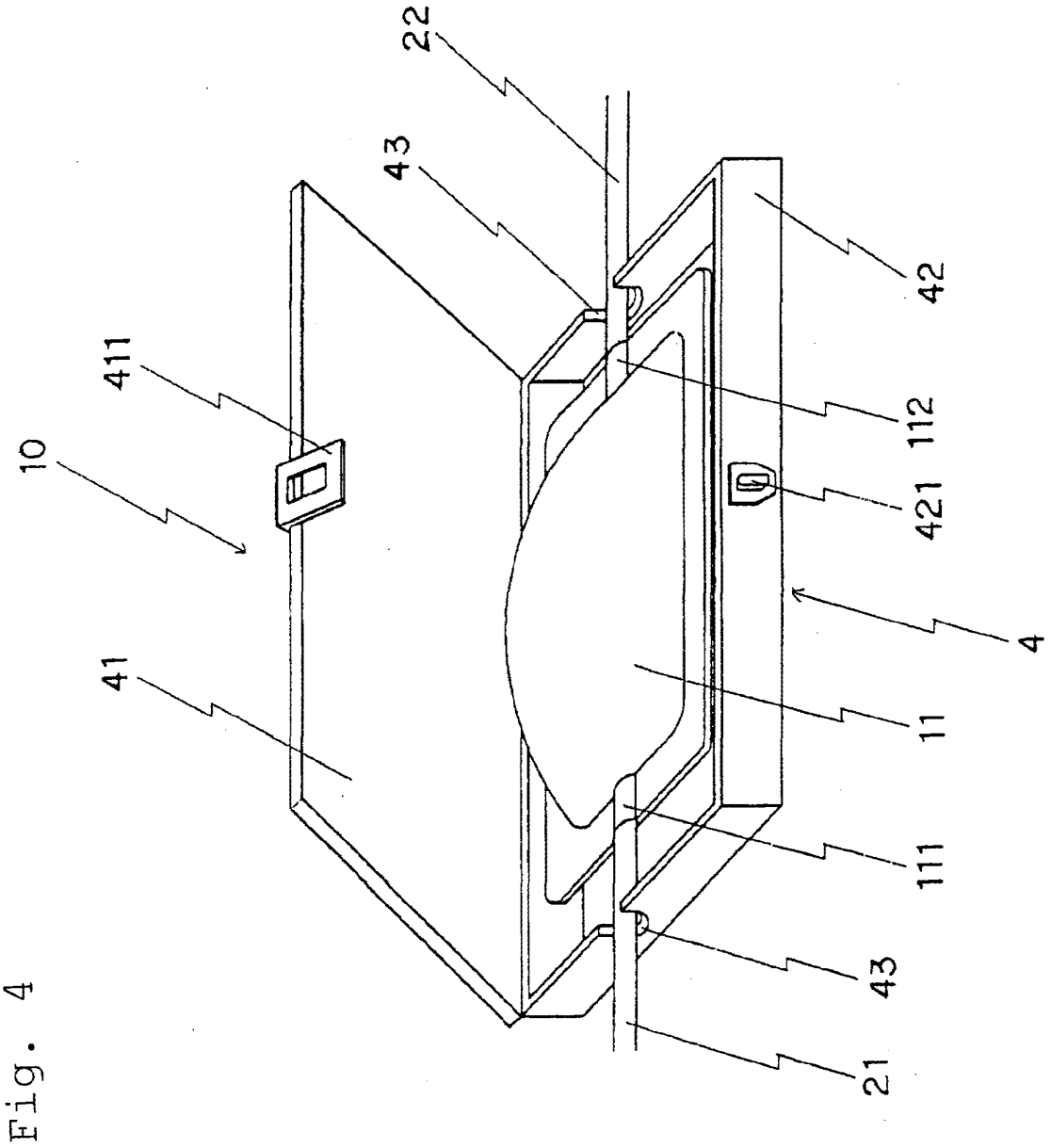
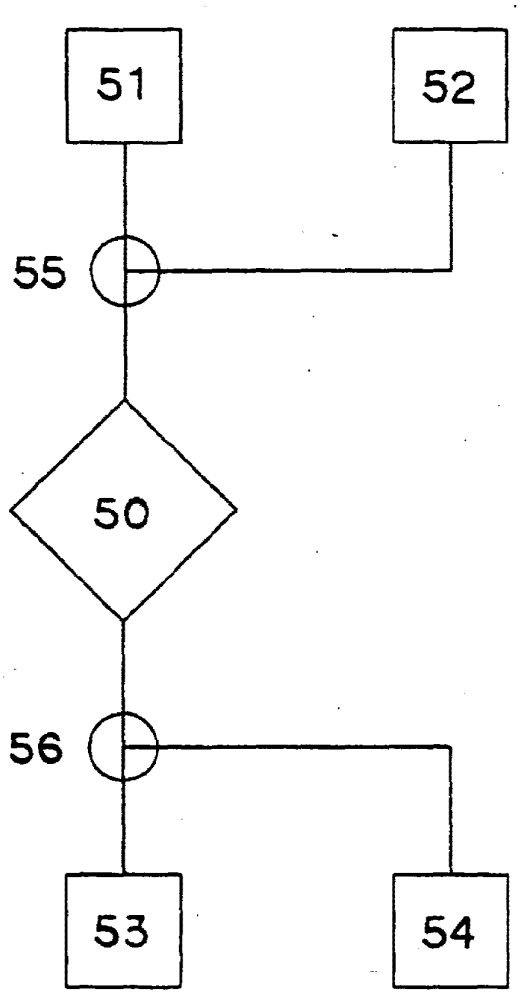


Fig. 4

Fig. 5



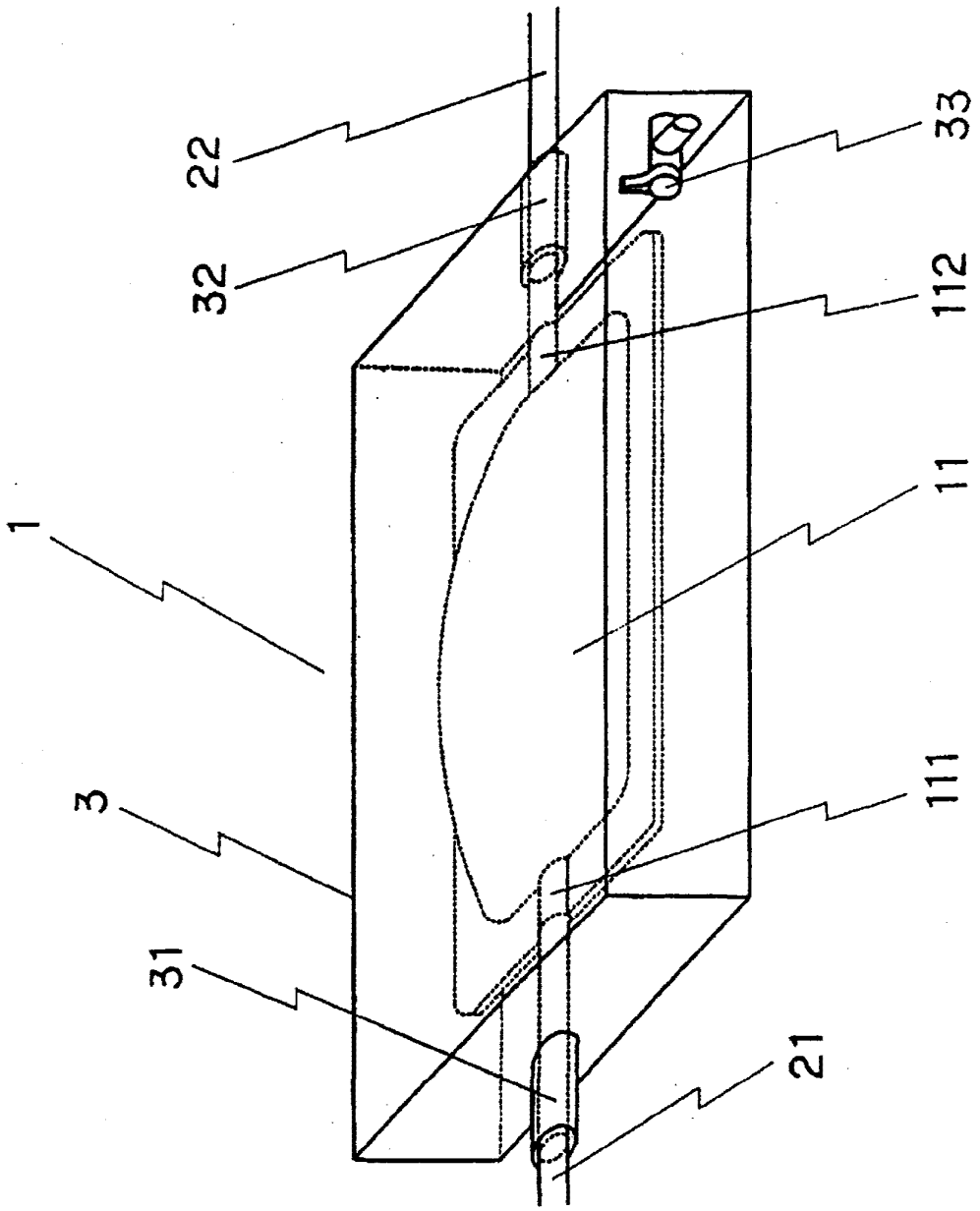


Fig. 6

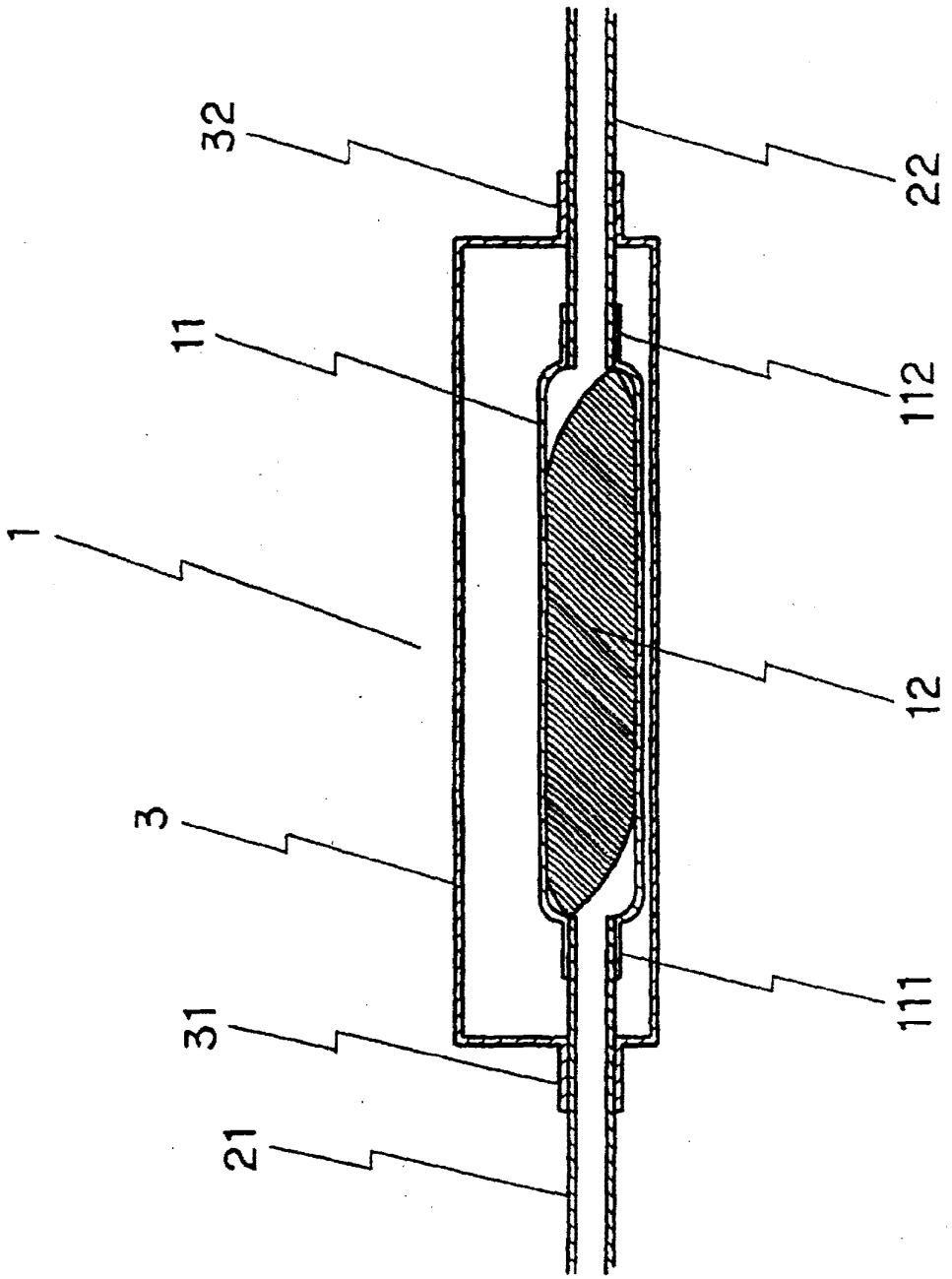


Fig. 7

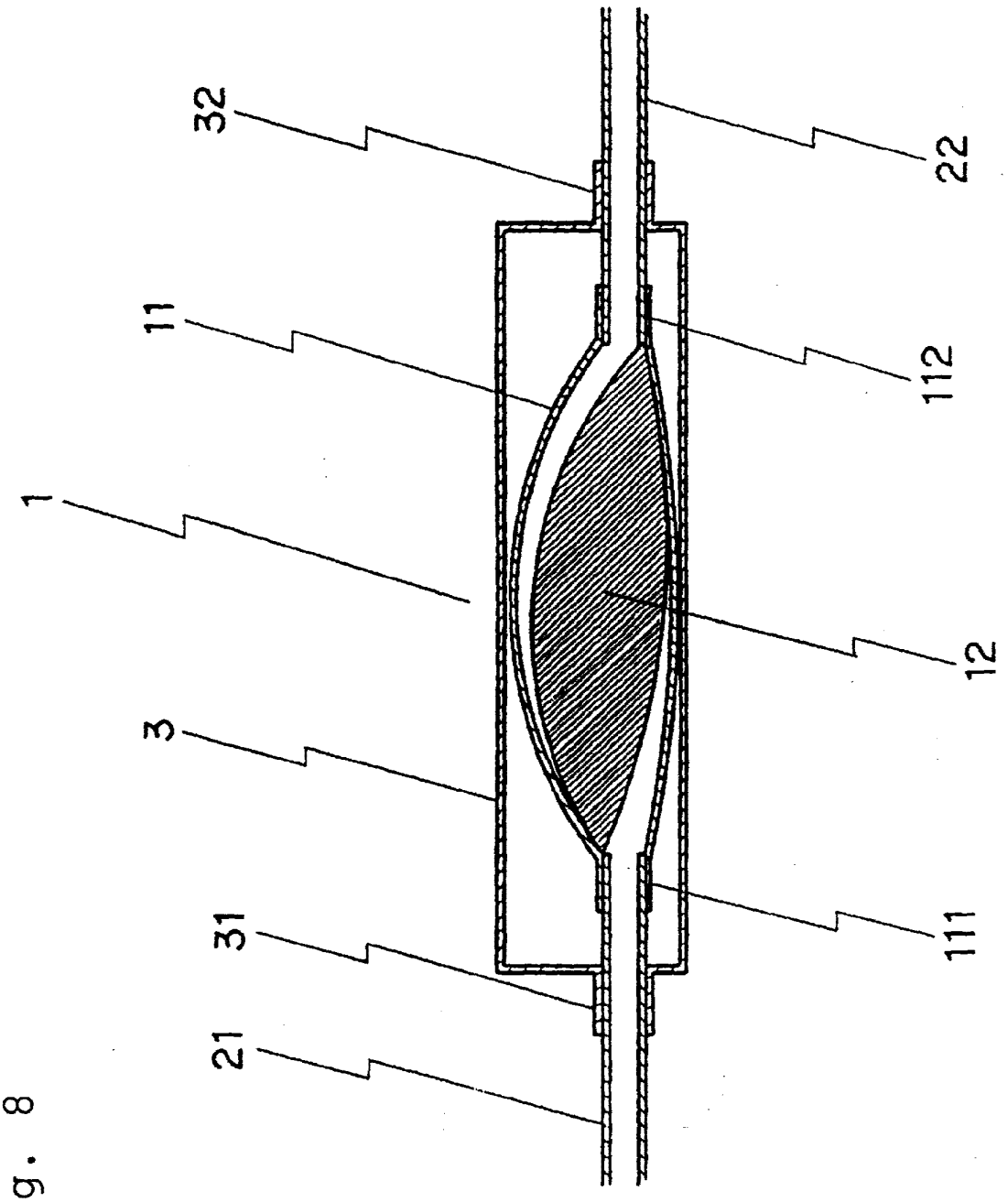


Fig. 8

Fig. 9

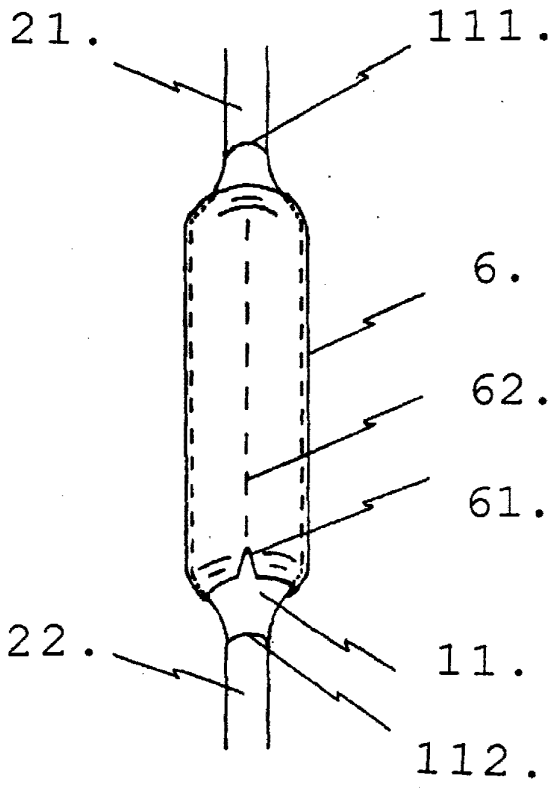


Fig. 10

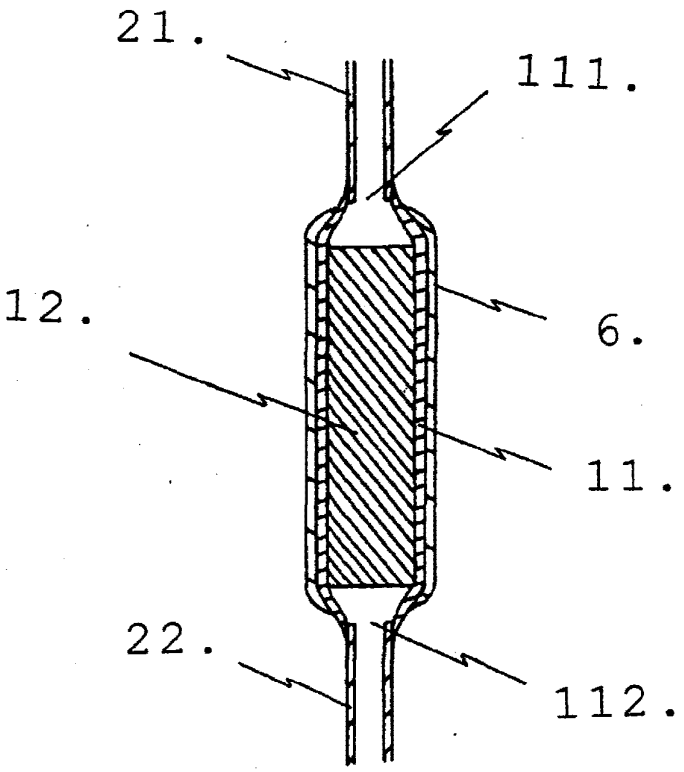
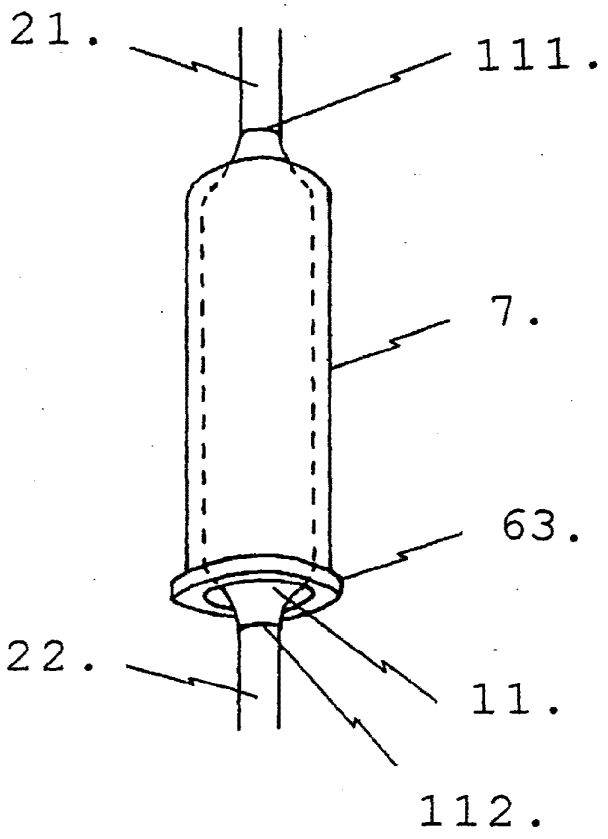


Fig. 11



European Patent Office

EUROPEAN SEARCH REPORT

Application Number
EP 98 12 1181

DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int.Cl.6)
A	EP 0 280 052 A (DONGBEI POWER COLLEGE) 31 August 1988 * column 5, line 17 - line 36 * * column 6, line 9 - line 47 * * figures *	1,4,6,7, 9,12,13, 15,20, 25,27	A61M1/36
A	US 4 416 777 A (KURODA TORU ET AL) 22 November 1983 * column 10, line 6 - line 18 * * column 11, line 3 - line 17 *		
			TECHNICAL FIELDS SEARCHED (Int.Cl.6)
			B01D A61M

The present search report has been drawn up for all claims

Place of search	Date of completion of the search	Examiner
THE HAGUE	17 February 1999	Vereecke, A

CATEGORY OF CITED DOCUMENTS

X : particularly relevant if taken alone
Y : particularly relevant if combined with another document of the same category
A : technological background
O : non-written disclosure
P : intermediate document

T : theory or principle underlying the invention
E : earlier patent document, but published on, or after the filing date
D : document cited in the application
L : document cited for other reasons

& : member of the same patent family, corresponding document

EPO FORM 1503 03.82 (P04C01)

ANNEX TO THE EUROPEAN SEARCH REPORT ON EUROPEAN PATENT APPLICATION NO. EP 98 12 1181

This annex lists the patent family members relating to the patent documents cited in the above-mentioned European search report. The members are as contained in the European Patent Office EDP file on
The European Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

17-02-1999

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
EP 0280052 A	31-08-1988	CN 1004400 B	07-06-1989
		DE 3850792 D	01-09-1994
		DE 3850792 T	24-11-1994
		DE 8804741 U	01-06-1988
		FI 880346 A,B	28-07-1988
		JP 2514997 B	10-07-1996
		JP 63229104 A	26-09-1988
		US 4851136 A	25-07-1989
US 4416777 A	22-11-1983	JP 1279473 C	29-08-1985
		JP 56053616 A	13-05-1981
		JP 60003367 B	28-01-1985
		DE 3038196 A	23-04-1981
		FR 2467403 A	17-04-1981
		GB 2062498 A,B	28-05-1981

EPO FORM P0459

For more details about this annex : see Official Journal of the European Patent Office, No. 12/82

(19) Europäisches Patentamt
European Patent Office
Office européen des brevets

(11) EP 1 421 960 A1

(12) EUROPEAN PATENT APPLICATION

(43) Date of publication:
26.05.2004 Bulletin 2004/22

(51) Int Cl.[7]: **A61M 5/165**

(21) Application number: **03025258.9**

(22) Date of filing: **06.11.2003**

(84) Designated Contracting States:
AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LI LU MC NL PT RO SE SI SK TR
Designated Extension States:
AL LT LV MK

(30) Priority: **21.11.2002 IT MI20022473**

(71) Applicant: **GVS S.p.A.**
40069 Zola Predosa (Bologna) (IT)

(72) Inventors:
- **Scagliarini, Massimo**
  40136 Bologna (IT)
- **Bettini, Emanuele**
  40050 Monte San Pietro (Bologna) (IT)

(74) Representative: **Ripamonti, Enrico, Dr. Ing. et al**
Ing. A. Giambrocono & C. s.r.l.,
19/B, Via Rosolino Pilo
20129 Milano (IT)

(54) Infusion filter operating in various tridimensional positions

(57) A filter (1) comprises a box casing (2) in which at least one cavity (37) is present between an outer element (3, 4) of said casing (2) and an inner surface (5A, 5B) presenting a plurality of channels (21) on which a corresponding hydrophilic filtering membrane (30) lies, said cavity (37) communicating with a conduit (27) for entry of the fluid into the filter (1) and said channels (21) being connected to a conduit (23) for exit of said fluid, in said outer element (3, 4) there being provided through apertures (40, 41) with which hydrophobic membranes (44) are associated. A surface (S1) bounded by the shortest possible ideal closed line (70), which totally comprises all the hydrophobic membranes (44), contains substantially within its interior the projection thereon of the useful hydrophilic surface (S2) of the hydrophilic filtering membrane (30), this enabling the filter (1) to be employed in a plurality of spatial positions during its use.

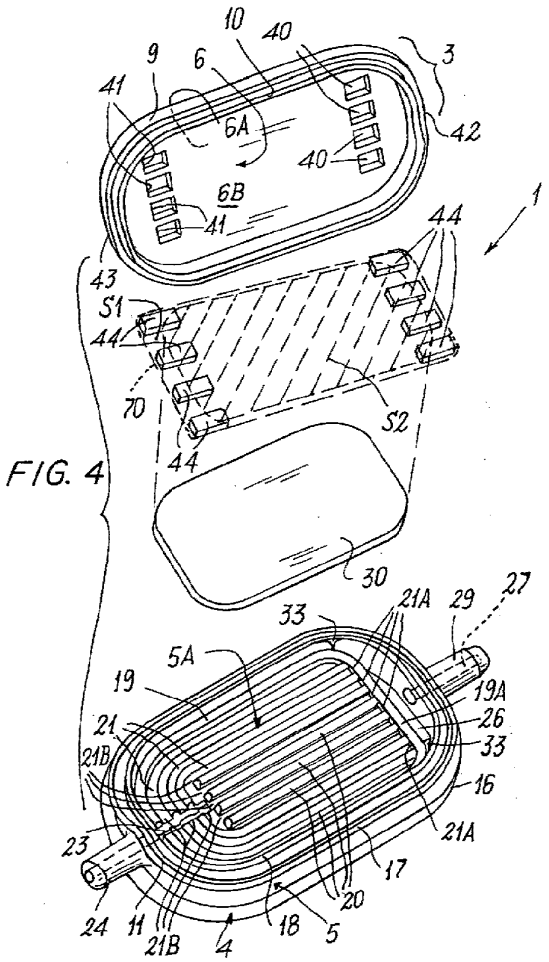


FIG. 4

EP 1 421 960 A1

Description

[0001] The present invention relaters to an infusion filter in accordance with the introduction to the main claim.

[0002] Filters of the same type as the present invention have been known for some time. They present small dimensions, but must be used in well defined spatial orientations to prevent the formation of air bubbles within the filter which, if they should reach the patient by being conveyed by the fluid, would result in serious well-known problems.

[0003] An object of the present invention is to provide an infusion filter which is improved with respect to similar known filters.

[0004] A particular object of the invention is to provide a filter of the stated type which during use can be disposed in a multiplicity of spatial positions without this involving risks to the correct fluid flow to a patient.

[0005] Another object is to provide a filter of the stated type which can be used reliably and safely.

[0006] These and other objects which will be apparent to the expert of the art are attained by a filter in accordance with the accompanying claims.

[0007] The present invention will be more apparent from the accompanying drawing, which is provided by way of non-limiting example and in which:

Figure 1 is a front view of a filter according to the invention;
Figure 2 is a side view of the filter of Figure 1;
Figure 3 is a section on the line 3-3 of Figure 1;
Figure 4 is an exploded view of the filter of Figure 1;
Figure 5 is a schematic view of a characteristic of Figure 1;
Figure 6 is a perspective view of a variant of the filter of Figure 1;
Figure 7 is a partial perspective view of another variant of the filter of Figure 1;
Figure 8 is a section on the line 8-8 of Figure 7;
Figure 9 is a partial perspective view of a further variant of the filter of Figure 1;
Figure 10 is a section on the line 10-10 of Figure 9;
Figure 11 is a partial perspective view of another variant of the filter of Figure 1;
Figure 12 is a section on the line 12-12 of Figure 11;
Figure 13 is a partial perspective view of another variant of the filter of Figure 1;
Figure 14 is a section on the line 14-14 of Figure 13;
Figure 15 is a perspective view from above of a further variant of the filter of Figure 1; and
Figure 16 is a section on the line 16-16 of Figure 15.

[0008] With reference to said Figures from 1 to 14, a filter according to the invention is indicated overall by 1 and comprises a box casing 2 defined, in the example under examination, by a first and a second outer element 3, 4 closing an intermediate element 5. These box casing elements 3, 4 and 5 are constructed preferably of plastic material in any known manner.

[0009] The outer elements 3 and 4 comprise a flat portion 6 and 7 having opposing faces 6A, 6B and 7A, 7B respectively. In proximity to the edge 9 of said portions 6, 7, there projects from their face 6B, 7B, which is internal with respect to the casing 2 (the face 6A and 7A being an external face of this latter), a shoulder 10 arranged to cooperate with a recess 11 provided in the facing surface of the element 5, in order to secure the elements 3 and 4 to the intermediate element 5. This fixing is obtained in any known manner, for example by ultrasonic bonding, gluing or other means.

[0010] The surface facing the face 6B is indicated in the figures by 5A, while the surface facing the face 7B is indicated by 5B.

[0011] Only one of the surfaces 5A and 5B is described hereinafter as these are identical. Likewise only one of the elements 3 and 4 is described hereinafter, it being understood that everything stated for the surface 5A and for the element 3 is also valid for the surface 5B and for the element 4.

[0012] The intermediate element 5 presents a rounded edge 16 and comprises on the face 5A, starting from its periphery and progressing towards its interior, a pair of spaced-apart parallel annular shoulders 17 and 18 defining the aforesaid recess 11, an annular step 19 and a plurality of parallel ribs 20, circumscribed by the step 19 and defining channels 21 closed at one end 21A by the step 19 and open at their other end 21B where they communicate with a conduit 23 leaving the element 5 via a stem 24 projecting from the edge 16 of said element.

[0013] The step 19 and the parallel ribs 20 have a height less than the shoulders 17 and 18. Between the step 19 and the shoulder 18 a cavity 26 is present communicating with an entry conduit 27 which penetrates into the element 5 (via the shoulders 17 and 18) by passing through a stem 29 projecting from the edge 16. Preferably the stem 29 is coaxial with the stem 24, they both lying along a central axis A of the element 5.

[0014] The step 19 and the ribs 20 can be formed directly in one piece with the element 5 or can be formed on a separate piece inserted within the shoulders 17 and 18 of the element 5 in such a manner as to rest along the shoulder 18 in correspondence with two of its side portions, but spaced from said shoulder 18 so as to define the cavity 26.

[0015] As stated, the free ends of the step 19 and of the ribs 20 lie at least in a plane distant from that in which the ends of the shoulders 17 and 18 lie. Within this space a hydrophilic filter membrane 30 is positioned to rest against the shoulder 18 but not to cover the cavity 26. In this respect, in correspondence with this latter, during filter assembly the hydrophilic membrane 30 is maintained distant from the shoulder 18 by cusp-shaped projections 33 jutting from this shoulder in correspondence with a transverse part 19A of the step 19 perpendicular

to said axis A. The membrane is finally rested on the ends of the ribs 20 and is finally fixed to the transverse part 19A and to the step 10 in known manner, for example by hot bonding.

[0016] When the intermediate element 5 is completed (i.e. also provided with the membranes 30), cavities 37 communicating with the aforesaid cavities 26 are present between its faces 5A and 5B and the adjacent faces 6B and 7B of the outer elements 3 and 4.

[0017] Each outer element 3, 4 (also having a rounded edge 9 such as that of the element 5) comprises at least two through apertures 40 and 41 each provided in proximity to sides 42 and 43 of said element which are perpendicular to the axis A. A hydrophobic membrane 44 of known type is positioned in correspondence with each of these apertures.

[0018] In particular, in Figures 1-4 each outer element 3, 4 comprises four apertures 40 and four adjacent apertures 41. However the number of these apertures can also be different: for example. in Figure 6, in correspondence with the sides 42 and 43 of the elements 3 and 4 a single aperture 40 and 41 is present having an evidently large transverse length. A single aperture 40 and 41 is also present in Figure 7, in proximity to said sides; however each of these apertures is connected to a large underlying recess 45 (rectangular in this example) provided within the interior face 6B of the portion 6 of the element 3 in correspondence with which a hydrophobic membrane 44 is present. In contrast, in Figure 9 in correspondence with each side 42 and 43 (only the side 42 is shown) a pair of apertures 40 and 41 are present, connected to an underlying recess 47 of larger dimensions provided within the face 6B of the portion 6; a step 48 is present between the aperture 40 (or 41) and the underlying recess 47, the hydrophobic membrane 44 being positioned in correspondence with this recess. In Figure 11, within the face 6B of the portion 6 of the element 3, in correspondence with each side 42 and 43, a substantially rectangular recess 50 is present, connected to two conduits 51 opening into the face 6A via corresponding apertures 40 (and 41). Finally in Figure 13, in the face 6B of the portion 6 (in proximity to the sides 42 and 43) a circular recess 53 is provided connected to the apertures 40 (or 41) via channels 54 with their axis inclined to the plane of the face 6A in which the apertures 40 (or 41) are located.

[0019] It should be noted that each membrane is preferably and advantageously associated with the relative aperture 40 or 41 or with the recess 45, 47, 50, 53 by being fixed to the face 6B of the part 3, rather than by being inserted into the respective hole or recess. This enables a filtering surface to be obtained which is larger than that obtained if the membrane were inserted into the corresponding hole or recess in that, in this latter case, a part of the useful volume of the membrane would be occupied by the bond between the membrane and the wall of the corresponding hole or recess.

[0020] The hydrophobic surfaces defined by the membrane 44 can be all connected together by a closed line 70, shown dashed in Figure 4 and full in Figure 5. Preferably, this line is the shortest which ideally connects together all the said surfaces of the membranes 44, i.e. it is defined by rectilinear portions in the example of the figures. According to the invention, this closed line defines a surface S1 within which the projection of the useful hydrophilic surface S2 of the underlying membrane 30 substantially falls, the "useful" surface meaning the effectively filtering surface of the membrane 30. The surface S1 is that enclosed by the line 70, the surface S2 being the hatched surface in Figures 4 and 5.

[0021] By virtue of this characteristic, after a usual line priming phase, proper filter effectiveness is achieved whatever its position in space during its use (vertical to, inclined to or parallel to an underlying plane). This is because the fluid entering the filter 1 is able to completely occupy the cavity 37 by expelling the air present therein and filtering through substantially the entire useful surface of the membrane (in the aforestated sense). In this manner, the filter is completely operative, and effective in filtering the entering fluid, in that substantially the entire useful surface of the hydrophilic membrane 30 (at most except for a peripheral portion) participates in the filtering. In addition, the channels 21 are completely filled by the fluid which filters through the membrane 30 such that from one end 21A (that facing the entry conduit 27) to their other end 21 B (that communicating with the exit conduit 23) they contain no residual air bubbles, with obvious positive implications for the fluid feed to the user.

[0022] It should be noted that at most, under utilization conditions, a possible minimum part of the useful surface S2 of the projection of the hydrophilic membrane 30 can lie outside the surface S1, provided that the geometry of the seat in which the membrane 30 is positioned enables the surface tension effect of the filtered fluid to be utilized, this effect occurring if the distance between the membrane 30 and the face 6B of the portion 6 (i.e. the depth of the cavity 37 measured perpendicular to the axis A) lies between 0.1 mm and 3 mm, preferably between 0.5 and 2 mm and advantageously between 0.5 mm and 1.5 mm. Under these conditions, the possible minimum (peripheral) surface part of the membrane 30, the projection of which does not fall within the surface S1, becomes in any event a fluid passage by capillary effect, with consequent complete use of the capacity of said membrane (i.e. the hydrophilic filtering surface of the membrane 30 is always 100% of its area).

[0023] By virtue of the invention, the described and claimed filter presents high functional capacity, exceeding that of known filters. This is because of the arrangement of the apertures 40 and 41 provided with the hydrophobic membranes 44, by virtue of which a high functional capacity of the filtering surface is obtained; this is also due to the fact that these apertures cooperate directly (as in Figures 1-6) or indirectly (as in Figures 7-14) with membranes 44 of considerable area (even greater

than that of said apertures, as in Figures 7-14), which ensure a high air flow from the casing 2 of the filter 1.

[0024] Other embodiments are evidently possible within the light of the present description, provided they remain within the scope of the accompanying claims. For example, each membrane 30 can be of any form, including complex (as can the arrangement of the underlying channels 21), the filter operating effectively provided the apertures present within the outer element 3 or 4 which face said membrane are such as to define, by means of the closed line which joins them together, the surface S1 with the aforedescribed characteristics. In the limit, a single aperture of large dimensions can be present in said element.

[0025] Another embodiment of the invention is shown in Figures 15 and 16 in which parts corresponding to those of the already described figures are indicated by the same reference numerals. In the figures under examination, the filter presents the apertures 40 and 41 connected to differently shaped recesses: the apertures 40 are associated with a recess 50 in accordance with the embodiment of Figure 11, while the aperture 41 is associated with a recess 45 in accordance with the embodiment of Figure 7.

[0026] The embodiment under examination also presents other differences with those already described; for example, in correspondence with the shoulder 17 and around the stems 24 and 29, the element 5 presents circular rims 93 spaced from the corresponding stems and defining therewith recesses 94 for accepting the end of a corresponding contact or tube connected to a vessel of liquid (for example physiological liquid), in the case of the stem 29, or connected to the patient in the case of the stem 24. The rim 93 is essentially a prolongation of the shoulder 17.

[0027] The shoulder 18 is originally formed of tapered shape (triangular in cross-section) such that when inserted into a recess 10A adjacent to the shoulder 10 and provided in each face 6B, 7B of the elements 3 and 4 towards the interior of the filter, it can be fused into this recess during for example the hot bonding, so securely joining the element 5 to the adjacent elements 3 and 4.

[0028] Finally, the apertures 40 and 41 are connected to recesses 97 formed in the external face 6A, 7A of the flat portions 6 and 7 to facilitate the escape of air from these apertures. These recesses lie parallel to the (longitudinal) axis A of the filter.

[0029] Said apertures, and those of the filter represented in the previously described figures, can be closed by suitable plugs (not shown) which can be maintained connected to the filter casing 2 (for example by a filiform connection element, for example of plastic material) or can be of the type completely separable from the filter. The purpose of these plugs is to prevent air being drawn from the outside into the filter interior when one of the tubes connected to the filter (in particular, that connected to a vessel of liquid) is subjected to vacuum caused for example by a syringe.

[0030] Embodiments in which the membrane element 5 presents two opposing surfaces 5A and 5B provided with channels 21 have been described and shown in the figures. However the scope of the present invention also comprises a filter in which this element 5 presents a single face (for example, 5A) provided with channels, whereas the other (the face 5B) is completely flat. In this case, the outer element 4 is not present and the face 5B of the element 5 closes the filter on the side opposite that on which the element 3 is present.

Claims

1. A filter (1) for filtering a fluid directed towards a patient, comprising a box casing (2) in which at least one cavity (37) is present defined by an outer element (3, 4) of said casing (2) and an inner surface (5A, 5B) presenting a plurality of channels (21) on which a corresponding hydrophilic filtering membrane (30) lies, said cavity (37) communicating with a conduit (27) for entry of the fluid into the filter (1) and said channels (21) being connected to a conduit (23) for exit of said fluid from the filter (1), in said element (3, 4) of the box casing (2) there being provided spaced-apart through apertures (40, 41) close to its opposing ends (42, 43) and with which hydrophobic membranes (44) are associated, **characterised in that** a surface (S1) bounded by an ideal closed line (70), which totally comprises all the hydrophobic membranes (44), contains substantially within its interior the projection thereon of the useful hydrophilic surface (S2) of the hydrophilic filtering membrane (30), this enabling the filter (1) to be employed in a plurality of spatial positions during its use.

2. A filter as claimed in claim 1, **characterised in that** the closed line bounding the surface (S1) comprising the hydrophobic membranes (44) is the shortest line which joins these latter together.

3. A filter as claimed in claim 1, **characterised in that** the distance between said element (3, 4) of the box casing (2) and the hydrophilic filtering membrane (30) lies between 0.1 mm and 3 mm, preferably between 0.5 mm and 2 mm.

4. A filter as claimed in claim 3, **characterised in that** the distance between said element (3, 4) of the box casing (2) and the hydrophilic filtering membrane (30) lies between 0.5 mm and 1.5 mm.

5. A filter as claimed in claim 1, **characterised in that** the through apertures (40, 41) have a size identical to that of the membranes (44) associated with them.

6. A filter as claimed in claim 1, **characterised in that**

the through apertures (40, 41) have a size less than that of the membranes (44) associated with them.

7. A filter as claimed in claim 6, **characterised in that** each membrane (44) is associated with a recess (45, 47, 50, 53) provided within a face (6B, 7B) of the element (3, 4) of the box casing (2) facing the hydrophilic membrane (30), with said recess (45, 47, 50, 53) there being associated at least one aperture (40, 41) opening into the opposing face (6A, 7A) of said element (3, 4), between said aperture and said recess there being present at least one step (48) so that the aperture has a size less than that of the recess.

8. A filter as claimed in claim 7, **characterised in that** the recess is of polygonal shape.

9. A filter as claimed in claim 7, **characterised in that** the recess is of circular shape.

10. A filter as claimed in claim 1, **characterised in that** each hydrophobic membrane (44) has a surface greater than that of the aperture (40, 41) with which it is associated.

11. A filter as claimed in claim 10, **characterised in that** the hydrophobic membrane is fixed to that face (6B, 7B) of the element (3, 4) of the box casing (2) facing the hydrophilic membrane (30), in correspondence with the relative aperture (40, 41).

12. A filter as claimed in claim 1, **characterised in that** the channels (21) of the inner surface (5A, 5B) present a closed end (21A) facing and close to the entry conduit (27), and the other end (21B) connected to the exit conduit (23).

13. A filter as claimed in claim 12, **characterised in that** the closed end (21 A) of said channels (21) is closed by an annular element (19) which surrounds said channels (21).

14. A filter as claimed in claim 1, **characterised in that** the entry conduit (27) and exit conduit (23) are provided within an element (5) of the box casing (2) presenting the surface (5A, 5B) with the channels (21) and connected to the outer element (3, 4) of said casing (2).

15. A filter as claimed in claim 14, **characterised in that** the entry conduit (27) and exit conduit (23) are provided within stems (29, 24) projecting from the box casing element (5) provided with channels (21).

16. A filter as claimed in claim 15, **characterised in that** around each stem (24, 29) an annular rim (93) is present defining with the corresponding stem (24, 29) a recess (94) for receiving the end of a corresponding conduit connected to the filter.

17. A filter as claimed in claim 14, **characterised in that** the element (5) with the surface (5A) provided with channels (21) presents a second surface (5B), opposing the surface (5A) with channels, but not provided with these latter.

18. A filter as claimed in claim 14, **characterised in that** the element (5) with the surface (5A) provided with channels (21) presents a second surface (5B), opposing the surface (5A) with channels (21) and shaped as this latter, to the front of said second surface (5B), also provided with channels (21) on which a hydrophilic membrane (30) is superposed, there being positioned a second outer element (4) of the box casing (2) provided with apertures (40, 41) with which hydrophobic membranes (44) are associated, between said second outer element (4) and the element (5) with the surfaces (5A., 5B) provided with channels (21) there being present a cavity (37) connected to the entry conduit (27), said element (5) with the surfaces (5A, 5B) provided with channels (21) being intermediate between the outer elements (3, 4) of the box casing (2).

19. A filter as claimed in claim 1, **characterised in that** the apertures (40, 41) are connected to recesses (97) provided in a free face (6A, 6B) of the corresponding outer element (3, 4).

20. A filter as claimed in claim 19, **characterised in that** the recesses (97) lie parallel to the longitudinal axis (A) of the filter.

21. A filter as claimed in claim 1, **characterised in that** the apertures (40, 41) cooperate with removable shut-off members.

22. A filter as claimed in claim 21, **characterised in that** the shut-off members are connected to the filter casing (2).

23. A filter as claimed in claim 22, **characterised in that** the shut-off members are completely separable from the filter casing (2).

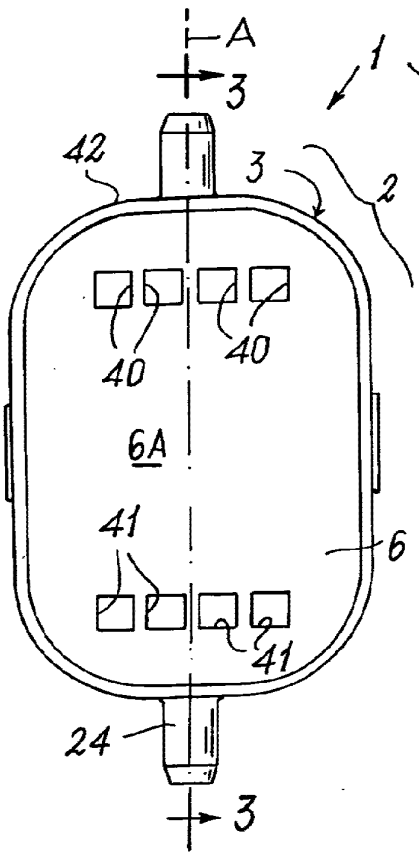


FIG. 1

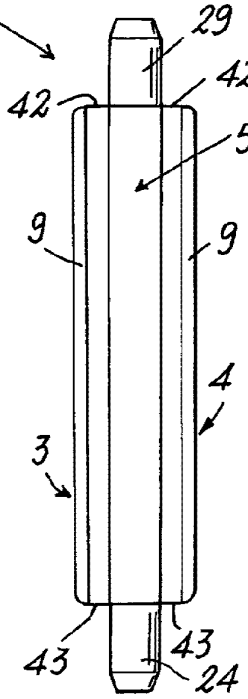


FIG. 2

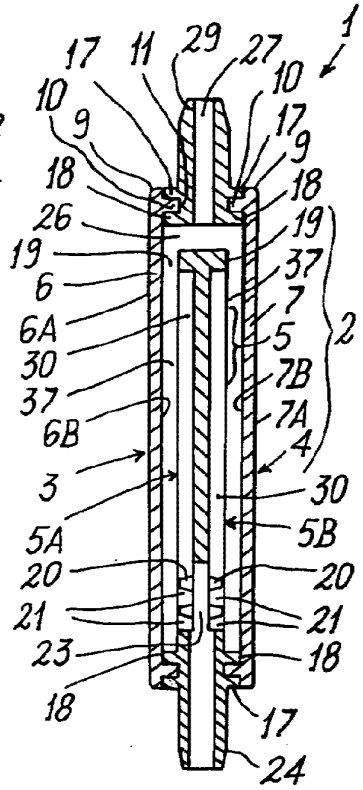


FIG. 3

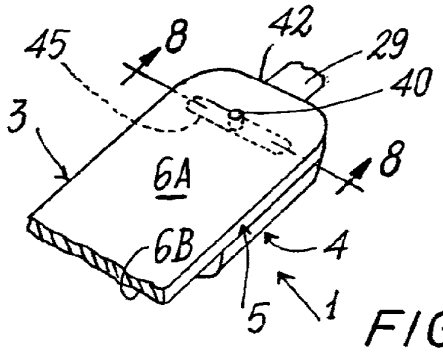


FIG. 7

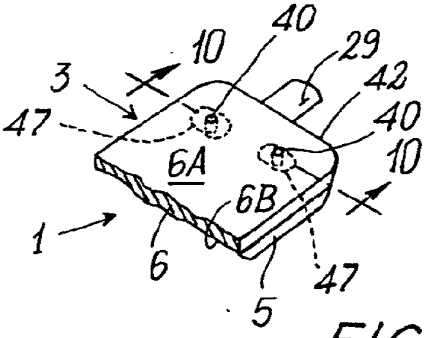


FIG. 9

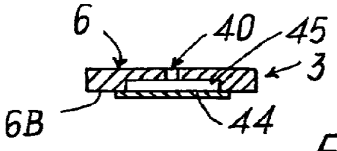


FIG. 8

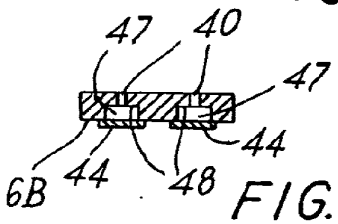


FIG. 10

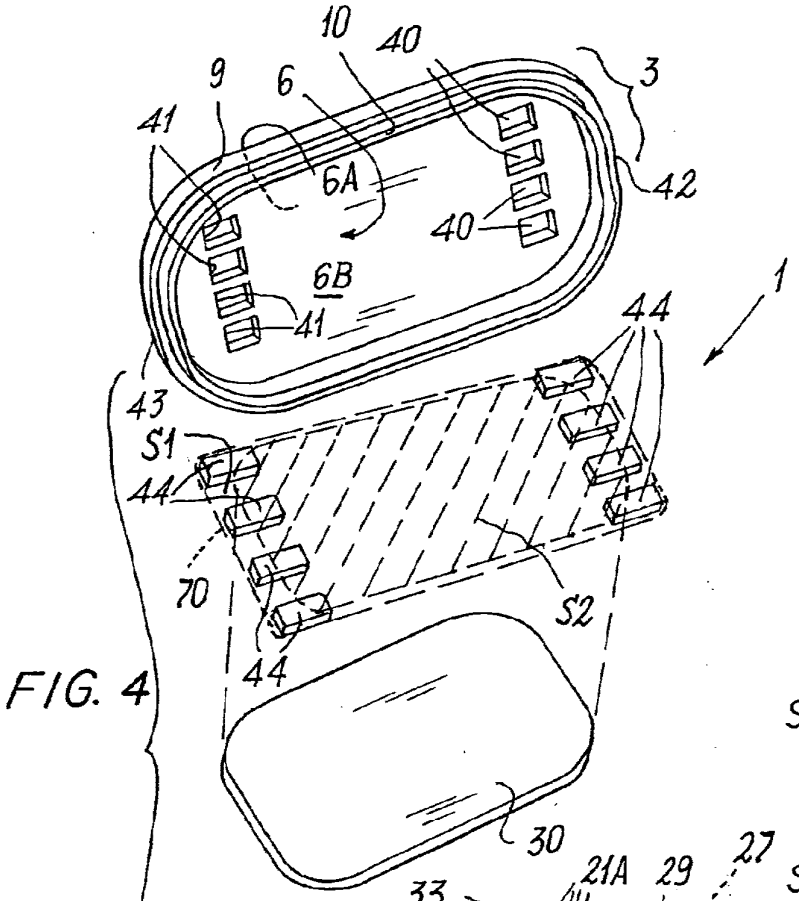


FIG. 4

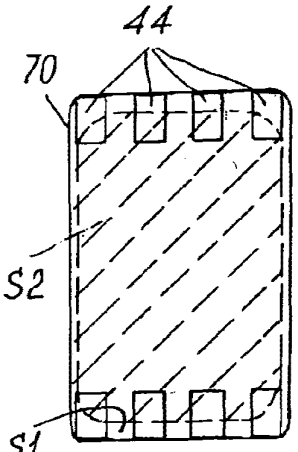
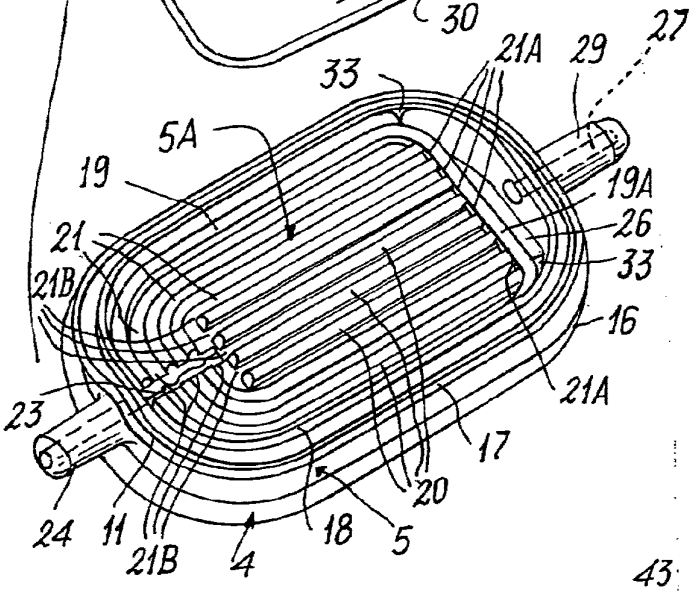


FIG. 5



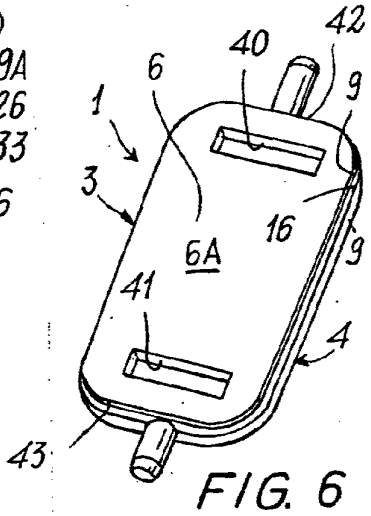


FIG. 6

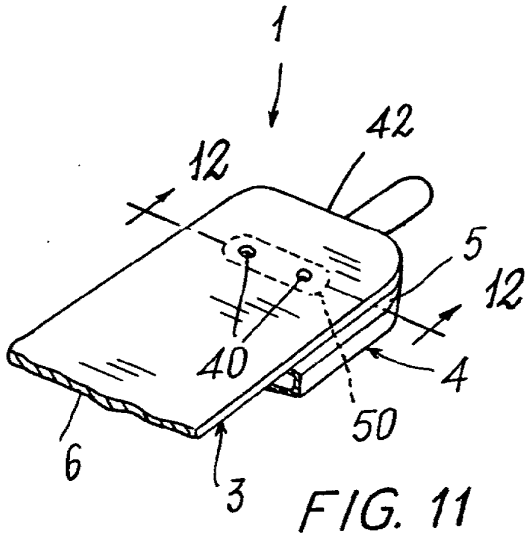


FIG. 11

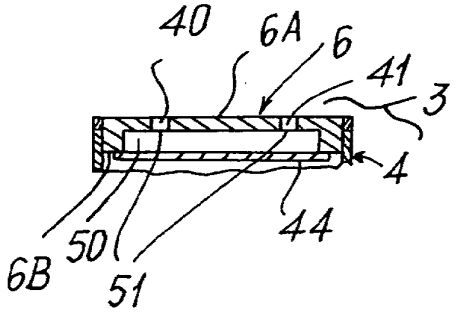


FIG.12

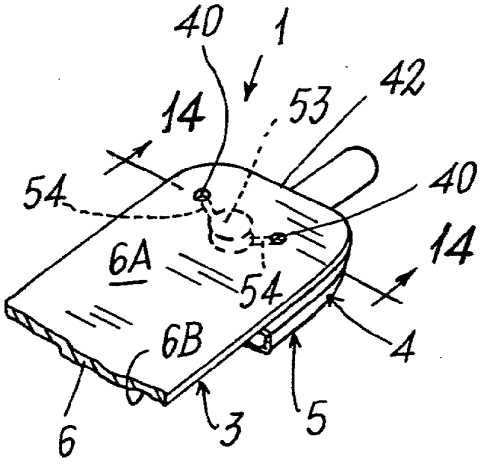


FIG.13

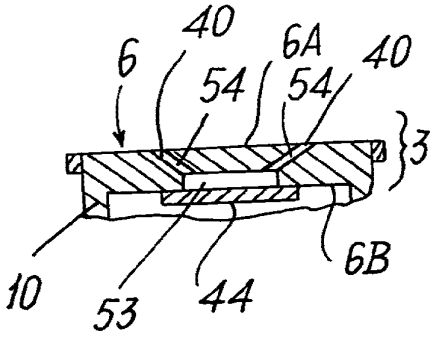


FIG.14

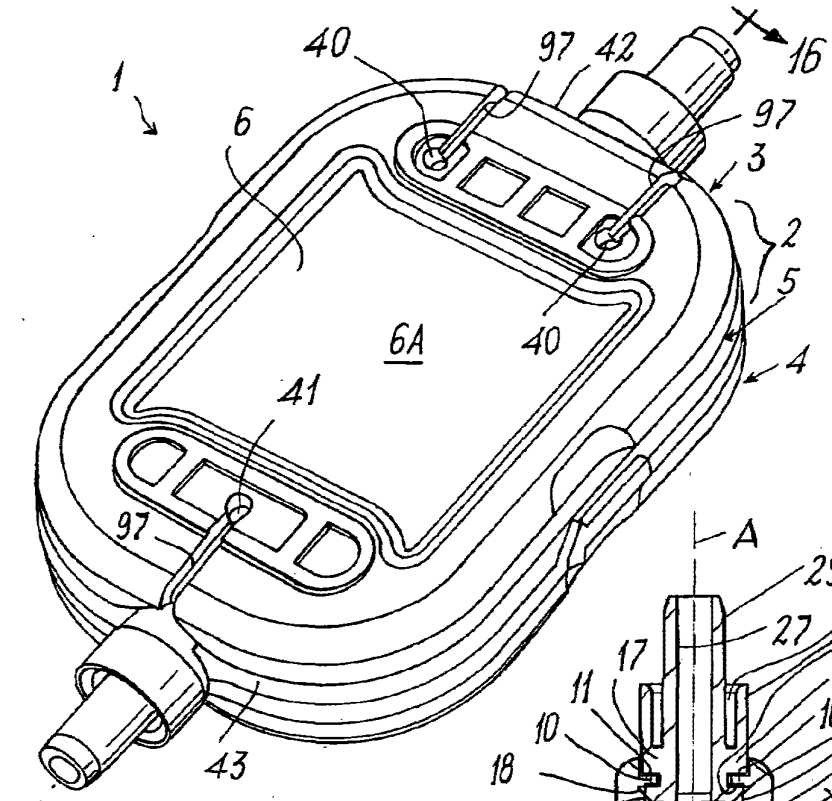

40
97
42
16
1
6
97
3
2
5
6A
40
4
41
97
43
16

FIG. 15

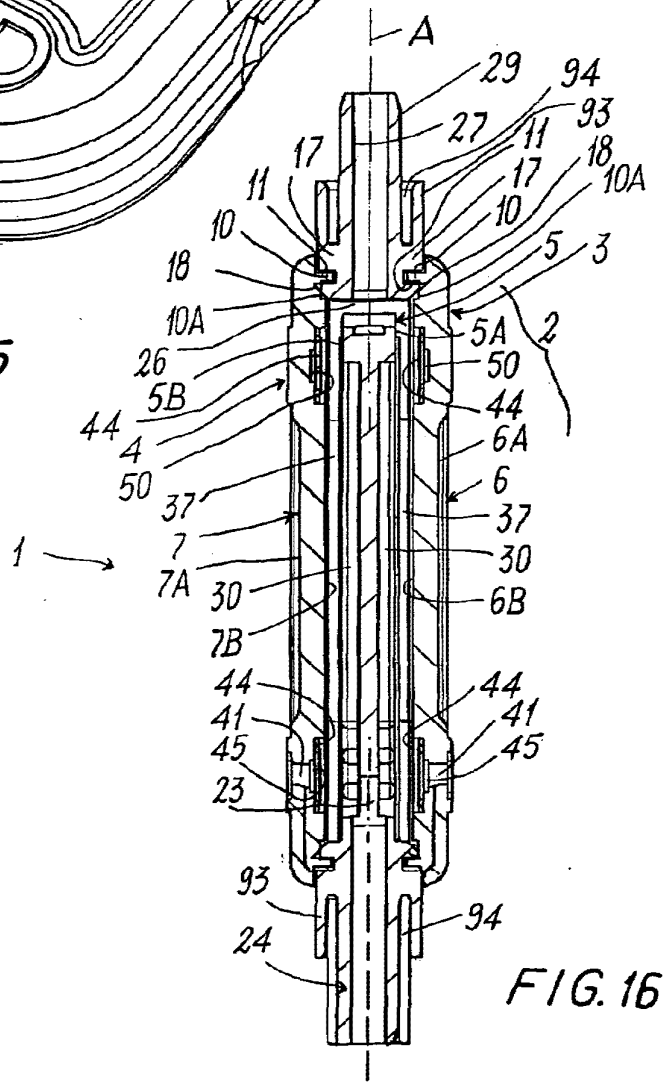

A
29
94
93
27
11
17
18
10A
11
17
10
10
18
5
3
10A
5A
2
26
50
5B
44
44
4
6A
50
6
37
37
7
30
1
7A
30
6B
7B
44
44
41
41
45
45
23
93
94
24

FIG. 16

European Patent Office

EUROPEAN SEARCH REPORT

Application Number
EP 03 02 5258

DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int.Cl.7)
X Y	EP 1 208 857 A (GVS S. R. L.) 29 May 2002 (2002-05-29) * paragraph [0007] - paragraph [0018] * * column 3, line 36 - line 47; figures 1-5 * ---	1,2,5-23 3,4	A61M5/165
Y	US 4 525 182 A (RISING DONALD B ET AL) 25 June 1985 (1985-06-25) * abstract * * column 1, line 17 - line 28 * * column 2, line 36 - line 56; figures 1-4,6 * ---	3,4	
A	WO 01 41844 A (KRAUS MENAHEM ;TEVA MEDICAL IND LTD (IL)) 14 June 2001 (2001-06-14) ---		
A	EP 0 784 988 A (FILTERTEK INC) 23 July 1997 (1997-07-23) ---		
A	EP 0 489 403 A (PALL CORP) 10 June 1992 (1992-06-10) ---		TECHNICAL FIELDS SEARCHED (Int.Cl.7)
A	US 5 622 626 A (MATKOVICH VLADO I ET AL) 22 April 1997 (1997-04-22) -----		A61M

The present search report has been drawn up for all claims

Place of search	Date of completion of the search	Examiner
THE HAGUE	29 January 2004	Michels, N

CATEGORY OF CITED DOCUMENTS

X : particularly relevant if taken alone
Y : particularly relevant if combined with another document of the same category
A : technological background
O : non-written disclosure
P : intermediate document

T : theory or principle underlying the invention
E : earlier patent document, but published on, or after the filing date
D : document cited in the application
L : document cited for other reasons

& : member of the same patent family, corresponding document

EPO FORM 1503 03.82 (P04C01)

ANNEX TO THE EUROPEAN SEARCH REPORT ON EUROPEAN PATENT APPLICATION NO. EP 03 02 5258

This annex lists the patent family members relating to the patent documents cited in the above-mentioned European search report. The members are as contained in the European Patent Office EDP file on
The European Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

29-01-2004

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
EP 1208857 A	29-05-2002	EP 1208857 A1	29-05-2002
		US 2002058913 A1	16-05-2002
US 4525182 A	25-06-1985	DE 3467718 D1	07-01-1988
		EP 0154645 A1	18-09-1985
		JP 60502091 T	05-12-1985
		WO 8500987 A1	14-03-1985
WO 0141844 A	14-06-2001	AU 7309200 A	18-06-2001
		EP 1237602 A1	11-09-2002
		WO 0141844 A1	14-06-2001
EP 0784988 A	23-07-1997	US 5827429 A	27-10-1998
		CA 2195360 A1	19-07-1997
		DE 69725629 D1	27-11-2003
		EP 0784988 A1	23-07-1997
EP 0489403 A	10-06-1992	US 5252222 A	12-10-1993
		CA 2054933 A1	04-06-1992
		DE 69131288 D1	08-07-1999
		DE 69131288 T2	23-09-1999
		EP 0489403 A2	10-06-1992
		JP 5184670 A	27-07-1993
		US 5536413 A	16-07-1996
US 5622626 A	22-04-1997	AU 3513595 A	10-11-1995
		DE 19580356 T0	24-04-1997
		EP 0792182 A1	03-09-1997
		JP 9511932 T	02-12-1997
		WO 9528215 A1	26-10-1995

EPO FORM P0459

For more details about this annex : see Official Journal of the European Patent Office, No. 12/82

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

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
17 December 2009 (17.12.2009)

PCT

(10) International Publication Number
WO 2009/152320 A2

(51) International Patent Classification:
A61M 5/14 (2006.01) *A61M 36/00* (2006.01)
G21F 5/015 (2006.01)

(21) International Application Number:
PCT/US2009/047027

(22) International Filing Date:
11 June 2009 (11.06.2009)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:

12/137,364	11 June 2008 (11.06.2008)	US
12/137,363	11 June 2008 (11.06.2008)	US
12/137,377	11 June 2008 (11.06.2008)	US
12/137,356	11 June 2008 (11.06.2008)	US

(71) Applicant *(for all designated States except US)*: **BRACCO DIAGNOSTICS INC.** [US/US]; 107 College Road East, Princeton, NJ 08540 (US).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: **QUIRICO, Charles, R.** [US/US]; 19 Robin Road, Warren, NJ 07059 (US). **BALESTRACCI, Ernest** [US/US]; 404 Hampton Lane, Iselin, NJ 08830 (US). **DARST, Daniel, D.** [US/US]; 25540 96th Street NW, Zimmerman, MN 55398 (US). **KRAUSE, Eric, J.** [US/US]; 3360 Lake Ridge Drive, Big Lake, MN 55309 (US). **LOKHANDE, Vishal, N.** [IN/US]; 100 North Whisman Road, Apartment . #1412, Mountain View, CA 94043 (US). **CHILDS, Jacob, S.** [US/US]; 30 W. 22nd Street, Apartment #202, Minneapolis, MN 55404 (US). **MADSON, Peter, B.** [US/CN]; 388 Furongjiang Lu, Building 3, Apartment 601, Changning District, Shanghai, 200051 (CN). **CLEMENTS, Daniel, V.** [US/US]; 4707 Emerson Avenue North, Minneapolis, MN 55430 (US).

(74) Agents: **BELDEN, Elisabeth, L.** et al.; Fredrikson & Byron, P.A., 200 South Sixth Street, Suite 4000, Minneapolis, MN 55402-1425 (US).

(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CL, 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, PE, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, 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, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, 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 (Rule 48.2(g))*

(54) Title: SHIELDING ASSEMBLIES FOR INFUSION SYSTEMS

(57) Abstract: A shielding assembly for an infusion system includes a plurality of compartments and a door for each compartment, and provides a radioactive radiation barrier for the compartments. One of the compartments contains one or more radioisotope generators of the infusion system and another of the compartments may contain a waste bottle of the infusion system. An opening into each of the generator and waste bottle compartments may be oriented upward, and the opening into the latter may be at a higher elevation than the opening into the former, for example, to facilitate independent removal and replacement of each. A door of at least one of the compartments, other than the generator compartment, when closed, may prevent the door of the generator compartment from being opened. A cabinet structure for the infusion system may enclose the shielding assembly and secure the generator.

WO 2009/152320 A2

SHIELDING ASSEMBLIES FOR INFUSION SYSTEMS

RELATED APPLICATIONS

The present application claims priority to the following U.S. patent applications: U.S. Patent Application No. 12/137,356, filed June 11, 2008; U.S. Patent Application No. 12/137,363, filed June 11, 2008; U.S. Patent Application No. 12/137,364, filed June 11, 2008; and U.S. Patent Application No. 12/137,377, filed June 11, 2008.

TECHNICAL FIELD

The present invention pertains to systems that generate and infuse radiopharmaceuticals, and, more particularly, to shielding assemblies thereof.

BACKGROUND

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

Whether the half-life of a particular radioactive isotope, employed by a radiopharmaceutical, is relatively short or long, a patient undergoing a nuclear imaging procedure is not typically exposed to a significant amount of radiation. However those personnel, whose job it is to set up and maintain radiopharmaceutical infusion systems, and to administer doses therefrom, are subject to more frequent exposures to radiation. Therefore, shielding assemblies, which provide a radiation barrier to protect these personnel from excessive exposure to radiation sources, are an important component of radiopharmaceutical generators and infusion systems. These shielding assemblies are typically formed with lead sidewalls, the bulk and weight of which can pose

difficulties for the personnel who regularly set up, maintain and use the systems. Thus, there is a need for improved shielding assemblies employed by systems that generate and infuse radiopharmaceuticals.

BRIEF DESCRIPTION OF THE DRAWINGS

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

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

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

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

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

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

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

Figure 2B is a perspective view of a framework of the system, according to some embodiments, with an enlarged detailed view of a component of the system, according to some embodiments.

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

DETAILED DESCRIPTION

The following detailed description is exemplary in nature and is not intended to limit the scope, applicability, or configuration of the invention in any way. Rather, the following description provides practical illustrations for implementing exemplary

embodiments. Utilizing the teaching provided herein, those skilled in the art will recognize that many of the examples have suitable alternatives that can be utilized.

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

Figure 1A further illustrates two pairs of wheels 121, 122, mounted to an underside of platform 113, to make system 10 mobile; handle 14 is shown located at an elevation suitable for a person to grasp in order to maneuver system 10, from one

location for another, upon pairs of wheels 121, 122. According to some preferred embodiments, one or both pairs of wheels 121, 122, are casters, allowing for rotation in a horizontal plane (swivel), in order to provide additional flexibility for maneuvering system 10 in relatively tight spaces.

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

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

Figure 1A further illustrates upper surface 131 of shell 13 including several openings 133, 135, 139 formed therein. Figure 1C is a partially exploded perspective

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

Turning now to Figure 1D, a schematic of an infusion circuit 300, which may be incorporated by system 10, is shown. Figure 1D illustrates circuit 300 generally divided into a first part 300A, which includes components mounted outside shell 13, and a second part 300B, which includes components mounted within the interior space surrounded by shell 13. (Parts 300A and 300B are delineated by dotted lines in Figure 1D.) Figure 1D further illustrates second part 300B of circuit 300 including a portion contained within a shielding assembly 200, which is designated schematically as a dashed line. Some embodiments of shielding assembly 200 will be described in greater detail, in conjunction with Figures 2A-B and 3A-B, below.

According to the illustrated embodiment, circuit 300 includes: an eluant reservoir 15, for example, a bag, bottle or other container, containing saline as the eluant, which is shown hanging from a post, or hanger 141 above upper surface 131 of shell 13 in Figure 1A; a syringe pump 33, for pumping the eluant from reservoir 15, and a pressure syringe 34 (or other device or sensor), for monitoring pumping pressure; a filter 37, which may also serve as a bubble trap, for the pumped eluant; a radioisotope generator 21, through which the filtered eluant is pumped to create a radioactive eluate, for example an eluate carrying Rubidium-82 that is generated by the decay of Strontium-82, via elution, within a column of generator 21; and an activity detector 25, for measuring the activity of the eluate discharged from generator 21, in

order to provide feedback for directing the flow of the eluate, via a divergence valve 35WP, either to a waste bottle 23 or through a patient line 305p, for example, to inject a dose of the radiopharmaceutical eluate into a patient. With reference back to Figure 1A, patient line 305p is shown extending out from shell 13, through opening 135, to a distal end thereof, which, according to some embodiments, includes a filter. Patient line 305p may be coupled to another line that includes a patient injection needle (not shown). Alternatively, patient line 305p may be coupled to another line (not shown), which extends from a source of another active substance, for example, a stress agent; the other line is coupled to the line that includes the patient injection needle, in order to permit injection of the additional active substance.

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

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

the eluate, at which time the feedback from activity detector 25 causes the controller to direct the corresponding servo-motor to re-set valve 35WP for diverting the flow of eluate into patient line 305p. According to some embodiments, once a prescribed volume of the eluate has passed through patient line 305p, the controller directs the corresponding servomotor to re-set divergence valve 35BG for diverting the flow of eluant through by-pass line 303 and into patient line 305p in order to flush, or push any eluate remaining in patient line 305p into the patient. According to some embodiments, the controller may also direct the corresponding servomotor to re-set divergence valve 35WP back toward waste bottle 23, prior to the flush through by-pass line 303, in order to prevent back flow of eluant, through line 305, toward generator 21. According to some preferred methods of operation, in certain situations, which will be described in greater detail below, eluant is pumped through by-pass line 303 immediately following the flow of the prescribed volume of eluate into patient line 305p, at a higher speed, in order to push the eluate in patient line 305, thereby increasing a flow rate of the injection of eluate out from patient line 305p and into patient. For example, once the prescribed volume of eluate has flowed into patient line 305p, and once divergence valve 35BG is set to divert flow through by-pass line 303, the speed of pump 33 may be adjusted to increase the flow rate of eluant to between approximately 70mL/min and approximately 100mL/min. This method for increasing the injection flow rate, is desirable, if a relatively high flow rate is desired for patient injection and a flow rate through generator 21 is limited, for example, to below approximately 70mL/min, maximum (typical flow rate may be approximately 50mL/min), in order to avoid an excessive back pressure created by the column of generator 21 in upstream portions of tubing circuit 300; the excessive back pressure could damage filter 37 or otherwise impede flow through eluant tubing line 302.

Although not shown in Figure 1D, a number of sensors, for example, to measure pressure and/or flow velocity, may be incorporated into circuit 300, according to some alternate embodiments, in order to monitor for flow anomalies, for example, related to occlusions/plugs in circuit 300 and/or leaks, and/or to provide feedback for control of an activity level of infused doses of radiopharmaceutical. Suitable sensors for any of the above purposes are known to those skilled in the art. Examples of flow meters that may be incorporated into circuit 300, include the Innova-Sonic® Model 205 Transit-Time Ultrasonic Liquid Flow Meter that employs digital signal processing

(available from Sierra Instruments, Inc.) and the Flocat LA10-C differential pressure flow meter. One example of a pressure sensor that may be employed to detect infusion circuit occlusions is the PRO / Pressure-Occlusion Detector (available from INTROTEK® of Edgewood, NY, a subsidiary of Magnetrol of Downers Grove, IL), which employs pulse-type ultrasound; this sensor detects subtle changes in positive and negative air pressure and produces a corresponding passive resistive output signal, which may be routed to the system controller and/or computer 17. On or more of this type of sensor may be incorporated into infusion circuit 300 by simply fitting the sensor around any of the tubing lines of infusion circuit 300; in fact, the PRO / Pressure-Occlusion Detector may be a suitable alternative to pressure syringe 34 of circuit 300. Other types of pressure sensors, for example, similar to those known in the art for blood pressure monitoring, may be employed in infusion circuit 300.

System 10 may further include sensors to detect fluid levels in eluant reservoir 15 and waste bottle 23. Some examples of such sensors, which also employ the aforementioned pulse-type ultrasound, are the Drip Chamber Liquid Level Sensor and the CLD / Continuous Level Detector (both available from INTROTEK®); alternatively, for example, an HPQ-T pipe mounted, self-contained liquid sensor (available from Yamatake Sensing Control, Ltd.), or an SL-630 Non-Invasive Disposable/Reusable Level Switch (available from Cosense, Inc. of Hauppauge, NY) may be employed to detect the fluid levels. Alternately or in addition, system 10 can include additional radiation and/or moisture detection sensors, which can detect leaks. With reference to Figure 1D, such sensors are preferably located in proximity to fittings 311, 312, 313, 314 and 315 that join portions of circuit 300 to one another. Some examples of leak detection sensors include, without limitation, those in the HPQ-D leak detection sensor family, and the HPF-D040 fiberoptic leak detector (all available from Yamatake Sensing Control, Ltd.). System 10 may further include additional sensors to detect contaminants and/or air bubbles within the tubing lines of circuit; examples of such sensors include the Point-air Detection (PAD) Sensor, that employs pulse-type ultrasound for air bubble detection, and the Blood Component Detector that employs optical sensing technology to perform Colorimetry-based fluid detection of unwanted elements in the tubing lines (both available from INTROTEK®).

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

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

directed to patient line 305p for infusion. Light projector 100 may further project a more rapidly flashing light, for example, for approximately five seconds, once a peak bolus of radioactivity is detected in the eluate, to provide further information to technical personnel. Alternative means of informing technical personnel that an infusion is taking place may also be incorporated by system 10, for example, including audible alarms or other types of visible or readable signals that are apparent at a distance from system, including in the control room.

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

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

maintenance procedures, such as changing out generator 21 and/or other components of circuit 300, as will be described below.

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

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

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

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

According to the embodiment illustrated in Figure 2A, opening 137 and door 221 are located at a lower elevation, for example, with respect to platform 113, than are opening 139 and lid 223, which provide access to the compartment being formed

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

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

According to the illustrated embodiment, doors 221, 225 are hinged to open in an upward direction, per arrows D and C, and, with reference back to Figure 1C, a

latch component 191 is provided to hold each of doors 221, 225 in an opened position, thereby, preventing doors 221, 225 from falling closed, which could pinch/crush fingers of technical personnel and/or tubing lines of circuit 300, when in the midst of a maintenance procedure. Figure 2B is a perspective view of framework 19 of the cabinet structure of system 10, according to some embodiments, to which latch component 191 is mounted; Figure 2B includes an enlarged detailed view of latch component 191, according to some embodiments. Figure 2B illustrates latch component 191 including a first pin 193, corresponding to door 225, and a second pin 195, corresponding to door 221; each pin 193, 195 includes a lever end 193A, 193B, respectively, and a holding end 193B, 195B, respectively. An edge of each door 221, 225, upon opening of doors 221, 225, may push past the holding end 195B, 193B of the corresponding pin 195, 193, in a first direction, per arrow F, and then may rest against a respective side S95 and S93 of each end 195B, 193B, until the corresponding lever end 195A, 193A is rotated in a counter-clockwise direction, per arrow cc, thereby moving the corresponding holding end 193B, 195B to make way for the closing of doors 221, 225. Doors 221, 225 being held by latch component 191 in an open position may be seen in Figure 3A.

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

Figure 3A is another perspective view of shielding assembly 200, according to some embodiments of the present invention. In Figure 3A, lid 223 and doors 221, 225, and 227 are opened to provide a view into openings 233, 235 and 231 of sidewalls 203, 205 and 201, respectively, and into a passageway 207, which is formed in

sidewall 203, opposite the compartment, which contains waste bottle 23. Passageway 207 is shown extending vertically along sidewall 203 and having a grooved extension 213 formed in a perimeter surface of opening 233. An optional retaining member 237, for example, formed from an elongate strip of resilient plastic having a generally c-shape cross-section, is shown being mounted along a length of passageway 207 to hold lines 305w and 305p in place within passageway 207. Figure 3A further illustrates a pair of passageways 251b and 251g, which are formed as grooves in a portion of sidewall 205, and another pair of passageways 215i and 215o, which are formed as grooves in a portion of sidewall 201. A routing of portions of tubing circuit 300 (Figure 1D) through passageways 207, 251b, 251c, 215i and 215o is shown in Figure 3B.

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

provide an indication to the user that an incorrect generator has been installed. Of course a user of system 10 may, alternately, manually enter information, that is provided on a generator label or marking, into computer 17, in order to either enable system 10, or to receive feedback from computer 17 that the incorrect generator is installed.

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

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

According to the illustrated embodiment, an end 404A, of eluant line 304, and an end 403, of by-pass line 303 extend from third side 393 of frame 39 to couple with divergence valve 35BG and an upstream section of eluant tubing line 302. Figure 3C further illustrates an opposite end 404B of eluant line extending from first side 391 of frame 39, alongside a similarly extending end 405 of eluate line 305, and ends 406 and

407 of patient line 305p and waste line 305w, respectively, extending from second side 392 of frame 39. Although ends 406, 407 are shown extending upward from tray 39a, as they would within shielding assembly 200, it should be appreciated that the tubing lines of circuit 300 are preferably flexible and would drop down under their own weight rather than extending upward, as shown, if not supported. Referring back to Figure 1D, in conjunction with Figure 3C, it can be seen that the aforementioned fittings are provided for coupling subassembly 390 into circuit 300: first fitting 311 couples the section of eluant line 302 to filter 37; second fitting 312 couples eluant line 304 to an inlet port of generator 21; third fitting 313, which may incorporate a check valve, couples eluate line 305 to an outlet port of generator 21; fourth fitting 314 couples waste line 305w to waste bottle 23; and fifth fitting 315 couples patient line 305p to an extension thereof, which extends outside shell 13 (designated by the dotted line). Each of the fittings 311, 312, 313, 314, 315 may be of the Luer type, may be a type suitable for relatively high pressure applications, or may be any other suitable type that is known to those skilled in the art.

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

With further reference to Figure 3B, other portions of tubing circuit 300 are shown. Figure 3B illustrates eluant tubing line 301 extending from reservoir 15, outside of shell 13 (Figure 1A), to syringe pump 33, which is mounted to an actuating platform 433. According to the illustrated embodiment, platform 433 is actuated by another servomotor (not shown) of system 10, which is controlled by the controller and computer 17 of system 10, to cause a plunger of pump 33 to move, per arrow I, so

as to draw in eluant, from reservoir 15, through tubing line 301, and then to cause the plunger to move in the opposite direction so as to pump the eluant, through tubing line 302, to either generator 21 or to by-pass line 303. Although the illustrated embodiment includes syringe pump 33, other suitable pumps, known to those skilled in the art, may be substituted for pump 33, in order to draw eluant from reservoir 15 and to pump the eluant throughout circuit 300. Although not shown, it should be appreciated that divergence valve 35BG is fitted into another valve actuating receptacle mounted within shell 13 and coupled to yet another servomotor (not shown) of system 10.

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

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

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

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

to some embodiments, computer 17 is pre-programmed to provide guidance in multiple languages.

Figure 4 is a screen shot of a main menu 470, which is presented by computer 17 on monitor 172, according to some embodiments. Main menu 470 includes a listing of each computer-facilitated operation that may be selected by the user, once the user has logged on. According to some multi-lingual embodiments, computer 17 presents a list of languages from which the user may select, prior to presenting main menu 470.

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

After the user enters the appropriate information into data entry fields of log in screen 570, computer 17 presents a request for the user to confirm the volume of eluant that is within reservoir 15 (e.g. saline in saline bag), via a screen 571, and then brings up main menu 470. If the user determines that the volume of eluant/saline is insufficient, the user selects a menu item 573, to replace the saline bag. If system 10 includes an encoded information reader, such as a bar code or RFID tag reader, confirmation that the selected reservoir is proper, i.e. contains the proper saline solution, may be carried out by computer 17, prior to connecting the reservoir into circuit 300, by processing information read from a label/tag attached to the reservoir. Alternatively, or in addition, tubing line 301 of circuit 300 may be provided with a

connector which only mates with the proper type of reservoir 15. According to some embodiments, system 10 may further include an osmolarity or charge detector, which is located just downstream of reservoir 15 and is linked to computer 17, so that an error message may be presented on monitor 172 stating that the wrong osmolarity or charge is detected in the eluant supplied by reservoir, indicating an improper solution. One example of a charge detector that may be employed by system 10 is the SciCon™ Conductivity Sensor (available from SciLog, Inc. of Middleton, WI).

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

In addition to tracking the volume of eluant in reservoir 15, computer 17 also tracks a volume of the eluate which is discharged from generator 21 into waste bottle 23. With reference to Figure 5C, an item 583 is provided in main menu 470, to be selected by the user when the user empties waste bottle 23. When the user selects item 583, computer 17 presents a screen 584, by which the user may effectively command computer 17 to set a waste bottle level indicator to zero, once the user has emptied waste bottle 23. Typically, the user, when powering up system 10 for operation, each

day, will either empty waste bottle 23, or confirm that waste bottle 23 was emptied at the end of operation the previous day, and utilize screen 584 to set the waste bottle level indicator to zero. Thus, computer 17, can track the filling of waste bottle 23 via monitoring of the operation of pump 33 and divergence valve 35WP, and provide an indication to the user when waste bottle 23 needs to be emptied, for example, via presentation of screen 584, in order to warn the user that, unless emptied, the waste bottle will overflow. According to some embodiments, system 10 automatically precludes any further operation of the system until the waste bottle is emptied. According to some alternative embodiments, a fluid level sensor may be coupled to waste bottle, for example, as mentioned above in conjunction with Figure 1D, in order to automatically detect when waste bottle is filled to a predetermined level and to provide, via computer 17, an indication to the user that waste bottle 23 needs to be emptied and/or to automatically preclude operation of system 10 until the waste bottle is emptied.

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

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

elution process is completed and informs the user of the time lapse, either in terms of the time countdown (screen 677), or in terms of a time from completion of the elution, for example, as will be described in conjunction with Figure 7B. According to an exemplary embodiment, wherein generator 21 is the CardioGen-82® that yields a saline solution of Rubidium-82, produced by the decay of Strontium-82, via the elution, a time required between two effective elution processes is approximately 10 minutes.

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

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

Upon completion of the elution process for breakthrough testing, computer 17 presents a screen 777, shown in Figure 7B, which, like screen 677, provides an indication of a time lapse since the completion of the elution, but now in terms of a time since completion of the breakthrough elution process. When the user transfers

the vial containing the sample of eluate into a dose calibrator, to measure the activity of the sample, the user may make a note of the time lapse indicated on screen 777. With further reference to Figure 7B, once the user has received the activity measure from the dose calibrator, the user proceeds to a screen 778, which includes data entry fields for the activity measure and the time between that at which the dose calibrator measured the activity of the sample and that at which the elution was completed. The user may enter the data via the touch-screen interface of monitor 172, or via any of the other aforementioned devices for user data entry. According to some alternate embodiments, computer 17 may receive the data, electronically, from the dose calibrator, either via wireless communication or a cable connection.

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

limits; the screen may further direct the user to contact the generator supplier, for example, to order a replacement generator.

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

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

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

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

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

974 presented by computer 17 includes data entry fields by which the user may establish parameters for the automatic infusion; all or some of the fields may be filled in with pre-programmed default parameters, which the user has an option to change, if necessary.

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

With further reference to Figure 9C, screen 976 shows an exemplary activity profile (activity - mCi/sec, on y-axis, versus time – sec, on x-axis) for the infusion/injected dose (designated between the two vertical lines). Those skilled in the art will appreciate that the shape of this profile depends upon the infusion flow rate,

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

Consistency of activity profiles among injected doses can greatly facilitate the use of PET scanning for the quantification of flow, for example, in coronary perfusion studies. Alternative infusion circuit configurations, operable according to alternative methods, to achieve consistency of activity profiles among injected doses, as well as a

more uniform level of radioactivity across each individual dose, will be described below, in conjunction with Figures 12A-C.

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

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

Turning now to Figure 10, an item 981 for computer-facilitated purging of the tubing lines of system 10 is shown included in main menu 470. When a user selects item 981, computer 17 guides the user to select either an air purge or a saline purge. The direction provided by computer 17 is not explicitly laid out herein, for a saline

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

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

The purge operations, which are facilitated by selecting item 981 from main menu 470, may also be accessed via the selection of an item 991 for generator setup.

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

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

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

Figure 12A illustrates circuit 1300A including, like the previously described circuit 300, eluant reservoir 15, pump 33, radioisotope generator 21, through which the

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

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

divergence valve 1335IO, similar to receptacle 253, shown in Figure 3A for divergence valve 35WP.

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

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

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

We claim:

1. A shielding assembly for an infusion system, the shielding assembly being mounted within a cabinet structure, and the shielding assembly comprising:
a first compartment sized to contain one or more radioisotope generators of the infusion system, the first compartment being enclosed by a first sidewall that forms a barrier to radioactive radiation, the first sidewall including an opening extending therethrough and a lid, 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 sized to contain a portion of an infusion tubing circuit 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, 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 sized to contain a waste bottle 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, 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.

2. The shielding assembly of claim 1, wherein the opening of the first sidewall is aligned with a first upper opening through a shell of the cabinet structure and the opening of the third sidewall is aligned with a second upper opening through the shell of the cabinet structure, the second upper opening being located at a greater elevation, with respect to the lowermost portion of the cabinet structure, than the first upper opening.

3. The shielding assembly of claim 1, wherein an opening through a shell of the cabinet structure provides access to both the lid of the first sidewall and to the lid portion of the second sidewall.

4. The shielding assembly of claim 1, wherein the lowermost portion of the cabinet structure is at approximately ground level and the first elevation is between approximately 12 inches and approximately 24 inches.

5. The shielding assembly of claim 1, wherein the lowermost portion of the cabinet structure is at approximately ground level and the second elevation is between approximately 24 inches and approximately 36 inches.

6. The shielding assembly of claim 1, further comprising:
a fourth compartment sized to contain another portion of the infusion tubing circuit of the infusion system downstream from the one or more generators, the fourth compartment being enclosed by a portion of the third sidewall and a door that forms a barrier to radioactive radiation, the door mating with the portion of the third sidewall to alternately enclose the fourth compartment and provide access to the fourth compartment; and
wherein the fourth compartment is immediately adjacent to the second compartment; the portion of the infusion tubing circuit contained in the second compartment includes an eluate line, extending from the one or more generators, a patient line, being coupled to the eluate line, and a waste line, being coupled to the eluate line; and
the other portion of the infusion tubing circuit contained in the fourth compartment includes an extension of the patient line, from the second compartment, and an extension of the waste line, from the second compartment.

7. The shielding assembly of claim 6, wherein the fourth compartment extends approximately vertically along the portion of the third sidewall, on an opposite side of the third sidewall from the third compartment.

8. The shielding assembly of claim 7, wherein the fourth compartment includes a retaining member to hold the extension of the patient line and the extension of the waste line in place within the fourth compartment.

9. The shielding assembly of claim 6, wherein the lid of the third sidewall, when mated with opening of the third sidewall, prevents the door of the fourth compartment from opening to provide access to the fourth compartment.

10. The shielding assembly of claim 9, wherein the door of the fourth compartment, when mated with the portion of the third sidewall, prevents the lid portion of the second sidewall from opening to provide access to the second compartment.

11. The shielding assembly of claim 10, wherein the lid portion of the second sidewall, when mated with the base portion of the second sidewall, prevents the lid of the first sidewall from opening to provide access to the first compartment.

12. The shielding assembly of claim 6, wherein the door of the fourth compartment, when mated with the portion of the third sidewall, prevents the lid portion of the second sidewall from opening to provide access to the second compartment.

13. The shielding assembly of any of claims 1-5, wherein the lid portion of the second sidewall, when mated with the base portion of the second sidewall, prevents the lid of the first sidewall from opening to provide access to the first compartment.

14. The shielding assembly of any of claims 1-5, wherein the lid of the first sidewall is hinged to open in an upward direction; and further comprising a latch component, mounted within the cabinet structure, to hold the lid of the first sidewall in an open position.

15. The shielding assembly of any of claims 1-5, wherein the lid portion of the second sidewall is hinged to open in an upward direction; and further comprising a latch component, mounted within the cabinet structure, to hold the lid portion of the second sidewall in an open position.

16. A method for setting up an infusion system, the method comprising:
opening a first door of a shielding assembly of the infusion system to access a first compartment of the assembly and to allow for a second door of the shielding assembly to be opened; and
opening the second door, after opening the first door, to access a second compartment of the shielding assembly, the second compartment being separate from, and outside of, the first compartment;
placing a radioisotope generator into the second compartment and connecting the generator to an infusion tubing circuit;
placing a portion of the infusion tubing circuit into the first compartment;
closing the second door to enclose the generator within the second compartment; and
closing the first door, after closing the second door, to enclose the portion of the infusion tubing circuit within the first compartment.

17. The method of claim 16, further comprising unlocking and removing an access panel from a shell of a cabinet structure, which encloses the shielding assembly, to access the first door and the second door of the shielding assembly.

18. The method of claim 16, further comprising:
opening a third door, prior to opening the first door, to access a third compartment of the shielding assembly and to allow for the first door to be opened;
placing another portion of the infusion tubing circuit into the third compartment; and
closing the third door, after closing the first door, to enclose the other portion of the infusion tubing circuit within the third compartment.

19. The method of claim 18, further comprising unlocking and removing an access panel from a shell of a cabinet structure, which encloses the shielding assembly, to access the first door, the second door and the third door of the shielding assembly.

20. The method of claim 18, further comprising:
opening a fourth door, prior to opening the third door, to access a fourth compartment of the shielding assembly and to allow for the third door to be opened;
connecting a waste line of the infusion tubing circuit to a waste bottle;
placing the waste bottle into the fourth compartment; and
closing the fourth door, after closing the third door, to enclose the waste bottle within the fourth compartment.

21. The method of any of claims 16-20, further comprising securing at least one of the first and second doors in an open position.

22. A shielding assembly for an infusion system, the shielding assembly comprising a plurality of compartments and providing a radioactive radiation barrier for the compartments, the assembly further comprising:
a first door 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 of the infusion system; and
a second door to alternately enclose and provide access to a second compartment 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 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.

23. The shielding assembly of claim 22, further comprising a third door to alternately enclose and provide access to a third compartment of the plurality of compartments, the third compartment sized to contain another portion of the infusion tubing circuit of the infusion system downstream from the one or more generators, the third door, when enclosing the third compartment, preventing the second door from opening to provide access to the second compartment.

24. The shielding assembly of claim 23, further comprising a fourth door to alternately enclose and provide access to a fourth compartment of the plurality of compartments,

the fourth compartment being sized to contain a waste bottle of the infusion system, the fourth door, when enclosing the fourth compartment, preventing the third door from opening to provide access to the third compartment.

25. The shielding assembly of claim 24, wherein the third compartment shares a sidewall with the fourth compartment and extends approximately vertically along the shared sidewall.

26. The shielding assembly of claim 25, wherein the third compartment includes a retaining member attached to the shared sidewall to hold the other portion of the infusion tubing circuit in place along the shared sidewall.

27. An infusion system comprising:

a cabinet structure including a shell defining an interior space thereof, the shell including a first opening, a second opening and an access panel, the access panel mating with the second opening and being removable therefrom;

a lock reversibly engaging the access panel to secure access to the interior space of the cabinet structure;

an eluant source;

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, 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 contained within a first compartment of the plurality of compartments of the shielding assembly and being accessible through the second opening of the shell of the cabinet structure, when the access panel is unlocked, and when a first door of the plurality of doors, which corresponds to the first compartment, is open;

an eluant line 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 coupled to the eluate line and extending out from the interior space of the cabinet structure through the first opening of the shell.

28. The assembly of claim 27, wherein the first door is hinged to open in an upward direction; and further comprising a latch component, mounted within the cabinet structure, to hold the first door in an open position.

29. The system of claim 27, further comprising:
a waste bottle contained within a second compartment of the plurality of compartments of the shielding assembly; and
a waste line coupled to the eluate line and to the waste bottle;
wherein the shell of the cabinet structure further includes a third opening; and
a second door of the plurality of doors, which corresponds to the second compartment, is aligned with the third opening of the shell, for access thereto, and is located at a higher elevation, with respect to a lowermost surface of the cabinet structure, than that of the second door.

30. The system of claim 27, further comprising:
a waste bottle contained within a second compartment of the plurality of compartments of the shielding assembly; and
a waste line coupled to the eluate line and to the waste bottle;
wherein a second door of the plurality of doors, which corresponds to the second compartment, when closed, prevents the first door from opening to provide access to the first compartment.

31. The system of claim 27, wherein:
the eluate line and at least a portion of the patient line are contained in a second compartment of the plurality of compartments of the shielding assembly; and
a second door of the plurality of doors, which corresponds to the second compartment, when closed, prevents the first door from opening to provide access to the first compartment.

32. The system of claim 31,wherein the second door is accessible only through the second opening of the shell of the cabinet structure, when the access panel is unlocked.

33. The system of claim 31, wherein the first door and the second door are both hinged to open in an upward direction; and further comprising at least one latch component, mounted within the cabinet structure, to hold the first door and the second door in an open position.

34. A shielding assembly for an infusion system, the shielding assembly being mounted within a cabinet structure, and the shielding assembly comprising:
a plurality of compartments having sidewalls providing barriers to radioactive radiation for the compartments;
a corresponding plurality of doors, 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 of the plurality of compartments enclosed by a first sidewall of the sidewalls and sized to contain one or more radioisotope generators 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.

35. The shielding assembly of claim 34, wherein the lowermost portion of the cabinet structure is at approximately ground level, the first sidewall opening is at an elevation of between approximately 12 inches and approximately 24 inches with respect to the lowermost portion of the cabinet.

36. The shielding assembly of claim 35, wherein the elevation of the upper surface of the shell is between approximately 24 inches and 36 inches, with respect to the lowermost portion of the cabinet structure.

37. The shielding assembly of claim 1, further comprising a second compartment of the plurality of compartments enclosed by a second sidewall of the sidewalls and sized to contain a waste bottle of the infusion system, the second sidewall including a second sidewall opening oriented upward and aligned with a second upper opening through the shell of the cabinet structure, the second upper opening being an opening in the upper surface of the shell.

Fig. 1A

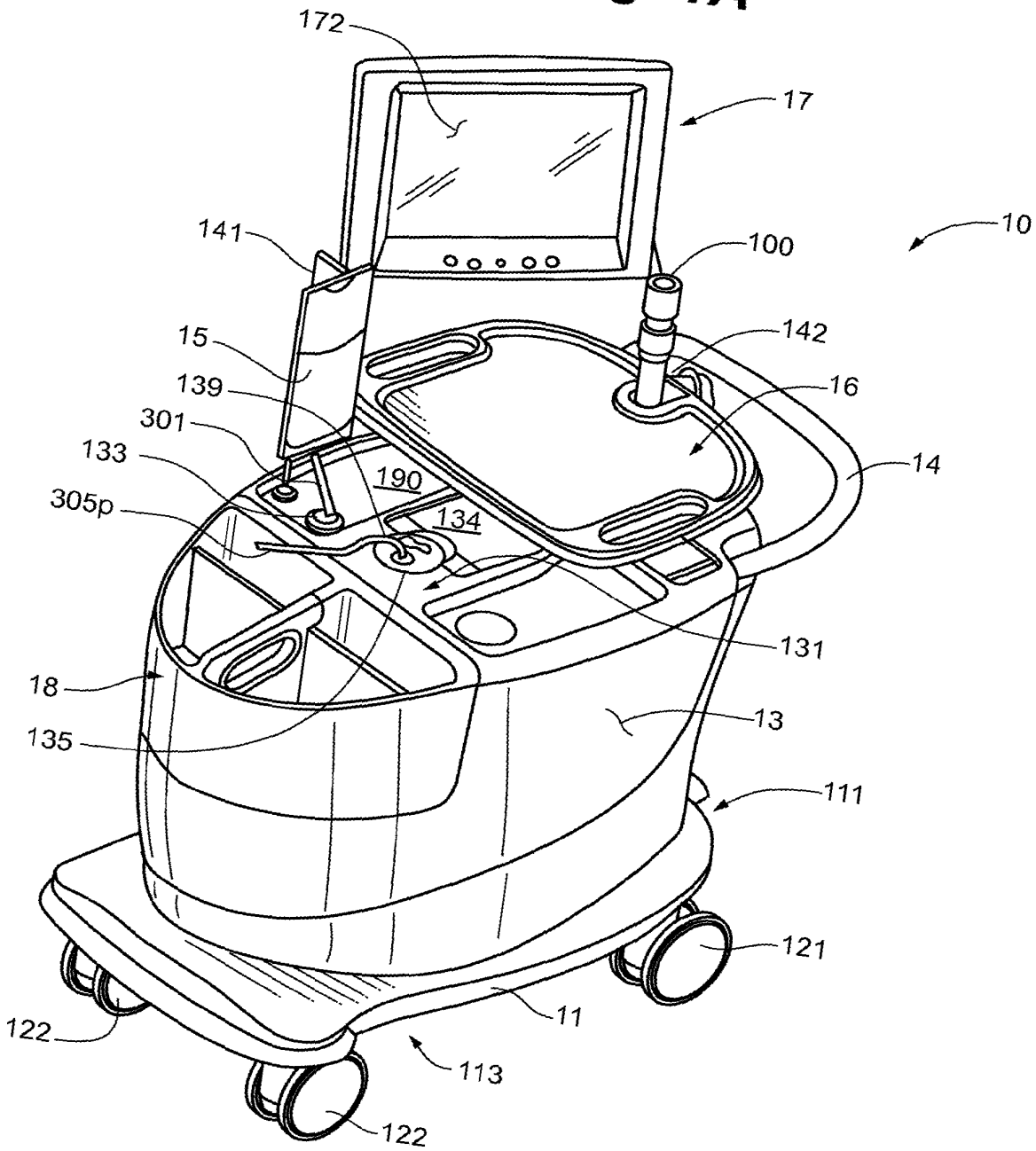

172
17
10
141
100
15
142
139
16
301
133
190
14
305p
134
131
18
13
135
111
121
11
122
113
122

Fig. 1B

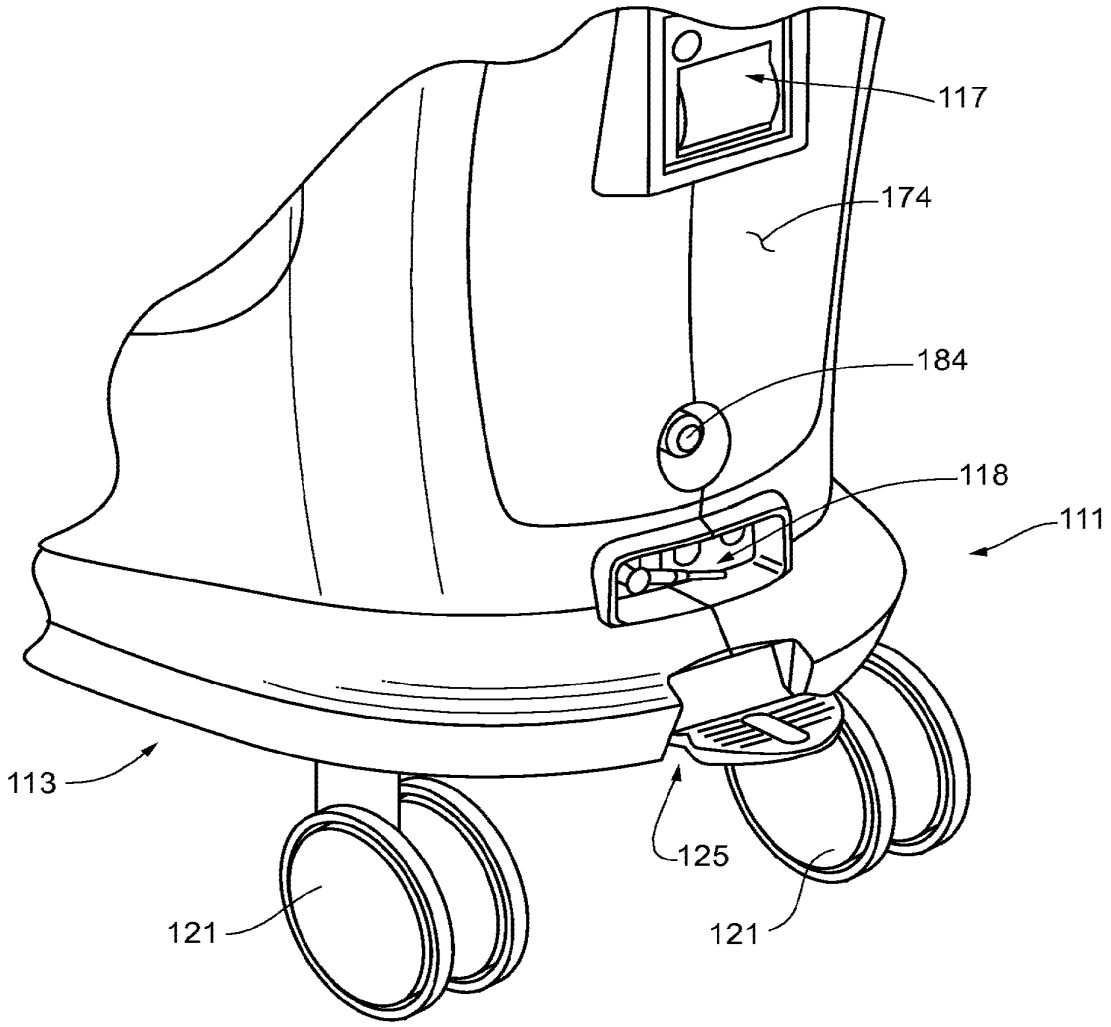
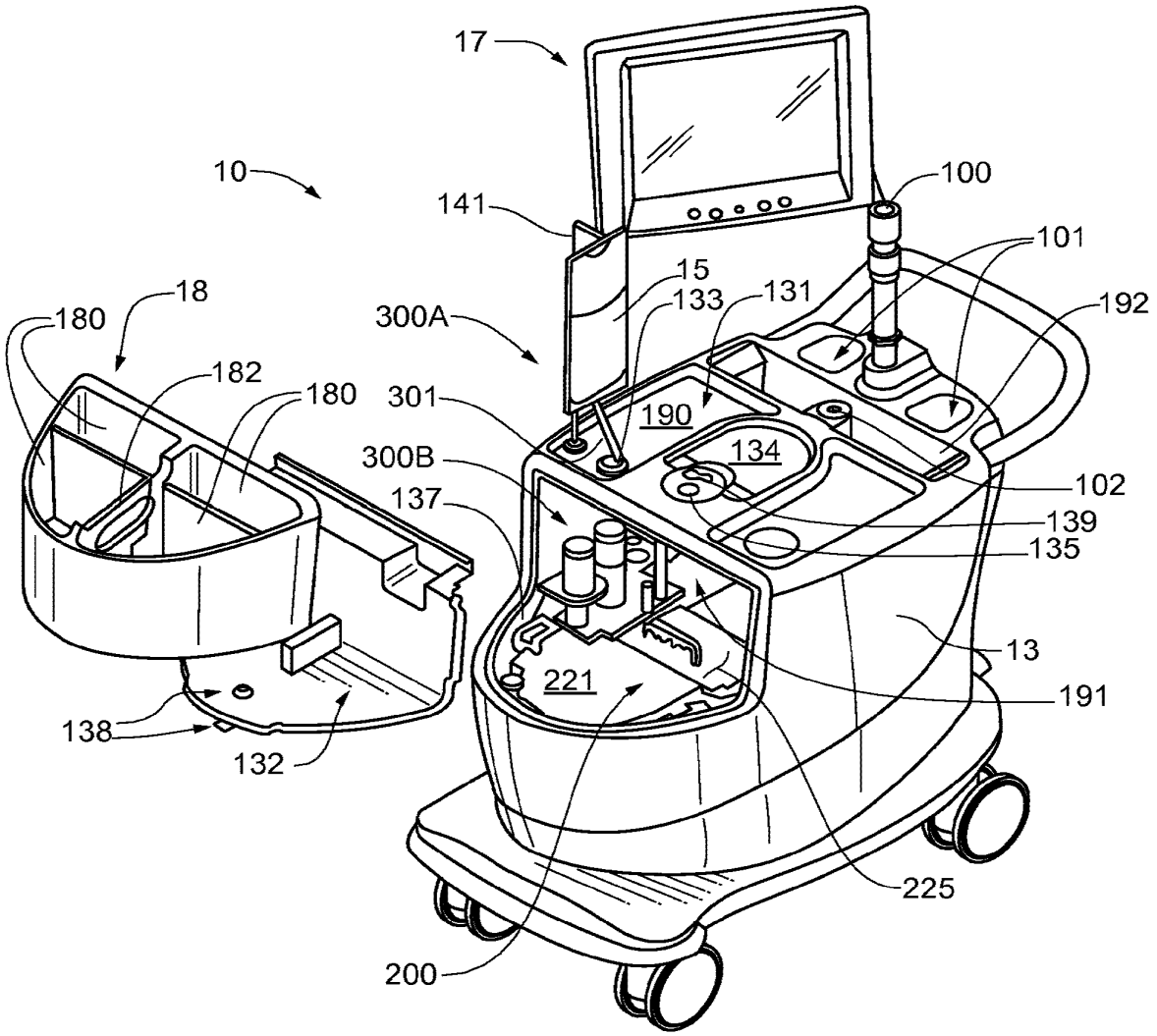


Fig. 1C


17
10
141
100
101
15
133
131
192
18
180
300A
182
180
301
190
134
300B
102
137
139
135
13
221
191
138
132
225
200

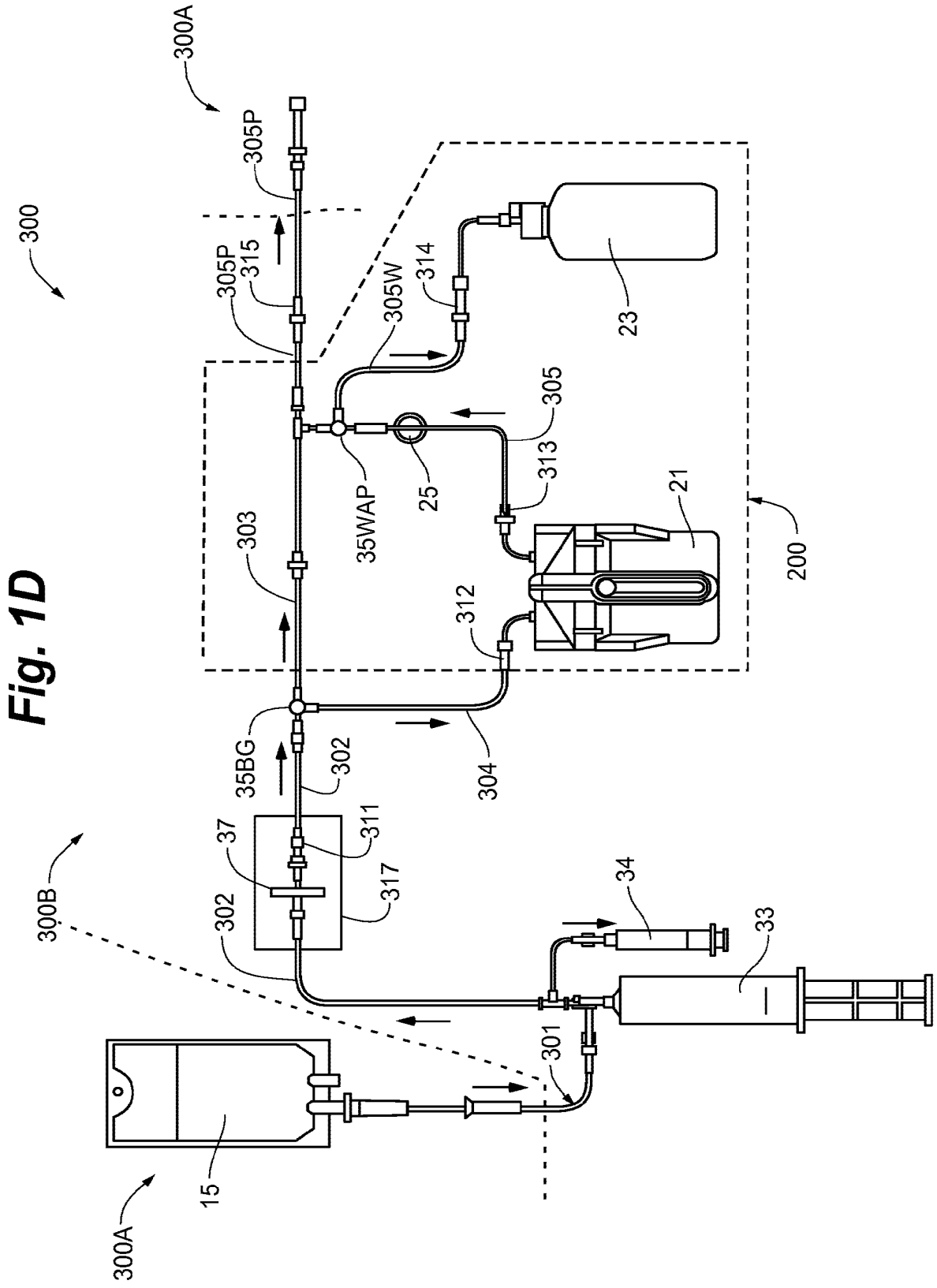

300A
305P
300
305P
315
314
305W
23
305
313
25
35WAP
21
303
200
312
35BG
302
304
37
311
317
300B
302
34
33
301
15
300A

Fig. 1D

Fig. 1E

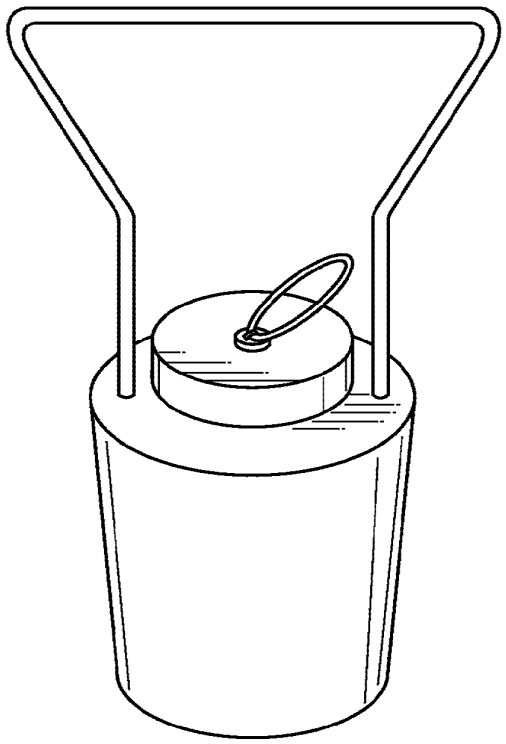


Fig. 2A

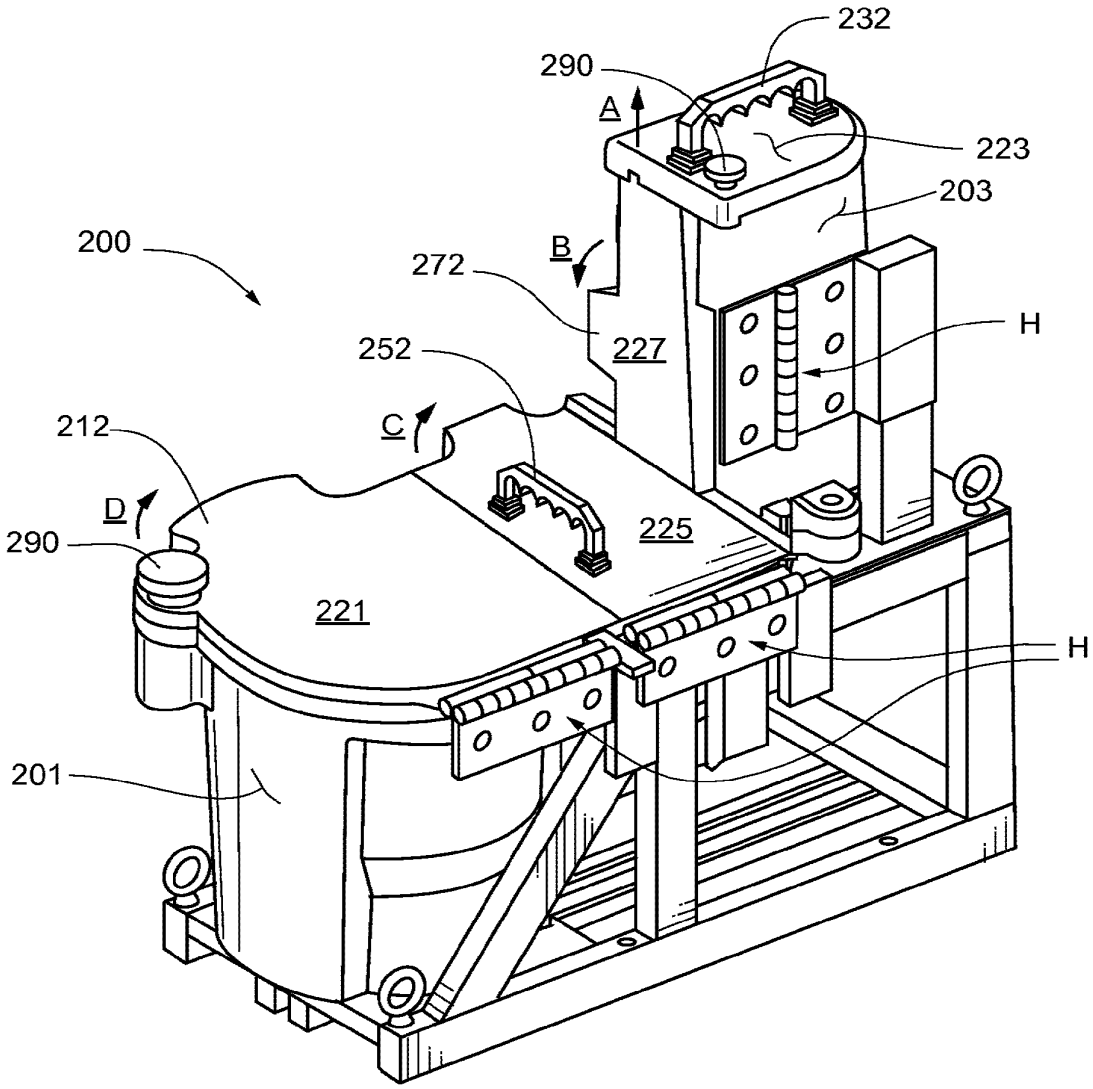


Fig. 2B-1

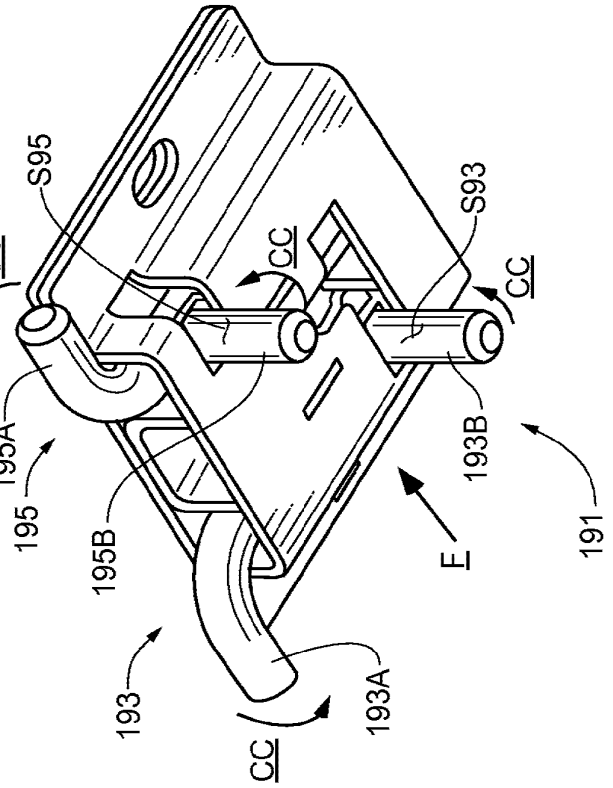


Fig. 2B

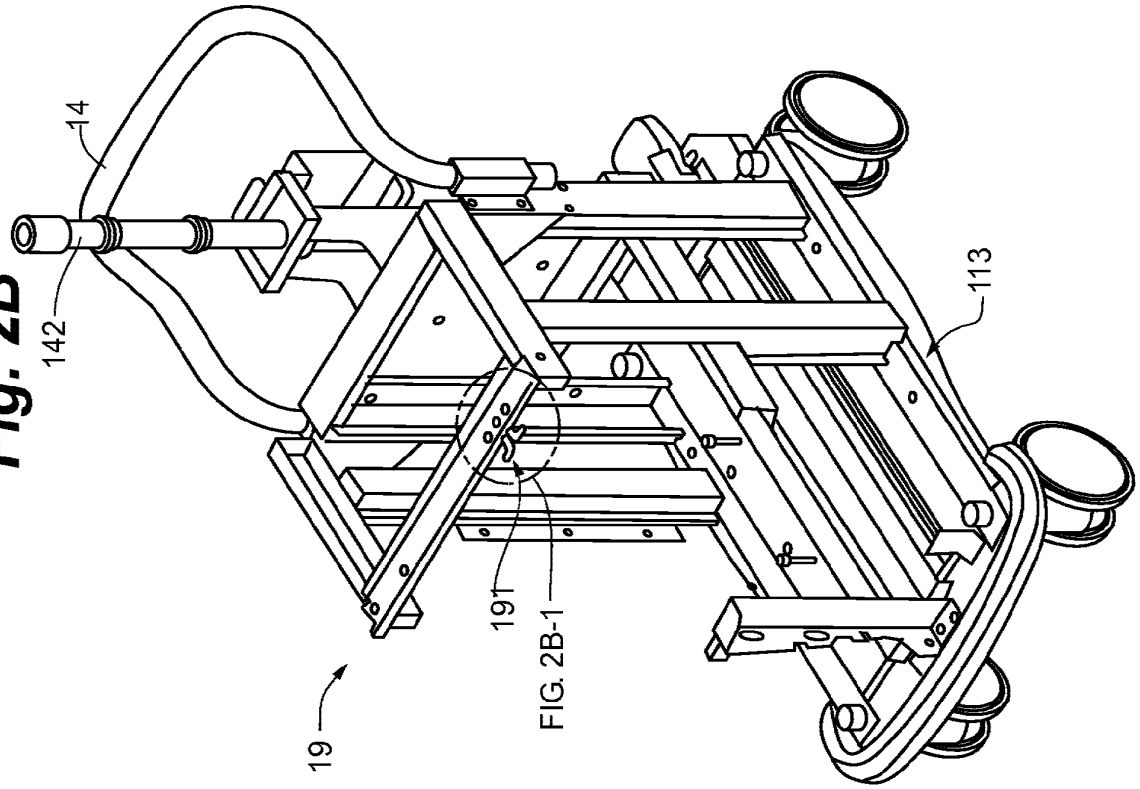


Fig. 3A

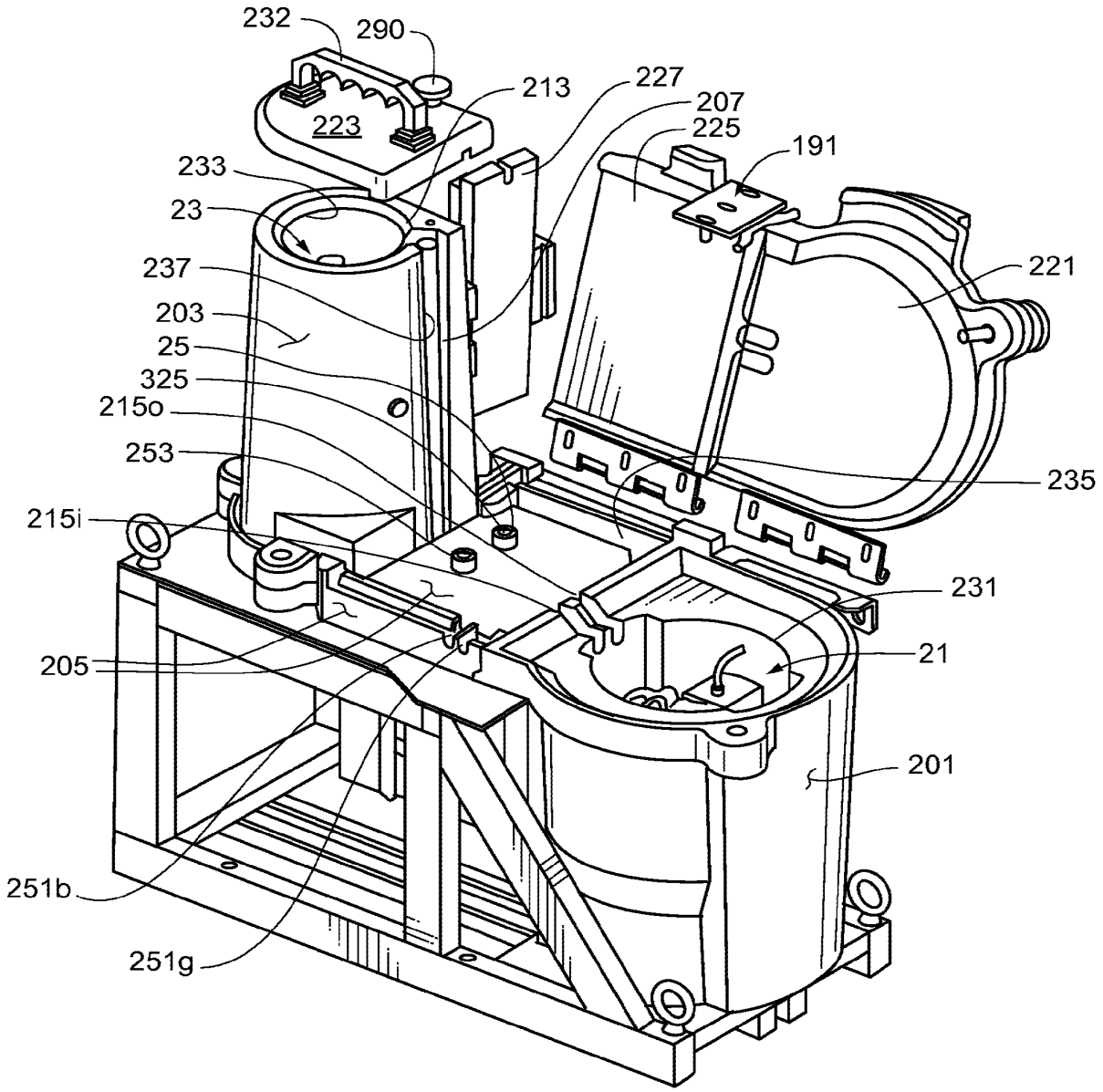
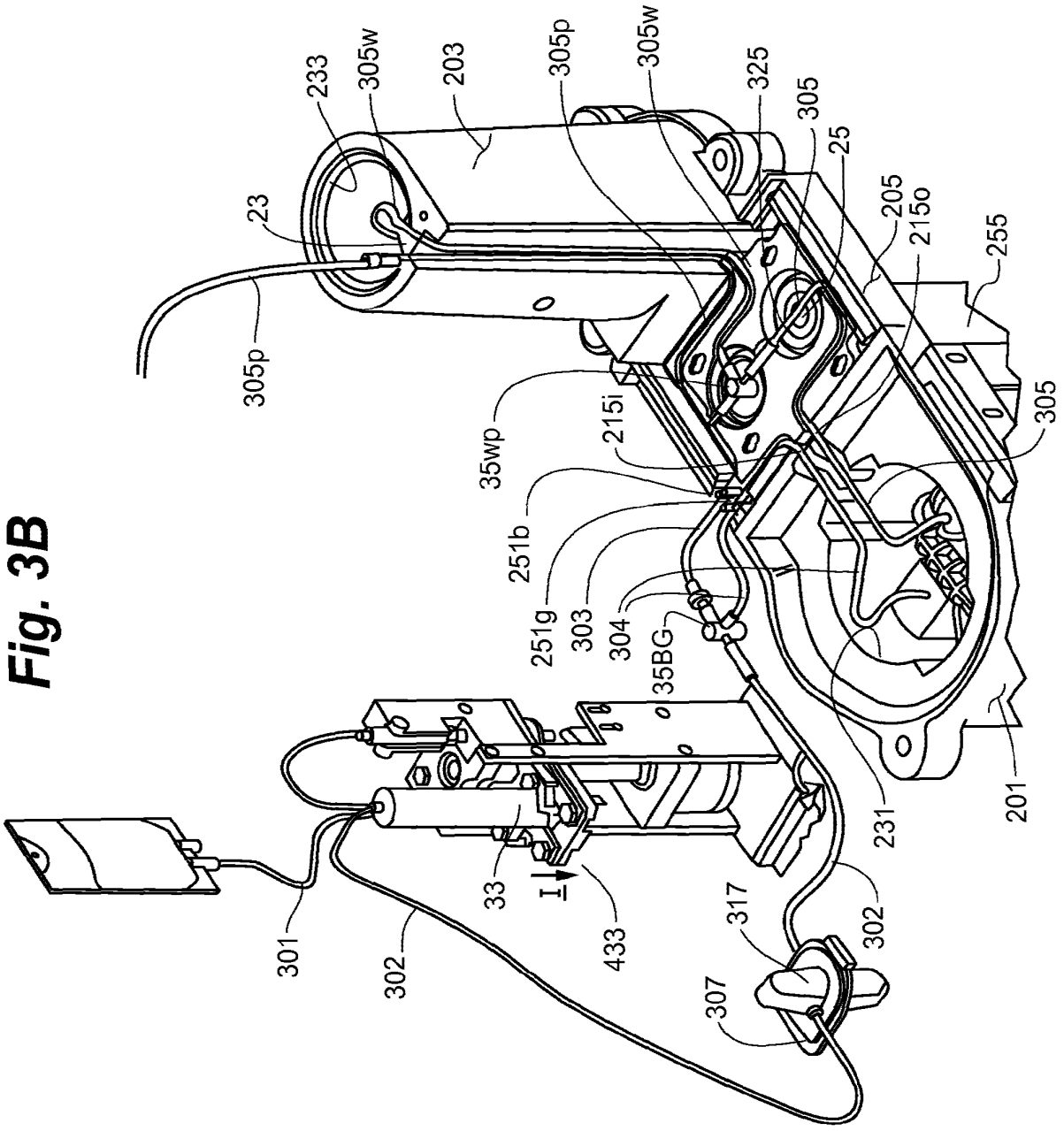

232
290
213
227
207
225
191
223
233
23
237
221
203
25
325
215o
253
235
215i
231
205
21
201
251b
251g

Fig. 3B


233
305w
203
305p
305w
325
305
25
205
215o
255
23
305p
35wp
215i
305
251b
251g
303
304
35BG
231
201
33
I
433
317
302
307
301
302

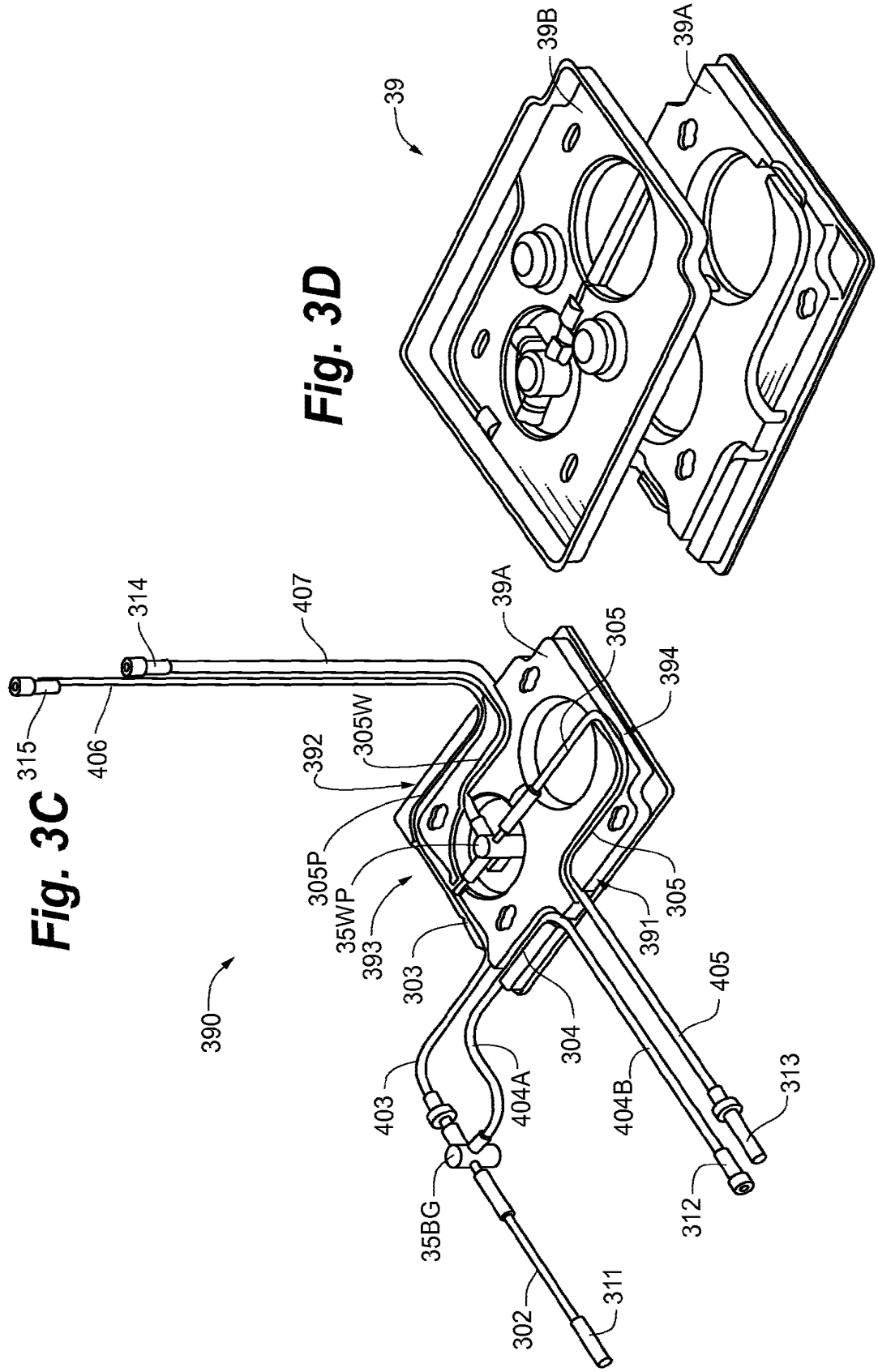

39
39B
39A
Fig. 3D
314
407
39A
305
394
315
406
392
305W
305P
35WP
393
303
390
Fig. 3C
403
404A
304
405
404B
313
312
35BG
302
311

Fig. 4

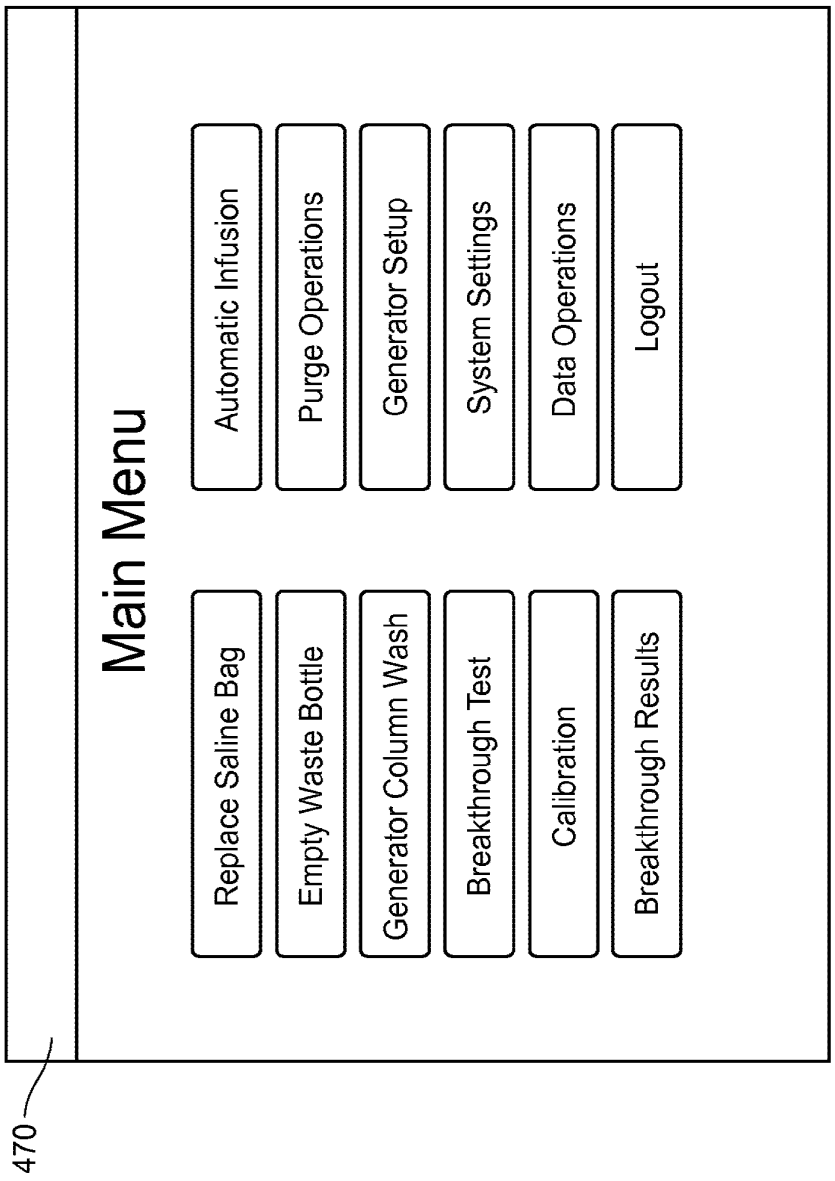

Main Menu
Automatic Infusion
Purge Operations
Generator Setup
System Settings
Data Operations
Logout
Replace Saline Bag
Empty Waste Bottle
Generator Column Wash
Breakthrough Test
Calibration
Breakthrough Results
470

Fig. 5A

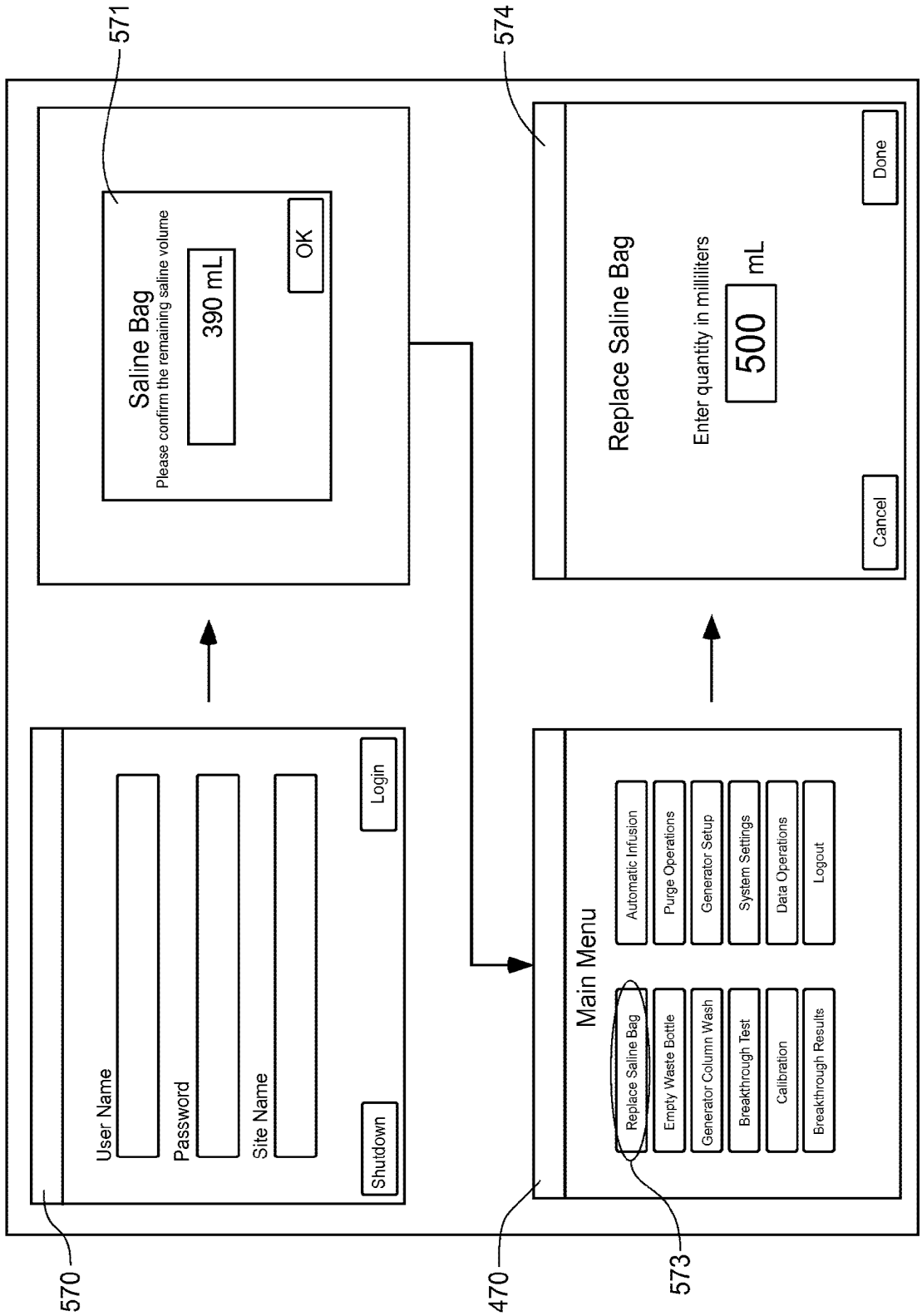
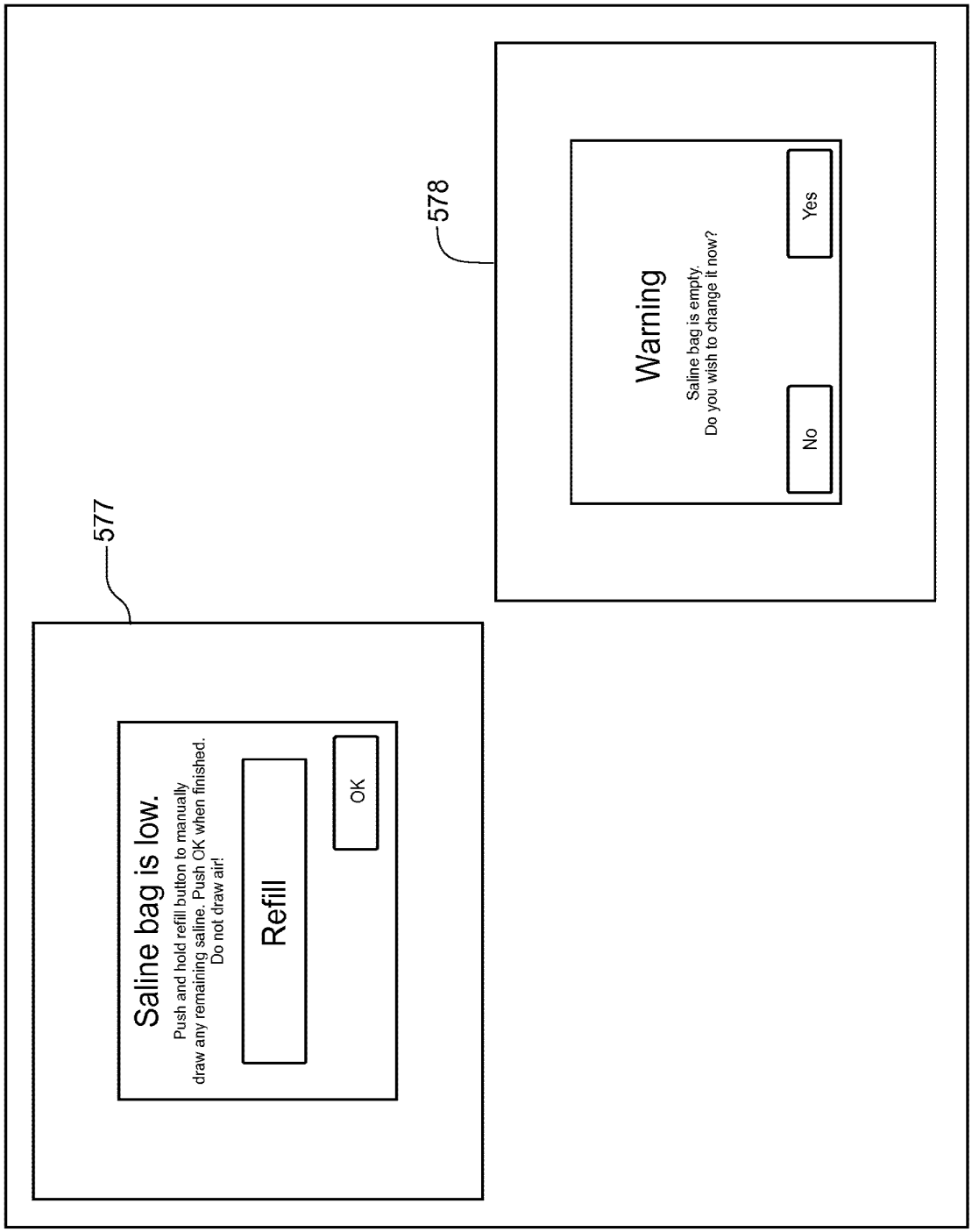

571
574
Saline Bag
Please confirm the remaining saline volume
390 mL
OK
Replace Saline Bag
Enter quantity in milliliters
500 mL
Done
Cancel
User Name
Password
Site Name
Login
Shutdown
Main Menu
Automatic Infusion
Purge Operations
Generator Setup
System Settings
Data Operations
Logout
Replace Saline Bag
Empty Waste Bottle
Generator Column Wash
Breakthrough Test
Calibration
Breakthrough Results
570
470
573

Fig. 5B


577
Saline bag is low.
Push and hold refill button to manually draw any remaining saline. Push OK when finished. Do not draw air!
Refill
OK
578
Warning
Saline bag is empty. Do you wish to change it now?
No
Yes

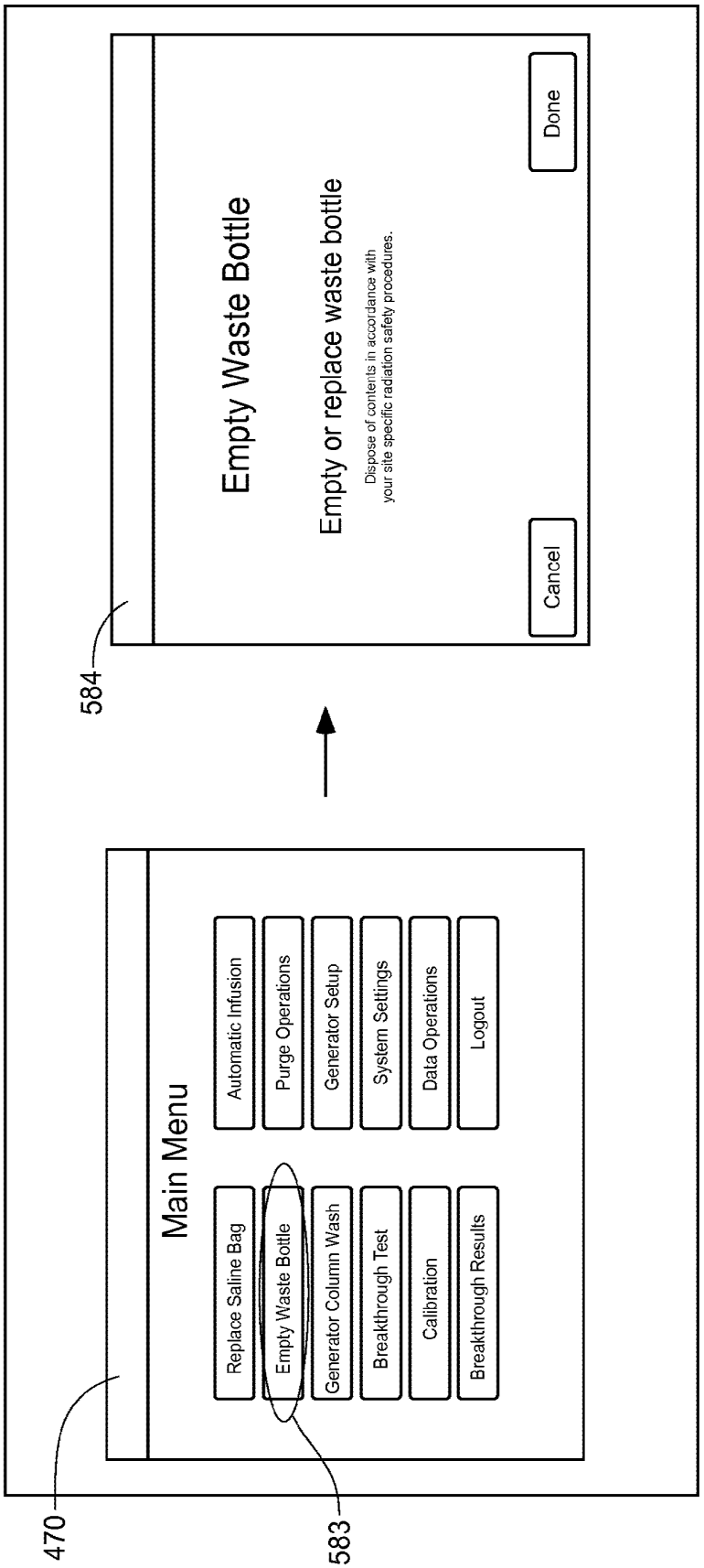

Main Menu
Replace Saline Bag
Empty Waste Bottle
Generator Column Wash
Breakthrough Test
Calibration
Breakthrough Results
Automatic Infusion
Purge Operations
Generator Setup
System Settings
Data Operations
Logout
470
583
584
Empty Waste Bottle
Empty or replace waste bottle
Dispose of contents in accordance with your site specific radiation safety procedures.
Cancel
Done

Fig. 5C

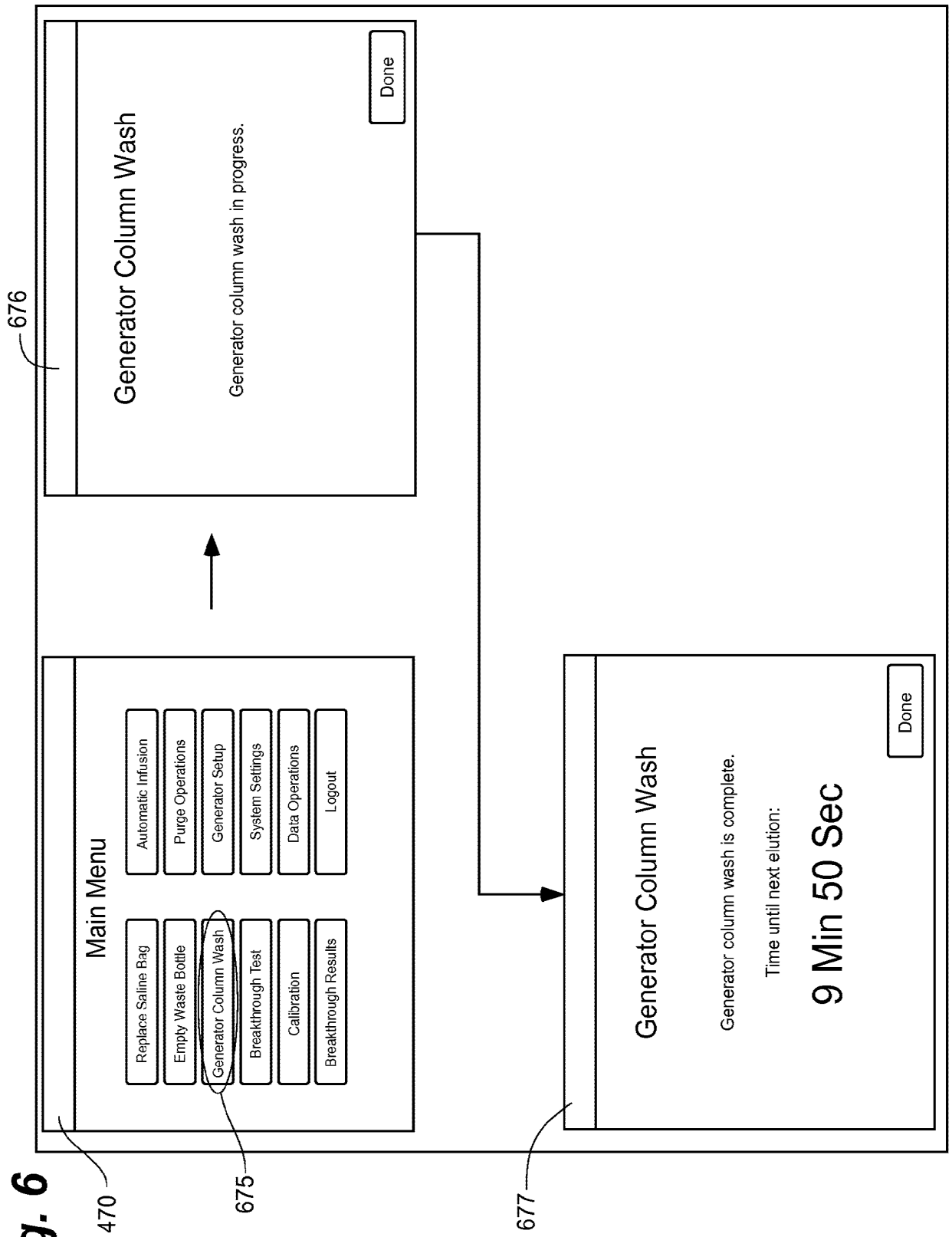

Generator Column Wash
Generator column wash in progress.
Done
676
Main Menu
Automatic Infusion
Purge Operations
Generator Setup
System Settings
Data Operations
Logout
Replace Saline Bag
Empty Waste Bottle
Generator Column Wash
Breakthrough Test
Calibration
Breakthrough Results
470
675
Generator Column Wash
Generator column wash is complete.
Time until next elution:
9 Min 50 Sec
Done
677

Fig. 6

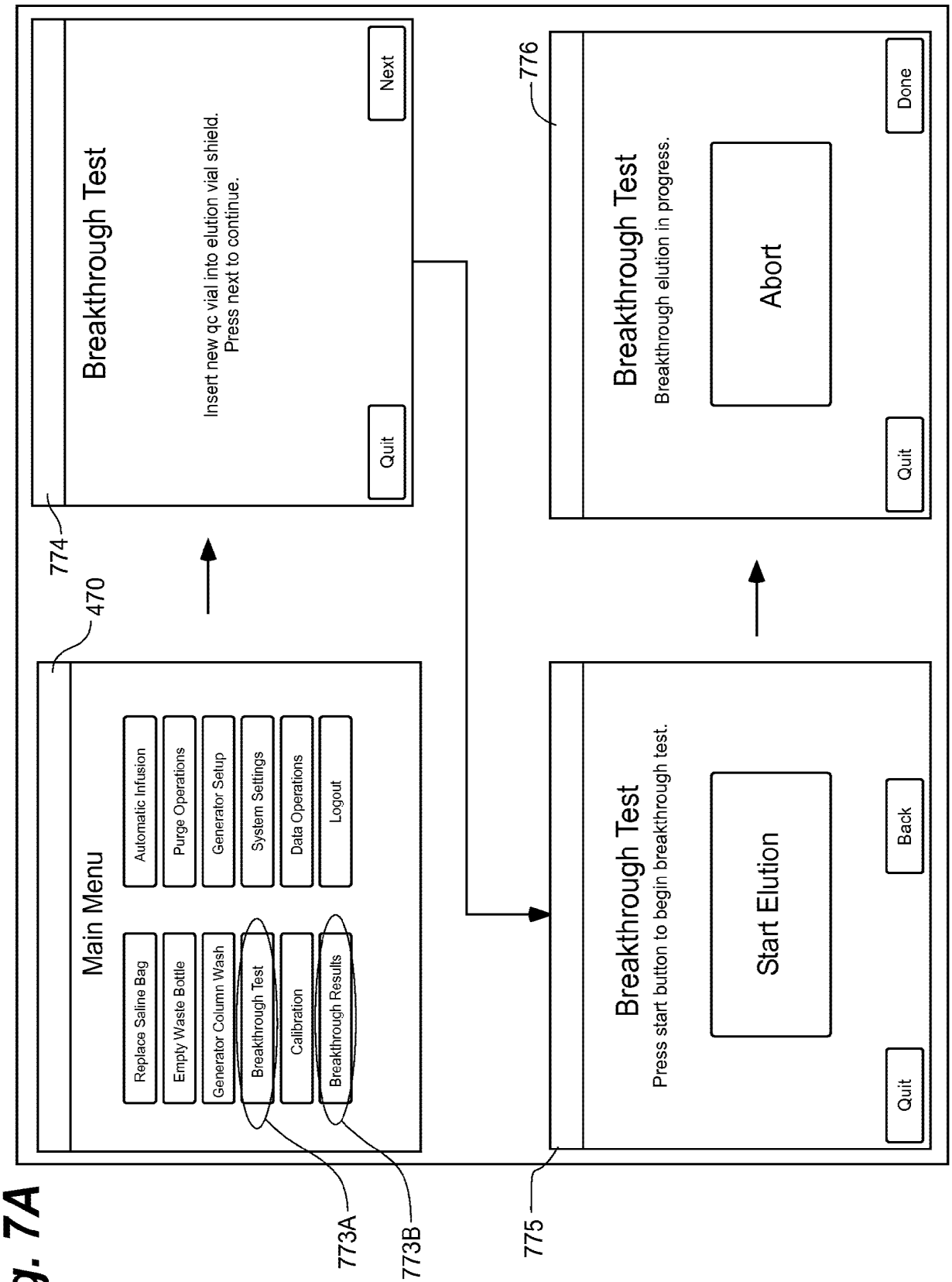

Breakthrough Test
Insert new qc vial into elution vial shield.
Press next to continue.
Next
Quit
774
776
Breakthrough Test
Breakthrough elution in progress.
Abort
Done
Quit
470
Main Menu
Automatic Infusion
Purge Operations
Generator Setup
System Settings
Data Operations
Logout
Replace Saline Bag
Empty Waste Bottle
Generator Column Wash
Breakthrough Test
Calibration
Breakthrough Results
773A
773B
775
Breakthrough Test
Press start button to begin breakthrough test.
Start Elution
Back
Quit

Fig. 7A

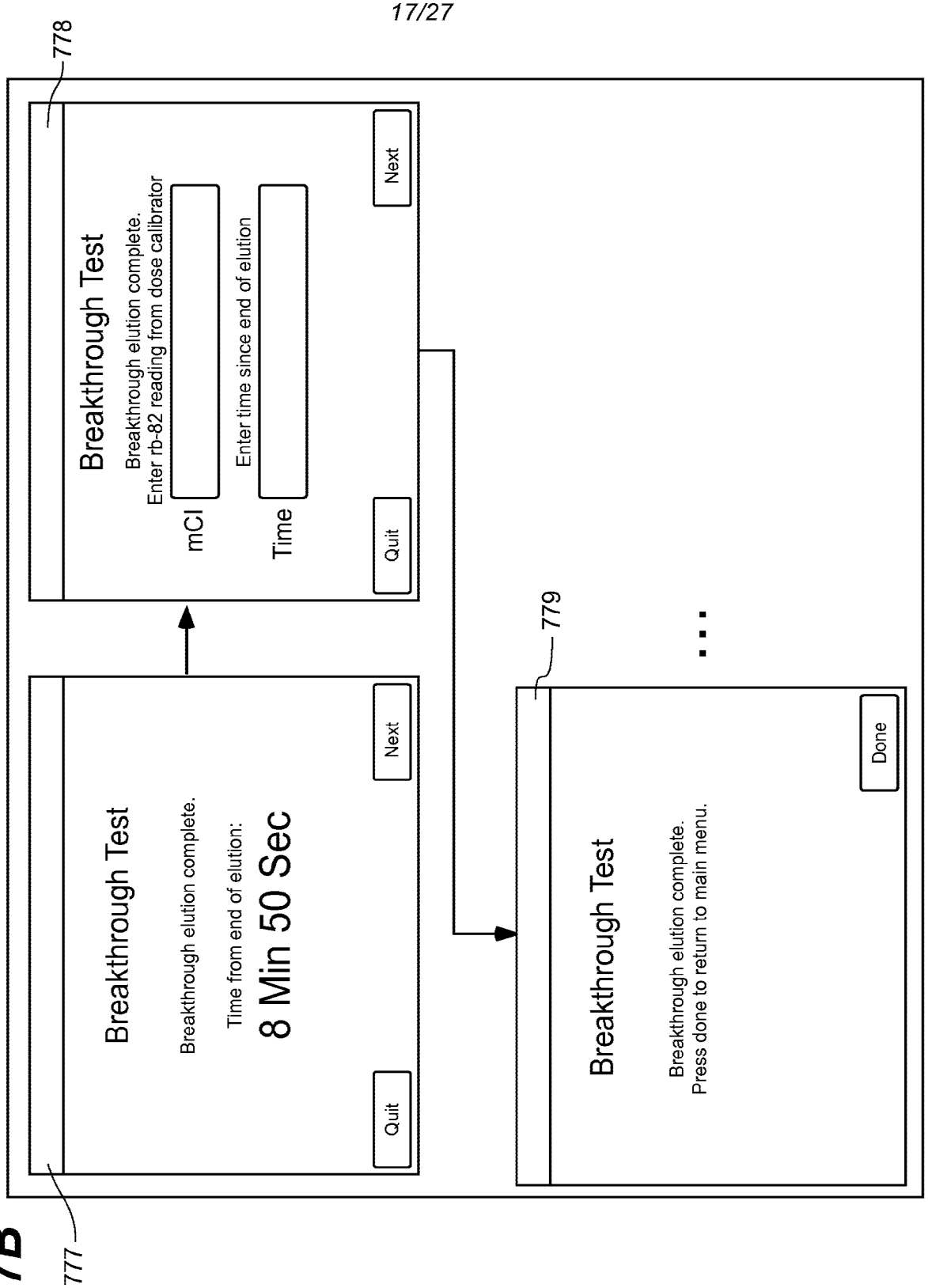

778
Breakthrough Test
Breakthrough elution complete.
Enter rb-82 reading from dose calibrator
mCi
Enter time since end of elution
Time
Next
Quit
777
Breakthrough Test
Breakthrough elution complete.
Time from end of elution:
8 Min 50 Sec
Next
Quit
779
Breakthrough Test
Breakthrough elution complete.
Press done to return to main menu.
Done

Fig. 7B

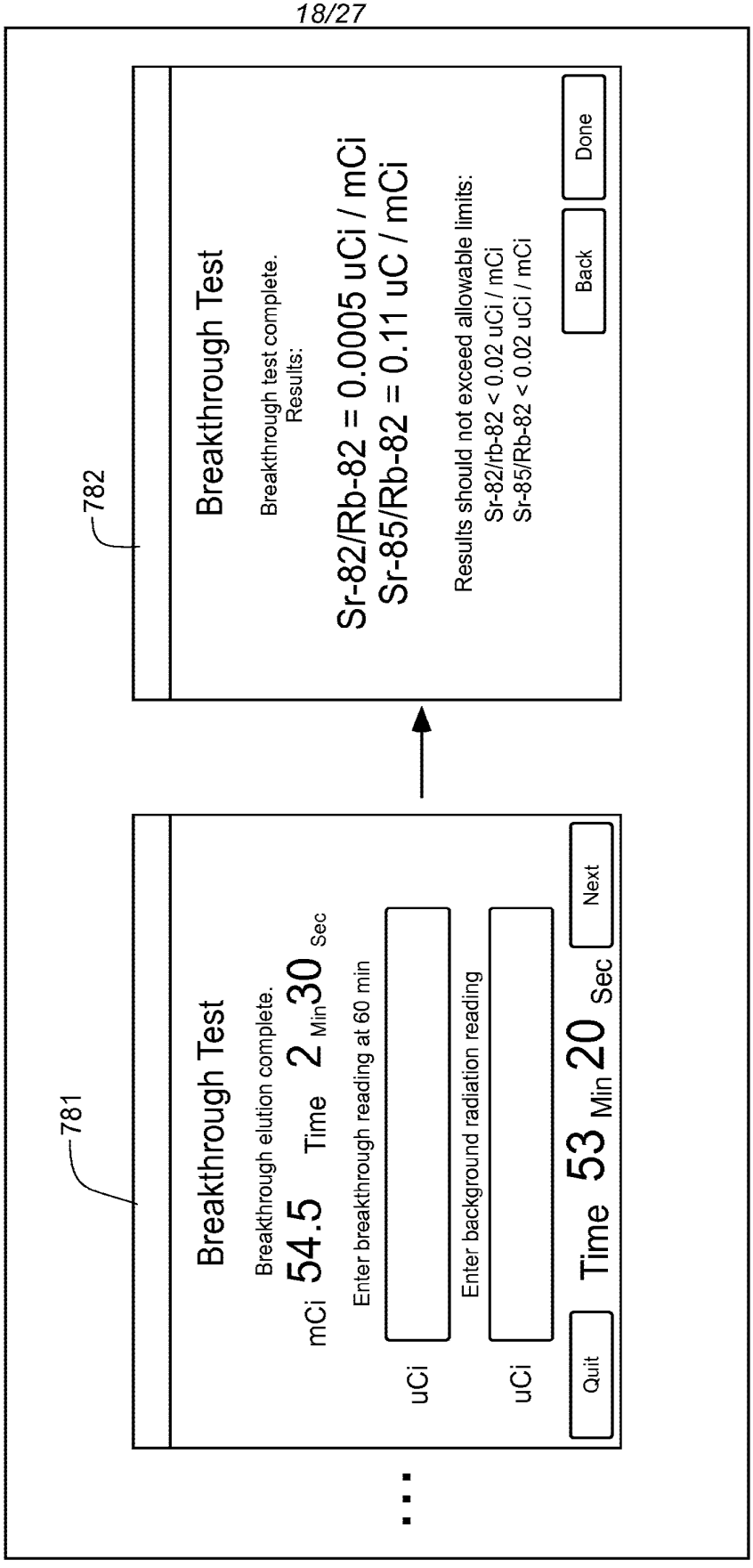

781
Breakthrough Test
Breakthrough elution complete.
mCi 54.5 Time 2 Min 30 Sec
Enter breakthrough reading at 60 min
uCi
Enter background radiation reading
uCi
Quit
Time 53 Min 20 Sec
Next
782
Breakthrough Test
Breakthrough test complete.
Results:
Sr-82/Rb-82 = 0.0005 uCi / mCi
Sr-85/Rb-82 = 0.11 uC / mCi
Results should not exceed allowable limits:
Sr-82/rb-82 < 0.02 uCi / mCi
Sr-85/Rb-82 < 0.02 uCi / mCi
Back
Done

Fig. 7C

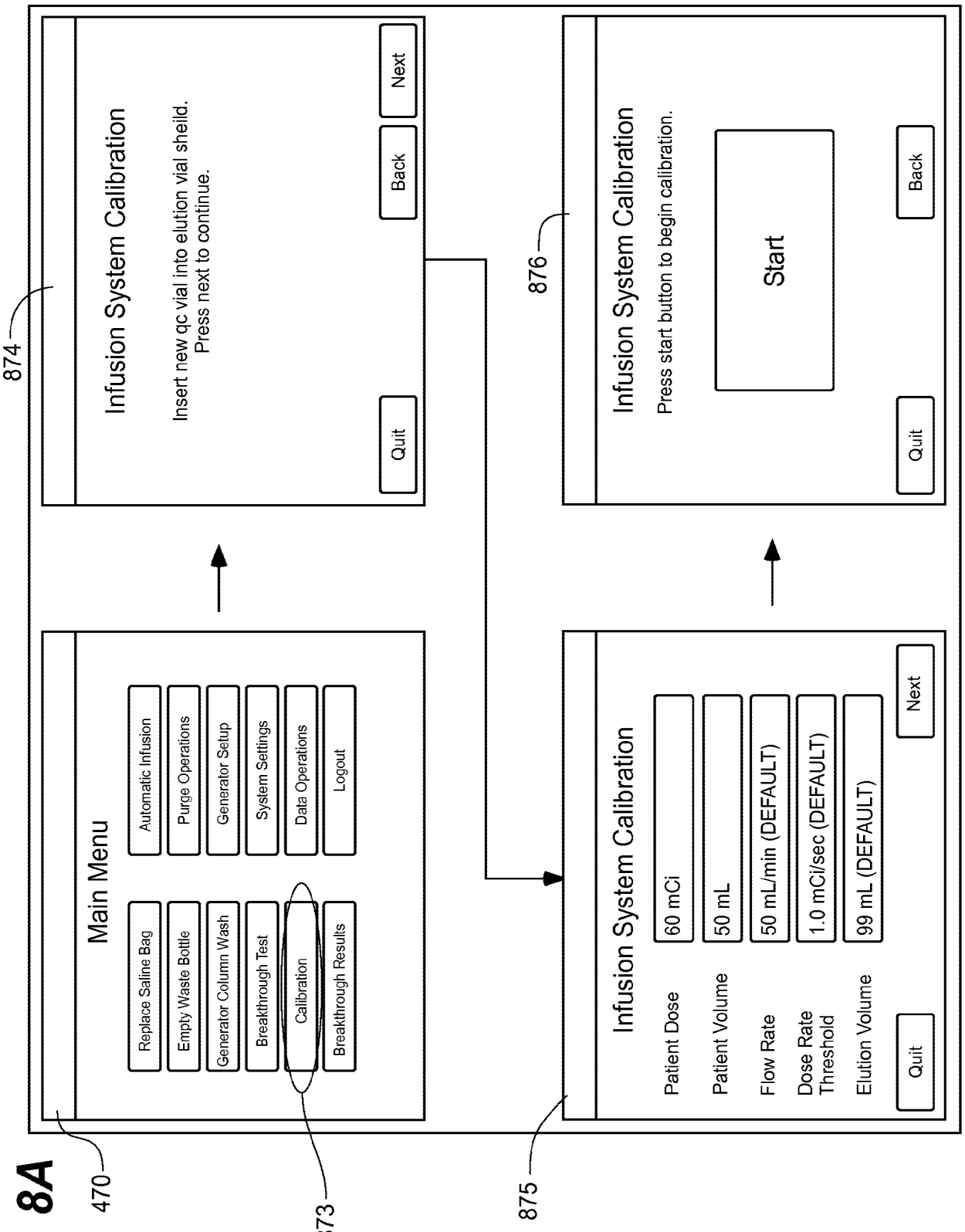

Main Menu
Automatic Infusion
Purge Operations
Generator Setup
System Settings
Data Operations
Logout
Replace Saline Bag
Empty Waste Bottle
Generator Column Wash
Breakthrough Test
Calibration
Breakthrough Results
470
873
Infusion System Calibration
Insert new qc vial into elution vial sheild.
Press next to continue.
Quit
Back
Next
874
Infusion System Calibration
Patient Dose
60 mCi
Patient Volume
50 mL
Flow Rate
50 mL/min (DEFAULT)
Dose Rate Threshold
1.0 mCi/sec (DEFAULT)
Elution Volume
99 mL (DEFAULT)
Quit
Next
875
Infusion System Calibration
Press start button to begin calibration.
Start
Quit
Back
876

Fig. 8A

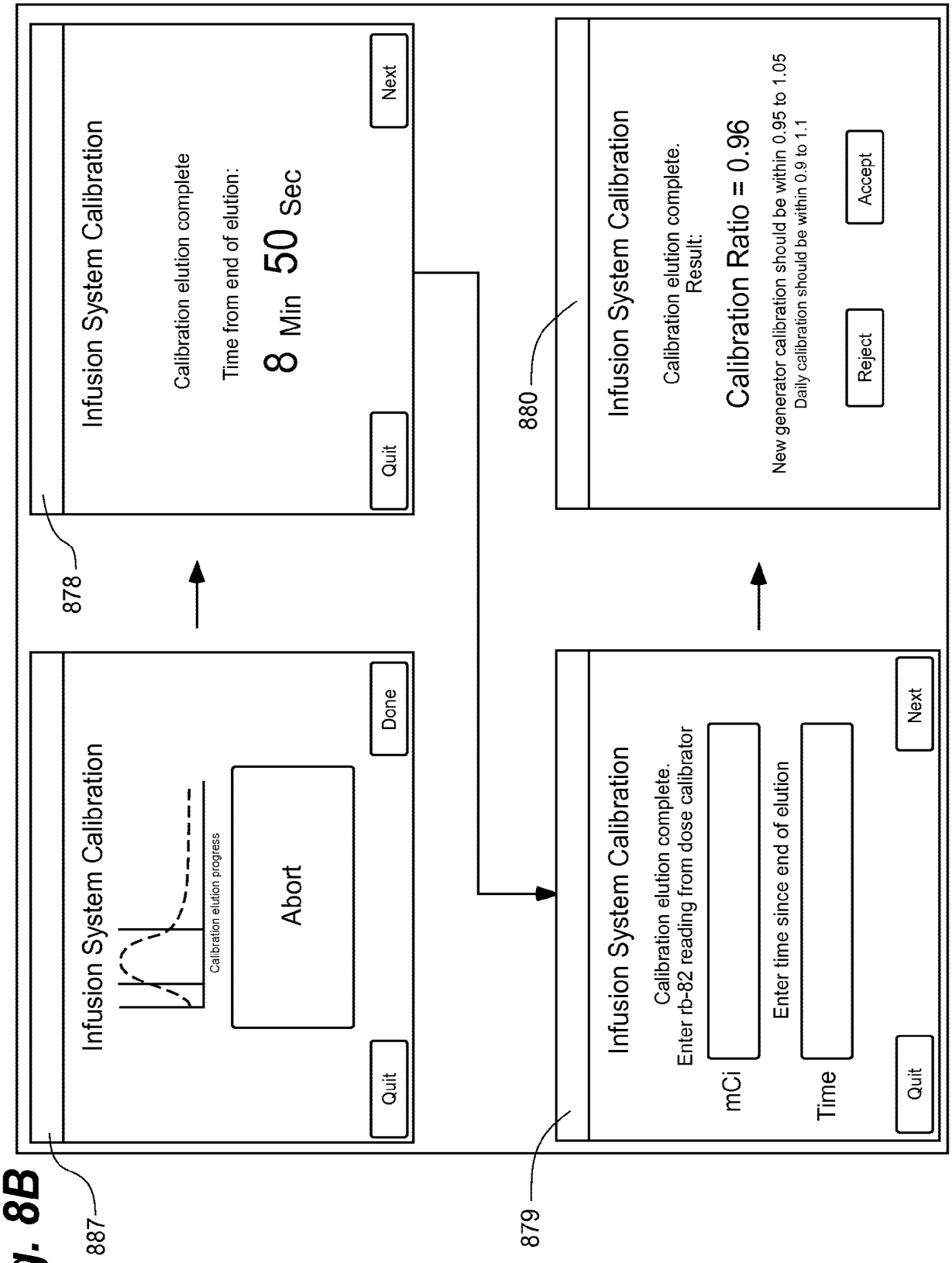

Infusion System Calibration
Calibration elution complete
Time from end of elution:
8 Min 50 Sec
Next
Quit
878
Infusion System Calibration
Calibration elution complete.
Result:
Calibration Ratio = 0.96
New generator calibration should be within 0.95 to 1.05
Daily calibration should be within 0.9 to 1.1
Reject
Accept
880
Infusion System Calibration
Calibration elution progress
Abort
Done
Quit
887
Infusion System Calibration
Calibration elution complete.
Enter rb-82 reading from dose calibrator
mCi
Enter time since end of elution
Time
Next
Quit
879

Fig. 8B

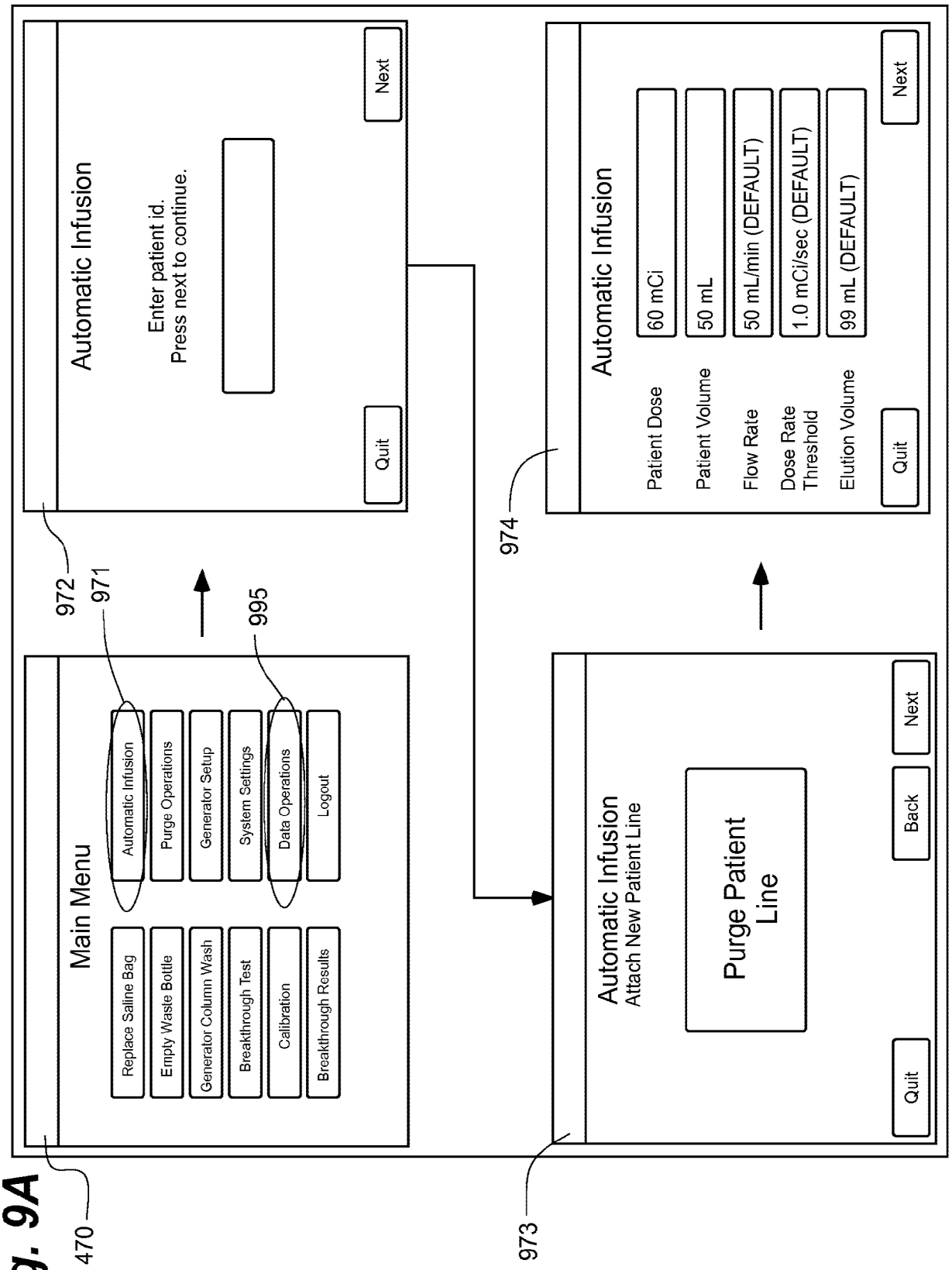

Main Menu
Automatic Infusion
Purge Operations
Generator Setup
System Settings
Data Operations
Logout
Replace Saline Bag
Empty Waste Bottle
Generator Column Wash
Breakthrough Test
Calibration
Breakthrough Results
Automatic Infusion
Enter patient id.
Press next to continue.
Quit
Next
Automatic Infusion
Attach New Patient Line
Purge Patient Line
Quit
Back
Next
Automatic Infusion
Patient Dose
60 mCi
Patient Volume
50 mL
Flow Rate
50 mL/min (DEFAULT)
Dose Rate Threshold
1.0 mCi/sec (DEFAULT)
Elution Volume
99 mL (DEFAULT)
Quit
Next
470
971
972
973
974
995

Fig. 9A

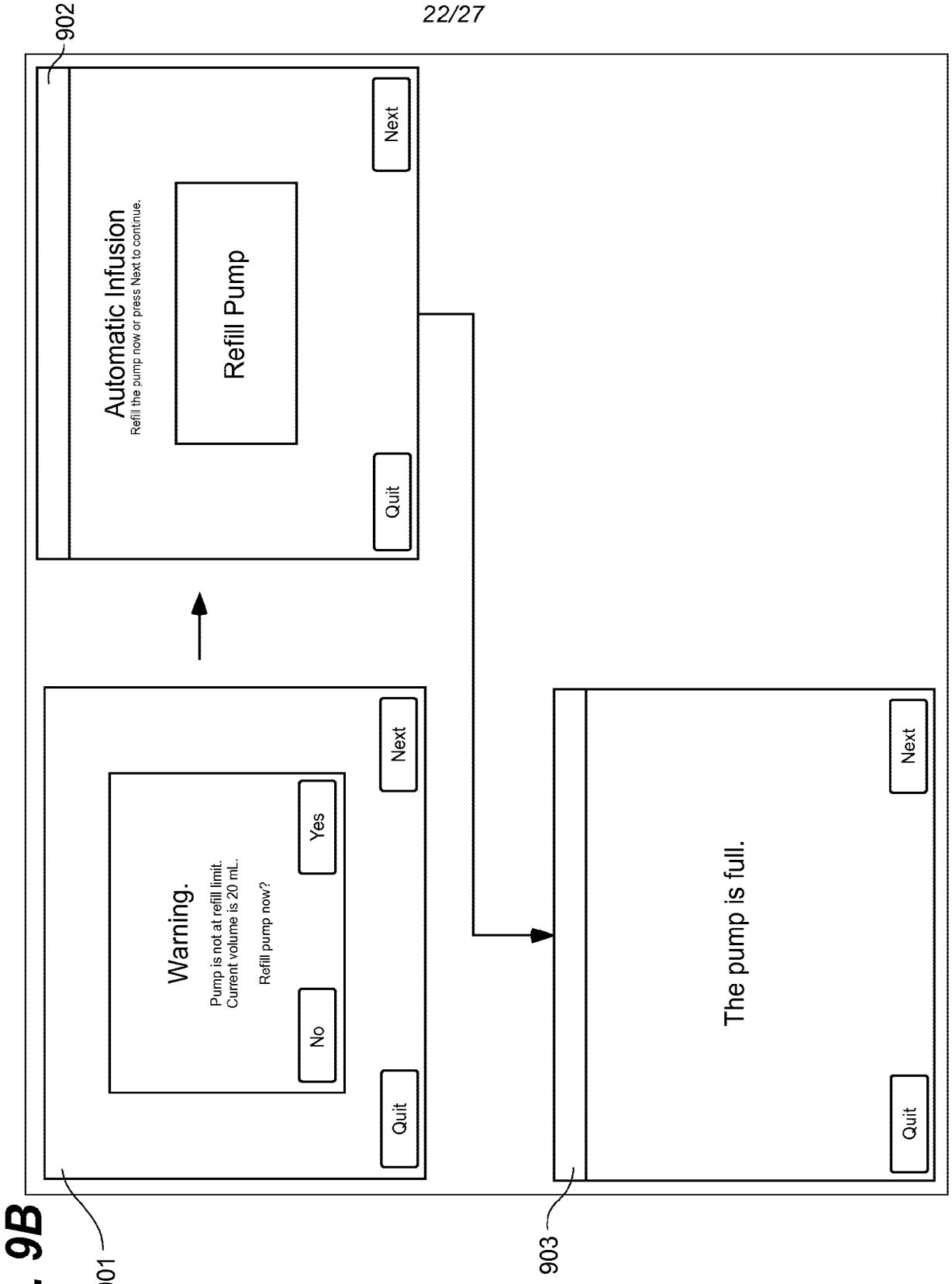

902
Automatic Infusion
Refill the pump now or press Next to continue.
Refill Pump
Next
Quit
Warning.
Pump is not at refill limit.
Current volume is 20 mL.
Refill pump now?
Yes
No
Next
Quit
The pump is full.
Next
Quit
901
903

Fig. 9B

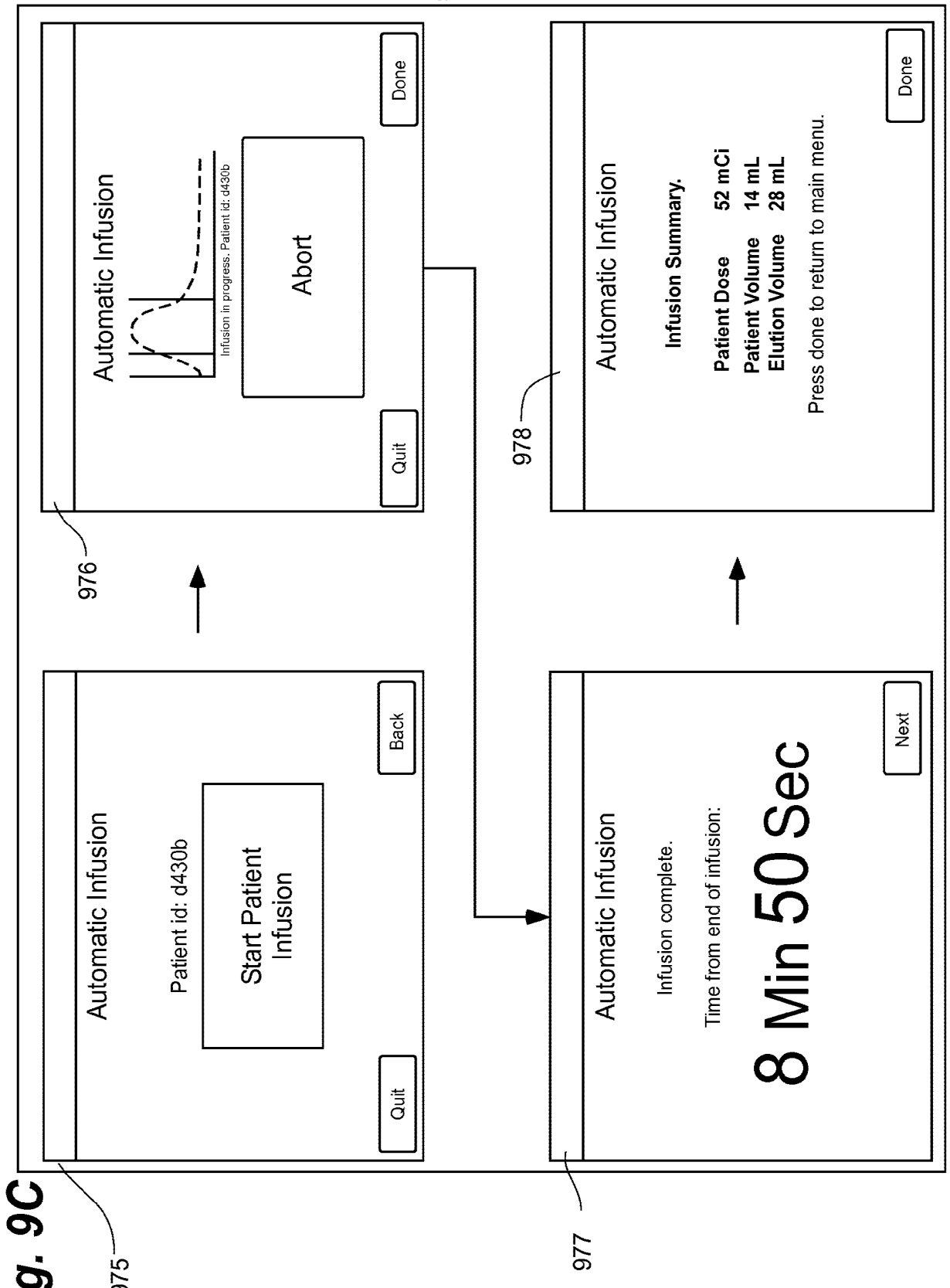

Automatic Infusion
Patient id: d430b
Start Patient Infusion
Back
Quit
975
Automatic Infusion
Infusion in progress. Patient id: d430b
Abort
Done
Quit
976
Automatic Infusion
Infusion complete.
Time from end of infusion:
8 Min 50 Sec
Next
977
Automatic Infusion
Infusion Summary.
Patient Dose 52 mCi
Patient Volume 14 mL
Elution Volume 28 mL
Press done to return to main menu.
Done
978

Fig. 9C

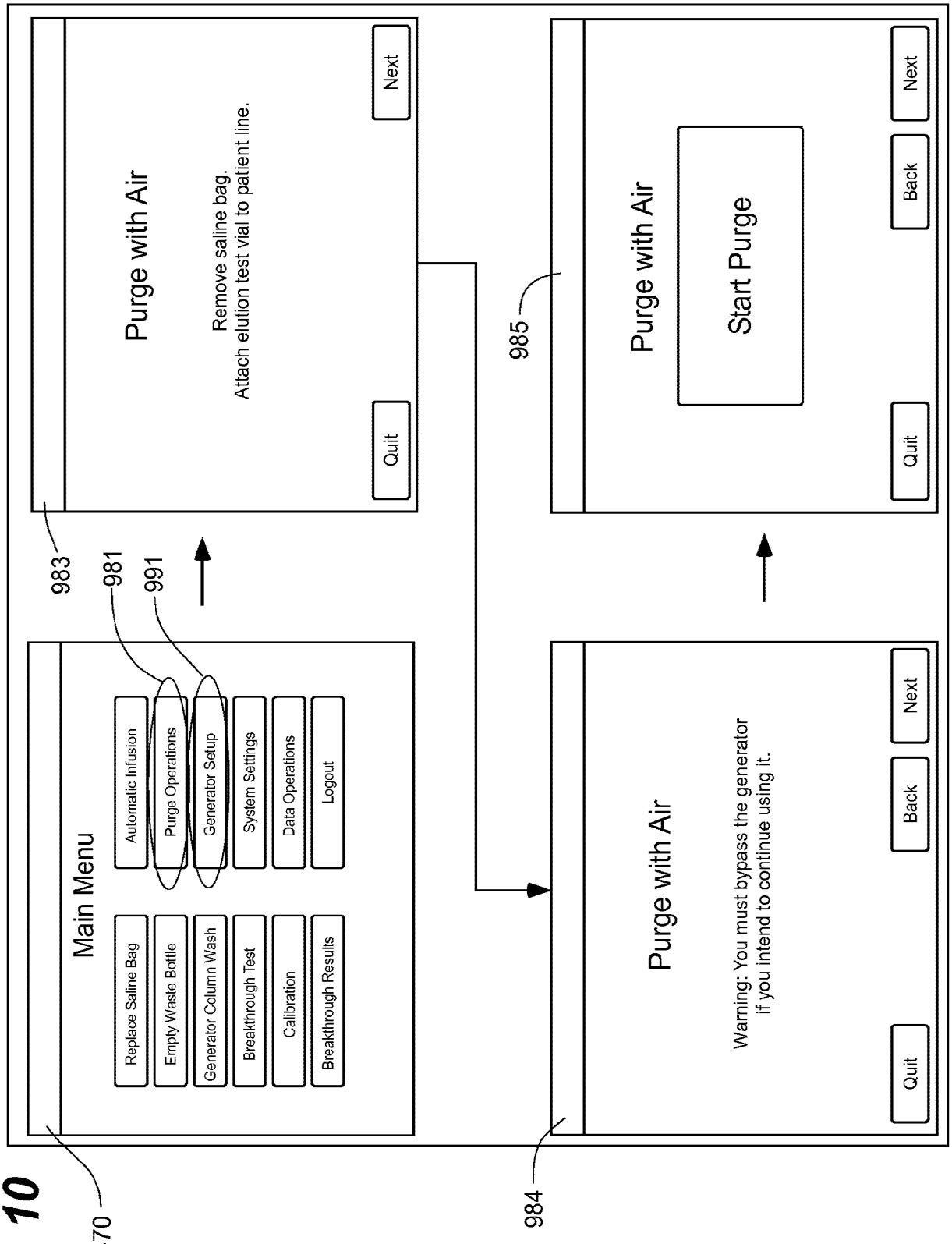
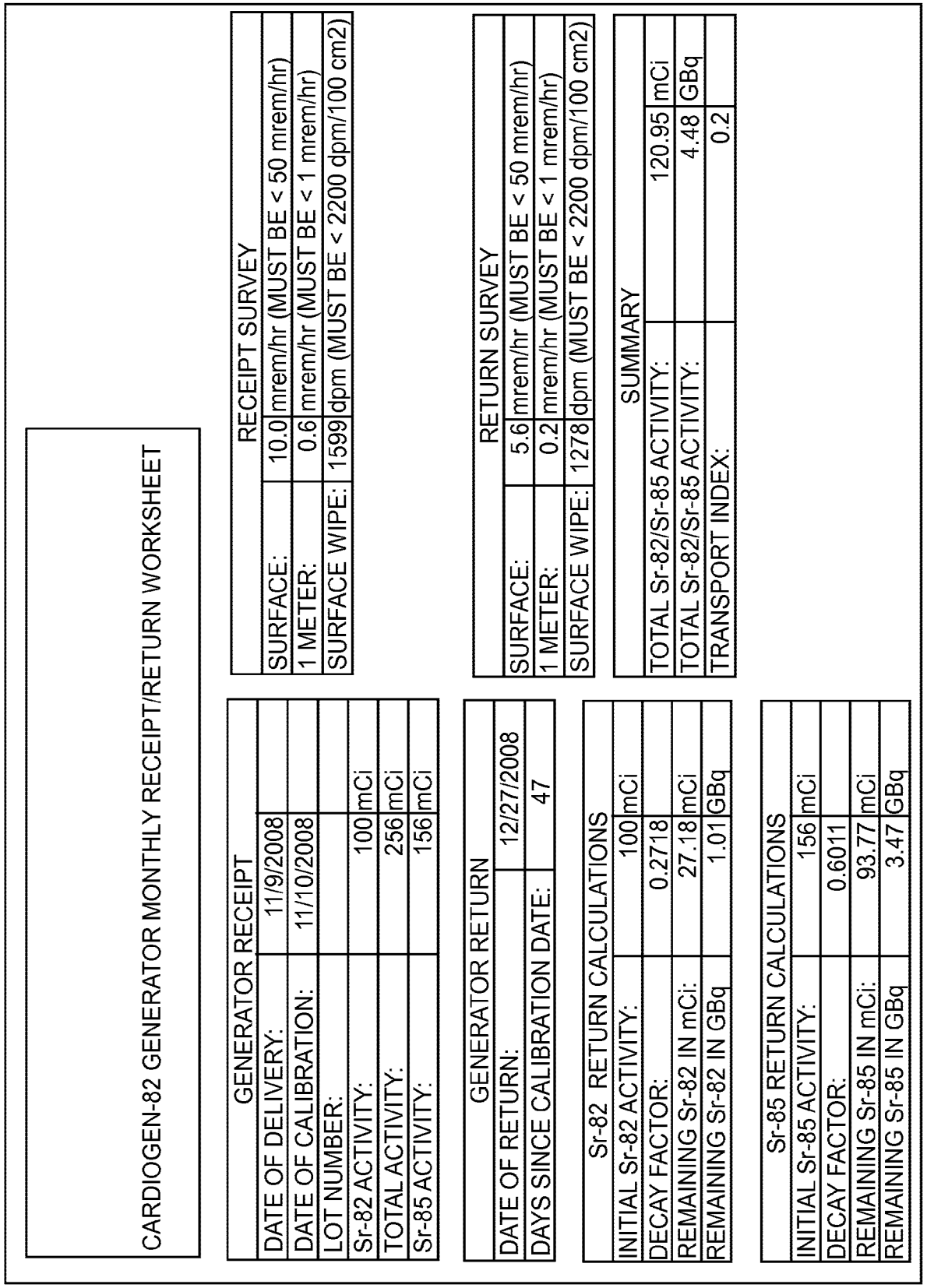

Main Menu
Automatic Infusion
Purge Operations
Generator Setup
System Settings
Data Operations
Logout
Replace Saline Bag
Empty Waste Bottle
Generator Column Wash
Breakthrough Test
Calibration
Breakthrough Results
Purge with Air
Remove saline bag.
Attach elution test vial to patient line.
Next
Quit
Purge with Air
Warning: You must bypass the generator if you intend to continue using it.
Quit
Back
Next
Purge with Air
Start Purge
Quit
Back
Next
470
981
983
984
985
991

Fig. 10

Fig. 11



CARDIOGEN-82 GENERATOR MONTHLY RECEIPT/RETURN WORKSHEET

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

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

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

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

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

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

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

Fig. 12A

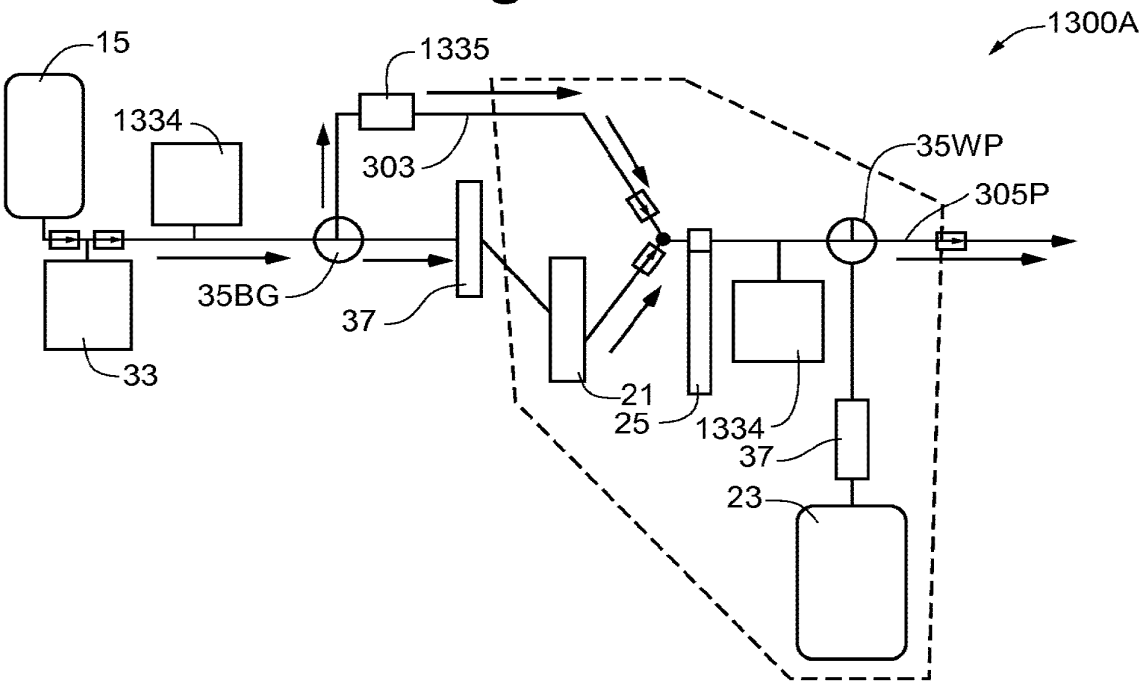


Fig. 12B

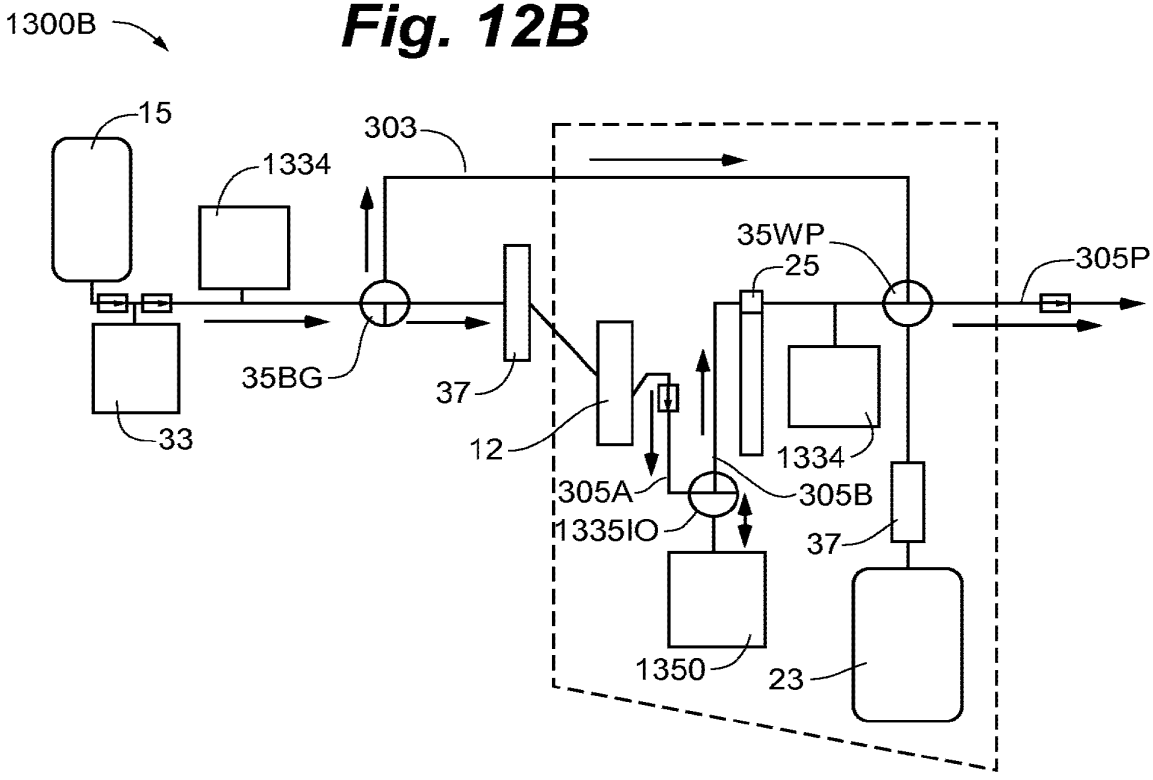
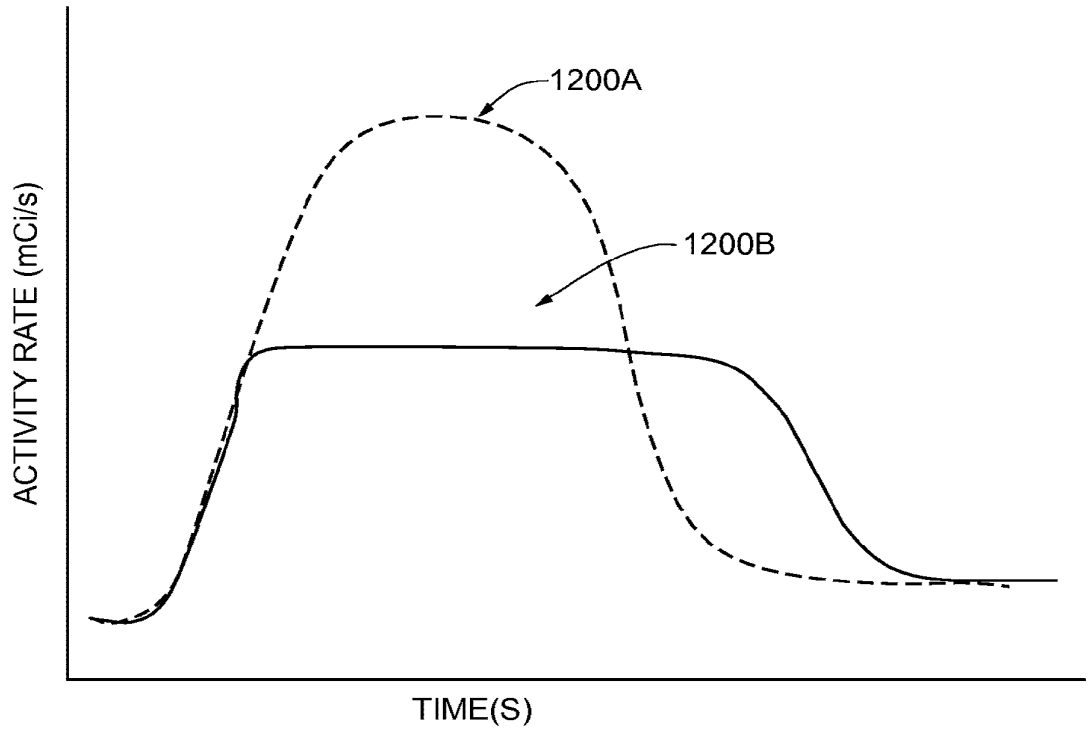


Fig. 12C



PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference	**FOR FURTHER ACTION**	see Form PCT/ISA/220 as well as, where applicable, item 5 below.
56782.1.9.1		
International application No.	International filing date *(day/month/year)*	(Earliest) Priority Date *(day/month/year)*
PCT/US2009/063788	10/11/2009	19/11/2008
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. [ ] **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. 1
      [X] as suggested by the applicant
      [ ] 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) (July 2009)

International application No
PCT/US2009/063788

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61M5/165 A61M5/14 A61M5/38
ADD. A61M5/00 A61M39/28

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

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 3 483 867 A (MARKOVITZ MEYER) 16 December 1969 (1969-12-16) figures 1-4 column 2, line 60 - column 7, line 9	1-10, 15-20
X	US 4 994 056 A (IKEDA DANIEL P [US]) 19 February 1991 (1991-02-19) figures 1-8 column 3, line 51 - column 5, line 68	1-10
X	US 4 466 888 A (VERKAART WESLEY H [US]) 21 August 1984 (1984-08-21) figures 1-16 column 3, line 48 - column 8, line 57	1-10

-/--

[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
24 March 2010	01/04/2010

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/US2009/063788

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 0 919 249 A1 (NISSHO KK [JP] NIPRO CORP [JP]) 2 June 1999 (1999-06-02) figures 1-11 paragraph [0021] - paragraph [0058] paragraph [0033]	1-10
A	EP 1 421 960 A1 (GVS S P A [IT]) 26 May 2004 (2004-05-26) figures 1-16 paragraph [0009] - paragraph [0030]	1-10, 15-20
E	WO 2009/152320 A2 (BRACCO DIAGNOSTICS INC [US]; QUIRICO CHARLES R [US]; BALESTRACCI ERNES) 17 December 2009 (2009-12-17) figure 3b page 19, line 10 - line 15	1-10, 15-20

3

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box II.1

Claims Nos.: 11-14

Claims 11 to 14 relate to a method for assembling a membrane filter. Said method is carried out within the human body because connecting a line to the fluid outlet filter is a connection with a catheter which is introduced to the patient. Consequently, the method defined in claims 11 to 14 is considered as a method for the treatment of the human body by surgery and therapy. The application does not meet the requirement of Rule 39.1)iv), because these claims are methods of treatment of the human body.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2009/063788

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.: 11-14
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:

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.

Patent document cited in search report		Publication date	Patent family member(s)		Publication date
US 3483867	A	16-12-1969	NONE		
US 4994056	A	19-02-1991	WO	9107205 A1	30-05-1991
US 4466888	A	21-08-1984	AT	16350 T	15-11-1985
			AU	7087681 A	26-11-1981
			DE	3172813 D1	12-12-1985
			DK	219881 A	21-11-1981
			EP	0040427 A1	25-11-1981
			ES	8300479 A1	01-02-1983
			JP	57049457 A	23-03-1982
EP 0919249	A1	02-06-1999	DE	69828571 D1	17-02-2005
			DE	69828571 T2	02-06-2005
			US	6129853 A	10-10-2000
EP 1421960	A1	26-05-2004	US	2004104160 A1	03-06-2004
WO 2009152320	A2	17-12-2009	WO	2009152322 A2	17-12-2009
			WO	2009152323 A2	17-12-2009
			WO	2009152326 A2	17-12-2009

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/US2009/063788	10.11.2009	19.11.2008

International Patent Classification (IPC) or both national classification and IPC
INV. A61M5/165 A61M5/14 A61M5/38
ADD. A61M5/00 A61M39/28

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. 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. 11-14

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. 11-14

☐ 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. 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	16-17, 20
	No:	Claims	1-10, 15, 18-19
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-10, 15-20
Industrial applicability (IA)	Yes:	Claims	1-10, 15-20
	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

Claims 11 to 14 relate to a method for assembling a membrane filter. Said method is carried out within the human body because connecting a line to the fluid outlet filter is a connection with a catheter which is introduced to the patient.

Consequently, the method defined in claims 11 to 14 is considered as a method for the treatment of the human body by surgery and therapy. The application does not meet the requirement of Rule 39.1)iv), because these claims are methods of treatment of the human body.

Thus, the subject-matter of these claims has not been searched and consequently no examination was carried out for those claims (Rule 66.1 (e) 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 US 3 483 867 A

D2 US 4 994 056 A

D3 US 4 466 888 A

D4 EP 0 919 249 A1

D5 EP 1 421 960 A1

D6 WO 2009/152320 A2

Novelty Article 33(2) PCT

2 The present application does not meet the criteria of Article 33 (1) PCT, because the subject-matter of **claims 1-10 and 15,18 and 19** does not seem to be 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) a removable clamp (10) for supporting a housing (52) of a membrane filter, the housing including a first major surface, a second major surface, opposite the first major surface, and a thickness, the thickness being defined from the first major surface to the second major surface, at a location around a common perimeter of the surfaces, and being less than a length and a width of each surface, the length

of each surface extending between a fluid inlet (60) and a fluid outlet (62) of the filter, the width of each surface extending approximately orthogonal to the length, and the clamp comprising:

a first support wall (14) including a first end and a second end, opposite the first end;

a second support wall (12), opposite the first support wall, including a first, terminal end and a second end, opposite the first, terminal end, the second end of the second support wall being fixedly and flexibly connected to the first end of the first support wall to allow the first, terminal end of the second support wall to move toward and away from the first support wall; and

a locking feature (18) connected to the second end of the first support wall and being configured to engage and disengage the first, terminal end of the second support wall (12);

wherein the first support wall has a width (see figure 4), defined from the first end thereof to the second end thereof, and the width of the first support wall spans the width of the housing of the filter, when the clamp is assembled about the housing;

the first support wall, in proximity to the first end thereof, is spaced apart from the second support wall, in proximity to the second end thereof, over a distance that spans the thickness of the housing when the clamp is assembled around the housing;

the clamp (10) supports the housing when the clamp is assembled around the housing and the locking feature engages the first, terminal end of the second support wall (figure 4);

and the clamp (10) is removable from around the housing when the locking feature disengages the first, terminal end of the second support wall.

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

2.2 Moreover the technical features of claims 2,6,7,15,18 and 19 are disclosed by the document D1. (infusion system (112)

2.3 Furthermore the technical features of claims 1 to 10 are shown by documents D2 to D4.

Document D2: figure 1 to 8, clamp (20), locking feature (46,48)

Document D3 : figure 1 to 16, clamp (20+22) having a first wall (20) and second wall (22), locking feature (39)

Document D4: figure 1 to 11, clamp (10) having a first wall (4) and second wall, locking feature (411)

Inventive Step Article 33(3) PCT

3 The present application does not meet the criteria of Article 33 (1) PCT, because the subject-matter of **claims 16,17 and 20** does not seem to involve an inventive step in the sense of Article 33 (3) PCT. Document D1 is the closest prior art.

The feature of claims 16,17 and 20 (cabinet) is 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. Consequently, the subject-matter of these claims also lacks an inventive step.

Further Comments

4 Contrary to the requirements of Rule 5.1(a)(ii) PCT, the **relevant background** art disclosed in the documents D1- D5 are not mentioned in the description, nor are these documents identified therein.

5 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).

6 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

7 Claim 1 does not meet the requirements of Article 6 PCT in that the matter for which protection is sought is not clearly defined. Claim 1 defines a removable clamp in combination with a housing of a membrane filter. However this housing of a membrane filter is not part of the subject matter of said claim 1. Therefore the definition of the subject - matter of said claim 1 is unclear, Article 6 PCT.

8 Furthermore, the removable clamp as defined in claim 1 is a definition of a normal clamp, which is already known from the skilled person in the art.

9 Claim 15 comprises all the features of claim 1 and is therefore not appropriately formulated as a claim dependent on the latter (Rule 6.4 PCT).

PTO/SB/30EFS (07-09)
Approved for use through 07/31/2012. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

REQUEST FOR CONTINUED EXAMINATION(RCE)TRANSMITTAL
(Submitted Only via EFS-Web)

Application Number	12137364	Filing Date	2008-06-11	Docket Number (if applicable)	56782.1.7	Art Unit	3763
First Named Inventor	Stephen E. Hidem			Examiner Name	Jenna Zhang		

This is a Request for Continued Examination (RCE) under 37 CFR 1.114 of the above-identified application.
Request for Continued Examination (RCE) practice under 37 CFR 1.114 does not apply to any utility or plant application filed prior to June 8, 1995, or to any design application. The Instruction Sheet for this form is located at WWW.USPTO.GOV

SUBMISSION REQUIRED UNDER 37 CFR 1.114

Note: If the RCE is proper, any previously filed unentered amendments and amendments enclosed with the RCE will be entered in the order in which they were filed unless applicant instructs otherwise. If applicant does not wish to have any previously filed unentered amendment(s) entered, applicant must request non-entry of such amendment(s).

☒ Previously submitted. If a final Office action is outstanding, any amendments filed after the final Office action may be considered as a submission even if this box is not checked.

- ☐ Consider the arguments in the Appeal Brief or Reply Brief previously filed on _____
- ☐ Other _____

☐ Enclosed

- ☐ Amendment/Reply
- ☐ Information Disclosure Statement (IDS)
- ☐ Affidavit(s)/ Declaration(s)
- ☐ Other _____

MISCELLANEOUS

☐ Suspension of action on the above-identified application is requested under 37 CFR 1.103(c) for a period of months _____
(Period of suspension shall not exceed 3 months; Fee under 37 CFR 1.17(i) required)

☐ Other _____

FEES

The RCE fee under 37 CFR 1.17(e) is required by 37 CFR 1.114 when the RCE is filed.
☒ The Director is hereby authorized to charge any underpayment of fees, or credit any overpayments, to Deposit Account No 061910

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT REQUIRED

☒ Patent Practitioner Signature
☐ Applicant Signature

PTO/SB/30EFS (07-09)
Approved for use through 07/31/2012. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Signature of Registered U.S. Patent Practitioner			
Signature	/Charles D. Segelbaum/	Date (YYYY-MM-DD)	2011-04-28
Name	Charles D. Segelbaum	Registration Number	42138

This collection of information is required by 37 CFR 1.114. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.11 and 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450.

If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.

Privacy Act Statement

The Privacy Act of 1974 (P.L. 93-579) requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that: (1) the general authority for the collection of this information is 35 U.S.C. 2(b)(2); (2) furnishing of the information solicited is voluntary; and (3) the principal purpose for which the information is used by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent application or patent. If you do not furnish the requested information, the U.S. Patent and Trademark Office may not be able to process and/or examine your submission, which may result in termination of proceedings or abandonment of the application or expiration of the patent.

The information provided by you in this form will be subject to the following routine uses:

1. The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C. 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether the Freedom of Information Act requires disclosure of these records.

2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.

3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.

4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).

5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent Cooperation Treaty.

6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).

7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (i.e., GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.

8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspections or an issued patent.

9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

Electronic Patent Application Fee Transmittal

Application Number:	12137364
Filing Date:	11-Jun-2008
Title of Invention:	INFUSION SYSTEMS INCLUDING COMPUTER-FACILITATED MAINTENANCE AND/OR OPERATION AND METHODS OF USE
First Named Inventor/Applicant Name:	Stephen E. Hidem
Filer:	Charles D. Segelbaum
Attorney Docket Number:	56782.1.7

Filed as Large Entity

Utility under 35 USC 111(a) Filing Fees

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Basic Filing:				
Pages:				
Claims:				
Miscellaneous-Filing:				
Petition:				
Patent-Appeals-and-Interference:				
Post-Allowance-and-Post-Issuance:				
Extension-of-Time:				

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Miscellaneous:				
Request for continued examination	1801	1	810	810
		Total in USD ($)		**810**

Electronic Acknowledgement Receipt

EFS ID:	9979176
Application Number:	12137364
International Application Number:	
Confirmation Number:	7377
Title of Invention:	INFUSION SYSTEMS INCLUDING COMPUTER-FACILITATED MAINTENANCE AND/OR OPERATION AND METHODS OF USE
First Named Inventor/Applicant Name:	Stephen E. Hidem
Customer Number:	22859
Filer:	Charles D. Segelbaum
Filer Authorized By:	
Attorney Docket Number:	56782.1.7
Receipt Date:	28-APR-2011
Filing Date:	11-JUN-2008
Time Stamp:	17:19:14
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	yes
Payment Type	Credit Card
Payment was successfully received in RAM	$810
RAM confirmation Number	4285
Deposit Account	
Authorized User	

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)

1	Request for Continued Examination (RCE)	56782_1_7_RCE.pdf	916446 0b87ab7d3fcac84d0a0b0d454f5b2d81de3bfaaa	no	3
Warnings:					
Information:					
2	Fee Worksheet (PTO-875)	fee-info.pdf	30565 73b45891407e33e87b4ce3574dae497df7eef8c2	no	2
Warnings:					
Information:					
			Total Files Size (in bytes):	947011	

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.

New Applications Under 35 U.S.C. 111
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.

National Stage of an International Application under 35 U.S.C. 371
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.

New International Application Filed with the USPTO as a Receiving Office
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.

PTO/SB/06 (07-06)
Approved for use through 1/31/2007. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

PATENT APPLICATION FEE DETERMINATION RECORD Substitute for Form PTO-875	Application or Docket Number 12/137,364	Filing Date 06/11/2008	☐ To be Mailed

APPLICATION AS FILED – PART I

	(Column 1)	(Column 2)	SMALL ENTITY ☐		OR	OTHER THAN SMALL ENTITY	
FOR	NUMBER FILED	NUMBER EXTRA	RATE ($)	FEE ($)		RATE ($)	FEE ($)
☐ BASIC FEE (37 CFR 1.16(a), (b), or (c))	N/A	N/A	N/A			N/A	
☐ SEARCH FEE (37 CFR 1.16(k), (i), or (m))	N/A	N/A	N/A			N/A	
☐ EXAMINATION FEE (37 CFR 1.16(o), (p), or (q))	N/A	N/A	N/A			N/A	
TOTAL CLAIMS (37 CFR 1.16(i))	minus 20 =	*	X $ =		OR	X $ =	
INDEPENDENT CLAIMS (37 CFR 1.16(h))	minus 3 =	*	X $ =			X $ =	
☐ APPLICATION SIZE FEE (37 CFR 1.16(s))	If the specification and drawings exceed 100 sheets of paper, the application size fee due is $250 ($125 for small entity) for each additional 50 sheets or fraction thereof. See 35 U.S.C. 41(a)(1)(G) and 37 CFR 1.16(s).						
☐ MULTIPLE DEPENDENT CLAIM PRESENT (37 CFR 1.16(j))							
* If the difference in column 1 is less than zero, enter "0" in column 2.			TOTAL			TOTAL	

APPLICATION AS AMENDED – PART II

AMENDMENT	04/28/2011	(Column 1) CLAIMS REMAINING AFTER AMENDMENT		(Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR	(Column 3) PRESENT EXTRA	SMALL ENTITY RATE ($)	ADDITIONAL FEE ($)	OR	OTHER THAN SMALL ENTITY RATE ($)	ADDITIONAL FEE ($)
	Total (37 CFR 1.16(i))	* 24	Minus	** 24	= 0	X $ =		OR	X $52=	0
	Independent (37 CFR 1.16(h))	* 5	Minus	***5	= 0	X $ =		OR	X $220=	0
	☐ Application Size Fee (37 CFR 1.16(s))									
	☐ FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))							OR		
						TOTAL ADD'L FEE		OR	TOTAL ADD'L FEE	0

AMENDMENT		(Column 1) CLAIMS REMAINING AFTER AMENDMENT		(Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR	(Column 3) PRESENT EXTRA	RATE ($)	ADDITIONAL FEE ($)		RATE ($)	ADDITIONAL FEE ($)
	Total (37 CFR 1.16(i))	*	Minus	**	=	X $ =		OR	X $ =	
	Independent (37 CFR 1.16(h))	*	Minus	***	=	X $ =		OR	X $ =	
	☐ Application Size Fee (37 CFR 1.16(s))									
	☐ FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))							OR		
						TOTAL ADD'L FEE		OR	TOTAL ADD'L FEE	

* If the entry in column 1 is less than the entry in column 2, write "0" in column 3.

** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 20, enter "20".

*** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 3, enter "3".

The "Highest Number Previously Paid For" (Total or Independent) is the highest number found in the appropriate box in column 1.

Legal Instrument Examiner:
/RUTH M. LLOYD/

This collection of information is required by 37 CFR 1.16. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.

DO NOT ENTER: /J.Z./

22859
Customer Number

Patent
Case No.: 56782.1.7

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

First Named Inventor:	Stephen E. Hidem		
Application No.:	12/137,364	Group Art Unit:	3763
Filed:	June 11, 2008	Examiner:	Jenna Zhang
Title:	INFUSION SYSTEMS INCLUDING COMPUTER-FACILITATED MAINTENANCE AND/OR OPERATION AND METHODS OF USE		

Mail Stop AF
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

AMENDMENT AFTER FINAL

In response to the Office Action mailed February 4, 2011, please amend the above-identified application as set forth below.

Amendments to the Claims are reflected in the listing of claims beginning on page 2 of this paper. Changes are shown with deletions being designated by strike-through or double-brackets and insertion of new language being underlined.

Remarks begin on page 10 of this paper.

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.
12/137,364	06/11/2008	Stephen E. Hidem	56782.1.7	7377

22859 7590 04/15/2011

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

EXAMINER	
ZHANG, JENNA	

ART UNIT	PAPER NUMBER
3763	

NOTIFICATION DATE	DELIVERY MODE
04/15/2011	ELECTRONIC

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.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

IP@FREDLAW.COM

Advisory Action Before the Filing of an Appeal Brief	**Application No.** 12/137,364	**Applicant(s)** HIDEM ET AL.	
	Examiner JENNA ZHANG	**Art Unit** 3763	

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

THE REPLY FILED 01 April 2011 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
   a) ☐ The period for reply expires _____months from the mailing date of the final rejection.
   b) ☒ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.
   Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☒ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☒ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.
   NOTE: *See Continuation Sheet*. (See 37 CFR 1.116 and 41.33(a)).
4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☐ Applicant's reply has overcome the following rejection(s): _____.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☒ will not be entered, or b) ☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: _____.
   Claim(s) objected to: _____.
   Claim(s) rejected: *1-17*.
   Claim(s) withdrawn from consideration: _____.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☐ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: _____.
12. ☐ Note the attached Information *Disclosure Statement*(s). (PTO/SB/08) Paper No(s). _____
13. ☐ Other: _____.

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

/J. Z./
Examiner, Art Unit 3763

Continuation of 3. NOTE: The amendment to claim 1 raises new considerations and elemental/operational features/functions and therefore change the scope of the applicant's claims and would require further additional search and consideration. Arguments for these amended claims are acknowledged but are considered moot because these amendments are not entered.

22859
Customer Number

Patent
Case No.: 56782.1.7

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

First Named Inventor:	Stephen E. Hidem		
Application No.:	12/137,364	Group Art Unit:	3763
Filed:	June 11, 2008	Examiner:	Jenna Zhang
Title:	INFUSION SYSTEMS INCLUDING COMPUTER-FACILITATED MAINTENANCE AND/OR OPERATION AND METHODS OF USE		

Mail Stop AF
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

AMENDMENT AFTER FINAL

In response to the Office Action mailed February 4, 2011, please amend the above-identified application as set forth below.

Amendments to the Claims are reflected in the listing of claims beginning on page 2 of this paper. Changes are shown with deletions being designated by strike-through or double-brackets and insertion of new language being underlined.

Remarks begin on page 10 of this paper.

Amendments to the Claims

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1. (Currently Amended) A method for operating an infusion system, the system comprising an eluant reservoir, a pump coupled to the reservoir, an infusion tubing circuit, a radioisotope generator, an activity detector, a waste bottle and a computer including a computer interface, the infusion tubing circuit including an eluant line coupled to the pump and to the generator, a waste line coupled to the generator and to the waste bottle, and a patient line coupled to the generator, the method comprising:

entering, into the computer, via the computer interface, a command to activate the pump in order to generate an eluate from a portion of a volume of eluant pumped through the generator, via an elution within the generator;

receiving an indication, from the computer, via the computer interface, that the elution is completed, when the pump has completed pumping the portion of the volume of eluant; and

receiving ~~an indication,~~ from the computer, via the computer interface, a display of time lapsed since the elution was completed.

2. (Original) The method of claim 1, further comprising:

entering, into the computer, via a computer interface, the volume of eluant contained in the reservoir, prior to the elution; and

receiving, from the computer interface, an indication of a volume of eluant in the reservoir, based upon tracking the portion of the volume of eluant that is pumped from the reservoir.

3. (Previously Presented) The method of claim 1, further comprising:

coupling the patient line of the infusion tubing circuit to a first shielded test vial, in order to collect a first sample of the eluate from the patient line during the elution;

measuring an activity of the first sample; and

entering into the computer, via the computer interface, the measured activity of the first sample and a time between completion of the elution and the measuring of the activity, the computer calculating a breakthrough of the generator.

4. (Original) The method of claim 3, further comprising:

selecting a breakthrough test procedure of the computer, via the computer interface, prior to entering the command to activate the pump; and

wherein coupling the patient line to the first shielded test vial is instructed by the computer interface, after selecting the breakthrough test.

5. (Previously Presented) The method of claim 3, further comprising:

exchanging the patient line of the infusion tubing circuit for a first new patient line, after collecting the first sample;

coupling the first new patient line to a second shielded test vial;

repeating the steps of claim 1, after exchanging the patient line, wherein the pump is activated a second time and a second elution takes place, in order to fill the second vial with a second sample of the eluate from the first new patient line;

measuring an activity of the second sample; and

entering into the computer, via the computer interface, the measured activity of the second sample and a time between completion of the second elution and the measuring of the activity of the second sample, the computer calculating a calibration coefficient for the infusion system based on the measured activity of the second sample and an activity of the eluate detected, during the second elution, by the activity detector of the system.

6. (Original) The method of claim 5, further comprising:

selecting a calibration procedure of the computer, via the computer interface, prior to entering the command to activate the pump for the second time; and

wherein coupling the first new patient line to the second shielded test vial is instructed by the computer interface, after selecting the calibration procedure.

7. (Original) The method of claim 5, further comprising:

exchanging the first new patient line of the infusion tubing circuit for a second new patient line, after the computer calculates the calibration coefficient;

purging air from the second patient line;

coupling the second new patient line to a patient, after purging; and

repeating the steps of claim 1, after exchanging the first new patient line for the second new patient line, wherein the pump is activated a third time and a third elution takes place, in order to inject a dose of the eluate to the patient from the second patient line.

8. (Original) The method of claim 7, further comprising receiving a report from the computer, upon completion of the third elution, the report including a patient identification number and at least one quantification of the dose of the eluate.

9. (Previously Presented) The method of claim 1, further comprising:

coupling the patient line to a shielded test vial in order to collect a sample of the eluate from the patient line during the elution;

measuring an activity of the sample; and

entering into the computer, via the computer interface, the measured activity of the sample and a time between completion of the elution and measuring of the activity, the computer calculating a calibration coefficient for the infusion system based on the measured activity and an activity of the eluate detected, during elution, by the activity detector of the system.

10. (Original) The method of claim 9, further comprising:

selecting a calibration procedure of the computer, via the computer interface, prior to entering the command to activate the pump; and

wherein coupling the patient line to the shielded test vial is instructed by the computer interface, after selecting the calibration procedure.

11. (Original) The method of claim 1, further comprising:

purging air from the patient line;

coupling the patient line to a patient, after purging, in order to inject a dose of the eluate to the patient from the patient line; and

receiving a report from the computer, upon completion of the elution, the report including a patient identification number and at least one quantification of the dose of the eluate.

12. (Original) The method of claim 1, wherein the computer interface comprises a touch-activated display screen.

13. (Original) The method of claim 1, further comprising:

receiving an indication, from the system, that the eluate is being diverted, from the generator, through the waste line of the infusion tubing circuit, when the pump is activated;

receiving an indication, from the system, that the eluate is being diverted from the generator, through the patient line of the infusion tubing circuit, when the pump is activated;

14. (Original) The method of claim 13, wherein:

the system further comprises a light projector;

the indication that the eluate is being diverted through the waste line comprises a flashing light projection from the light projector; and

the indication that the eluate is being diverted through the patient line comprises a solid light projection from the light projector.

15. (Original) The method of claim 13, further comprising receiving an indication from the system that a peak bolus of radioactivity has been detected, in the eluate, by the activity detector.

16. (Original) The method of claim 15, wherein:

the system further comprises a light projector; and

the indication that the peak bolus of radioactivity has been detected comprises a flashing light from the light projector.

17. (Original) The method of claim 1, further comprising:

entering, into the computer, via the computer interface, a command to set a waste bottle level indicator to zero, when the waste bottle is empty and prior to entering the command to activate the pump; and

receiving, from the computer, via the computer interface, an indication that the waste bottle needs to be emptied, based upon the computer tracking a volume of the eluate that is diverted, from the generator, through the waste line of the infusion tubing circuit.

18. (Withdrawn) A computer readable medium having computer executable instructions for executing a method for maintaining an infusion system, the method comprising:

receiving, via a graphical user interface, a volume of eluant contained in a reservoir of the infusion system prior to activating a pump of the infusion system to pump a portion of the volume of eluant through a radioisotope generator of the system in order to generate, via elution, an eluate;

tracking the portion of the volume of eluant that is pumped from the reservoir;

providing an indication of a volume of eluant within the reservoir; and

tracking a volume of the eluate that is diverted from the generator to the waste bottle;

providing an indication that the waste bottle needs to be emptied.

19. (Withdrawn) The computer readable medium of claim 18, further including receiving, via the graphical user interface, a command to set a waste bottle level indicator to zero when the waste bottle is empty.

20. (Withdrawn) A computer readable medium having computer executable instructions for executing a method of calibrating an activity detector of an infusion system, the method comprising:

receiving a calibration command;

receiving calibration parameters relating to an elution process;

activating a pump of the infusion system to initiate the elution process, the elution process producing a sample of an eluate;

tracking a time from the end of the elution process;

receiving from the activity detector of the infusion system an activity level detected during the elution process;

receiving a measured activity level of the eluate sample obtained from a dose calibrator;

receiving a time measured from the completion of the elution process to the measurement of the activity level by the dose calibrator;

calculating a calibration coefficient for the infusion system based on the measured activity level of the eluate sample and activity level detected during the elution process; and

providing the calibration coefficient as an output.

21. (Withdrawn) A computer readable medium having computer executable instructions for executing a method of conducting a breakthrough test of a radioisotope generator of an infusion system, the method comprising:

receiving a breakthrough test command;

activating a pump of the infusion system to initiate an elution process, the elution process using the generator to produce a sample of an eluate from a patient line;

tracking a time lapsed from the end of the elution process;

receiving a measured activity level of the eluate sample obtained from a dose calibrator;

receiving a time measured from the completion of the elution process to the measurement of the activity level by the dose calibrator;

calculating a breakthrough of the radioisotope generator based on the measured activity level and the time between completion of the elution process and the measuring of the activity level; and

providing the breakthrough of the generator as an output.

22. (Withdrawn) The computer readable medium of claim 21, further comprising:

receiving a second measured activity level of the eluate sample obtained from a dose calibrator, the second measured activity level being a measurement taken at predetermined time period after the completion of the elution process.

23. (Withdrawn) The computer readable medium of claim 21, wherein the predetermined time period is 60 minutes after completion of the elution process.

24. (Withdrawn) A method for purging a tubing circuit of an infusion system with air, the system comprising a pump coupled to the tubing circuit, a radioisotope generator, a waste bottle and a computer including a computer interface, the method comprising:

receiving instructions from the computer, via the computer interface, to disconnect the pump from an eluant reservoir of the system, and to by-pass the generator by disconnecting an eluant line and an eluate line, of the tubing circuit, from the generator, and connecting the eluant line to the eluate line; and

entering, into the computer, via the computer interface, a command to perform an air purge of the tubing circuit, the air purge being automated, via the computer, to perform purges of individual portions of the tubing circuit, in sequence, via control of the pump and of two divergence valves of the tubing circuit;

wherein a first valve, of the two divergence valves, is located between a first portion of the eluate line and two downstream portions of the eluate line, a first of the two downstream

portions extending to a waste bottle of the system and a second of the two downstream portions extending to a vial outside the system;

a second valve, of the two divergence valves, is located between a first portion of the eluant line, extending from the pump, and two downstream portions of the eluant line, a first of the two downstream portions of the eluant line being connected to the first portion of the eluate line, and a second of the two downstream portions of the eluant line being connected to the second of the two downstream portions of the eluate line.

Remarks

This communication responds to the Office Action mailed February 4, 2011 for the application captioned above. The following remarks are respectfully submitted

§103 Rejection

Claims 1, 2, 9, and 11 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Bergner (US Pat. No. 4,585,941).

Claims 3-8 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Bergner (US Pat. No. 4,585,941) in view of Gerhart (US Pat. No. 3,774,036).

Claim 12 stands rejected under 35 U.S.C. 103(a) as being unpatentable over Bergner (US Pat. No. 4,585,941) in view of Graves et al. (US Pat. No. 7,163,031 B2).

Claim 17 stands rejected under 35 U.S.C. 103(a) as being unpatentable over Bergner (US Pat. No. 4,585,941) in view of Agarwal et al (US Pat. No. 4,096,859).

In the Office Action, the Examiner rejects claims 1-3, 9, and 11 are rejected under 35 USC §103(a) based on Bergner. With respect to claim 1, the Examiner contends that Bergner discloses the elements of the claim, including "receiving an indication, from the computer, via the computer interface, of time lapsed since the elution was completed." Although Applicant respectfully disagrees, Applicant has amended claim 1 to clarify the invention. In light of the amendment to claim 1, Applicant requests reconsideration. As amended, this limitation now reads, "receiving from the computer, via the computer interface, a display of time lapsed since the elution was completed."

In support of the rejection of claim 1, the Examiner cites to col. 4, line 7 to col. 6, line 19. Applicant has reviewed Bergner and does not see such an indication. This portion of Bergner references and describes Figs. 2-4.

Fig. 2, which is copied below for ease of reference, shows the front panel of the infusion pump controller 60. As may be seen from this panel, it does not provide a display of time lapsed since the elution was completed. Instead, it shows information such as the total volume 74,

volume eluted 76, an LED 82 that lights when the end of travel of the plunger is indicated. No mention is made of time after elution is completed.

Fig. 2

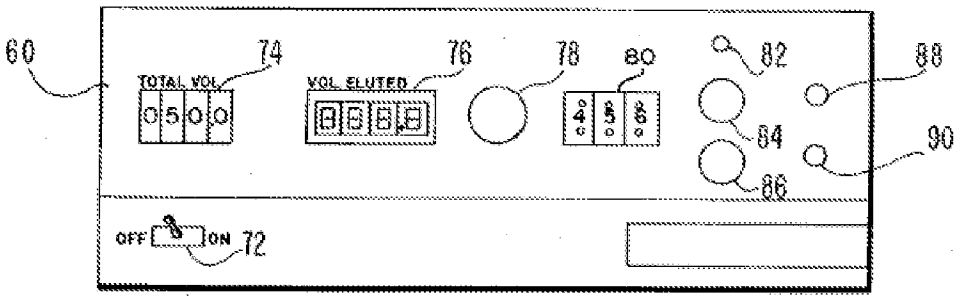


Fig. 3, which is copied below for ease of reference, shows front view of the dosimetry control used with the strontium-rubidium infusion system. As may be seen from this panel, it does not provide a display of time lapsed since the elution was completed. Instead, it shows information such as the volume to be infused 94, the volume of eluate which has been infused 96, the total dose to be infused 98, the total dose which has been infused 100, the dose rate 102, the actual dose rate present 104, the flow rate 112. No mention is made of time after elution is completed.

Fig. 3

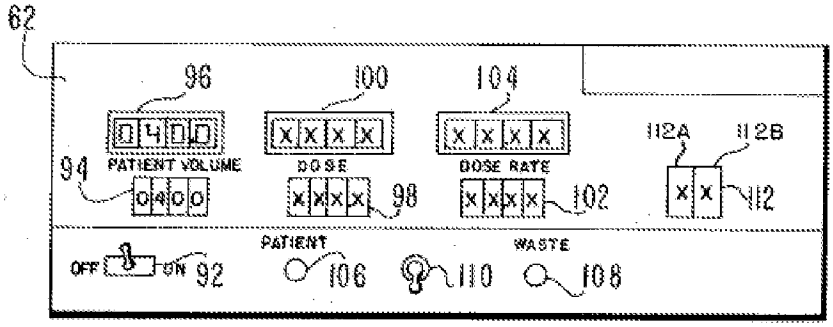


Fig. 4, which is copied below for ease of reference, provides an explanatory graph of radioactivity measured (on the y-axis) by the dosimeter probe versus time (on the x-axis). This graph is used for explanatory purposes; it is not information displayed to a user. It is not information received from a computer interface. In addition, the information displayed in the graph is merely an indication of a typical dosage level over time, stopping when the elution stops. It does not track the time after the elution stops nor is it intended to display any such information to a user.

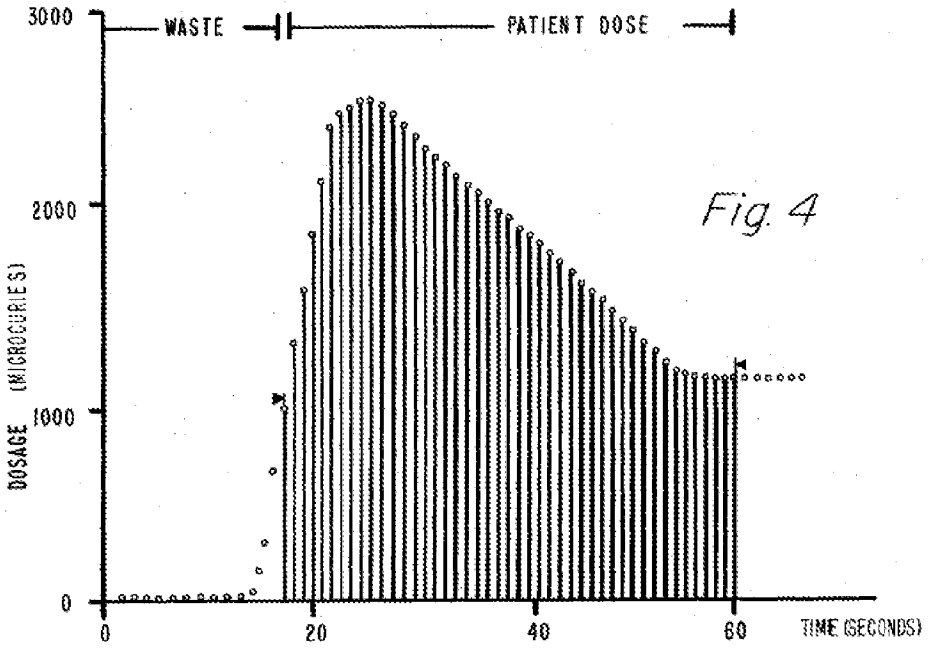


Fig. 4

In the Office Action, the Examiner combines Bergner with Gerhart, Graves, or Agarwal in rejecting other pending claims. Gerhart, Graves, or Agarwal also fail to disclose the limitation from independent claim 1 of "receiving an indication, from the computer, via the computer interface, of time lapsed since the elution was completed."

Graves discloses an automated bulk dispensing system that includes an eluate shield or pig and/or recipient shield or pig that has been disassembled and a second container, e.g., eluate vial, or recipient container, e.g., recipient vial. (See, e.g., Fig. 5). Gerhart does not disclose "a display of time lapsed since the elution was completed."

Gerhart discloses a method and apparatus for generating and maintaining an available supply of a radioactive eluate with at least a minimum level of activity. Gerhart does not appear to mention a computer, a computer interface, or a display of time lapsed since the elution was completed.

Agarwal discloses an apparatus for peritoneal dialysis. Agarwal does not disclose an elution process.

Accordingly, since none of the references cited by the Examiner in the Office Action discloses "receiving from the computer, via the computer interface, a display of time lapsed since the elution was completed," as required by claim 1, Applicant submits that the rejection of claim 1 and its associated dependent claims should be withdrawn.

In view of the foregoing, it is submitted that this application is in condition for allowance. Favorable consideration and prompt allowance of the application is respectfully requested. Applicant believes no fee is due to enter the present Amendment. The Commissioner is hereby authorized to charge any additional filing fees required to Deposit Account No. 061910. The Examiner is invited to telephone the undersigned if the Examiner believes it would be useful to advance prosecution.

Respectfully submitted,

Dated: April 1, 2011

/Charles D. Segelbaum/
Charles D. Segelbaum
Reg. No. 42,138
(612) 492-7115

Fredrikson & Byron, P.A.
200 South Sixth Street, Suite 4000
Minneapolis, MN 55402-1425 USA
Facsimile: (612) 492-7077

Please grant any extension of time necessary for entry; charge any fee due to Deposit Account No. 06-1910.

Electronic Acknowledgement Receipt

EFS ID:	9794579
Application Number:	12137364
International Application Number:	
Confirmation Number:	7377
Title of Invention:	INFUSION SYSTEMS INCLUDING COMPUTER-FACILITATED MAINTENANCE AND/OR OPERATION AND METHODS OF USE
First Named Inventor/Applicant Name:	Stephen E. Hidem
Customer Number:	22859
Filer:	Charles D. Segelbaum
Filer Authorized By:	
Attorney Docket Number:	56782.1.7
Receipt Date:	01-APR-2011
Filing Date:	11-JUN-2008
Time Stamp:	17:05:24
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		56782_1_7_ResponseToFOA.pdf	183885 3825f94254014e6c6040277b92a426103277fcbc	yes	13

	Multipart Description/PDF files in .zip description		
	Document Description	**Start**	**End**
	Amendment After Final	1	1
	Claims	2	9
	Applicant Arguments/Remarks Made in an Amendment	10	13
Warnings:			
Information:			
	Total Files Size (in bytes):	183885	

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.

New Applications Under 35 U.S.C. 111
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.

National Stage of an International Application under 35 U.S.C. 371
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.

New International Application Filed with the USPTO as a Receiving Office
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.

PTO/SB/06 (07-06)
Approved for use through 1/31/2007. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

PATENT APPLICATION FEE DETERMINATION RECORD

Substitute for Form PTO-875

Application or Docket Number	Filing Date	☐ To be Mailed
12/137,364	06/11/2008	

APPLICATION AS FILED – PART I

FOR	(Column 1) NUMBER FILED	(Column 2) NUMBER EXTRA	SMALL ENTITY ☐ RATE ($)	SMALL ENTITY ☐ FEE ($)	OR	OTHER THAN SMALL ENTITY RATE ($)	OTHER THAN SMALL ENTITY FEE ($)
☐ BASIC FEE (37 CFR 1.16(a), (b), or (c))	N/A	N/A	N/A			N/A	
☐ SEARCH FEE (37 CFR 1.16(k), (i), or (m))	N/A	N/A	N/A			N/A	
☐ EXAMINATION FEE (37 CFR 1.16(o), (p), or (q))	N/A	N/A	N/A			N/A	
TOTAL CLAIMS (37 CFR 1.16(i))	minus 20 =	*	X $ =		OR	X $ =	
INDEPENDENT CLAIMS (37 CFR 1.16(h))	minus 3 =	*	X $ =			X $ =	
☐ APPLICATION SIZE FEE (37 CFR 1.16(s))	If the specification and drawings exceed 100 sheets of paper, the application size fee due is $250 ($125 for small entity) for each additional 50 sheets or fraction thereof. See 35 U.S.C. 41(a)(1)(G) and 37 CFR 1.16(s).						
☐ MULTIPLE DEPENDENT CLAIM PRESENT (37 CFR 1.16(j))							
			TOTAL			TOTAL	

* If the difference in column 1 is less than zero, enter "0" in column 2.

APPLICATION AS AMENDED – PART II

AMENDMENT	04/01/2011	(Column 1) CLAIMS REMAINING AFTER AMENDMENT		(Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR	(Column 3) PRESENT EXTRA	SMALL ENTITY RATE ($)	SMALL ENTITY ADDITIONAL FEE ($)	OR	OTHER THAN SMALL ENTITY RATE ($)	OTHER THAN SMALL ENTITY ADDITIONAL FEE ($)
	Total (37 CFR 1.16(i))	* 24	Minus	** 24	= 0	X $ =		OR	X $52=	0
	Independent (37 CFR 1.16(h))	* 5	Minus	***5	= 0	X $ =		OR	X $220=	0
	☐ Application Size Fee (37 CFR 1.16(s))									
	☐ FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))							OR		
						TOTAL ADD'L FEE		OR	TOTAL ADD'L FEE	0

AMENDMENT		(Column 1) CLAIMS REMAINING AFTER AMENDMENT		(Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR	(Column 3) PRESENT EXTRA	RATE ($)	ADDITIONAL FEE ($)		RATE ($)	ADDITIONAL FEE ($)
	Total (37 CFR 1.16(i))	*	Minus	**	=	X $ =		OR	X $ =	
	Independent (37 CFR 1.16(h))	*	Minus	***	=	X $ =		OR	X $ =	
	☐ Application Size Fee (37 CFR 1.16(s))									
	☐ FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))							OR		
						TOTAL ADD'L FEE		OR	TOTAL ADD'L FEE	

* If the entry in column 1 is less than the entry in column 2, write "0" in column 3.

** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 20, enter "20".

*** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 3, enter "3".

The "Highest Number Previously Paid For" (Total or Independent) is the highest number found in the appropriate box in column 1.

Legal Instrument Examiner:
/BURNELL L. ROSS/

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.
12/137,364	06/11/2008	Stephen E. Hidem	56782.1.7	7377

22859 7590 02/04/2011

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

EXAMINER	
ZHANG, JENNA	
ART UNIT	**PAPER NUMBER**
3763	

NOTIFICATION DATE	DELIVERY MODE
02/04/2011	ELECTRONIC

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.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

IP@FREDLAW.COM

Office Action Summary	Application No.	Applicant(s)	
	12/137,364	HIDEM 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 *3* 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 *03 January 2011*.

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) *1-17* 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) *1-17* is/are rejected.

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

8)☐ Claim(s) _____ 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 *24 October 2008* 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

1. In response to the Amendments filed on January 3, 2011, claims 3, 5, and 9 are amended. Currently, claims 1-17 are pending.

Election/Restrictions

2. **Claims 18-24** are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected Inventions, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on January 3, 2011.

Claim Rejections - 35 USC § 112

3. The amendments to claims 3, 5, and 9 are accepted and are considered sufficient to overcoming the previous 35 U.S.C. 112, second paragraph, rejections to claims 3, 5, and 9, which are hereby withdrawn.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

5. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

6. **Claims 1, 2, 9, and 11** are rejected under 35 U.S.C. 103(a) as being unpatentable over Bergner (US Pat. No. 4,585,941).

Regarding **claim 1**, Bergner teaches a method for operating an infusion system, the system comprising: an eluant reservoir, a pump (64) coupled to the reservoir, an infusion tubing circuit (Fig. 1), a radioisotope generator (28), an activity detector (58), a waste bottle (42) and a computer (60, 62) including a computer interface, the infusion tubing circuit including an eluant line coupled to the pump and to the generator, a waste line coupled to the generator and to the waste bottle, and a patient line coupled to the generator (col. 3, line 23 until col. 4, line 53; Fig. 1), the method comprising:

entering, into the computer, via the computer interface, a command to activate the pump in order to generate an eluate from a portion of a volume of eluant pumped through the generator, via an elution within the generator;

receiving an indication, from the computer, via the computer interface, that the elution is completed, when the pump has completed pumping the portion of the volume of eluant; and

receiving an indication, from the computer, via the computer interface, of time lapsed since the elution was completed (col. 4, line 7 until col. 6, line 19).

Regarding **claim 2**, Bergner teaches entering, into the computer (60, 62), via a computer interface, the volume of eluant contained in the reservoir, prior to the elution; and receiving, from the computer interface, an indication of a volume of eluant in the reservoir, based upon tracking the portion of the volume of eluant that is pumped from the reservoir (col. 4, line 4 until col. 5, line 32).

Regarding **claim 9**, Bergner teaches coupling the patient line to a shielded test vial in order to collect a sample of the eluate from the patient line during the elution; measuring an activity of the sample; and entering into the computer, via the computer interface, the measured activity of the sample and a time between completion of the elution and measuring of the activity, so that the computer may calculate a calibration coefficient for the infusion system based on the measured activity and an activity of the eluate detected, during elution, by the activity detector of the system (col. 6, line 21 until col. 9, line 48).

Regarding **claim 10**, Bergner teaches selecting a calibration procedure of the computer, via the computer interface, prior to entering the command to activate the pump (col. 4, line 26 until col. 9, line 48) but does not teach that the step of coupling the patient line to the shielded test vial is instructed by the computer interface, after selecting the calibration procedure. However, it would have been obvious to one of ordinary skill in the art at the time of the invention to modify the device of Bergner so that the controllers 60, 62 would notify the user to perform the step of coupling the patient line to the shielded test vial for an automated reminder to the user to increase the safety of the treatment.

Regarding **claim 11**, Bergner teaches purging air from the patient line; coupling the patient line to a patient, after purging, in order to inject a dose of the eluate to the patient from the patient line; and receiving a report from the computer, upon completion of the elution, the report including a patient identification number and at least one quantification of the dose of the eluate (col. 3, line 63 until col. 4, line 6 and lines 36-53; col. 6, lines 1-19).

Regarding **claims 13-16**, Bergner teaches

> receiving an indication, from the system, that the eluate is being diverted, from the generator, through the waste line of the infusion tubing circuit, when the pump is activated; and receiving an indication, from the system, that the eluate is being diverted from the generator, through the patient line of the infusion tubing circuit, when the pump is activated (col. 5, lines 8-24);

receiving an indication from the system that a peak bolus of radioactivity has been detected, in the eluate, by the activity detector (col. 7, line 1 until col. 9, line 47); and

wherein the system further comprises a light projector (104, 96, 100, 108; col. 9, line 49 until col. 10, line 11);

Although Bergner teaches the use of flashing and solid light projections from the light projector (106, 108) as alerting notifications (col. 11, line 46 until col. 12, line 29), Bergner does not teach that the indication that the eluate is being diverted through the waste line is a flashing light projection, the indication that the eluate is being diverted through the patient line comprises a solid light projection from the light projector, and the indication that the peak bolus of radioactivity has been detected comprises a flashing light from the light projector. However, it would have been obvious to one of ordinary skill in the art at the time of the invention to modify the device of Bergner with the use of flashing and solid light projections as the indication that the eluate is being diverted through the waste line is a flashing light projection, the indication that the eluate is being diverted through the patient line comprises a solid light projection, and the indication that the peak bolus of radioactivity has been detected comprises a flashing light from the light projector, to provide a notification that alerts the user.

7. **Claims 3-8** are rejected under 35 U.S.C. 103(a) as being unpatentable over Bergner (US Pat. No. 4,585,941) in view of Gerhart (US Pat. No. 3,774,036).

Regarding **claim 3**, Bergner teaches coupling the patient line of the infusion tubing circuit to a first shielded test vial, in order to collect a first sample of the eluate from the patient line during the elution; measuring an activity of the first sample; and entering into the computer, via the computer interface, the measured activity of the first sample and a time between completion of the elution and the measuring of the activity (col. 3, line 55 until col. 5, line 68). However, Bergner does not teach method step of the computer calculating a breakthrough of the generator as required by the amended instant claim. It is noted that Gerhart teaches that breakthrough testing is performed to ensure the safety of a radioactive treatment dosage (col. 2, lines 27-39). Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to modify the method of Bergner with a breakthrough test procedure as taught by Gerhart to ensure the safety level of the treatment. Furthermore, it would have been obvious to one of ordinary skill in the art at the time of the invention to modify the device of Bergner so that the controllers 60, 62 perform the breakthrough test to calculate a breakthrough of the generator since the controllers 60, 62 controls the operations of the device of Bergner.

Regarding **claim 4**, Bergner does not teach selecting a breakthrough test procedure of the computer, via the computer interface, prior to entering the command to activate the pump; and wherein coupling the patient line to the first shielded test vial is instructed by the computer interface, after selecting the breakthrough test. However, as explained for claim 3 above, Bergner in view of Gerhart teaches performing a breakthrough test procedure prior to entering the command to activate the pump to

ensure the safety level of the treatment. Furthermore, it would have been obvious to one of ordinary skill in the art at the time of the invention to modify the device of Bergner so that the controllers 60, 62 would notify the user to perform the step of coupling the patient line to the shielded test vial for an automated reminder to the user to increase the safety of the treatment. Hence, the modified method of Bergner in view of Gerhart discloses selecting a breakthrough test procedure of the computer, via the computer interface, prior to entering the command to activate the pump; and wherein coupling the patient line to the first shielded test vial is instructed by the computer interface, after selecting the breakthrough test.

Regarding **claim 6**, the modified method of Bergner further teaches selecting a calibration procedure of the computer, via the computer interface, prior to entering the command to activate the pump for the second time; and wherein coupling the first new patient line to the second shielded test vial is instructed by the computer interface, after selecting the calibration procedure, as set forth for claim 10 (col. 6, line 21 until col. 9, line 48).

Regarding **claims 5 and 7**, Bergner further teaches repeating the steps of claim 1, wherein the pump is activated a second time and a second elution takes place, in order to fill the second vial with a second sample of the eluate from the first new patient line; measuring an activity of the second sample; and entering into the computer, via the computer interface, the measured activity of the second sample and a time between completion of the second elution and the measuring of the activity of the second sample, so that the computer may calculate a calibration coefficient for the infusion

system based on the measured activity of the second sample and an activity of the eluate detected, during the second elution, by the activity detector of the system. Bergner also teaches purging air from the second patient line; and repeating the steps of claim 1, wherein the pump is activated a third time and a third elution takes place, in order to inject a dose of the eluate to the patient from the second patient line (col. 6, line 21 until col. 9, line 48).

Regarding **claim 8**, Bergner further teaches receiving a report from the computer, upon completion of the third elution, the report including a patient identification number and at least one quantification of the dose of the eluate (col. 5, lines 41-68 and col. 9, line 49 until col. 10, line 11).

8. **Claim 12** is rejected under 35 U.S.C. 103(a) as being unpatentable over Bergner (US Pat. No. 4,585,941) in view of Graves et al (US Pat. No. 7,163,031 B2).

Regarding **claim 12**, Bergner teaches the use of displays but does not teach a touch-activated display screen. However, it is noted that Graves et al teaches the use of a touch screen electronic display screen for inputting and outputting into a computer for a radiopharmaceutical delivery device (col. 4, line 53 until col. 5, line 2). Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to modify the device of Bergner with using a system that has a touch-activated display screen as disclosed by Graves et al to consolidate the number of components required for inputting and outputting commands and notifications in an infusion device.

9. **Claim 17** is rejected under 35 U.S.C. 103(a) as being unpatentable over Bergner (US Pat. No. 4,585,941) in view of Agarwal et al (US Pat. No. 4,096,859).

Regarding **claim 17**, Bergner teaches the use of a waste bottle and tracking the waste level to determine the trigger point (col. 10, lines 12-68) but does not explicitly teach entering, into the computer, via the computer interface, a command to set a waste bottle level indicator to zero, when the waste bottle is empty and prior to entering the command to activate the pump; and receiving, from the computer, via the computer interface, an indication that the waste bottle needs to be emptied, based upon the computer tracking a volume of the eluate that is diverted, from the generator, through the waste line of the infusion tubing circuit. However, Agarwal et al teaches a medical delivery device with a waste container in which a controller tracks the waste level to alert the user to empty the waste container (col. 5, line 38 until col. 6, line 36). It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the method of Bergner with the steps of setting initial waste bottle level to zero when the bottle is empty and tracking the waste bottle level so that an alert is given to the user that the waste bottle is full and needs to be emptied as taught by Agarwal et al, to prevent overflowing of waste from the waste bottle.

It is noted that the modified method of Bergner and Agarwal et al teaches entering, into the computer, via the computer interface, a command to set a waste bottle level indicator to zero, when the waste bottle is empty and prior to entering the command to activate the pump; and receiving, from the computer, via the computer interface, an indication that the waste bottle needs to be emptied, based upon the

computer tracking a volume of the eluate that is diverted, from the generator, through the waste line of the infusion tubing circuit

Response to Arguments

10. Applicant's arguments filed January 3, 2011 have been fully considered but they are not persuasive.

Applicant argues that Bergner does not disclose the limitation of "receiving an indication, from the computer, via the computer interface, of time lapsed since the elution was completed." However, the Examiner respectfully disagrees. It is noted that total volume 74, volume eluted 76, volume to be infused 94, volume of eluate infused 96, total dose to be infused 98, total dose infused 100, dose rate 102, actual dose rate 104, and the flow rate 112 are all indicators that can be used to determine the time elapsed since the elution was completed, since the radioactive decay of Rubidium-82 is known. For example, one of ordinary skill in the art can use the volume infused 100, an indicator from the computer, to determine the time lapsed since elution was completed using the known half life of the radioactive element.

Furthermore, in response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., receiving the actual time lapse since elution was completed and displaying this time after elution stops) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification

are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

In response to applicant's arguments that Gerhart does not teach of a computer, a computer interface, or a receipt of a time lapsed since an elution was completed, it is noted Bergner teaches a computer (60, 62) with a computer interface and receiving an indication, from the computer, via the computer interface, of time lapsed since the elution was completed. Gerhart discloses the feature of using of breakthrough testing to ensure the safety level of radioactive treatment dosage but the combination of Bergner in view of Gerhart discloses a computer with a computer interface that performs a breakthrough test and receiving an indication, from the computer, via the computer interface, of time lapsed since the elution was completed.

In response to applicant's arguments that Graves does not teach of the step of receiving an indication, from the computer, via the computer interface, of time lapsed since the elution was completed, it is noted Bergner teaches receiving an indication, from the computer, via the computer interface, of time lapsed since the elution was completed, as explained above. Graves discloses an automated dispensing system for radiopharmaceutical delivery, wherein the system includes a touch screen electronic display for inputting and outputting into a computer. Therefore, Grave teaches a feature of consolidating the components required for inputting and outputting commands and notifications in an infusion device such as the individual LED displays and switches of Bergner into a touch screen electronic display screen. The combination of Bergner in view of Graves discloses the device having a touch-activated display screen and

receiving an indication, from the computer, via the computer interface, of time lapsed since the elution was completed.

In response to applicant's arguments that Agarwal does not teach of an elution process, it is noted Bergner teaches an elution process for a radiopharmaceutical delivery device that includes a waste bottle and tracking the waste level. It is noted that Agarwal discloses an automated medical delivery device with a waste container and a controller tracking the waste level to alert the user to empty the waste container. Therefore, the combination of Bergner in view of Agarwal discloses an elution process with the features for waste management.

Conclusion

11. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

12. 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
1/31/11

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

Notice of References Cited	Application/Control No. 12/137,364	Applicant(s)/Patent Under Reexamination HIDEM ET AL.	
	Examiner JENNA ZHANG	Art Unit 3763	Page 1 of 1

U.S. PATENT DOCUMENTS

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Name	Classification
*	A	US-4,585,941	04-1986	Bergner, Brian C.	250/363.02
*	B	US-3,774,036	11-1973	Gerhart, James M.	252/645
*	C	US-4,096,859	06-1978	Agarwal et al.	604/28
*	D	US-7,163,031 B2	01-2007	Graves et al.	141/9
	E	US-			
	F	US-			
	G	US-			
	H	US-			
	I	US-			
	J	US-			
	K	US-			
	L	US-			
	M	US-			

FOREIGN PATENT DOCUMENTS

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Country	Name	Classification
	N					
	O					
	P					
	Q					
	R					
	S					
	T					

NON-PATENT DOCUMENTS

*		Include as applicable: Author, Title Date, Publisher, Edition or Volume, Pertinent Pages)
	U	
	V	
	W	
	X	

*A copy of this reference is not being furnished with this Office action. (See MPEP § 707.05(a).)
Dates in MM-YYYY format are publication dates. Classifications may be US or foreign.

Index of Claims	Application/Control No.	Applicant(s)/Patent Under Reexamination
	12137364	HIDEM ET AL.
	Examiner	**Art Unit**
	JENNA ZHANG	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	09/27/2010	01/31/2011							
	1	✓	✓							
	2	✓	✓							
	3	✓	✓							
	4	✓	✓							
	5	✓	✓							
	6	✓	✓							
	7	✓	✓							
	8	✓	✓							
	9	✓	✓							
	10	✓	✓							
	11	✓	✓							
	12	✓	✓							
	13	✓	✓							
	14	✓	✓							
	15	✓	✓							
	16	✓	✓							
	17	✓	✓							
	18	✓	N							
	19	✓	N							
	20	✓	N							
	21	✓	N							
	22	✓	N							
	23	✓	N							
	24	✓	N							

Search Notes	Application/Control No.	Applicant(s)/Patent Under Reexamination
	12137364	HIDEM ET AL.
	Examiner	**Art Unit**
	JENNA ZHANG	3763

SEARCHED

Class	Subclass	Date	Examiner
604	236, and 65-67 with text	9/27/2010	JZ
312	209	9/27/2010	JZ
600	5	9/27/2010	JZ
600	4, and 600/431, 1-8, and 301 with text	9/29/2010	JZ

SEARCH NOTES

Search Notes	Date	Examiner
Inventor Search	9/27/2010	JZ
Assignee Search	9/27/2010	JZ
Consulted Chris Koharski	9/28/2010	JZ
EAST Search	9/27-29/2010	JZ
Updated EAST Search	1/31/2011	JZ

INTERFERENCE SEARCH

Class	Subclass	Date	Examiner

22859
Customer Number

Patent
Case No.: 56782.1.7

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

First Named Inventor:	Stephen E. Hidem		
Application No.:	12/137,364	Group Art Unit:	3763
Filed:	June 11, 2008	Examiner:	Jenna Zhang
Title:	INFUSION SYSTEMS INCLUDING COMPUTER-FACILITATED MAINTENANCE AND/OR OPERATION AND METHODS OF USE		

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

AMENDMENT

In response to the Office Action mailed October 5, 2010, please amend the above-identified application as set forth below.

Amendments to the Claims are reflected in the listing of claims beginning on page 2 of this paper. Changes are shown with deletions being designated by strike-through or double-brackets and insertion of new language being underlined.

Remarks begin on page 10 of this paper.

Amendments to the Claims

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1. (Original) A method for operating an infusion system, the system comprising an eluant reservoir, a pump coupled to the reservoir, an infusion tubing circuit, a radioisotope generator, an activity detector, a waste bottle and a computer including a computer interface, the infusion tubing circuit including an eluant line coupled to the pump and to the generator, a waste line coupled to the generator and to the waste bottle, and a patient line coupled to the generator, the method comprising:

entering, into the computer, via the computer interface, a command to activate the pump in order to generate an eluate from a portion of a volume of eluant pumped through the generator, via an elution within the generator;

receiving an indication, from the computer, via the computer interface, that the elution is completed, when the pump has completed pumping the portion of the volume of eluant; and

receiving an indication, from the computer, via the computer interface, of time lapsed since the elution was completed.

2. (Original) The method of claim 1, further comprising:

entering, into the computer, via a computer interface, the volume of eluant contained in the reservoir, prior to the elution; and

receiving, from the computer interface, an indication of a volume of eluant in the reservoir, based upon tracking the portion of the volume of eluant that is pumped from the reservoir.

3. (Currently amended) The method of claim 1, further comprising:

coupling the patient line of the infusion tubing circuit to a first shielded test vial, in order to collect a first sample of the eluate from the patient line during the elution;

measuring an activity of the first sample; and

entering into the computer, via the computer interface, the measured activity of the first sample and a time between completion of the elution and the measuring of the activity, ~~so that~~ the computer ~~may calculate~~ calculating a breakthrough of the generator.

4. (Original) The method of claim 3, further comprising:

selecting a breakthrough test procedure of the computer, via the computer interface, prior to entering the command to activate the pump; and

wherein coupling the patient line to the first shielded test vial is instructed by the computer interface, after selecting the breakthrough test.

5. (Currently amended) The method of claim 3, further comprising:

exchanging the patient line of the infusion tubing circuit for a first new patient line, after collecting the first sample;

coupling the first new patient line to a second shielded test vial;

repeating the steps of claim 1, after exchanging the patient line, wherein the pump is activated a second time and a second elution takes place, in order to fill the second vial with a second sample of the eluate from the first new patient line;

measuring an activity of the second sample; and

entering into the computer, via the computer interface, the measured activity of the second sample and a time between completion of the second elution and the measuring of the activity of the second sample, ~~so that~~ the computer ~~may calculate~~ calculating a calibration coefficient for the infusion system based on the measured activity of the second sample and an activity of the eluate detected, during the second elution, by the activity detector of the system.

6. (Original) The method of claim 5, further comprising:

selecting a calibration procedure of the computer, via the computer interface, prior to entering the command to activate the pump for the second time; and

wherein coupling the first new patient line to the second shielded test vial is instructed by the computer interface, after selecting the calibration procedure.

7. (Original) The method of claim 5, further comprising:

exchanging the first new patient line of the infusion tubing circuit for a second new patient line, after the computer calculates the calibration coefficient;

purging air from the second patient line;

coupling the second new patient line to a patient, after purging; and

repeating the steps of claim 1, after exchanging the first new patient line for the second new patient line, wherein the pump is activated a third time and a third elution takes place, in order to inject a dose of the eluate to the patient from the second patient line.

8. (Original) The method of claim 7, further comprising receiving a report from the computer, upon completion of the third elution, the report including a patient identification number and at least one quantification of the dose of the eluate.

9. (Currently amended) The method of claim 1, further comprising:

coupling the patient line to a shielded test vial in order to collect a sample of the eluate from the patient line during the elution;

measuring an activity of the sample; and

entering into the computer, via the computer interface, the measured activity of the sample and a time between completion of the elution and measuring of the activity, ~~so that~~ the computer ~~may calculate~~ calculating a calibration coefficient for the infusion system based on the measured activity and an activity of the eluate detected, during elution, by the activity detector of the system.

10. (Original) The method of claim 9, further comprising:

selecting a calibration procedure of the computer, via the computer interface, prior to entering the command to activate the pump; and

wherein coupling the patient line to the shielded test vial is instructed by the computer interface, after selecting the calibration procedure.

11. (Original) The method of claim 1, further comprising:

purging air from the patient line;

coupling the patient line to a patient, after purging, in order to inject a dose of the eluate to the patient from the patient line; and

receiving a report from the computer, upon completion of the elution, the report including a patient identification number and at least one quantification of the dose of the eluate.

12. (Original) The method of claim 1, wherein the computer interface comprises a touch-activated display screen.

13. (Original) The method of claim 1, further comprising:

receiving an indication, from the system, that the eluate is being diverted, from the generator, through the waste line of the infusion tubing circuit, when the pump is activated;

receiving an indication, from the system, that the eluate is being diverted from the generator, through the patient line of the infusion tubing circuit, when the pump is activated;

14. (Original) The method of claim 13, wherein:

the system further comprises a light projector;

the indication that the eluate is being diverted through the waste line comprises a flashing light projection from the light projector; and

the indication that the eluate is being diverted through the patient line comprises a solid light projection from the light projector.

15. (Original) The method of claim 13, further comprising receiving an indication from the system that a peak bolus of radioactivity has been detected, in the eluate, by the activity detector.

16. (Original) The method of claim 15, wherein:

the system further comprises a light projector; and

the indication that the peak bolus of radioactivity has been detected comprises a flashing light from the light projector.

17. (Original) The method of claim 1, further comprising:

entering, into the computer, via the computer interface, a command to set a waste bottle level indicator to zero, when the waste bottle is empty and prior to entering the command to activate the pump; and

receiving, from the computer, via the computer interface, an indication that the waste bottle needs to be emptied, based upon the computer tracking a volume of the eluate that is diverted, from the generator, through the waste line of the infusion tubing circuit.

18. (Withdrawn) A computer readable medium having computer executable instructions for executing a method for maintaining an infusion system, the method comprising:

receiving, via a graphical user interface, a volume of eluant contained in a reservoir of the infusion system prior to activating a pump of the infusion system to pump a portion of the volume of eluant through a radioisotope generator of the system in order to generate, via elution, an eluate;

tracking the portion of the volume of eluant that is pumped from the reservoir;

providing an indication of a volume of eluant within the reservoir; and

tracking a volume of the eluate that is diverted from the generator to the waste bottle;

providing an indication that the waste bottle needs to be emptied.

19. (Withdrawn) The computer readable medium of claim 18, further including receiving, via the graphical user interface, a command to set a waste bottle level indicator to zero when the waste bottle is empty.

20. (Withdrawn) A computer readable medium having computer executable instructions for executing a method of calibrating an activity detector of an infusion system, the method comprising:

receiving a calibration command;

receiving calibration parameters relating to an elution process;

activating a pump of the infusion system to initiate the elution process, the elution process producing a sample of an eluate;

tracking a time from the end of the elution process;

receiving from the activity detector of the infusion system an activity level detected during the elution process;

receiving a measured activity level of the eluate sample obtained from a dose calibrator;

receiving a time measured from the completion of the elution process to the measurement of the activity level by the dose calibrator;

calculating a calibration coefficient for the infusion system based on the measured activity level of the eluate sample and activity level detected during the elution process; and

providing the calibration coefficient as an output.

21. (Withdrawn) A computer readable medium having computer executable instructions for executing a method of conducting a breakthrough test of a radioisotope generator of an infusion system, the method comprising:

receiving a breakthrough test command;

activating a pump of the infusion system to initiate an elution process, the elution process using the generator to produce a sample of an eluate from a patient line;

tracking a time lapsed from the end of the elution process;

receiving a measured activity level of the eluate sample obtained from a dose calibrator;

receiving a time measured from the completion of the elution process to the measurement of the activity level by the dose calibrator;

calculating a breakthrough of the radioisotope generator based on the measured activity level and the time between completion of the elution process and the measuring of the activity level; and

providing the breakthrough of the generator as an output.

22. (Withdrawn) The computer readable medium of claim 21, further comprising:

receiving a second measured activity level of the eluate sample obtained from a dose calibrator, the second measured activity level being a measurement taken at predetermined time period after the completion of the elution process.

23. (Withdrawn) The computer readable medium of claim 21, wherein the predetermined time period is 60 minutes after completion of the elution process.

24. (Withdrawn) A method for purging a tubing circuit of an infusion system with air, the system comprising a pump coupled to the tubing circuit, a radioisotope generator, a waste bottle and a computer including a computer interface, the method comprising:

receiving instructions from the computer, via the computer interface, to disconnect the pump from an eluant reservoir of the system, and to by-pass the generator by disconnecting an eluant line and an eluate line, of the tubing circuit, from the generator, and connecting the eluant line to the eluate line; and

entering, into the computer, via the computer interface, a command to perform an air purge of the tubing circuit, the air purge being automated, via the computer, to perform purges of individual portions of the tubing circuit, in sequence, via control of the pump and of two divergence valves of the tubing circuit;

wherein a first valve, of the two divergence valves, is located between a first portion of the eluate line and two downstream portions of the eluate line, a first of the two downstream

portions extending to a waste bottle of the system and a second of the two downstream portions extending to a vial outside the system;

a second valve, of the two divergence valves, is located between a first portion of the eluant line, extending from the pump, and two downstream portions of the eluant line, a first of the two downstream portions of the eluant line being connected to the first portion of the eluate line, and a second of the two downstream portions of the eluant line being connected to the second of the two downstream portions of the eluate line.

Remarks

This communication responds to the Office Action mailed October 5, 2010 for the application captioned above. The following remarks are respectfully submitted

Election of Restriction

The Examiner indicated that restriction to one of the following inventions is required under 35 U.S.C. 121:

I. **Claims 1-17**, drawn to a method for operating an infusion system, classified in class 604, subclass 503.

II. **Claims 18-19**, drawn to a computer readable medium having computer executable instructions for executing a method for maintaining an infusion system, classified in class 700, subclass 1.

III. **Claims 20-23**, drawn to a computer readable medium having computer executable instructions for executing methods of calibrating and testing, classified in class 702, subclass 85.

IV. **Claim 24**, drawn to a method for purging a tubing circuit of an infusion system with air, classified in claim 128, subclass 898.

In a telephone conversation between Examiner Zhang and Elisabeth Belden on July 16, 2010, a provisional election was made without traverse to prosecute the invention of Group 1, Claims 1-17. Claims 18-24 were withdrawn from further consideration by the Examiner. In response to the restriction requirement, Applicant respectfully elects, without traverse, Group 1, Claims 1-17.

§112 Rejection

Claims 3, 5, and 9, stand rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Applicant has amended claims 3, 5, and 9 above to replace the "may calculate" language with a "calculating" limitation. Applicant submits that the rejections under §112 should now be withdrawn.

§103 Rejection

Claims 1-3, 9, and 11 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Bergner (US Pat. No. 4,585,941).

Claims 10 and 13-16 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Bergner (US Pat. No. 4,585,941).

Claims 4-8 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Bergner (US Pat. No. 4,585,941) in view of Gerhart (US Pat. No. 3,774,036).

Claim 12 stands rejected under 35 U.S.C. 103(a) as being unpatentable over Bergner (US Pat. No. 4,585,941) in view of Graves et al. (US Pat. No. 7,163,031 B2).

Claim 17 stands rejected under 35 U.S.C. 103(a) as being unpatentable over Bergner (US Pat. No. 4,585,941) in view of Agarwal et al (US Pat. No. 4,096,859).

In the Office Action, the Examiner rejects claims 1-3, 9, and 11 are rejected under 35 USC §103(a) based on Bergner. With respect to claim 1, the Examiner contends that Bergner discloses the elements of the claim, including "receiving an indication, from the computer, via the computer interface, of time lapsed since the elution was completed." Applicant respectfully disagrees, and requests reconsideration.

In support of the rejection of claim 1, the Examiner cites to col. 4, line 7 to col. 6, line 19 as the portion of the Bergner that discloses "receiving an indication, from the computer, via the computer interface, of time lapsed since the elution was completed." Applicant has reviewed Bergner and does not see such an indication. This portion of Bergner references and describes Figs. 2-4.

Fig. 2, which is copied below for ease of reference, shows the front panel of the infusion pump controller 60. As may be seen from this panel, it does not provide an indication of the time lapsed since the elution was completed. Instead, it shows information such as the total

volume 74, volume eluted 76, an LED 82 that lights when the end of travel of the plunger is indicated. No mention is made of time after elution is completed.

Fig. 2

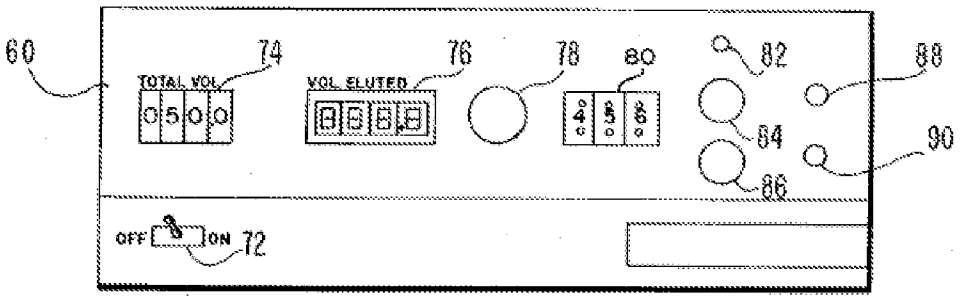


Fig. 3, which is copied below for ease of reference, shows front view of the dosimetry control used with the strontium-rubidium infusion system. As may be seen from this panel, it does not provide an indication of the time lapsed since the elution was completed. Instead, it shows information such as the volume to be infused 94, the volume of eluate which has been infused 96, the total dose to be infused 98, the total dose which has been infused 100, the dose rate 102, the actual dose rate present 104, the flow rate 112. No mention is made of time after elution is completed.

Fig. 3

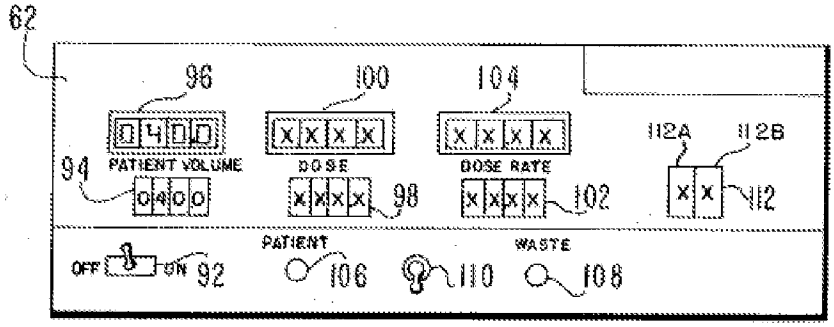


Fig. 4, which is copied below for ease of reference, provides an explanatory graph of radioactivity measured (on the y-axis) by the dosimeter probe versus time (on the x-axis). This graph is used for explanatory purposes; it is not information displayed to a user. It is not information received from a computer interface. In addition, the information displayed in the graph is merely an indication of a typical dosage level over time, stopping when the elution stops. It does not track the time after the elution stops nor is it intended to display any such information to a user.

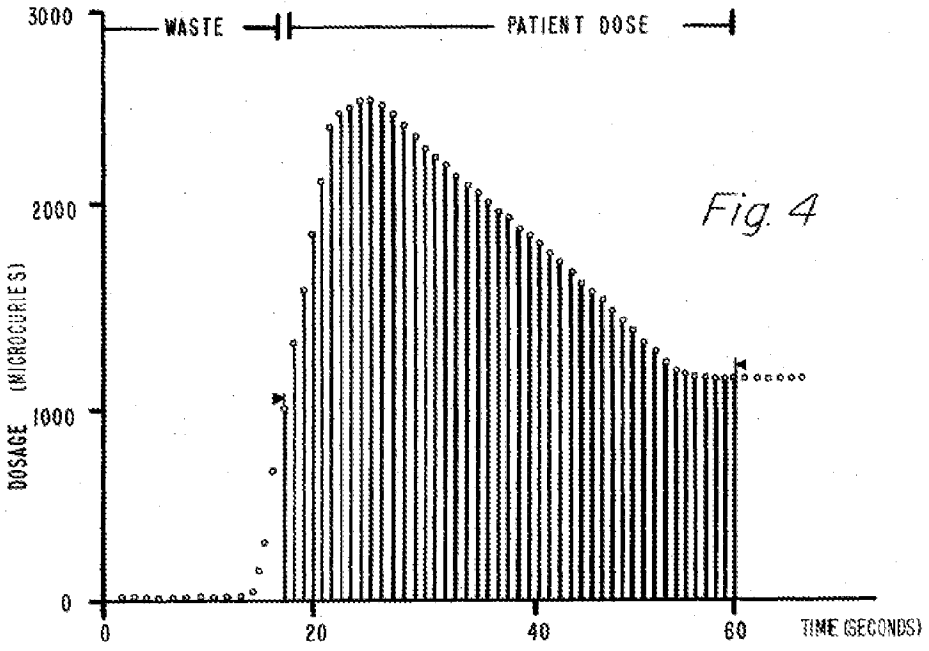


Fig. 4

In the Office Action, the Examiner combines Bergner with Gerhart, Graves, or Agarwal in rejecting other pending claims. Gerhart, Graves, or Agarwal also fail to disclose the limitation from independent claim 1 of "receiving an indication, from the computer, via the computer interface, of time lapsed since the elution was completed."

Graves discloses an automated bulk dispensing system that includes an eluate shield or pig and/or recipient shield or pig that has been disassembled and a second container, e.g., eluate vial, or recipient container, e.g., recipient vial. (See, e.g., Fig. 5). Gerhart does not disclose "receiving an indication, from the computer, via the computer interface, of time lapsed since the elution was completed."

Gerhart discloses a method and apparatus for generating and maintaining an available supply of a radioactive eluate with at least a minimum level of activity. Gerhart does not appear to mention a computer, a computer interface, or receipt of a time lapsed since an elution was completed.

Agarwal discloses an apparatus for peritoneal dialysis. Agarwal does not disclose an elution process.

Accordingly, since none of the references cited by the Examiner in the Office Action discloses "receiving an indication, from the computer, via the computer interface, of time lapsed since the elution was completed," as required by claim 1, Applicant submits that the rejection of claim 1 and its associated dependent claims should be withdrawn.

In view of the foregoing, it is submitted that this application is in condition for allowance. Favorable consideration and prompt allowance of the application is respectfully requested. Applicant believes no fee is due to enter the present Amendment. The Commissioner is hereby authorized to charge any additional filing fees required to Deposit Account No. 061910. The Examiner is invited to telephone the undersigned if the Examiner believes it would be useful to advance prosecution.

Respectfully submitted,

Dated: January 3, 2011

/Charles D. Segelbaum/
Charles D. Segelbaum
Reg. No. 42,138
(612) 492-7115

Fredrikson & Byron, P.A.
200 South Sixth Street, Suite 4000
Minneapolis, MN 55402-1425 USA
Facsimile: (612) 492-7077

Please grant any extension of time necessary for entry; charge any fee due to Deposit Account No. 06-1910.

Electronic Acknowledgement Receipt

EFS ID:	9152136
Application Number:	12137364
International Application Number:	
Confirmation Number:	7377
Title of Invention:	INFUSION SYSTEMS INCLUDING COMPUTER-FACILITATED MAINTENANCE AND/OR OPERATION AND METHODS OF USE
First Named Inventor/Applicant Name:	Stephen E. Hidem
Customer Number:	22859
Filer:	Charles D. Segelbaum
Filer Authorized By:	
Attorney Docket Number:	56782.1.7
Receipt Date:	03-JAN-2011
Filing Date:	11-JUN-2008
Time Stamp:	16:58:10
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		56782_1_7_Response.pdf	187220 46555f58a6546b1ebeaa005a3bd6ed9ab515fa64	yes	14

	Multipart Description/PDF files in .zip description		
	Document Description	**Start**	**End**
	Amendment/Req. Reconsideration-After Non-Final Reject	1	1
	Claims	2	9
	Applicant Arguments/Remarks Made in an Amendment	10	14
Warnings:			
Information:			
	Total Files Size (in bytes):	187220	

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.

New Applications Under 35 U.S.C. 111
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.

National Stage of an International Application under 35 U.S.C. 371
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.

New International Application Filed with the USPTO as a Receiving Office
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.
12/137,364	06/11/2008	Stephen E. Hidem	56782.1.7	7377

22859 7590 10/05/2010

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
10/05/2010	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.

Office Action Summary	Application No.	Applicant(s)	
	12/137,364	HIDEM 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 *3* 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 2008*.

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) *1-24* is/are pending in the application.

4a) Of the above claim(s) *18-24* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-17* is/are rejected.

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

8)☐ Claim(s) _____ 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 *24 October 2008* 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 *See Continuation Sheet*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continuation of Attachment(s) 3). Information Disclosure Statement(s) (PTO/SB/08), Paper No(s)/Mail Date :10/24/2008; 1/20/2009; 5/20/2009; 7/15/2009; 10/16/2009; 3/12/2010; 8/4/2010.

DETAILED ACTION

Election/Restrictions

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

I. **Claims 1-17**, drawn to method for operating an infusion system, classified in class 604, subclass 503.

II. **Claims 18-19**, drawn to a computer readable medium having computer executable instructions for executing a method for maintaining an infusion system, classified in class 700, subclass 1.

III. **Claims 20-23**, drawn to a computer readable medium having computer executable instructions for executing methods of calibrating and testing, classified in class 702, subclass 85.

IV. **Claim 24**, drawn to a method for purging a tubing circuit of an infusion system with air, classified in class 128, subclass 898.

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

Inventions I and II are related as process and apparatus for its practice. The inventions are distinct if it can be shown that either: (1) the process as claimed can be practiced by another and materially different apparatus or by hand, or (2) the apparatus as claimed can be used to practice another and materially different process. (MPEP § 806.05(e)). In this case, the apparatus can be used to practice another and materially different process such as performing the step of tracking a volume of the eluate that is diverted from the generator to the waste bottle.

Inventions I and III are related as process and apparatus for its practice. The inventions are distinct if it can be shown that either: (1) the process as claimed can be practiced by another and materially different apparatus or by hand, or (2) the apparatus as claimed can be used to practice another and materially different process. (MPEP § 806.05(e)). In this case, the apparatus can be used to practice another and materially different process such as performing the step of tracking a time from the end of the elution process.

Inventions II and IV are related as process and apparatus for its practice. The inventions are distinct if it can be shown that either: (1) the process as claimed can be practiced by another and materially different apparatus or by hand, or (2) the apparatus as claimed can be used to practice another and materially different process. (MPEP § 806.05(e)). In this case, the apparatus can be used to practice another and materially different process such as performing the steps for calibrating an activity detector of an infusion system.

Inventions III and IV are related as process and apparatus for its practice. The inventions are distinct if it can be shown that either: (1) the process as claimed can be practiced by another and materially different apparatus or by hand, or (2) the apparatus as claimed can be used to practice another and materially different process. (MPEP § 806.05(e)). In this case, the apparatus can be used to practice another and materially different process such as performing the steps for conducting a breakthrough test of a radioisotope generator of an infusion system.

Inventions I and IV are related as subcombinations disclosed as usable together in a single combination. The subcombinations are distinct if they do not overlap in scope and are not obvious variants, and if it is shown that at least one subcombination is separately usable. In the instant case, subcombination of Invention I has separate utility such as the steps for calibration and breakthrough testing. See MPEP § 806.05(d).

Inventions II and III are related as subcombinations disclosed as usable together in a single combination. The subcombinations are distinct if they do not overlap in scope and are not obvious variants, and if it is shown that at least one subcombination is separately usable. In the instant case, subcombination of Invention III has separate utility such as the steps for calibration and breakthrough testing. See MPEP § 806.05(d).

The examiner has required restriction between subcombinations usable together. 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.

2. 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/or examination burden if restriction were not required because at least the following reason(s) apply: the inventions have acquired a separate status in the art in view of their different classification, and the inventions require a different field of search (e.g., searching different classes /subclasses or electronic resources, or employing different search strategies or search queries).

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**.

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 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.

3. During a telephone conversation with Elizabeth Balden on July 16, 2010 a provisional election was made without traverse to prosecute the invention of **Group I, claims 1-17**. Affirmation of this election must be made by applicant in replying to this Office action. Claims 18-24 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

4. 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).

Claim Rejections - 35 USC § 112

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. **Claims 3, 5, and 9** are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. It is noted that the recitation of "the computer

may calculate" is indefinite as this recitation fails to require the performance of the subsequent limitation. Therefore, since the limitation following the recitation of "the computer may calculate" is not positively recited, no patentable weight would be given to the claim limitations of "the computer may calculate a breakthrough of the generator" (as per claim 3); "the computer may calculate a calibration coefficient for the infusion system based on the measured activity of the second sample and an activity of the eluate detected, during the second elution, by the activity detector of the system" (as per claim 5); and "the computer may calculate a calibration coefficient for the infusion system based on the measured activity and an activity of the eluate detected, during elution, by the activity detector of the system" (as per claim 9).

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

8. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

9. **Claims 1-3, 9, and 11** are rejected under 35 U.S.C. 103(a) as being unpatentable over Bergner (US Pat. No. 4,585,941).

Regarding **claim 1**, Bergner teaches a method for operating an infusion system, the system comprising: an eluant reservoir, a pump (64) coupled to the reservoir, an infusion tubing circuit (Fig. 1), a radioisotope generator (28), an activity detector (58), a waste bottle (42) and a computer (60, 62) including a computer interface, the infusion tubing circuit including an eluant line coupled to the pump and to the generator, a waste line coupled to the generator and to the waste bottle, and a patient line coupled to the generator (col. 3, line 23 until col. 4, line 53; Fig. 1), the method comprising:

> entering, into the computer, via the computer interface, a command to activate the pump in order to generate an eluate from a portion of a volume of eluant pumped through the generator, via an elution within the generator;

receiving an indication, from the computer, via the computer interface, that the elution is completed, when the pump has completed pumping the portion of the volume of eluant; and

receiving an indication, from the computer, via the computer interface, of time lapsed since the elution was completed (col. 4, line 7 until col. 6, line 19).

Regarding **claim 2**, Bergner teaches entering, into the computer (60, 62), via a computer interface, the volume of eluant contained in the reservoir, prior to the elution; and receiving, from the computer interface, an indication of a volume of eluant in the reservoir, based upon tracking the portion of the volume of eluant that is pumped from the reservoir (col. 4, line 4 until col. 5, line 32).

Regarding **claim 3**, Bergner teaches coupling the patient line of the infusion tubing circuit to a first shielded test vial, in order to collect a first sample of the eluate from the patient line during the elution; measuring an activity of the first sample; and entering into the computer, via the computer interface, the measured activity of the first sample and a time between completion of the elution and the measuring of the activity (col. 3, line 55 until col. 5, line 68).

Regarding **claim 9**, Bergner teaches coupling the patient line to a shielded test vial in order to collect a sample of the eluate from the patient line during the elution; measuring an activity of the sample; and entering into the computer, via the computer interface, the measured activity of the sample and a time between completion of the elution and measuring of the activity, so that the computer may calculate a calibration coefficient for the infusion system based on the measured activity and an activity of the

eluate detected, during elution, by the activity detector of the system (col. 6, line 21 until col. 9, line 48).

Regarding **claim 11**, Bergner teaches purging air from the patient line; coupling the patient line to a patient, after purging, in order to inject a dose of the eluate to the patient from the patient line; and receiving a report from the computer, upon completion of the elution, the report including a patient identification number and at least one quantification of the dose of the eluate (col. 3, line 63 until col. 4, line 6 and lines 36-53; col. 6, lines 1-19).

Claim Rejections - 35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

11. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of

the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

12. **Claims 10 and 13-16** are rejected under 35 U.S.C. 103(a) as being unpatentable over Bergner (US Pat. No. 4,585,941).

Regarding **claims 13-16**, Bergner teaches

receiving an indication, from the system, that the eluate is being diverted, from the generator, through the waste line of the infusion tubing circuit, when the pump is activated; and receiving an indication, from the system, that the eluate is being diverted from the generator, through the patient line of the infusion tubing circuit, when the pump is activated (col. 5, lines 8-24);

receiving an indication from the system that a peak bolus of radioactivity has been detected, in the eluate, by the activity detector (col. 7, line 1 until col. 9, line 47); and

wherein the system further comprises a light projector (104, 96, 100, 108; col. 9, line 49 until col. 10, line 11);

Although Bergner teaches the use of flashing and solid light projections from the light projector (106, 108) as alerting notifications (col. 11, line 46 until col. 12, line 29),

Bergner does not teach that the indication that the eluate is being diverted through the waste line is a flashing light projection, the indication that the eluate is being diverted through the patient line comprises a solid light projection from the light projector, and the indication that the peak bolus of radioactivity has been detected comprises a flashing light from the light projector. However, it would have been obvious to one of ordinary skill in the art at the time of the invention to modify the device of Bergner with the use of flashing and solid light projections as the indication that the eluate is being diverted through the waste line is a flashing light projection, the indication that the eluate is being diverted through the patient line comprises a solid light projection, and the indication that the peak bolus of radioactivity has been detected comprises a flashing light from the light projector, to provide a notification that alerts the user.

Regarding **claim 10**, Bergner teaches selecting a calibration procedure of the computer, via the computer interface, prior to entering the command to activate the pump (col. 4, line 26 until col. 9, line 48) but does not teach that the step of coupling the patient line to the shielded test vial is instructed by the computer interface, after selecting the calibration procedure. However, it would have been obvious to one of ordinary skill in the art at the time of the invention to modify the device of Bergner so that the controllers 60, 62 would notify the user to perform the step of coupling the patient line to the shielded test vial for an automated reminder to the user to increase the safety of the treatment.

13. **Claims 4-8** are rejected under 35 U.S.C. 103(a) as being unpatentable over Bergner (US Pat. No. 4,585,941) in view of Gerhart (US Pat. No. 3,774,036).

Regarding **claim 4**, Bergner does not teach selecting a breakthrough test procedure of the computer, via the computer interface, prior to entering the command to activate the pump; and wherein coupling the patient line to the first shielded test vial is instructed by the computer interface, after selecting the breakthrough test. However, it is noted that Gerhart teaches that breakthrough testing is performed to ensure the safety of a radioactive treatment dosage (col. 2, lines 27-39). Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to modify the method of Bergner with breakthrough test procedure prior to entering the command to activate the pump as taught by Gerhart to ensure the safety level of the treatment. Furthermore, it would have been obvious to one of ordinary skill in the art at the time of the invention to modify the device of Bergner so that the controllers 60, 62 would notify the user to perform the step of coupling the patient line to the shielded test vial for an automated reminder to the user to increase the safety of the treatment. Hence, the modified method of Bergner in view of Gerhart discloses selecting a breakthrough test procedure of the computer, via the computer interface, prior to entering the command to activate the pump; and wherein coupling the patient line to the first shielded test vial is instructed by the computer interface, after selecting the breakthrough test.

Regarding **claim 6**, the modified method of Bergner further teaches selecting a calibration procedure of the computer, via the computer interface, prior to entering the command to activate the pump for the second time; and wherein coupling the first new

patient line to the second shielded test vial is instructed by the computer interface, after selecting the calibration procedure, as set forth for claim 10 (col. 6, line 21 until col. 9, line 48).

Regarding **claims 5 and 7**, Bergner further teaches repeating the steps of claim 1, wherein the pump is activated a second time and a second elution takes place, in order to fill the second vial with a second sample of the eluate from the first new patient line; measuring an activity of the second sample; and entering into the computer, via the computer interface, the measured activity of the second sample and a time between completion of the second elution and the measuring of the activity of the second sample, so that the computer may calculate a calibration coefficient for the infusion system based on the measured activity of the second sample and an activity of the eluate detected, during the second elution, by the activity detector of the system. Bergner also teaches purging air from the second patient line; and repeating the steps of claim 1, wherein the pump is activated a third time and a third elution takes place, in order to inject a dose of the eluate to the patient from the second patient line (col. 6, line 21 until col. 9, line 48).

Regarding **claim 8**, Bergner further teaches receiving a report from the computer, upon completion of the third elution, the report including a patient identification number and at least one quantification of the dose of the eluate (col. 5, lines 41-68 and col. 9, line 49 until col. 10, line 11).

14. **Claim 12** is rejected under 35 U.S.C. 103(a) as being unpatentable over Bergner (US Pat. No. 4,585,941) in view of Graves et al (US Pat. No. 7,163,031 B2).

Regarding **claim 12**, Bergner teaches the use of displays but does not teach a touch-activated display screen. However, it is noted that Graves et al teaches the use of a touch screen electronic display screen for inputting and outputting into a computer for a radiopharmaceutical delivery device (col. 4, line 53 until col. 5, line 2). Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to modify the device of Bergner with using a system that has a touch-activated display screen as disclosed by Graves et al to consolidate the number of components required for inputting and outputting commands and notifications in an infusion device.

15. **Claim 17** is rejected under 35 U.S.C. 103(a) as being unpatentable over Bergner (US Pat. No. 4,585,941) in view of Agarwal et al (US Pat. No. 4,096,859).

Regarding **claim 17**, Bergner teaches the use of a waste bottle and tracking the waste level to determine the trigger point (col. 10, lines 12-68) but does not explicitly teach entering, into the computer, via the computer interface, a command to set a waste bottle level indicator to zero, when the waste bottle is empty and prior to entering the command to activate the pump; and receiving, from the computer, via the computer interface, an indication that the waste bottle needs to be emptied, based upon the computer tracking a volume of the eluate that is diverted, from the generator, through the waste line of the infusion tubing circuit. However, Agarwal et al teaches a medical delivery device with a waste container in which a controller tracks the waste level to

alert the user to empty the waste container (col. 5, line 38 until col. 6, line 36). It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the method of Bergner with the steps of setting initial waste bottle level to zero when the bottle is empty and tracking the waste bottle level so that an alert is given to the user that the waste bottle is full and needs to be emptied as taught by Agarwal et al, to prevent overflowing of waste from the waste bottle.

It is noted that the modified method of Bergner and Agarwal et al teaches entering, into the computer, via the computer interface, a command to set a waste bottle level indicator to zero, when the waste bottle is empty and prior to entering the command to activate the pump; and receiving, from the computer, via the computer interface, an indication that the waste bottle needs to be emptied, based upon the computer tracking a volume of the eluate that is diverted, from the generator, through the waste line of the infusion tubing circuit

Conclusion

16. 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
09/28/2010

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

Notice of References Cited	Application/Control No. 12/137,364	Applicant(s)/Patent Under Reexamination HIDEM ET AL.	
	Examiner JENNA ZHANG	Art Unit 3763	Page 1 of 1

U.S. PATENT DOCUMENTS

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Name	Classification
*	A	US-4,096,859	06-1978	Agarwal et al.	604/28
	B	US-			
	C	US-			
	D	US-			
	E	US-			
	F	US-			
	G	US-			
	H	US-			
	I	US-			
	J	US-			
	K	US-			
	L	US-			
	M	US-			

FOREIGN PATENT DOCUMENTS

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Country	Name	Classification
	N					
	O					
	P					
	Q					
	R					
	S					
	T					

NON-PATENT DOCUMENTS

*		Include as applicable: Author, Title Date, Publisher, Edition or Volume, Pertinent Pages)
	U	
	V	
	W	
	X	

*A copy of this reference is not being furnished with this Office action. (See MPEP § 707.05(a).)
Dates in MM-YYYY format are publication dates. Classifications may be US or foreign.

Index of Claims	Application/Control No.	Applicant(s)/Patent Under Reexamination
	12137364	HIDEM ET AL.
	Examiner	Art Unit
	JENNA ZHANG	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	09/27/2010								
	1	✓								
	2	✓								
	3	✓								
	4	✓								
	5	✓								
	6	✓								
	7	✓								
	8	✓								
	9	✓								
	10	✓								
	11	✓								
	12	✓								
	13	✓								
	14	✓								
	15	✓								
	16	✓								
	17	✓								
	18	✓								
	19	✓								
	20	✓								
	21	✓								
	22	✓								
	23	✓								
	24	✓								

Search Notes	Application/Control No.	Applicant(s)/Patent Under Reexamination
	12137364	HIDEM ET AL.
	Examiner	Art Unit
	JENNA ZHANG	3763

SEARCHED

Class	Subclass	Date	Examiner
604	236, and 65-67 with text	9/27/2010	JZ
312	209	9/27/2010	JZ
600	5	9/27/2010	JZ
600	4, and 600/431, 1-8, and 301 with text	9/29/2010	JZ

SEARCH NOTES

Search Notes	Date	Examiner
Inventor Search	9/27/2010	JZ
Assignee Search	9/27/2010	JZ
Consulted Chris Koharski	9/28/2010	JZ
EAST Search	9/27-29/2010	JZ

INTERFERENCE SEARCH

Class	Subclass	Date	Examiner

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

BIB DATA SHEET

CONFIRMATION NO. 7377

SERIAL NUMBER	FILING or 371(c) DATE RULE	CLASS	GROUP ART UNIT	ATTORNEY DOCKET NO.
12/137,364	06/11/2008	~~345~~ 604	3763	56782.1.7

APPLICANTS

Stephen E. Hidem, Plymouth, MN;
Aaron M. Fontaine, Fridley, MN;
Janet L. Gelbach, New Albany, IN;
Patrick M. McDonald, Omaha, NE;
Kathryn M. Hunter, Knoxville, TN;

**** CONTINUING DATA ***************************

**** FOREIGN APPLICATIONS ***************************

**** IF REQUIRED, FOREIGN FILING LICENSE GRANTED ****
06/23/2008

Foreign Priority claimed	35 USC 119(a-d) conditions met	Verified and Acknowledged	Met after Allowance	STATE OR COUNTRY	SHEETS DRAWINGS	TOTAL CLAIMS	INDEPENDENT CLAIMS
☐ Yes ☑ No	☐ Yes ☑ No	/JENNA ZHANG/ (Examiner's Signature)	☐ (Initials)	MN	23	24	5

ADDRESS

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

TITLE

INFUSION SYSTEMS INCLUDING COMPUTER-FACILITATED MAINTENANCE AND/OR OPERATION AND METHODS OF USE

FILING FEE RECEIVED		
1780	FEES: Authority has been given in Paper No._____ to charge/credit DEPOSIT ACCOUNT No._____ for following:	☐ All Fees ☐ 1.16 Fees (Filing) ☐ 1.17 Fees (Processing Ext. of time) ☐ 1.18 Fees (Issue) ☐ Other _____ ☐ Credit

BIB (Rev. 05/07).

PTO/SB/08a (03-08)
Approved for use through 06/30/2008. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Not for submission under 37 CFR 1.99)

Application Number	12137364
Filing Date	2008-06-11
First Named Inventor	Stephen E. Hidem
Art Unit	2628
Examiner Name	
Attorney Docket Number	56782.1.7

U.S.PATENTS Remove

Examiner Initial*	Cite No	Patent Number	Kind Code[1]	Issue Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1					

If you wish to add additional U.S. Patent citation information please click the Add button. Add

U.S.PATENT APPLICATION PUBLICATIONS Remove

Examiner Initial*	Cite No	Publication Number	Kind Code[1]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1					

If you wish to add additional U.S. Published Application citation information please click the Add button. Add

FOREIGN PATENT DOCUMENTS Remove

Examiner Initial*	Cite No	Foreign Document Number[3]	Country Code[2] i	Kind Code[4]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear	T[5]
	1	2008140351	WO	A1	2008-11-20			☒

If you wish to add additional Foreign Patent Document citation information please click the Add button Add

NON-PATENT LITERATURE DOCUMENTS Remove

Examiner Initials*	Cite No	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc), date, pages(s), volume-issue number(s), publisher, city and/or country where published.	T[5]

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /J.Z./

Receipt date: 01/20/2009	Application Number	12137364	12137364 - GAU: 3763
INFORMATION DISCLOSURE STATEMENT BY APPLICANT (**Not for submission under 37 CFR 1.99)**	Filing Date	2008-06-11	
	First Named Inventor	Stephen E. Hidem	
	Art Unit	2628	
	Examiner Name		
	Attorney Docket Number	56782.1.7	

	1		☐

If you wish to add additional non-patent literature document citation information please click the Add button Add

EXAMINER SIGNATURE

Examiner Signature	/Jenna Zhang/	Date Considered	09/27/2010

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through a citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

[1] See Kind Codes of USPTO Patent Documents at www.USPTO.GOV or MPEP 901.04. [2] Enter office that issued the document, by the two-letter code (WIPO Standard ST.3). [3] For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. [4] Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. [5] Applicant is to place a check mark here if English language translation is attached.

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /J.Z./

PTO/SB/08a (01-10)
Approved for use through 07/31/2012. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Not for submission under 37 CFR 1.99)

Application Number	12137364
Filing Date	2008-06-11
First Named Inventor	Stephen E. Hidem
Art Unit	3763
Examiner Name	Jenna Zhang
Attorney Docket Number	56782.1.7

U.S.PATENTS

Examiner Initial*	Cite No	Patent Number	Kind Code[1]	Issue Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1	5590648		1997-01-07	Mitchell et al.	

If you wish to add additional U.S. Patent citation information please click the Add button.

U.S.PATENT APPLICATION PUBLICATIONS

Examiner Initial*	Cite No	Publication Number	Kind Code[1]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1	20070213848		2007-09-13	DeKemp et al.	
	2	20080093564		2008-04-24	Tartaglia et al.	
	3	20080242915		2008-10-02	Jackson et al.	

If you wish to add additional U.S. Published Application citation information please click the Add button.

FOREIGN PATENT DOCUMENTS

Examiner Initial*	Cite No	Foreign Document Number[3]	Country Code[2] ¡	Kind Code[4]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear	T[5]
	1	9615337	WO		1996-05-23	Nilsson		☐

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /J.Z./

Receipt date: 03/12/2010	Application Number	12137364 12137364 - GAU: 3763
INFORMATION DISCLOSURE STATEMENT BY APPLICANT (**Not for submission under 37 CFR 1.99**)	Filing Date	2008-06-11
	First Named Inventor	Stephen E. Hidem
	Art Unit	3763
	Examiner Name	Jenna Zhang
	Attorney Docket Number	56782.1.7

	2	02096335	WO		2002-12-05	Hill ROM Services		☐
	3	2006074473	WO		2006-07-13	Atlas Systems		☐
	4	2008028165	WO		2008-03-06	Catholic Health		☐

If you wish to add additional Foreign Patent Document citation information please click the Add button

NON-PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc), date, pages(s), volume-issue number(s), publisher, city and/or country where published.	T[5]
	1	NEIL J. EPSTEIN, et al., "A Rb82 infusion system for quantitative perfusion imaging with 3D PET" Applied Radiation and Isotopes, vol. 60, 9 February 2004, pages 921-927, XP002557544 DOI:10, 1016/j. apradiso.2004.02.002	☐
	2	R. KLEIN, et al., "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, pages 659-673, XP002557545 DOI:10, 1088/0031-9155/52/3/009	☐
	3	International Search Report and Written Opinion, dated 02-25-2010 for PCT Application No. PCT/US2009/047027, 22 pages	☐
	4	International Search Report and Written Opinion, dated 02-17-2010 for PCT Application No. PCT/US2009/047030, 17 pages	☐
	5	International Search Report and Written Opinion, dated 03-01-2010 for PCT Application No. PCT/US2009/047031, 20 pages	☐
	6	International Search Report and Written Opinion, dated 02-25-2010 for PCT Application No. PCT/US2009/047034, 15 pages	☐

If you wish to add additional non-patent literature document citation information please click the Add button

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /J.Z./

Receipt date: 03/12/2010	Application Number	12137364 12137364 - GAU: 3763
INFORMATION DISCLOSURE STATEMENT BY APPLICANT (**Not for submission under 37 CFR 1.99)**	Filing Date	2008-06-11
	First Named Inventor	Stephen E. Hidem
	Art Unit	3763
	Examiner Name	Jenna Zhang
	Attorney Docket Number	56782.1.7

EXAMINER SIGNATURE			
Examiner Signature	/Jenna Zhang/	Date Considered	09/27/2010

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through a citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

[1] See Kind Codes of USPTO Patent Documents at www.USPTO.GOV or MPEP 901.04. [2] Enter office that issued the document, by the two-letter code (WIPO Standard ST.3). [3] For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. [4] Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. [5] Applicant is to place a check mark here if English language translation is attached.

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /J.Z./

PTO/SB/08a (03-08)
Approved for use through 06/30/2008. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Not for submission under 37 CFR 1.99)

Application Number	12137364
Filing Date	2008-06-11
First Named Inventor	Stephen E. Hidem
Art Unit	2628
Examiner Name	
Attorney Docket Number	56782.1.7

U.S.PATENTS Remove

Examiner Initial*	Cite No	Patent Number	Kind Code[1]	Issue Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1					

If you wish to add additional U.S. Patent citation information please click the Add button. Add

U.S.PATENT APPLICATION PUBLICATIONS Remove

Examiner Initial*	Cite No	Publication Number	Kind Code[1]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1					

If you wish to add additional U.S. Published Application citation information please click the Add button. Add

FOREIGN PATENT DOCUMENTS Remove

Examiner Initial*	Cite No	Foreign Document Number[3]	Country Code[2] i	Kind Code[4]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear	T[5]
	1	2007071022	WO	A1	2007-06-28	Robert A. Dekemp		☐
	2	2007104133	WO	A1	2007-09-20	Robert A. Dekemp		☐

If you wish to add additional Foreign Patent Document citation information please click the Add button Add

NON-PATENT LITERATURE DOCUMENTS Remove

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /J.Z./

Receipt date: 05/20/2009	Application Number	12137364 12137364 - GAU: 3763
INFORMATION DISCLOSURE STATEMENT BY APPLICANT (**Not for submission under 37 CFR 1.99)**	Filing Date	2008-06-11
	First Named Inventor	Stephen E. Hidem
	Art Unit	2628
	Examiner Name	
	Attorney Docket Number	56782.1.7

Examiner Initials*	Cite No	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc), date, pages(s), volume-issue number(s), publisher, city and/or country where published.	T[5]
	1		☐
	2		☐
	3		☐

If you wish to add additional non-patent literature document citation information please click the Add button Add

EXAMINER SIGNATURE

Examiner Signature	/Jenna Zhang/	Date Considered	09/27/2010

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through a citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

[1] See Kind Codes of USPTO Patent Documents at www.USPTO.GOV or MPEP 901.04. [2] Enter office that issued the document, by the two-letter code (WIPO Standard ST.3). [3] For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. [4] Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. [5] Applicant is to place a check mark here if English language translation is attached.

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /J.Z./

INFORMATION DISCLOSURE STATEMENT BY APPLICANT
(Not for submission under 37 CFR 1.99)

Application Number	12137364
Filing Date	2008-06-11
First Named Inventor	Stephen E. Hidem
Art Unit	3737
Examiner Name	
Attorney Docket Number	56782.1.7

U.S.PATENTS Remove

Examiner Initial*	Cite No	Patent Number	Kind Code[1]	Issue Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1	3774036		1973-11-20	Gerhart	
	2	3997784		1976-12-14	Picunko, et al.	
	3	4286169		1981-08-25	Rossem	
	4	4625118		1986-11-25	Kriwetz et al.	
	5	4679142		1987-07-07	Lee	
	6	4755679		1988-07-05	Wong	
	7	4853546		1989-08-01	Abe et al.	
	8	5039863		1991-08-13	Matsuno et al.	

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /J.Z./

Receipt date: 07/15/2009	Application Number	12137364	12137364 - GAU: 3763
INFORMATION DISCLOSURE STATEMENT BY APPLICANT (**Not for submission under 37 CFR 1.99)**	Filing Date	2008-06-11	
	First Named Inventor	Stephen E. Hidem	
	Art Unit	3737	
	Examiner Name		
	Attorney Docket Number	56782.1.7	

	9	5258906		1993-11-02	Kroll et al.	
	10	5274239		1993-12-28	Lane et al.	
	11	5475232		1995-12-12	Powers et al.	
	12	5485831		1996-01-23	Holdsworth et al.	
	13	5739508		1998-04-14	Uber, III	
	14	5840026		1998-11-24	Uber, III et al.	
	15	5885216		1999-03-23	Evans, III et al.	
	16	6157036		2000-12-05	Whiting et al.	
	17	6442418	B1	2002-08-27	Evans, III et al.	
	18	6626862	B1	2003-09-30	Duchon et al.	
	19	6767319	B2	2004-07-27	Reilly et al.	

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /J.Z./

Receipt date: 07/15/2009	Application Number	12137364	12137364 - GAU: 3763
INFORMATION DISCLOSURE STATEMENT BY APPLICANT (**Not for submission under 37 CFR 1.99)**	Filing Date	2008-06-11	
	First Named Inventor	Stephen E. Hidem	
	Art Unit	3737	
	Examiner Name		
	Attorney Docket Number	56782.1.7	

	20	6901283	B2	2005-05-31	Evans, III et al.	
	21	7169135	B2	2007-01-30	Duchon et al.	
	22	7256888	B2	2007-08-14	Staehr et al.	
	23	7413123	B2	2008-08-19	Ortenzi	

If you wish to add additional U.S. Patent citation information please click the Add button. Add

U.S.PATENT APPLICATION PUBLICATIONS Remove

Examiner Initial*	Cite No	Publication Number	Kind Code[1]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1	20070282263	A1	2007-12-06	Kalafut et al.	
	2	20080071219	A1	2008-03-20	Rhinehart et al.	
	3	20080166292	A1	2008-07-10	Levin et al.	

If you wish to add additional U.S. Published Application citation information please click the Add button. Add

FOREIGN PATENT DOCUMENTS Remove

Examiner Initial*	Cite No	Foreign Document Number[3]	Country Code[2] i	Kind Code[4]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear	T[5]

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /J.Z./

Receipt date: 07/15/2009	Application Number	12137364	12137364 - GAU: 3763
INFORMATION DISCLOSURE STATEMENT BY APPLICANT (**Not for submission under 37 CFR 1.99)**	Filing Date	2008-06-11	
	First Named Inventor	Stephen E. Hidem	
	Art Unit	3737	
	Examiner Name		
	Attorney Docket Number	56782.1.7	

	1	2006007750	WO	A1	2006-01-26	UNIVERSITÄT ZÜRICH		☐

If you wish to add additional Foreign Patent Document citation information please click the Add button Add

NON-PATENT LITERATURE DOCUMENTS Remove

Examiner Initials*	Cite No	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc), date, pages(s), volume-issue number(s), publisher, city and/or country where published.	T[5]
	1		☐

If you wish to add additional non-patent literature document citation information please click the Add button Add

EXAMINER SIGNATURE

Examiner Signature	/Jenna Zhang/	Date Considered	09/27/2010

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through a citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

[1] See Kind Codes of USPTO Patent Documents at www.USPTO.GOV or MPEP 901.04. [2] Enter office that issued the document, by the two-letter code (WIPO Standard ST.3). [3] For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. [4] Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. [5] Applicant is to place a check mark here if English language translation is attached.

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /J.Z./

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Not for submission under 37 CFR 1.99)

Application Number	12137364
Filing Date	2008-06-11
First Named Inventor	Stephen E. Hidem
Art Unit	3763
Examiner Name	Jenna Zhang
Attorney Docket Number	56782.1.7

U.S.PATENTS Remove

Examiner Initial*	Cite No	Patent Number	Kind Code[1]	Issue Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1	6908598		2005-06-21	Sylvester	
	2	7163031		2007-01-16	Graves et al.	
	3	7476377		2009-01-13	Moller	
	4	7504646		2009-03-17	Balestracci	

If you wish to add additional U.S. Patent citation information please click the Add button. Add

U.S.PATENT APPLICATION PUBLICATIONS Remove

Examiner Initial*	Cite No	Publication Number	Kind Code[1]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1	20070232980		2007-10-04	Felt	
	2	20090312635		2009-12-17	Shimchuk	

If you wish to add additional U.S. Published Application citation information please click the Add button. Add

FOREIGN PATENT DOCUMENTS Remove

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /J.Z./

Receipt date: 08/04/2010

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Not for submission under 37 CFR 1.99)

Application Number	12137364 12137364 - GAU: 3763
Filing Date	2008-06-11
First Named Inventor	Stephen E. Hidem
Art Unit	3763
Examiner Name	Jenna Zhang
Attorney Docket Number	56782.1.7

Examiner Initial*	Cite No	Foreign Document Number[3]	Country Code[2]	Kind Code[4]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear	T[5]
	1	2004059661	WO		2004-07-15	Lynntech, Inc.		☐
	2	2006026603	WO		2006-03-09	Bracco Diagnostics		☐
	3	2006135374	WO		2006-12-21	Lynntech Inc.		☐
	4	2008140351	WO		2008-11-20	Obshchestvo		☐
	5	2010020596	WO		2010-02-25	Stichting Jeroen Bosch		☐

If you wish to add additional Foreign Patent Document citation information please click the Add button Add

NON-PATENT LITERATURE DOCUMENTS Remove

Examiner Initials*	Cite No	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc), date, pages(s), volume-issue number(s), publisher, city and/or country where published.	T[5]
	1		☐

If you wish to add additional non-patent literature document citation information please click the Add button Add

EXAMINER SIGNATURE

Examiner Signature	/Jenna Zhang/	Date Considered	09/27/2010

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through a citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /J.Z./

Receipt date: 08/04/2010	Application Number	12137364 12137364 - GAU: 3763
INFORMATION DISCLOSURE STATEMENT BY APPLICANT (**Not for submission under 37 CFR 1.99)**	Filing Date	2008-06-11
	First Named Inventor	Stephen E. Hidem
	Art Unit	3763
	Examiner Name	Jenna Zhang
	Attorney Docket Number	56782.1.7

[1] See Kind Codes of USPTO Patent Documents at www.USPTO.GOV or MPEP 901.04. [2] Enter office that issued the document, by the two-letter code (WIPO Standard ST.3). [3] For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. [4] Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. [5] Applicant is to place a check mark here if English language translation is attached.

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /J.Z./

PTO/SB/08a (07-09)
Approved for use through 07/31/2012. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Not for submission under 37 CFR 1.99)

Application Number	12137364
Filing Date	2008-06-11
First Named Inventor	Stephen E. Hidem
Art Unit	3737
Examiner Name	
Attorney Docket Number	56782.1.7

U.S.PATENTS Remove

Examiner Initial*	Cite No	Patent Number	Kind Code[1]	Issue Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1					

If you wish to add additional U.S. Patent citation information please click the Add button. Add

U.S.PATENT APPLICATION PUBLICATIONS Remove

Examiner Initial*	Cite No	Publication Number	Kind Code[1]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1	20030004463	A1	2003-01-02	Reilly	
	2	20070140958	A1	2007-06-21	DeKemp	

If you wish to add additional U.S. Published Application citation information please click the Add button. Add

FOREIGN PATENT DOCUMENTS Remove

Examiner Initial*	Cite No	Foreign Document Number[3]	Country Code[2] i	Kind Code[4]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear	T[5]
	1	9956117	WO		1999-11-04	General Hospital Corp		☐
	2	20050002971	WO		2005-01-13	Iphase Technologies		☐

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /J.Z./

Receipt date: 10/16/2009	Application Number	12137364	12137364 - GAU: 3763
INFORMATION DISCLOSURE STATEMENT BY APPLICANT (**Not for submission under 37 CFR 1.99)**	Filing Date	2008-06-11	
	First Named Inventor	Stephen E. Hidem	
	Art Unit	3737	
	Examiner Name		
	Attorney Docket Number	56782.1.7	

	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		☐
	9	2006325826	JP		2006-12-07	S.D. Giken		☐
	10	2000350783	JP		2000-12-19	Sumitomo Heavy Ind Ltd		☐

If you wish to add additional Foreign Patent Document citation information please click the Add button Add

NON-PATENT LITERATURE DOCUMENTS Remove

Examiner Initials*	Cite No	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc), date, pages(s), volume-issue number(s), publisher, city and/or country where published.	T[5]
	1		☐

If you wish to add additional non-patent literature document citation information please click the Add button Add

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /J.Z./

Receipt date: 10/16/2009	Application Number	12137364 12137364 - GAU: 3763
INFORMATION DISCLOSURE STATEMENT BY APPLICANT (**Not for submission under 37 CFR 1.99)**	Filing Date	2008-06-11
	First Named Inventor	Stephen E. Hidem
	Art Unit	3737
	Examiner Name	
	Attorney Docket Number	56782.1.7

EXAMINER SIGNATURE			
Examiner Signature	/Jenna Zhang/	Date Considered	09/27/2010

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through a citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

[1] See Kind Codes of USPTO Patent Documents at www.USPTO.GOV or MPEP 901.04. [2] Enter office that issued the document, by the two-letter code (WIPO Standard ST.3). [3] For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. [4] Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. [5] Applicant is to place a check mark here if English language translation is attached.

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /J.Z./

PTO/SB/08a (03-08)
Approved for use through 06/30/2008. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Not for submission under 37 CFR 1.99)

Application Number	12137364
Filing Date	2008-06-11
First Named Inventor	Stephen E. Hidem
Art Unit	2628
Examiner Name	
Attorney Docket Number	56782.1.7

U.S.PATENTS Remove

Examiner Initial*	Cite No	Patent Number	Kind Code[1]	Issue Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1	3710118		1973-01-09	Holgate et al.	
	2	4562829		1986-01-07	Bergner	
	3	4585009		1986-04-29	Barker et al.	
	4	4585941		1986-04-29	Bergner	
	5	6870175	B2	2005-03-22	Dell et al.	
	6	7204797	B2	2007-04-17	Reilly et al.	

If you wish to add additional U.S. Patent citation information please click the Add button. Add

U.S.PATENT APPLICATION PUBLICATIONS Remove

Examiner Initial*	Cite No	Publication Number	Kind Code[1]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /J.Z./

Receipt date: 10/24/2008	Application Number	12137364	12137364 - GAU: 3763
INFORMATION DISCLOSURE STATEMENT BY APPLICANT (**Not for submission under 37 CFR 1.99)**	Filing Date	2008-06-11	
	First Named Inventor	Stephen E. Hidem	
	Art Unit	2628	
	Examiner Name		
	Attorney Docket Number	56782.1.7	

	1	20050278066	A1	2005-12-15	Graves et al.	

If you wish to add additional U.S. Published Application citation information please click the Add button. Add

FOREIGN PATENT DOCUMENTS Remove

Examiner Initial*	Cite No	Foreign Document Number[3]	Country Code[2] i	Kind Code[4]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear	T[5]
	1	0102121	EP	A1	1984-03-07	DeJong, Rudolf et all		☐
	2	2007016170	WO	A1	2007-02-08	Fago		☐
	3	2007030249	WO	A2	2007-03-15	Gibson		☐
	4	2007149108	WO	A2	2007-12-27	Pollard		☐

If you wish to add additional Foreign Patent Document citation information please click the Add button Add

NON-PATENT LITERATURE DOCUMENTS Remove

Examiner Initials*	Cite No	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc), date, pages(s), volume-issue number(s), publisher, city and/or country where published.	T[5]
	1	BRACCO Brochure, "Rubidium 82 Infusion System, Easy to Operate...Automated...Complete", (C)Bracco Diagnostics, Inc., 0605-002NA, June 2001. (2 pages)	☐
	2	BRACCO, "Cardio-Gen82(R) Infusion System User's Guide", pages 1-42	☐

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /J.Z./

Receipt date: 10/24/2008	Application Number	12137364 12137364 - GAU: 3763
INFORMATION DISCLOSURE STATEMENT BY APPLICANT (**Not for submission under 37 CFR 1.99**)	Filing Date	2008-06-11
	First Named Inventor	Stephen E. Hidem
	Art Unit	2628
	Examiner Name	
	Attorney Docket Number	56782.1.7

	3	IMAGING TECHNOLOGY NEWS, web exclusive: "FDG-PET Injector Thrusts New Life into Molecular Imaging", April 2008, 2 pages.	☐

If you wish to add additional non-patent literature document citation information please click the Add button Add

EXAMINER SIGNATURE

Examiner Signature	/Jenna Zhang/	Date Considered	09/27/2010

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through a citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

[1] See Kind Codes of USPTO Patent Documents at www.USPTO.GOV or MPEP 901.04. [2] Enter office that issued the document, by the two-letter code (WIPO Standard ST.3). [3] For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. [4] Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. [5] Applicant is to place a check mark here if English language translation is attached.

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /J.Z./

EAST Search History

EAST Search History (Prior Art)

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
S35	22	("4401108" | "4409966" | "4472403" | "4562829" | "4585009" | "4883459" | "5383858" | "5472403" | "5514071" | "5520653" | "5918443" | "5927351" | "5947890" | "6267717" | "6450936" | "6471674" | "6520930").PN. OR ("6767319").URPN.	US-PGPUB; USPAT; USOCR	OR	ON	2010/05/06 15:44
S36	23	("3866608" | "3918453" | "4781707" | "5055198" | "5378227" | "5407425"). PN. OR ("5656027"). URPN.	US-PGPUB; USPAT; USOCR	OR	ON	2010/05/06 15:54
S37	91	("2804075" | "3896733" | "3965896" | "3993067" | "4006745" | "4014329" | "4033345" | "4047526" | "4631050" | "4744785" | "4772256" | "4796644" | "4798578" | "4867738" | "4874359" | "4886487" | "4898572" | "4976682"). PN. OR ("5055198"). URPN.	US-PGPUB; USPAT; USOCR	OR	ON	2010/05/06 15:57
S50	10	("3996017" | "4911807" | "5193990" | "5260028" | "5372695" | "5989423" | "6325775" | "6582386" | "6605223" | "6712963"). PN. OR ("7001513"). URPN.	US-PGPUB; USPAT; USOCR	OR	ON	2010/05/06 17:31
S78	2	(stephen near3 hidem). in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2010/09/27 19:21
S79	1	(aaron near3 fontaine). in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2010/09/27 19:21

S80	1	(janet near3 gelbach).in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2010/09/27 19:21
S81	74	(patrick near3 mcdonald).in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2010/09/27 19:21
S82	1	(kathryn near3 hunter).in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2010/09/27 19:22
S83	75	(S78 S79 S80 S81 S82)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2010/09/27 19:22
S84	1	(S78 S79 S80 S81 S82) and (radioisotope radioactive PET (positron adj emission adj tomography) radiation rubidium strontium)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2010/09/27 19:23
S85	46	("20030004463" | "20050278066" | "20070213848" | "20070140958" | "20070232980" | "20070282263" | "20080093564" | "20080242915" | "20080071219" | "20080166292" | "20090312635" | "3710118" | "3774036" | "3997784" | "4286169" | "4562829" | "4585009" | "4585941" | "4625118" | "4679142" | "4755679" | "4853546" | "5590648" | "5039863" | "5258906" | "5274239" | "5475232" | "5485831" | "5739508" | "5840026" | "5885216" | "6157036" | "6442418" | "6626862" | "6767319" | "6870175" | "6901283" | "6908598" | "7163031" |	US-PGPUB; USPAT; USOCR	OR	ON	2010/09/27 19:35

		"7169135" | "7204797" | "7256888" | "7413123" | "7476377" | "7504646").PN.				
S86	128	(BRACCO near3 DIAGNOSTICS).as.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2010/09/27 19:37
S87	33	S86 and (radioisotope radioactive PET (positron adj emission adj tomography) radiation rubidium strontium)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2010/09/27 19:37
S88	68	(S87 S85) and (command $3 activat$3 enter$3 receiv$3 indicat$3 tim$3 select$3 measur$4 test$3 purg$3 calibrat$3)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2010/09/27 19:41
S89	147150	("128" "600" "604" "606" "607" "623" "312" "345" "700" "702" "705" "715" "417" "514").clas. and (radioisotope radioactive PET (positron adj emission adj tomography) radiation rubidium strontium)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2010/09/27 19:44
S90	145900	S89 and (command$3 activat$3 enter$3 receiv $3 indicat$3 tim$3 select $3 measur$4 test$3 purg $3 calibrat$3)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2010/09/27 19:44
S91	149	S89 and (command$3 activat$3 enter$3 receiv $3 indicat$3 tim$3 select $3 measur$4 test$3 purg $3 calibrat$3)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	AND	ON	2010/09/27 19:44
S92	282	S89 and (command$3 activat$3 enter$3 receiv $3 indicat$3 tim$3 select $3 measur$4 test$3 purg $3 (calibrat$3 or initial$3 or initiat$3))	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	AND	ON	2010/09/27 19:45

S93	73	S89 and (command$3 enter$3 receiv$3 indicat $3 tim$3 (select$3 or choos$3) measur$4 test $3 ((purg$3 or remov$3 or releas$3) near3 (air gas)) (calibrat$3 or initial $3 or activat$3 or initiat $3))	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	AND	ON	2010/09/27 19:46
S94	961	312/209.ccls.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2010/09/27 19:54
S95	300	604/236.ccls.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2010/09/27 19:54
S96	301	604/65,66,67.ccls. and (radioisotope radioactive PET (positron adj emission adj tomography) radiation rubidium strontium)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2010/09/27 19:54
S97	87	600/5.ccls.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2010/09/27 19:55
S98	174	(radio$1pharmaceutical $1) and "604".clas.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2010/09/27 19:56
S99	11522	"604".clas. and (radioisotope radioactive PET (positron adj emission adj tomography) radiation rubidium strontium radio $1pharmaceutic$4)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2010/09/28 10:38

S101	23	S99 and (command$3 enter$3 receiv$3 indicat $3 tim$3 (select$3 or choos$3) measur$4 test $3 ((purg$3 or remov$3 or releas$3) near3 (air gas)) (calibrat$3 or initial $3 or activat$3 or initiat $3))	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	AND	ON	2010/09/28 10:39
S103	23	S99 and (command$3 enter$3 receiv$3 (indicat $3 or flash$3 or blink$3 or light) tim$3 (select$3 or choos$3) measur$4 test$3 ((purg$3 or remov $3 or releas$3) near3 (air gas)) (calibrat$3 or initial $3 or activat$3 or initiat $3))	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	AND	ON	2010/09/28 12:28
S104	1786	"604".clas. and (radioisotope radioactive radio$1pharmaceutic$4)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2010/09/28 12:29
S105	0	S104 and (command$3 enter$3 receiv$3 (indicat $3 or flash$3 or blink$3 or light) tim$3 (select$3 or choos$3) measur$4 test$3 ((purg$3 or remov $3 or releas$3) near3 (air gas)) (calibrat$3 or initial $3 or activat$3 or initiat $3))	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	AND	ON	2010/09/28 12:29
S106	133999	(radioisotope radioactive radio$1pharmaceutic$4) and (medica$4 medicin$2 therapy therapeutic$5 diagnos$4 drug)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2010/09/28 12:31
S110	5	("20060151048" "20030216609" "20030004463" "20050238576" "2010030009" "20080177126").pn.	US-PGPUB; USPAT; USOCR	OR	ON	2010/09/28 12:47
S111	8	("20080242915" "6773673" "4562829" "20080093564" "20080224065" "20030216609" "20030004463" "20050238576").pn.	US-PGPUB; USPAT; USOCR	OR	ON	2010/09/28 12:50

S112	4	("4585941" "4585009" "20070140958" "20070213848").pn.	US-PGPUB; USPAT; USOCR	OR	ON	2010/09/28 12:52
S113	14	S110 S111 S112	US-PGPUB; USPAT; USOCR	OR	ON	2010/09/28 12:53
S114	6	("5168901" | "5223434" | "5326532" | "5468355" | "5482865" | "5514071").PN. OR ("6773673").URPN.	US-PGPUB; USPAT; USOCR	OR	ON	2010/09/28 13:12
S115	42	("3528407" | "3827427" | "4091287").PN. OR ("4585941").URPN.	US-PGPUB; USPAT; USOCR	OR	ON	2010/09/28 13:12
S116	30	("4006736").PN. OR ("4585009").URPN.	US-PGPUB; USPAT; USOCR	OR	ON	2010/09/28 13:12
S117	14	("4202345").PN. OR ("4562829").URPN.	US-PGPUB; USPAT; USOCR	OR	ON	2010/09/28 13:12
S118	77	S114 S115 S116 S117	US-PGPUB; USPAT; USOCR	OR	ON	2010/09/28 13:12
S120	5	("20060151048" "20030216609" "20030004463" "20050238576" "2010030009" "20080177126").pn.	US-PGPUB; USPAT; USOCR	OR	ON	2010/09/28 17:24
S121	8	("20080242915" "6773673" "4562829" "20080093564" "20080224065" "20030216609" "20030004463" "20050238576").pn.	US-PGPUB; USPAT; USOCR	OR	ON	2010/09/28 17:24
S122	4	("4585941" "4585009" "20070140958" "20070213848").pn.	US-PGPUB; USPAT; USOCR	OR	ON	2010/09/28 17:24
S123	14	S120 S121 S122	US-PGPUB; USPAT; USOCR	OR	ON	2010/09/28 17:24
S125	14	S123 and (command$3 enter$3 receiv$3 (indicat $3 flash$3 blink$3 light) tim$3 (select$3 or choos $3) measur$4 test$3 ((purg$3 remov$3 releas $3) near3 (air gas)) (calibrat$3 initial$3 activat $3 initiat$3))	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2010/09/28 17:26
S127	6	("5168901" | "5223434" | "5326532" | "5468355" | "5482865" | "5514071").PN. OR ("6773673").URPN.	US-PGPUB; USPAT; USOCR	OR	ON	2010/09/28 17:49

S128	42	("3528407" | "3827427" | "4091287").PN. OR ("4585941").URPN.	US-PGPUB; USPAT; USOCR	OR	ON	2010/09/28 17:49
S129	30	("4006736").PN. OR ("4585009").URPN.	US-PGPUB; USPAT; USOCR	OR	ON	2010/09/28 17:49
S130	14	("4202345").PN. OR ("4562829").URPN.	US-PGPUB; USPAT; USOCR	OR	ON	2010/09/28 17:49
S131	77	S127 S128 S129 S130	US-PGPUB; USPAT; USOCR	OR	ON	2010/09/28 17:49
S133	76	S131 and (command$3 enter$3 receiv$3 (indicat $3 flash$3 blink$3 light) tim$3 (select$3 or choos $3) measur$4 test$3 ((purg$3 remov$3 releas $3) near3 (air gas)) (calibrat$3 initial$3 activat $3 initiat$3))	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2010/09/28 17:50
S134	54	S133 and (radioisotope radioactive PET (positron adj emission adj tomography) radiation rubidium strontium)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2010/09/28 17:50
S135	11	(S131 S123) and (elution eluate eluant)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2010/09/28 17:52
S136	1272	600/431.ccls.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2010/09/28 18:16
S137	772	S136 and (radioisotope radioactive PET (positron adj emission adj tomography) radiation rubidium strontium)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2010/09/28 18:16
S138	141	600/4.ccls.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2010/09/29 19:06

S139	3552	600/1-8,301.ccls. and (command$3 enter$3 receiv$3 (indicat$3 flash $3 blink$3 light) tim$3 (select$3 or choos$3) measur$4 test$3 ((purg $3 remov$3 releas$3) near3 (air gas)) (calibrat $3 initial$3 activat$3 initiat$3))	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2010/09/29 19:08
S140	2	600/1-8,301.ccls. (command$3 enter$3 receiv$3 (indicat$3 or flash$3 or blink$3 or light) tim$3 (select$3 or choos$3) measur$4 test $3 ((purg$3 or remov$3 or releas$3) near3 (air gas)) (calibrat$3 or initial $3 or activat$3 or initiat $3))	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	AND	ON	2010/09/29 19:12
S141	86	600/1-8,301.ccls. and (eluant elution eluate)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2010/09/29 19:13
S142	71	600/1-8,301.ccls. and (eluant elution eluate) and (computer processor control$4)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2010/09/29 19:13
S143	66	600/1-8,301.ccls. and (eluant elution eluate) and (computer processor control$4) and (radioisotope radioactive PET (positron adj emission adj tomography) radiation rubidium strontium)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2010/09/29 19:14

9/30/2010 4:47:08 PM
C:\Documents and Settings\jzhang1\My Documents\EAST\Workspaces\12137364.wsp

PTO/SB/08a (01-10)
Approved for use through 07/31/2012. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Not for submission under 37 CFR 1.99)

Application Number	12137364
Filing Date	2008-06-11
First Named Inventor	Stephen E. Hidem
Art Unit	3763
Examiner Name	Jenna Zhang
Attorney Docket Number	56782.1.7

U.S.PATENTS Remove

Examiner Initial*	Cite No	Patent Number	Kind Code[1]	Issue Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1	6908598		2005-06-21	Sylvester	
	2	7163031		2007-01-16	Graves et al.	
	3	7476377		2009-01-13	Moller	
	4	7504646		2009-03-17	Balestracci	

If you wish to add additional U.S. Patent citation information please click the Add button. Add

U.S.PATENT APPLICATION PUBLICATIONS Remove

Examiner Initial*	Cite No	Publication Number	Kind Code[1]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1	20070232980		2007-10-04	Felt	
	2	20090312635		2009-12-17	Shimchuk	

If you wish to add additional U.S. Published Application citation information please click the Add button. Add

FOREIGN PATENT DOCUMENTS Remove

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	12137364
	Filing Date	2008-06-11
	First Named Inventor	Stephen E. Hidem
	Art Unit	3763
	Examiner Name	Jenna Zhang
	Attorney Docket Number	56782.1.7

Examiner Initial*	Cite No	Foreign Document Number[3]	Country Code[2] ¡	Kind Code[4]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear	T[5]
	1	2004059661	WO		2004-07-15	Lynntech, Inc.		☐
	2	2006026603	WO		2006-03-09	Bracco Diagnostics		☐
	3	2006135374	WO		2006-12-21	Lynntech Inc.		☐
	4	2008140351	WO		2008-11-20	Obshchestvo		☐
	5	2010020596	WO		2010-02-25	Stichting Jeroen Bosch		☐

If you wish to add additional Foreign Patent Document citation information please click the Add button Add

NON-PATENT LITERATURE DOCUMENTS Remove

Examiner Initials*	Cite No	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc), date, pages(s), volume-issue number(s), publisher, city and/or country where published.	T[5]
	1		☐

If you wish to add additional non-patent literature document citation information please click the Add button Add

EXAMINER SIGNATURE

Examiner Signature		Date Considered	

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through a citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	12137364
	Filing Date	2008-06-11
	First Named Inventor	Stephen E. Hidem
	Art Unit	3763
	Examiner Name	Jenna Zhang
	Attorney Docket Number	56782.1.7

[1] See Kind Codes of USPTO Patent Documents at www.USPTO.GOV or MPEP 901.04. [2] Enter office that issued the document, by the two-letter code (WIPO Standard ST.3). [3] For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. [4] Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. [5] Applicant is to place a check mark here if English language translation is attached.

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	12137364
	Filing Date	2008-06-11
	First Named Inventor	Stephen E. Hidem
	Art Unit	3763
	Examiner Name	Jenna Zhang
	Attorney Docket Number	56782.1.7

CERTIFICATION STATEMENT

Please see 37 CFR 1.97 and 1.98 to make the appropriate selection(s):

☐ That each item of information contained in the information disclosure statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(1).

OR

☐ That no item of information contained in the information disclosure statement was cited in a communication from a foreign patent office in a counterpart foreign application, and, to the knowledge of the person signing the certification after making reasonable inquiry, no item of information contained in the information disclosure statement was known to any individual designated in 37 CFR 1.56(c) more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(2).

☐ 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)	2010-08-04
Name/Print	Elisabeth L. BELDEN	Registration Number	50,751

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 1 hour to complete, including gathering, preparing and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

Privacy Act Statement

The Privacy Act of 1974 (P.L. 93-579) requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that: (1) the general authority for the collection of this information is 35 U.S.C. 2(b)(2); (2) furnishing of the information solicited is voluntary; and (3) the principal purpose for which the information is used by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent application or patent. If you do not furnish the requested information, the U.S. Patent and Trademark Office may not be able to process and/or examine your submission, which may result in termination of proceedings or abandonment of the application or expiration of the patent.

The information provided by you in this form will be subject to the following routine uses:

1. The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C. 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether the Freedom of Information Act requires disclosure of these record s.

2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.

3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.

4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).

5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent Cooperation Treaty.

6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).

7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (i.e., GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.

8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspections or an issued patent.

9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

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

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
15 July 2004 (15.07.2004)

PCT

(10) International Publication Number
WO 2004/059661 A1

(51) International Patent Classification[7]: G21G 4/08

(21) International Application Number:
PCT/US2002/041676

(22) International Filing Date:
30 December 2002 (30.12.2002)

(25) Filing Language: English

(26) Publication Language: English

(71) Applicant: **LYNNTECH, INC.** [US/US]; 7610 Eastmark Drive, College Station, TX 77845 (US).

(72) Inventor: **SYLVESTER, Paul**; 80 N. Warren, Apt.16, Woburn, MA 01801 (US).

(74) Agent: **STREETS, Jeffrey, L.**; Streets & Steele, 13831 Northwest Freeway, Suite 355, Houston, TX 77040 (US).

(81) Designated States *(national)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, 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, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW.

(84) Designated States *(regional)*: ARIPO patent (GH, GM, KE, LS, MW, MZ, 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, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

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.

WO 2004/059661 A1

(54) Title: RUBIDIUM-82 GENERATOR BASED ON SODIUM NONATITANATE SUPPORT, AND SEPARATION METHODS FOR THE RECOVERY OF THE RECOVERY OF STRONTIUM-82 FROM IRRADIATED TARGETS

(57) Abstract: Sodium nonatitanate compositions, a method using the composition for recovery of 82Sr from irradiated targets, and a method using the composition for generating 82Rb. The sodium nonatitanate materials of the invention are highly selective at separating strontium from solutions derived from the dissolution of irradiated target materials, thus reducing target processing times. The compositions also have a very low affinity for rubidium, making it an ideal material for use as a 82Rb generator. Sodium nonatitanate materials of this type both improve the recovery of 82Sr and provide a safer, more effective 82Rb generator system.

RUBIDIUM-82 GENERATOR BASED ON SODIUM NONATITANATE SUPPORT, AND SEPARATION METHODS FOR THE RECOVERY OF STRONTIUM-82 FROM IRRADIATED TARGETS

BACKGROUND OF THE INVENTION

Field of the Invention

This invention relates to the selective separation of strontium-82 from other radioisotopes, such as those resulting from an irradiated molybdenum target, and in the manufacture of a rubidium-82 generator.

Background of the Related Art

The use of radioisotopes as diagnostic and imaging agents in medicine has expanded rapidly in recent years. Positron (β+) emitters are particularly useful in the study of metabolic processes because the positron-electron annihilation reaction produces a pair of gamma rays with an energy level of 511 keV travelling in opposite directions. By placing a series of detectors around a patient who has been administered a positron emitter, both the location and amount of radioactivity can be accurately determined. This property is utilized in Positron Emission Tomography (PET) to image metabolic processes *in vivo*. Rubidium-82 (82Rb) is a short-lived positron-emitting isotope ($T_{1/2}$ = 75 seconds) that is increasingly being used to study blood flow through the heart and brain. Physiologically, rubidium is an analogue of potassium, and consequently enters the body's large potassium pool, which has a comparatively slow turnover. Thus, after 82Rb is injected intravenously, the tracer's uptake in tissue reflects the rate of delivery, i.e. blood flow, and thus 82Rb rapidly builds up in the heart. This can be used, for example, to study blood-brain barrier leakage and heart muscle perfusion.

The short half-life of 82Rb means that it must be supplied to physicians in the form of a generator, where the parent 82Sr ($T_{1/2}$ = 25 days) is immobilized on a solid substrate or support and 82Rb eluted as required. The generators that are currently available use hydrous tin oxide to immobilize the 82Sr and allow the elution of 82Rb by saline or other appropriate eluant. The 82Sr ($T_{1/2}$ = 25 days) is accompanied by unwanted 85Sr ($T_{1/2}$ = 64 days), generated as a by-product during the manufacture of 82Sr, wherein both isotopes have a relatively long half-life and a high radiotoxicity due to their tendency to accumulate in bone. Thus, it is essential to minimize or eliminate the introduction of 82Sr and 85Sr into a patient during the administration of 82Rb. Although hydrous tin oxide has proved acceptable to date

for use in generators, new materials exhibiting far higher strontium affinities, improved strontium/rubidium separation factors and greater radiolytic stability are needed in order to lower the amount of 82Sr and 85Sr released during elution of the 82Rb.

The parent 82Sr is generated by the proton irradiation of rubidium, rubidium chloride or molybdenum targets followed by dissolution and processing to isolate the 82Sr. The demand for 82Rb generators has grown so great that there is a need to reduce processing times and to increase the yield of 82Sr from processed targets. One method of improving the supply of 82Sr is to improve the processes used to extract 82Sr from irradiated targets. Current methods utilize organic ion exchange or chelating resins to extract very low levels of strontium from dissolved targets containing molar concentrations of inert ions. However, a satisfactory separation of 82Sr from the target materials and other radioisotopes generated during the irradiation procedure requires multiple treatment steps due to the relatively low affinity and low selectivity of the organic ion exchange resins for 82Sr.

82Sr is produced by the proton irradiation of molybdenum metal, rubidium metal and rubidium chloride targets. The irradiation process also produces a range of other radioactive isotopes (e.g. 88Y, 88Zr, 85Sr) and as a consequence, a series of carefully designed separation procedures have been designed to separate the desired 82Sr from other radioisotopes and inactive species present. The primary method used to separate 82Sr is by a series of ion exchange and selective elution steps. Typically, AG 50 W-X8 ion exchange resin is used to separate 82Sr from dissolved targets. However, this resin is relatively non-selective and will absorb numerous polyvalent cations (e.g., 88Y) in addition to the desired 82Sr. Consequently, multiple separation steps are required to isolate 82Sr from the other isotopes present.

82Rb can be conveniently supplied to physicians in the form of a generator in which the parent 82Sr is immobilized on an ion exchange material and the 82Rb eluted when required. This means that 82Rb PET can be performed at clinical facilities where a typical generator may last several months before the yield of 82Rb diminishes below a usable level.

To be suitable for use in a 82Rb generator, an ion exchange material must exhibit a high affinity for strontium but a low affinity for rubidium, allowing the 82Rb daughter to be eluted from a column containing immobilized 82Sr. Generators have been proposed that were based on a number of separation media including Chelex 100, Al_2O_3, Sb(V) hexacyanoferrate, polyantimonic acid, titanium vanadate and hydrated tin(IV) oxide, with the hydrated tin(IV) oxide being the most widely used.

However, the crucial component of any system is the actual ion exchange material containing the immobilized 82Sr parent. Current systems using hydrous tin

oxide have a limited life due to the breakdown of the hydrous tin dioxide, necessitating frequent replacement.

Therefore, there is a need for a highly strontium selective ion exchange material in place of ion exchange resins and hydrated tin(IV) oxide, so that the separation and recovery of 82Sr from Rb, RbCl and Mo targets is greatly facilitated. This will lead to a reduction in processing steps, a decrease in target processing times and thus a decrease in the cost of the 82Sr product. There is also a need for an ion exchange material suitable for use as a 82Rb generator having a very high selectivity for 82Sr and a very low selectivity for 82Rb to allow elution of the 82Rb by isotonic saline or other solutions.

SUMMARY OF THE INVENTION

The present invention provides a method of chemically isolating strontium-82 from proton-irradiated molybdenum targets. This comprises dissolving the molybdenum metal target containing the strontium-82, adjusting the pH of the dissolved molybdenum target solution to an alkaline pH, removing precipitates from the solution, and then absorbing the strontium-82 from the solution onto a support comprising sodium nonatitanate. Sodium nonatitanate can also be applied to the efficient recovery of strontium-82 from alkaline RbCl solutions produced during the processing of proton-irradiated rubidium metal and rubidium chloride targets.

The present invention also provides a rubidium-82 generator, comprising a strontium-82 support medium comprising sodium nonatitanate. Preferably, the sodium nonatitanate is characterized by a strontium selectivity greater than 250,000 mL/g at an alkaline pH, and/or the sodium nonatitanate is characterized by a rubidium selectivity less than 100 mL/g at an alkaline pH. More preferably, the sodium nonatitanate is characterized by a strontium/rubidium separation factor greater than 1,000, and even more preferably greater than 100,000.

The rubidium-82 generator is prepared by a process comprising: preparing sodium nonatitanate from titanium isopropoxide and aqueous sodium hydroxide; heating the sodium nonatitanate at a temperature between 100°C and 250°C for a period between 12 hours and 2 weeks; and absorbing strontium-82 on the sodium nonatitanate from an aqueous solution comprising strontium-82 and a soluble sodium salt, wherein the sodium salt concentration is between 0.1 and 1 molar. It is also preferred that the titanium isopropoxide and the aqueous sodium hydroxide solution are provided at a sodium hydroxide to titanium isopropoxide molar ratio of greater than 0.44, but preferably providing a large molar excess of sodium

hydroxide. The sodium hydroxide to titanium isopropoxide molar ratio is preferably between 1 and 10, more preferably between 2 and 6, and most preferably about 4.

Furthermore, the invention provides a process for preparing a solution containing rubidium-82. The process comprises providing a solution containing strontium-82 at a pH between 10 and 14, absorbing the strontium-82 from the solution onto a sodium nonatitanate support medium, and eluting rubidium-82 from the sodium nonatitanate support medium with a solvent. The solvent is preferably selected from the group consisting of water and saline solutions. More particularly, the solvent may be an aqueous solution having a sodium chloride concentration between 0.001 molar and 1 molar, preferably between 0.2 molar and 1 molar. The solvent may also be a pharmaceutical grade isotonic saline and buffer solution.

DETAILED DESCRIPTION OF THE INVENTION

The present invention provides improved sodium nonatitanate compositions, a method using the composition for recovery of 82Sr from irradiated targets, and a method using the composition for generating 82Rb. The sodium nonatitanate materials of the invention are far more selective at separating strontium from solutions derived from the dissolution of irradiated target materials than current ion exchange resins used in the production of 82Sr. The present invention reduces the number of processing steps required, and thus leads to a decrease in target processing times and a reduction in the cost of the 82Sr product. Waste generation and disposal are also decreased.

According to the present invention, synthetic conditions are adjusted to produce a material with improved properties more applicable to 82Sr processing. The sodium nonatitanate of the present invention has been found to have a very low affinity for rubidium in addition to an exceptionally high affinity for strontium, making it ideal for use as a replacement for the hydrous tin dioxide used in current 82Rb generators. Sodium nonatitanate materials of this type will both improve the recovery of 82Sr and lead to a safer, more effective 82Rb generator system for clinical applications.

Sodium nonatitanate, $Na_4Ti_9O_{20}.xH_2O$, is an inorganic ion exchange material that has been used for the removal of 90Sr from neutral and alkaline nuclear wastes. The sodium nonatitanate of the present invention has a number of advantages over conventional organic ion exchange resins (e.g., Chelex 100) that include: very high selectivity for trace levels of strontium in the presence of molar concentrations of other ions at alkaline pH; very low affinity for rubidium; excellent radiation, chemical and thermal stability so that there is no release of contaminants (e.g. Ti) into the 82Rb product; rapid reaction kinetics; high cation exchange capacity; absorbed ions readily stripped by treatment with dilute mineral acid allowing the sodium nonatitanate to be recycled, if desired; scale up of similar synthesis has

already been demonstrated; and the sodium nonatitanate powder can be manufactured into pellets appropriate for column operations. Other chemically related sodium titanate materials suitable for use in the same manner as the aforementioned sodium nonatitanate ($Na_4Ti_9O_{20}.xH_2O$) include other titanate materials exhibiting high Sr affinity and low Rb affinity, including Sr-Treat (available from Selion Oy) and monosodium titanate (available from Boulder Scientific) It is also anticipated that analogous zirconates may exhibit similar properties.

The invention also provides important improvements in the processing of irradiated targets to recover 82Sr. Sodium nonatitanate has a much greater affinity for 82Sr than currently used ion exchange resins, and a low affinity for other radioactive isotopes. Consequently, the use of sodium nonatitanate greatly simplifies the extraction process by reducing the number of separation steps that are required to produce chemically pure 82Sr. Thus, targets can be processed more rapidly and the recovery of 82Sr improved. Improved isotope selectivity may also facilitate the isolation of other useful isotopes from the targets, leading to greater payback from target processing operations.

Furthermore, less than 1g of sodium nonatitanate material is needed in a 82Rb generator and 1 kg of this material is expected to be sufficient to process a large number of targets, even if the sodium nonatitanate material is not recycled and is disposed of after one use. Consequently, the additional cost incurred by the use of sodium nonatitanate will be negligible in comparison with the cost savings achieved in the 82Sr production.

It has been determined that replacing hydrous tin dioxide with sodium nonatitanate reduces the amount of 82Sr released during the operation of the 82Rb generator, thereby reducing the exposure of the patient to 82Sr. Sodium nonatitanate is also more chemically stable and less likely to leach non-radioactive contaminants into solution during operation of the generator. The sodium nonatitanate is also more amenable to recycling since the 82Sr can readily be stripped with mineral acid without producing additional impurities. Recycling of 82Sr generators is already being used as a source of additional 82Sr, and improvements to the recycling procedure (obtained by using a superior ion exchange material) will facilitate the recovery of 82Sr from this source.

Although the sodium nonatitanate may be used as a direct replacement for hydrous tin dioxide in the 82Rb generator, it is also possible to use sodium nonatitanate in the form of a disposable add-on filter that could be used to trap any 82Sr that is leached from the generator during the production of 82Rb.

The first step in preparing a 82Rb generator is to load the parent 82Sr onto the sodium nonatitanate material and place the ion exchange material into a suitable column. It is essential that sufficient time be allowed for the 82Sr to be absorbed by the sodium

nonatitanate material in order to maximize the loading of the parent radioisotope per gram of ion exchange material.

Sodium nonatitanate should be loaded with 82Sr before being placed in an ion exchange column, to avoid preferential loading of the 82Sr on the top of the ion exchange column rather than uniformly throughout the material. This high concentration of radioactivity on a very small volume may result in undesirable radiolytic problems. Although sodium nonatitanate has been shown to be highly resistant to radiation damage, it is considered prudent to avoid any potential problems.

EXAMPLES

These Examples investigated the suitability of sodium nonatitanate for the use in separating 82Sr from irradiated targets and in the construction of a 82Sr/82Rb generator. Initial batch experiments compared the rubidium and strontium selectivities of a number of different sodium nonatitanate samples with commercially available ion exchange materials (e.g. AW 500, Chelex 100) and some experimental materials that had also exhibited high strontium selectivities (e.g. sodium titanosilicate). Column experiments were then performed using target simulants and generator simulants on materials that exhibited favorable selectivity characteristics. Some work was also performed to investigate the likely interference from other isotopes present in irradiated targets on the production of 82Sr.

Example 1 - Preparation of Sodium Nonatitanate

Sodium nonatitanate (NaTi) was synthesized hydrothermally as follows. 77.5 g of titanium isopropoxide was added to 84.35 g of a 50 wt.% solution of NaOH with vigorous stirring and 60 mL of deionized water was added. The resultant gel was heated at approximately 108°C for 3 hours, transferred to a hydrothermal pressure vessel with an additional 90 mL of deionized water, and heated at either 170°C or 200°C for times ranging from 21 hours to 1 week. After the allotted time, the materials were filtered, washed with ethanol to remove residual base and dried at 60°C. The mass of sodium nonatitanate produced was approximately 31 g. Each sample was characterized using x-ray powder diffraction (XRD). The reaction is outlined in Equation 1.

$$9\ Ti(OC_3H_7)_4 + 4\ NaOH(aq) \text{ ----> } Na_4Ti_9O_{20}.xH_2O + 9\ C_3H_7OH \quad (1)$$

The crystallinity of the material was shown to be dependent upon the reaction time and temperature, with the most crystalline materials being produced after 1 week of hydrothermal treatment (200°C for 7 days). Samples that received no hydrothermal treatment,

or only a few days, were virtually amorphous with only a few very broad reflections visible on the XRD pattern.

The theoretical cation exchange capacity (CEC) of sodium nonatitanate is quite high and has a value of 4.74 meq/g, which compares favorably with organic ion exchange resins.

Alternative titanium salts that could be used to manufacture sodium nonatitanate include titanium tetrachloride, $TiCl_4$, and titanium sulfate, $TiOSO_4.xH_2SO_4.yH_2O$. However, hydrolysis of these salts leads to the generation of hydrochloric acid and sulfuric acid, respectively, and thus additional base is required during the hydrothermal process. The final product also needed to be exhaustively washed to remove residual sodium chloride or sodium sulfate. Consequently, titanium isopropoxide (which hydrolyzes to form propanol) is the preferred starting material because the final product is free from additional sodium salts.

Example 2 - Determination of Strontium Selectivity

Sodium nonatitanate and a variety of other ion exchange materials were obtained and evaluated for use in the separation of 82Sr from targets and in a 82Rb generator. These materials are described below in Table 1.

Table 1. Characteristics of ion exchange materials evaluated in this study.

Material	Source	Sample Preparation
Na-Clinoptilolite	GSA Resources, AZ	Ground to powder.
AW500	Aldrich (1.6 mm Pellets)	Ground to powder.
Hydrous SnO_2	Synthesized in house	$NaOH + SnCl_4$. Washed with acetic acid/sodium acetate buffer.
K+ Pharmacosiderite ($K_3H(TiO)_4(SiO_4)_3.4H_2O$)	Synthesized according to literature method.	None. Used as synthesized.
Sodium Titanosilicate ($Na_2Ti_2O_3SiO_4.2H_2O$)	Synthesized according to literature method.	None. Used as synthesized.
AG 50W-X8 (Na+) (25 - 50 Mesh)	BioRad. Strong acid ion exchange resin.	Converted to Na+ form (for alkaline solutions only)
Chelex 100 (Na+) (50 - 100 Mesh)	BioRad. Chelating resin with iminodiacetic acid functionality.	None. Used as received.
Sodium Nonatitanate	Honeywell, IL	None. Used as received.
Hydrous SiO_2	Synthesized in house	Acetic acid hydrolysis of tetraethyl orthosilicate. Washed with H_2O

Hydrous TiO_2	Synthesized in house	Hydrolysis of titanium isopropoxide. Washed with H_2O
Hydrous ZrO_2	Synthesized in house	$ZrOCl_2$ + NaOH. Washed with deionized water.

The strontium selectivity of the ion exchange materials of Table 1 was evaluated in sodium chloride and rubidium chloride solutions using radiotracer techniques. Samples were evaluated using a simple batch technique to allow the rapid screening of a large number of materials over a range of ionic strengths. Blanks were run for each matrix to check for any loss of strontium during filtration or absorption of strontium onto the scintillation vials. In all solutions evaluated, strontium absorption was negligible.

0.05g of each of the ion exchange materials was contacted with 10 mL of a solution, spiked with 89Sr, in a capped scintillation vial. (The total strontium content was approximately 1.6 ppm, thus preventing any loss of strontium in solution due to precipitation of sparingly soluble $Sr(OH)_2$ at alkaline pH values.) The mixtures were shaken for 6 hours, filtered through a 0.2 μm syringe filter and the residual activity determined using liquid scintillation counting (LSC). Distribution Coefficients (K_d values) were then determined according to Equation 2:

$$K_d = (A_i - A_f) / A_f * v/m \qquad (2)$$

where: A_i = initial activity in solution (counts per minute (cpm)/mL)

A_f = final activity in solution (cpm/mL)

v = volume of solution (mL)

m = mass of exchanger (g)

The final pH of the solution was also noted. The period of 6 hours was chosen to allow equilibrium to be reached for each of the ion exchange materials. However, previous work on the titanosilicates and titanates had shown the reaction rates to be rapid with the majority of the uptake occurring in only a few minutes. The concentration of the chloride solutions was varied from 1M to 0.001M to evaluate the effect of increasing Rb+ and Na+ concentrations on the uptake of Sr^{2+}. All experiments were performed in duplicate, and if significant variations between duplicate samples occurred, the experiments were repeated until good agreements on the K_d values were obtained. The results are shown in Tables 2 and 3 and represented the average K_d obtained, quoted to 3 significant figures.

Table 2. Strontium selectivity data from unbuffered sodium chloride solutions.

Ion Exchange Material	K_d mL/g 1M NaCl	0.1M NaCl	0.01M NaCl	0.001M
NaCl				
Na-Clinoptilolite	8	124	3,260	36,900
AW500	1,860	88,300	1,270,000	1,210,000
Hydrous SnO_2	767	43,000	124,000	51,800
K+ Pharmacosiderite	18,300	251,000	594,000	281,000
Sodium Titanosilicate	556,000	273,000	119,000	42,900
AG 50W (Na+)	32	3,380	365,000	2,510,000
Chelex 100 (Na+)	610	26,400	726,000	1,300,000
NaTi (Honeywell)	80,600	1,030,000	258,000	166,000
NaTi (No hydrothermal)	1,530,000	2,570,000	739,000	372,000
NaTi (170°C, 21hr)	1,030,000	1,240,000	272,000	172,000
NaTi (170°C, 3d)	959,000	633,000	218,000	93,100
NaTi (170°C, 7d)	167,000	834,000	264,000	90,400
NaTi (200°C, 21hr)	439,000	1,390,000	197,000	120,000
NaTi (200°C, 3 d)	261,000	898,000	251,000	158,000
NaTi (200°C, 7d)	195,000	955,000	265,000	214,000
ZrO_2	3,360	52,200	213,000	232,000

Table 3. *Strontium* selectivity data from unbuffered rubidium chloride solutions

Material	K_d mL/g 1M RbCl	0.1M RbCl	0.01M RbCl	0.001M
RbCl				
Na-Clinoptilolite	19	3	88	11,000
AW500	9,750	107,000	1,020,000	1,280,000
Hydrous SnO_2	766	66,100	104,000	51,800
K+ Pharmacosiderite	1,950	40,800	419,000	427,000
Sodium Titanosilicate	12,600	94,700	164,000	179,000
AG-50W (Na+)	44	3,870	237,000	800,000
Chelex 100 (Na+)	1,580	38,400	555,000	977,000
NaTi (Honeywell)	13,900	108,000	279,000	324,000
NaTi (No hydrothermal)	14,220	116,000	345,000	429,000
NaTi (170°C, 21hr)	10,500	71,700	193,000	205,000
NaTi (170°C, 3d)	15,100	39,500	68,000	95,200
NaTi (170°C, 7d)	23,000	55,800	31,200	110,000
NaTi (200°C, 21hr)	11,000	66,400	110,000	103,000
NaTi (200°C, 3 d)	10,600	56,800	146,000	158,000
NaTi (200°C, 7d)	10,500	57,400	146,000	158,000
ZrO_2	3,000	42,400	184,000	221,000

Comparing the selectivity data from sodium and rubidium solutions, it is evident that rubidium ions cause a reduction in affinity for the strontium ion for all of the exchangers indicating that the affinity of these materials for rubidium is significantly higher than the affinity for sodium ions. The pH of the final solutions was generally alkaline for the nonatitanates (NaTi) and titanosilicates, with pH values as high as 12 being measured. This was due to hydrolysis of the exchangers resulting in the absorption of protons and the release

of sodium ions, thus increasing the pH of the aqueous phase. This effect can be overcome, if desired, by buffering the solution.

The most distinct trend was observed in 1M NaCl solutions for the sodium nonatitanate samples. The highest K_d was observed for the non-hydrothermal material and the K_d values decreased with increasing reaction time for both the 200°C and 170°C materials. Clearly, strontium uptake is facilitated by having a low-crystallinity material. This suggests that as the crystallinity increases and the size of the nonatitanate crystallites also increases, it becomes thermodynamically less favorable for exchange of the sodium ions by strontium. It is also interesting to note that the majority of the sodium nonatitanates exhibit a higher selectivity for strontium in 1M NaCl than in 0.001M NaCl. This indicates that the higher ionic strength facilitates the Na^+/Sr^{2+} exchange reaction and more than compensates for the increased competition for the ion exchange sites from the additional Na+ ions.

This data shows that sodium nonatitanate is an ideal material for the recovery of 82-Sr from irradiated rubidium and rubidium chloride targets and in the manufacture of a 82-Rb generator.

Example 3 - Rubidium Selectivity from NaCl Solutions

For an ion exchange material to be suitable for use in a 82Rb generator, it must have a very high selectivity for strontium to prevent any loss of 82Sr from the ion exchange column and release to the patient undergoing a PET scan. This property was clearly demonstrated in Example 2. It must also have a very low selectivity towards rubidium, thus allowing 82Rb to be released into solution as saline is passed through the 82Rb generator. Consequently, the rubidium selectivity of the ion exchange materials was evaluated in sodium chloride media following the procedure described in Example 2. The same procedure was followed using 86Rb to spike the solutions to give an activity of approximately 200,000 cpm/mL. Total rubidium in solution was < 0.05 ppm. The selectivities of the materials are shown below in Table 4.

Table 4. Rubidium selectivity data from unbuffered sodium chloride solutions.

Material	86Rb K_d mL/g			
	1M NaCl	0.1M NaCl	0.01M NaCl	0.001M
NaCl				
AW500	116	620	4,920	21,900
Hydrous SnO_2	1	6	36	290
K+ Pharmacosiderite	148	475	2,030	4,020
Sodium Titanosilicate	8,010	194,000	114,000	75,800
AG 50W (Na+)	7	75	688	6,680
Chelex 100 (Na+)	3	8	43	256
NaTi (Honeywell)	9	102	488	817

NaTi (No hydrothermal)	4	59	280	446
NaTi (170°C, 21hr)	9	56	209	297
NaTi (170_oC, 3d)	7	46	198	311
NaTi (170°C, 7d)	3	15	47	71
NaTi (200°C, 21hr)	8	79	334	502
NaTi (200°C, 3d)	8	52	207	307
NaTi (200°C, 7d)	4	25	111	178
ZrO_2	1	12	60	154

From the data in Table 4, it is clear that the all of the sodium nonatitanate materials have a very low affinity for rubidium, particularly in the presence of relatively high amounts of sodium ions. In general, the rubidium selectivity decreased with increasing reaction time for both series of nonatitanates (170°C and 200°C) with the lowest affinity being demonstrated by the sample that was heated hydrothermally at 170°C for 1 week. Uptake was negligible in 1M NaCl and the very low reduction in activity that was noted could be accounted for by absorption of rubidium during filtration and by pipetting errors during the counting procedure. Consequently, samples with K_d values that were below 10 mL/g can be considered to have no affinity at all for 86Rb. Some rubidium uptake was evident in very dilute sodium solutions, but the K_d values were low for all of the titanate samples. This suggests that the uptake of rubidium was more likely due to the materials having an exceptionally low affinity for sodium rather than any real affinity for rubidium. All of the sodium nonatitanate materials performed better than the commercially available sample obtained from Honeywell Inc. The materials are clearly ideal for use in a 82-Rb generator.

Hydrous tin dioxide exhibited some of the lowest rubidium affinities and was comparable with Chelex 100, the best of the nonatitanates and the hydrous zirconium dioxide. However, hydrous tin dioxide exhibited much lower strontium K_d values than the nonatitanates. Therefore, nonatitanate materials are preferred because they have higher strontium/rubidium separation factors. Hydrous tin dioxide also has a limited pH stability range and significant dissolution and release of absorbed strontium is likely to occur should any significant pH perturbations occur outside the range of pH 4 to pH 9. Radiation stability of hydrous tin dioxide is also limited, with particle breakdown causing current 82-Rb generators to be replaced before decay has reduced the 82-Rb below useable levels.

The rubidium selectivity data also indicates that AW500, potassium Pharmacosiderite and the sodium titanosilicate have a strong affinity for rubidium in a range of saline solutions. Consequently, these materials will be unsuitable for use in a 82Rb generator and have only limited applications in the processing of irradiated target materials.

Example 4 - Sr and Rb Selectivity in 0.1M Sodium Acetate/Acetic Acid Buffer

In order to prevent hydrolysis reactions from raising the pH as described above, some strontium and rubidium selectivity experiments were performed in a 0.1M sodium acetate / acetic acid buffer solution. In these tests, the final pH remained between 5.2 and 6.3, which is a more clinically acceptable pH for an 82Rb infusion. Rubidium K_d values remained low, as expected, following the trend observed in Table 5. Strontium K_d values were considerably lower, with a maximum K_d value of 80,000 mL/g being obtained for the sodium nonatitanate sample that was heated hydrothermally at 170°C for 21 hours. This is considerably lower than the K_d value of over 1,200,00 mL/g that was obtained in unbuffered 0.1M NaCl. The K_d values obtained for the other ion exchange materials were also considerably lower. However, the Sr/Rb separation factors remained high and the sodium nonatitanates still outperformed hydrous tin dioxide and the organic ion exchange resins. The affinity of sodium nonatitanate for strontium is greatest at higher pH values.

Example 5 - Molybdenum Targets

The basic steps of a proposed process to obtain 82Sr from irradiated molybdenum targets are as follows:

1. Dissolve the irradiated molybdenum target in 30% hydrogen peroxide, ensuring excess hydrogen peroxide is destroyed.
2. Add sodium hydroxide to bring the pH to approximately 12.
3. Filter the solution to remove any precipitate. It is predicted that the majority of 88Zr and 59Fe will be found in the precipitate, and experiments already performed have confirmed that 99% or more of the 88Y precipitated out of solution on the addition of NaOH.
4. Pass the solution through a column of sodium nonatitanate and wash the column with two bed volumes of 0.1M NaCl, adjusted to pH 12 with NaOH. 82Sr and 85Sr will be absorbed. 82Rb and other Rb isotopes will remain in the aqueous phase. Molybdate anions will also pass through the column.
5. The column can then be stripped using dilute mineral acid to recover the 82Sr and the sodium nonatitanate reused or discarded.

There is a range of other isotopes present in addition to 82Sr, including 75Se, 73As, 74As, 7Be, 68Ge, 48V, 60Co (and other Co isotopes), 54Mn, 51Cr and 95mTc. In the alkaline target solution, Se, As, V, Ge, Cr, Mn and Tc are expected to be present as anions and thus will not be absorbed onto the sodium nonatitanate. Significant amounts of Co would be expected to precipitate when the target solution is neutralized, and thus little is expected to be available under alkaline conditions to absorb onto the sodium nonatitanate. The most

likely isotope to be absorbed is beryllium, because it is a Group II metal with a similar aqueous chemistry to strontium. However, the affinity of sodium nonatitanate for Group II metals decreases in the order Sr > Ca > Mg. No data is available for beryllium, but if the trend continues, the affinity would be expected to be low. Thus, any absorbed 7Be would be readily removed by an alkaline sodium chloride (or similar) wash.

The current process for recovering 82Sr from irradiated rubidium metal and rubidium chloride targets requires minimal modification to facilitate the use of sodium nonatitanate. Both targets are processed following standard processing procedures to generate rubidium chloride solutions in an ammonia/ammonium chloride buffer solution. These solutions are then passed through a sodium nonatitanate column and washed with additional buffer to remove any weakly held rubidium cations. Strontium and possibly some other cationic species present will be absorbed onto the nonatitanate column, whereas rubidium cations, ammonium cations and anions will rapidly pass through the column. If additional cations are absorbed onto the sodium nonatitanate, they can be selectively removed by washing with an appropriate eluant (e.g. citrate, nitrilotriacetate.) The strontium selectivity of sodium nonatitanate has been shown to be unaffected by a number of common complexants and as a consequence, it should be a relatively simple manner to elute any undesirable cations from the column, leaving pure 82/85Sr.

Figure 1 clearly shows the exceptionally high affinity of the sodium nonatitanate materials in comparison with the currently utilized organic resin Chelex 100. All of the sodium nonatitanates performed equally well in the buffered rubidium target solutions indicating that the synthetic conditions are not too important when the material is being used in solutions containing high concentrations of rubidium ions. Thus, by replacing the Chelex 100 with sodium nonatitanate, a more efficient 82Sr isolation can be achieved.

It has also been shown that it is possible to tailor the selectivity of the sodium nonatitanate to achieve the optimum Sr/Rb separation by manipulating the reaction conditions. The differing selectivities were most obvious in sodium solutions, with the less crystalline materials exhibiting the highest strontium distribution coefficients. However, the series of nonatitanates showed little difference in behavior when the predominant cation in solution was Rb+. The materials synthesized clearly demonstrated superior characteristics to the commercially available sample in almost all matrices evaluated. The majority of the sodium nonatitanate samples also exhibited greater strontium selectivities than hydrous tin dioxide in a range of sodium chloride solutions, from 1M to 0.001M. Rubidium selectivities were low, making the sodium nonatitanate ideal as a replacement for hydrous tin dioxide in a 82Rb generator.

Commercially, one method of 82-Sr production is via the proton spallation reaction with natural molybdenum metal targets. A simulated molybdate target solution was prepared as follows. 12.5 g of molybdenum powder was carefully dissolved in 30% H_2O_2 solution and made up to a total volume of 500 mL to produce a clear yellow solution of molybdic acid, H_2MoO_4. Solid sodium hydroxide granules totaling 10.9 g were then carefully added to neutralize the solution and bring the pH to approximately 12.3. The colorless solution was then filtered to remove any precipitate. This alkaline molybdate solution was spiked with either 86Rb or 89Sr and K_d values determined as described previously. Separation factors for the strontium/rubidium selectivity were also calculated by dividing the strontium K_d by the rubidium K_d, thus allowing the relative affinities of the ion exchange materials to be directly compared. The results are illustrated below in Table 5.

Table 5. Strontium and rubidium absorption from simulated molybdate target solutions

Material	Sr K_d mL/g	Rb K_d mL/g	Separation Factor
AW500	7,070	194	36.4
K+ Pharmacosiderite	187,000	142	1320
Sodium Titanosilicate	547,000	6500	84.2
Chelex 100 (Na+)	3,120	5	624
AG 50W-X8 (Na+)	69	18	3.83
NaTi (Honeywell)	337,000	27	12,500
NaTi (No hydrothermal)	1,690,000	12	141,000
NaTi (170°C, 21hr)	1,000,000	12	83,300
NaTi (170°C, 3d)	829,000	14	59,200
NaTi (170°C, 7d)	324,000	3	108,000
NaTi (200°C, 21hr)	954,000	12	79,500
NaTi (200°C, 3 d)	687,000	11	62,500
NaTi (200°C, 7d)	772,000	9	85,800
ZrO_2	168,000	8	21,000

From this data, it is clear that the sodium nonatitanate materials are far superior to Chelex 100 and AG 50W-X8 ion exchange resins for the recovery of 82Sr from irradiated molybdenum targets. High K_d values in excess of 500,000 mL/g indicate that almost 100% strontium removal was achieved by some of the nonatitanate samples, with the residual strontium in solution approaching background levels. In the alkaline conditions used in this test, the Chelex 100 resin had the lowest affinity for strontium of all of the materials evaluated. The selectivity of the sodium nonatitanate for rubidium was lowest for the sodium nonatitanate material that was prepared by heating for 1 week at 170°C to obtain a relatively crystalline product. However, strontium selectivity also decreased with increasing reaction time.

The best overall strontium/rubidium separation factor was obtained for the material that had not undergone any hydrothermal treatment. All of the materials performed better than the commercially available nonatitanate materials. Thus, it is possible to alter the selectivity of the material by controlling the reaction conditions to produce an improved sodium nonatitanate material for use in 82Sr separations. Rubidium selectivities were very low for all of the nonatitanates, indicating minimal rubidium absorption would occur in a column process and that any rubidium absorbed would be readily removed by a dilute saline wash.

The sodium titanosilicate, potassium Pharmacosiderite and AW500 exhibit selectivities for rubidium that are too high to allow their use in the selective removal of 82Sr from irradiated molybdenum targets. This high selectivity would result in some rubidium being retained on the column that would not be readily removed by a simple saline wash, thus leading to contamination of the 82Sr product with both radioactive and stable rubidium isotopes. Hydrous tin oxide was not evaluated because, due to the amphoteric nature of tin, significant dissolution would be expected at a pH in excess of 12.

Example 6 - Acid Molybdate Target Solutions

Sodium nonatitanate has a relatively low affinity for strontium at pH values less than 6, and was not expected to exhibit any affinity for strontium from the acidic molybdate target solutions prior to the addition of sodium hydroxide. K_d values were determined to confirm this and to compare it with the K_d values for both Chelex 100 and AG 50W-X8 under identical conditions. The data obtained is shown below in Table 6.

Table 6. The affinity of selected ion exchange materials for strontium in acidic molybdate target solutions

Ion Exchange Material	Sr K_d mL/g	Final pH of Solution
Chelex 100	25	1.43
AG 50W-X8	18,300	1.42
Sodium Nonatitanate (Honeywell)	1,260	1.53

These data clearly indicate that for the processing of acid molybdate solutions, the strong acid ion exchange resin AG 50W-X8 is the preferred medium. However, the Sr K_d value of 18,300 mL/g in the acidic media is nearly two orders of magnitude lower than the K_d value of 1,690,000 mL/g that was obtained for the best of the sodium nonatitanate materials in alkaline molybdate solutions. Consequently, it is evident that 82Sr can be recovered more effectively from alkaline solution using sodium nonatitanate than is currently achieved using AG 50W-X8 from acidic media.

Example 7 - Rubidium and Rubidium Chloride Target Solutions

The processing of either rubidium chloride or rubidium metal targets follows a similar procedure once the target has been successfully dissolved. In essence, 82Sr needs to be selectively extracted from a solution of RbCl in a 0.1 M NH_3 / 0.1M NH_4Cl buffer adjusted to a pH of between 9 and 10. Batch experiments were performed in simulated buffer solutions to determine the strontium selectivity in the presence of high concentrations of rubidium ions. Only the ion exchange materials that exhibited high strontium selectivities in the initial scoping studies with NaCl solutions were evaluated. K_d values were obtained as described previously. Two rubidium chloride solutions were selected which represent typical rubidium concentrations obtained during the processing of rubidium metal (1.95 M Rb+) and rubidium chloride targets (0.68 M Rb+). In both cases, Chelex 100 is used in the preliminary step to remove the 82Sr from the buffered rubidium solutions. The K_d values for the ion exchange materials are shown in Figure 1.

In the buffered rubidium solutions, there is little difference between the different nonatitanates evaluated. This is in stark contrast to the sodium molybdate solutions where a large variation in the performance of the titanates was observed. The nonatitanates were clearly the most effective materials at removing strontium from the buffered solutions with strontium K_d values of around 15,000 mL/g in 0.68 M Rb+ solutions and approximately 5,000 mL/g in 1.96 M Rb+ solutions. By contrast, Chelex 100 ion exchange resin gave K_d values of less than 1,000 mL/g in both solutions. Hydrous titanium oxide and hydrous tin oxide also exhibited appreciable K_d values, but they performed less efficiently than the nonatitanates in both solutions. Consequently, this data demonstrates that using sodium nonatitanate in place of Chelex 100 ion exchange resin will greatly increase the amount of strontium extracted from the target solutions.

The ion exchange materials were also evaluated for their rubidium selectivity from 0.1 M NH_3 / 0.1M NH_4Cl buffer solution. The buffer was prepared, spiked with 86Rb and the pH adjusted to approximately 9.25 with concentrated ammonia. 86Rb K_d values were then determined following the method described earlier. All of the sodium nonatitanates had a K_d < 20 mL/g. The very low rubidium selectivity in the pure buffer is almost certainly due to competition from NH_4+ ions for the available ion exchange sites. Consequently, absorption of rubidium during the processing of rubidium and rubidium chloride targets will be minimal, and any rubidium absorbed will be readily removed by washing with additional 0.1 M NH_3 / 0.1M NH_4Cl buffer solution. Thus, a clean separation of 82Sr from these targets can be obtained using sodium nonatitanate.

The performance could also be improved by removing the buffer and increasing the pH to improve the amounts of strontium absorbed. (Buffers were initially utilized to maximize the performance of the organic ion exchange resins currently used and are not essential to the 82Sr recovery process.)

Example 9 - Kinetic Experiments

In order for the sodium nonatitanate materials to find applications in the processing of irradiated target solutions, they must exhibit fast ion exchange kinetics allowing solutions to be passed through an ion exchange column at an acceptable rate. The kinetics of strontium absorption from alkaline molybdate target solutions was evaluated using a simple batch procedure. Ion exchange material, in the amount of 0.05 g, was shaken with 10 mL of molybdate solution spiked with 89Sr to give a total activity of approximately 155,000 cpm/mL. After an allotted time, the material was filtered through a 0.2 m syringe filter and the activity in the aqueous phase determined by LSC. The results are shown below in Figure 2.

From the data in Figure 2, it is clear that the reaction kinetics for the sodium nonatitanate powder is extremely rapid, with over 99 % of the 89Sr removed in only 1 minute. By contrast, the reaction kinetics of the organic ion exchanged resins was much slower and the total amount of 89Sr removed after 1 hour was much less.

The exceedingly rapid kinetics can partly be explained by the fact that the nonatitanate was in the form of a fine powder, whereas the two resins were in the form of beads (see Table 1). As a consequence, a relatively slow reaction rate would be expected for the beads because the uptake of 82Sr will be dependent upon the rate of diffusion of the 82Sr to the internal functional groups. The rate of uptake of a sample of sodium nonatitanate pellets (using hydrous titanium dioxide as a binder) was significantly slower than the powdered form, but the kinetics and amount of 82Sr absorbed was still significantly better than for either of the two organic resins. As the pelletization process is improved, it is expected that the kinetics and selectivity of the pelletized sodium nonatitanate will improve substantially. Other sodium nonatitanate powders of varying crystallinities also showed rapid kinetics. Other potentially suitable binders for forming suitable pellets include titanium isopropoxide or tetraethyl orthosilicate (TEOS) as a binder precursor.

Example 10 - 82Sr Removal from Irradiated Targets Using Pelletized Sodium Nonatitanate

A sample of sodium nonatitanate was mixed with titanium isopropoxide as a binder and the resulting paste dried at 105°C for 12 hours. The material was gently broken up using a mortar and pestle and then sieved to produce particles in the range 40 to 60 mesh. The binder content was approximately 20%. These particles were then used to assess the extraction of 89Sr from simulated target solutions.

1 mL of pelletized sodium nonatitanate was slurried into a column and the target simulant that had been spiked with 89Sr to give an activity of approximately 200,000 cpm/mL was passed through the column at a flow rate of 15 mL per hour. The amount of activity removed from solution was then determined. The results are given below in Table 1.

Table 1. Removal of 82Sr From Irradiated Target Solutions

Target (%)	Solution Composition	Volume (mL)	82Sr Removed
Rubidium Metal	1.95M RbCl in 0.1M NH_3/NH_4Cl Buffer, pH10	20	97.3
Rubidium Chloride	0.68M RbCl in 0.1M NH_3/NH_4Cl Buffer, pH 10	20	98.8
Molybdenum Metal	0.26M Na_2MoO_4, pH 12	20	99.9

This data clearly shows the effectiveness of sodium nonatitanate at removing strontium isotopes from 82Sr target materials. Rubidium absorption under these conditions is minimal.

Example 11 - Elution of Strontium

Strontium was quantitatively eluted from the sodium nonatitanate column of Example 10 using 6M nitric acid. Hydrochloric acid was found to be much less effective and also resulted in breakdown of the sodium nonatitanate particles and blocked the ion exchange column.

While the foregoing is directed to the preferred embodiment of the present invention, other and further embodiments of the invention may be devised without

departing from the basic scope thereof, and the scope thereof is determined by the claims that follow.

What is claimed is:

1. A rubidium-82 generator, comprising:

(a) a strontium-82 support medium comprising sodium nonatitanate.

2. The rubidium-82 generator of claim 1, wherein the sodium nonatitanate is characterized by a strontium selectivity greater than 250,000 mL/g at an alkaline pH.

3. The rubidium-82 generator of claim 1, wherein the sodium nonatitanate is characterized by a rubidium selectivity less than 100 mL/g at an alkaline pH.

4. The rubidium-82 generator of claim 1, wherein the sodium nonatitanate is characterized by a strontium/rubidium separation factor greater than 1,000.

5. The rubidium-82 generator of claim 1, wherein the sodium nonatitanate is characterized by a strontium/rubidium separation factor greater than 100,000.

6. A process for preparing a rubidium-82 generator, comprising:

(a) preparing sodium nonatitanate from titanium isopropoxide and aqueous sodium hydroxide;

(b) heating the sodium nonatitanate at a temperature between 100°C and 250°C for a period between 12 hours and 2 weeks; and

(c) absorbing strontium-82 on the sodium nonatitanate from an aqueous solution comprising strontium-82 and sodium chloride, wherein the sodium chloride concentration is between 0.1 and 1 molar.

7. The process of claim 6, wherein the molar ratio of aqueous sodium hydroxide to titanium isopropoxide is in excess of 0.44.

8. The process of claim 6, wherein the molar ratio of aqueous sodium hydroxide to titanium isopropoxide is between 2 and 6.

9. A method of chemically isolating strontium-82 from a proton-irradiated molybdenum target, comprising:

(a) dissolving the molybdenum metal target containing the strontium-82;

(b) adjusting the pH of the dissolved molybdenum target solution to an alkaline pH;

(c) removing precipitates from the solution; and then

(d) absorbing the strontium-82 from the solution onto a support comprising sodium nonatitanate.

10. A process for preparing a solution containing rubidium-82, comprising:

(a) providing a solution containing strontium-82 at a pH between 10 and 14;

(b) absorbing strontium-82 onto a sodium nonatitanate support medium; and

(c) eluting rubidium-82 from the sodium nonatitanate support medium with a solvent.

11. The process of claim 10, wherein the solvent is selected from the group consisting of water and saline solutions.

12. The process of claim 10, wherein the solvent is an aqueous solution having a sodium chloride concentration between 0.001 molar and 1 molar.

13. The process of claim 10, wherein the solvent is an aqueous solution having a sodium chloride concentration between 0.2 molar and 1 molar.

14. The process of claim 10, wherein the solvent is a pharmaceutical-grade saline and buffer solution.

15. A method of chemically isolating strontium-82 from a proton-irradiated rubidium or rubidium chloride target, comprising:

(a) dissolving the target containing the strontium-82;

(b) adjusting the pH of the dissolved target solution to an alkaline pH;

(c) removing precipitates from the solution; and then

(d) absorbing the strontium-82 from the solution onto a support comprising sodium nonatitanate without absorbing rubidium.

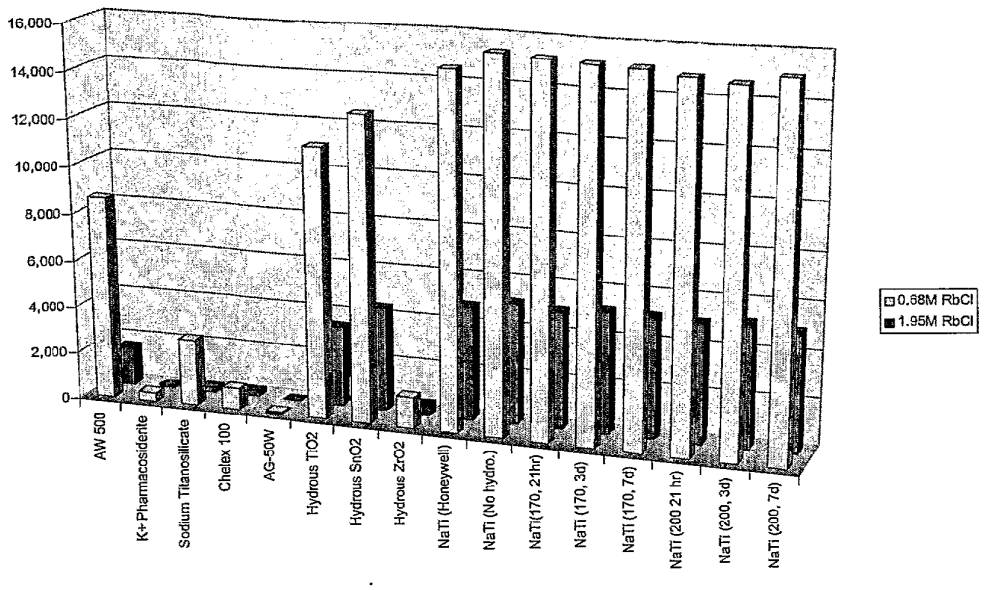


Figure 1. 82Sr K_d Values for the ion exchange materials from simulated rubidium and rubidium chloride target solutions

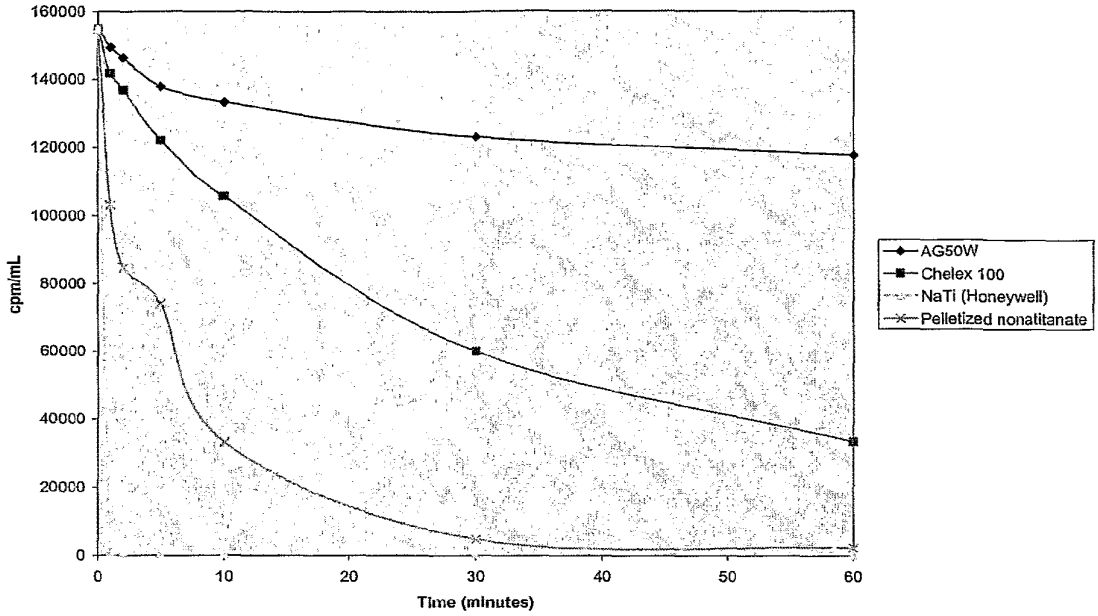


Figure 2. The reduction of 82Sr activity with increasing time.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 02/41676

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 G21G4/08

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)
IPC 7 G21G

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, COMPENDEX

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	EP 0 043 650 A (SQUIBB & SONS INC) 13 January 1982 (1982-01-13) the whole document	1-15
A	US 3 953 567 A (GRANT PATRICK M ET AL) 27 April 1976 (1976-04-27) the whole document	1-15
A	US 4 406 877 A (NEIRINCKX RUDI D ET AL) 27 September 1983 (1983-09-27) the whole document	1-15
A	US 3 957 945 A (GRANT PATRICK M ET AL) 18 May 1976 (1976-05-18) the whole document	9

-/--

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

[X] Patent family members are listed in 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
15 September 2003	25/09/2003

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, Tx. 31 651 epo nl, Fax: (+31–70) 340–3016	Ludi, M

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

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication,where appropriate, of the relevant passages	Relevant to claim No.
A	SYLVESTER P ET AL: "AN ASSESSMENT OF INORGANIC ION-EXCHANGE MATERIALS FOR THE REMOVAL OF STRONTIUM FROM SIMULATED HANFORD TANK WASTES" SEPARATION SCIENCE AND TECHNOLOGY, DEKKER,,NEW YORK,NY,, US, vol. 34, no. 10, 1999, pages 1981-1992, XP009013438 ISSN: 0149-6395 the whole document ---	1-15
A	SAHA G B ET AL: "USE OF THE 82SR/82RB GENERATOR IN CLINICAL PET STUDIES" INTERNATIONAL JOURNAL OF RADIATION APPLICATIONS AND INSTRUMENTATION PART B: NUCLEAR MEDICINE AND BIOLOGY, ELSEVIER SCIENCE PUBLISHERS, NEW YORK, NY, US, vol. 17, no. 8, 1990, pages 763-768, XP000166064 ISSN: 0883-2897 the whole document -----	1

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/US 02/41676

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
EP 0043650 A	13-01-1982	US 4400358 A	23-08-1983
		AT 22188 T	15-09-1986
		AU 548918 B2	09-01-1986
		AU 7135281 A	07-01-1982
		CA 1176618 A1	23-10-1984
		DE 3175292 D1	16-10-1986
		EP 0043650 A2	13-01-1982
		IE 51449 B1	24-12-1986
		JP 1662587 C	19-05-1992
		JP 3025760 B	08-04-1991
		JP 57030545 A	18-02-1982
		ZA 8103677 A	30-06-1982
US 3953567 A	27-04-1976	CA 1057946 A1	10-07-1979
		CH 591750 A5	30-09-1977
		DE 2542415 A1	15-04-1976
		FR 2286480 A1	23-04-1976
		JP 51060900 A	27-05-1976
US 4406877 A	27-09-1983	AU 7068681 A	10-12-1981
		CA 1171354 A1	24-07-1984
		EP 0041356 A1	09-12-1981
		JP 57031624 A	20-02-1982
		ZA 8103320 A	26-05-1982
US 3957945 A	18-05-1976	NONE	

Form PCT/ISA/210 (patent family annex) (July 1992)

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

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
9 March 2006 (09.03.2006)

PCT

(10) International Publication Number
WO 2006/026603 A2

(51) International Patent Classification:
A61K 51/00 (2006.01)

(21) International Application Number:
PCT/US2005/030796

(22) International Filing Date: 30 August 2005 (30.08.2005)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/605,481 30 August 2004 (30.08.2004) US

(71) Applicant *(for all designated States except US)*: **BRACCO DIAGNOSTICS INC.** [US/US]; 107 College Road East, Princeton, NJ 08540 (US).

(72) Inventors; and
(75) Inventors/Applicants *(for US only)*: **BALESTRACCI, Ernest** [US/US]; Woodbridge Hills, 404 Hampton Lane, Iselin, NJ 08830 (US). **MELCHORE, James, A., Jr.** [US/US]; 12 Staats Road, Bloomsbury, NJ 08804 (US). **MONTEFERRANTE, Jo, Anna** [US/US]; 18 Johnston Drive, Flemington, NJ 08822 (US). **KUCHAREWICZ ROPIAK, Irene** [US/US]; 15122 East Run Drive, Lawrenceville, NJ 08648 (US). **SCHRAMM, Ernest** [DE/US]; 815 Prospect Avenue, Milltown, NJ 08850 (US). **ZODDA, Julius, P.** [US/US]; 3 Tigers Court, Mercerville, NJ 08619 (US).

(74) Agents: **SUTTON, Paul, J.** et al.; Greenberg Traurig, LLP, Met Life Building, 200 Park Avenue, New York, NY 10166 (US).

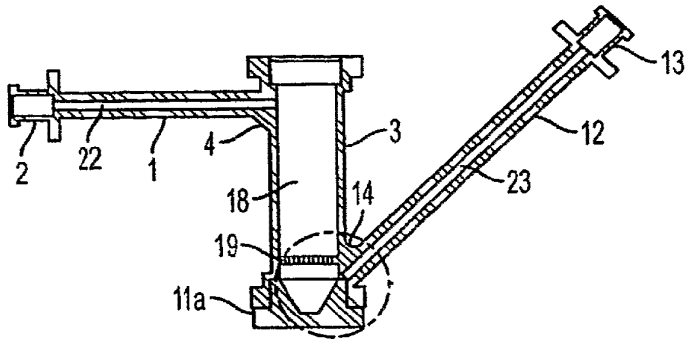
(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, 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: IMPROVED CONTAINERS FOR PHARMACEUTICALS, PARTICULARLY FOR USE IN RADIOISOTOPE GENERATORS



(57) Abstract: The invention is directed to improved containers for pharmaceuticals and any tubing and tubing connectors associated therewith, particularly containers for pharmaceuticals which are irradiated, heated or otherwise subjected to increased pressure. In a preferred embodiment, the invention is directed to an improved container for use in a radioisotope generator, such as a rubidium-82 generator.

WO 2006/026603 A2

IMPROVED CONTAINERS FOR PHARMACEUTICALS, PARTICULARLY FOR USE IN RADIOISOTOPE GENERATORS

TECHNICAL FIELD OF THE INVENTION

The invention is directed to improved containers for pharmaceuticals and the tubing and tubing connectors associated therewith, particularly containers for pharmaceuticals which are heated, irradiated or otherwise subjected to increased pressure. In a preferred embodiment, the invention is directed to an improved container for use in a radioisotope generator. Specifically, the designs and materials of the column container and its closure and associated tubing and tubing connectors have been improved.

SUMMARY OF THE INVENTION

The invention includes improved pharmaceutical containers, particularly improved containers for pharmaceuticals that are subjected to increased pressure (such as by heating or other means) and/or are subjected to radioactivity. In a preferred embodiment, the invention is directed to an improved container, also called a column, for use in a radioisotope generator. In an especially preferred embodiment, the improved column is for use with rubidium-82 generator such as those disclosed in U.S. Patent Nos. 3,953,567; 4,400,358; 4,406,877; 4,562,829; 4,585,009; 4,585,941; and 5,497,951, incorporated herein by reference in their entirety. In a particularly preferred embodiment, the improved column is used in a rubidium-82 generator such as that sold under the trade name CardioGen®.

The improved pharmaceutical container of the invention includes an improved seal and crimping process, as well as changes to the design of the stopper and the container to prevent blockages and improve consistency in packing and closing the container, which improves flow rate and elution from the column.

Further improvements include constructing the container and stopper out of radiation resistant or tolerant materials. In addition, flexible tubing used with the container is made of a radiation resistant or tolerant material, and the Luer locks used to fasten the flexible tubing to the container is made of a radiation resistant or tolerant material and is further improved to insure a tight, secure lock which will not inadvertently loosen or disconnect.

Specifically, the improved container has a new, stronger seal which is used to crimp the stopper in a pharmaceutical container and particularly, which is used to seal a radioisotope generator column/stopper assembly system, such as the CardioGen® system. This improved seal prevents leakage, even at increased pressure, and reduces ballooning of the rubber stopper material. The seal has a configuration similar to one of those shown in Fig. **5**B through Fig. **5**F and Fig. **6** and is made of any suitably strong material including

metal or plastic. A pneumatically operated automatic or semi-automatic crimper, set at optimized pressure, is preferably used to crimp the seal during assembly of a pharmaceutical container such as a radioisotope generator column/stopper assembly system. The invention includes identification of optimized crimping pressure(s) for crimping the seal (regardless of material) to a pharmaceutical container such as a glass or plastic vial or column and thus securing in place a rubber closure(s) when using an automatic crimping system and/or manual crimping.

The stopper which is crimped into place is also improved. Specifically, it is made of a material which is radiation resistant or tolerant, is resistant to ballooning and can withstand at least the pressures at which the container operates. Additionally, the configuration and placement of the stopper are improved. For example, the improved stoppers form tight seals with the column and reduce the "dead volume" at the bottom of the column– space where non-radioactive, decayed eluate could mix with (and dilute) fresh, radioactive eluate, reducing the efficacy of the eluent.

The improved pharmaceutical container also includes improvements to the design which improve its packing/assembly and thus ensure specified flow of eluent through the container.

These improvements are illustrated in the context of a radioisotope generator column container. Flow rate of the eluent through the column could be partially or completely blocked if the stopper blocks the outlet arm of the column. As shown in Figure **1**, the outlet arm of the container of the invention has been repositioned slightly and a small piece of plastic removed from the inside edge of the column to create a recess or notch where the outlet arm enters the column lumen to prevent a stopper from blocking flow. See Figure **4.** A small reinforcement piece of resin is added to the outside of the column between the outlet arm and column body to provide additional strength.

Another improvement in the containers of the invention addresses consistency of assembly and packing of the containers. In prior columns for a radioisotope generator, a plastic basket or spacer was supplied separately and was placed on the top of the column packing before the seal was inserted and the seal crimped into place. In these prior columns, placement of the baskets or spacers, which hold the column packing in place, could vary significantly, potentially creating some problems with consistency in packing. In the improved columns, two small orientation knobs have been added to the outside of the top basket/spacer and the orientation knobs are positioned 180° apart. These knobs fit into two small slots cut into the wall of the column. This combination eliminates the potential variability of manual alignment and depth placement of the basket/spacer into the column and ensures a consistent fit every time. Critical to the function of the column is the alignment of the basket/spacer openings with the column inlet in the top arm. This prevents potential misalignment and consequent restricted flow and possible back pressure and also ensures consistent and timely output of eluent to the patient.

Another improvement is to make the column assembly out of a radiation resistant or tolerant material, such as radiation resistant polypropylene. Likewise, the flexible tubing and Luer connector are made of radiation resistant or tolerant materials, such as radiation resistant polyvinylchloride. Furthermore, the Luer connector on the flexible tube and its counterpart Luer connector on the column assembly are configured to provide for a tight lock which will not leak and which will not loosen or inadvertently disconnect during use.

THE TECHNICAL PROBLEM AND ITS SOLUTION

The invention was designed to solve a number of technical problems experienced with prior art pharmaceutical containers.

1. Leakage From the Stopper/Column Interface

Leakage from the flange (or other area) of the seal of prior pharmaceutical containers such as column/stopper assembly systems was found to occur when the system was exposed to increasing pressure.

The new seal, consisting of a stronger material crimped at optimized crimping pressure, prevents leakage at the flange seal area even at increasing pressure.

2. Ballooning

Ballooning and/or burst of rubber materials (both before and after irradiation) through the center hole of current aluminum seals has been observed when they are subject to repeated pulsations of pressure cycling. The seals of the invention, which are stronger and are crimped at optimized pressure, reduce the likelihood of this problem. However, in a preferred embodiment the seal used in the improved container of the invention has a center hole of reduced size. For example, a seal with the configuration of those in Fig. **5**B, Fig. **5**C, Fig. **5**E or Fig. **6** may preferably be used. Due to the small center hole and strength of these seals, and crimping at optimized pressure, ballooning and/or burst of rubber materials is prevented. Consequently, pharmaceutical containers of the invention, and particularly column/stopper systems of the invention, can be exposed to much higher pressures during use of the system in the field.

In addition, the larger surface area of the crimp resulting from the reduction of the diameter of the center hole serves as additional support for the rubber closure and inhibits possible rupture as it is weakened over time due to the cumulative effect of exposure to radiation from the column or container content.

Also, the stopper is made of a radiation resistant or tolerant material. This also helps prevent ballooning and bursting.

3. Leakage Through Puncture Points

Leakage through puncture points has been observed in prior art pharmaceutical containers. Such leakage may be eliminated in containers of the invention through a combination of the stronger seal material, preferably a smaller center hole, and crimping at optimized pressure.

4. Splitting of the Seal

Splitting or tearing of current aluminum seals has been observed at pressures intended for use with a pharmaceutical container system (or pressures to which the system can potentially be exposed during intended usage in the field).

Due to the strength of the new seal material, no splitting or rupture of seal material is observed at pressures intended for use. For example, the seals on the columns of the invention do not split or rupture when used in, for example, a rubidium generator at intended pressures.

5. Inconsistent Manual Crimping Procedure

The manual crimping procedure commonly used with many prior container systems, including radioisotope column systems, is not always consistent and thus may not result in reproducible crimping pressures. Over-pressuring can result in buckling and collapse of the skirt of the seal material, the closure and/or the container. Under-pressuring can result in a loose overseal. Use of the automatic or semi-automatic crimping procedure of the invention with compressed or pressurized air results in consistent/reproducible crimping pressures, and enables selection of optimized crimping pressures when crimping various seal materials.

6. Maintenance of Consistent Flow/Reduction of Back Pressure

In some prior pharmaceutical columns, flow rate of the eluent through the column could be partially or completely blocked because the stopper blocked the outlet arm of the column. The outlet arm of the container of the invention has been repositioned slightly and a small piece of plastic removed from the inside edge of the column to create a recess or notch where the outlet arm enters the column lumen to prevent a stopper from blocking flow. A small reinforcement piece of resin is added to the outside of the column between the outlet arm and column body to provide additional strength. The recessed outlet arm and notch near the bottom of the column body greatly reduces the chance of back pressure due to a stopper blocking the outlet arm.

7. Inconsistent Positioning Within Column

In a column for a radioisotope generator, a plastic basket or spacer is supplied separately and is placed on the top of the packed column before the seal or closure is inserted and the seal crimped into place. In prior columns, the baskets/spacers, which hold the column packing in place, were not easily positioned consistently both in terms of depth and orientation. In the improved columns of the invention, two small orientation knobs have been added to the outside of the top basket/spacer and these orientation knobs are positioned 180° apart. These knobs fit into two small slots cut into the wall of the column. This combination eliminates the potential variability of manual placement of the basket into the column, ensuring a consistent fit from generator to generator and reducing the variability in packing density associated with this manual process.

8. Degradation Due To Radiation

Many materials degrade when exposed to radiation. Degradation includes possible changes in color, loss of flexibility, increased brittleness and the leaching out of various substances from the materials. To avoid these potential problems, the column assembly,

stopper, flexible tubing and Luer connectors are made out of radiation resistant or tolerant materials.

Frequently, when a material is said to be radiation resistant or tolerant, that means the material can withstand the amount of radiation used for sterilization, which is typically about 25 kGy. For the purposes of the present invention, however, a material is radiation resistant or tolerant when it can be exposed to about 145 kGy radiation and not degrade to the point where the functioning of the column assembly will be adversely affected.

9. Properly Closed Luer Locks

Luer locks are known in the art. However, it can be difficult to determine when a Luer lock has been sufficiently tightened to form a tight, non-leaking lock. Thus, one improvement is to provide for one or more tabs on each Luer connector. When the tabs achieve a certain orientation with respect to each other, for example when the tabs line up, such orientation means that the Luer lock has been sufficiently tightened.

Another potential difficulty with Luer locks is that they can come loose, i.e. disconnect, during use, which has the potential of causing a leak. To overcome this potential difficulty, the Luer connectors screw together and are each provided with one or more tabs. As the Luer connectors approach their fully tightened position, the tabs overlap. Further tightening causes the overlapping tabs to pass by each other, which can cause a clicking sound or sensation. When this occurs, the Luer lock is sufficiently tightened. Also, the Luer locks cannot become loose, e.g. unscrew, because the overlapping tabs will inhibit this action.

BRIEF DESCRIPTION OF THE FIGURES

Figs. **1A** through **1G** illustrate the inventive column assembly from different angles and cross sections.

Figs. **2A** through **2D** illustrate an alternative embodiment of the inventive assembly from different angles and cross sections.

Figs. **3A** throu gh **3D** illustrate a spacer or basket used in the inventive column assembly.

Fig. **4** illustrates a detailed view of the bottom of the inventive column assembly.

Fig. **5A** is a prior art crimp seal.

Figs. **5B** through **5F** illustrate various crimp seals that may be used with the inventive column assembly.

Figs. **6A** and **6B** illustrate a preferred crimp seal.

Figs. **7A** through **7D** illustrate a stopper for use with the inventive column assembly.

Figs. **8A** through **8D** illustrate an improved Luer lock.

DETAILED DESCRIPTION OF THE INVENTION

Referring now to Fig. **1**, Fig. **1A** shows a side view and Fig. **1B** shows a bottom view of the inventive container (e.g., column assembly) of one embodiment of the invention. Fig. **1C** is another side view of the inventive column assembly, cut along line A-A of Fig. **1B**. Fig. **1D** is detail B from Fig. **1C**, at a scale of 3:1 compared to Fig. **1C**. Fig. **1E** is a top view of the inventive column assembly, cut along line E-E of Fig. **1A**. Fig. **1F** is another side view of the inventive column assembly, cut along line C-C of Fig. **1B**. Fig. **1G** is detail D of Fig. **1F**, at a scale of 2:1 compared to Fig. **1F**.

Fig. **1**A has an inlet arm **1** which has an inlet arm female Luer cap **2** at its distal end. The proximal end of the inlet arm **1** attaches to the upper portion of a column **3**. There is also an inlet arm support means **4** to support the inlet arm **1**. The support means is preferably material which is added to support the inlet arm **1**. Preferably, this material is the same material used to construct the column assembly. As shown, the inlet arm support means **4** is a triangular shaped member attached to the inlet arm **1** and the column **3**, although the shape of the support is not limited to a triangle. It can be square, a bar passing from the inlet arm **1** to the column **3**, or any other suitable shape.

The column **3** has a top portion **5** and a bottom portion **6**. The top portion **5** comprises a first top portion **7** and a second top portion **8**. The first top portion **7** is on top of and has a diameter greater then the second top portion **8**, which is on top of and has a greater diameter than the column **3**.

The bottom portion **6** of the column **3** has a similar configuration. It has a first bottom portion **9** and a second bottom portion **10**. The first bottom portion **9** sits below and has a greater diameter than the second bottom portion **10**, which sits below and has a greater diameter than the column **3**. Also shown is a bottom stopper **11**.

An outlet arm **12** is attached to the bottom portion of the column **3**. The distal end of the outlet arm **12** terminates in an outlet arm female Luer cap **13**. There is also an outlet arm support means **14** to support the outlet arm **12**. The support means is preferably material which is added to support the outlet arm **12**. Preferably, this material is the same material used to construct the column assembly. As shown, the outlet arm support means **14** is a triangular shaped member which attaches to the column and the outlet arm **12**, although the shape of the support is not limited to a triangle. It can be a square, a bar passing from the outlet arm **12** to the column **3**, or any other suitable shape.

Fig. **1**C shows a cross section of the inventive column assembly, cut through line A-A of Fig. **1**B. As shown, the inlet arm **1**, column **3** and outlet arm **12** are hollow.

Turning to the hollow interior or lumen of the column **3**, it first defines a top stopper receptacle area **15**. Below that and in communication with it is a top basket receptacle area **16**. As shown in Fig. **1C**, the top basket receptacle area **16** contains a top basket or spacer **17**. Following that is a packing material containing area **18**. Underneath the packing material containing area **18** is a bottom screen **19**, followed by a bottom open area **20**. Underneath the bottom open area **20** is a bottom stopper receptacle area **21**.

Fig. **1**C shows the bottom stopper **11** inserted into the bottom stopper receptacle area **21** of the column **3**. Note that the bottom stopper **11** consumes most of the bottom stopper receptacle area **21**. This minimizes the dead volume in the bottom stopper receptacle area **21**. Minimization of the dead volume minimizes mixing of fresh, radioactive eluent with non-radioactive or decayed eluent, which could dilute the fresh eluent, thereby maintaining a narrow rubidium-82 bolus profile.

The inlet arm **1** and outlet arm **12** are each hollow, the hollow portions being **22** and **23** respectively, and are in communication with the hollow portion of the column **3**. As

shown in Fig. **1C**, the hollow portion **22** of the inlet arm **1** is in communication with the top basket receptacle area **16**.

The intersection of the column **3** and the outflow arm **12** is shown in more detail in Fig. **1D**. As shown therein, no portion of the outflow arm **12** extends into the hollow portion of the column **3**, as was the case with certain prior art column assemblies. Also, the hollow portion **23** of the outflow arm **12** intersects the hollow portion of column **3** at the top of the bottom stopper receptacle area **21** or at about the place the bottom stopper receptacle area **21** and the bottom open area **20** intersect. This configuration, not found in prior art column assemblies, prevents the bottom stopper **11** from blocking the outflow arm **12**.

In a preferred embodiment, an outflow notch **25** is formed where the hollow portion **23** of the outflow arm **12** intersects the hollow interior of the column **3**, thus further preventing any blockage of the outflow arm **12** by the bottom stopper **11**. This embodiment is shown in more detail in Fig. **4**.

Fig. **1E** is a top view of the inventive column assembly. Visible from this perspective are, for example, the top basket or spacer **17** and the top basket receptacle area **16**. Also shown are notches **24a** and **24b**.

The notches **24a** and **24b** are made in the wall of the top basket receptacle area **16**. As shown in Fig. **1E**, they are 180 degrees opposed to each other. They are configured to cooperate with a pair of protrusions which appear on a top basket (discussed below with respect to Fig. **3**) such that the protrusions fit into notches **24a** and **24b**. This configuration insures proper placement of the top basket into the top basket receptacle area **16** so that the top basket is straight and at the correct depth. In prior art column assemblies, which lacked these notches and protrusions, it was possible to insert the top basket in such a manner that it was not straight and/or at the wrong depth, which adversely affected the function of the column assembly.

Fig. **1E** shows two notches **24a** and **24b** 180° opposed to each other. It is understood that the present invention is not limited to this configuration. Rather, there can be 1, 3, 4, 5, 6 or more notches or even a ledge present in the wall of the top basket receptacle area **16** in any configuration, so long as these notches (or ledge) cooperate with protrusions on the top basket to insure its proper fit.

Fig. **1F** shows a side view of the inventive column assembly, cut along line C-C of Fig. **1B**. Fig. **1G** is detail D of Fig. **1E**, showing an alternative embodiment for the first top portion **7a**. As shown in Fig. **1G**, this first top portion **7a** slopes downwardly from its top, whereas the first top portion **7** of Fig. **1F** is squared off, i.e., non-sloping.

Fig. **2** shows an alternative embodiment of the inventive column assembly. As shown in Fig. **2D**, which is detail B from Fig. **2C** at a scale of 3:1, the bottom stopper **11a** is configured to fit into substantially all of the space of the bottom stopper receptacle area **21**. This insures a better fit between the outer wall of the bottom stopper **11a** and the inner wall of the bottom stopper receptacle area **21**, thus further insuring against any leaks. In addition, the stopper **11a** reduces the dead volume in the bottom stopper receptacle area **21**. Minimization of the dead volume minimizes mixing with non-radioactive or decayed eluent, which could dilute the fresh eluent, thereby maintaining a narrow rubidium-82 bolus profile. The bottom stopper **11a** further comprises a bottom stopper hollow space **11b**. This bottom stopper hollow space **11b** helps prevent the bottom stopper **11a** from blocking the outflow arm **12**.

The column assembly is preferably made of polypropylene. Prior art column assemblies were made with H5820 polypropylene. While that product can still be used, in a preferred embodiment the polyproplylene random copolymers PP P5M4R-034 or PP 13R9A (Huntsman Polymers (The Woodlands, TX)) can be used because they are more resistant to radiation than the prior art H5820 polypropylene. See the Prospector X5 data sheets with

ATSM and ISO properties for PP P5M4R-034 and PP 13R9A, which are incorporated herein by reference in their entirety. Of the two Huntsman polypropylenes, PP 13R9A is the more preferred, based upon UV profile, Instron stress testing and appearance after gamma-irradiation.

The manufacturing process for the inventive column assembly has also been improved. A new automatic mold has been designed which improves the quality and appearance of the column assembly, and which increases the efficiency of the manufacturing process. Manufacturing is presently done by Duerr Molding (Union, N.J.).

For example, pins are used to form the hollow portions of the inlet arm **22** and outflow arm **23**. In the prior art molding process, these pins were not fixed, so they floated. As a result, the side wall thickness of the inlet arm **1** and outlet arm **12** varied. In the present process, the pins are fixed. Therefore, the thickness of the side walls is more uniform.

Also, as described above, the position of the outflow arm **12** has been moved, the outflow arm no longer protrudes into the hollow interior or lumen of the column **3**, and the outflow arm resides in a recess or notch. This prevents the outflow arm from being blocked. Furthermore, support means **4, 14** are provided to strengthen the inlet arm **1** and the outflow arm **12**. In addition, notches **24a** and **24b** are provided for the proper placement of the top basket.

Further improvement to the manufacturing process and column assembly are described throughout the instant specification.

The packing material area **18** of the column **3** is designed to receive packing material. The type of packing material used depends upon the intended use of the column arrangement.

When used as, for example, a rubidium-82 generator, such as CardioGen®, the packing material is one which will adhere strontium-82 but will allow for the elution of rubidium-82. Strontium(II)-82 decays into rubidium(I)-82. Elution of strontium-82 is not

desired because it binds to bone and exposes the patient to unnecessary radiation exposure. Presently, stannic oxide is the preferred packing material.

The packing material is loaded into the column **3** in a conventional manner. The column **3** is then loaded with strontium-82 in a conventional manner. For example, the closure is punctured by a needle (or similar device) containing the strontium-82 solution. The strontium-82 solution is slowly added to the top of the packed column and allowed to flow through it by the force of gravity. If necessary, a small vacuum can be used. Also, the packing material is preferably wetted before the strontium-82 is added. Slow addition of the strontium-82 is preferred because it will result in the strontium-82 being absorbed as close to the top of the column as possible.

Filters, preferably fiberglass filters, can also be used in this conventional loading procedure. For example, two fiberglass filters are first placed in the column **3**, then a portion of the packing material is added, followed by a single fiberglass filter, then the remainder of the packing material, then two more fiberglass filters. Once filled, the top basket or spacer **17** is inserted into the top basket receptacle area **16**. The top basket **17** acts as a retainer to hold the packing material in place.

Fig. **3** shows schematics of the spacer or top basket **26** of the inventive column assembly. The spacer or top basket **26** is cylindrical in shape with an open top portion **27** and a screen **28** at the bottom portion **29**. Another top basket or spacer **17** of similar configuration is shown in Fig. **1**, placed in the top basket receptacle area **16**.

As shown in the embodiment of Figs. **3B** and **3D**, the top basket **26** actually has three cylindrical areas, a top cylindrical area **30**, a middle cylindrical area **31** and a lower cylindrical area **32**. The top **30** and bottom **32** cylindrical areas have diameters about equal to each other, and their diameters are greater than the diameter of the middle cylindrical area **31**.

The top basket **26** also contains protrusions **33a**, **33b** which are designed to cooperate with notches **24a**, **24b** in the top basket receptacle area **16**. In operation, the protrusions **33a**, **33b** fit into the notches **24a**, **24b** to insure proper alignment of the top basket **26** in the top basket receptacle area **16**. When so positioned, the top basket **26** acts as a retainer to hold the packing material in place.

As shown in Figs. **3A** and **3C**, the two protrusions **33a**, **33b** are 180° opposed to each other. They are located at the top cylindrical area **30**. As was the case with the notches **24a**, **24b**, the present invention is not limited to this configuration. Rather, there can be 1, 3, 4, 5, 6 or more protrusions, in any orientation, so long as they cooperate with the notches to help insure a proper fit for the top basket **26** .

The top basket **26** also contains a side opening **34**. As shown in Figs. **3B** and **3D**, the side opening is in the middle cylindrical area **31** of the top basket **26**. The purpose of the side opening is to line up with the inlet arm **1** when the top basket **26** is placed in the top basket receptacle area **16**. In this arrangement, when a liquid is introduced into the inlet arm **1**, it will pass through the side opening **34** into the top basket **26**.

The top basket **26** can be made of any suitable material, such as polypropylene. Preferably, the material will be radiation resistant, i.e. resistant to degradation in the presence of a radioactive material. More preferably, the top basket **26** is made of the same material used to construct the column assembly. In a preferred embodiment, that material is PP P5M4-R-034 or PP 13R9A polypropylene (Huntsman Polymers (The Woodlands, TX). Even more preferably, the material is the PP 13R9A polypropylene. In a yet further preferred embodiment, the top basket **26** is molded at the same time the rest of the column assembly is molded.

As discussed above, Fig. **4** shows a detailed view of the bottom **6** portion of the column **3**. Fig. **4** shows the outflow notch **25** where the hollow portion **23** of the outflow arm

12 intersects the hollow interior of the column 3. The outlet notch 25 prevents blockage of the hollow portion 23 of the outflow arm 12 by the bottom stopper 11 (not shown in Fig. 4).

Fig. 5 shows various types of crimp seals to use with the present invention. Fig. 5A shows the current, prior art crimp seal. Figs 5B-5F show various alternate embodiments of the crimp seal.

The function of the crimp seal is to form a tight, crimped seal between the stoppers (described below) and the pharmaceutical container to prevent leakage. Also, a central hole is provided in the crimp seal to allow for the insertion of a needle or similar device. In one preferred embodiment the pharmaceutical container is a column, or column assembly, such as one used in a rubidium generator.

The crimp seal can be made of any material, such as plastic or metal. The material should preferably be radiation resistant, and of sufficient strength to withstand pressures of at least 90 psi and preferably up to 160 psi. More preferably, the material should be metal. Preferred metals comprise aluminum, steel and tin, or suitable alloys or mixtures thereof. The metal can be optionally coated. For example, tin coated steel can be used.

The diameter of the crimp seal will vary according to use, for example, vary according to the diameter of the pharmaceutical container which is to be crimped. With respect to a column assembly to be used as a rubidium–82 generator, such as CardioGen®, the diameter of the crimp seal is preferably about 20 mm across its top.

Fig. 5A shows a conventional prior art crimp seal 35. It is made out of aluminum which is about 0.2 mm thick, has a flat top portion 36 with a diameter of about 20 mm with central hole 37 of about 9.5mm in diameter and a skirt 38 about 7.5mm high.

There are several potential problems with this prior art crimp seal. First, because aluminum with a thickness of only about 0.2 mm is used, the crimp seal might not be strong enough to insure a strong, leakproof seal. Second, the central hole 37 is large, and therefore

the stopper might not be properly supported. Also, the larger central hole **37** may allow for ballooning of the stopper. Third, this crimp seal is manually crimped to the column **3**. Manual crimping can result in undesirable variability of crimping pressure and, accordingly, can affect how well the crimp seal **35** seals the column **3** to prevent leakage.

Fig. **5B** shows one type of useful crimp seal **39**. This crimp seal **39** comprises two parts, a top crimp member **40** and a bottom washer **41**. Both the top crimp member **40** and the bottom washer **41** are made of aluminum (vendor –West). The thickness of the aluminum for each part can vary depending upon the intended use, but the aluminum used for each member is generally about 0.2 mm thick.

The top crimp member **40** has a central hole **42** and a skirt **43**. The size of each, and the diameter of the crimp seal, can vary depending upon use. As shown in Fig. **5B**, the central hole **42** has a diameter of about 6.4mm and the skirt **43** is about 7.6mm high. The diameter of the top crimp member **40** is about 20 mm. The top crimp member **40** also has a cover **44**, which covers the central hole **42** when not in use but can be pulled or pealed back when in use. Also, while none of Figs. **5C** through **5F** or Fig. **6** show a cover, it is understood that each of these embodiments can employ a cover if desired.

Fig. **5B** also employs a bottom washer **41**. The bottom washer **41** contains a central hole **45**. The bottom washer central hole **45** can have a diameter greater than, the same as or smaller than the diameter of the central hole **42** in the top crimp member **40**. As shown in Fig. **5B**, both central holes **45**, **42** have about the same diameter, i.e. about 6.4mm. The bottom washer **41** does not have a skirt. The diameter of the bottom washer **41** is about 20 mm.

When used, the bottom washer **41** is placed below the top crimp member **40** and both are crimped into place. Crimping is preferably performed via an automatic or semi-automatic

crimper, which is discussed in more detail below. In the alternative, other processes which control the crimping pressure applied can be used.

Fig. **5C** shows another embodiment of the inventive crimp seals. This crimp seal **46** comprises a single member. It is made out of steel (vendor – Microliter). The thickness of the steel can vary according to the intended use, but is generally about 0.2 mm thick. This crimp seal **46** is about 20 mm in diameter, contains a central hole **47** of about 5.0mm in diameter and has a skirt **48** about 7.2mm high. The crimp seal **46** is preferably crimped into place using an automatic or semi-automatic crimper, although other processes which control the pressure applied can be used.

Fig **5D** shows yet another embodiment of the inventive crimp seals. This crimp seal **49** comprises a single member. It is made out of steel (vendor – Microliter). The thickness of the steel can vary according to the intended use, but is generally about 0.2 mm thick. This crimp seal **49** has a diameter of about 20mm, contains a central hole **50** of about 8.0mm in diameter and a skirt **51** about 7.2mm high. The crimp seal **49** is preferably crimped into place using an automatic crimper, although other processes which control the pressure applied can be used.

Fig. **5E** is yet still another embodiment of the inventive crimp seals. This embodiment comprises two parts, a top crimp member **52** and a bottom washer **53**. Both the top crimp member **52** and the bottom washer **53** are made of aluminum (vendor – Microliter). The thickness of the aluminum can vary depending upon the intended use, but the aluminum used for each member is generally about 0.2 mm thick.

The top crimp member **52** has a central hole **54** and a skirt **55**. The central hole **54** has a diameter of about 9.6 mm and the skirt **55** is about 7.6 mm high. The top crimp member **52** has a diameter of about 20mm.

The top crimp member **52** also contains an insert **56**, which is seated in or under the central hole **54**. The insert **56** can be made of any suitable substance, but is preferable made of metal, such as steel, aluminum or tin, or plastic. The insert **56** also contains an insert central hole **57,** which has a diameter of about 5 mm.

The bottom washer **53** also has a central hole **58**, which has a diameter of about 5 mm. The bottom washer **53** is about 20 mm in diameter and it does not have a skirt.

When used, the bottom washer **53** is placed below the top crimp member **52** and the insert **56** and then all are crimped into place. Crimping is preferably performed using an automatic or semi-automatic crimper, although other processes which control the pressure applied can be used.

Fig. **5F** shows yet another embodiment of the inventive crimp seals. Like Fig. **5E**, Fig. **5F** employs two members, a top crimp member **59** and a bottom washer **60**. Both members are made of aluminum (vendor-Microliter). While the thickness of the aluminum can vary with the intended use, generally each member is about 0.2 mm thick.

The top crimp member **59** contains a central hole **61** and a skirt **62**. The central hole **61** has a diameter of about 9.6 mm and the skirt **62** is about 7.6 mm high. The top crimp member **59** has a diameter of about 20mm.

The bottom washer **60** also has a central hole **63**. The bottom washer central hole **63** has a diameter of about 11.4 mm. The diameter of the entire bottom washer **60** is about 20mm. The bottom washer **60** does not have a skirt.

When used, the bottom washer **60** is placed below the top crimp member **59**. Both are then crimped into place. Preferably, an automatic crimper is employed, although other processes which control the pressure applied can be used.

Fig. **6** is an alternate and preferred embodiment of the inventive crimp seals. This crimp seal **64** comprises a single member. It is made out of steel (vendor – Microliter), code

#20-000 M. See the Microliter Product Catalog, which is incorporated herein by reference in its entirety. The thickness of the steel is about 0.20 mm.

The crimp seal **64** contains a central hole **65** and a skirt **66**. The central hole **65** is about 5.00 mm $\pm$ 0.25 mm in diameter and the skirt **66** is about 7.00 mm $\pm$ 0.25 mm high. The entire crimp seal **64** has a diameter of about 20.75 mm $\pm$ 0.25 mm. The crimp seal **64** is preferably crimped into place using an automatic or semi-automatic crimper.

Fig. **7** shows an improved stopper **67** to be used with the inventive column assembly. The stopper **67** is preferably made from a material which will form a tight seal with the column assembly. In a preferred embodiment the stopper **67** is made of a material which is also resistant to radiation.

Prior art stoppers were made of materials such as Itran-Tompkins PT-29 green neoprene rubber. This material had two potential disadvantages. First, it could degrade when exposed to radiation. Second, it contained latex, which could cause allergic reactions.

Various materials were compared to the PT-29 green neoprene used in the prior art. These materials included neoprene, isoprene, bromobutyl, chlorobutyl, nitrile, isoprene/chlorobutyl, EPDM (ethylene propylene diene monomer) and Viton®. These materials were coated, uncoated, siliconized and non-siliconized.

These materials were made into column assembly stoppers and were irradiated simulating the exposure from a 100mCi generator over a time period of 45 days (about 145 kGy). Irradiated stoppers were compared to non-irradiated controls by integrity (pressure) testing of the column/stopper assemblies. Assemblies were pressurized to determine load pressure required to cause ballooning of rubber materials or leaks/burst at the seal closure (up to about 200 psi). In addition, for the purpose of determining potential rubber extractables and/or leechables, additional column/stopper assemblies were irradiated in the presence of

0.9% saline solution. The saline solution was then scanned at 250mm for UV absorbing extractables.

Three elastomeric compositions were identified as suitable to use in the stoppers of the invention: West Pharmaceutical Services (Lionville, PA) 4588/40 isoprene/chlorobutyl; American Stelmi (Princeton, NJ) 6720 bromobutyl; and Helvoet-Pharma (Pennsauken, NJ) Helvoet FM 140/0 chlorobutyl. Of these materials, the most preferred product to use is the West 4588/40 isoprene/chlorobutyl. Other materials may be used as long as they provide the stopper characteristics specified herein.

The stopper **67** should be configured so that it forms a tight seal with the column assembly and minimizes the dead volume (mixing), thus maintaining a narrow rubidium-82 bolus profile and maximizing efficiency. One preferred structure for the stopper is shown in Fig **7**.

Referring to Fig **7B**, the stopper **67** comprises a generally cylindrical top section **68** and a generally cylindrical bottom section **69**. The diameter of the stopper bottom section **69** is about the same as or slightly larger than the inside diameter of the first top portion **7** and first bottom portion **9** of the cylinder **3**, assuming both of these portions **7, 9** have the same diameter. If these portions have different diameters, then the cylindrical bottom section **69** of the stopper **67** will have about the same or slightly larger inside diameter as the portion **7, 9** it is intended to be inserted into. The reason for this configuration is to insure a tight fit between the stopper **67** and the first top **7** and first bottom **9** portions of the cylinder **3**. A tight cylinder **3**/ stopper **67** interface helps prevent leakage.

The stopper top section **68** has a greater diameter than the stopper bottom section **69** to prevent the stopper **67** from being inserted too far into the cylinder **3**. In addition, optionally the stopper top section **68** can have a curved upper edge **70**.

The stopper bottom section **69**, in one preferred embodiment, contains a U-shaped groove **71** in its base. See Fig **7A**. The U-shaped groove **71** traverses greater than half the length of the stopper bottom section **69**, and it terminates in a semi-circular section **72**. Preferably, the center point **73** of the semicircular section **72** should be about at the center point of the stopper bottom section **69**.

The stopper top section **68** contains a central circular indentation **74** in its top surface. See Fig **7C**. Preferably, the diameter of the central circular indentation **74** has a diameter about equal to the width of the U-shape groove **71**. As shown in Figs **7B** and **7D**, the central circular indentation **74** and the U-shaped groove **71** should preferably line up with each other when the stopper is viewed through its cross-section. The central circular indentation **74** and U-shaped groove **71** allow for easy insertion of a needle or similar device into the stopper **67**.

The surface of the stopper top section **68** also contains three spherical dots **75a**, **75b**, **75c** and an indicia, such as a spherical lug **76**. They are spaced equidistant from each other around the central circular indentation **74**. Also, the spherical lug **76** is placed so that it is above the U-shaped grove **71**. In this configuration, when the stopper **67** is inserted into the first top portion **7** of the column **3**, the spherical lug **76** can be lined up with the inlet arm **1**. Thus, the open end of the U-shaped groove **71** will face the inlet arm **1**, thus preventing its blockage.

The same holds true for the first bottom portion **9** of the column **3**. When the stopper **67** (stopper **11** shown in Fig. **1** and stopper **11b** in Fig. **2** can have the same or different configurations from stopper **67**) is inserted therein, the spherical lug **76** is lined up with the outlet arm **12**. The open end of the U-shaped groove **71** will then face the outlet arm **12** and prevent its blockage.

It is understood that the present invention is not limited to a U-shaped groove **71**. Any other configuration, such as a notch, can be used so long as any potential blockage is

avoided. In fact, if there is no potential for blockage, the U-shaped groove **71** or alternative structure can be eliminated.

The stopper **67** is affixed to the column **3** via crimping, using the crimping seals described above in Figs. **5** and **6**. In the prior art, crimping was performed manually. The disadvantage of manual crimping is that it is not always uniform. One problem this can cause is leakage. To overcome this potential problem, the present invention preferably uses automatic or semi-automatic crimping.

Any automatic or semi-automatic crimper can be used for the present invention, so long as it can consistently crimp seals at a specified, controlled pressure. One preferred type of automatic crimper is a pneumatic crimper, which is powered by gas. One example of a pneumatic crimper suitable for the present invention as an AP/CP2000 Lightweight Air Crimper/Decapper (Laboratory Precision Limited, UK). See Laboratory Precision Limited brochure copyrighted April 4, 2001, which is incorporated herein by reference in its entirety.

In the crimping process, a stopper **67** is inserted into the top portion **5** or bottom portion **6** of the column **3**, so that it is seated in the first top portion **7** or first bottom portion **9**, respectively. A crimp seal or a crimp seal and washer (see Figs. **5** and **6**) is/are placed over the stopper **67**. The crimp seal or crimp seal and washer are then crimped into place, either manually or, preferably, automatically or semi-automatically. While the crimping pressure used is optimized based upon the configuration and material of the crimp seal and stopper, generally about 117 ± 3 psi pressure is used.

The resulting crimped crimp seal/stopper configuration can withstand the operative pressures of the system and can further withstand pressures of at least 90 psi and preferably up to 200 psi.

When in operation, connector tubes (not shown) are connected to the column assembly. Referring to Fig **1A**, both the inlet arm **1** and the outlet arm **12** have a female Luer

cap **2**, **13** at their distal ends. These female Luer caps **2**, **13** engage male Luer caps at the proximal ends of the connector tubes.

Prior art connector tubes can discolor from clear to brown and harden upon prolonged exposure to radiation. Also, the Luer connector can discolor and become brittle. In addition, the Luer connectors can loosen or become unintentionally disconnected during shipping or use.

Accordingly, the present invention includes constructing connector tubing out of radiation resistant materials. Preferably, the tubing is made from a flexible radiation resistant polyvinyl chloride (PVC) and the Luer connector is made from a rigid radiation resistant PVC. For example, a preferred material for constructing the tubing is AlphaGary PVC 2232 A/R-78S Clear 030X. See AlphaGary Test Result Certificate, Report Date 8/20/99; Technical Data, Date of Origin 8/99; and Material Safety Data Sheet printed 04/05/00; which are incorporated herein by reference in their entirety. A preferred material for constructing the Luer connector is AlphaGary PVC 2212 RHT/1-118 Clear 080X. See AlphaGary Data Sheet, Revision Date 4/02, which is incorporated herein by reference in its entirety. Also, using this AlphaGary rigid PVC for the Luer connector allows the heat bonding of tubing to the Luer connector.

The present invention further includes an improved Luer lock. The improvements are described below. An embodiment of this improved Luer lock is set forth in Fig. **8**. These improved Luer locks can be used with the pharmaceutical containers of the present invention, or in any other indication where it is desirable to have a connection that will not inadvertently loosen or disconnect.

In the embodiment of Fig. **8**, Fig **8A** show a side view of the inventive column assembly with the inlet arm **1** projecting forward. Also shown is the female Luer cap **2** at the distal end of the inlet arm **1**.

As shown in Fig. **8C**, the female Luer cap **2** terminates in a flange **77**. The flange **77** can be flat or, as shown, contain a groove **78**. Other configurations, known in the art, can also be used.

The flange **77** is configured to engage and mate with threads **78** in a male Luer cap **79**. When the two caps **2, 79** are screwed together, they form a tight Luer lock which will be leak resistant. This configuration is shown in Fig. **8D**.

One difficulty with a Luer lock is to know when the male and female caps **79, 2** have been connected sufficiently to form a tight lock. To overcome this problem, one or more tabs are provided on each of the male **79** and female Luer caps **2.** As shown for example in Figs. **8C** and **8D**, two tabs are provided on each cap **80a, 80b, 81a** and **81b**, although it is understood that the invention is not limited to this configuration only. For example, each of the Luer caps can also contain 1, 3, 4, 5, 6 or more tabs.

In one embodiment, the female Luer cap tabs **80a, 80b** and the male Luer cap tabs **81a, 81b** are so positioned that when the Luer locks is sufficiently tight, the tabs line up with each other. This way, a user knows when tightening is completed. The present invention, however, is not limited to this one configuration, so long as the tab or tabs on each of the Luer connectors **79, 2** are arranged in a desired configuration to demonstrate that the Luer connectors **79, 2** are sufficiently tightened. In another preferred embodiment, as shown in Fig **8D**, the male Luer cap tabs **81a, 81b** overlap with the female Luer cap tabs **80a, 80b**. The tabs are so positioned that this overlap occurs when the tightening is complete. At the point of desired tightening, the tabs **80a, 80b, 81a, 81b** pass by or click past each other. That way, the Luer locks cannot be over- or under-tightened. Also, inadvertent loosening or disconnection of the Luer lock during use or shipping is prevented by the overlapping of the tabs, preventing the Luer connectors **79, 2** from turning in a loosening direction.

When the inventive column assembly is used as, for example, a rubidium-82 generator, it is pre-packaged with strontium-82 in the factory. That is, the product shipped to the customer is radioactive. Therefore, the radioactive column assembly is shipped in a shielded (e.g. lead) container.

Nevertheless, leakage is still a concern upon shipping. Thus, to improve safety when the radioactive column assembly is shipped, an inventive improvement is to ship the product with a liquid absorbent pad. Preferably, the shipping pad is a GP100 absorbent pad (Shell Packaging Corporation, Springfield, NJ). GP100 is a 100% polypropylene non-woven mat of randomly oriented micro-fibers (2-10 micron diameters). See SPC General Product Specifications for GP100 dated May 26, 2003, which is incorporated herein by reference in its entirety. This type of shipping pad, which may have various configurations, thicknesses or absorbent capacities, is useful in absorbing any leaks which may occur.

SUMMARY OF THE PREFERRED EMBODIMENTS

Improved Seal

The new seal, which is used to crimp the rubber stopper in place in a pharmaceutical container and particularly, which is used to seal a radioisotope generator column/stopper assembly system, such as CardioGen®, is preferably made of a sufficiently strong material to eliminate the problems discussed above. Figs. **5B** through **5F** and Fig. **6** illustrate various method of reinforcing the top portion of the seal by use of a second layer (washer) or use of a stronger material such as steel/tin in addition to reducing the size of the center hole. The material may include metal or plastic, but is preferably metal. The metal may include heavy gauge aluminum, steel or tin, but is preferably steel or tin. The seal generally has the configuration shown in Fig. **5B** through **5F** and Fig. **6** and may have a small or large central hole, a shorter or longer skirt and optionally, a cover (e.g., plastic or aluminum over the central hole). The dimensions of the seal will vary, and one skilled in the art will understand that they should be appropriate to the container which is being sealed. Approximate dimensions for seals for a radioisotope generator column are shown in the various examples in Figure **5** and in Fig. **6**. These dimensions are approximate and are not intended to be limiting.

The central hole of the seals of the invention may vary in size. In a preferred embodiment the seal has a smaller central hole such as, for example, those proportional to the central holes shown in Fig. **5B**, Fig. **5C**, Fig. **5E** and Fig **6**.

In one embodiment, seals of Fig. **5B** through Fig **5F** and Fig. **6** are used to seal a radioisotope generator column. These seals are available from the vendors West Pharmaceutical Services (Lionville, PA) and Microliter Analytical Supplies Inc. (Suwannee, GA). In a particularly preferred embodiment, the central hole of the seal is reduced in size such as in the seals in Fig. **5B**, Fig. **5C**, Fig. **5E** and Fig. **6**. The preferred configuration for

this application is a 1-piece steel/tin crimp with a center hole of approximately 4-5 mm diameter and a skirt length of approximately 7.2 to 7.5mm as shown in Fig. **6**.

The combination of using a stronger material such as steel/tin or heavier gauge aluminum and reduction of the center hole results in optimum performance in maintaining a secure leakage free seal under high pressure and particularly repeated exposure (pulsing or cycling) to high pressure as occurs with the use of the rubidium-82 generator as the enlarged surface area of the crimp limits excessive expansion of the rubber closure under pressure.

The use of a stronger material such as steel/tin or heavy gauge aluminum further improves the performance of the crimp by reducing the likelihood of failure due to relaxation or fatigue of the seal flange which is formed at the point where the crimp skirt is folded under the column or container flange when exposed to high or pulsating pressures. It is understood that the skirt length can be varied to provide a proper fit with the container/rubber seal combination to which it is applied.

Improved Seal

In a preferred embodiment improved stoppers are used. Such stoppers are made of a radiation resistant material, preferably isoprene/chlorobutyl and most preferably West 4588/40 isoprene/chlorobutyl. Additionally, the configuration and placement of the stoppers are improved so that they form tight seals with the column, do not block the inlet or outlet arms and reduce the "dead volume" at the bottom of the column. In a preferred embodiment the stoppers are designed to facilitate insertion of a needle or similar device and contain indicia indicating proper insertion orientation. In the most preferred embodiment, the stoppers have the configuration shown in Fig 7A, Fig 7B and Fig. 7C.

Automatic Crimper and Improved Crimping Process

In a preferred embodiment, an automatic or semi-automatic crimper is used to crimp the seals of the invention. The automatic or semi-automatic crimper is set at an optimized

pressure and is able to crimp seals of any material during assembly of a pharmaceutical container such as a radioisotope generator column/stopper assembly system. Suitable automatic crimpers include pressurized and/or compressed air crimpers such as those available from Laboratory Precision Limited under the trade name/model number AP/CP2000. Use of the automatic or semi-automatic crimping procedure of the invention with compressed or pressurized air results in consistent/reproducible crimping pressures, and enables selection of optimized crimping pressures when crimping various seal materials.

Use of optimized pressures improves the performance of the seals of the invention and also improves performance of seals of only moderate strength, such as lighter gauge aluminum and some plastics.

The automatic or semi-automatic, pneumatically powered crimper used to apply the seal is preferably operated at an optimized pressure of between 60 – 140 psi. However, although automatic or semi-automatic crimpers are preferred, it should be noted that application of the seal is not limited to automated equipment, and systems ranging from manual to fully automatic may be used, provided their operation can be optimized to produce repeatable and consistent predetermined pressures in applying the seals.

Column Design Improvements

Manufacturing Process: To create the new column design, a new automatic mold has been designed. The mold and the new columns produced therein exhibit improved column quality and appearance. The new mold also increases the efficiency of the manufacturing process. The increased speed of the new automated mold enables one operator to run the process efficiently.

Column Design: The improved pharmaceutical container also includes improvements to the design which ensure specified flow of eluent through the container and improve its packing and consistency. In one embodiment the improved container comprises a column

used in a radioisotope generator. The improved column includes a repositioned outlet arm, and the column outlet resides in a recess or notch in the inside ledge of the column where the outlet arm enters the column lumen, to prevent a stopper from blocking the flow. These improvements further include introducing small reinforcement pieces of resin to the outside of the column between the outlet arm and column body and between the inlet arm and column body to provide additional strength. Additionally, the seam of the inlet and outlet arms has been eliminated by changing the mold runners. This change has improved the consistency of the inlet and outlet arm diameters and made the arms stronger.

Furthermore, to address consistency of packing of the containers, two small alignment slots have been cut into the wall of the column to receive the orientation knobs on the baskets that properly align and seat the basket in the column and limit the insertion depth into the column. This improves the consistency of packing density and eliminates potential blockage of the inlet arm. Additionally, in one embodiment, the improved column has stopper flanges and Luer flanges with much smoother surfaces with sharper edges to improve the sealing ability of the crimp. These attributes improve stopper and Luer contact to the column and greatly reduce the chance of leakage. Also, the flashing on the column is reduced greatly to enhance the appearance of the part.

Finally, the column assembly is made from a radiation resistant or tolerant material. The most preferred material is Huntsman PP 13R9A polypropylene.

Luer Lock and Connector Tube Improvements

The Luer locks and connector tubes used with the column have also been improved. First, the connector tubes are made from a radiation resistant or tolerant material. Preferably, this material is AlphaGary PVC 2232 A/R-78S clear 030X.

Second, the terminal end of the connector tube which attaches to the column contains a male Luer cap. This male Luer cap is made of a radiation resistant material, preferably AlphaGary PVC 2212RHT/1-118 clear 080X.

Third, the male and female Luer caps screw together and each contains tabs, preferably two tabs each. When the tabs line up with each other in one embodiment or overlap with each other in another embodiment, that indicates that the two Luer caps are sufficiently tightened or screwed together to form a tight seal or lock. Also, in a preferred embodiment the overlapping tabs prevent the Luer caps from becoming loose, ie unscrewing inadvertently.

Shipping Improvements

The columns can be shipped pre-loaded with, for example, strontium-82. Therefore, the columns are shipped in sealed containers containing GP-100 absorbent material to absorb any leakage.

The above description is to be taken as illustrative and not in the limiting sense. Many modifications can be made to the design without deviating from the scope thereof.

What Is Claimed Is:

1. An improved pharmaceutical container for containing a pharmaceutical agent which is heated, subjected to increased pressure or radioactive, comprising:

a. an inlet arm,

b. a hollow column, and

c. an outlet arm,

wherein the improvement comprises configuring the outlet arm so that it does not protrude into the hollow portion of the column, and support means to support the inlet arm and the outlet arm.

2. The improved pharmaceutical container of claim 1, wherein the container is constructed of a material which is resistant to radiation.

3. The improved pharmaceutical container of claim 1 or 2, wherein the container is constructed of a radiation resistant polypropylene.

4. The improved pharmaceutical container of any of claims 1 through 3, wherein the container is constructed of PP 13R9A polypropylene.

5. An improved pharmaceutical container of any one of claims 1 through 4, wherein a notch is provided in the hollow column at the point where the outflow arm intersects the hollow column.

6. The improved pharmaceutical container of any one of claims 1 through 5, further comprising a basket receptacle area inside the column for receiving a basket where the inlet arm intersects the column, said basket receptacle area further comprising one or more notches, said notches configured to cooperate with one or more protrusions on a basket to be inserted into the basket receptacle area in such a way so as to insure that the basket is properly seated in the basket receptacle area.

7. The improved pharmaceutical container of any one of claims 1 through 6, further comprising two stoppers which form tight seals with and prevent leakage from an open top end and an open bottom end of the column, wherein said stoppers are made of a material which is resistant to radiation, optionally further comprising a packing material and/or a pharmaceutical agent.

8. The improved pharmaceutical container of claim 7, wherein the bottom stopper takes up substantially all of the space at the open bottom end of the column, without blocking the outlet arm, so as to reduce the amount of the dead volume at the bottom of the column.

9. The improved pharmaceutical container of claim 7 or 8, wherein said stoppers are made of a material selected from the group consisting of isoprene/chlorobutyl, bromobutyl and FM 140/0 chlorobutyl.

10. The improved pharmaceutical container of claim any one of claims 7 through 9, wherein said stoppers are made of isoprene/chlorobutyl.

11. The improved pharmaceutical container of any one of claims 7 through 10, wherein each of said stoppers comprises a top cylindrical portion and a bottom cylindrical portion, said bottom cylindrical portion having a diameter sufficient to insure a tight seal between the stopper and the cylinder interface, and said top cylindrical portion having a diameter greater than the bottom cylindrical portion.

12. The improved pharmaceutical container of claim 11, wherein the bottom cylindrical portion contains a U-shaped channel at its base.

13. The improved pharmaceutical container of claim 12, wherein the top cylindrical portion has indicia disposed on its surface, said indicia disposed so that it indicates the direction of the open end of the U-shaped channel.

14. The improved pharmaceutical container of any one of claims 8 through 13, further comprising a centrally located indentation at a top end of the stopper.

15. The improved pharmaceutical container of any one of claims 8 through 14, wherein the stoppers are held in place by crimping a crimp seal around the stoppers to affix them to the container.

16. The improved pharmaceutical container of claim 15, wherein the crimping is performed with an automatic or semi-automatic crimper.

17. The improved pharmaceutical container of claim 15 or 16, wherein the automatic crimper is a pneumatic crimper.

18. The improved pharmaceutical container of any one of claims 15 through 17, wherein the crimp seal is crimped at a pressure of about 60-140 psi.

19. The improved pharmaceutical container of any one of claims 15 through 18, wherein the crimp seal is constructed of a material which is resistant to radiation.

20. The improved pharmaceutical container of any one of any one of claims 15 through 19, wherein the crimp seal is constructed of a material selected from the group consisting of aluminum, steel and tin.

21. The improved pharmaceutical container of any one of claims 15 through 20, wherein the crimped stopper is able to withstand a pressure of between 90 psi and 200 psi inside the sealed container.

22. The improved pharmaceutical container of any one of claims 15 through 21, wherein the crimp seal is made of aluminum and comprises a top crimp member and a bottom washer.

23. The improved pharmaceutical container of claims 15 through 21, wherein the crimp seal is made of steel and comprises a single crimp seal member.

24. The improved pharmaceutical container of claim 22, wherein the top crimp member comprises a generally circular surface with a central hole and a skirt, and the bottom washer comprises a generally circular surface with a central hole.

25. The improved pharmaceutical container of claim 23, wherein the crimp seal member comprises a generally circular surface with a central hole and a skirt.

26. The improved pharmaceutical container of claim 22 or 24, wherein the top crimp member further comprises an insert, said insert being seated in or under the central hole, and further wherein said insert contains a central hole whose diameter is less than the diameter of the central hole in the top crimp member.

27. The improved pharmaceutical container of any one of claims 15 through 21, 23 and 25, wherein said crimp seal comprises a single crimp seal member made of steel with a generally circular surface having a diameter of about 20.75 mm ± 0.25 mm and a skirt with a height of about 7.00 mm ± 0.25 mm, and wherein said generally circular surface has a central hole with a diameter of about 5.00 mm ± 0.25 mm.

28. The improved pharmaceutical container of any one of claims 15 through 27, further comprising a removable cover which covers the central hole in the top crimp member.

29. The improved pharmaceutical container of any one of claims 1 through 28, for generating rubidium-82.

30. The improved pharmaceutical container of any one of claims 1 through 29, further comprising a first connector tube which attaches to the inlet arm via a Luer lock, and a second connector tube which attaches to the outlet arm via a Luer lock, wherein a portion of each Luer lock is affixed to each of the connector tubes and another portion of the Luer locks is affixed to each of the inlet arm and outlet arm.

31. The improved pharmaceutical container of claim 30, wherein the connector tubes and the Luer lock portions attached to the connector tubes are made of materials which are resistant to radiation.

32. The improved pharmaceutical container of claim 30 or 31, wherein the connector tubes are made of a flexible, radiation resistant polyvinyl chloride and the Luer lock portions attached to the connector tubes are made of a rigid, radiation resistant polyvinyl chloride.

33. The improved pharmaceutical container of any one of claims 30 through 32, wherein the connector tubes are made of PVC 2232 A/R-78S clear 030X and the Luer lock portions attached to the connector tubes are made of PVC 2212 RHT/1-118 clear 080X.

34. An improved Luer lock comprising a female Luer cap and a male Luer cap, wherein one of said Luer caps contains a flange and the other of said Luer caps contains threads, configured so that the flange and threads cooperate with each other in such a way that the female Luer cap and male Luer cap can be screwed together, wherein the improvement comprises providing for one or a plurality of tabs on each of the male and female Luer caps, wherein the tabs on the male Luer cap and the tabs on the female Luer cap achieve a desired configuration with respect to each other when the tightening of the two Luer caps together is complete.

35. The improved Luer lock of claim 34, wherein the male and female Luer caps each contain two tabs.

36. The improved Luer lock of claim 34 or 35, wherein the desired configuration is where the respective tabs on the male Luer cap and the female Luer cap line up with each other.

37. The improved Luer lock of claim 34 or 35, wherein the desired configuration is where the respective tabs on the male Luer cap and the female Luer cap overlap with each other, thus preventing overtightening or inadvertent loosening of the Luer lock.

38. The improved pharmaceutical container of any one of claims 1 through 33, which is shipped or packed in with an absorbent material.

39. The improved pharmaceutical container of claim 38, wherein the absorbent material is GP-100.

40. An improved rubiduim -82 generator comprising:

a. a hollow column with a top portion, a middle portion and a bottom portion, said top portion including one or more notches, and a screen separating the middle portion and the bottom portion;

b. a top basket with one or more protrusions, said one or more protrusions configured to cooperate with the one or more notches in the top portion of the hollow column so as to cause the proper seating of the top basket in the top portion of the hollow column, said top basket further comprising a screen at its base and a side opening;

c. an inlet arm which intersects the hollow column at its top portion at a point where the inlet arm is aligned with the side opening in the top basket, and further wherein the inlet arm has a female Luer cap at its distal end, said female Luer cap containing one or more tabs on its outer surface;

d. an outlet arm which intersects but does not protrude into the hollow column at its bottom portion, wherein a notch is provided at the point of intersection on the bottom portion's inner surface, and further

wherein the outlet arm has a female Luer cap at its distal end, said female Luer cap containing one or more tabs on its outer surface;

e. support means to support the inlet arm and the outlet arm to the hollow column

wherein said hollow column, top basket, inlet arm, outlet arm and support means are constructed of a radiation resistant polypropylene;

f. a packing material comprising stannic oxide with strontium-82 adhered to it, said packing material placed in the middle portion of the hollow column above the bottom screen and below the screen of the top basket;

g. a top stopper comprising a radiation resistant material, said top stopper configured to form a tight seal with the top portion of the hollow column but which does not block the inlet arm;

h. a bottom stopper comprising a radiation resistant material, said bottom stopper configured to form a tight seal with the bottom portion of the hollow column and minimizing the dead space in the bottom portion of the hollow column, without blocking the outlet arm;

i. first a crimp seal to crimp the top stopper to the top portion of the hollow column and a second crimp seal to crimp the bottom stopper to the bottom portion of the hollow column, wherein each crimp seal comprises steel with a thickness of about 0.2mm and a central hole about 5.0mm in diameter, wherein each crimp seal is crimped to a pressure of about 117 psi;

j. a first flexible tube comprising a flexible, radiation resistant polyvinyl chloride with a first male Luer cap comprising a rigid, radiation

resistant polyvinyl chloride at one end of said first flexible tube, said first male Luer cap being configured to cooperate with the female Luer cap at the distal end of the inlet arm so that the two Luer caps can be screwed together to form a tight Luer lock, and wherein said first male Luer cap contains one or more tabs on its outer surface which will align with the one or more tabs on the outer surface of the female Luer cap at the distal end of the inlet arm, such that when the two Luer caps are screwed together these tabs achieve a desired configuration with respect to each other when the tightening of the Luer caps is complete; and

k. a second flexible tube comprising a flexible, radiation resistant polyvinyl chloride with a second male Luer cap comprising a rigid, radiation resistant polyvinyl chloride at one end of said second flexible tube, said second male Luer cap being configured to cooperate with the female Luer cap at the distal end of the outlet arm so that the two of them can be screwed together to form a tight Luer lock, and wherein said second male Luer cap contains one or more tabs which will align with the one or more tabs on the female Luer cap at the distal end of the outlet arm, such that when the two Luer caps are screwed together these tabs achieve a desired configuration with respect to each other when the tightening of the Luer caps is complete.

41. An improved rubiduim-82 generator comprising:

a. a hollow column with a top portion, a middle portion and a bottom portion, said top portion including one or more notches, and a screen separating the middle portion and the bottom portion;

b. a top basket with one or more protrusions, said one or more protrusions configured to cooperate with the one or more notches in the top portion of the hollow column so as to cause the proper seating of the top basket in the top portion of the hollow column, said top basket further comprising a screen at its base and a side opening;

c. an inlet arm which intersects the hollow column at its top portion at a point where the inlet arm is aligned with the side opening in the top basket, and further wherein the inlet arm has a female Luer cap at its distal end, said female Luer cap containing one or more tabs on its outer surface;

d. an outlet arm which intersects but does not protrude into the hollow column at its bottom portion, wherein a notch is provided at the point of intersection on the bottom portion's inner surface, and further wherein the outlet arm has a female Luer cap at its distal end, said female Luer cap containing one or more tabs on its outer surface;

e. support means to support the inlet arm and the outlet arm to the hollow column

wherein said hollow column, top basket, inlet arm, outlet arm and support means are constructed of a radiation resistant polypropylene;

f. a packing material comprising stannic oxide with strontium-82 adhered to it, said packing material placed in the middle portion of the hollow column above the bottom screen and below the screen of the top basket;

g. a top stopper comprising a radiation resistant material, said top stopper configured to form a tight seal with the top portion of the hollow column but which does not block the inlet arm;

h. a bottom stopper comprising a radiation resistant material, said bottom stopper configured to form a tight seal with the bottom portion of the hollow column and minimizing the dead space in the bottom portion of the hollow column, without blocking the outlet arm;

i. first a crimp seal to crimp the top stopper to the top portion of the hollow column and a second crimp seal to crimp the bottom stopper to the bottom portion of the hollow column, wherein each crimp seal comprises steel with a thickness of about 0.2mm and a central hole about 5.0mm in diameter, wherein each crimp seal is crimped to a pressure of about 117 psi;

j. a first flexible tube comprising a flexible, radiation resistant polyvinyl chloride with a first male Luer cap comprising a rigid, radiation resistant polyvinyl chloride at one end of said first flexible tube, said first male Luer cap being configured to cooperate with the female Luer cap at the distal end of the inlet arm so that the two Luer caps can be screwed together to form a tight Luer lock and where said first male Luer cap contains one or more tabs on its outer surface which will overlap with the one or more tabs on the outer surface of the female Luer cap at the distal end of the inlet arm, such that when the two Luer caps are screwed together these tabs overlap and are pushed past each other, and a tight Luer lock which is resistant to inadvertent loosening is formed; and

k. a second flexible tube comprising a flexible, radiation resistant polyvinyl chloride with a second male Luer cap comprising a rigid, radiation resistant polyvinyl chloride at one end of said second flexible tube, said second male Luer cap being configured to cooperate with the female Luer cap at the distal end of the outlet arm so that the two of them can be screwed together to form a tight Luer lock, and wherein said second male Luer cap contains one or more tabs which will overlap with the one or more tabs on the female Luer cap at the distal end of the outlet arm, such that when the two Luer caps are screwed together these tabs overlap and are pushed past each other, and a tight Luer lock which is resistant to inadvertent loosening is formed.

42. The improved pharmaceutical container of any one of claims 30 through 33 wherein the Luer locks comprise a female Luer cap and a male Luer cap, wherein one of said Luer caps contains a flange and the other of said Luer caps contains threads, configured so that the flange and threads cooperate with each other in such a way that the female Luer cap and male Luer cap can be screwed together, wherein the improvement comprises providing for one or a plurality of tabs on each of the male and female Luer caps, wherein the tabs on the male Luer cap and the tabs on the female Luer cap achieve a desired configuration with respect to each other when the tightening of the two Luer caps together is complete.

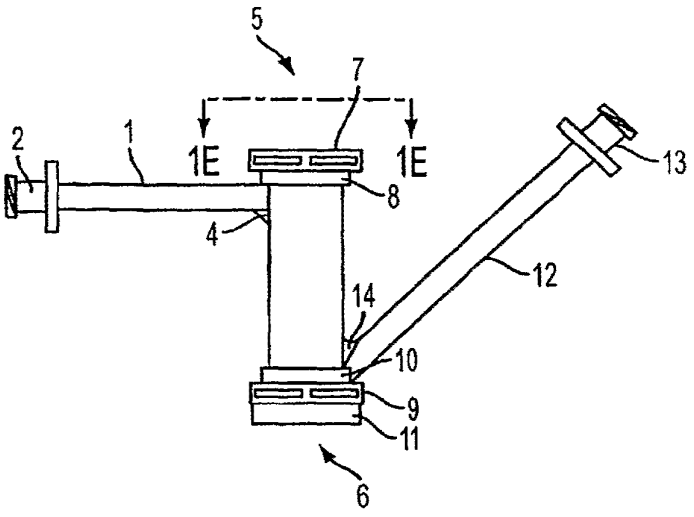


FIG. 1A

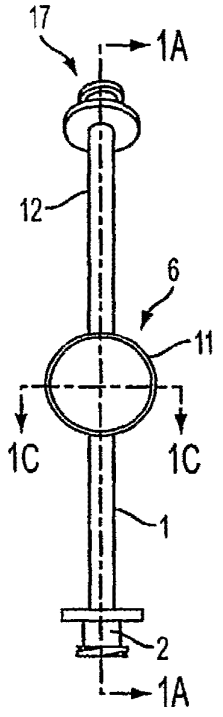


FIG. 1B

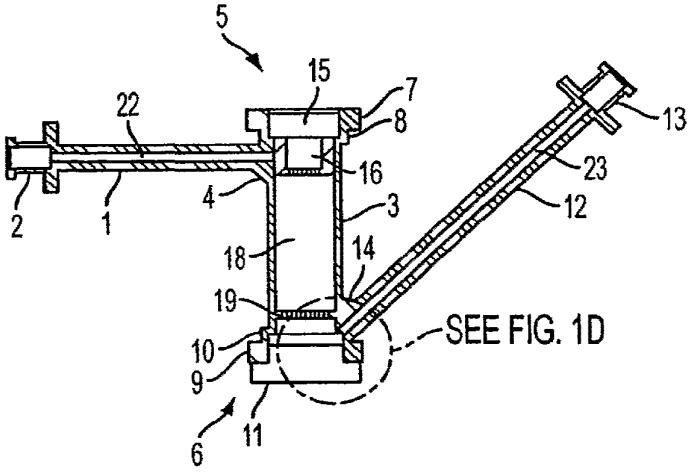

5
15
7
8
22
13
16
23
4
3
12
2
1
18
14
19
SEE FIG. 1D
10
9
6
11

FIG. 1C

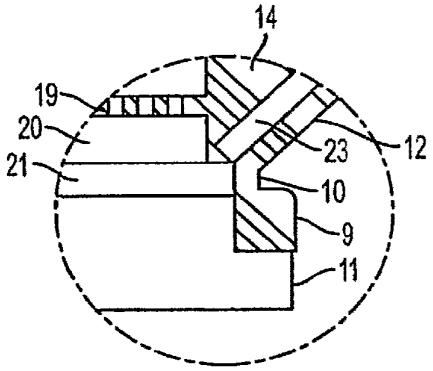

14
19
20
23
12
21
10
9
11

FIG. 1D

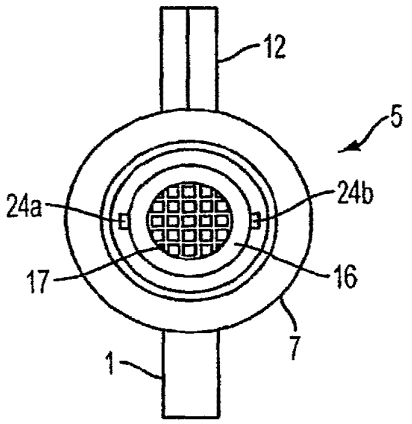


FIG. 1E

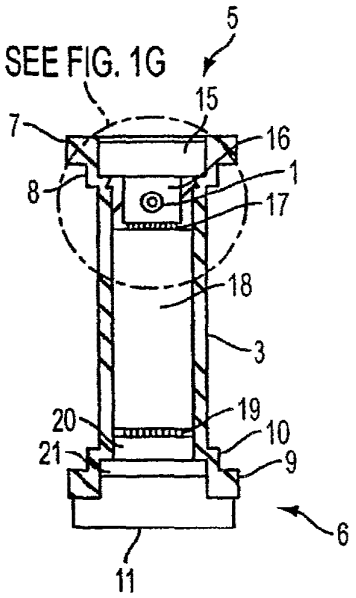


FIG. 1F

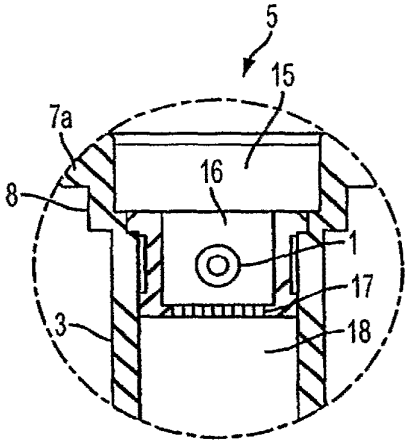


FIG. 1G

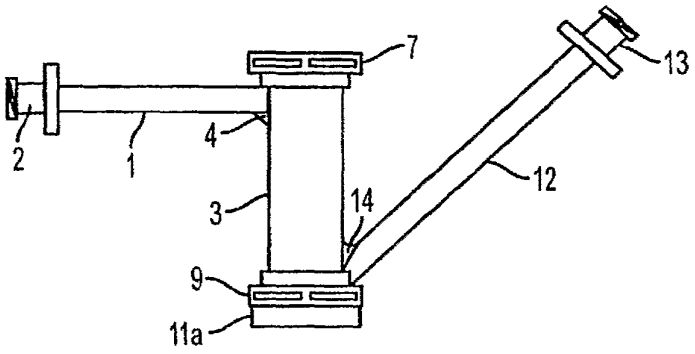


FIG. 2A

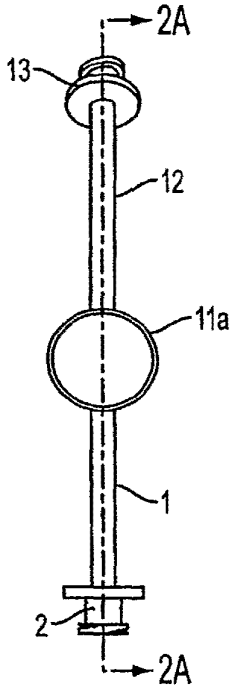


FIG. 2B

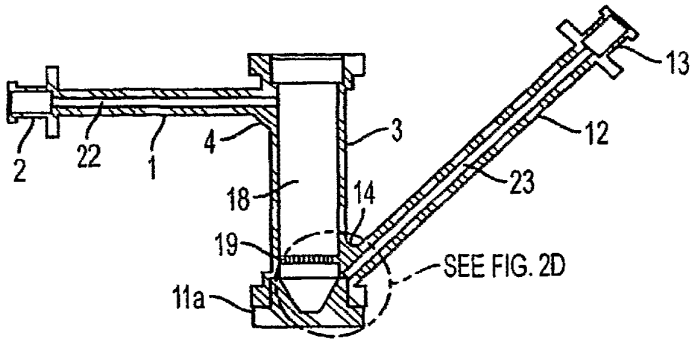


FIG. 2C

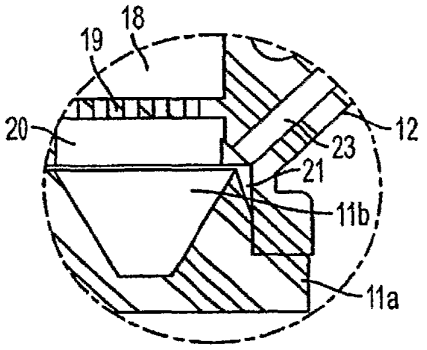


FIG. 2D

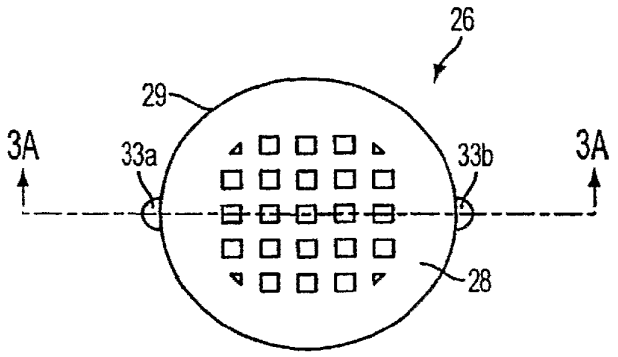


FIG. 3A

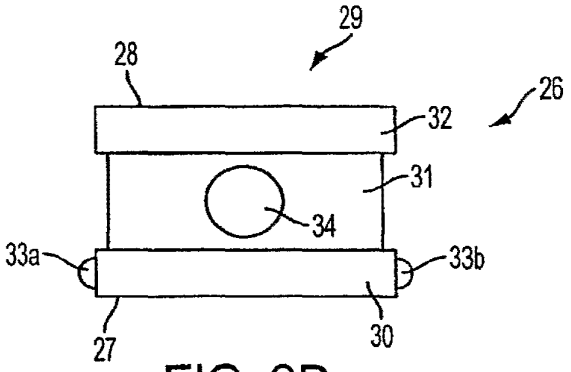


FIG. 3B

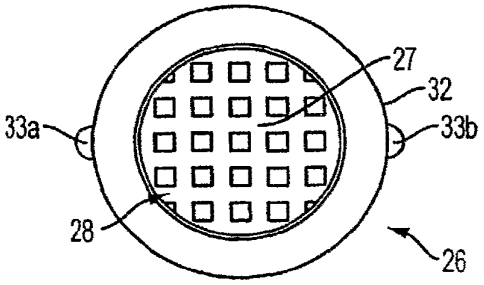


FIG. 3C

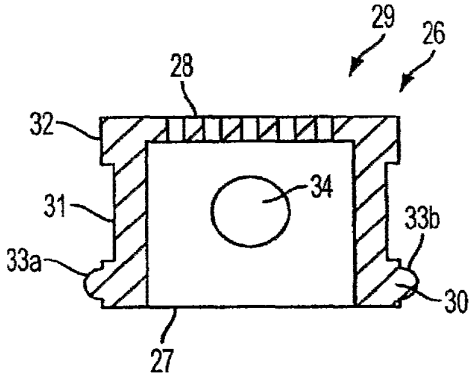


FIG. 3D

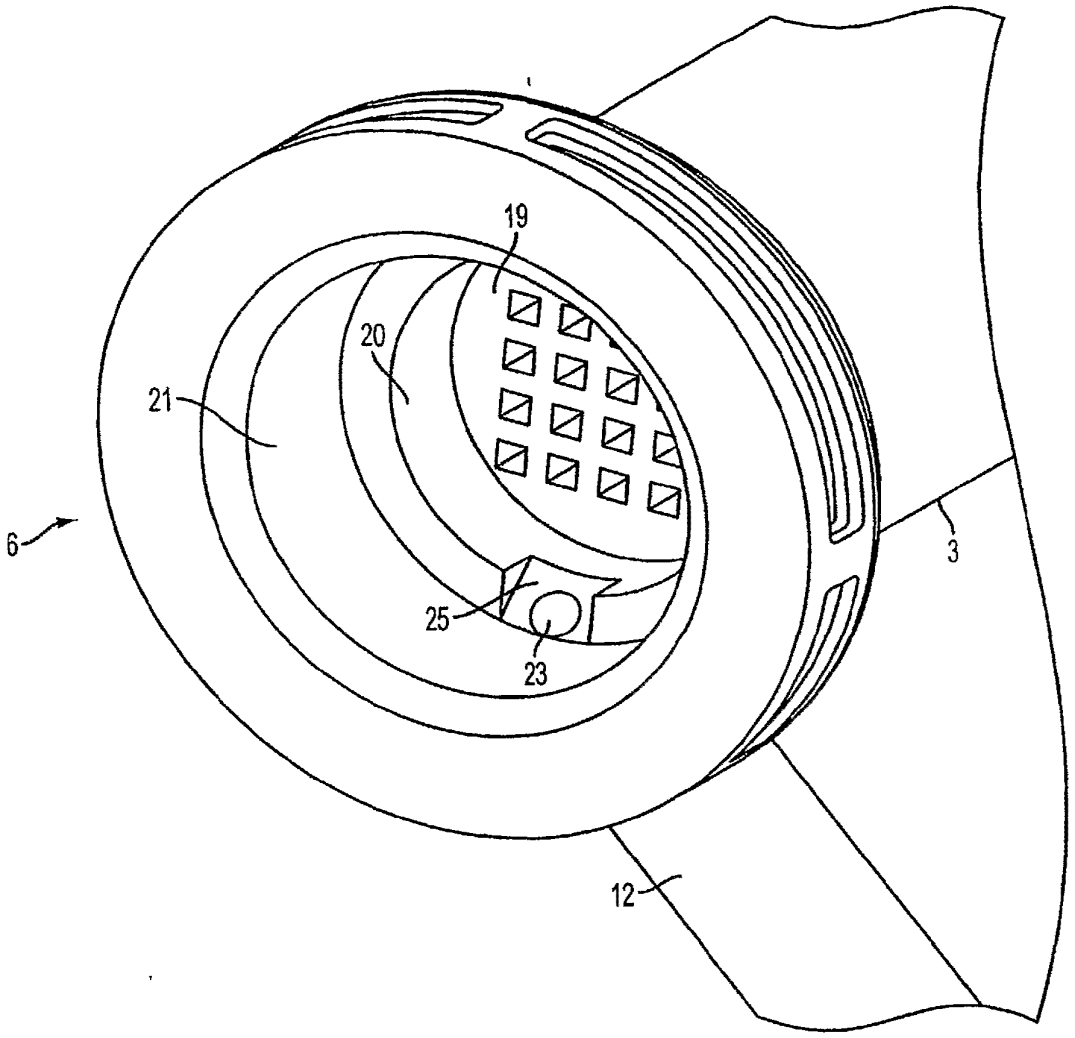


FIG. 4

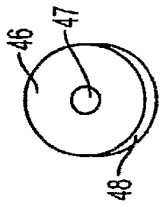


FIG. 5C

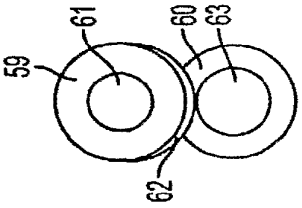


FIG. 5F

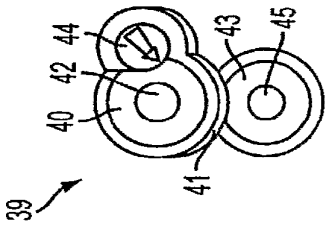


FIG. 5B

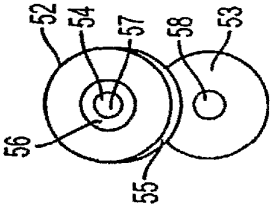


FIG. 5E

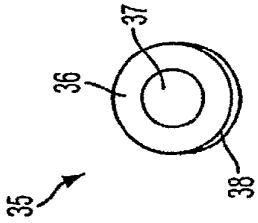


FIG. 5A
PRIOR ART

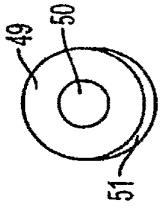


FIG. 5D

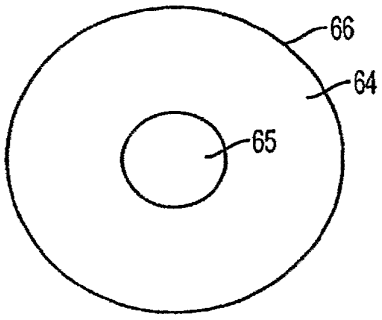


FIG.6A

FIG.6B

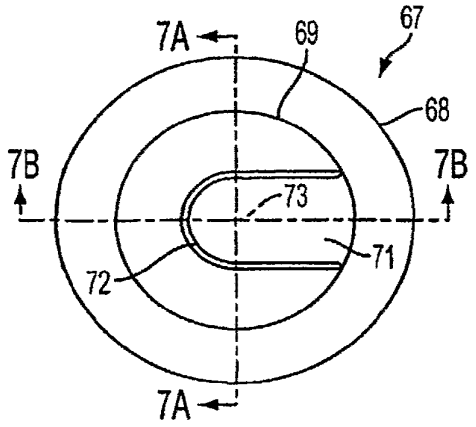


FIG. 7A

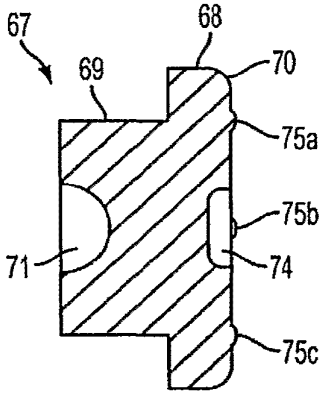


FIG. 7B

1214

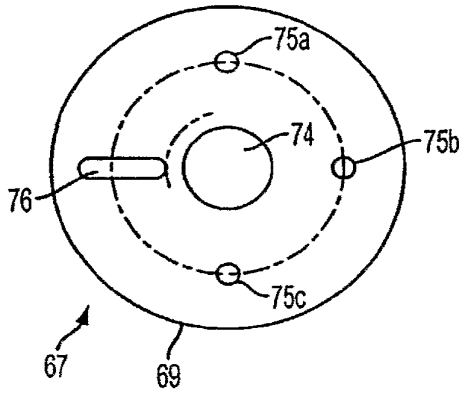


FIG. 7C

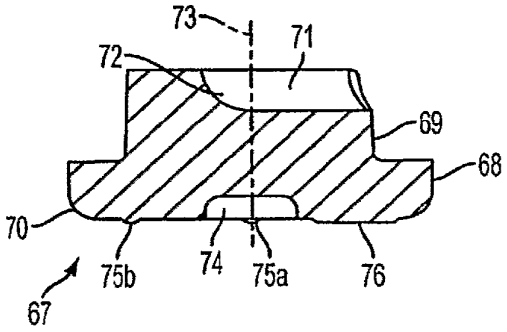


FIG. 7D

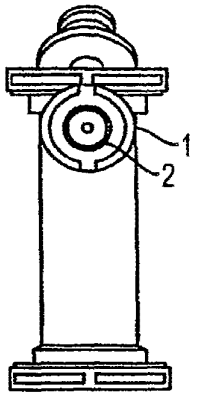


FIG. 8A

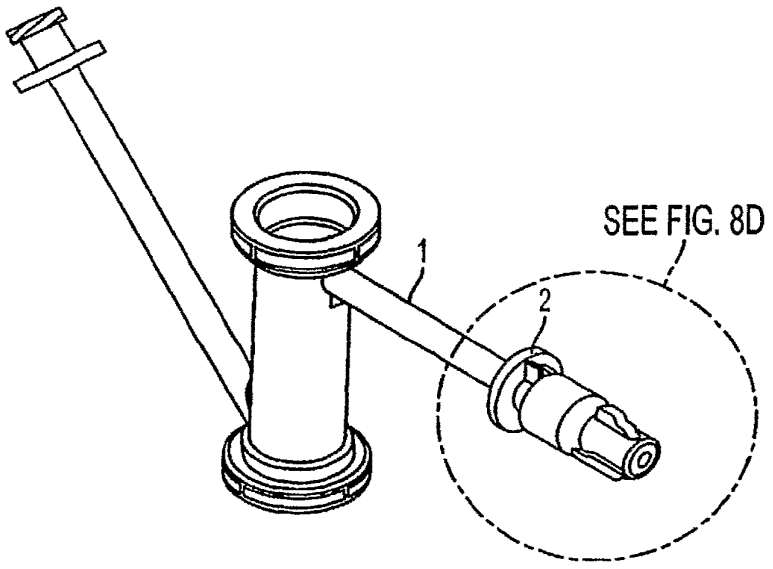


FIG. 8B

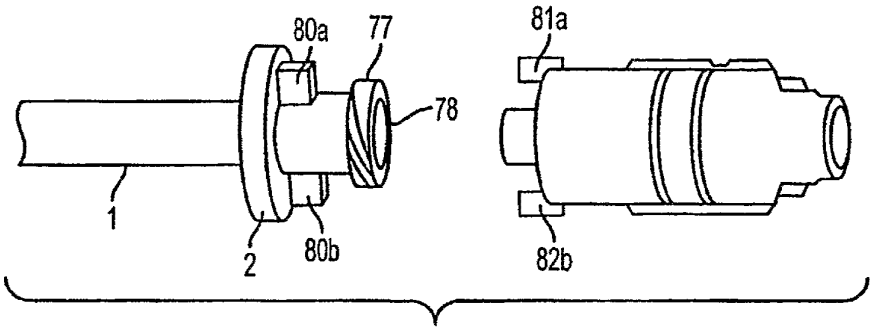


FIG. 8C

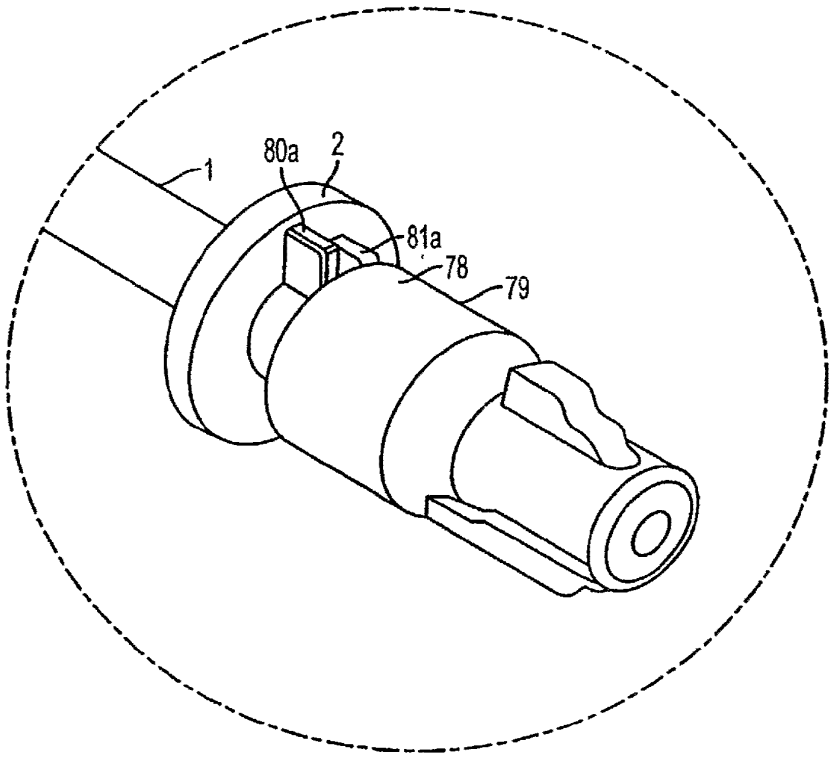


FIG. 8D

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

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
21 December 2006 (21.12.2006)

PCT

(10) International Publication Number
WO 2006/135374 A2

(51) International Patent Classification:
G21G 4/08 (2006.01) *A61K 51/00* (2006.01)
A61K 51/12 (2006.01) *B01D 15/00* (2006.01)

(21) International Application Number:
PCT/US2005/025605

(22) International Filing Date: 19 July 2005 (19.07.2005)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
10/894,870 19 July 2004 (19.07.2004) US

(71) Applicant *(for all designated States except US)*: **LYNNTECH, INC.** [US/US]; 7607 Eastmark Drive, College Station, TX 77840 (US).

(72) Inventors; and
(75) Inventors/Applicants *(for US only)*: **MOLLER, Teresia** [FI/US]; 702 San Saba, College Station, TX 77845 (US). **ADAMS, Todd** [US/US]; 9388 Haney Road, Franklin, TX 77856 (US). **CISAR, Alan** [US/US]; 15603 Juniper Hollow Way, Cypress, TX 77433 (US). **GALI, Hariprasad** [IN/US]; 7600 Central Park Lane #1603, College Station, TX 77840 (US). **SYLVESTER, Paul** [GB/US]; 14 Florence Road, Waltham MA 02453 (GB).

(74) Agent: **CAMPIGOTTO, Frank, J.**; STREETS & STEELE, 13831 Northwest Freeway, Suite 355, Houston, TX 77040 (US).

(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, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, 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.

WO 2006/135374 A2

(54) Title: RUBIDIUM-82 GENERATOR BASED ON SODIUM NONATITANATE SUPPORT, AND IMPROVED SEPARATION METHODS FOR THE RECOVERY OF STRONTIUM-82 FROM IRRADIATED TARGETS

(57) Abstract: Sodium nonatitanate compositions, a method using the composition for recovery of ^{82}Sr from irradiated targets, and a method using the composition for generating ^{82}Rb. The sodium nonatitanate materials of the invention are highly selective at separating strontium from solutions derived from the dissolution of irradiated target materials, thus reducing target processing times. The compositions also have a very low affinity for rubidium, making it an ideal material for use as a ^{82}Rb generator. Sodium nonatitanate materials of this type both improve the recovery of ^{82}Sr and provide a safer, more effective ^{82}Rb generator system.

RUBIDIUM-82 GENERATOR BASED ON SODIUM NONATITANATE SUPPORT, AND IMPROVED SEPARATION METHODS FOR THE RECOVERY OF STRONTIUM-82 FROM IRRADIATED TARGETS

BACKGROUND OF THE INVENTION

Field of the Invention

[001] This invention relates to the selective separation of strontium-82 from other radioisotopes, such as those resulting from irradiated molybdenum or rubidium targets, and in the manufacture of a rubidium-82 generator.

Background of the Related Art

[002] The use of radioisotopes as diagnostic and imaging agents in medicine has expanded rapidly in recent years. Positron (β+) emitters are particularly useful in the study of metabolic processes because the positron-electron annihilation reaction produces a pair of gamma rays with an energy level of 511 keV travelling in opposite directions. By placing a series of detectors around a patient who has been administered a positron emitter, both the location and amount of radioactivity can be accurately determined. This property is utilized in Positron Emission Tomography (PET) to image metabolic processes *in vivo*. Rubidium-82 (^{82}Rb) is a short-lived positron-emitting isotope ($T_{½}$ = 76 seconds) that is increasingly being used to study blood flow through the heart and brain. Physiologically, rubidium is an analogue of potassium, and consequently enters the body's large potassium pool, which has a comparatively slow turnover. Thus, after ^{82}Rb is injected intravenously, the tracer's uptake in tissue reflects the rate of delivery, *i.e.*, blood flow, and thus ^{82}Rb rapidly builds up in the heart. This can be used, for example, to study blood-brain barrier leakage and heart muscle perfusion.

[003] The short half-life of ^{82}Rb means that it must be supplied to physicians in the form of a generator, where the parent ^{82}Sr ($T_{½}$ = 25 days) is immobilized on a solid substrate or support and ^{82}Rb eluted as required. The generators that are currently available use hydrous tin oxide to immobilize the ^{82}Sr and allow the elution of ^{82}Rb by saline or other appropriate eluant. The ^{82}Sr ($T_{½}$ = 25 days) is accompanied by unwanted ^{85}Sr ($T_{½}$ = 64 days), generated as a by-product during the manufacture of ^{82}Sr, wherein both isotopes have a relatively long half-life and

a high radiotoxicity due to their tendency to accumulate in bone. Thus, it is essential to minimize or eliminate the introduction of ^{82}Sr and ^{85}Sr into a patient during the administration of ^{82}Rb. Although hydrous tin oxide has proved acceptable to date for use in generators, new materials exhibiting far higher strontium affinities, improved strontium/rubidium separation factors and greater radiolytic stability are needed in order to lower the amount of ^{82}Sr and ^{85}Sr released during elution of the ^{82}Rb.

[004] The parent ^{82}Sr is generated by the proton irradiation of rubidium, rubidium chloride or molybdenum targets followed by dissolution and processing to isolate the ^{82}Sr. The demand for ^{82}Rb generators has grown so great that there is a need to reduce processing times and to increase the yield of ^{82}Sr from processed targets. One method of improving the supply of ^{82}Sr is to improve the processes used to extract ^{82}Sr from irradiated targets. Current methods utilize organic ion exchange or chelating resins to extract very low levels of strontium from dissolved targets containing molar concentrations of inert ions. However, a satisfactory separation of ^{82}Sr from the target materials and other radioisotopes generated during the irradiation procedure requires multiple treatment steps due to the relatively low affinity and low selectivity of the organic ion exchange resins for ^{82}Sr.

[005] ^{82}Sr is produced by the proton irradiation of molybdenum metal, rubidium metal and rubidium chloride targets. The irradiation process also produces a range of other radioactive isotopes (*e.g.*, ^{88}Y, ^{88}Zr, ^{85}Sr) and as a consequence, a series of carefully designed separation procedures have been designed to separate the desired ^{82}Sr from other radioisotopes and inactive species present. The primary method used to separate ^{82}Sr is by a series of ion exchange and selective elution steps. Typically, AG 50 W-X8 ion exchange resin is used to separate ^{82}Sr from dissolved targets. However, this resin is relatively non-selective and will absorb numerous polyvalent cations (*e.g.*, ^{88}Y) in addition to the desired ^{82}Sr. Consequently, multiple separation steps are required to isolate ^{82}Sr from the other isotopes present.

[006] ^{82}Rb can be conveniently supplied to physicians in the form of a generator in which the parent ^{82}Sr is immobilized on an ion exchange material and the ^{82}Rb eluted when required. This means that ^{82}Rb PET can be performed at clinical facilities where a typical generator lasts about a month before the yield of ^{82}Rb diminishes below a usable level.

[007] To be suitable for use in a ^{82}Rb generator, an ion exchange material must exhibit a high affinity for strontium but a low affinity for rubidium, allowing the ^{82}Rb daughter to be eluted from a column containing immobilized ^{82}Sr. Generators have been proposed that were

based on a number of separation media including Chelex 100, Al_2O_3, Sb(V) hexacyanoferrate, polyantimonic acid, titanium vanadate and hydrated tin(IV) oxide, with the hydrated tin(IV) oxide being the most widely used.

[008] However, the crucial component of any system is the actual ion exchange material containing the immobilized ^{82}Sr parent. Current systems using hydrous tin oxide have a limited life due to the breakdown of the hydrous tin dioxide, necessitating frequent replacement.

[009] Therefore, there is a need for a highly strontium selective ion exchange material for use in place of ion exchange resins and hydrated tin(IV) oxide, so that the separation and recovery of ^{82}Sr from Rb, RbCl and Mo targets is greatly facilitated. A replacement for the ion exchange resin will lead to a reduction in processing steps, a decrease in target processing times and thus a decrease in the cost of the ^{82}Sr product. An ion exchange material suitable for use as a ^{82}Rb generator will have a very high selectivity for ^{82}Sr and a very low selectivity for ^{82}Rb to allow elution of the ^{82}Rb by isotonic saline or other solutions and will offer a longer operating life or improved operating conditions compared to hydrated tin(IV) oxide.

SUMMARY OF THE INVENTION

[010] The present invention provides a method of chemically isolating strontium-82 from proton-irradiated molybdenum targets. This comprises dissolving the molybdenum metal target containing the strontium-82, adjusting the pH of the dissolved molybdenum target solution to an alkaline pH, removing precipitates from the solution, and then absorbing the strontium-82 from the solution onto a support comprising sodium nonatitanate. Sodium nonatitanate can also be applied to the efficient recovery of strontium-82 from alkaline RbCl solutions produced during the processing of proton-irradiated rubidium metal and rubidium chloride targets.

[011] The present invention also provides a rubidium-82 generator, comprising a strontium-82 support medium comprising sodium nonatitanate. Preferably, the sodium nonatitanate is characterized by a strontium selectivity greater than 250,000 mL/g at an alkaline pH, and/or the sodium nonatitanate is characterized by a rubidium selectivity less than 100 mL/g at an alkaline pH. More preferably, the sodium nonatitanate is characterized by a strontium/rubidium separation factor greater than 1,000, and even more preferably greater than 100,000.

[012] The rubidium-82 generator is prepared by a process comprising: preparing sodium nonatitanate from titanium isopropoxide and aqueous sodium hydroxide; heating the sodium

nonatitanate at a temperature between 100°C and 250°C for a period between 12 hours and 2 weeks; and absorbing strontium-82 on the sodium nonatitanate from an aqueous solution comprising strontium-82 and a soluble sodium salt, wherein the sodium salt concentration is between 0.1 and 1 molar. It is also preferred that the titanium isopropoxide and the aqueous sodium hydroxide solution are provided at a sodium hydroxide to titanium isopropoxide molar ratio of greater than 0.44, but preferably providing a large molar excess of sodium hydroxide. The sodium hydroxide to titanium isopropoxide molar ratio is preferably between 1 and 10, more preferably between 2 and 6, and most preferably about 4.

[013] Furthermore, the invention provides a process for preparing a solution containing rubidium-82. The process comprises providing a solution containing strontium-82 at a pH between 10 and 14, absorbing the strontium-82 from the solution onto a sodium nonatitanate support medium, and eluting rubidium-82 from the sodium nonatitanate support medium with a solvent. The solvent is preferably selected from the group consisting of water and saline solutions. More particularly, the solvent may be an aqueous solution having a sodium chloride concentration between 0.001 molar and 1 molar, preferably between 0.1 molar and 1 molar. The solvent may also be a pharmaceutical grade isotonic saline and buffer solution.

BRIEF DESCRIPTION OF THE DRAWINGS

[014] FIG. **1** is a graph showing ^{82}Sr K_d values for the ion exchange materials from simulated rubidium and rubidium chloride target solutions.

[015] FIG. **2** is a graph showing the reduction of ^{82}Sr activity with increasing time.

[016] FIG. **3** is a graph showing the effect of pH on the uptake of ^{85}Sr using normal saline as an eluant.

[017] FIG. **4** is a graph showing ^{85}Sr K_d values in normal saline for NaTi samples of various pellet size.

[018] FIG. **5** is a schematic drawing of a system having a sodium nonatitanate column in accordance with the present invention.

[019] FIGS. **6A-6B** are graphs showing the pH of saline solutions at the inlet and outlet of a $^{82}Sr/^{82}Rb$ column.