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(54) **PORTABLE SAMPLING OR TESTING DEVICE AND METHOD FOR PHARMACOKINETICS AND PHYSIOLOGY STUDIES**

TRAGBARE ABTAST- ODER TESTVORRICHTUNG UND VERFAHREN FÜR PHARMAKOKINETISCHE UND PHYSIOLOGISCHE UNTERSUCHUNGEN

DISPOSITIF PORTABLE D'ECHANTILLONNAGE OU D'ESSAI ET PROCEDE PERMETTANT D'EFFECTUER DES ETUDES PHARMACOCINETIQUES ET PHYSIOLOGIQUES

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## Description

### Background of the Invention

**[0001]** This invention relates to a device for use in biomedical research, and, in particular, to a system for conducting tests and monitoring conscious and freely-moving animals.

**[0002]** Working with living animals is a requirement for important biomedical research techniques, such as infusion, in vivo microdialysis, in vivo ultrafiltration, in vivo electrochemistry, and electrocardiology. All of these techniques study the performance of living organs, such as the brain, heart, circulatory system, muscles, etc. These techniques also require connections between one or more external devices and one or more sensors or implants in the animal's body. Examples of devices include syringe pumps, fraction collectors, electrometers, vacuum sources, light sources, and potentiostats. Examples of implants include infusion cannulae, ultrafiltration probes, microdialysis probes, and electrodes.

**[0003]** U.S. Patent No. 6,062,224 discloses an apparatus and a method for conducting automated blood sampling (ABS). The method disclosed in that patent includes the step of returning unused blood, that was withdrawn from the test subject and was still remaining in the catheter and associated tubing after collection, back into the animal. The injection of unused blood back into a test subject is important when the subject is a small animal, because in that instance one must be concerned with the conservation of red blood cells (erythrocytes) in the small animal. Red blood cell replenishment requires a period of 10 to 14 days in rodents, therefore a study running over a period of only 1 to 4 days is not long enough for the body to replace any blood cells removed during automated sampling. If too many red blood cells are removed, the animal is at risk of anemia and its associated complications. The return of withdrawn blood into some larger animals, such as humans, may also be needed to conserve erythrocytes if the animal is sufficiently small (e.g. human infants), but in other cases may not be desirable since returned blood would be accompanied by anticoagulants to keep the blood from clotting while in the automated blood sampling device. Although the required concentration of an anticoagulant, such as heparin, when used in blood return, is less than 2% of the typical therapeutic dose, it may be desirable to seek an alternative approach to automated blood sampling which either does not re-inject blood into the animal being monitored, or returns blood using an alternative means of preventing coagulation of the blood while it is out of the body during connection to the automated blood sampler.

**[0004]** As discussed in U.S. Patent No. 6,062,224, it is sometimes desirable to monitor the animal while it is active and/or to allow the animal to engage in various types of activity during the testing or monitoring of the animal. For example, rotational and vertical behavior in

laboratory rodents is a well-established indicator of neurochemical changes occurring in the animal during testing. The clockwise or counterclockwise preference of the animal, the frequency of such rotation, and similar information concerning the vertical movement of the animal are valuable data. Accordingly, U.S. Patent No. 6,062,224 and U.S. Patent No. 5,816,256 disclose movement-responsive systems that include a container for housing the animal and a mechanism for rotating the container in response to rotational movement of the animal.

**[0005]** The devices disclosed in the above-referenced patents are very useful in monitoring small animals because these devices allow for monitoring the animal without undue interference with the movement or normal activities of the animal, and the automation eliminates the need for human handling and the stress associated with such handling. Although this same concept can be envisioned for some larger mammals (e.g. pigs), it would not be practical for all human studies. The exception would be studies in neonatal intensive care units where premature infants are not much different in weight than an average guinea pig, have similar sized veins, and are much less mobile. In the case of neonatal intensive care, a traditional incubator would be substituted for a cage, and automated blood sampling would be conducted under continuous supervision by medical personnel. The advantage of automated blood sampling in premature infants would be to alleviate the trauma associated with multiple "sticks" (insertion of a needle into a vein or artery) during the repeated blood sampling that is necessary to monitor disposition of drug treatments. These patients are highly medicated and because they have undeveloped organs for drug metabolism and excretion, the therapeutic concentration of the drugs used is highly variable. Neonates must be constantly monitored to avoid toxic reactions due to overdose. In these patients, the extremely tiny blood vessels make the process of blood sampling extremely difficult for the phlebotomist (blood sampling technician), traumatic for the patient, and emotionally challenging for the parents and all associated medical personnel.

**[0006]** In human studies that involve the collection of blood for Phase 1 Clinical Trials, there are several other reasons that would justify the use of automated blood sampling, and specifically a mobile device for conducting this process. For example, mobility would be useful to allow a human subject to utilize a private restroom facility without interrupting a test or monitoring session. Humans are more likely to participate in automated blood sampling studies if their movements are unrestricted, and they can move to different rooms within the clinic to eat, watch television, or engage in entertainment like card playing or board games. Automated blood sampling, as well as the automation of other tests conducted during Phase 1 Clinical Trials (such as electrocardiography, blood pressure recording, and body temperature monitoring) can potentially be done with greater temporal accuracy (i.e. the collection of samples at a specific time),

and the use of less human personnel, than manual methods of acquiring the same samples and data.

**[0007]** Large animals, such as dogs or pigs, may not respond well to the tethering and movement-responsive caging required for operation of the 6,062,224 and 5,816,256 device. Furthermore, that device may be incompatible with an animal that is agile (monkeys, primates), or able to jump high (monkeys, dogs, rabbits). The movement-responsive cage for a strong animal (pig, horse, sheep, cow, goat) would have to be constructed of even stronger materials, increasing the cost and weight of the device. Tethering would necessarily restrict the animal's movement to the confines of the test cage and may induce test-related stress for the animal. Stress involves release of various hormones, and such hormones have a profound effect on the redirection of blood flow as well as the function of many physiological systems in the body. Therefore, the test conditions should be designed to reduce this stress effect as much as possible. It is therefore desirable to provide a system which does not unduly restrict movement of the animal, does not induce significant test related stress, is reasonable in size, can be manufactured, operated and maintained at reasonable cost, and which is may be adapted for larger animals including, but not limited to, pigs, cows, horses, dogs, primates, and humans.

**[0008]** US Patent No. 4,696,309 describes a portable apparatus for repeatedly taking samples of blood or other body fluid from a person or animal, which comprises a housing adapted to be attached to the person or animal from which the samples are to be taken. The housing contains a pump having an inlet connected to a catheter inserted in the body of the person or animal and an outlet connected through a conduit and a multiple position first control valve to a storage receptacle having provision for separately storing a plurality of individual samples. A reservoir for rinsing fluid is connected through a second control valve to the conduit just downstream of the pump. A control system comprising a radio receiver for remote control controls the pump and second control valve to admit body fluid and rinsing fluid alternately to the conduit and controls the first control valve to direct individual samples of body fluid to the storage receptacle and to discharge rinsing fluid from the conduit. The storage receptacle comprises a plurality of small receptacles for individual samples or a continuous tube in which samples are spaced by gas.

### **Summary of the Invention**

**[0009]** The invention relates to a portable device for automated blood sampling, comprising a mobile apparatus suitable for collecting blood samples from a freely-moving human or animal subject. The apparatus comprises a mobile base provided with means to allow free movement of the device, a first conduit for moving fluid between the subject and the mobile apparatus, a second conduit and a third conduit operatively connected to each

other and to the first conduit, a sample collector comprising a fluid reservoir, operatively connected to the second conduit, a syringe pump for moving fluid, operatively connected to the third conduit, a first valve that controls flow through the first conduit, a second valve that controls flow through the second conduit, a controller for controlling the automated blood sampling, the controller being operatively coupled to the pump and the valves, an uninterruptible power supply operatively connected to the controller and having an internal battery, such that power may typically be provided to the uninterruptible power supply from an external power source but when external power is not being supplied, power is maintained by the internal battery, and an audible and/or visible alarm configured to indicate an interruption of external power to the device. The controller is configured to cause collection of a blood sample by a method which comprises: providing sterile solution in the conduits, with the first valve in the closed position, and the second valve in the open position; pushing sterile solution into the third conduit using the pump, thereby flushing the second conduit with sterile solution; closing the second valve and opening the first valve; withdrawing sterile solution from the third conduit with the pump, thereby withdrawing a discreet amount of blood from the freely moving subject, sufficient to fill the first conduit with sterile solution and to fill the third conduit with the desired blood sample; opening the second valve and closing the first valve; with the pump, pushing into the third conduit a volume of sterile solution equal to the volume of the second conduit, thereby forcing the blood sample to the end of the second conduit; and pushing from the pump an amount of sterile solution into the third conduit equal to the volume of the blood sample, thereby depositing the blood sample into the fluid reservoir of the sample collector.

**[0010]** According to one embodiment, an ABS apparatus is connected to a freely-moving animal by resiliently compressible tubing. The tubing is operably connected to a refrigerated fraction collector having sealed vials for receipt of blood samples. The tubing is also operably connected to a syringe pump and a source of sterile fluid, such as saline (0.9% sodium chloride solution). The apparatus further includes valves operatively connected to the resilient tubing. The apparatus also includes a sample collection control means, such as a personal computer (PC), a microcontroller, a computer chip with embedded software code, an electronic controller, a timer, or other regulating device.

**[0011]** The tubing of the present invention provides fluid communication between the test animal, the refrigerated fraction collector, and the syringe pump through a three-way connector such as a "Y" or "T" connector. The valves are located so as to control fluid flow to and from these three areas. The valves associated with the tubing which connects the test animal and the refrigerated fraction collector may comprise pinch valves and may be combined within a common housing and utilize individual or common pinch bars. In this manner, the system em-

plays a pinch valve that operates such that whenever one selected tube is open, another is shut. In this embodiment, the test lead, tubing, and "T" connector all have anticoagulant properties, either inherent in the non-thrombogenic (i.e. material not likely to induce blood clotting) plastic used in their construction, or via a permanent or renewable anticoagulant coating in the interior thereof. Because all surfaces in contact with the blood sample in this embodiment are non-thrombogenic, it is possible to use saline solutions, without added heparin or other anticoagulant additives, to flush the system and to move blood samples within the apparatus.

**[0012]** In some cases, it may still be necessary or desirable to use an added anticoagulant as part of the biomedical test. In such case, the added anticoagulant would form a renewable non-thrombogenic film on the interior surface of all tubing and other connections through which it was flushed. Therefore, this system should be able to function either with, or without, anticoagulants such as heparin, sodium citrate or other materials added to the saline used to move blood in and out of the automated blood sampler.

**[0013]** In one embodiment, the control means (controller) coordinates the valve positions, fraction collector, and syringe activity so as to flush the system, withdraw a blood sample from the animal, move that blood sample to the refrigerated fraction collector, and advance the fraction collector to the next vial position or to waste. The controller can also regulate the refilling of the syringe pump with sterile saline solution from a sterile saline solution supply means. Because the controller is easily programmed with various test protocols, the controller can be programmed such that no blood is re-injected into the test subject. In that case, blood would be continuously sampled in small volumes on the order of microliters, at intervals spanning as short a time as possible (less than 3 minutes). If desired, blood which is withdrawn during a particular cycle and not used as a sample may be flushed out of the apparatus and associated catheter during an ensuing cycle.

**[0014]** In one embodiment, the ABS apparatus, the controller, and an uninterruptible power supply are situated on a carriage of a size that allows the freely-moving animal, a mobile human subject, or a human technician to easily move the entire device. Accordingly, the freely-moving animal is not overly restricted in its activities. The animal may be allowed to roam within a larger area such as a room, or containment area, and perform normal functions such as eating, sleeping, and/or elimination without affecting the biomedical test. In the case of a human test subject, the human may recline in a bed, lounge in a chair, walk down a hallway, and use a wheelchair-compatible toilet stall without interfering with the biomedical test. Such a device may be less stressful than systems or protocols which restrain movement.

## **Brief Description of the Drawings**

### **[0015]**

- 5 Fig. 1 shows a perspective front view of one embodiment of the apparatus of the present invention that might be used for large animals or human subjects. Fig. 1A shows an embodiment of the apparatus in Fig. 1 modified for use above an incubator used in a neonatal intensive care environment
- 10 Fig. 2 shows a side view of the tray section of the apparatus of Fig. 1.
- 15 Fig. 3 shows a diagrammatic view of one embodiment of an apparatus for automated sampling of blood
- 20 Fig. 4 shows a flowchart of one embodiment of the method of the present invention for conducting automated micro sampling of blood.
- 25 Fig. 5 shows a flowchart of a modification of the method of Fig. 4.
- 30 Fig. 6 shows a perspective view of an alternative embodiment of the apparatus of the present invention that might be used for a large animal moving on its own recognizance.
- 35 Fig. 6A shows the same apparatus as Fig. 6, but with an added shield which would prevent the apparatus from being wedged in the corner of a square or rectangular cage surrounding a containment area.
- 40 Fig. 7 shows a perspective view of the embodiment of Fig. 6 in use within a containment area.
- 45 Fig. 8 shows an exploded, partial cutaway, partial perspective view of an embodiment of the present invention incorporating a "lazy susan" bearing.

### **Detailed Description of the Invention**

- 50 **[0016]** Referring now to Fig. 1, there is shown a perspective front view of one embodiment of the apparatus of the present invention. Specifically, in this embodiment, portable device 100 is capable of being moved by a test subject, such as a human, or by a laboratory assistant when the test subject is a different type of large animal. In this embodiment, portable device 100 comprises equipment section 102 and mobile base 104. Mobile base 104, in this embodiment, includes legs 106, 108, 110, 112 and 114, each of which have a wheel attached thereto to permit base 104 to be wheeled about in any direction. The number of legs, and the height and shape of the legs, is a design choice, and are all contemplated to be within the scope of the invention. The use of wheels, roller balls, or other means to allow free movement of this device is likewise a design choice, and are all contemplated to be within the scope of the invention. For example, it may be desired to provide devices of various heights to accommodate test subjects of various heights. Alternatively, a single unit with a varying height may be designed. All of these variations are within the scope of the present invention.

**[0017]** Continuing with Fig. 1, equipment section 102 includes an apparatus for performing a biomedical test on the test subject, which, in this embodiment, comprises ABS 116. Also shown in Fig. 1 are refrigerated fraction collectors 118 and 120. Referring now to Fig. 2, a partial side view of the device of Fig. 1 is shown, showing additional detail of equipment section 102. Equipment section 102 comprises lower support 122 and bracket support 124 which comprises bracket 126 and bracket 128. Bracket support 124 is used in this embodiment to mount ABS 116 above refrigerated fraction collector 120. Refrigerated fraction collector 120 is supported by lower support 122.

**[0018]** Also shown in Fig. 2 is portable power supply 130, which in this embodiment comprises an uninterruptible power supply (UPS) and a microprocessor. Power for portable supply 130 is typically provided through cord 132 and extension cord unit 134 hanging from hook 136. Extension cord 137 of extension cord unit 134 is connected to a power source such as a wall socket. Control means 130 also comprises speaker 138 and warning light 140. When no power is sensed from cord 132, control means 130 causes an intermittent audible alarm to be sounded through speaker 138 to ensure those in the vicinity are aware that external power is not being supplied. In this embodiment, alarm light 140 flashes one color (e.g. yellow) when external power is not being supplied, and flashes another color (e.g. red) when the internal battery in the portable power supply reaches a predetermined discharge level. While the mains power is disconnected, such as by removal of cord 137 from the wall socket, power to all units plugged into the power supply is maintained by its internal battery. Units plugged into control means 130 in Fig. 2 include ABS 116, collector 120, laptop computer 139, but could include additional devices being transported by the portable pharmacokinetic and physiologic sampling and monitoring system.

**[0019]** Continuing with Fig. 2, control means 130 may also incorporate location monitor 144, which could also be placed on bracket 126, bracket 128, lower support 122, ABS 116, fraction collector 120, or other places on the system. Location monitor 144 comprises a transponder and/or transceiver that is used to find the location of a mobile unit within a research facility. A unique code associated with each cart is transmitted to a receiving unit mounted in the ceiling, wall, door or floor of each room in the facility. This code is then displayed on a view screen at a central monitoring station receiving information from each individual receiving station, enabling technicians to locate a specific cart within the confines of the research facility. An optional panic button 145 can be activated by the patient or a technician to alert personnel at the central monitoring station of an emergency situation. Fig. 2 also shows computer 139, which is used to upload information about the blood sampling protocol to a controlling computer chip located inside ABS 116, and to receive downloads from that chip confirming all sampling steps and operations of ABS 116 and fraction col-

lector 120. In the embodiment in Fig. 1 and 2, computer 139 is a laptop computer also receiving power from power supply 130. It is also envisioned that such a computer could be located in a central station with uploads and downloads communicated to the portable device via a choice of mechanisms, examples of which include (a) a portable flash card which transfers to a USB or other hard-wired connection port on the computer and also on the ABS 116 unit (b) a wireless network transmission of data to and from the central computer (c) a temporary connection of a cable between the ABS 116 unit and the external computer or (d) an infrared transmission between the computer and the ABS 116 unit or (e) other common means of communication between a computer and a peripheral device.

**[0020]** The selection of the means for support is a design choice, and fewer or more supports of the same or differing form may be used, and all are contemplated to be within the scope of the invention. Supports or combinations of supports may include additional brackets, shelves, trays, hooks, drawers, rods, hangers and others. The combination of bracket support 124 and lower support 122 provides the ability to mount equipment in a variety of horizontal and vertical relationships. Moreover, incorporation of additional equipment is facilitated. By way of example, but not of limitation, a transceiver may be attached or supported by either bracket support 124 or lower support 122 to allow for wireless transmission of data from portable device 100 to a remote device, such as a computer, in the event test control means 130 does not include a transceiver or in the event additional bandwidth is desired. The data transmitted may comprise test data and/or data from a global positioning receiver or other tracking device. Similarly, in the event physiological monitoring is desired, the requisite equipment for such monitoring may be easily incorporated into portable device 100.

**[0021]** Fig. 3 shows a diagrammatic view of ABS 116. In this embodiment, one end of catheter tubing 300 is operably connected to test lead 299 which is a catheter which has its distal end inserted into a vein or artery in the test subject using devices and methods well-known in the art. Catheter tubing 300 is routed through first pinch valve 302 to first intersection or "T" 304, where catheter tubing 300 is joined with collector tubing 306 and reservoir tubing 308. Collector tubing 306 extends from first "T" 304 through second pinch valve 310 to refrigerated fraction collector 118. Fraction collector 118 includes sealed vials 312 for receiving blood samples, and also includes drain 314, all as is well known in the art. The present invention includes within its scope use of sample collection means other than refrigerated fraction collectors. For example, it will be appreciated by those skilled in the art that for performance of some experiments, the sample collection means will not require a drain, and the saline and sample may be intentionally intermixed.

**[0022]** Connector tubing 308 extends from first "T" 304 and reservoir 298 to second intersection or "T" 316. It will

be appreciated by those skilled in the art that reservoir 298 can alternatively be an extension of tubing 308 or the enlarged section of tubing as depicted for reservoir 298 in Fig. 3. Extending from second "T" 316 is syringe tubing 318 which is, in turn, connected to syringe pump 320. Syringe pump 320 is of the type that can be controlled to move fluid to or from syringe tubing 318, and may comprise, for example, the Culex ABS syringe drive manufactured by Bioanalytical Systems, Inc. of West Lafayette, Indiana. It will be appreciated by those skilled in the art that other means for moving fluid can be substituted for syringe pump 320 and are considered within the scope of this invention. Other means for moving fluid include, but are not limited to, a reciprocal piston pump, peristaltic pump, or any other vacuum/pressure source.

**[0023]** Reservoir tubing 322 extends from second "T" 316, goes through third pinch valve 324 and is connected to sterile saline reservoir 326. Sterile saline or any other physiologically compatible solution, such as Ringer's solution, may be housed within saline reservoir 326. First, second and third pinch valves 302, 310 and 324, respectively, in the embodiment of Fig. 3, are intended for use with only a single tube - to open or close that tube - and may comprise, for example, Model 161P, manufactured by NR Research of Caldwell, New Jersey. It is also anticipated that with a double pinch valve, such as that used in the Empis Automated Dosing device, manufactured by Bioanalytical Systems Inc., West Lafayette, Indiana, could be used in situations where two different blood vessels are alternately being sampled. In that example, a second syringe drive, tubing set and saline reservoir would mount to the front panel of ABS 116. The fraction collector, such as the HoneyComb model manufactured by Bioanalytical Systems Inc., West Lafayette, Indiana, would possess dual sampling needles so that only one collector would be required.

**[0024]** It will be appreciated by those skilled in the art that a wide variety of fluid control means can be used in place of first pinch valve 302, second pinch valve 310 and third pinch valve 324. For example, first pinch valve 302 and second pinch valve 310 may be replaced with a single three-way pinch valve, alternatively, in-line valves may be used. It will be further appreciated by those skilled in the art that it is not necessary to have sterile saline reservoir 326 in the apparatus for performing automated micro blood sampling. For example, in another embodiment, syringe pump 320 is connected to syringe tubing 318 which is in turn connected to first "T" 304. In this other embodiment, second "T" 316, connector tubing 308, and third pinch valve 324 are omitted.

**[0025]** The blood sampling system of Fig. 3 also includes controller 130 for automated control of the system as is described in greater detail herein. Controller 130, which comprises, in this embodiment, a computer chip with embedded software code, is operatively connected, by means well-known in the art to: (a) first pinch valve 302; (b) second pinch valve 310; (c) third pinch valve 324; (d) syringe pump 320; and (e) fraction collector 118.

In addition, there must be a transfer of information to controller 130 chip from user interface software located in an external computer 129 which uploads user preferences to controller 130 by means of (a) a cable (b) a flash card (c) a wireless network connection (d) a Bluetooth connection, or any another established method of communication between the external computer and peripheral devices. By its operable connections, controller 130 controls the positions of first pinch valve 302 and second pinch valve 310 to cause the alternate opening and closing of test lead 300 and collector tubing 306; controls the open and closed position of third pinch valve 324, to cause the opening and closing of reservoir tubing 322; controls syringe pump 320 for delivering fluid into or withdrawing fluid from syringe tubing 318; and instructs fraction collector 118 to either receive blood samples into the vials 312 or to pass fluid coming from collector tubing 306 into drain 314.

**[0026]** The present invention may be used to sample body fluids other than blood, either separately or in combination with blood sampling and other biomedical testing. Cerebrospinal fluid (CSF), for example, may be sampled using the present invention. The combination of CSF and blood sampling allows for a complete picture of the disposition of a drug, metabolite or biomarker on both sides of the blood brain barrier. Other applications will be known to those skilled in the art and are within the scope of the present invention.

**[0027]** Operation of one embodiment of ABS 116 is explained by referring to Fig. 4. Fig. 4 is a flow chart of one method for conducting automated blood sampling according to the present invention. At step 400, the operator outlines the blood sampling method to be used in the study, using the user interface software on a computer. This method includes, among other information, the time of the sample, the volume of the sample and whether or not the sample will be diluted with saline. These decisions are translated by the computer software into a series of instructions which are then uploaded to the automated blood sampler in step 402. During step 402, automated internal system checks would verify the correct operation of the fraction collector (Fig. 1, 118 or 120) and controller (Fig. 1, 116) prior to accepting the upload of the method defined by the user in step 400.

**[0028]** Prior to step 400, the tubing and syringe pump would already be loaded and flushed with saline. The catheter in the test subject would be connected to ABS 116 only after this flushing procedure was complete. This process is described in detail in the next paragraphs.

**[0029]** Catheter tubing 300, collector tubing 306, reservoir 298, connector tubing 308, syringe tubing 318, and saline tubing 322 are all filled with sterile saline solution residing in saline bag 326 according to the following steps:

- (a) Pinch valve 302 and pinch valve 310 are placed in the closed position and pinch valve 324 is placed in the open position.

(b) Syringe pump 320 is operated to withdraw a predetermined amount of saline from saline reservoir 326. The predetermined amount is determined by the maximal volume of the syringe on syringe pump 320. One or more refills of the syringe may be required to accomplish complete flushing of all tubing. The required volume must be at least as great as the total volume of catheter 299, catheter tubing 300, twice the volume of collector tubing 306, reservoir 298, connector tubing 308, syringe tubing 318, and reservoir tubing 322, plus the volume of first and second "T"s 304 and 316, respectively, if first and second "T"s 304 and 316 introduce additional volume as would be the case if first and second "T"s comprise separate connectors, and the volume of any desired flush (as described at step 412 below).

(c) Pinch valve 324 is then closed.

(d) Pinch valve 302, or pinch valve 310, is then opened and Syringe pump 320 is instructed to deliver saline until syringe pump 320 is empty. During this delivery of saline, reservoir 298, tubing 304 and tubing 308 are all inverted so that as the fluid enters reservoir 298, any associated air bubbles will rise with the fluid front and be pushed out more easily into fraction collector 306 tubing. If this procedure is not followed, air bubbles will rise towards "T" 316 and be harder to expel from the system. If there was insufficient fluid in the line to accomplish the purge of all air and air bubbles from the system, then pinch valve 324 is opened again, pinch valve 302 and 310 are closed again, and the plunger of the syringe on syringe pump 320 is retracted again to refill the syringe. Valve 324 is then closed, valve 302 remains closed, and valve 310 is opened again. Step (d) is then repeated until tubing 318, 308, 322 and 306 are all filled with saline and free of air and air bubbles.

(e) The syringe is refilled again as described in step (e).

(f) Tubing 304 and 308 are returned to the original position shown in Fig. 3, and valve 306 and 324 are closed, while valve 302 is opened. Then syringe pump 320 is instructed to deliver fluid to catheter tubing 300 through opened valve 302 until all air is expelled from tubing 300.

(g) A connection can now be made between catheter tubing 300 and catheter 299. Valve 302 will then be opened, while valves 310 and 324 remain closed. Syringe pump 320 is instructed to withdraw fluid from tubing 318 and thus withdraw fluid from all fluid lines connected to tubing 318, including tubing 308, 304, 300 and catheter 299. This action draws blood into each successive tubing until the syringe pump is instructed to stop. Typically, this process will draw only enough blood to capture any air bubble which may have been formed during connection of catheter 299 to catheter tubing 300. Once the air bubble passes into "T" 304 or enters reservoir 298, valve 302 is closed. Then valve 310 is opened and syringe pump

320 is instructed to deliver fluid to line 318, "T" 316, tubing 308, reservoir 298, "T" 304, and fraction collector tubing 306 in order to flush the air bubble, and all blood in these connections, to the drain on the fraction collector.

(h) Valve 310 and 324 are then closed, and valve 302 is opened. The syringe pump continues to deliver fluid to line 318 and thus flushes blood in the catheter tubing and catheter back to the test subject.

(i) At any time in this process, if there is insufficient fluid in the syringe, the system can be refilled according to the method outlined in step (e).

(j) At any time in this process, if there is too much fluid in the syringe, thereby preventing syringe plunger 320 from being retracted because the syringe is already full, the system can purge excess fluid by opening only valve 310 and expelling the extra fluid.

**[0030]** Returning to Fig. 4, in step 404 blood is withdrawn from the test subject of an amount sufficient to produce a blood sample. To withdraw blood, first pinch valve 302 (Fig. 3) must be opened and pinch valves 310 and 324 must be closed. Then, syringe pump 320 is controlled to withdraw saline of a volume equal to the volume of catheter 299, catheter tubing 300 and first "T" 304 plus an amount equal to the volume of the desired blood sample. This results in catheter 299, catheter tubing 300, first "T" 304 and some or all of reservoir 298 being filled with blood.

**[0031]** To place the withdrawn blood sample volume into fraction collector 118, indicated as step 406 (Fig. 4), the following steps are then taken:

(a) First pinch valve 302 and 324 are closed and pinch valve 310 is opened.

(b) Fraction collector 118 is controlled so that fluid goes to drain 314.

(c) Syringe pump 320 is instructed to deliver saline of a volume at least equal to the volume of collector tubing 306 and the remaining volume of first "T" 304 that is not yet filled with blood from step 404. This step moves blood into collector tubing 306 and to the end of collector tubing 306 nearest fraction collector 118, thus displacing the saline that was previously filling that line

(d) Fraction collector 118 is instructed to advance one of the vials 312 so that fluid passes to one of vials 312.

(e) Syringe pump 320 is controlled to introduce saline of a volume equal to the volume of the blood sample, thereby forcing the blood sample into one of vials 312.

**[0032]** Returning to Fig. 4, if, at step 408, it is determined that no additional blood samples are necessary or desired, the method of blood sampling ends at step 410 with the flushing of blood from all tubing and the catheter during step 411. If, on the other hand, additional

blood samples are necessary or desired, in step 412 the same flush is performed, fraction collector 118 is realigned over the drain, and syringe pump 320 is refilled in anticipation of the next sample.

**[0033]** At step 414, it is determined, by controller 130, whether syringe pump 320 has a sufficient volume of sterile saline available to perform another blood test. If enough saline is available, the method returns to step 404 to withdraw additional blood. If insufficient saline is available, syringe pump 320 is filled with additional saline at step 416.

**[0034]** The situation described above reflects a situation wherein the unused withdrawn blood or other fluid, remaining in test lead 300 and some of first "T" 304, is returned to the test subject to conserve blood cells and prevent anemia. There may be other examples, in which it is not desirable to do this. For example, when the test subject is a human, there may be conditions in which anticoagulant use in the automated blood sampler may be contraindicated by a test subject's use of therapeutic anticoagulants, such as warfarin, due to a pre-existing medical need. In such cases, it may be undesirable to re-introduce blood back into the test subject when an anticoagulant is required due to the nature of the tubing being used on the ABS. In these situations, reintroduction is avoided by maintaining pinch valve 302 in the closed position until such time as a sample is to be withdrawn. This means that all blood passing through pinch valve 302 is prevented from returning along the same path by the subsequent closure of pinch valve 302. However, because blood is maintained outside of the body in catheter 299 and catheter tubing 300, care must be taken to rapidly flush blood from the tubing beyond valve 302 and advance to the next withdrawal of blood in order to avoid keep the blood moving in the catheter 299 and catheter tubing 300 and avoid the situation where blood is stationary for prolonged periods of time, since this would increase the potential for blood clotting and obstructing catheter 299 and catheter tubing 300.

**[0035]** According to one embodiment, a near continuous withdrawal is conducted, with each withdrawal taking place over a period measured in seconds, and totaling between 5 and 250 microliters to avoid significant loss of blood from the test subject. According to this method, the time between sampling is minimized. The withdrawal step may be relatively slow to preserve the integrity of the blood cells during their passage through the narrow bore tubing of the catheter 299 and catheter tubing 300, while the intervening steps are conducted somewhat faster through larger bore tubing in fraction collector tubing 306. Thus, blood is not allowed to remain stagnant in test lead 300, or anywhere in the system, for a significant amount of time. This approach is useful in situations wherein a discreet sample at a given time is not needed.

**[0036]** If the time between samples is short enough to avoid blood coagulation in the catheter and catheter tubing, then the process may be modified as shown in Fig. 5. In this procedure, the process of Fig. 4 is modified by

removing step 411 and changing step 412 to new step 413. At step 413, the flush is restricted only to tubing 318, "T" 316, tubing 308, reservoir 298, "T" 304, tubing 306 and fraction collector 118. Valve 302 remains closed throughout the flushing step and blood remains in half of "T" 304, catheter tubing 300 and catheter 299. Syringe pump 320 can refill at any time by closing valve 310 and 302, opening valve 324 and retracting the plunger on syringe pump 320 as described previously. After blood has been flushed, valve 302 is opened and the next aliquot of blood is pulled into "T" 304 and reservoir 298. This process continues until such time as the last blood sample is taken. Then, the process ends when the catheter is physically removed from the test subject and the syringe, saline 326 and all tubing on controller 116 are removed and discarded..

**[0037]** It will be appreciated by those of skill in the art that, with the exception of connecting catheter 299 to catheter tubing 300, steps 404-416 may be controlled by controller 130 to result in an automated blood sampling method. Steps 400-402 cover the selection and initiation of the blood sampling method to be automated. A blood sampling method would define (a) when a blood sample was taken, (b) how much blood was taken and (c) whether the blood was to be intentionally diluted with saline, or not. Controller 130 must be able to send control signals to pinch valve 302, pinch valve 310, pinch valve 324, syringe pump 320, and fraction collector 118, all of which are operably connected to controller 130. In one embodiment, controller 130 receives a signal from syringe pump 320 indicative of the saline volume in syringe pump 320 to ensure proper volumes of saline are pumped and withdrawn, and/or are available for obtaining the next blood sample.

**[0038]** Referring now to Fig. 6, there is shown a perspective view of an alternative embodiment of the present invention, which is intended for use with freely-moving animals. In this embodiment, portable sampling or monitoring device 600 comprises base section 602. Wheels 604, 606, 608 and 610 are connected to base 602 by legs 612, 614, 616 and 618 respectively.

**[0039]** Testing or sampling device 620 is positioned above the test subject on base section 602. Thus, base section 602 serves as an equipment section in this embodiment. Testing device 620 is connected to test subject 622 by test lead 624. Test lead 624 passes through hole 626 in base section 602. Keeping test lead 624 within the space defined by portable device 600 protects tube 624 from becoming trampled, twisted, entangled or crushed.

**[0040]** In this embodiment, portable sampling or monitoring device 600 comprises harness 627. Harness 627 includes sling 628 and strap 630. Sling 628 is connected to portable device 600 by passing strap 630 through holes 631 in base section 602.

**[0041]** Fig. 7 shows a perspective view of the embodiment of Fig. 6 in use within a means for constraining the movement of the test subject within a confined area, such

as the space below a video monitoring camera. Portable sampling or monitoring device 600 is attached by test lead 624 and harness 627 to test subject 622. Portable sampling or monitoring device 600 and test subject 622 are located within an area defined by an obstruction. In this embodiment, fence 640, defines a containment area. Sampling or monitoring device 600 cannot pass beyond fence 640, thus test subject 622 is maintained within the containment area.

**[0042]** As will be appreciated by those of skill in the art, the means for containing the movement of the test subject installed in portable sampling or testing device 600 may also comprise the attachment of a lead, leash, or tether, having one end constrained to an immobile object such as a ceiling. Alternatively, additional shapes of the cage enclosure 640 may be used as a containment area, including such permutations as mazes which would allow the test subject to be trained to navigate the maze, and/or challenged with various maze-related problems while simultaneously being sampled or monitored, and such permutations are contemplated to be within the scope of the invention. However, construction of a containment area should take into account the configuration of the portable device 600. By way of example, but not of limitation, if the portable device 600 is substantially rectangular as shown in Fig. 7, then a containment area of a generally circular shape should be used so as to avoid having a test subject become trapped within a corner of the containment area. Alternatively, the addition of a generally round shield, of a height less than the height of the cage wall, as shown in Fig. 6A, would enable the portable sampling and monitoring device 600 to be used in containment areas of virtually any configuration.

**[0043]** The potential of entrapping the test subject may be further avoided by allowing the test subject to rotate within the confines of device 600, and the associated test equipment to rotate with the test subject, with respect to the rest of the portable device. Referring to Fig. 8, an exploded, partially cutaway, partially perspective view of the present invention incorporates a ball bearing assembly and bearing race, as manufactured by Bioanalytical Systems Inc., West Lafayette, Indiana. Equipment support plate 800 comprises hollow pipe 802. Base 812 comprises hole 814. Harness holder 816 comprises sleeve 818, hole 820, and holes 822. Also shown is bearing 806 which comprises upper plate 804, ball bearings 805, hole 807, bearing race 808, lower plate 810 and support bracket 807. Upper plate 804 and lower plate 810 are in a fixed rotatable relationship with each other.

**[0044]** In use, equipment support plate 800 is fixedly attached to upper plate 804 of bearing 806 and lower plate 810 is fixedly attached to base 812. Hollow pipe 802 extends through hole 808 and beyond lower plate 810 and base 812, and acts as a conduit for various test leads operably connected to the test subject, including infusion catheters, wires, cables, blood sampling catheters and similar devices. Sleeve 818 protects the test leads from the test subject and is attached to hollow pipe

802. In this configuration, equipment may be placed on equipment support plate 800, and a test lead passed through hollow pipe 802, through hole 820 of harness holder 816, and connected to a test subject. The test subject is placed within, for example, a sling, which is then attached by straps or cord to harness holder 816 using holes 822.

**[0045]** Accordingly, when the test subject turns beneath base 812, torque is applied through the sling to harness holder 816. The torque is passed through sleeve 818, hollow pipe 802 and equipment plate 800 to upper plate 804 of bearing 806. Thus, upper plate 804, equipment plate 800 and harness holder 816 all rotate without kinking or placing stress on the tube connected to the test subject. Moreover, this allows the test subject to change direction even if base 812 is entrapped within a containment area, allowing the test subject to change course and extract himself along with portable device 600 and move out of the entrapment.

**[0046]** It will be appreciated by those skilled in the art that the above apparatus and method for monitoring and sampling is a significant improvement over the prior art. It permits the collection of blood samples, the continuous or intermittent infusion of a drug, the acquisition of heart rate and electrocardiograms, the collection of microdialysis or ultrafiltration samples, the acquisition of body temperature readings, and other data or samples that can be obtained by connection of a test lead or catheter between an animal and an external device. The use of such portable devices permits testing of larger animals, including but not limited to humans, pigs, cows, horses, dogs, sheep and goats while the animal is engaged in other activities. The device described in Fig. 1, when used with a human, would enable that human to utilize a private restroom facility without interrupting a test or monitoring session.

**[0047]** Additionally, the present invention eliminates test-related stress for an animal resulting from tethering or restriction, for the animal is not tethered and has freedom of movement. It is likely that the use of a mobile, automated blood sampling device would be less stressful for humans in a Phase 1 Clinical Trial, than repeated needle sticks over the course of a one or two day study that could demand as many as 24 blood samples from each test subject. It is anticipated that a portable automated blood sampling device, that could be wheeled over an incubator by medical personnel, could greatly alleviate the pain and emotional burden of repeated blood sticks from premature infants in neonatal intensive care wards by reducing the problem to a single insertion of an intravenous catheter. Thus, data retrieved by the present invention is free from artifacts that may be introduced due to induced stress. Moreover, the present invention allows for a number of additional devices to be easily incorporated into the device without significant reduction in the mobility of the test subject.

**[0048]** While the present invention has been described in detail with reference to certain exemplary embodi-

ments thereof, such are offered by way of non-limiting examples of the invention, as other versions are possible. Moreover, a number of design choices exist within the scope of the present invention, some of which have been discussed above. It is anticipated that a variety of other modifications and changes will be apparent to those having ordinary skill in the art and that such modifications and changes are intended to be encompassed within scope of the invention as defined by the following claims.

## Claims

1. A portable device (100) for automated blood sampling, comprising a mobile apparatus (116) suitable for collecting blood samples from a freely-moving human or animal subject, the apparatus comprising:

a first conduit (300) for moving fluid between the subject and the mobile apparatus,  
 a second conduit (306) and a third conduit (318) operatively connected to each other and to the first conduit,  
 a sample collector (120) comprising a fluid reservoir, operatively connected to the second conduit,  
 a syringe pump (320) for moving fluid, operatively connected to the third conduit,  
 a first valve (302) that controls flow through the first conduit,  
 a second valve (310) that controls flow through the second conduit,  
 a controller (130) for controlling the automated blood sampling, the controller being operatively coupled to the pump and the valves,

### characterized by:

a mobile base (104) provided with a number of legs (106, 108, 110, 112, 114) and means attached thereto to allow free movement of the device,  
 an uninterruptible power supply operatively connected to the controller and having an internal battery, such that power may typically be provided to the uninterruptible power supply from an external power source but when external power is not being supplied, power is maintained by the internal battery, and  
 an audible and/or visible alarm (138, 140) configured to indicate an interruption of external power to the device;

wherein the controller is configured to cause collection of a blood sample by a method which comprises:

providing sterile solution in the conduits, with the first valve in the closed position, and the second

valve in the open position;  
 pushing sterile solution into the third conduit using the pump, thereby flushing the second conduit with sterile solution;  
 closing the second valve and opening the first valve;  
 withdrawing sterile solution from the third conduit with the pump, thereby withdrawing a discreet amount of blood from the freely moving subject, sufficient to fill the first conduit with sterile solution and to fill the third conduit with the desired blood sample;  
 opening the second valve and closing the first valve;  
 with the pump, pushing into the third conduit a volume of sterile solution equal to the volume of the second conduit, thereby forcing the blood sample to the end of the second conduit; and pushing from the pump an amount of sterile solution into the third conduit equal to the volume of the blood sample, thereby depositing the blood sample into the fluid reservoir of the sample collector.

2. The portable device of Claim 1 further comprising a physiological monitoring device capable of being operably connected to the test subject.
3. The portable device of Claim 1 further comprising a transmitter in communication with other devices not physically connected to the device of claim 1.
4. The portable device of Claim 3, further comprising a transponder or transceiver connected to the device.
5. The portable device of Claim 3, further comprising a computer (139) connected by a wireless network, infrared communication, or other wireless means to the portable device of Claim 3.
6. The portable device of Claim 1 wherein the fluid reservoir of the sample collector comprises a plurality of vials (312) for receiving one or more fluids from the freely moving subject, the plurality of vials capable of being operably connected to the second conduit.
7. The portable device of Claim 1, wherein a plurality of wheels are connected to the base; and wherein the device further comprises a support member (122, 124), wherein at least a portion of the apparatus is supported by the support member.
8. The portable device of Claim 1, wherein the controller for controlling the automated blood sampling comprises a microprocessor.
9. The portable device of Claim 1, wherein the alarm

is operatively connected to the uninterruptible power supply, such that after mains power from a wall socket to the uninterruptible power supply is interrupted, the alarm is activated until such time as the power is restored.

10. The portable device of Claim 1, wherein the apparatus is sized so as to be easily transported by the freely moving subject.

11. The portable device of Claim 1 wherein a plurality of wheels are connected to the base; and wherein the device further comprises a support member, wherein the apparatus is connected to the support member and wherein the sample collector is a fraction collector.

12. A method for performing automated fluid sampling, the method comprising the steps of: providing the apparatus of Claim 1, wherein the first, second, and third conduits are filled with fluid, and wherein the first fluid control means is in the closed position, and the second fluid control means is in the open position;

pushing solution into the third conduit using the means for moving fluid, thereby flushing the second conduit with solution;

closing the second fluid control means and opening the first fluid control means; withdrawing solution from the third conduit with the means for moving fluid, thereby withdrawing a discreet amount of bodily fluid from the freely moving subject, sufficient to fill the first conduit with bodily fluid and to fill the third conduit with the desired bodily fluid sample;

opening the second fluid control means and closing the first fluid control means;

with the means for moving fluid, pushing into the third conduit a volume of solution equal to the volume of the second conduit, thereby forcing the bodily fluid sample to the end of the second conduit; and

pushing from the means for moving fluid an amount of solution into the third conduit equal to the volume of the bodily fluid sample, thereby depositing the bodily fluid sample into the fluid reservoir of the sample collector.

13. The method of Claim 12, wherein the step of withdrawing solution from the third conduit comprises the step of:

withdrawing a volume of solution from the third conduit with the means for moving fluid of at least twice the volume of the first conduit plus the volume of the bodily fluid sample, thereby withdrawing a discreet amount of bodily fluid from the freely moving subject, sufficient to fill the first

conduit with bodily fluid and to fill the third conduit with the desired bodily fluid sample and a volume of bodily fluid equal to the volume of the first conduit;

and wherein the step of pushing solution into the third conduit comprises the step of:

with the means for moving fluid, pushing into the third conduit a volume of solution equal to the volume of the first conduit, thereby forcing the volume of bodily fluid equal to the volume of the first conduit from the third conduit into the second conduit.

14. The method of Claim 13, further including the steps of:

providing a means for supplying solution;

providing a fourth tube operatively connected to the means for supplying solution and the means for moving fluid, such that the means for supplying solution is in communication with the means for moving fluid;

providing a third and fourth fluid control means each having a closed and an open position, operatively connected to the third and the fourth tube, respectively, such that when the third or fourth fluid control means is in the closed position, fluid is restricted from flowing in the respective tube, and when the third or fourth fluid control means is in the open position, fluid is free to flow in the respective tube;

opening the fourth fluid control means, and closing the third fluid control means;

withdrawing solution with the means for moving fluid from the means for supplying solution, thereby refilling the means for moving fluid with solution;

closing the fourth fluid control means; and opening the third fluid control means.

15. The method of Claim 14, further comprising, before the step of pushing solution into the third tube, the steps of:

providing a sample collection control means for controlling fluid flow, the sample collection control means operatively connected to the means for moving fluid, and the first and second fluid control means; and

activating the sample collection control means, such that subsequent steps are controlled by the sample collection control means.

16. The method of Claim 15, further comprising, after the step of pushing into the third tube with the means for moving fluid a volume of solution equal to the volume of the second tube, thereby forcing the fluid sample to the end of the second tube, the step of:

positioning the means for receiving fluid so as to collect the fluid sample.

### Patentansprüche

1. Ortsveränderliches Gerät (100) für eine automatische Blutentnahme, eine mobile Vorrichtung (116) aufweisend, die geeignet ist für die Entnahme von Blutproben von einem menschlichen oder tierischen Probanden, der sich frei bewegen kann, wobei die Vorrichtung aufweist:

eine erste Leitung (300), die ein Fluid zwischen dem Probanden und dem mobilen Gerät bewegt,

eine zweite Leitung (306) und eine dritte Leitung (318), die betriebswirksam miteinander und mit der ersten Leitung verbunden sind,

einen Probensammler (120), der einen Fluidbehälter aufweist, der betriebswirksam mit der zweiten Leitung verbunden ist,

eine Spritzenpumpe (320) zum Bewegen von Fluid, die betriebswirksam mit der dritten Leitung verbunden ist,

ein erstes Ventil (302), das einen Durchfluss durch die erste Leitung steuert,

ein zweites Ventil (310), das einen Durchfluss durch die zweite Leitung steuert,

eine Steuereinrichtung (130) zum Steuern der automatischen Blutentnahme, wobei die Steuereinrichtung betriebswirksam mit der Pumpe und den Ventilen verbunden ist,

### gekennzeichnet durch:

eine mobile Basis (104) mit einer Anzahl von Beinen (106, 108, 110, 112, 114) und daran angebrachten Einrichtungen, welche die freie Bewegung der Vorrichtung ermöglichen,

eine unterbrechungsfreie Leistungszufuhreinrichtung, die betriebswirksam mit der Steuereinrichtung verbunden ist und eine interne Batterie aufweist, so dass die unterbrechungsfreie Leistungszufuhreinrichtung in der Regel von einer externen Leistungsquelle mit Leistung versorgt werden kann, aber die Leistungszufuhr, wenn keine externe Leistung geliefert wird, **durch** die interne Batterie aufrechterhalten wird, und

eine akustische und/oder visuelle Alarmeinrichtung (138, 140), die dafür ausgelegt ist, eine Unterbrechung der externen Leistung für die Vorrichtung anzuzeigen;

wobei die Steuereinrichtung dafür ausgelegt ist, eine Blutentnahme anhand eines Verfahrens zu bewirken, das Folgendes umfasst:

Bereitstellen einer sterilen Lösung in den Leitungen, wobei das erste Ventil die geschlossene

Stellung einnimmt und das zweite Ventil die offene Stellung einnimmt;

Drücken der sterilen Lösung in die dritte Leitung mittels der Pumpe, wodurch die zweite Leitung mit steriler Lösung durchspült wird;

Schließen des zweiten Ventils und Öffnen des ersten Ventils;

Ziehen von steriler Lösung aus der dritten Leitung mittels der Pumpe, wodurch eine abgemessene Menge an Blut, die ausreicht, um die erste Leitung mit steriler Lösung zu füllen und die dritte Leitung mit der gewünschten Blutprobe zu füllen, von dem Probanden entnommen wird, der sich frei bewegen kann;

Öffnen des zweiten Ventils und Schließen des ersten Ventils;

Drücken eines Volumens der sterilen Lösung, das dem Volumen der zweiten Leitung gleich ist, in die dritte Leitung mittels der Pumpe, wodurch die Blutprobe ans Ende der zweiten Leitung gedrängt wird; und

Drücken einer Menge der sterilen Lösung, die dem Volumen der Blutprobe gleich ist, von der Pumpe in die dritte Leitung, wodurch die Blutprobe in den Fluidbehälter des Probensammlers eingebracht wird.

2. Ortsveränderliches Gerät nach Anspruch 1, ferner ein physiologisches Überwachungsgerät aufweisend, das betriebswirksam mit dem Probanden verbunden werden kann.

3. Ortsveränderliches Gerät nach Anspruch 1, ferner einen Sender aufweisend, der mit anderen Geräten kommuniziert, die nicht physisch mit dem Gerät nach Anspruch 1 verbunden sind.

4. Ortsveränderliches Gerät nach Anspruch 3, ferner einen Transponder oder Transceiver aufweisend, der mit dem Gerät verbunden ist.

5. Ortsveränderliches Gerät nach Anspruch 3, ferner einen Computer (139) aufweisend, der über ein Drahtlosnetz, eine Infrarotverbindung oder eine andere drahtlose Einrichtung mit dem ortsveränderlichen Gerät nach Anspruch 3 verbunden ist.

6. Ortsveränderliches Gerät nach Anspruch 1, wobei der Fluidbehälter des Probensammlers eine Mehrzahl von Ampullen (312) aufweist, die eines oder mehrere Fluide von dem Probanden aufnehmen, der sich frei bewegen kann, wobei die in Mehrzahl vorhandenen Ampullen betriebswirksam mit der zweiten Leitung verbunden werden können.

7. Ortsveränderliches Gerät nach Anspruch 1, wobei in Mehrzahl vorhandene Räder mit der Basis verbunden sind, und wobei das Gerät ferner ein tragen-

- des Element (122, 124) aufweist, wobei mindestens ein Teil der Vorrichtung auf dem tragenden Element liegt.
8. Ortsveränderliches Gerät nach Anspruch 1, wobei die Steuereinrichtung zum Steuern der automatischen Blutentnahme einen Mikroprozessor aufweist. 5
9. Ortsveränderliches Gerät nach Anspruch 1, wobei die Alarmeinrichtung betriebswirksam mit der unterbrechungsfreien Leistungszufuhreinrichtung verbunden ist, so dass nach einer Unterbrechung einer Netzleistungszufuhr von einer Wandsteckdose zur unterbrechungsfreien Leistungszufuhreinrichtung der Alarm aktiviert wird, bis die Leistungsversorgung wiederhergestellt wird. 10 15
10. Ortsveränderliches Gerät nach Anspruch 1, wobei die Vorrichtung so bemessen ist, dass sie von dem Probanden, der sich frei bewegen kann, mühelos transportiert werden kann. 20
11. Ortsveränderliches Gerät nach Anspruch 1, wobei in Mehrzahl vorhandene Räder mit der Basis verbunden sind; und wobei das Gerät ferner ein tragendes Element aufweist, wobei die Vorrichtung mit dem tragenden Element verbunden ist, und wobei der Probensammler ein Fraktionssammler ist. 25 30
12. Verfahren zur Durchführung einer automatischen Fluidentnahme, wobei das Verfahren die folgenden Schritte umfasst: Bereitstellen des Geräts nach Anspruch 1, wobei die ersten, zweiten und dritten Leitungen mit Fluid gefüllt sind, und wobei eine erste Fluidsteuereinrichtung eine geschlossene Stellung einnimmt und eine zweite Fluidsteuereinrichtung eine geschlossene Stellung einnimmt; 35 40
- Drücken von Lösung in die dritte Leitung unter Verwendung einer Einrichtung zum Bewegen des Fluids, wodurch die zweite Leitung mit der Lösung durchspült wird;
- Schließen der zweiten Fluidsteuereinrichtung und Öffnen der ersten Fluidsteuereinrichtung; 45
- Ziehen von Lösung aus der dritten Leitung mit der Einrichtung zum Bewegen des Fluids, wodurch eine abgemessene Menge an Körperfluid, die ausreicht, um die erste Leitung mit Körperfluid zu füllen und die dritte Leitung mit der gewünschten Körperfluidprobe zu füllen, von dem Probanden entnommen wird, der sich frei bewegen kann; 50
- Öffnen der zweiten Fluidsteuereinrichtung und Schließen der ersten Fluidsteuereinrichtung; 55
- Drücken eines Lösungsvolumens, das dem Volumen der zweiten Leitung gleich ist, in die dritte Leitung mittels der Einrichtung zum Bewegen des Fluids, wodurch die Körperfluidprobe ans Ende der zweiten Leitung gedrängt wird; und Drücken einer Lösungsmenge, die dem Volumen der Körperfluidprobe gleich ist, in die dritte Leitung mittels der Einrichtung zum Bewegen des Fluids, wodurch die Körperfluidprobe in den Fluidbehälter des Probensammlers eingebracht wird.
13. Verfahren nach Anspruch 12, wobei der Schritt des Ziehens der Lösung aus der dritten Leitung den folgenden Schritt umfasst:
- Ziehen eines Lösungsvolumens, das mindestens dem doppelten Volumen der ersten Leitung plus dem Volumen der Körperfluidprobe entspricht, aus der dritten Leitung mittels der Einrichtung zum Bewegen des Fluids, wodurch dem Probanden, der sich frei bewegen kann, eine abgemessene Menge an Körperfluid, die ausreicht, um die erste Leitung mit Körperfluid zu füllen und die dritte Leitung mit der gewünschten Körperfluidprobe zu füllen, und ein Volumen an Körperfluid, das dem Volumen der ersten Leitung gleich ist, entnommen wird; und wobei der Schritt des Drückens der Lösung in die dritte Leitung den folgenden Schritt umfasst:
- Drücken eines Lösungsvolumens, das dem Volumen der ersten Leitung gleich ist, in die dritte Leitung mittels der Einrichtung zum Bewegen des Fluids, wodurch das Volumen an Körperfluid, das dem Volumen der ersten Leitung gleich ist, aus der dritten Leitung in die zweite Leitung gedrängt wird.
14. Verfahren nach Anspruch 13, ferner die folgenden Schritte umfassend:
- Bereitstellen einer Einrichtung zum Zuführen einer Lösung;
- Bereitstellen eines vierten Schlauchs, der betriebswirksam mit der Einrichtung zum Zuführen von Lösung und der Einrichtung zum Bewegen von Fluid verbunden ist, so dass die Einrichtung zum Zuführen von Lösung mit der Einrichtung zum Zuführen von Fluid in Verbindung steht;
- Bereitstellen einer dritten und einer vierten Fluidsteuereinrichtung, die jeweils eine geschlossene und eine offene Stellung aufweisen und die betriebswirksam mit dem dritten und dem vierten Schlauch verbunden sind, so dass, wenn die dritte oder die vierte Fluidsteuereinrichtung die geschlossene Stellung einnimmt, kein Fluid in einen entsprechenden Schlauch fließen kann, und wenn die dritte oder die vierte Fluidsteuereinrichtung die offene Stellung einnimmt, Fluid in einen entsprechenden Schlauch

fließen kann;  
 Öffnen der vierten Fluidsteuereinrichtung und  
 Schließen der dritten Fluidsteuereinrichtung;  
 Ziehen von Lösung aus der Einrichtung zum Zu-  
 führen von Fluid mittels der Einrichtung zum Be-  
 wegen von Fluid, wodurch die Einrichtung zum  
 Bewegen von Fluid mit Lösung gefüllt wird;  
 Schließen der vierten Fluidsteuereinrichtung;  
 und  
 Öffnen der dritten Fluidsteuereinrichtung.

15. Verfahren nach Anspruch 14, ferner vor dem Schritt  
 des Drückens von Lösung in einen dritten Schlauch  
 die folgenden Schritte umfassend:

Bereitstellen einer Probensammelungs-Steuer-  
 einrichtung zum Steuern eines Fluidstroms, wo-  
 bei die Probensammelungs-Steuerinrichtung  
 betriebswirksam mit der Einrichtung zum Bewe-  
 gen von Fluid und den ersten und zweiten Fluid-  
 steuereinrichtungen verbunden ist; und  
 Aktivieren der Probensammelungs-Steuerin-  
 richtung, so dass nachfolgende Schritte von der  
 Probensammelungs-Steuerinrichtung gesteu-  
 ert werden.

16. Verfahren nach Anspruch 15, ferner nach dem  
 Schritt des Drückens eines Lösungsvolumens, das  
 dem Volumen eines zweiten Schlauchs gleich ist, in  
 den dritten Schlauch mittels der Einrichtung zum Be-  
 wegen von Fluid, durch den die Fluidprobe ans Ende  
 des zweiten Schlauchs gedrängt wird, den folgen-  
 den Schritt umfassend:

Positionieren der Einrichtung zum Aufnehmen  
 von Fluid, damit diese die Fluidprobe sammelt.

## Revendications

1. Cette invention concerne un dispositif portable (100)  
 d'échantillonnage de sang automatisé, comprenant  
 un appareil mobile (116) adapté au recueil d'échan-  
 tillons de sang d'un être humain ou d'un sujet animal  
 évoluant librement, l'appareil comprenant :

une première conduite (300) pour transférer le  
 fluide entre le sujet et l'appareil mobile,  
 une deuxième conduite (306) et une troisième  
 conduite (318) opérationnellement reliées l'une  
 à l'autre et à la première conduite,  
 un collecteur d'échantillons (120) comprenant  
 un réservoir de fluide opérationnellement relié  
 à la deuxième conduite,  
 une pompe à seringue (320) pour transférer le  
 fluide, opérationnellement reliée à la troisième  
 conduite,  
 une première valve (302) qui régule l'écoule-

ment à travers la première conduite,  
 une deuxième valve (310) qui régule l'écoule-  
 ment à travers la deuxième conduite,  
 un contrôleur (130) qui régule l'échantillonnage  
 de sang automatisé, le contrôleur étant opéra-  
 tionnellement relié à la pompe et aux valves,

## caractérisé par :

une base mobile (104) dotée d'un certain nom-  
 bre de pieds (106, 108, 110, 112, 114) et de  
 moyens qui lui sont attachés pour permettre le  
 libre mouvement du dispositif,  
 une alimentation sans coupure opérationnelle-  
 ment reliée au contrôleur et ayant une batterie  
 interne, de manière à ce qu'une alimentation  
 puisse être normalement fournie à l'alimentation  
 sans coupure à partir d'une source d'alimenta-  
 tion externe mais lorsque l'alimentation externe  
 n'est pas fournie, l'alimentation est maintenue  
 par la batterie interne, et  
 une alarme sonore et/ou visible (138, 140) con-  
 figurée pour signaler une interruption de l'ali-  
 mentation externe allant au dispositif ;

dans lequel le contrôleur est configuré de manière  
 à provoquer le recueil d'un échantillon de sang par  
 une méthode qui consiste à :

établir la circulation de la solution stérile dans  
 les conduites, avec la première valve en position  
 fermée et la deuxième valve en position  
 ouverte ;  
 pousser la solution stérile dans la troisième con-  
 duite en utilisant la pompe, en établissant ainsi  
 la circulation de la solution stérile dans la deuxiè-  
 me conduite ;  
 fermer la deuxième valve et ouvrir la première  
 valve ;  
 retirer la solution stérile de la troisième conduite  
 avec la pompe, en prélevant ainsi une quantité  
 de sang discrète du sujet évoluant librement,  
 suffisante pour remplir la première conduite de  
 solution stérile et pour remplir la troisième con-  
 duite de l'échantillon de sang souhaité ;  
 ouvrir la deuxième valve et fermer la première  
 valve ;  
 avec la pompe, pousser dans la troisième con-  
 duite un volume de solution stérile égal au vo-  
 lume de la deuxième conduite, en forçant ainsi  
 l'échantillon de sang jusqu'à l'extrémité de la  
 deuxième conduite ; et  
 pousser de la pompe dans la troisième conduite  
 une quantité de solution stérile égale au volume  
 de l'échantillon de sang, en déposant par ce  
 moyen l'échantillon de sang dans le réservoir  
 de fluide du collecteur d'échantillons.

2. Dispositif portable selon la Revendication 1 comprenant en outre un dispositif de surveillance physiologique apte à être opérationnellement relié au sujet d'étude.
3. Dispositif portable selon la Revendication 1, comprenant en outre un émetteur en communication avec d'autres dispositifs non physiquement raccordés au dispositif de la revendication 1.
4. Dispositif portable selon la Revendication 3, comprenant en outre un transpondeur ou un émetteur/récepteur raccordé au dispositif.
5. Dispositif portable selon la Revendication 3, comprenant en outre un ordinateur (139) raccordé par un réseau sans fil, des communications infrarouges ou d'autres moyens sans fil au dispositif portable de la Revendication 3.
6. Dispositif portable selon la Revendication 1, dans lequel le réservoir de fluide du collecteur d'échantillons comprend une pluralité de flacons (312) pour recevoir un ou plusieurs fluides du sujet évoluant librement, la pluralité de flacons étant apte à être opérationnellement reliée à la deuxième conduite.
7. Dispositif portable selon la Revendication 1, dans lequel une pluralité de roues est reliée à la base ; et dans lequel le dispositif comprend en outre un élément support (122, 124), au moins une partie de l'appareil étant soutenue par l'élément de support.
8. Dispositif portable selon la Revendication 1, dans lequel le contrôleur destiné à la régulation de l'échantillonnage de sang automatisé comprend un microprocesseur.
9. Dispositif portable selon la Revendication 1, dans lequel l'alarme est opérationnellement reliée à l'alimentation sans coupure, de sorte qu'après que l'alimentation secteur de la prise murale allant à l'alimentation sans coupure a été interrompue, l'alarme est activée jusqu'au moment où l'alimentation est rétablie.
10. Dispositif portable selon la Revendication 1, dans lequel l'appareil est dimensionné de manière à pouvoir être facilement transporté par le sujet évoluant librement.
11. Dispositif portable selon la Revendication 1, dans lequel une pluralité de roues est reliée à la base ; et dans lequel le dispositif comprend en outre un élément support, l'appareil étant relié à l'élément support et le collecteur d'échantillons étant un dispositif de recueil de fractions.
12. Procédé de réalisation d'un échantillonnage de fluide automatisé, le procédé comprenant les étapes consistant à :
- 5 fournir le dispositif de la Revendication 1, dans lequel les première, deuxième et troisième conduites sont remplies de fluide, et dans lequel le premier moyen de commande de fluide est en position fermée et le deuxième moyen de commande de fluide est en position ouverte ;
- 10 pousser la solution dans la troisième conduite en utilisant les moyens pour transférer le fluide, établissant ainsi la circulation de la solution dans la deuxième conduite ;
- 15 fermer le deuxième moyen de commande de fluide et ouvrir le premier moyen de commande de fluide ; retirer la solution de la troisième conduite avec les moyens pour transférer le fluide, en prélevant ainsi une quantité discrète des fluides corporels du sujet évoluant librement, suffisante pour remplir la première conduite de fluides corporels et pour remplir la troisième conduite de l'échantillon de fluides corporels souhaité ;
- 20 ouvrir le deuxième moyen de commande de fluide et fermer le troisième moyen de commande de fluide ;
- 25 avec les moyens pour transférer le fluide, pousser dans la troisième conduite un volume de solution égal au volume de la deuxième conduite, en forçant ainsi l'échantillon de fluides corporels jusqu'à l'extrémité de la deuxième conduite ; et pousser à partir des moyens pour transférer le fluide dans la troisième conduite une quantité de solution égale au volume de l'échantillon de fluides corporels, en déposant ainsi l'échantillon de fluides corporels dans le réservoir de fluide du collecteur d'échantillons.
- 30
- 35
- 40 13. Procédé selon la Revendication 12, dans lequel l'étape de retrait de la solution à partir de la troisième conduite comprend les étapes consistant à :
- 45 retirer de la troisième conduite avec les moyens pour transférer le fluide un volume de solution d'au moins deux fois le volume de la première conduite plus le volume de l'échantillon de fluides corporels, prélevant ainsi une quantité discrète de fluides corporels du sujet évoluant librement, suffisante pour remplir la première conduite de fluides corporels et pour remplir la troisième conduite de l'échantillon de fluides corporels souhaité et d'un volume de fluides corporels égal au volume de la première conduite ; et dans lequel l'étape de poussée de la solution dans la troisième conduite comprend les étapes consistant à :
- 50 avec les moyens pour transférer le fluide, pousser
- 55

ser dans la troisième conduite un volume de solution égal au volume de la première conduite, forçant ainsi le volume de fluides corporels égal au volume de la première conduite de la troisième conduite à la deuxième conduite.

5

14. Procédé selon la Revendication 13, comprenant en outre les étapes consistant à :

fournir des moyens pour alimenter la solution ; 10  
 fournir un quatrième tube opérationnellement relié aux moyens pour alimenter la solution et aux moyens pour transférer le fluide, de sorte que les moyens pour alimenter la solution soient en communication avec les moyens pour transférer le fluide ; 15  
 fournir un troisième et un quatrième moyen de commande de fluide ayant chacun une position ouverte et fermée, opérationnellement reliés au troisième et au quatrième tube, respectivement, de sorte que lorsque le troisième ou le quatrième moyen de commande de fluide est en position fermée, l'écoulement du fluide est limité dans le tube respectif, et lorsque le troisième ou le quatrième moyen de commande de fluide est en position ouverte, le fluide est libre de s'écouler dans le tube respectif ; 20  
 ouvrir le quatrième moyen de commande de fluide et fermer le troisième moyen de commande de fluide ; 25  
 retirer la solution avec les moyens pour transférer le fluide à partir des moyens pour alimenter la solution, en remplissant ainsi à nouveau les moyens pour transférer le fluide avec la solution ; 30  
 fermer le quatrième moyen de commande de fluide ; et 35  
 ouvrir le troisième moyen de commande de fluide. 40

15. Procédé selon la Revendication 14, comprenant en outre, avant l'étape de poussée de la solution dans le troisième tube, les étapes consistant à :

fournir des moyens de commande du recueil d'échantillons afin de réguler l'écoulement de fluide, les moyens de commande du recueil d'échantillons étant opérationnellement reliés aux moyens pour transférer le fluide et aux premier et deuxième moyens de commande de fluide ; et 45  
 activer les moyens de commande du recueil d'échantillons de manière à ce que les étapes ultérieures soient régulées par les moyens de commande du recueil d'échantillons. 50  
 55

16. Procédé selon la Revendication 15, comprenant en outre, après l'étape de poussée dans le troisième

tube avec les moyens pour transférer le fluide un volume de solution égal au volume du deuxième tube, en forçant ainsi l'échantillon de fluide jusqu'à l'extrémité du deuxième tube, l'étape consistant à :

positionner les moyens pour recevoir le fluide de manière à recueillir l'échantillon de fluide.

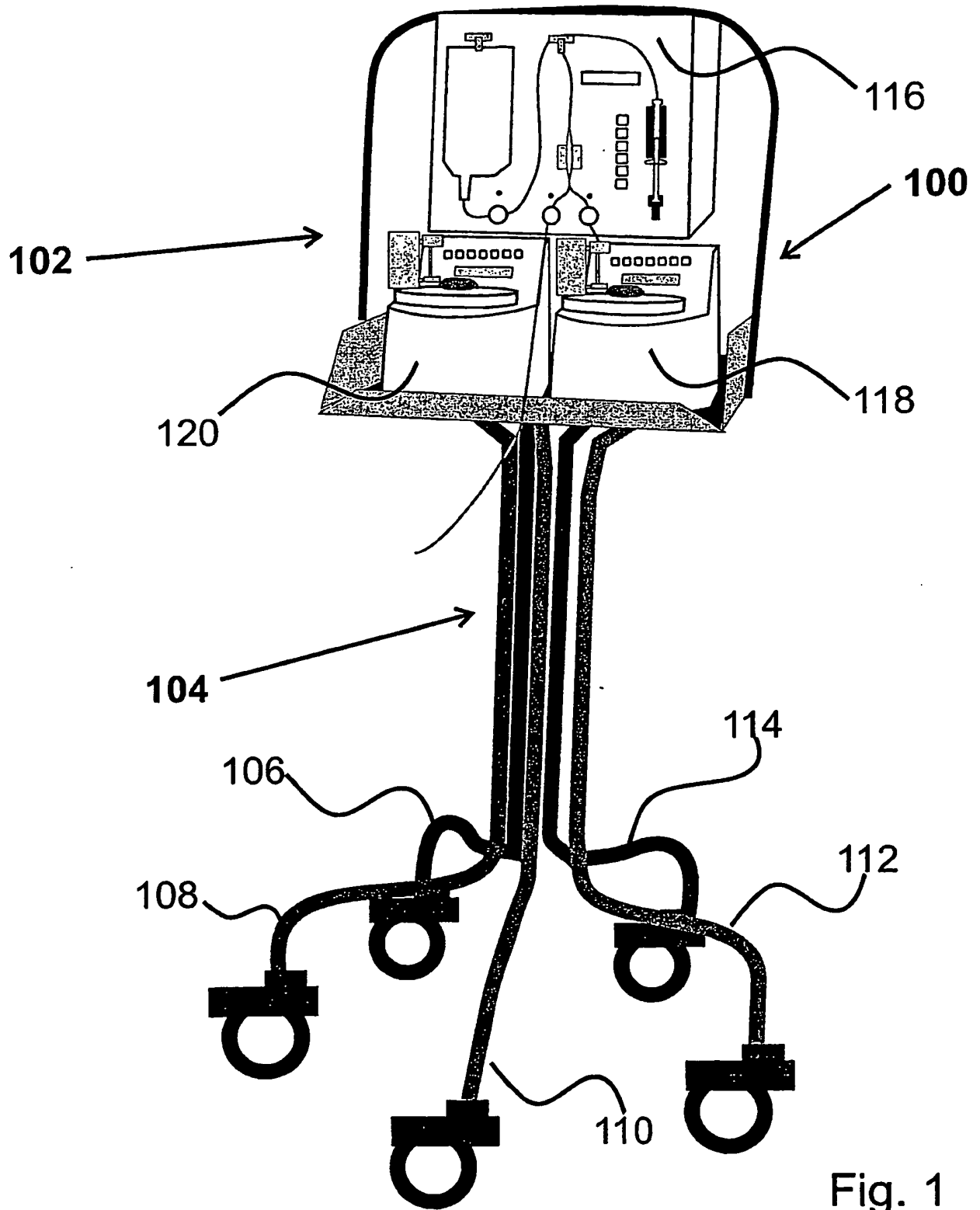


Fig. 1

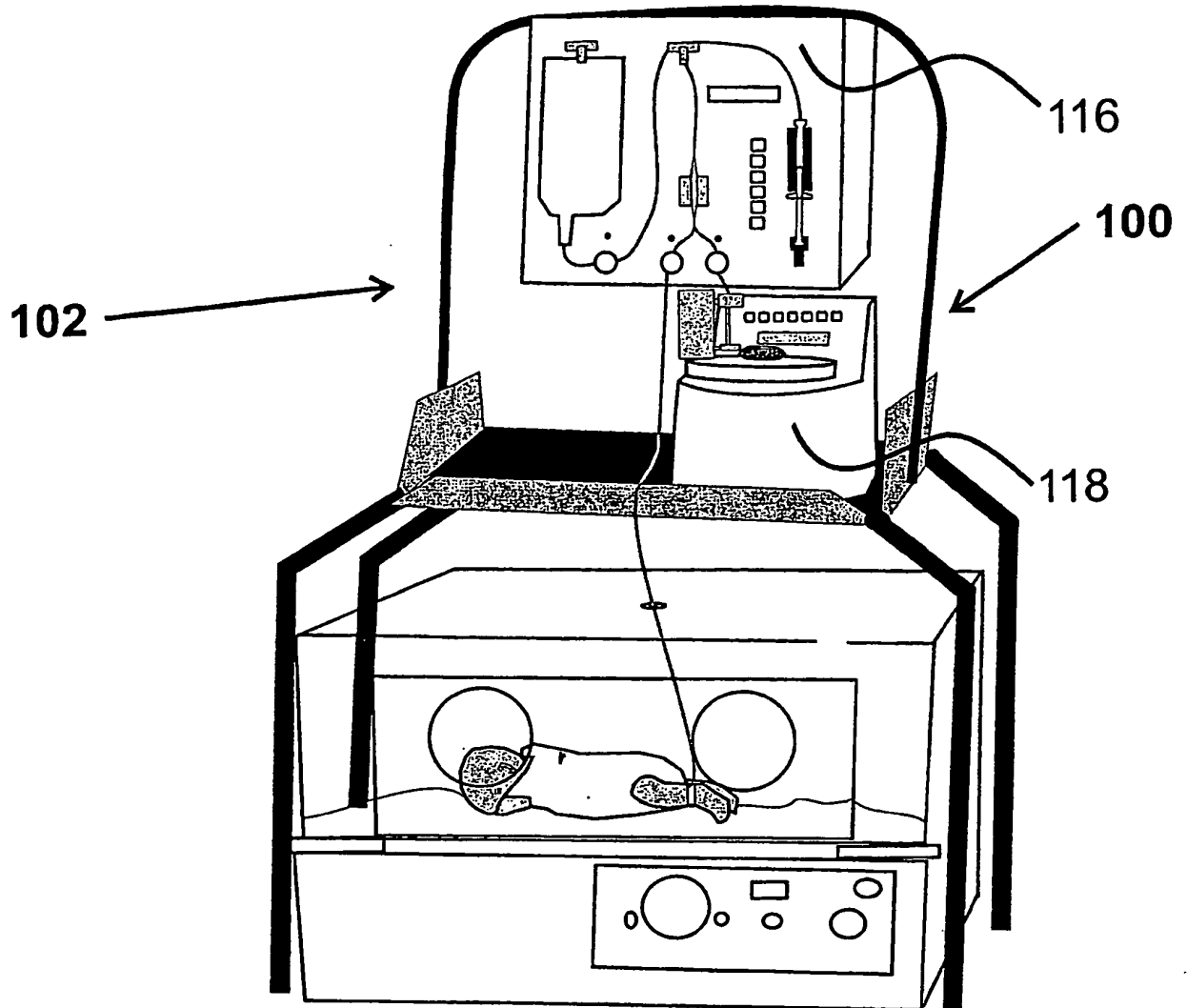


Fig. 1A

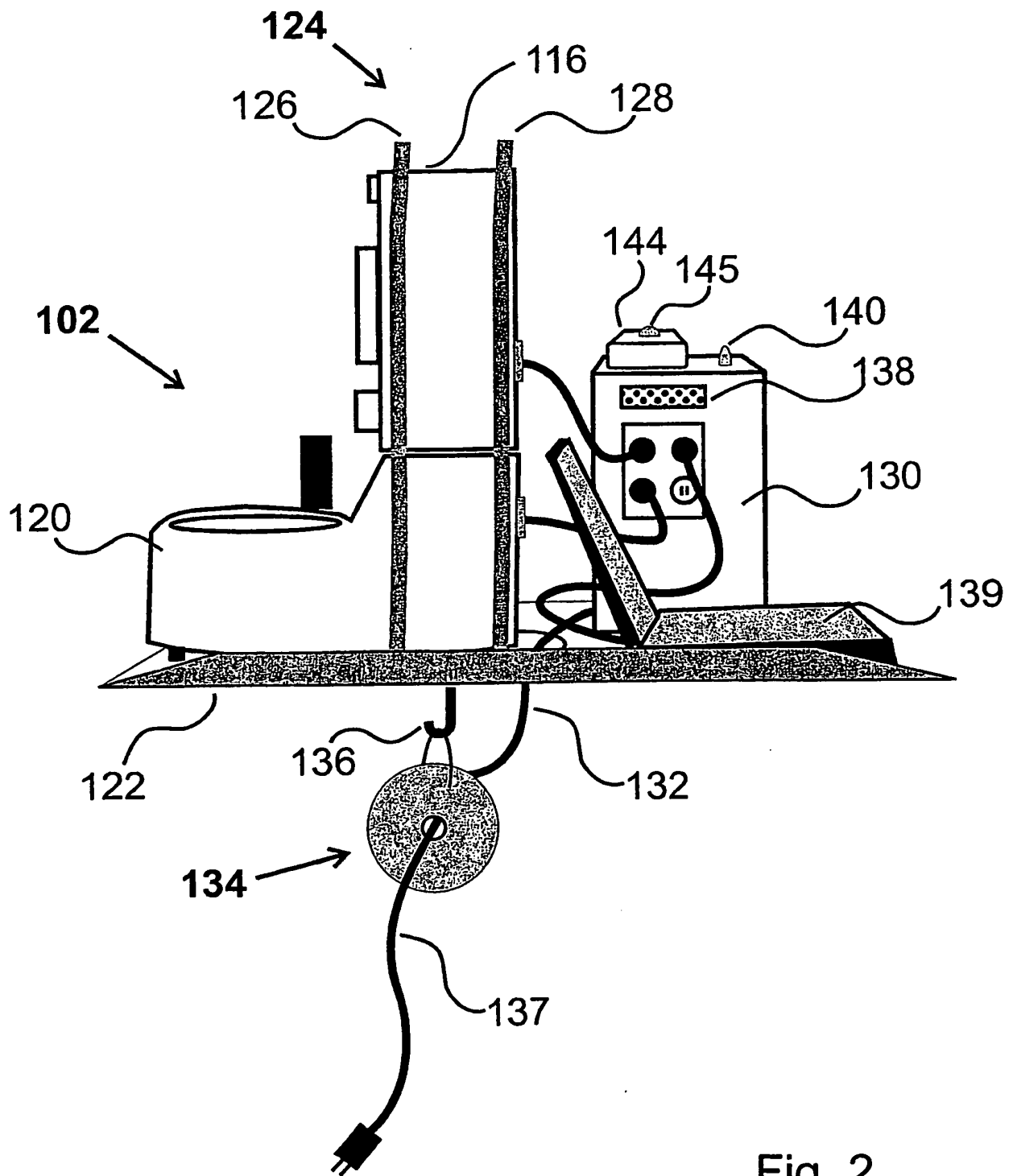


Fig. 2

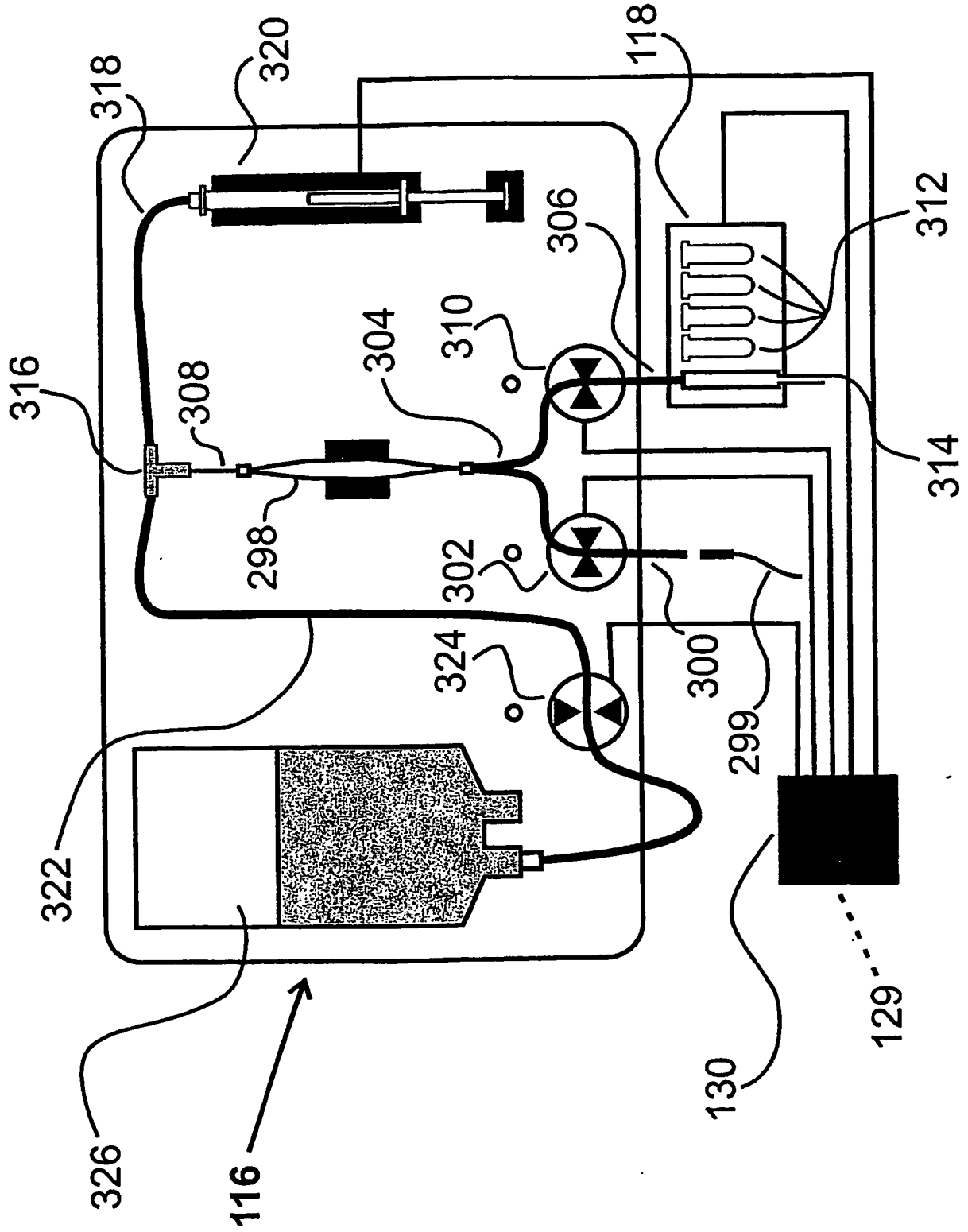


Fig. 3

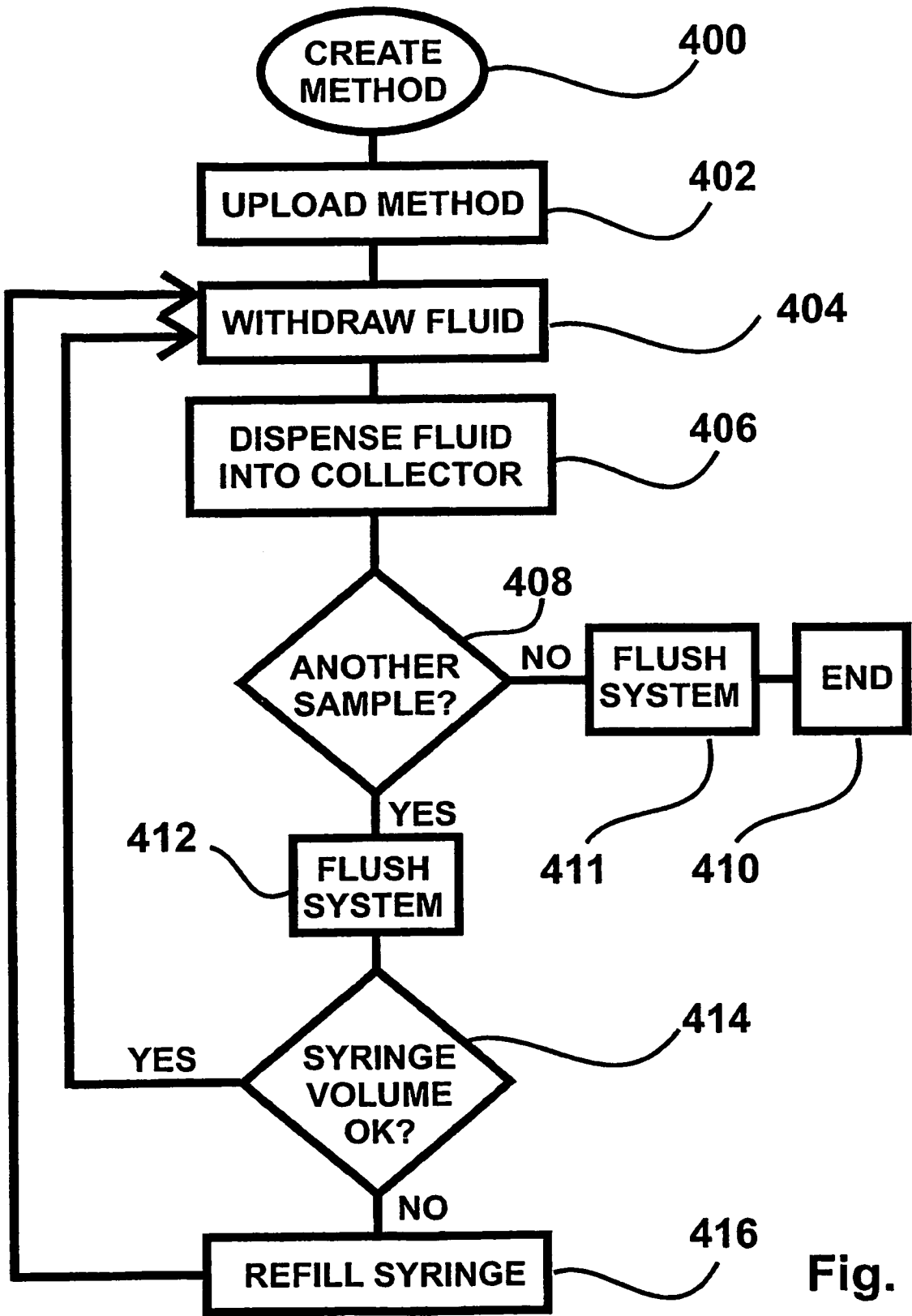


Fig. 4

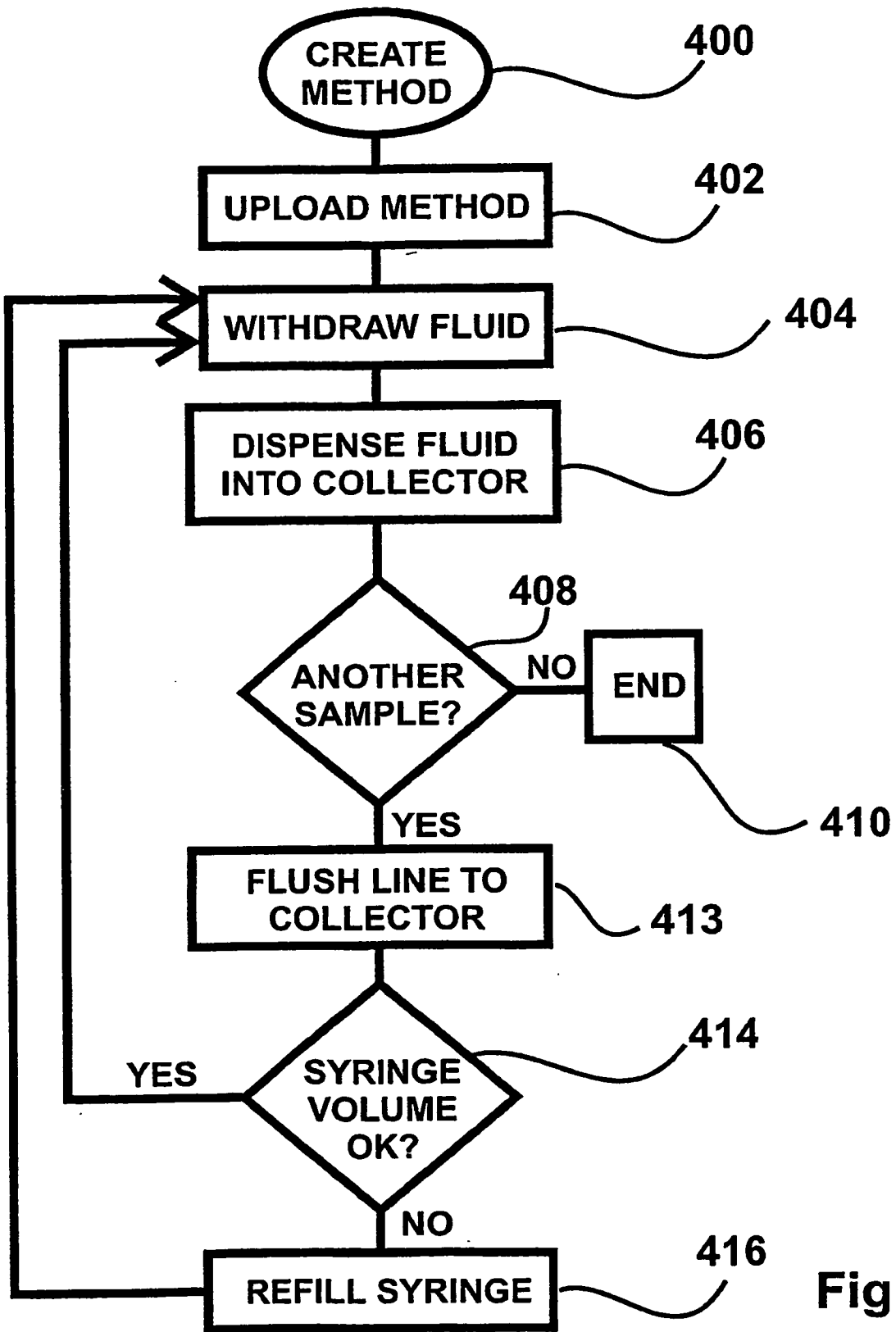


Fig. 5

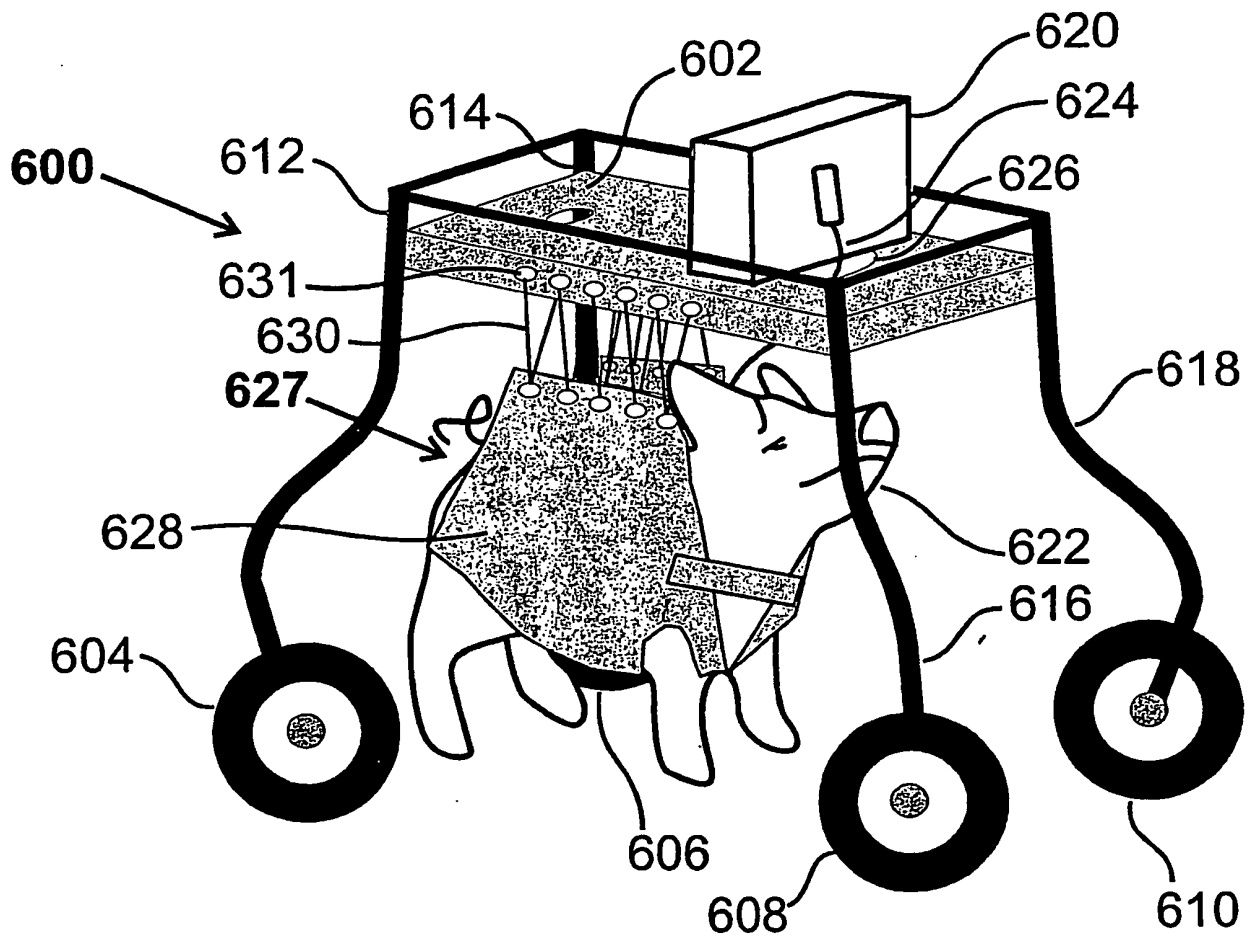


Fig. 6

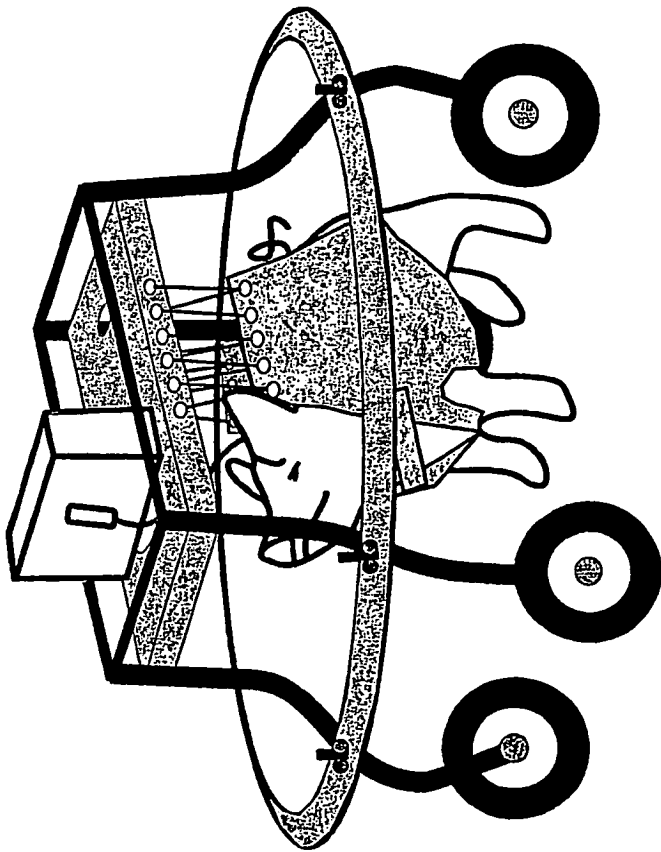


Fig. 6A

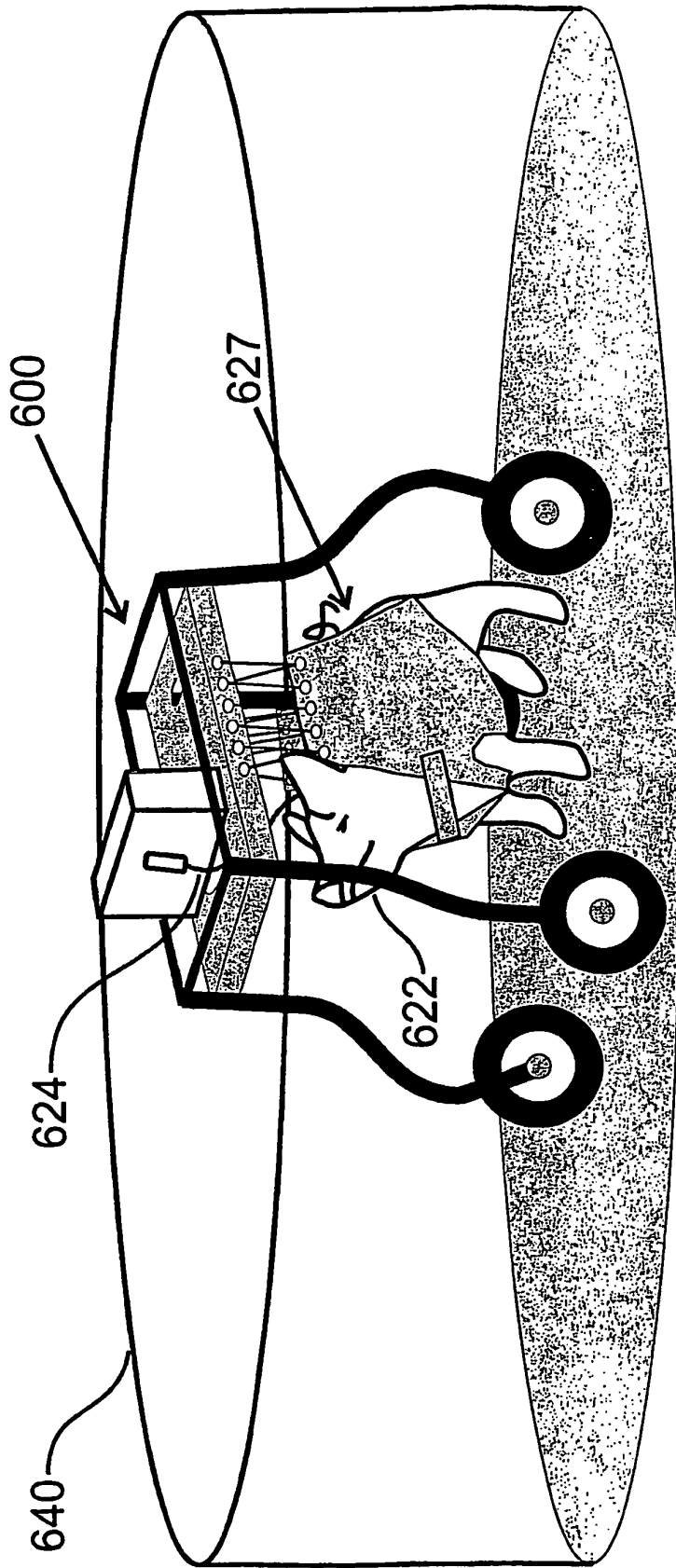


Fig. 7

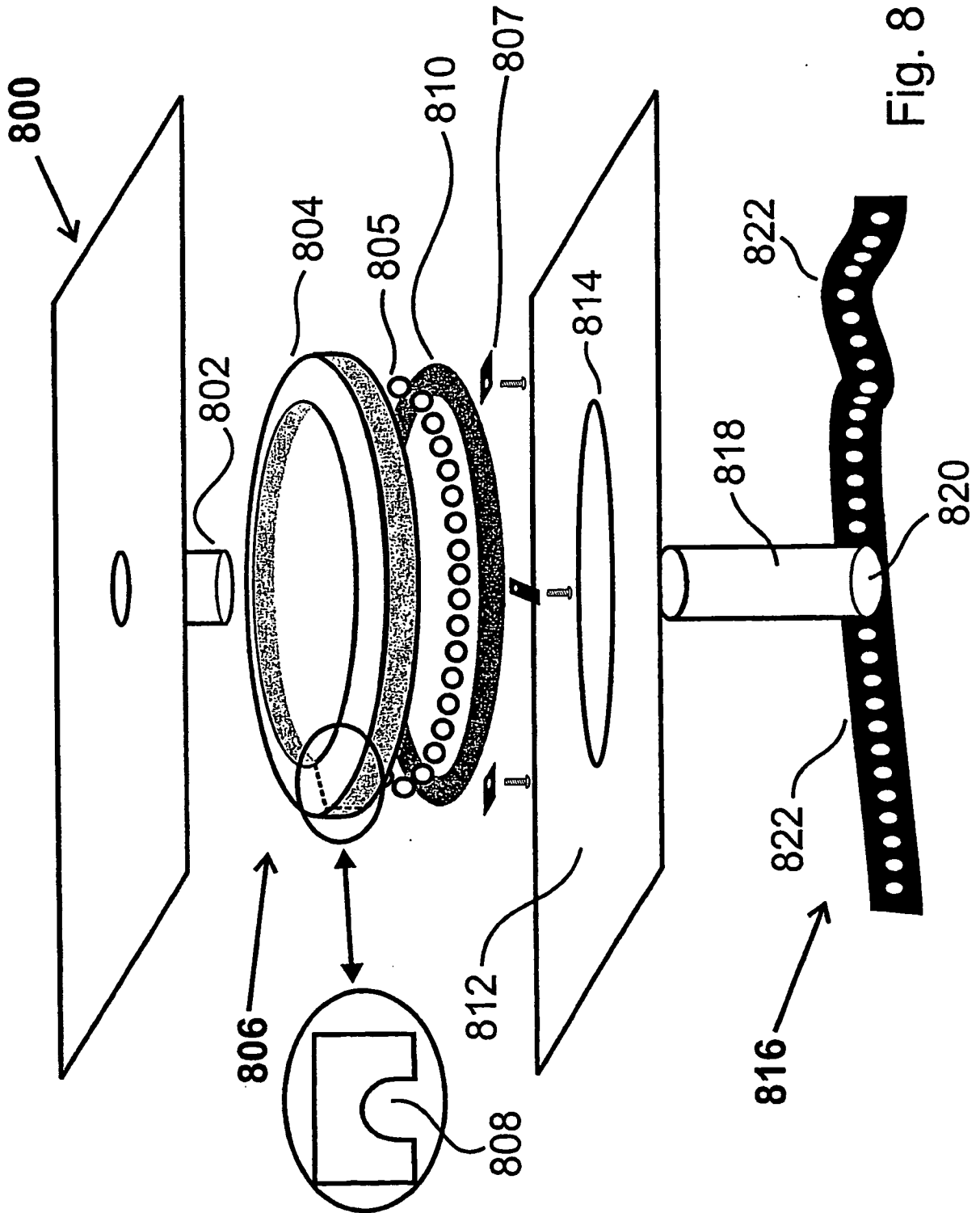


Fig. 8

**REFERENCES CITED IN THE DESCRIPTION**

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**Patent documents cited in the description**

- US 6062224 A [0003] [0004] [0007]
- US 5816256 A [0004] [0007]
- US 4696309 A [0008]

专利名称(译)	用于药代动力学和生理学研究的便携式取样或测试装置和方法		
公开(公告)号	<a href="#">EP1793888A4</a>	公开(公告)日	2009-08-19
申请号	EP2005817257	申请日	2005-08-09
[标]申请(专利权)人(译)	生物分析SYST		
申请(专利权)人(译)	生物分析系统公司		
当前申请(专利权)人(译)	生物分析系统公司		
[标]发明人	KISSINGER CANDICE B		
发明人	KISSINGER, CANDICE, B.		
IPC分类号	A61M37/00 A61B5/00 A01K1/03		
CPC分类号	A61B5/1113 A61B5/15003 A61B5/150221 A61B5/150229 A61B5/150236 A61B5/150244 A61B5/150305 A61B5/150366 A61B5/150755 A61B5/150809 A61B5/150824 A61B5/150862 A61B5/150992 A61B5/153 A61B5/154 A61B5/157 A61B2503/045 A61B2503/40 A61B2560/0437		
优先权	10/914733 2004-08-09 US		
其他公开文献	EP1793888A2 EP1793888B1		
外部链接	<a href="#">Espacenet</a>		

摘要(译)

公开了一种用于药代动力学和生理学研究的便携式取样或测试装置以及使用该装置对静止或移动动物或人类测试对象进行测试的方法。该装置包括用于对自由移动的对象进行测试的装置，或者可以由技术人员移动以定位在固定对象上的装置，例如重症监护病房中的早产儿或无意识的人类对象。该设备的设计和尺寸适合移动。在一个实施例中，该装置包括轮式推车，该轮式推车可由可操作地连接到其上的人体测试对象移动。在另一个实施例中，该装置包括位于动物上方的带轮托架，该托架磨损连接到该装置的吊索。该设备可以包括不间断电源。该方法提供对体液采样或从测试对象获取生理读数。该方法提供了在有或没有将取出的体液重新引入自由移动的对象中的情况下去除体液。

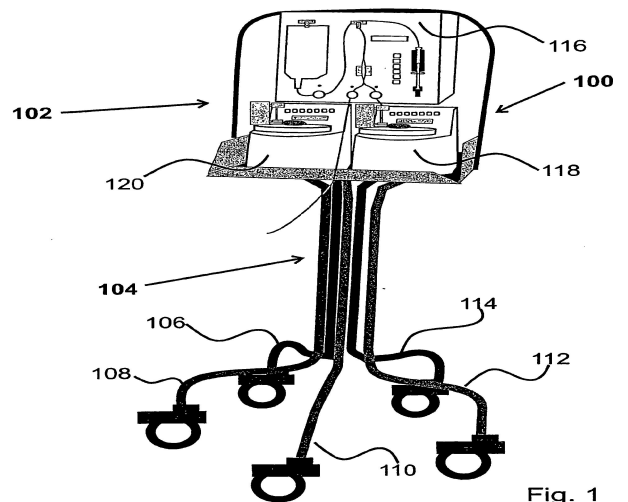


Fig. 1