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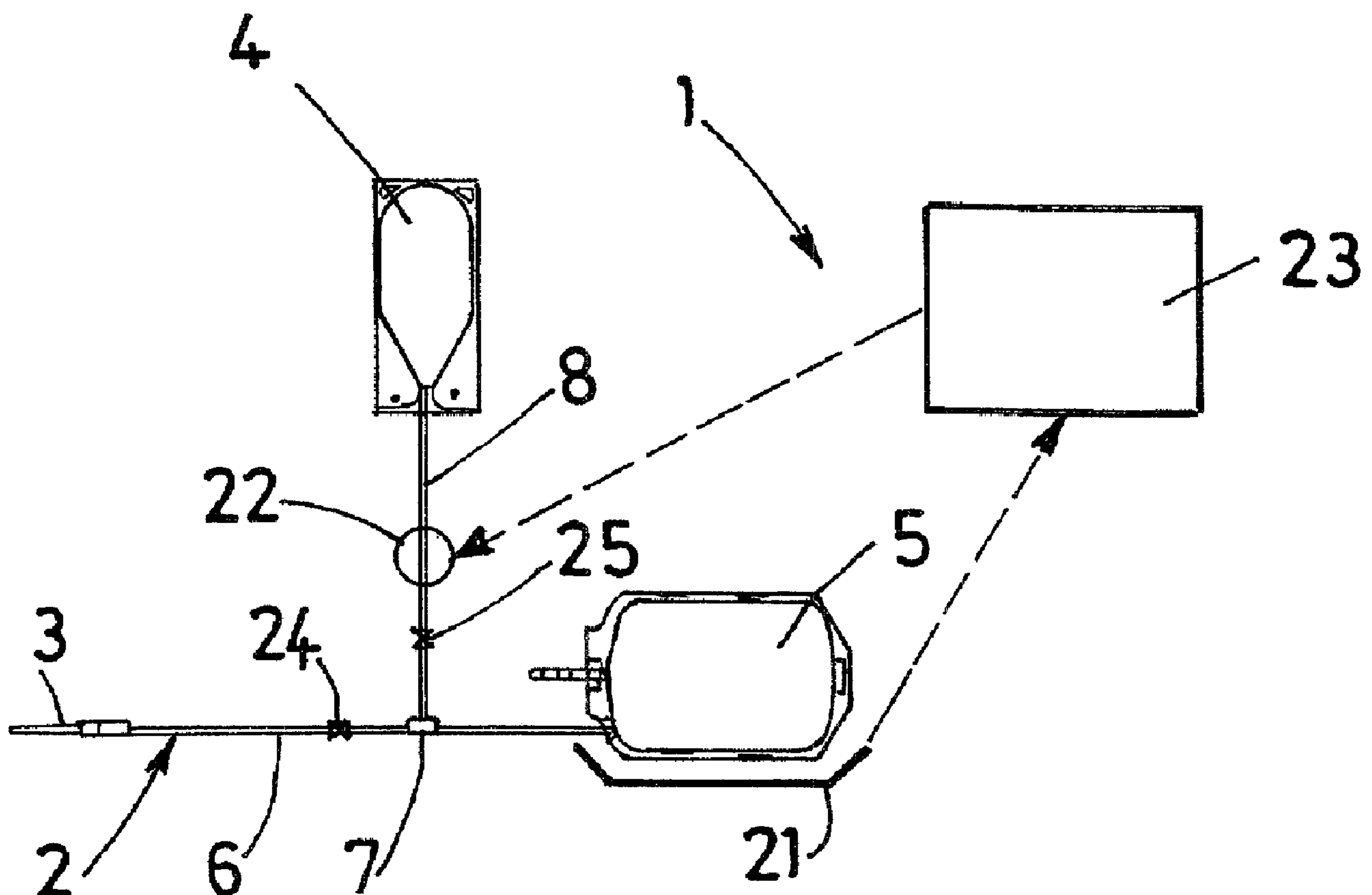
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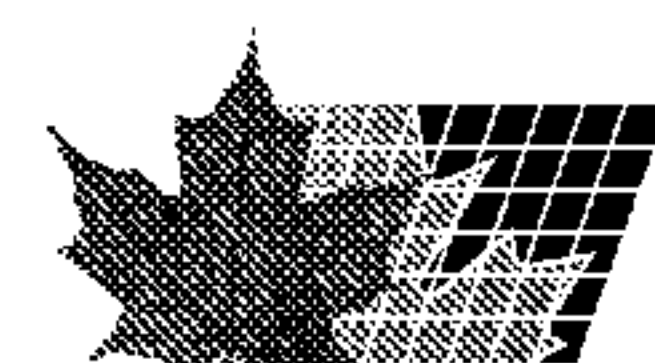
(54) Titre : METHODE ET DISPOSITIF D'ECHANTILLONNAGE D'UN LIQUIDE BIOLOGIQUE AUQUEL UNE SOLUTION
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(54) Title: A METHOD AND MACHINE FOR TAKING BIOLOGICAL FLUID TO WHICH A SOLUTION IS ADDED IN
ACCORDANCE WITH A DESIRED RATIO



(57) Abrégé/Abstract:

The invention concerns a method of taking a biological fluid, in particular blood, with an anticoagulant and/or preservation solution added, in which the biological fluid is taken by natural flow and the anticoagulant and/or preservation solution is added by pumping,



(57) **Abrégé(suite)/Abstract(continued):**

the said method making provision for measuring the flow of fluid taken and slaving the pumping speed to the measured flow, so as to obtain continuously during sampling a given ratio between the quantity of fluid taken and the quantity of anticoagulant and/or preservation solution added.

The invention also concerns the sampling machine (1) and the bag system (2) for implementing the said method.

ABSTRACT

**A method and machine for taking biological fluid to which a solution is
added in accordance with a desired ratio**

5 The invention concerns a method of taking a biological fluid, in particular blood,
with an anticoagulant and/or preservation solution added, in which the biological
fluid is taken by natural flow and the anticoagulant and/or preservation solution is
added by pumping, the said method making provision for measuring the flow of
fluid taken and slaving the pumping speed to the measured flow, so as to obtain
10 continuously during sampling a given ratio between the quantity of fluid taken and
the quantity of anticoagulant and/or preservation solution added.

The invention also concerns the sampling machine (1) and the bag system (2) for
implementing the said method.

Figure 1.

**A METHOD AND MACHINE FOR TAKING BIOLOGICAL FLUID TO WHICH A SOLUTION IS
ADDED IN ACCORDANCE WITH A DESIRED RATIO**

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The invention concerns a method of taking a biological fluid with an anticoagulant and/or preservation solution added, a sampling machine for implementing this method and a bag system for taking a biological fluid by means of such a machine.

5 It applies typically to the case where the biological fluid is whole blood which is to be taken from a donor in a collecting bag. This is because it is recommended that the blood be taken in a sterile fashion and have an anticoagulant and/or preservation solution added at the time of sampling so as to allow its subsequent use and the best sanitary safety conditions.

10 To do this, it is known, prior to the sampling, how to fill the collecting bag with the anticoagulant and/or preservation solution and then to fill the collecting bag with fluid during sampling.

One of the problems which is then posed is that, in order to attempt to produce a homogeneous mixture between the fluid and the solution contained in the bag, it
15 is necessary to stir the collecting bag, which complicates the sampling process and does not entirely give satisfaction.

Another problem which is posed concerns the obtaining of a given ratio between the quantity of fluid taken and the quantity of anticoagulant and/or preservation solution added. This is because, in particular in the field of sampling blood, the
20 quantity of anticoagulant and/or preservation fluid present in the collecting bag is fixed at a certain value so that the blood can be used in the medical field.

And, when the anticoagulant and/or preservation solution is present in the collecting bag prior to the sampling, the ratio is correct only for a given quantity of fluid taken. However, this ratio is considerably higher at the start of the sampling
25 or when the sampling is interrupted before the entire quantity of fluid required is taken. In the case of blood, there may result a reduction in the quality of the blood by lysis of the red corpuscles and deterioration of the functionality of the platelets, or even an impossibility of using the blood taken.

To resolve this problem, it has been proposed, in particular through the
30 documents FR-2 808 693 and US-6 113 554, to place the anticoagulant and/or

preservation solution in a bag separate from the collecting bag and to supply the collecting bag with solution simultaneously with the sampling of the fluid.

These solutions do not give satisfaction entirely, in particular on two levels.

5 The first problem concerns the obtaining of the ratio between the quantity of fluid taken and the quantity of anticoagulant and/or preservation solution added. This is because, in these documents, the ratio is obtained either by using a specific bag system or by using a complex pump structure, which complicates their use and substantially increases the cost of sampling.

10 The second problem relates to the pumping of the fluid which, by imposing a flow of fluid taken, is necessary for obtaining the ratio. This is because, for reasons of safety and in the case of the sampling of blood from a donor, it is then desirable to use a pressure sensor for the fluid upstream of the pump, in order to prevent any risk of collapse of the vein of the donor. This sensor, apart from its complexity and cost, may give rise to problems of asepsis if it is based on a
15 gaseous exchange between the inside and outside of the sampling system. In addition, the pumping is a source of discomfort and insecurity for the donor.

The invention aims to resolve all these problems by proposing in particular a sampling method which is particularly simple to implement, which is comfortable and safe for the donor and which makes it possible to obtain continuously during
20 the sampling a given ratio between the quantity of fluid taken and the quantity of anticoagulant and/or preservation solution added.

To this end, and according to a first aspect, the invention concerns a method of taking a biological fluid, in particular blood, with an anticoagulant and/or preservation solution added, in which the biological fluid is taken by natural flow
25 and the anticoagulant and/or preservation fluid is added by pumping, the said method making provision for measuring the flow of fluid taken and slaving the pumping speed to the measured flow rate, so as to obtain continuously during the sampling a given ratio between the quantity of fluid taken and the quantity of anticoagulant and/or preservation solution added.

30 According to one embodiment, the measurement of the flow of fluid taken is made

by calculating the variation in weight of the fluid taken, and the pumping of the anticoagulant and/or preservation solution is carried out by means of a peristaltic pump whose speed of rotation is variable according to the flow rate measured.

According to a second aspect, the invention concerns a sampling machine for
5 implementing the method according to the invention, comprising a device for measuring the flow of fluid taken and a device for pumping the anticoagulant and/or preservation solution, the said pumping device comprising a means of slaving the pumping speed according to the value of the flow of fluid issuing from the measuring device.

10 According to one embodiment, the measuring device comprises a means of measuring the weight and calculating the variation in the weight of fluid taken, and the pumping device comprises a peristaltic pump with a single head which is able to move in rotation at variable speeds.

According to a third aspect, the invention concerns a bag system for taking a
15 biological fluid by means of a machine according to the invention, the said system comprising, in closed circuit, means of taking the fluid, a bag containing an anticoagulant and/or preservation solution for the fluid taken, and a collecting bag intended to receive the fluid taken with the anticoagulant and/or preservation solution added. The collecting bag is in fluid communication with the sampling
20 means by means of a first flexible tube and with the bag containing the anticoagulant and/or preservation solution by means of a second flexible tube.

According to one embodiment, the bag system may have no means for measuring the pressure within the said system.

Other objects and advantages of the invention will emerge during the description
25 which follows with reference to the accompanying drawings.

In one aspect, the present invention relates to a machine for sampling a biological fluid, in particular blood, with an added anticoagulant and/or preservative solution, comprising a device for measuring the flow of sampled fluid and a device for pumping the anticoagulant and/or preservative solution, said pumping device comprising means
30 for adjusting the pumping speed according to the value of the flow of fluid coming from

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the measuring device, wherein said machine lacks means for pumping the biological fluid, which is sampled by natural discharge.

In another aspect, the present invention related to a system of bags for sampling a biological fluid by means of the machine as defined above, said system comprising, in a
5 closed circuit, means for sampling the fluid, a bag containing an anticoagulant and/or preservative solution for the sampled fluid, and a receiving bag designed to receive the sampled fluid with the added anticoagulant and/or preservative solution, wherein the receiving bag is in fluidic communication with the sampling means by means of a first flexible tube and with the bag containing the anticoagulant and/or preservative solution
10 by means of a second flexible tube, wherein in said system at least the part of the second tube designed to be squeezed by the head of the peristaltic pump has a hardness that is less than that of the first tube.

Figure 1 depicts schematically the functioning of a sampling machine according to a first embodiment of the invention, in which a bag system is disposed.

15 Figure 2 depicts schematically the functioning of a sampling machine according to a second embodiment of the invention, in which a bag system is disposed.

Figure 3 depicts schematically a bag system disposed on the placement device of a sampling machine according to the invention.

Figure 4a depicts a front perspective view of the sampling machine.

Figure 4b depicts a rear perspective view of the sampling machine.

5 Figure 5 depicts a flow diagram relating to the functioning of the sampling machine for obtaining the given ratio between the quantity of fluid taken and the quantity of anticoagulant and/or preservation solution added.

10 Figure 1 depicts a bag system 2 comprising means 3 of taking the fluid from a patient, at least one bag 4 containing an anticoagulant and/or preservation solution for the fluid taken, and at least one collecting bag 5 intended to receive the fluid taken with the anticoagulant and/or preservation solution added.

For example, the bag system 2 is sterilised and packaged in sterile packaging.

15 The sampling means 3 consist in particular of a needle 42 allowing access to the vein of the donor and a cap 43 protecting the needle 42. In addition, a needle protector 44 can be placed slidably on a first tube 6.

20 The collecting bag 5 is in fluid communication with the sampling means 3 by means of the first flexible tube 6. The bag 4 containing an anticoagulant and/or preservation solution is in fluid communication with the collecting bag 5 by means of a second flexible tube 8 connected at a connector 7 to the first tube 6. This connector is a three-way junction to which there are connected firstly a first part of the first tube 6 coming from the sampling means 3 and the second tube 8 and secondly a second part of the first tube 6 in the direction of the collecting bag 5.

25 According to one embodiment, the part of the first tube 6 included between the connector 7 and the collecting bag 5 is of sufficient length to obtain a homogeneous mixture between the fluid taken and the anticoagulant and/or preservation solution, when the mixture reaches the inlet orifice of the collecting bag 5. The length of this part of the first tube 6 is appreciably greater than 15 cm, for example around 25 cm.

Figure 2 depicts a bag system 2 comprising, apart from the bag system depicted in Figure 1, a sampling bag 9 intended to receive the first millilitres of blood taken, and a lateral sampling device 10 associated with the said sampling bag 9 so as to allow the taking of samples by means of tubes under vacuum. The sampling bag 9 is in fluid communication with the collecting bag 5 by means of two flexible tubes 6, 11 connected at a connector 12 in the form of a three-way junction.

The filling of the sampling bag 9 and collecting bag 5 results from natural flow, that is to say gravity and the venous pressure of the donor. A natural flow based on venous pressure and gravity offers a superior comfort and safety to the donor.

Clamps 13, 14 can be situated respectively on the first flexible tube 6, downstream of the connector 12, and on the flexible tube 11. The said clamps 13, 14 make it possible to orient to the sampling bag 9 the first millilitres of fluid taken, the clamp 13 is then closed whilst the clamp 14 is open. When the sampling bag 9 is full, the clamp 14 is closed and the clamp 13 is opened so as to orient the fluid taken to the collecting bag 5.

Circuit openers can be provided at the connector 12 and at the inlet and outlet orifices of the bags containing blood or blood components. A circuit opener 41 is in particular disposed on the second tube, at its end in fluid communication with the bag 4 containing the anticoagulant and/or preservation solution, in order to prevent the anticoagulant and/or preservation solution going back during sterilisation of the system, in particular by steam.

Moreover, it is preferable for the circuit opener not to be situated on the passage of flow of the blood lying between the sampling means 3 and the collecting bag 5 in order to prevent any risk of haemolysis of the blood taken at the time of taking.

In order to perform the steps of filtration and separation of the various constituents of the blood, the collecting bag 5 can be in fluid communication, by means of a fourth flexible tube 15, with a satellite bag 16. A leukocyte-removing filter 17 is situated between the collecting bag 5 and the satellite bag 16.

The satellite bag 16 can be in fluid communication with one or more other satellite bags, for example the satellite bag 16 can be in fluid communication with two

other satellite bags 18, 19.

A clamp 20 can be provided on the flexible tube 15 between the collecting bag 5 and the leukocyte-removing filter 17.

5 The bag system described above is intended to be disposed in the placement device of a sampling machine as depicted in Figures 4a and 4b.

Figure 4a is a perspective view of the front face of the sampling machine 1. It comprises the weighing device 21, of sufficiently large size to accept a bag system 2 as described above.

10 The sampling machine also comprises a pumping device 22 comprising a peristaltic pump with a single head which is able to move in rotation at variable speeds in order to pump the anticoagulant and/or preservation solution, the taking of the fluid resulting from natural flow, that is to say gravity and the venous pressure of the donor. Thus the bag system 2 may have no means for measuring the pressure within the said system.

15 Depicted in Figures 1 and 2, the weighing device 21 makes it possible to know instantaneously the weight and the variations in weight of the fluid taken and thus the flow of fluid taken. For this purpose the whole of the bag system 2 as depicted in Figures 2 and 3 is placed on this weighing device 21, the tare weight is weighed by the weighing device 21 after the placement of the bag system 2, in
20 order to take account of the weight of the said bag system 2 before sampling. After a negligible short period (corresponding to the circulation of the solution in the tubes 6, 8), the variations in weight determined by the weighing device 21 are thus uniquely correlated with the flow of fluid taken. This is because the anticoagulant passes from the bag 4 containing the anticoagulant and/or
25 preservation solution to the collecting bag 5, these two bags 4, 5 being on the weighing device 21, and the circulation of the solution does not give rise to any variations in weight.

30 The peristaltic pump 22 comprises a squashing head around which there is disposed part of the second flexible tube 8, making it possible to slave the flow of the solution with respect to the calculation of the variations in weight of the fluid

taken, by means of control electronics for the motor of the pump 23.

The control electronics 23 transcribe the calculations of variations in weight into flow of fluid taken, by means of a calculation taking account of the density of the fluid taken. The control electronics 23 then determine the flow of the anticoagulant and/or preservation solution to be fixed, according to the ratio determined, and adjust the speed of rotation of the peristaltic pump 22 in order, according to this flow determined, to supply the collecting bag 5 with a anticoagulant and/or preservation solution.

According to an embodiment depicted in Figure 1, it can also be envisaged placing the whole of the bag system except for the bag 4 containing the anticoagulant and/or preservation solution on the weighing device 21, as depicted in Figure 1, but it is then necessary to take account, in addition to the tare weighing normally carried out, of a constant which is the variation in weight related to the introduction of anticoagulant and/or preservation solution into the collecting bag 5.

According to a particular embodiment of the invention, optical sensors can be added to the machine 1. A first optical sensor 24 can be placed on the first tube 6 between the sampling means 3 and the connector 7, preferably between the connectors 7 and 12. This sensor 24 detects the presence of blood, in order to verify that the blood is circulating suitably within the first tube 6. It also checks that there is no air or anticoagulant and/or preservation solution going back towards the sampling means 3, and therefore towards the donor. This optical sensor can for example be replaced or supplemented by an ultrasonic sensor for detecting flow reversals more finely.

A second optical sensor 25 can be placed on the second tube 8 between the head of the peristaltic pump 22 and the connector 7. This sensor 25 detects the presence of anticoagulant and/or preservation solution in order to check that the anticoagulant and/or preservation solution is circulating suitably within the second tube 8.

The machine 1 also comprises a placement device designed to receive the bag system 2 as depicted in Figure 3. The placement device comprises a groove 26

in which the user places the tubes 6, 8, a curved device 30 which can be provided for supporting the second tube 8 on the peristaltic pump 22 in order to allow correct functioning of the latter. The machine 1 also comprises an automatic clamp 39 and a cap 34 which protects and ensures optimum maintenance of the placement of the bag system in the groove 26 of the machine 1. The curved device 30 provided for supporting the second tube 8 on the peristaltic pump 22 moves away from the second tube 8 when the cap 34 is opened.

When the peristaltic pump 22 is in movement, the rollers of the pump head 22 successively compress the section of the second tube 8 against the curved device 30 so as to ensure the movement of the anticoagulant and/or preservation solution in the second tube.

The sampling machine 1 also comprises an interface 31 which is divided into two areas, a display 32 and a keyboard 33, as depicted in Figure 4a. The display 32 gives the user of the machine various information: it displays general information such as the date, time or the battery level; information concerning the current sampling, the number of the sample, the volume sampled, the duration of the sampling or the volume of blood required; as well as error messages when the flow of fluid taken is not correct or when the cap 34 of the machine 1 is not closed.

The keyboard 33 comprises a certain number of keys having various functions. The standby key 35 switches the sampling machine 1 on and off. The stop key 36 stops the sampling in the event of an emergency. The alarm light 37 comes on in order to warn the user of faulty functioning, for example when the flow of fluid being taken is not situated within the authorised range, the values of which are between 30 and 350 millilitres per minute, in particular between 50 and 250 millilitres per minute. The navigation keys 38 enable the user to navigate in the various menus offered by the machine 1, the principal menus being the modification of the parameters, the performance of a self-test and the carrying out of sampling.

The machine 1 can also comprise connectors provided at the area 40 for inputting and outputting data to a printer, a barcode reader or a microcomputer, as

depicted in Figure 4b.

The placing of the bag system 2 in the placement device of the machine 1, as depicted in Figure 3, can be facilitated by the formation of a loop, when the said system is manufactured, associating the first tube 6 and the second tube 8, using an association means 27. This association means consists of a straight connector 28 in the form of a cylindrical housing in which the second tube 8 is inserted, and a lateral clip 29 in the form of a U in which the tube 6 is clipped, thus allowing fixing of the first tube 6 and the second tube 8.

In order to fix the two tubes 6 and 8 to each other, the assembly of the tubes and association means 27 is carried out for example by solvent bonding.

The loop thus formed facilitates the positioning of the bag system on the sampling machine 1 and serves as a foolproof locating device, since because of this it can be positioned only in one direction in the placement device.

This loop also prevents the driving of the second tube 8 by the peristaltic pump 22 since the association means 27 and the three-way junction 7 are locked in housings provided for this purpose in the groove 26 of the sampling machine 1, when the straight connector is integrated in the second tube 8 and the two tubes 6 and 8 are attached to each other. When a tube is driven by the rotation of the peristaltic pump, the circulation of the fluid within this tube is interfered with. The immobilisation of the second tube 8 therefore allows optimum functioning of the peristaltic pump 22.

According to one embodiment, the part of the second tube 8 which is situated between the connector 7 and the association means 26 has appropriate physical characteristics so as to correctly control the flow created by the said peristaltic pump 22.

For example, the part of the second tube 8 forming the loop can have a hardness less than that of the first tube 6. In particular, the second tube 8 has a hardness of between 60 and 70 Shore A, in particular 65 Shore A. The other tubes have a hardness greater than 70 Shore A, in particular 78.

Figure 5 is a flow diagram relating to the functioning of the sampling machine for

obtaining the desired ratio between the quantity of blood taken and the quantity of anticoagulant and/or preservation solution added.

A sampling sequence carried out according to the method of the invention and using the sampling machine 1 will now be described.

5 To start up the sampling machine 1, the user presses the standby key 35. Using the navigation keys 38, the user next chooses the main menu relating to the performance of a sampling. The display 32 indicates that it is possible to proceed with the installation of the bag system 2. Then the user closes the cover 34. By means of the information collected by the sensors 24, 25, the display 32 states
10 whether the bag system 2 is correctly placed.

Before starting the sampling proper, the machine 1 performs a step of initialising the sampling (A).

The machine 1 makes the anticoagulant solution circulate as far as the connector 7, and this makes it possible to take blood without the risk of coagulation. The
15 sensor 25 detects the presence of an anticoagulant and/or preservation solution in order to check whether this has reached the connector 7. It is possible to cause the peristaltic pump 22 to make at least one additional rotation after the sensor 25 has detected the presence of the solution, so that the anticoagulant and/or preservation solution is present within the first tube 6 before the blood
20 circulates therein.

During this step (A), the user introduces the sampling means 3 into the vein of the donor and then proceeds with the taking of samples by means of the lateral sampling device 10 associated with the sampling bag 9 and clamps 13, 14.

25 When this step (A) is correctly performed, the display 32 indicates that the sampling can be initiated.

The step of initiating the sampling (B) commences with the opening of the automatic clamp 39, when the user presses on the corresponding navigation key 38.

The blood detection step (C) is performed by means of the optical sensor 24.

This optical sensor 24 detects the presence of blood in order to check that the blood is present in the first tube 6 level with this sensor 24. It is thus possible to estimate that the fluid is circulating suitably within the first tube 6.

As from step (D), the machine 1 uses the weighing device 21, the peristaltic pump 22 and the control electronics 23 in order to obtain a desired ratio between the quantity of blood taken and the quantity of anticoagulant and/or preservation solution added.

The step of calculating the variation in weight (D) is performed by the weighing device 21. Step (E) of calculating the flow of blood is performed using the results obtained during step (D). Steps (F) and (G) concern respectively the adjustment of the speed of rotation of the peristaltic pump 22 and the verification of the value of the flow of blood. Concerning the adjustment of the speed of the peristaltic pump 22, the control electronics 23 calculate, from the blood flow obtained at step (E), the flow of anticoagulant to be obtained. In particular, the ratio between the quantity of anticoagulant and/or preservation solution and that of blood can be fixed at 1/7. The control electronics 23 next transcribe this flow of anticoagulant into a certain speed of rotation of the peristaltic pump 22. The frequency of adjustment of the speed of rotation of the peristaltic pump 22 is such that the period between two adjustments is less than one second, more particularly around a tenth of a second.

Step (H) concerning the obtaining of the programmed volume of blood is performed by the weighing device 21. The programmed volume corresponds to a certain weight, and when the weighing device 21 measures this weight, the sampling stops. As long as this weight is not attained, the machine 1 continues the loop consisting of steps (D) to (G).

Step I marks the end of the sampling.

The volume of blood taken is variable according to the geographic area. One advantage of the device according to the invention is that it is possible to choose the volume of blood taken at the time of collection, and that it is not necessary to provide different bag systems containing different volumes of anticoagulant. Moreover, should the user have to interrupt the sampling before the programmed

end of the sampling, by pressing on the stop key 36, the blood is usable since the ratio between the quantity of blood taken and the quantity of anticoagulant and/or preservation solution is correct throughout the sampling.

CLAIMS

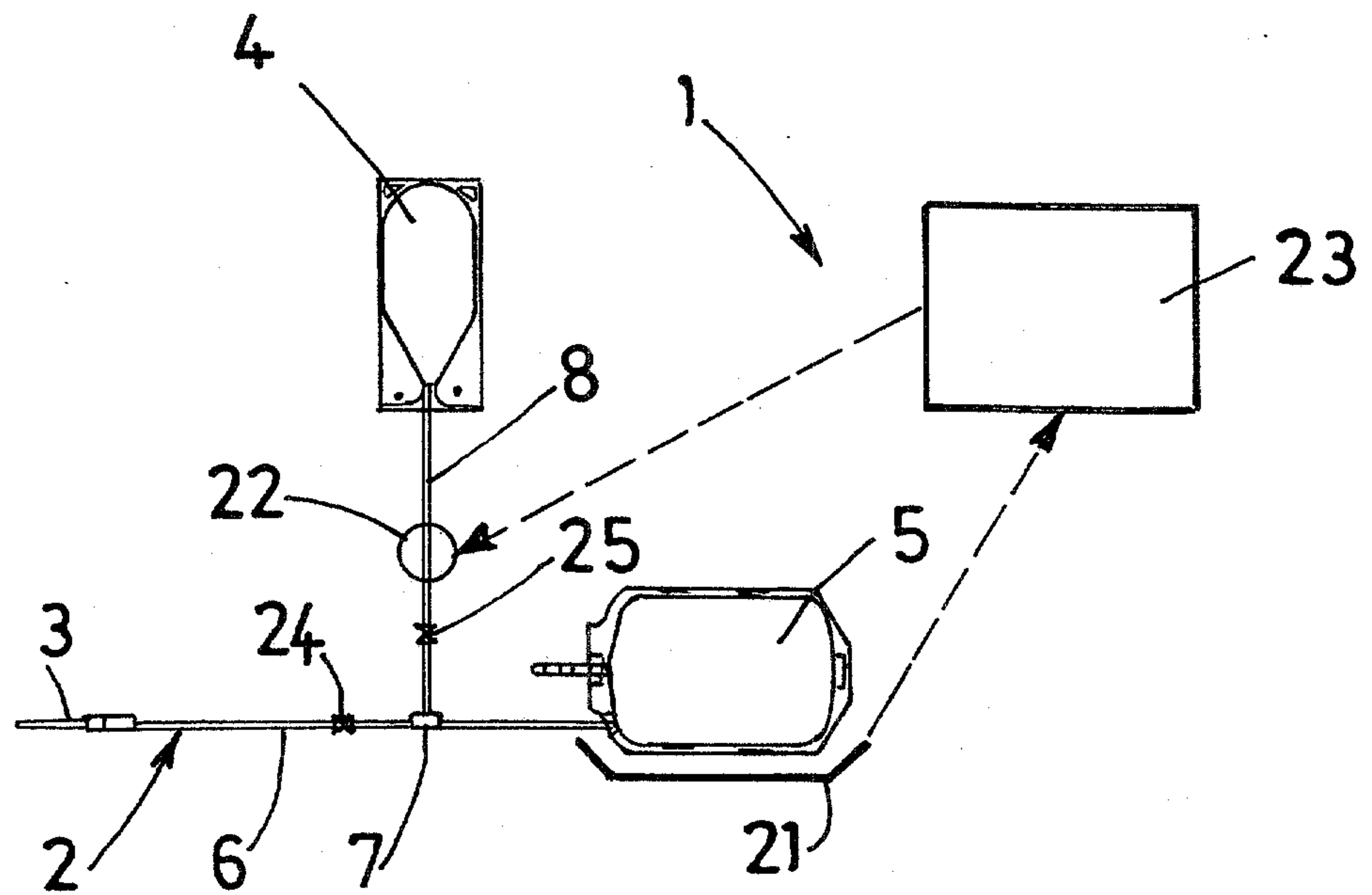
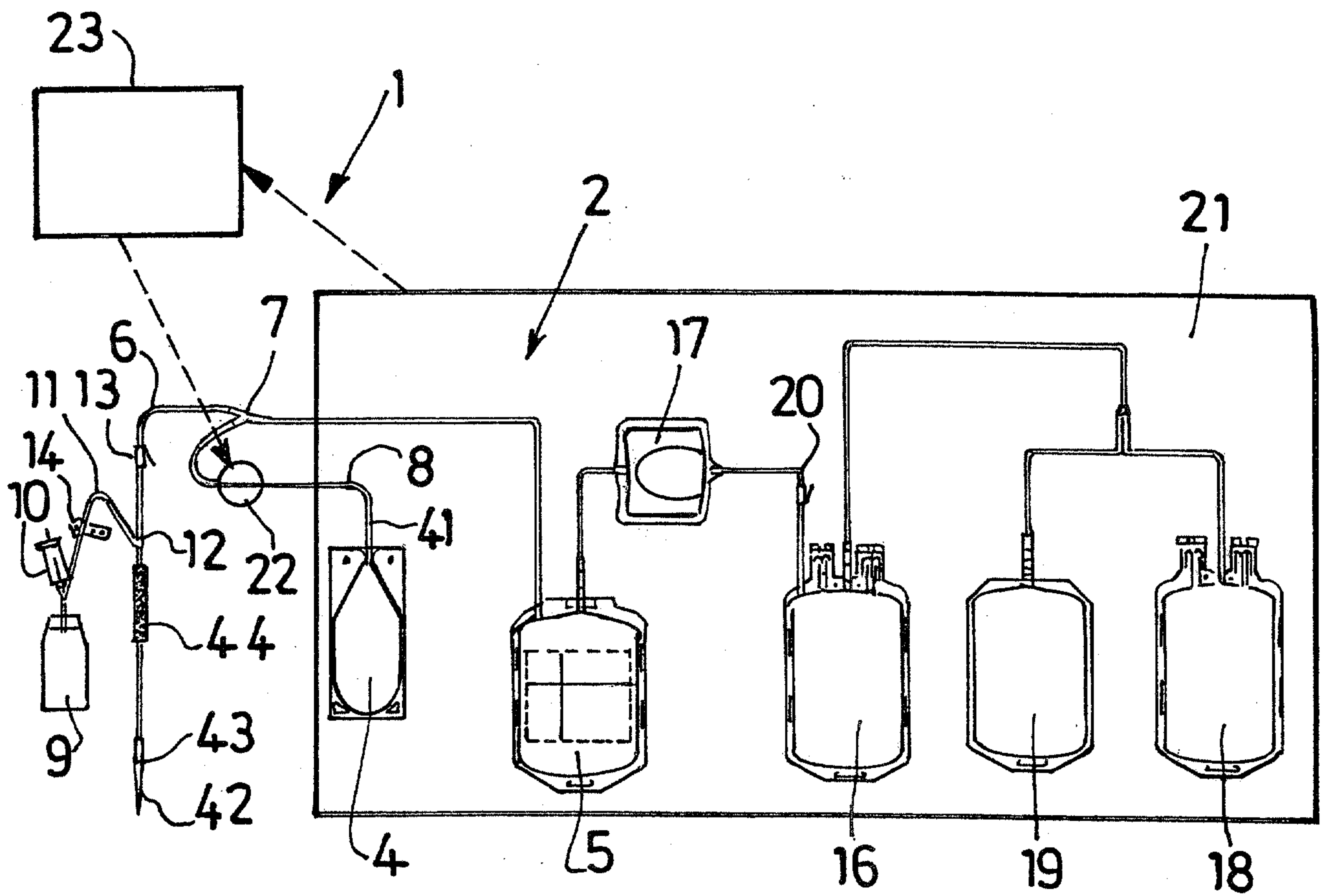
1. Machine for sampling a biological fluid, in particular blood, with an added anticoagulant and/or preservative solution, comprising a device for measuring the flow of sampled fluid and a device for pumping the anticoagulant and/or preservative solution,
5 said pumping device comprising means for adjusting the pumping speed according to the value of the flow of fluid coming from the measuring device, wherein said machine lacks means for pumping the biological fluid, which is sampled by natural discharge.
2. Machine according to claim 1, wherein the measurement device comprises means for measuring the weight and calculating the variation in the weight of the
10 sampled fluid.
3. Machine according to claim 1 or 2, wherein the pumping device comprises a peristaltic pump with a single head, which is rotatingly mobile at variable speeds.
4. System of bags for sampling a biological fluid by means of the machine according to claim 3, said system comprising, in a closed circuit, means for sampling the fluid, a
15 bag containing an anticoagulant and/or preservative solution for the sampled fluid, and a receiving bag designed to receive the sampled fluid with the added anticoagulant and/or preservative solution, wherein the receiving bag is in fluidic communication with the sampling means by means of a first flexible tube and with the bag containing the anticoagulant and/or preservative solution by means of a second flexible tube, wherein
20 in said system at least the part of the second tube designed to be squeezed by the head of the peristaltic pump has a hardness that is less than that of the first tube.
5. System according to claim 4, wherein said system lacks means for measuring the pressure inside said system.
6. System according to claim 4 or 5, wherein the second tube is equipped with a
25 circuit opener arranged near its end in fluidic communication with the bag containing the anticoagulant and/or preservative solution.
7. System according to any one of claims 4 to 6, wherein the second tube is connected to the first tube by means of a connector.
8. System according to claim 7, wherein the length of the first tube measured
30 between the connector and the intake orifice of the receiving bag is greater than 15 cm.

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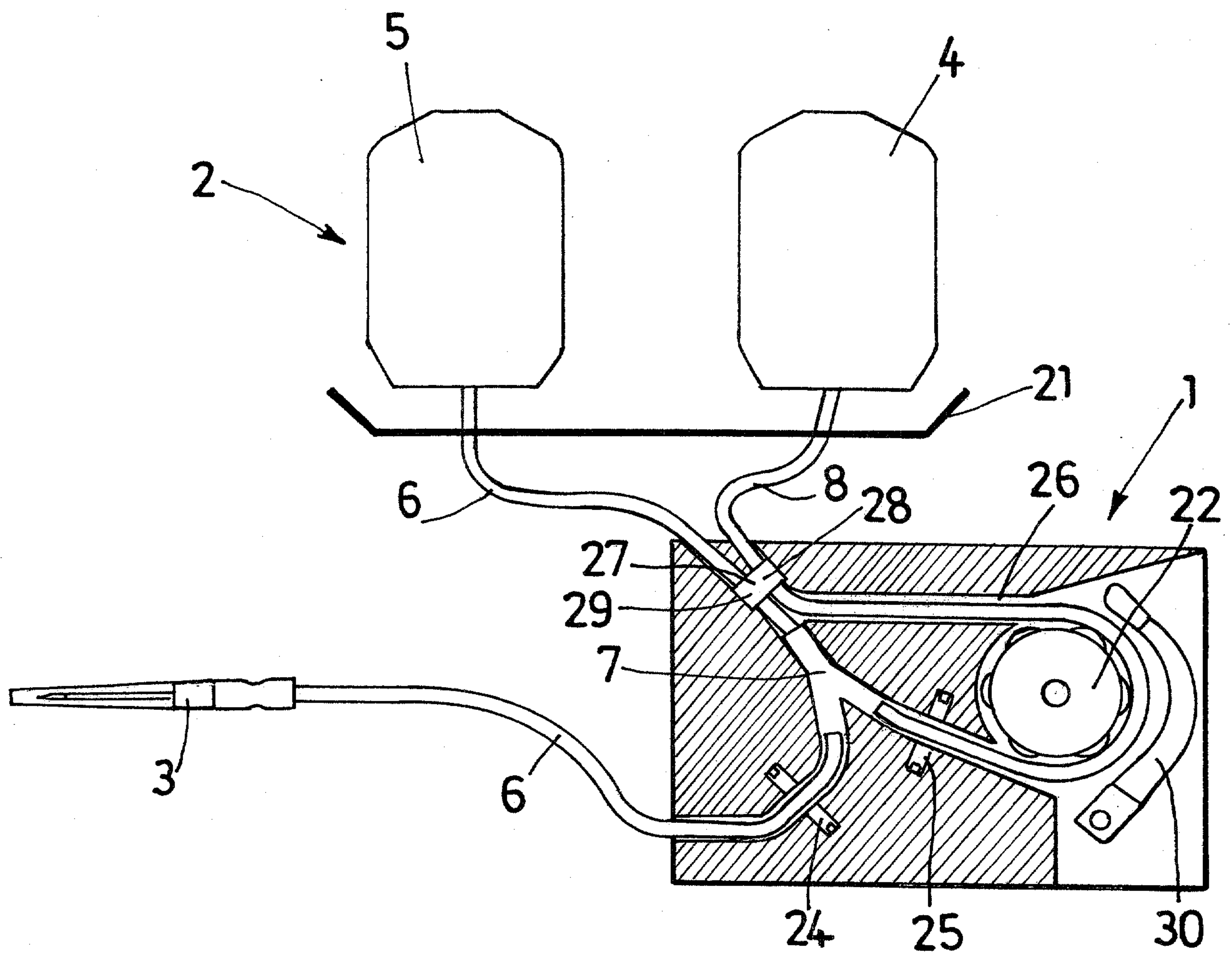
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9. System according to claim 7, wherein the length of the first tube measured between the connector and the intake orifice of the receiving bag is around 25cm.

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FIG. 1FIG. 2

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FIG.3

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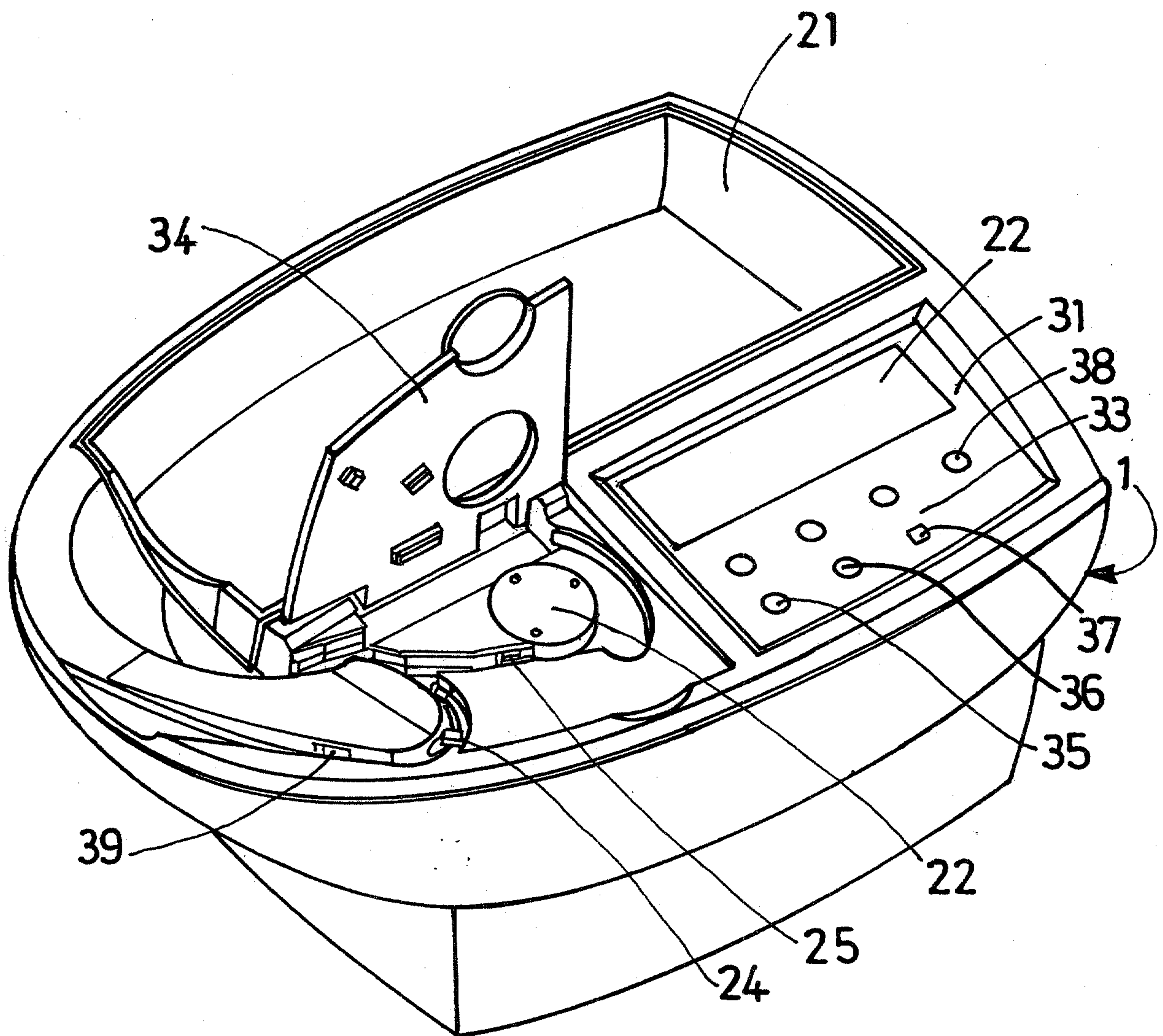


FIG.4a

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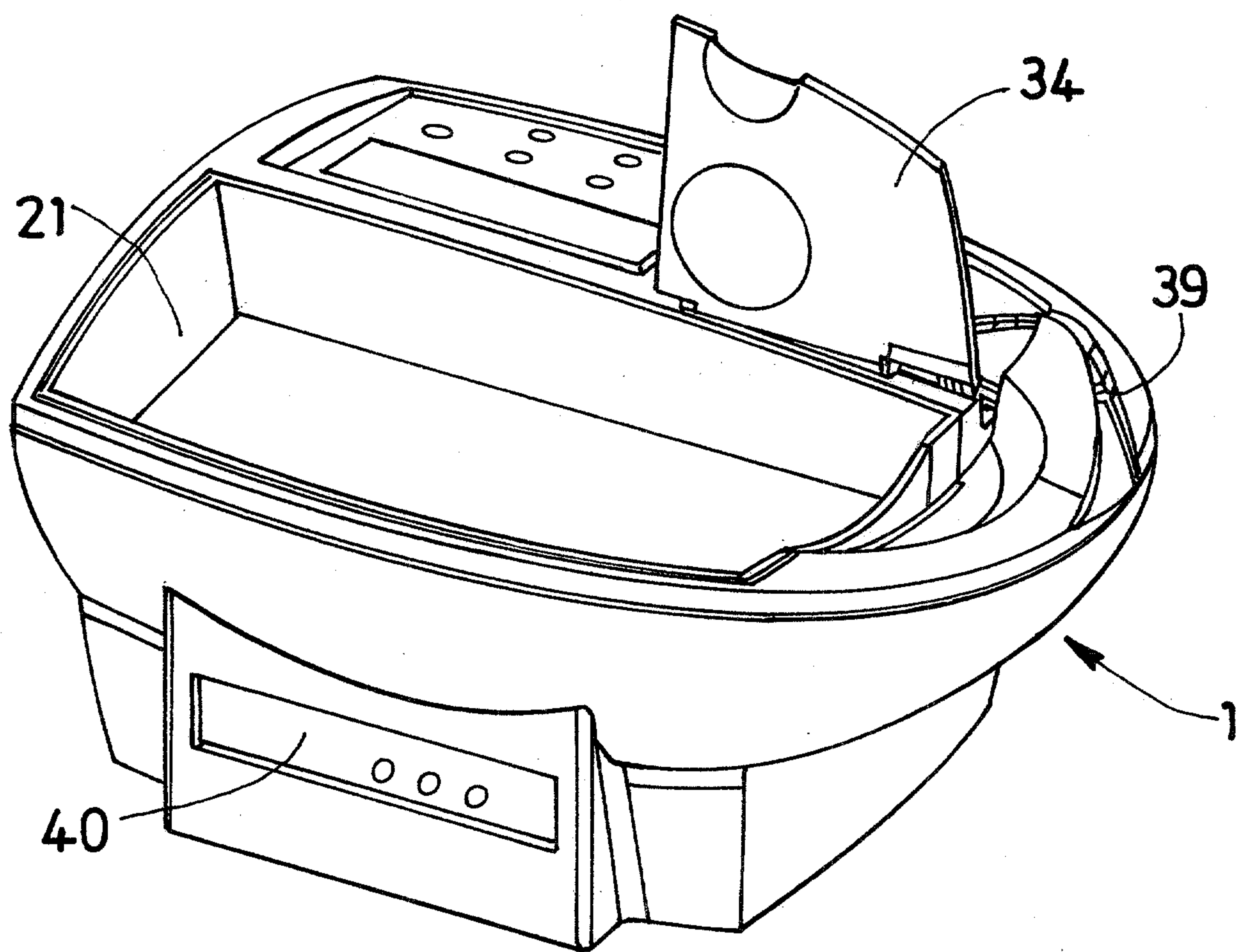
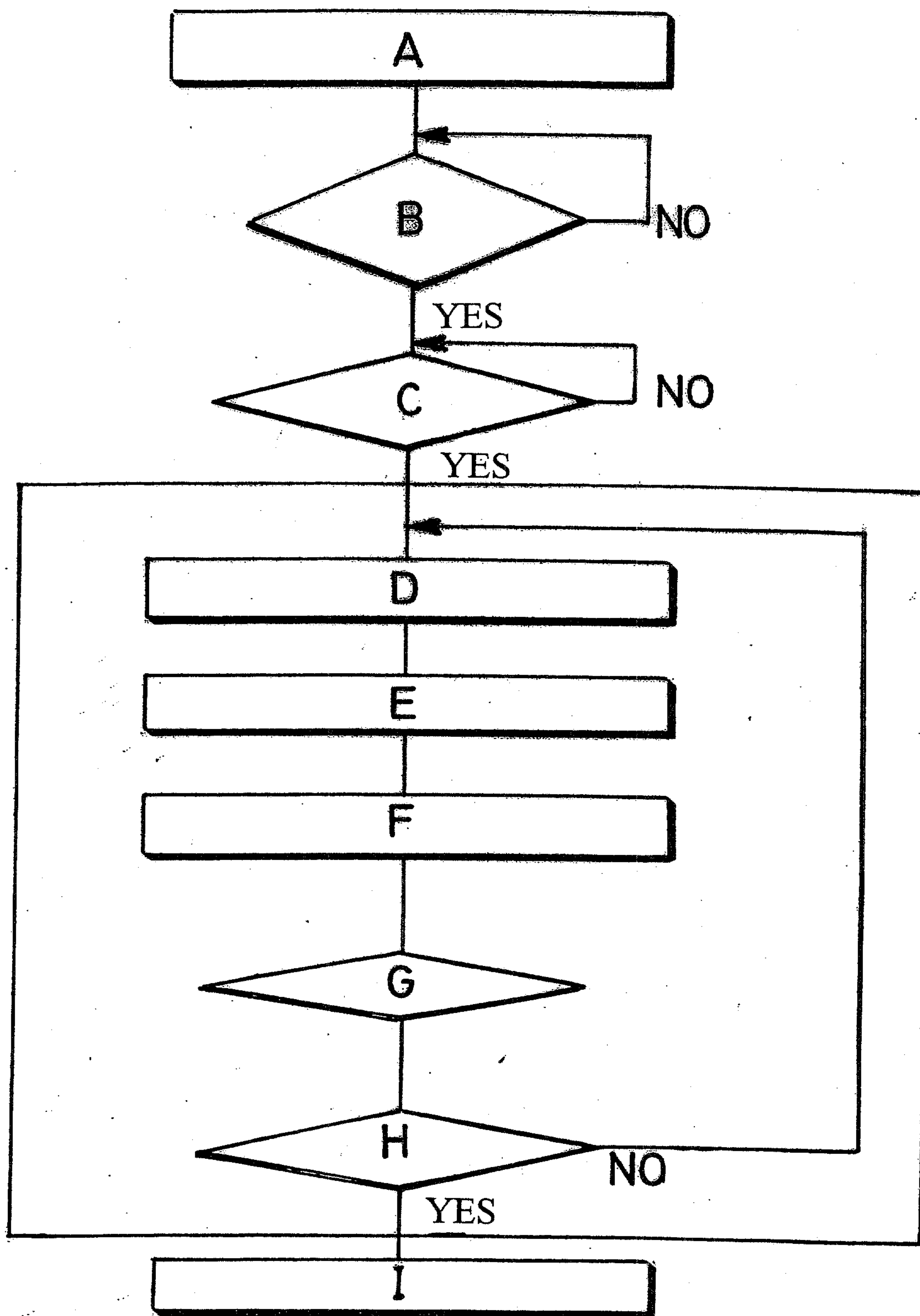


FIG. 4b

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FIG. 5

