Office de la Propriété Intellectuelle du Canada
Un organisme d'Industrie Canada

Canadian Intellectual Property Office
An agency of Industry Canada

CA 2582170 C 2010/09/21

(11)(21) 2 582 170

(12) BREVET CANADIEN
CANADIAN PATENT

(13) C

(22) Date de dépôt/Filing Date: 1999/03/19

(41) Mise à la disp. pub./Open to Public Insp.: 1999/09/23

(45) Date de délivrance/Issue Date: 2010/09/21

(62) Demande originale/Original Application: 2 327 665

(30) Priorités/Priorities: 1998/03/20 (US60/078,848);
1998/04/29 (US60/083,484)

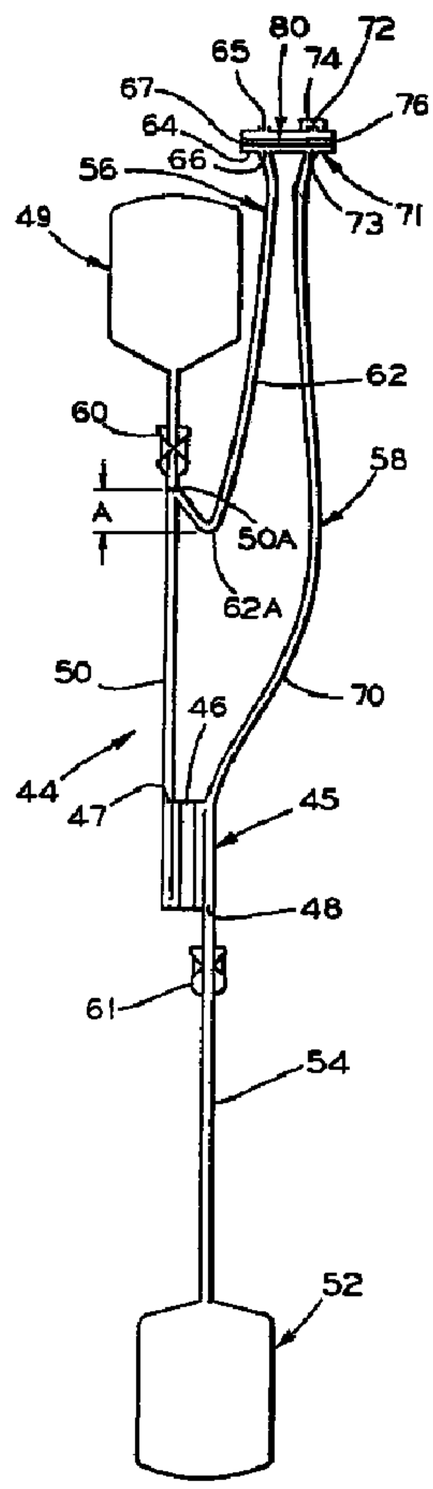
(51) Cl.Int./Int.Cl. *B01D 35/02* (2006.01),
A61M 1/00 (2006.01), *A61M 1/36* (2006.01),
B01D 35/01 (2006.01), *B01D 35/30* (2006.01)

(72) Inventeurs/Inventors:
ZIA, MAJID, US;
KHAMIS, CHAOUKI A., US

(73) Propriétaire/Owner:
HEMERUS MEDICAL, LLC, US

(74) Agent: BERESKIN & PARR LLP/S.E.N.C.R.L.,S.R.L.

(54) Titre : PROCEDE ET APPAREIL DE FILTRATION D'UN FLUIDE BIOLOGIQUE
(54) Title: BIOLOGICAL FLUID FILTRATION METHOD AND APPARATUS



(57) Abrégé/Abstract:
A biological fluid processing or fluid filtration system is provided having novel open and closed loop processing systems (44) wherein the gases transferred into and out of the system (55) during processing pass through a porous medium (67) in upstream

CA 2582170 C 2010/09/21

(11)(21) 2 582 170

(13) C

(57) Abrégé(suite)/Abstract(continued):
and/or downstream gas inlet or outlet housings or vents (64, 71) in a manner which precludes the fluid being processed or filtered from ever contacting the housings or vents (64, 71). Each housing or vent (64, 71) is separated from the fluid by a column of gas in its respective transfer line (50, 54). The upstream gas inlet housing or vent (64) is in communication with the unfiltered biological fluid, and the downstream gas inlet housing or vent (71) is in communication with the filtered biological fluid.

ABSTRACT

A biological fluid processing or fluid filtration system is provided having novel open and closed loop processing systems (44) wherein the gases transferred into and out of the system (55) during processing pass through a porous medium (67) in upstream and/or downstream gas inlet or outlet housings or vents (64, 71) in a manner which precludes the fluid being processed or filtered from ever contacting the housings or vents (64, 71). Each housing or vent (64, 71) is separated from the fluid by a column of gas in its respective transfer line (50, 54). The upstream gas inlet housing or vent (64) is in communication with the unfiltered biological fluid, and the downstream gas inlet housing or vent (71) is in communication with the filtered biological fluid.

TITLE

BIOLOGICAL FLUID FILTRATION METHOD AND APPARATUS

BACKGROUND OF THE INVENTION

1. Field of the Invention

The present invention relates to a method and apparatus for processing biological fluids into their therapeutically valuable components. More particularly, the present invention relates to a method and apparatus for processing donated blood into its therapeutically valuable components. Most particularly, the present invention relates to an improved method and apparatus for processing donated blood into its therapeutically valuable components which uses improved open-loop and closed-loop systems to substantially increase the recovery of all the blood products from the donated blood.

2. Discussion of the Related Art

Methods and apparatus for processing blood are well known in the prior art. U.S. Patent No. 3,892,236 to Djerassi shows an apparatus for the continuous withdrawal of blood from a human donor, forced extracorporeal circulation of blood of the donor with separation of granulocytes, and return by gravity of the leukocyte-poor whole blood to the donor.

U.S. Patent No. 5,126,054 to Matkovich shows a venting means for venting gas from the transfer line of a liquid delivery system comprising a housing, a first, liquid-wettable, microporous membrane carried in said housing so as to be in communication with the transfer line, and a second, non-liquid-wettable, gas permeable microporous membrane superimposed on said microporous membrane to the outward side of the housing. Gas in the delivery system is vented from the system so long as the

first microporous membrane remains unwetted by the delivery liquid.

U.S. Patent No. 5,451,321 to Matkovich shows biological fluid processing assemblies having a gas inlet, and/or a gas outlet.

While these devices are generally satisfactory, some of the methods and apparatus of the prior art leave a large amount of biological fluid trapped in various elements of the fluid processing apparatus. While the aforementioned patent 5,451,321 to Matkovich provides for liquid trapped in various elements of the blood processing system to be recovered either by causing a volume of gas behind the entrapped liquid to push the liquid through those elements and into the designated collection bag, or by pulling the entrapped liquid into the designated collection bag by a pressure differential (e.g. gravity head, pressure cuff, suction and the like), the system still has several drawbacks. One drawback is that they require one or more nonwettable, gas permeable, membranes. This requirement can lead to increased costs over wettable membranes.

Therefore, those skilled in the art continue to search for a method and apparatus to provide for optimal recovery of the biological fluid from biological fluid processing systems, cost reduction and ease of use, and have developed novel open and closed loop systems and methods associated therewith to achieve this goal.

SUMMARY OF THE INVENTION

The problems of the prior art are solved by the present invention utilizing novel open and closed loop biological fluid processing systems which all share the concept that the gases transferred into, out of, or within the biological fluid processing system have the transfer lines arranged or configured in a manner which precludes

the biological fluid from ever contacting the upstream and downstream gas inlet or outlet housings or vents, or bypassing the fluid filtration or leukocyte depletion device. Gases are transferred into and out of the biological fluid processing systems through a porous medium in the upstream and downstream gas inlet housings or vents. Each housing or vent is separated from, and in communication with the biological fluid by a column of gas in the transfer lines. The upstream gas inlet housing or vent is in communication with the unfiltered biological fluid and the downstream inlet or vent is in communication with the filtered biological fluid.

In one embodiment of the present invention, a biological fluid filtration apparatus is provided which includes a fluid filtration or leukocyte depletion device having an inlet and an outlet, a fluid container upstream from and elevated above said fluid filtration or leukocyte depletion device and having an outlet, a first conduit in fluid communication with the outlet of said fluid container and the inlet of said fluid filtration or leukocyte depletion device, a receiving container downstream of said fluid filtration or leukocyte depletion device and having an inlet, a second conduit in fluid communication with the inlet of said receiving container and the outlet of said fluid filtration or leukocyte depletion device, an upstream gas inlet having one of its' ends elevated above said fluid container, and having its' other end in fluid communication with said first conduit, and a downstream gas inlet having one of its' end elevated above said fluid container, and having its' other end in fluid communication with said or leukocyte depletion or fluid filtration device.

In another embodiment of the present invention, there is provided a closed loop fluid filtration or leukocyte depletion device including a fluid filtration or leukocyte

depletion device having an inlet and an outlet, a fluid container upstream from, and elevated above, said fluid filtration or leukocyte depletion device and having an outlet, a first conduit in communication with the outlet of said fluid container and the inlet of said fluid filtration or leukocyte depletion device, a receiving container downstream of said fluid filtration or leukocyte depletion device and having an inlet, a second conduit in fluid communication with the inlet of said receiving container and the outlet of said fluid depletion device and a bypass line in fluid communication with said fluid container and said receiving container and having a loop portion elevated above said fluid container.

In yet another embodiment of the present invention the upstream gas inlet is eliminated and the downstream gas inlet is connected to the receiving container instead of the fluid filtration or leukocyte depletion device.

In another embodiment of the present invention, the downstream gas inlet may be eliminated.

In still another modification of the present invention, the upstream gas inlet housing or vent and the downstream gas inlet housing or vent may be part of the same inlet device.

Thus, it is an object of the present invention to provide an improved method and apparatus for filtering biological fluids.

It is a further object of the present invention to provide an open gas vent that prevents premature gas introduction into the fluid stream in a biological fluid processing system.

It is a further object of the present invention to provide an open loop biological fluid processing system with transfer lines or conduits arranged or configured in a matter which precludes the biological fluid from contacting the upstream and downstream gas inlet housings

or vents, or bypassing the biological fluid depletion device.

Another object of the present invention is to offer a wider choice of materials which may be used in the gas inlet housings or gas outlet housings or vents of biological fluid filtration systems. The present invention does not require wettable membranes. The choice of membranes for the present invention is not limited.

Another object of the present invention is to provide a system of the foregoing nature where gas is transferred into and out of the biological fluid processor through porous medium in the upstream and downstream gas vents.

A still further object of the present invention is to provide an open loop system of the foregoing nature where each gas vent is separated from, and in communication with the biological fluid by a column of gas in the transfer lines or conduits.

A still further object of the present invention is to provide an open loop biological fluid filtration system of the foregoing nature wherein the upstream gas inlet housing or vent, and the downstream gas inlet housing or vent may be a portion of the same inlet device.

A still further object of the present invention is to provide a closed loop biological fluid filtration system having a bypass line bypassing the biological fluid filtration device, the bypass line is arranged such that a column of gas separates the unfiltered biological fluid upstream of the filtration device from the filtered biological fluid downstream of the biological fluid filtration device.

A further object of the present invention is to provide an open loop biological fluid filtration system having an upstream gas inlet elevated above the level of the biological fluid container and having a satellite bag connected to the biological receiving fluid container.

Further objects and advantages of the present invention will be apparent from the following description and appended claims, reference being made to the accompanying drawings forming a part of the specification, wherein like reference characters designate corresponding parts in the several views.

BRIEF DESCRIPTION OF THE DRAWINGS

Fig. 1 is an elevational view of a prior art biological fluid filtration system.

Fig. 2 is an elevational view of a construction embodying the present invention.

Fig. 3 is an elevational view showing a modification of the construction shown in Fig. 2.

Fig. 4 is an elevational view of a further modification of the construction shown in Fig. 2.

Fig. 5 is an elevational view showing a further modification of the construction shown in Fig. 2.

Fig. 6 is an elevational view of a closed loop construction embodying the present invention.

Fig. 7 is an elevational view showing a modification of the construction shown in Fig. 6.

Fig. 8 is an elevational view of a further modification of the construction shown in Fig. 6.

Fig. 9 is an elevational view showing a further modification of the construction shown in Fig. 6.

Fig. 10 is an elevational view showing a further modification of the construction shown in Fig. 6.

Fig. 11 is an elevational view showing a further modification of the construction shown in Fig. 6.

Fig. 12 is an elevational view of a construction embodying the present invention utilizing a satellite bag.

DESCRIPTION OF THE PREFERRED EMBODIMENT

The aforementioned U.S. Patent No. 5,451,321 to Matkovich shows a biological fluid processing assembly for filter biological processes such as blood. An example of the Matkovich apparatus is illustrated in Fig. 1. The apparatus has a blood collection bag 30 connected by a first conduit 31 to a leukocyte depletion device 32. The leukocyte depletion device 32 is connected by a second conduit 33 to a blood receiving bag 34. A gas inlet 35 having a cover or cap 36, is provided in fluid communication with the first conduit 31 downstream of said collection bag 30, and a gas outlet 37 is provided in second conduit 33 downstream of the leukocyte depletion device 32.

In one embodiment of the prior art, a first clamp 38 is placed on first conduit 31 downstream of the blood collection bag 30 and upstream of the gas inlet 35, and a second clamp 39 is placed on the second conduit 33 downstream of the gas outlet 37. In a typical operation the blood collection bag 30 is sterile and is connected to the conduit 31 as illustrated. The gas inlet 35 is comprised of a housing 41 and a porous medium barrier 42 in addition to cover or cap 36. Additional details of the barrier 42 may be obtained by reference to U.S. Patent No. 5,451,321.

Prior to the start of blood processing, the inlet clamp 38, the outlet clamp 39, and the gas inlet 35 are all closed. The blood processing is initiated by opening the inlet clamp 38, and allowing the blood to drain from the blood collection bag 30. A column of blood flows through the first conduit 31 into the leukocyte depletion device 32 displacing any gas within the blood processing system. No blood enters the gas inlet device 35 since the gas inlet is closed. The displaced gas is expelled from the system through the gas outlet 37 since the second

clamp 39 is closed. As substantially all the gas is expelled from the first conduit 31 and the portion of the second conduit 33 leading to the gas outlet 37, the porous medium is wetted by the blood, and the blood flow seizes or stops at the liquiphobic bearer in the gas outlet 37.

Once the gas outlet 37 is wetted, the second or outlet clamp 39 is opened, and filtered blood flows into the blood receiving bag 34. The gas outlet 37 need not be closed prior to opening of the outlet clamp since the gas outlet is sealed by the wetted porous medium. Blood flows from the collapsible blood container or bag 30 through the leukocyte depletion device 32 and into the blood receiving bag 34 until equilibrium is reached within the system and blood ceases to flow. At this point, all of the blood has not been processed through the leukocyte depletion device 32. The first conduit 31, the filter device 32, and the second conduit 33 are filled with blood.

Removing the cover or cap 36 from the gas inlet 35 allows gas to enter the processing system and drive the blood through the leukocyte depletion device 32. However, since the filter medium 32A within the leukocyte depletion device 32 is wetted, the flow of blood seizes when gas fills the upstream chamber of the filter. When the blood flow seizes, the second or outlet clamp 39 is closed.

It can be seen that, at this point, the downstream side of the leukocyte depletion device 32, and the entire second conduit 33 are filled with blood. With ever increasing need for blood and blood products, those skilled in the prior art have strived to increase the recovery of blood, and such a relatively large quantity of blood being left in the device of the prior art is no longer satisfactory.

In order to solve the recovery problems present in the prior art devices, the open-loop construction shown in Fig. 2 has been developed. There is shown a biological

fluid filtration system 44 having a leukocyte depletion device 45 with a filter medium 46, an inlet 47, and an outlet 48. The leukocyte depletion device may be such as the biological fluid filter shown in US Patent No. 6,171,493, or any other suitable fluid filtration or leukocyte depletion device.

A blood container 49 is provided upstream from, and elevated above said leukocyte depletion device 45. Blood container 49 is connected to, or in fluid communication with, said leukocyte depletion device 45 through first conduit 50.

There is also provided a blood receiving container 52 downstream of said leukocyte depletion device 45. Leukocyte depletion device 45 is connected to blood receiving container 52 through second conduit 54. An upstream gas inlet 56 is provided in fluid communication with said first conduit 50, and a downstream gas inlet 58 is provided in fluid communication with said leukocyte depletion device 45, downstream of said filter medium 46.

An inlet clamp 60 and an outlet clamp 61 may be provided. It should be understood that one or more of inlet clamp 60 and/or outlet clamp 61 may be provided, and be well within the scope of the present invention.

Upstream gas inlet 56 may take the form of a vent line 62 being connected to an upstream gas inlet housing 64. Vent line 62 may have a U-shaped portion 62A to prevent drawing of gas into biological fluid filtration system 44 until substantially all of the biological fluid has drained from the biological fluid container 49. The other end of vent line 62 should be at a sufficient height such that it is always positioned above the level of the fluid in the biological fluid container 49.

Upstream gas inlet housing or vent 64 has an inlet 65 and an outlet 66. Interposed between the inlet 65 and the

outlet 66 in a sealing relationship is at least one layer of a porous medium 67. The porous medium may be such as a bacterial retention medium, a viral retention medium, or other suitable medium.

In a similar manner, the downstream gas inlet 58 may comprise a second vent line 70 connected to a downstream gas inlet housing or vent 71 having an inlet 72 and an outlet 73. A cap or other closure 74 may be used in connection with the opening and the closing of inlet 72. Interposed in the housing 71, between the inlet 72 and the outlet 73 is a second porous medium 76. The second porous medium 76 may also be such as a bacterial retention medium, a viral retention medium, or other suitable medium.

As illustrated, upstream gas inlet housing 64 and downstream gas inlet housing 71 may be provided in a single novel inlet device 80 having a barrier or wall 81 which prevents fluid communication between the upstream gas inlet porous medium 67 and the downstream gas inlet porous medium 76. The upstream medium 67 and the downstream medium 76 may then be formed of a single sheet.

The upstream gas inlet 56 and the downstream gas inlet 58 may be placed in any practicable location as long as they are located such that the blood product being filtered never contacts the porous medium 67. In the preferred embodiment illustrated the porous medium 67 contained within the housing 64 is elevated above the blood container 49, but other locations are well within the scope of the present invention.

In the method of blood processing embodying the present invention, the inlet clamp 60 and the outlet clamp 61 are initially closed. The cap or closure 74 covering the inlet 72 of downstream gas inlet device, housing, or housing portion 71 is also in place.

The blood processing is initiated by opening the inlet clamp 60 and allowing the biological fluid to flow through the first conduit 50. As the fluid flows past the junction 50A, some of the fluid will flow into the upstream gas inlet 56 through vent line 62. A column of liquid of a predetermined, desired, length (shown as dimension A in Fig. 2), between the junction 50A and the bottom of the loop portion of 62A, prevents gas entry into the system until substantially all of the biological fluid has been drained from the biological fluid container 49.

The upstream gas vent may be thought of as a manometer measuring the pressure at the junction 50A. As the level of fluid within the biological fluid container 49 decreases, the pressure at the junction 50A decreases and, therefore, the height of the fluid in the vent line 62 decreases. When substantially all of the biological fluid has drained from the biological fluid container 49, the atmospheric pressure acting on the column of fluid within the vent line 62 will cause all of the fluid within the upstream gas inlet 56 to drain into the conduit 50. The remaining fluid contained with the upstream gas inlet line 62 is drained into the conduit 50 because the upstream gas inlet is open to atmosphere. Thus, dimension A in Fig. 2 must be of sufficient distance such that the above described sequence of events occur. At this point, the leukocyte depletion device 45 downstream of the filter medium 46 and the second conduit 54 between the leukocyte depletion device 45 and the blood receiving container 52, are all filled with filtered biological fluid.

The filtered biological fluid or blood downstream of the filter medium 46 in the leukocyte depletion device 45 may now be recovered by opening the cap or closure 74 covering the inlet 72 of downstream gas inlet device, housing, or housing portion 71. In place of cap 74, a clamp (not shown) could be used on second vent 70.

After this step substantially all of the blood previously unrecovered by the prior art devices is in the blood receiving container 52. Any gas in the receiving container 52 and/or second conduit 54 downstream of the disconnecting point of the blood receiving container 52 may be pushed back up into the second conduit 54 by gently squeezing the blood receiving container 52, and then the outlet clamp 61 can be closed.

As is now evident, the construction shown in Fig. 2 provides an easy method of drainage of substantially all of the biological fluid from the receiving bag 52 through the leukocyte depletion device 45. In addition, the biological fluid filtration system 44 in its preferred embodiment utilizes only a single housing in the inlet device 80, and a single layer of porous medium and substantially all of the filtered biological fluid is recovered. The system has a lower number of parts, is easier to manufacture, and recovers more biological fluid at a lower per unit biological fluid processing cost.

Alternate embodiments of the construction shown in Fig. 2 are illustrated in Figs. 3-5, with like numerals designating corresponding parts in the several views. Their operation can easily be understood by those skilled in the art in view of the foregoing description.

A modification of the present invention utilizing only the upstream gas inlet 56 and a satellite bag 83 is shown in Fig. 12. Satellite bag 83 is connected in fluid communication with blood receiving container 52 by satellite conduit 84. Satellite clamp 85 opens and closes satellite conduit 84. In this embodiment of the present invention, the satellite bag is used to vent the gas displaced from the receiving container 52. The volume of the satellite bag 83 should be sufficient to accept all of the gas displaced. After all the blood has flowed into the receiving container 52, the container is gently

squeezed until all of the gas is vented past the satellite clamp 85, at which time the satellite clamp 85 is closed.

Referring now to Fig. 6, there is shown a closed loop biological fluid filtration system 90. As in previous embodiments of the present invention, there is a leukocyte depletion device 45 having a filter medium 46, an inlet 47, and an outlet 48. The filter medium 46 is interposed in a sealing relationship between the inlet 47 and the outlet 48. The system 90 also includes a blood container 49 connected by first conduit 50 to the inlet 47 of leukocyte depletion device 45. Inlet clamp 60 is provided as before.

Provided downstream of the leukocyte depletion device 45 is a blood receiving container 52. A second conduit 54 is connected between the outlet 48 of the leukocyte depletion device 45 and the inlet of the blood receiving container 52. Used in place of the upstream gas inlet 56 and a downstream gas inlet 58 is a by-pass line 91, which may be opened and closed by by-pass clamp 92. A first end of the by-pass line 91 is connected in fluid communication with the blood container 49 proximate the outlet thereof, and the other end of the by-pass line 91 is connected in fluid communication with the blood receiving container 52 proximate the inlet thereof. The loop portion 93 of the by-pass line 91 is positioned such that when the blood container 49 is full of blood, the blood will not reach the loop portion 93 and thus, there can be no flow of blood through the by-pass line. One such position is illustrated in Fig. 6 with the loop portion 93 elevated above the blood container 49.

In place of loop portion 93, a one way check valve or other device may be used such that a column of gas will always separate the unfiltered biological fluid upstream of the filtration device from the filtered biological fluid downstream of the leukocyte depletion device 45.

The positioning of the loop portion 93, and the bypass line 91 may also be varied to accomplish this.

The method of operating the the closed loop embodiment of the invention differs in several respects from the method used with the open loop embodiment. As illustrated in Fig. 6, the additional by-pass clamp 92 is needed because no gas inlet or gas outlet devices are provided, as were necessary in the prior art. Prior to the start of blood processing, the inlet clamp 60 is closed and the by-pass clamp 92 is open. The blood processing is initiated by opening the inlet clamp 60 and allowing blood to drain from the blood container 49 through first conduit 50 into the leukocyte depletion device 45 and therethrough to the blood receiving container 52. The blood does not by-pass the leukocyte depletion device 45 because of the loop portion 93 of the by-pass line 91 being elevated to a sufficient height. The gas within the closed loop biological fluid filtration system 90 is displaced by the blood flow into the blood receiving container 52. As the blood container 49 approaches its nearly empty condition, the gas stored within the receiving container 52 automatically flows through the by-pass line 91 into the blood container 49 and allows substantially all of the blood to be processed through the leukocyte filtration device 45. It is important to note that the chamber of the leukocyte depletion device 45 downstream of the filter media 46 at this point will be filled with blood, as will the second conduit 54 between the leukocyte depletion device and the blood receiving container 52. If there is any gas left in the receiving container 52 it may be displaced into the by-pass line 91 by closing the outlet clamp 61, gently squeezing the blood receiving container 52 and closing the by-pass clamp 92. In this embodiment of the invention comprising the closed loop biological fluid filtration

system, the chamber downstream of the filter medium 46 in the leukocyte depletion device 45 is not drained of blood, nor is second conduct 54. However, the inlet device and the outlet devices of the prior art are eliminated, and a simplified system is provided.

Additional modifications of the closed loop biological fluid filtration system 90 are shown in Figs. 7-11. Their operation can be understood by those skilled in the art from the foregoing description.

Therefore, by carefully studying the problems present in prior art biological filtration fluid systems, I have developed a novel method and apparatus for biological fluid filtration.

CLAIMS

1. A closed loop leukocyte depletion system including:

a) a leukocyte depletion device having an inlet and an outlet,

b) a blood container upstream from, and elevated above, said leukocyte depletion device and having an outlet,

c) a first conduit in fluid communication with the outlet of said blood container and the inlet of said leukocyte depletion device,

d) a receiving container downstream of said leukocyte depletion device and having an inlet,

e) a second conduit in fluid communication with the inlet of said receiving container and the outlet of said leukocyte depletion device,

f) a bypass line in fluid communication with said blood container and said receiving container and having a loop portion elevated above said blood container.

2. The system defined in claim 1, wherein said bypass line is in fluid communication with said blood container proximate the bottom thereof and said bypass line has a loop portion elevated above said blood container.

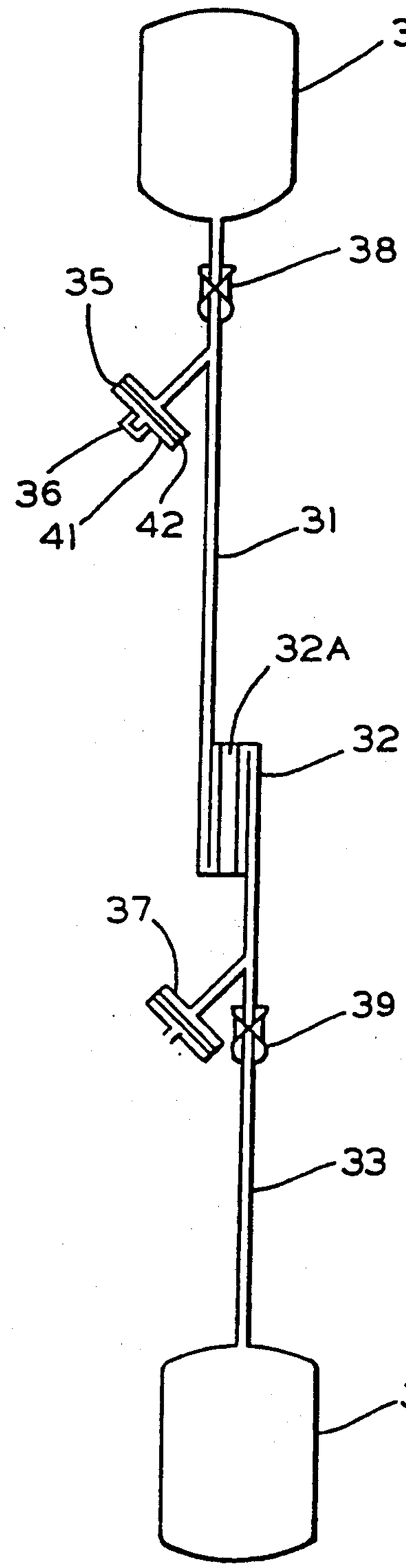


FIG. 1
(PRIOR ART)

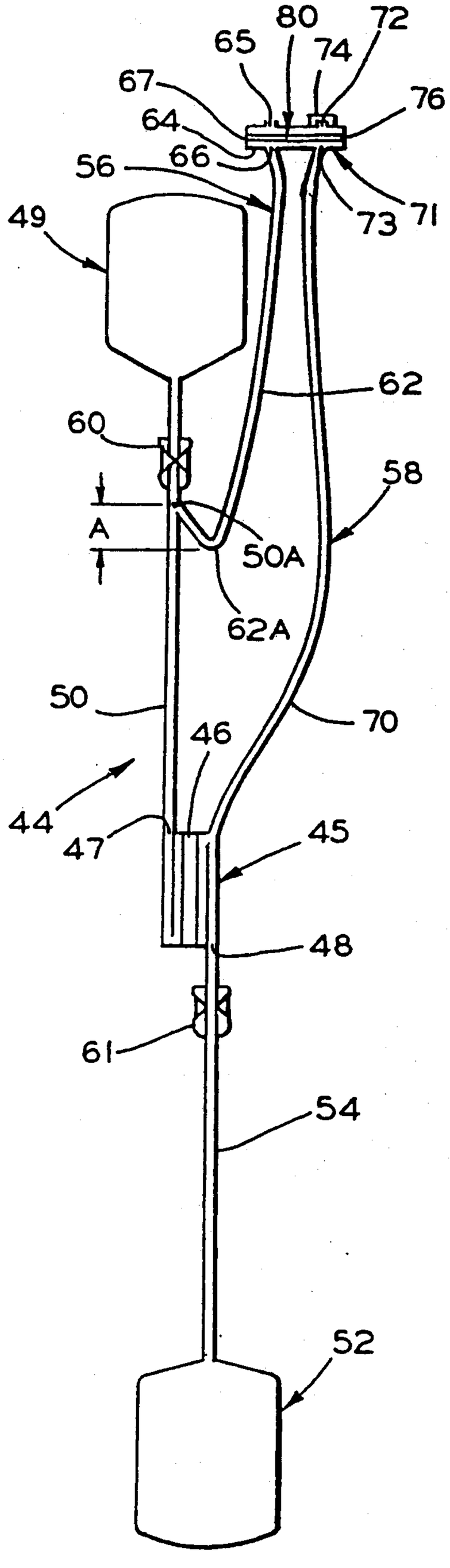


FIG. 2

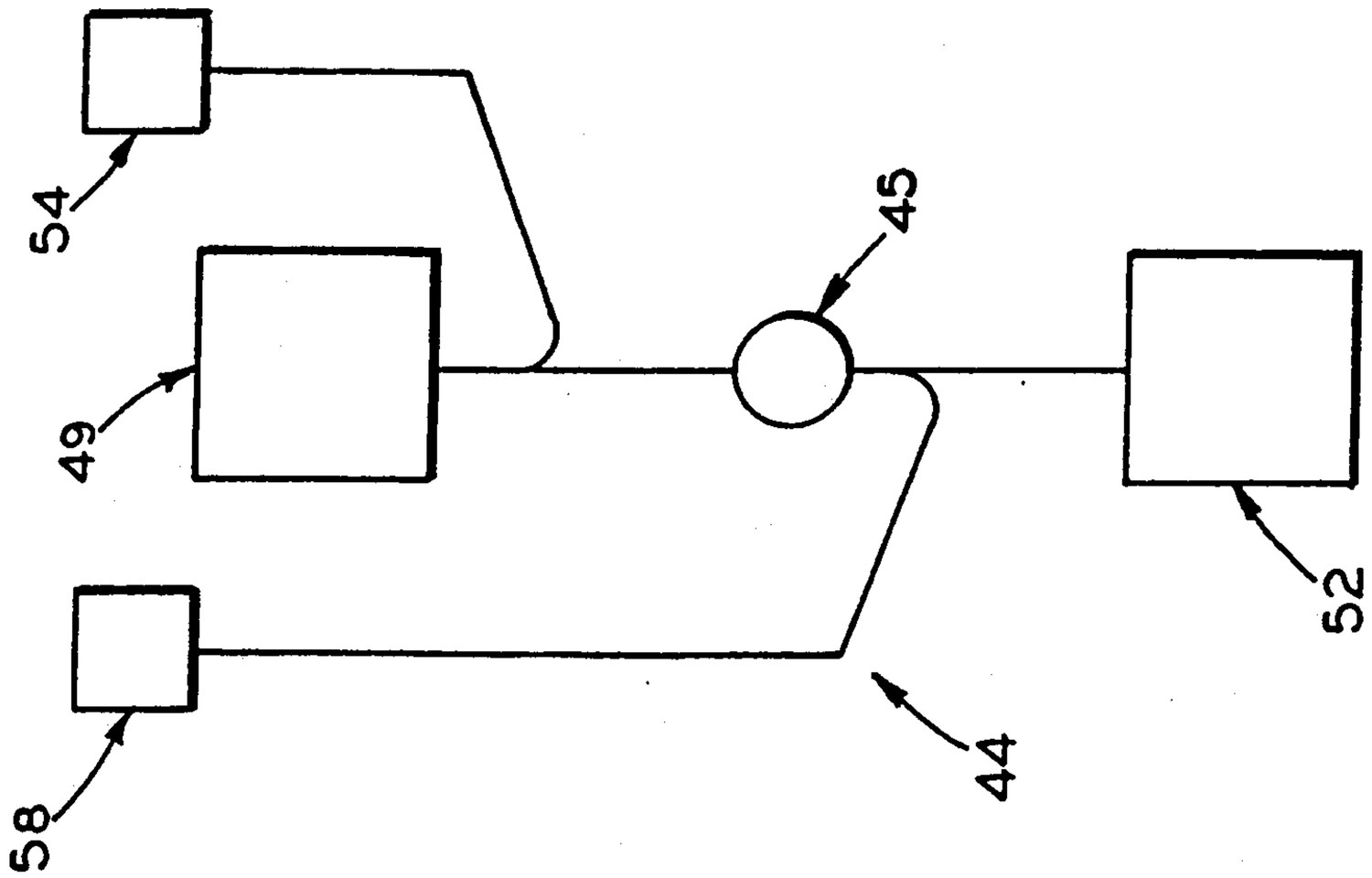


FIG. 5

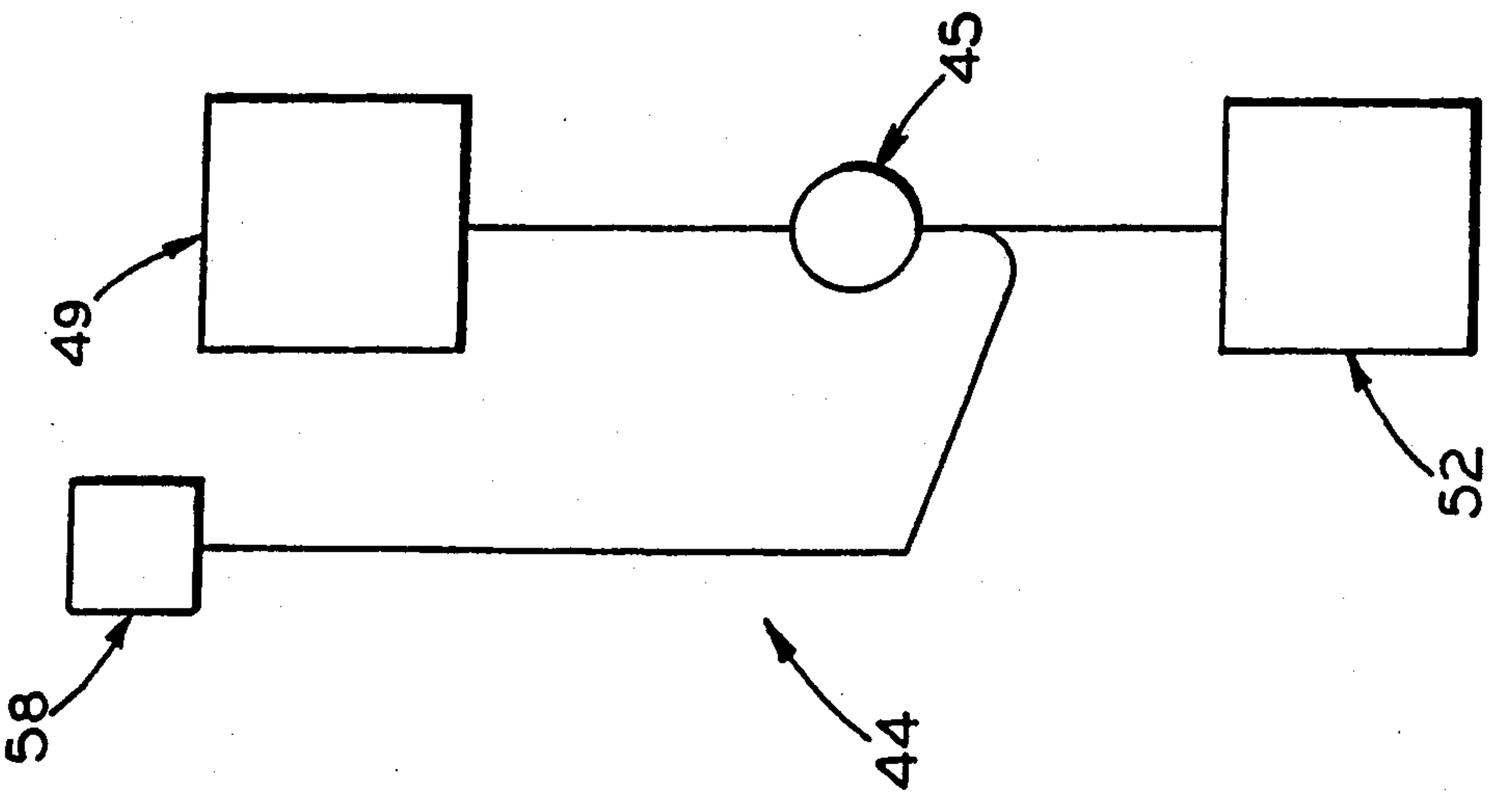


FIG. 4

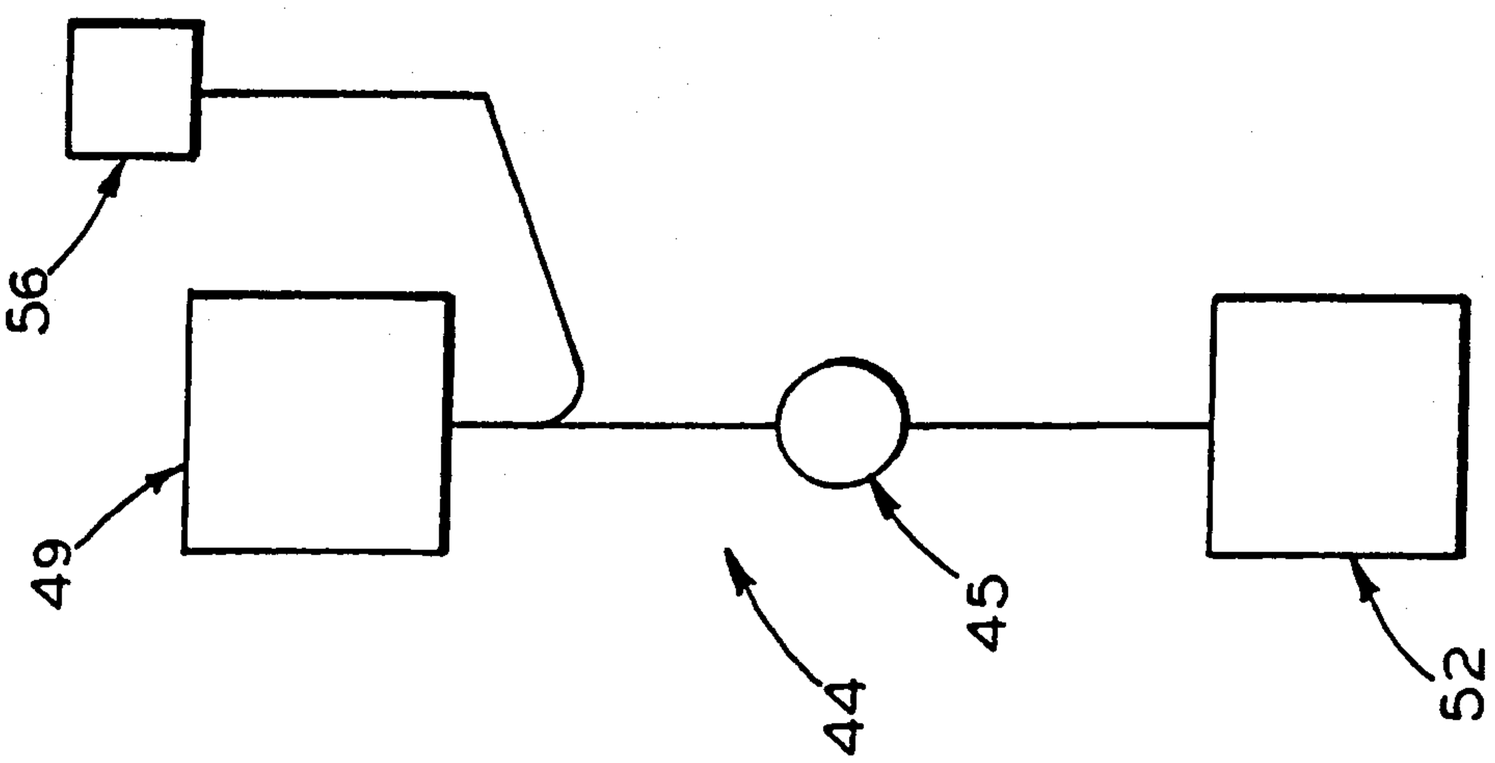


FIG. 3

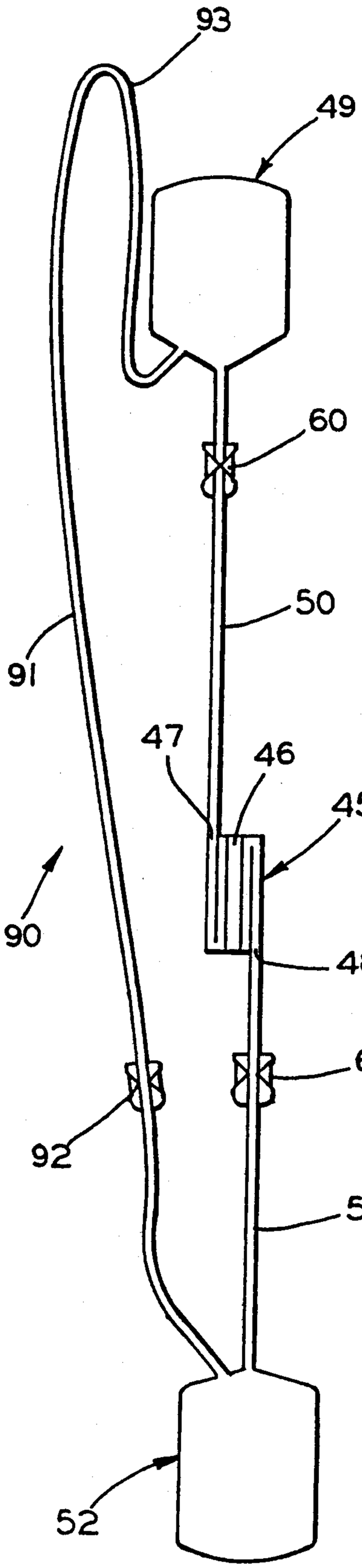

93
49
60
50
91
47
46
45
90
48
61
92
54
52

FIG. 6

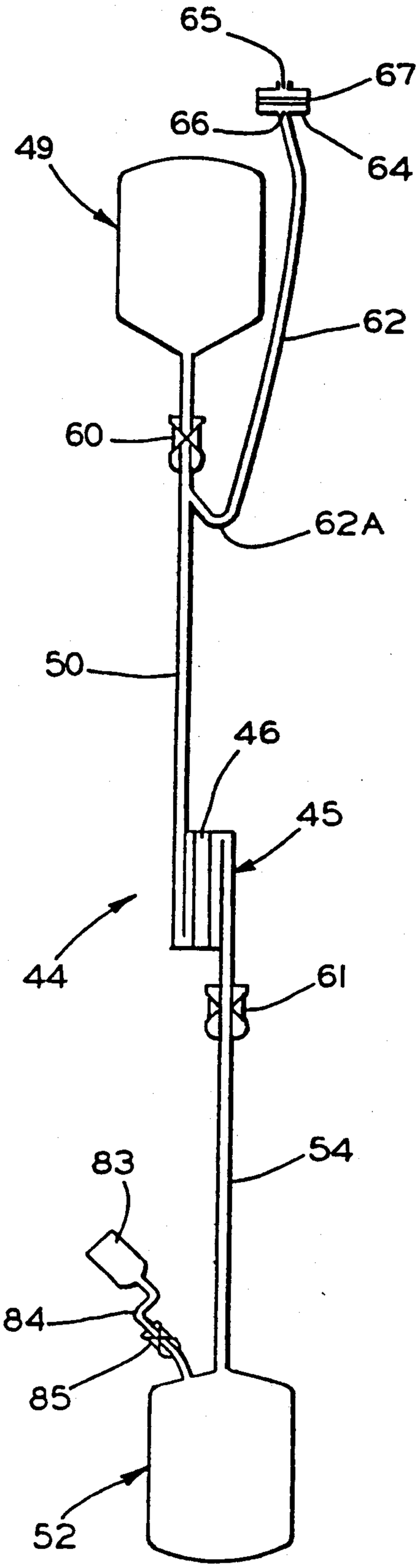

65
67
66
64
49
62
60
62A
50
46
45
44
61
54
83
84
85
52

FIG. 12

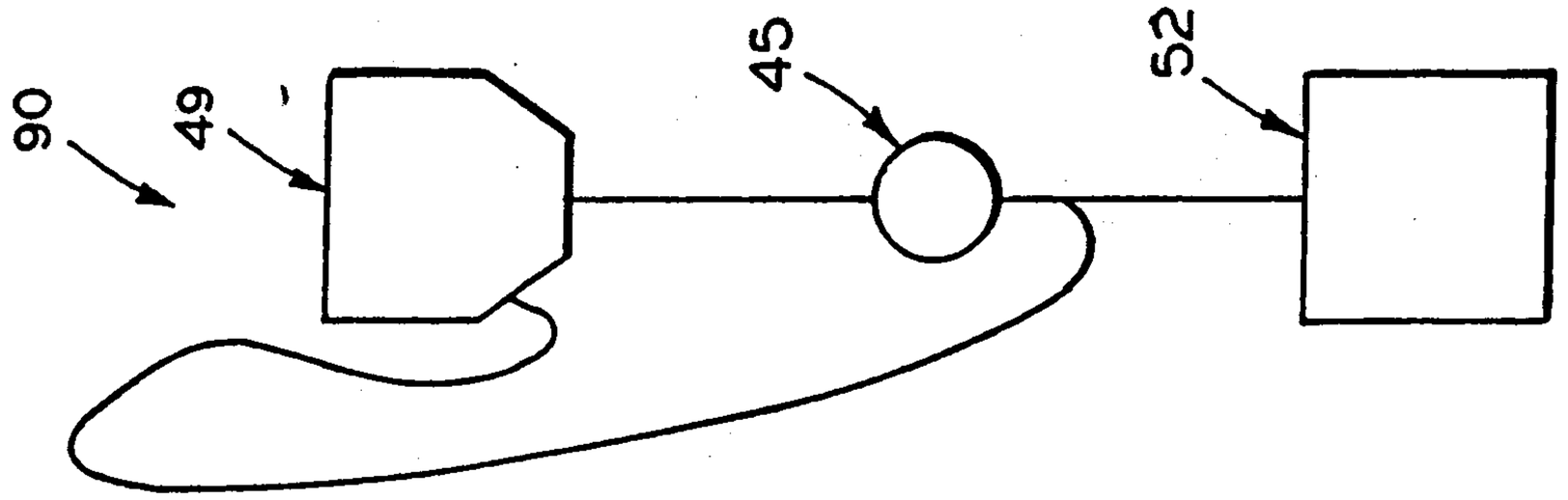


FIG. 11

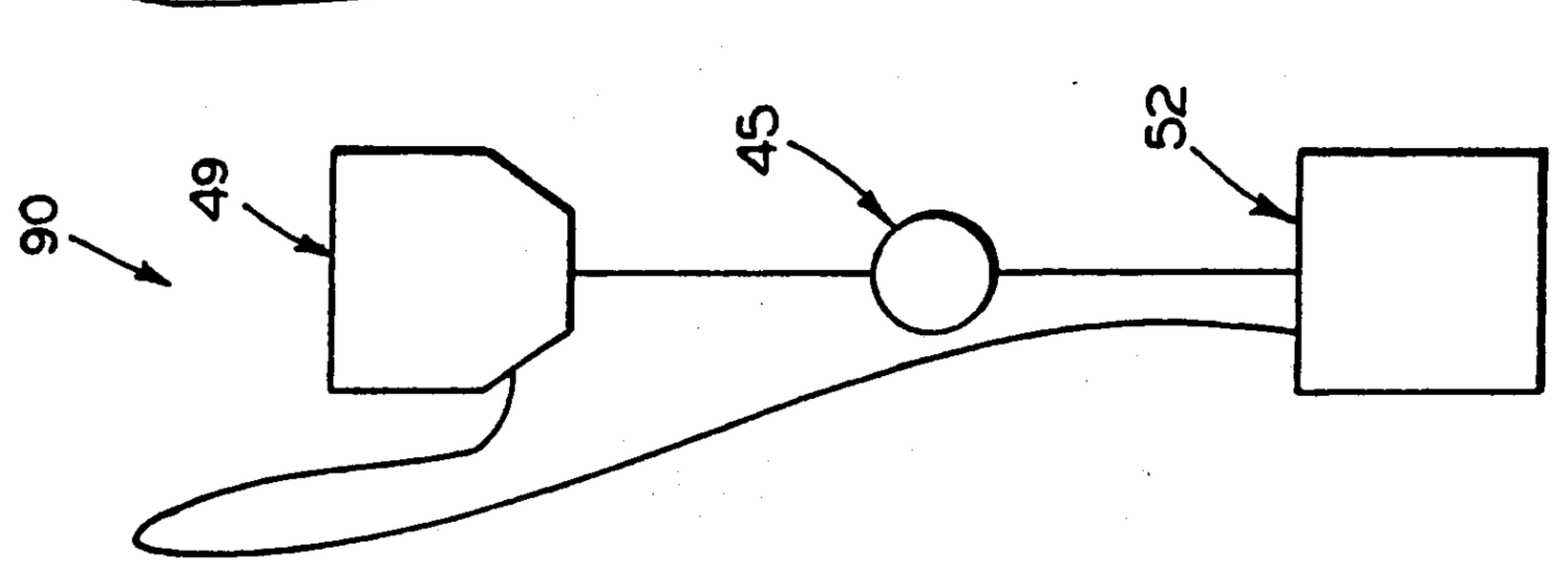


FIG. 10

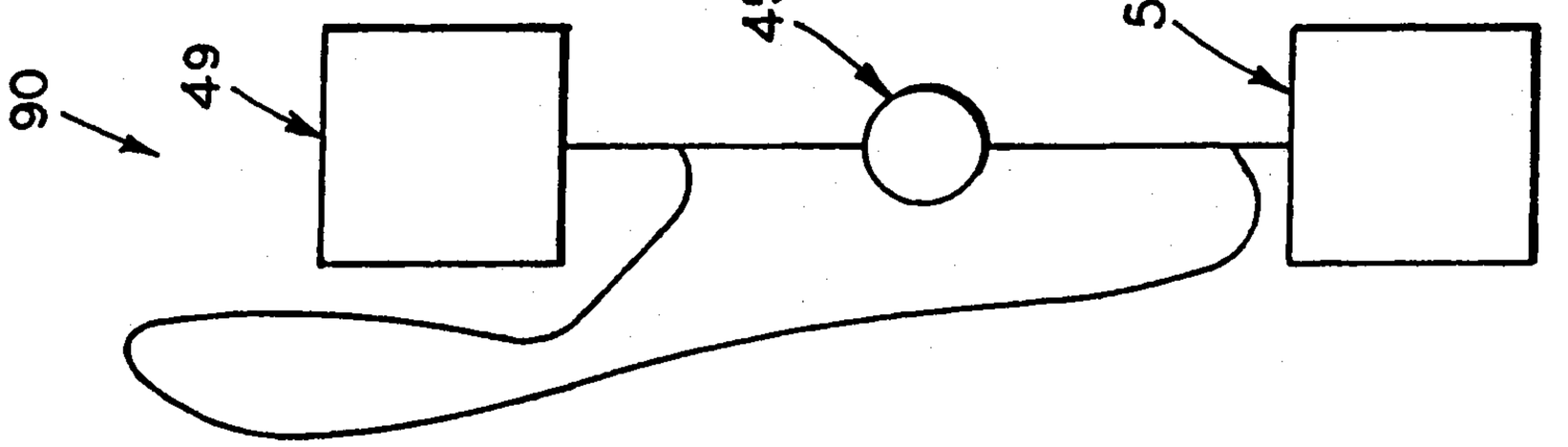


FIG. 9

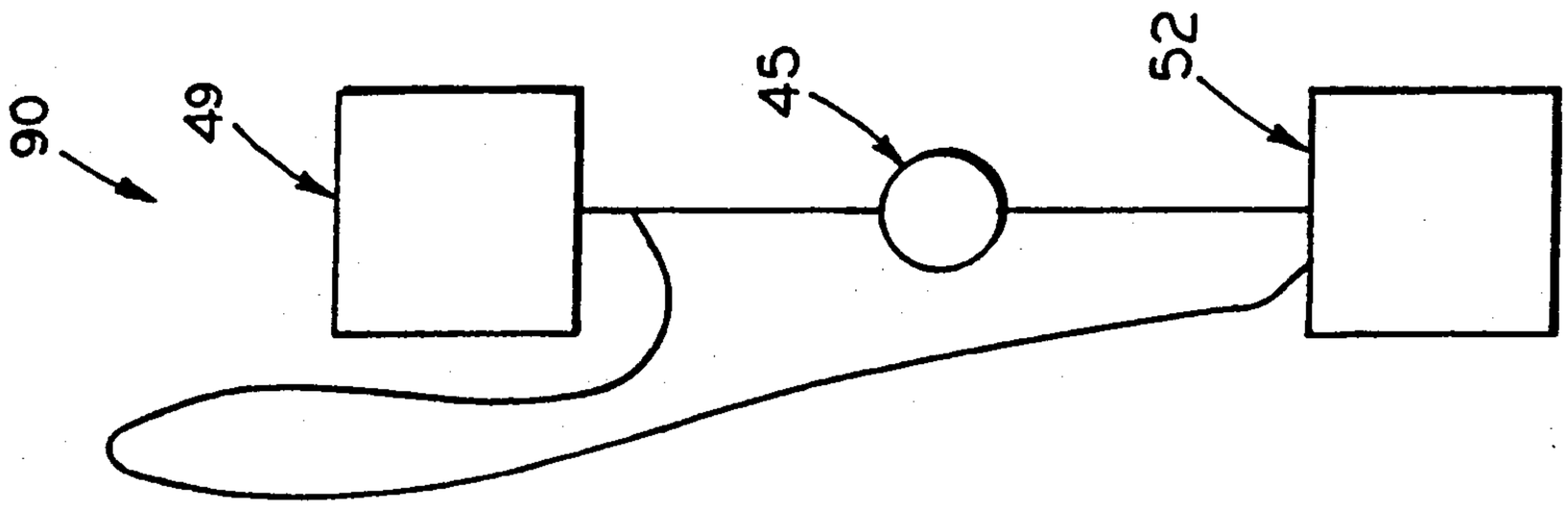


FIG. 8

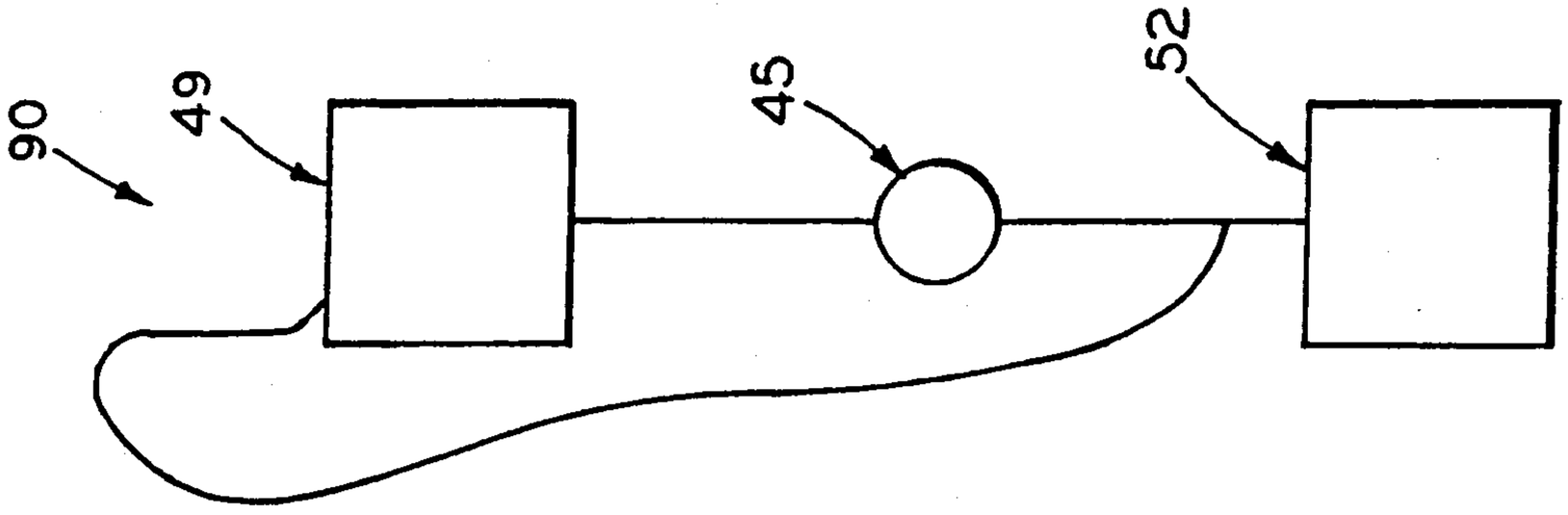
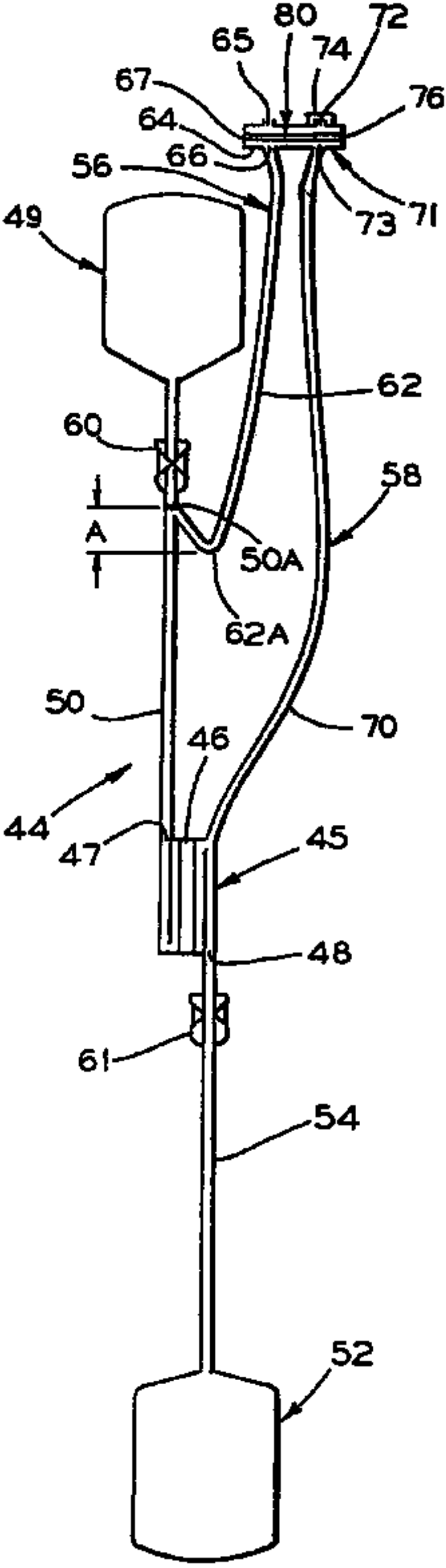


FIG. 7


80
72
65
74
67
76
64
66
56
73
71
49
62
60
58
A
50A
62A
50
70
46
44
47
45
48
61
54
52