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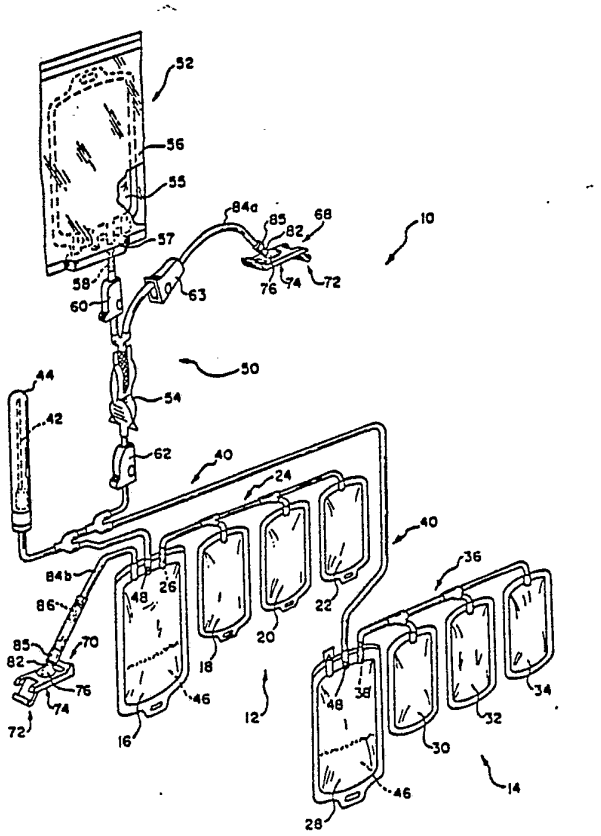
(54) Title: INCREASED YIELD BLOOD COLLECTION SYSTEMS AND METHODS

(57) Abstract

A blood collection and separation system (10) including first and second blood collection and separation assemblies (12, 14). The first collection assembly (12) includes a primary container (16) and transfer containers (18, 20, and 22). A branch conduit (24) establishes a fluid path between the primary container (16) and each of the transfer containers (18, 20, and 22). The second blood collection assembly (14) also includes a primary container (28) and transfer containers (30, 32, and 34). A branch conduit (36) establishes a fluid path between the primary container (26) and each of the transfer containers (30, 32, and 34). The system (10) further includes a primary conduit (40) for establishing a fluid path between a phlebotomy needle (42) and the primary containers (16, 28). In order to return a portion of the collected blood components to the donor during the procedure, the system includes an auxiliary conduit assembly (50) for establishing a fluid path between the primary conduit (40) and a source (52) of sterile saline solution. The system further includes a connector assembly (68, 70)which is operative for forming a fluid path between the collection assemblies (12, 14) and the auxiliary conduit assembly (5) so that a portion of the collected blood components can be returned to the donor through the primary conduit (4) and the phlebotomy needle (42).



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INCREASED YIELD BLOOD COLLECTION SYSTEMS AND METHODS

RELATED APPLICATION:

This application is a continuation-in-part of United States Patent Application Serial No. 316,918, filed October 30, 1981 and entitled "METHOD AND SYSTEM FOR WITHDRAWING TWO UNITS OF WHOLE BLOOD FROM A DONOR, ONE FOR EXTRACTING PLASMA AND ONE FOR STORAGE".

FIELD OF THE INVENTION:

This application generally relates to systems and methods which enable the collection and separation of whole blood into its therapeutic components, such as red cells, plasma, platelets, and various clotting factors. This application also

generally relates to whole blood collection and separation systems and methods which enable the storage of whole blood and its various therapeutic components for the maximum allowable periods.

BACKGROUND AND OBJECTS OF THE INVENTION:

At the present time, over 12 million units of whole blood are collected from volunteer donors in the United States each year. With the advent of blood component therapy, approximately 60% to 80% of the whole blood collected today is not itself stored and used for transfusion. Instead, the whole blood is first separated into its clinically proven components, which are themselves individually stored and used to treat a multiplicity of specific conditions and diseased states.

The clinically proven components of whole blood include red cells, which can be used to treat chronic anemia; platelets, which can be used to treat thrombo-cytopenia; cryoprecipitate, which is rich in Clotting Factor VIII (also known as AHF) and can be used to treat hemophilia; plasma, which can be used to restore all of the clotting factors to patients; as well as numerous other plasma-based fractions, such as albumin, protein fraction, gamma globulin, and various other specific coagulation protein concentrates.

The present consensus is that care of a patient is improved by providing only the therapeutic components of whole blood which are required to treat the specific disease. The demand for therapeutic components of whole blood is thus ever-increasing. Likewise, the demand for safe and effective systems and methods for collecting, separating, and storing the therapeutic components of whole blood grows accordingly.

One desirable feature for a blood collection and separation system and method is its capability to maximize, to the greatest extent possible, the yield of clinically proven blood components during a single collection procedure. The importance of this feature stems in large part from the traditionally limited number of individuals who volunteer to donate whole blood on a regular basis. The importance of this feature also stems from the periodic nature of blood collection procedures themselves. In the United States, for example, a collection of one unit of whole blood from an individual volunteer donor for separation into its various components can be undertaken only once every 8 weeks if the red cells are retained for storage. Maximizing the component yield for each procedure can help to offset these supply-side factors which together limit the supply of available whole blood.

Another desirable feature for a blood collection and separation system and method is its capability of yielding components which are suited for storage for prolonged periods. This feature,

which also helps to offset the limited supply of available whole blood, is closely related to the degree of sterility a given blood collection system can assure.

For example, in the United States, whole blood and components which are collected and processed in a nonsterile, or "open", system must be transfused within twenty-four (24) hours of collection. On the other hand, in the United States, whole blood and red cells which are collected in a sterile, or "closed", system may be stored for upwards to thirty-five days, depending upon the type of anticoagulant and storage medium used. Similarly, in the United States platelets which are collected in a sterile, or "closed", system may be stored for upwards to five days, depending upon the ability of the storage container to maintain proper pH levels.

In the United States, Federal Regulations [Title 21 C.F.R. §640.16(b)] define a "closed" blood collection system as one in which the initially sterile blood collection and transfer containers are integrally attached to each other and not open to communication with the atmosphere. Furthermore, to remain a "closed" blood collection system in the United States, the blood collection container of the system cannot be "entered" in a non-sterile fashion after blood collection. By United States standards, an entry into a blood collection system which presents the probability of non-sterility which exceeds one in a million (i.e., greater than 10^{-6})

constitutes a "non-sterile" entry. A non-sterile entry "opens" a heretofore "closed" system and dictates the significantly shortened storage periods for the blood and components collected and processed within the system.

Representative examples of known whole blood collection assemblies include the following United States Patents:

Earl	3,064,647
Wandell et al	3,078,847
Bellamy Jr.	3,110,308
Tenczar Jr.	3,187,750
Viguier	3,870,042
Garber et al	3,986,506
Djerassi	4,111,199
Smith	4,222,379

Representative examples of known commercially available whole blood collection assemblies are sold by Fenwal Laboratories, Inc. (a division of Travenol Laboratories, Inc., Deerfield, Illinois); Delmed Corp., Irvine, California; and Cutter Laboratories, Inc., Berkeley, California.

It should be noted that most, if not all, of the above-cited blood collection assemblies are "closed" as judged by United States standards. The assemblies thereby enable the storage of blood and its various components for the maximum allowable periods. However, none of the above-cited systems enables the collection and processing of more than

one unit of whole blood during a given procedure. Thus, none of these assemblies has the capability of effectively increasing the component yield per procedure.

In addressing the desirability of extending the component yield of conventional blood collection systems, it has been suggested to utilize a plasmapheresis-type procedure.

Plasmapheresis is a procedure which facilitates the collection of source plasma for commercial fractionation into AHF, albumin, and other plasma-based protein fractions. During conventional plasmapheresis, a unit of whole blood is collected and separated into red cells and plasma. The red cells are returned to the donor, and the plasma is retained for fractionation purposes. Another unit of whole blood is then drawn from the same donor and again separated into red cells and plasma. Again, the red cells are returned to the donor, and only the plasma is retained.

The end result is, for each plasmapheresis procedure, two units of source plasma. Because, during plasmapheresis, no red cells are retained for storage, the plasmapheresis procedure can be repeated twice in a seven day period, allowing the collection of four units of plasma from each donor per week.

Representative examples of plasmapheresis assemblies include the following United States Patents:

Naftulin	3,459,182
Naftulin et al	3,782,382
Dabney	3,945,380

Representative examples of known commercially available plasmapheresis assemblies include those sold by Fenwal Laboratories, Cutter Laboratories; Delmed; and Terumo Company, Ltd., (Japan).

By utilizing a plasmapheresis-type procedure for blood and blood component collection purposes, it has been suggested to initially collect one unit of whole blood for separation into red cells and plasma. As in conventional plasmapheresis, the red cells would be returned to the donor. The plasma woud be retained for separation into various therapeutic components. Utilizing the same phlebotomy, another unit of whole blood would be collected. Unlike conventional plasmapheresis, this unit of whole blood would be retained in its entirety and could be separated into red cells and various other therapeutic components.

The end result would be, for each plasmapheresis-type procedure, one unit of red cells and two units of plasma and plasma-based components, such as platelets, cryoprecipitate, etc.

No known conventional plasmapheresis assembly can be utilized to perform this "increased-yield" procedure and, at the same time, provide blood components which are suited for

prolonged storage in the United States. This is because no known conventional plasmapheresis assembly has means for returning the initially collected unit of red cells to the donor in a manner which does not at the same time "open" the system, as judged by the applicable United States standards heretofore discussed. Indeed, no known conventional plasmapheresis assembly can return the initially collected unit of red cells to the donor with even a probability of nonsterility of one in a thousand (10^{-3}), which falls significantly short of the demanding 10^{-6} standard in the United States.

Because of this, only source plasma can be collected by conventional plasmapheresis assemblies. This source plasma must be frozen within 4 hours of collection for storage and can be used only for fractionation, which includes a subsequent sterilization step.

One of the principal objects of this invention is to provide a blood collection system and method which maximizes, to the greatest extent possible, the yield of blood components obtained during a single collection procedure in a manner which also assures the maximum available storage period for each of the components collected, as measured by applicable United States standards.

In addition to the above-discussed matters, yet another desirable feature for a blood collection and separation system and method is that it constitutes a compact and easily handled system which can be efficiently manufactured, stored, and utilized by the operator.

To this end, it is another one of the principal objects of this invention is to provide a blood collection system which is formed of two or more initially separate, closed subsystems which are compact and easily handled and which can be sequentially joined together without compromising the sterile integrity of any of the subsystems, as measured by applicable United States standards.

SUMMARY OF THE INVENTION:

To achieve these and other objects, the invention provides an increased yield blood collection system which maximizes, to the greatest extent possible, the yield of blood components obtained during a single collection procedure in a manner which also assures the maximum permissible storage period for each of the components collected.

The system which embodies the features of the invention comprises first and second blood collection assemblies, each of which includes a primary collection container. The first blood collection assembly also includes at least one transfer container which communicates with the associated primary container by means of a fluid path

which is closed from communication with the atmosphere. The system further includes primary conduit means which establishes between a phlebotomy needle and each of the primary collection containers a fluid path which is closed from communication with the atmosphere, as well as auxiliary conduit means which establishes between a source of sterile saline and the primary conduit means a fluid path which is likewise closed from communication with the atmosphere. These containers and the conduit means which interconnect them collectively constitute, after sterilization, a "closed" system as measured by applicable standards in the United States.

To enable an increased yield of components by utilizing the system, the system includes means for selectively forming a fluid pathway between a selected one of the primary containers and the auxiliary conduit means in a manner which does not compromise the overall closed integrity of the system as measured by applicable standards in the United States.

To this end, the system includes normally closed first and second connector means which communicate, respectively, with the auxiliary conduit means and the primary container of the first collection assembly. Each of the connector means includes means for selectively mechanically coupling the first and second connector means together with a portion of each in facing contact. The facing portions, in turn, each includes means which is

meltable to form a fluid path through the facing portions, but only in response to exposure to an energy source sufficient to effectively sterilize the meltable means as the fluid path is being formed.

In the preferred embodiment, the fluid path which is formed is hermetically closed to communication with the atmosphere. It has been demonstrated that the probability of nonsterility which is occasioned by the formation of this fluid path exceeds one in a million (10^{-6}), thereby maintaining the closed integrity of the associated system, as measured by United States Standards.

The system as just described enables the an increased yield blood collection method which utilizes a single phlebotomy to sequentially collect two units of whole blood for separation into red cells and plasma. In accordance with the method, the red cells of the first unit collected are returned to the donor utilizing the just described connector means, with the plasma being retained for further separation and storage. The second unit of whole blood is collected after the red cells from the first unit are returned. The second unit of whole blood is retained in its entirety for storage or for separation and storage of its components.

Because the method utilizes the just described connector means, the system remains closed during the entire procedure, despite the return of red cells to the donor midway through the procedure. Prolonged storage periods for each collected

component is thereby realized. In addition, the system enables the yield of plasma and plasma-based components collected during a single procedure to be doubled.

The invention also provides a blood collection system which is formed of a series of initially separate, compact subsystems which can be selectively joined together by the operator without compromising the sterile integrity of any of the subsystems or the formed system as a whole.

In one embodiment, the system shares the same basic elements and operative objectives of the heretofore described increased yield blood collection system. In this embodiment, the first and second blood collection assemblies and the primary conduit means together comprise an initially separate, closed first subassembly. Similarly, the auxiliary conduit means likewise comprises another initially separate, closed second subassembly, as does the source of saline. In this embodiment, the connector means as heretofore described is associated with each subassembly. Utilizing the connector means, the subassemblies may be selectively coupled together in a manner which does not compromise the closed integrity of any of the subassemblies or of the combined system as a whole.

In one embodiment, the transfer containers, which may be associated with each of the first and second blood collection assemblies of the heretofore described increased yield blood collection system,

or, indeed, with any blood collection system, each comprises an initially separate entity which can be selectively coupled in flow communication with the primary collection container utilizing the connector means as above-described.

The blood collection system which embodies the features of the invention as described in the preceding two paragraphs comprises a series of individual, closed subsystems. It is thus compact and easily handled by the operator. The system also provides a substantial amount of "in the field" flexibility, so that the operator can readily tailor the specific configuration of the system to the particular collection objectives at hand. All these desirable features are realized without compromise to the desired overall closed integrity of the formed system.

Other features and advantages of the invention will be pointed out in, or will be apparent from, the specification and claims, as will obvious modification of the embodiments shown in the drawings.

DESCRIPTION OF THE DRAWINGS:

Fig. 1 is a perspective view, with a portion broken away and in section, of an increased yield blood collection system which embodies various of the features of the invention;

Fig. 2 is a perspective view of the increased yield blood collection system shown in Fig. 1 after a first unit of whole blood has been collected from a donor;

Fig. 3 is a plan view of the increased yield blood collection system shown in Fig. 1 as the red cells of the first unit of whole blood are being returned to the donor;

Fig. 4 is a plan view of the increased yield blood collection system shown in Fig. 1 after the collection of the second unit of whole blood from the donor;

Fig. 5 is an enlarged view of a portion of the increased yield blood collection system shown in Fig. 3 prior to the return of the red cells of the first unit of whole blood to the donor;

Fig. 6 is a further enlarged view, with portions broken away and in section, of a portion the system shown in Fig. 5, showing the connector means associated with the system in an uncoupled relationship;

Fig. 7 is an enlarged view, with portions broken away and in section, of the connector means shown in Fig. 6 in a coupled relationship and being exposed to a radiant energy-induced melting apparatus to open a fluid path therethrough;

Fig. 8 is an enlarged view, with portions broken away and in section, of the connector means shown in Fig. 7 after the fluid path has been opened therethrough;

Fig. 9 is a plan view of a blood collection system which takes the form of an increased yield blood collection system and which includes a series of initially separate subsystems; and

Fig. 10 is a plan view of a blood collection system which takes the form of a blood collection assembly and which includes a series of initially separate transfer containers.

Before explaining the embodiments of the invention in detail, it is to be understood that the invention is not limited in its application to the details of construction and the arrangement of components as set forth in the following description or as illustrated in the accompanying drawings. The invention is capable of other embodiments and of being practiced or carried out in various ways. Furthermore, it is to be understood that the phraseology and terminology employed herein is for the purpose of description and should not be regarded as limiting.

DESCRIPTION OF THE PREFERRED EMBODIMENT:

A blood collection and separation system 10 is shown in Fig. 1. As illustrated, the system 10 includes first and second blood collection and separation assemblies, respectively 12 and 14.

The first collection assembly 12 includes a primary container 16 and at least one transfer container 18. While the number of transfer containers provided can vary according to the

collection and storage objectives of the operator, in the embodiment illustrated in Fig. 1, three transfer containers 18, 20, and 22 are shown.

Branch conduit means 24 establishes a fluid path between the primary container 16 and each of the transfer containers 18, 20, and 22. The branch conduit means 24 is preferably formed of a flexible plastic material suited for blood contact, such as plasticized polyvinyl chloride.

As shown in Fig. 1, the branch conduit means 24 is integrally connected with each transfer container 18, 20, and 22, as well as with the primary container 16. The fluid path which is established by the branch conduit means 24 is thereby closed from communication with the atmosphere. The first collection assembly 12 itself thereby constitutes, after sterilization, a closed system as judged by applicable standards in the United States.

Fluid communication between the primary container 16 and the first adjacent transfer container 18 is normally closed by a member 26 (shown in phantom lines in Fig. 1) which can be selectively opened by the operator. The closure member 26 may be variously constructed, and constitute, for example, an external roller clamp. In the illustrated embodiment, however the closure member 26 takes the form of a manually frangible valve member which is located within the fluid path and which can be similar in construction and operation to the valve member disclosed in Carter et al U.S. Patent 4,294,247.

The second blood collection assembly 14 also includes a primary container 28. While it is not essential that the second blood collection assembly 14 also include transfer containers, it is usually desirable that one or more transfer containers be provided. Thus, as in the first collection assembly 12, three transfer containers 30, 32, and 34 are provided.

As in the first collection assembly 12, branch conduit means 36 establishes a fluid path between the primary container 26 and each of the transfer containers 30, 32, and 34. Also as in the first collection assembly 12, the branch conduit means 36 of the second assembly 14 is formed of a flexible plastic material, such as plasticized polyvinyl chloride.

As shown in Fig. 1, the branch conduit means 36 of the second collection assembly 13 is integrally connected with each of the transfer containers 30, 32, and 34 as well as with the primary container 28, so that the fluid path which is established by the branch conduit means 36 is closed from communication with the atmosphere. The second collection assembly 14, like the first collection assembly 12, thereby constitutes, after sterilization, a closed system as judged by applicable standards in the United States.

Fluid communication between the primary container 28 and the first adjacent transfer container 30 in the second collection assembly 14 is, as in the first collection assembly 12, normally

closed by a closure member 38 (shown in phantom lines in Fig. 1). In the illustrated embodiment, the closure member 38 takes the form of a manually frangible valve member which is disposed within the fluid path and which is identical to the valve member 26 associated with the first collection assembly 12.

The construction and the materials of the primary containers 16 and 28 and the transfer containers 18, 20, 22 and 30, 32, 34 may vary to suit the objectives of the operator. In the illustrated embodiment, each of the primary containers 16 and 28 takes the form of a bag made of a plasticized polyvinyl chloride material. However, other similar materials which are approved for whole blood or red cell contact and storage can be utilized.

The transfer containers 18, 20, 22 and 30, 32, 34 may take the form of bags formed of the same plasticized polyvinyl chloride material as the primary containers 16 and 28. Alternately, the one or more of the transfer containers 18, 20, 22 and 30, 32, 34 may be fabricated of other materials which are known to be beneficial to their intended storage function, as is taught in Smith U. S. Patent 4,222,379. For example, one of the transfer containers may be fabricated from a polyolefin material which is disclosed in Gajewski et al U.S. Patent 4,140,162 and which is suited for prolonged platelet storage because of its gas transmission capabilities. Still alternatively, the transfer container which is intended to receive source plasma

for fractionation purposes may take the form of the container (not shown) which is the subject of Bacehowski et al U.S. Patent 4,253,458.

In order to introduce whole blood into the first and second collection assemblies 12 and 14, the system 10 further includes primary conduit means 40 for establishing a fluid path between a phlebotomy needle 42 and the primary containers 16 and 28 of each of the blood collection assemblies 12 and 14. The needle 42 includes a removable cover or sheath 44 which normally closes the needle 42 from communication with the atmosphere.

The primary conduit means 40 is preferably formed of a flexible plastic material, such as plasticized polyvinyl chloride. As shown in Fig. 1, the primary conduit means 40 is integrally connected with each of the primary containers 16 and 28 and the needle 42, so that the fluid path which is established by the primary conduit means 40 is closed from communication with the atmosphere. The entire subsystem defined by the primary conduit means 40 and the first and second collection assemblies 12 and 14 thereby constitutes, after sterilization, a closed system as judged by standards in the United States.

To prevent blood from clotting during the course of the blood collection procedure, each of the primary containers 16 and 28 is prefilled with a predetermined amount of an anticoagulant solution 46, such as ACD, CPD, or CPDA.

Fluid communication between the primary conduit means 40 and each primary container 16 and 28 is normally blocked by valve means 48 which is situated at the junction of the primary conduit means 40 and each of the primary containers 16 and 28. The valve means 48 serves to retain the desired supply of anticoagulant solution in the containers 16 and 28 prior to use and also acts as a fluid control mechanism during the course of the blood collection procedure. The valve means 48 may be variously constructed, In the illustrated embodiment, however, the valve means 48 takes the form of a ball valve which is sealingly lodged in the fluid path and which can be manually squeezed out of the path and into the associated container 16 or 28 to open fluid flow communication at the desired time.

In order to return a portion of the collected blood components to the donor during the procedure, the system 10 further includes auxiliary conduit means 50 for establishing a fluid path between the primary conduit means 40 and a source 52 of sterile saline or other suitable I.V. solution. In the preferred embodiment, the auxiliary conduit means 50 includes an inline filter and drip chamber 54 of conventional construction.

The source 52 of sterile saline may be variously constructed. In the illustrated embodiment, the source 52 includes a bag 55 made of a plasticized polyvinyl chloride material which contains the sterile saline. However, other

materials which are approved for contact with parenteral solutions may be utilized. A suitable overwrap 56 may be provided to prevent evaporation of the saline from the container source 52 during storage.

In the embodiment illustrated in Fig. 1, the auxiliary conduit means 50 is integrally connected with the saline container 52 as well as with the primary conduit means 40 to thereby form a fluid path which is closed from communication with the atmosphere.

The integral connection between the saline container 52 and the auxiliary conduit means 50 may be variously made. In the embodiment illustrated in Fig. 1, a port block assembly 57 is used, such as the one disclosed in Boggs et al, U.S. Patent application Serial Number 282,894, filed July 13, 1981.

The auxiliary conduit means 50 and the integrally connected saline container 52 constitute, after sterilization, a closed system as judged by standards in the United States.

Like the branch conduit means 24 and 36 and the primary conduit means 40, the auxiliary conduit means 50 is preferably formed of a flexible plastic material, such as plasticized polyvinyl chloride.

In this arrangement, a member 58 (shown in phantom lines in Fig. 1) normally closes fluid communication between the saline container 52 and the auxiliary conduit means 50 to retain saline in the integrally connected container 52 prior to use. As

with closure members 26 and 48, in the illustrated embodiment, the closure member 58 takes the form of an inline, manually frangible valve member.

In order to control fluid flow through the auxiliary conduit means 50 after the frangible valve member 58 is opened, external roller clamps 60 and 62 are provided upstream and downstream of the filter and drip chamber 54.

The system 10 as heretofore described may be sterilized, such as by autoclaving, as a unit.

To commence a blood collection and separation procedure which utilizes the heretofore described system 10, the frangible valve member 58 in the auxiliary conduit means 50 is manually broken. The associated roller clamps 60 and 62 are opened to initially prime the system 10 with saline solution.

After the system is suitably primed, the roller clamp 62 downstream of the filter and drip chamber 54 is closed. This temporarily isolates the auxiliary conduit means 50 from the primary conduit means 40. The needle cover 44 is removed and a venipuncture is made (see Fig. 2). The closure ball valve member 48 associated with the primary container 16 of the first blood collection assembly 12 is squeezed into the container 16. Whole blood thus flows from the donor through the primary conduit means 40 only into the primary container 16.

Referring now principally to Fig. 2, after a unit of whole blood has been collected in the primary container 16, the primary conduit means 40 upstream

of the container 16 is sealed closed. This closure can be accomplished by using a spaced-apart pair of hand seal clips 64, or by the formation of a hermetic, snap-apart seal using a HEMATRON® dielectric sealer (not shown) sold by the Fenwal Division of Travenol Laboratories, Inc. The primary conduit means 40 is thereafter severed between the hand seal clips 64 or along the snap-apart seal. The whole blood-filled primary container 16, along with the rest of the first collection assembly 12, is separated from the system 10.

The primary container 16 is next placed in a centrifugal device (not shown) or the like to separate the collected unit of whole blood into red cells and platelet-and-cyroprecipitate-rich plasma.

During the time the whole blood in the first collection assembly 12 is being processed, it is desirable to reintroduce a flow of saline through the auxiliary conduit means 50 and primary conduit means 40 to flush traces of blood from the fluid paths, as well as to maintain the patency of the needle 42. This is accomplished by opening the heretofore closed roller clamp 62.

Once the whole blood in the primary container 16 of the first collection assembly 12 has been suitably separated, the branch conduit means 24 downstream of the first adjacent transfer container 18 is temporarily closed, such as by use of a hemostat 66 (see Fig. 2). The frangible valve member 26 in the branch conduit means 24 upstream of the

first adjacent transfer container 18 is opened, and the unit of platelet-and-cyroprecipitate-rich plasma is expressed from the primary container 16 into the first transfer container 18, utilizing known manual or automatic expression methods, leaving behind only red cells in the primary container 16.

Referring now principally to Fig. 3, the branch conduit means 24 between the primary container 16 and transfer container 18 is next sealed closed, again utilizing a pair of hand seal clips 65 or the snap-apart hermetic seal. The branch conduit means 24 is then severed between the clips 65 to separate the primary container 16 from the rest of the first collection assembly 12, i.e., the transfer containers 18, 20, and 22.

The platelet-and-cyroprecipitate-rich plasma in the first-utilized transfer container 18 can now be further separated by centrifugation or the like into various therapeutic components. For example, the plasma can be sequentially processed to yield a unit of platelets, a unit of cyroprecipitate, and a unit of source plasma for fractionation purposes. During this step of the procedure, the hemostat 66 (shown in phantom lines in Fig. 3) is sequentially moved along the branch conduit means 24, and these plasma-based components are sequentially transferred from the first transfer container 18 into the other transfer containers 20 and 22. The branch conduit means 24 between the transfer containers 18, 20, and

22, is sequentially sealed after each transfer as heretofore described to permit separation of the individual transfer containers 18, 20, and 22 for storage.

Alternately, the platelet and cyroprecipitate-rich plasma in the transfer container 18 may itself be frozen for later use without further processing.

By sealing the various conduits prior to separation of the primary container 16 and each transfer container 18, 20, and 22, the closed integrity of the system 10 is maintained as measured by applicable United States Standards.

The red cells which remain in the primary container 16 of the first collection assembly 12 are next returned to the donor. To enable this step, the system 10 further includes means 67 (see Fig. 3) for establishing a fluid path between the the primary container 16 and the phlebotomy needle 42 in a manner which does not compromise the sterile closed integrity of the system 10 as a whole.

More particularly, and as is best seen in Figs. 1, 2, and 5, the means 67 includes normally closed first and second connector means 68 and 70 which communicate, respectively, with the auxiliary conduit means 50 and the primary container 16. As is best shown in Figs. 5 and 6, each connector means 68 and 70 includes means 72 for selectively mechanically coupling the first and second connector means 68 and 70 together (as also shown in Figs. 3 and 4) with a

portion 74 of each in facing contact (see also Fig. 7). The facing portions 74 include means 80 operative for melting to form a fluid path through the connector means 68 and 70, but only in response to exposure to an energy source sufficient in itself to effectively sterilize the means 80 as they melt. This constitutes an active sterilization step which occurs simultaneously with the formation of the fluid path.

Furthermore, during the act of melting, the means 80 are preferably operative for fusing together to form a hermetic seal about the periphery of the fluid path. The resulting connection is thus internally sterile and closed from communication with the atmosphere.

The connector means 68 and 70 may be variously constructed and employ different means of operation. However, to meet the desired increased-yield objectives of the system 10, the connector means 68 and 70 each must meet certain operative requirements.

More particularly, each connector means 68 and 70 must (1) normally close the associated subassembly from communication with the atmosphere; (2) be opened only in conjunction with an active sterilization step which serves to sterilize the regions adjacent to the fluid path as the fluid path is formed; and (3) be capable of hermetically sealing the fluid path at the time it is formed.

It has been determined that the sterile connector generally described in Granzow et al U.S. Patents 4,157,723 and 4,265,280 meets all of the above criteria and, for this reason, such a connector is shown in the illustrated embodiment.

The construction and operation of such a connector can be best seen in Figs. 5 through 8. More particularly, each connector means 68 and 70 includes a housing 76 which defines a hollow interior 78 which communicates with its associated part of the system 10. The heretofore described meltable means 80 associated with the facing portions 74 of the connector means 68 or 70 takes the form of meltable wall means, each of which normally seals or closes the associated interior 78 from communication with the atmosphere.

The housing 76 further includes a tubular conduit portion 82 which communicates with the interior 78 and which serves to interconnect the connector means 68 and 70 with a length of a tubing, respectively, 84a and 84b.

While the connector means 68 and 70 may be variously attached to the end of the tubing 84, in the illustrated embodiment, a hermetic, friction fit between the tubular conduit portion 82 is envisioned. An elastic band 85, such as made from a latex material, preferably encircles the outer periphery of the junction to assure a fluid tight, hermetic fit between the tubular portion 22 and the respective tubing 84a and b.

The tubing 84a associated with the first connector means 68 is integrally connected with the upstream side of the filter and drip chamber 54. A roller clamp 63 is provided to control fluid flow through the tubing 84a in this arrangement.

The tubing 84b associated with the second connector means 68 is integrally connected with the primary container 16. To normally prevent fluid flow communication with the interior 78 of the connector means 70 in this arrangement, an inline valve member 86 (shown in phantom lines in Fig. 5) is provided. While the valve member 86 may be variously constructed, in the illustrated embodiment, it takes the form of an inline frangible valve member 86 like that associated with the saline container 52 and branch conduit means 24 and 36.

Alternately, the frangible valve member 86 can form an integral part of the connector housing 76, as is shown in Granzow et al, U.S. Patent 4,265,280.

In the illustrated embodiment, the wall means 80 is fabricated from a radiant energy absorbing material. It is thus operative for melting in response to exposure to a source of radiant energy. Furthermore, the material from which the wall means 80 is constructed is purposefully preselected so that it melts only at temperatures which result in the rapid destruction of any bacterial contaminant on the surface of the material (i.e., over 200°C). To permit the transmission of

radiant energy through the housing 76 to the meltable wall means 80, the housing 76 is made of a material which does not absorb the particular type of radiant energy selected.

In the preferred embodiment, the wall means 80 is made of a material fabricated from poly(4-methyl-1-pentene), which is sold under the trademark TPX by Mitsui Chemical Company. This material has a crystalline melting point of approximately 235°C, and is further discussed in Boggs et al U.S. Patent 4,325,417. The material of the wall means 80 is colored black so as to absorb infrared radiation. The housing 76 is made of a clear TPX material which is generally transparent to the passage of infrared radiation.

As can be best seen in Fig. 5, the connecting means 72 takes the form of mating bayonet-type coupling mechanisms, which serve to interlock the connector means 68 and 70 together with their radiant energy absorbing wall means 80 in facing contact (see Fig. 7). When exposed to a light-induced melting apparatus 90, which, in the illustrated embodiment, consists of an incandescent quartz lamp 91 focused on the opaque, light-absorbing wall means 80, the radiant energy absorbing wall means 80 melt and fuse together, as can be seen in Fig. 8. In the process of melting, the wall means 80

form a hermetically sealed opening 88 which establishes through the connector means 68 and 70 a fluid path which is at once sterile and closed to communication with the atmosphere.

As the following Example demonstrates, the utilization of the illustrated connector means 68 and 70 assures a probability of non-sterility which exceeds 10^{-6}.

EXAMPLE

A methanol suspension of 1.5×10^8 Bacillus subtilis var niger (globiguii) spores per milliliter was prepared. This organism was chosen because of its high resistance to dry heat (see Angelotti, et al, "Influence of Spore Masture Content on the Dry Heat Resistance of Bacillus subtilis var niger", Appl. Microbiol., v 16 (5): 735-745, 1968).

Eighty (80) uncoupled sterilized connector members (i.e., forty (40) pairs) identical to the connector means 68 and 70 shown in Figs. 5 through 8, were inoculated with 0.01 milliliter of the B subtilis var niger (globiguii) suspension. This constituted exposure of the associated wall means 80 of each connector member 68 and 70 to approximately one million (i.e., 10^6) spores of the organisms.

Forty (40) of the inoculated uncoupled connectors were each attached to empty, sterile containers. The other forty (40) were each attached

to containers containing a sterile microbiological growth medium (soybean casien digest (SCD) broth). These inoculated pairs of connector members will hereafter be referred to as the Test Connectors.

Sixteen (16) additional uncoupled and sterilized connector members (i.e., eight (8) pairs) were inoculated only with methanol. Eight (8) of the connectors were each attached to empty, sterile containers, and eight (8) were each attached to sterile containers containing the SCD broth. These will hereafter be referred to as Negative Control Connectors.

The Test Connectors were coupled together, forming forty (40) connections between the empty containers and the SCD broth containers. The noninoculated Negative Control Connectors were also coupled together, forming eight (8) connections between the empty containers and the SCD broth containers. Each connection was placed within the light-induced melting apparatus 90 as heretofore described to fuse the membranes together and open a fluid path. The medium was then passed through the connections.

Eight (8) additional and already fused connector members were inoculated as Positive Controls. Two of these connections were inoculated with a theoretical challenge of 10^6 B subtilis var niger (globigii) spores per connection; two were inoculated with a theoretical challenge of 10^4 spores per connection; two were inoculated with a

theoretical challenge of 10^2 spores per connection; and two were inoculated with a theoretical challenge of 10^1 spores per connection. Medium was the flushed through the fluid path of these Positive Control Connectors.

All units were incubated at approximately 32° to 37°C for up to seven days. After incubation, all turbid broths were subcultured to SCD agar and incubated for 18 to 24 hours at approximately 32° to 37°C. The subcultures were examined for the presence of orange colonies, which is characteristic of the indicator organism.

Upon examination of the forty (40) Test Connections, no turbid broths were observed.

All eight (8) Negative Controls also remained negative during incubation.

All eight (8) Positive Controls demonstrated growth of the indicator organism at all inoculum levels.

Attention is next directed principally to Figs. 3 and 4, and to the utilization of the connector means 68 and 70 which have just been described in detail.

To return red cells to the donor, the connector means 68 and 70 are joined together (as shown in detail in Fig. 5). The coupled connector means 68 and 70 are next exposed to the source of infrared radiation by utilizing the light-induced melting 90 apparatus (as shown in detail in Fig. 7). As heretofore described (and as shown in detail in

Fig. 8), the fluid path 88 is established which is at once internally sterile and hermetically closed to communication with the atmosphere.

The frangible valve member 86 associated with the connector means 70 is broken, and the roller clamps 60, 62, and 63 are opened. Red cells from the primary container 16 of the first collection assembly 12, along with saline, are thereby introduced into the auxiliary conduit means 50 through the filter and drip chamber 54 for return to the donor.

As heretofore demonstrated, the closed integrity of the primary container 16, the auxiliary conduit means 50, and the overall system 10 is not compromised by virtue of this connection, as measured against applicable standards in the United States.

After the red cells in the primary container 16 have been returned to the donor, the heretofore opened roller clamp 63, which controls the red cell flow, is closed. Traces of red cells are flushed from the auxiliary and primary conduit means 50 and 40 by the saline.

In the next step, the roller clamps 60 and 62 are both closed to terminate the flow of saline into the primary conduit means 40 and to prevent a backflow of fluids from the primary conduit means 40 into the filter and drip chamber 54. The closed ball valve member 48 associated with the primary container 28 of the second collection assembly 14 is squeezed into the container 28, and whole blood again flows

from the donor through the primary conduit means 40, this time for collection only in the primary container 28 of the second collection assembly 14.

As is next shown in Fig. 4, after a unit of whole blood has been collected in the primary container 28, the primary conduit means 40 upstream of the second collection assembly 14 is sealed closed by another pair of hand seal clips 69 or the formation of a hermetic, snap-apart seal. The primary conduit means 40 is severed between the clips 69 to separate the entire second collection assembly 14 from the system 10. The whole blood collected in the primary container 28 is processed into red cells and the other therapeutic components heretofore discussed with regard to the first collection assembly 12. However, in contrast to the first collection assembly 12, none of the components collected in the second collection assembly 14 is returned to the donor.

This terminates the increased yield blood collection and separation procedure utilizing the system 10 shown in Fig. 1.

It is important to recognize that all of the components which are collected in the first and second collection assemblies 12 and 14 of the system 10 are suitable for prolonged storage, because

utilizing the heretofore described connector means 68 and 70 does not constitute a non-sterile entry of the system 10, when measured by applicable United States Standards. The system 10 remains closed throughout the procedure, despite the return of red cells.

The increased yield collection system 10 permits, during a single procedure, the collection of twice the amount of plasma-based components than can be ordinarily collected utilizing conventional systems and methods. Utilizing the system 10, a blood collection facility can significantly increase its yield of valuable blood components collected without additional donors and without altering the 8-week collection interval in the United States, all with significant savings in time and expense.

For example, by utilizing the system 10 and method heretofore described, a therapeutic dose of ten (10) units of platelets, or a comparable therapeutic dose of another component, can be collected from five individual donors, instead of ten. Overall collection time and expense per unit of collected component are thus cut in half. As a further example, by utilizing any of the system 10 and method heretofore described, the number of more costly and time consuming mobile collections procedures, which are conducted away from the blood processing facility, and which require the return of the whole blood collected to the facility for centrifigation within four hours of collection, can be reduced without adversely effecting the supply of components.

Attention is now directed to the blood collection system 11 which is shown in Fig. 9. Generally, the system 11 includes separate, closed first, second, and third subassemblies, respectively 92, 94 and 96. Each subassembly 92, 94, and 96 can be selectively joined by the operator to another subassembly to form the system 11 in a manner which does not compromise the closed integrity of any of the subassemblies 92, 94, 96 or the formed system 11 as a whole.

The blood collection system 11 may be variously configured according to the operative objectives desired. As shown in Fig. 9, the illustrated system 11 generally shares the same basic elements and objectives of the increased yield blood collection system 10 shown in Fig. 1. Elements which are common to the embodiment shown in Fig. 1 are therefore assigned the same reference numerals in Fig. 9.

More particularly, the first subassembly 92 of the system 11 includes the heretofore described first and second collection assemblies 12 and 14, including connector means 70, and the heretofore described primary conduit means 40 and the phlebotomy needle 42.

The second subassembly 94 of the system 11 includes the heretofore described auxiliary conduit means 50, including connector means 68. Last, the third subassembly 96 of the system 11 includes the

source 52 of saline in the form of the bag 55 which is filled with sterile saline and which is carried within a tear-away overwrap 56.

Connector means as heretofore described enables the physical attachment of the subassemblies 92, 94, and 96 one to another, as well as the establishment of interconnecting sterile fluid pathways between the first, second, and third subassemblies 92, 94, and 96, all in a manner which does not compromise the closed integrity of any subassembly 92 or 94 or 96 or the formed system 11 as a whole.

More particularly, the first subassembly 92 includes a single connector means 93; the second subassembly 94 includes a pair of connector means 95 a and b; and the third subassembly 96 includes a single connector means 97.

Each of these connector means 93, 95a and b, and 97 is constructed the same as the connector means 68 or 70 heretofore described and shown in Figs. 5 through 8. Each includes the meltable wall means 80 as heretofore described, as well as the mating bayonet-type coupling mechanism 72 for mechanically coupling pairs of the connector means 93, 95a and b, and 97 together to bring the wall means 80 into facing contact. Each connector means 93, 95a and b,

and 97 is integrally attached to its associated subassembly 92, 94 and 96 utilizing the same friction fit arrangement which has heretofore been described and which preferably includes the elastic latex band 85.

As can be seen in phantom line Connection A in Fig. 9, the connector means 93 and 95a can be coupled together to physically join the first subassembly 92 with the second subassembly 94. As can be seen in phantom line Connection B in Fig. 9, the connector means 95b and 97 can likewise be coupled together to physically join the second subassembly 94 with the third subassembly 96.

By exposing the coupled pairs of connector means 93, 95a, and 95b, 97 to the radiant energy-induced melting apparatus 90, the associated wall means 80 will melt and fuse together. Sterile, hermetically sealed fluid pathways will be opened to interconnect each of the various subassemblies 92, 94, and 96 together and form the blood collection system 11.

Furthermore, as can be seen in phantom line Connection C in Fig. 9, by later coupling together connector means 68 and 70, the primary container 16 can be interconnected with the auxiliary conduit means 50 during the course of an increased yield blood collection procedure. The system 11, once formed, can thus be utilized in the same manner as the system 10 heretofore described.

The blood collection system 11 in Fig. 9 could also serve to collect source plasma for fractionation purposes. Since it is not essential during the collection of source plasma to maintain the closed integrity of the system 11, in this environment, the connector means 70 associated with the first collection container 16 of the first subassembly 92 could be replaced by a conventional port assembly (not shown) having a normally closed, piercable membrane. In this arrangement, and for the same reasons, the connector means 68 associated with the second subassembly 92 could be replaced by a conventional spike (also not shown) which would serve to puncture the membrane associated with the first collection assembly 12. This would enable the necessary return of red cells from the first collection container 16 to the donor via the second subassembly 92 during the course of the plasmapheresis procedure.

However, in this alternate arrangement, the connector means 93 of the first subassembly 92, the connector means 95a and 95b of the second subassembly 94, and the connector means 97 of the third subassembly 96 would all remain as shown in Fig. 9 to enable each of the subassemblies 92, 94, and 96 to be interconnected in the manner heretofore described.

Attention is now directed to the blood collection system 13 which is shown in Fig. 10. The system 13 generally shares the same basic elements and objectives of each of the first and second collection assemblies 12 and 14 heretofore discussed;

namely, the collection of a unit of whole blood and its separation into various therapeutic components. For the sake of illustration, Fig. 10 shows the system 13 in the configuration of the first collection assembly 12 shown in Figs. 1 and 9, although it should be appreciated that the same arrangement can be utilized for the second collection assembly 14, or virtually any blood collection assembly.

More particularly, as shown in Fig. 10, the system 13 includes the primary container 16 which is integrally connected with the primary conduit means 40. The primary conduit means 40 can communicate with the system 10 shown in Fig. 1 or the system 11 shown in Fig. 9. The primary conduit means 40 can also constitute a donor tube of a blood collection assembly which is unattached to other blood collection assemblies, such as those sold as single BLOOD-PACK® units by Fenwal Laboratories.

The system 13 also includes the branch conduit means 24 heretofore identified. However, in this embodiment, the branch conduit means 24 is configured as a series of interrupted lengths 24a. One interrupted length 24a is integrally connected with the primary container 16, and two interrupted lengths 24a are integrally connected with each transfer container 18, 20, 22. Each interrupted length 24a terminates with a connector means 98 which is constructed the same as the connector means 68 or 70 heretofore discussed.

As is shown in phantom lines in Fig. 10, by coupling selected pairs of these connector means 98 together, and by then exposing the coupled pairs of connector means 98 to the apparatus 90, the operator is able to configure the blood collection assembly 12 or any blood collection assembly, as desired, utilizing only the number and arrangement of transfer containers 18 or 20 or 22 which match the specific collection objectives at hand.

The systems 11 and 13 shown, respectively, in Figs. 9 and 10 each provides a blood collection assembly which comprises a series of initially separate subassemblies which can be easily manufactured, packaged, sterilized, shipped, and stored. The assembly so provided gives the operator the flexibility, not found in conventional blood collection assemblies, to conveniently tailor the configuration of the system to meet the collection objectives of the particular procedure. These significant benefits are achieved without a substantial probability of non-sterility to the system 10, thereby permitting the maximum permissible storage periods for the collected components.

Various of the features of the invention are set forth in the following claims.

CLAIMS:

1. An increased yield blood collection system comprising

a first blood collection assembly including a first primary container, at least one transfer container, and branch conduit means for establishing between said primary container and said transfer container a fluid path which is closed from communication with the atmosphere,

a second blood collection assembly including a second primary container,

primary conduit means for establishing between a phlebotomy needle and each of said first and second primary containers a fluid path which is closed from communication with the atmosphere,

auxiliary conduit means for establishing between said primary conduit means and a source of sterile saline a fluid path which is closed from communication with the atmosphere, and

normally closed first and second connector means communicating, respectively, with said auxiliary conduit means and said first primary container, each of said connecor means including means for selectively mechanically coupling said first and second connector means together with a portion of each in facing contact, said facing

portions including means operative for melting to form a fluid path through said facing portions only in response to exposure to an energy source sufficient to effectively sterilize said meltable means of said facing portions.

2. A system according to claim 1 wherein said meltable means of said facing portions are further operative for fusing together about the periphery of said fluid path during melting to hermetically seal said fluid path.

3. A system according to claim 1 or 2 wherein each of said meltable means of said facing portions is made of a radiant energy absorbing material and melts in response to exposure to a source of radiant energy sufficient to effectively sterilize said meltable means.

4. An increased yield blood collection system comprising

a first blood collection assembly including a first primary container, at least one transfer container, and branch conduit means for establishing between said primary container and said transfer container a fluid path which is closed from communication with the atmosphere,

a second blood collection assembly including a second primary container,

primary conduit means for establishing between a phlebotomy needle and each of said first and second primary containers a fluid path which is closed from communication with the atmosphere,

auxiliary conduit means for establishing between said primary conduit means and a source of sterile saline a fluid path which is closed from communication with the atmosphere, and

first connector means having an interior communicating with said auxiliary conduit means and including wall means for normally closing said interior from communication with the atmosphere,

second connector means having an interior communicating with said first primary container and including wall means for normally closing said interior from communication with the atmosphere,

each of said first and second connector means further including means for mechanically coupling said first and second connector means together with said wall means in facing contact, and

said wall means being further operative for melting only in response to exposure to sterilizing temperatures and, when disposed in said facing contact and exposed to said sterilizing temperatures, for fusing together and forming an opening to establish through said first and second connector means a fluid path which is sterile and closed to communication with the atmosphere.

5. An increased yield blood collection system comprising

a phlebotomy needle,

a source of sterile saline,

a first blood collection assembly including a first primary container, at least one transfer container, and branch conduit means for establishing between said primary container and said transfer container a fluid path which is closed from communication with the atmosphere,

a second blood collection assembly including a second primary container,

primary conduit means for establishing between said phlebotomy needle and each of said first and second primary containers a fluid path which is closed from communication with the atmosphere,

auxiliary conduit means for establishing between said primary conduit means and said source of sterile saline a fluid path which is closed from communication with the atmosphere, and

first connector means having an interior communicating with said auxiliary conduit means and including wall means for normally closing said interior from communication with the atmosphere,

second connector means having an interior communicating with said first primary container and including wall means for normally closing said interior from communication with the atmosphere,

each of said first and second connector means further including means for mechanically coupling said first and second connector means together with said wall means in facing contact, and

said wall means being further operative for melting only in response to exposure to sterilizing temperatures and, when disposed in facing contact and exposed to said sterilizing temperatures, for fusing together and forming an opening to establish through said first and second connector means a fluid path which is sterile and closed to communication with the atmosphere.

6. A system according to claim 1 or 2 or 4 or 5

wherein said branch conduit means integrally connects each of said transfer containers with said primary container.

7. A system according to claim 1 or 2 or 4 or 5

wherein said branch conduit means includes an interrupted first portion having an end integrally connected with said primary container and an opposite end, an interrupted second portion having an end integrally connected with said transfer container and an opposite end, and normally closed first and second connector means communicating, respectively, with said opposite ends of said first portion and said second portion, each of said connector means including means for selectively mechanically coupling said connector means together with a portion of each

in facing contact, said facing portions including means for melting to form a fluid flow path through said facing portions only in response to exposure to an energy source sufficient to effectively sterilize said meltable means of said facing portions.

8. A system according to claim 1 or 2 or 4 or 5

wherein said auxiliary conduit means is integrally connected with said primary conduit means and the source of saline.

9. A system according to claim 1 or 2 or 4 or 5

wherein said auxiliary conduit means includes oppositely spaced end portions and connector means communicating with each of said end portions,

wherein said source of saline includes connector means communicating therewith, and

wherein said primary conduit means includes connector means communicating therewith,

each of said connector means including means for selectively mechanically coupling a selected pair of said connector means together with a portion of each in facing contact, said facing portions including means for normally closing said connector means from communication with the atmosphere and for melting to form a fluid flow path through said facing portions of said selected pair only in response to exposure to an energy source sufficient to effectively sterilize said meltable means of said facing portions.

10. A system according to claim 1 or 2 or 4 or 5

wherein said second blood collection assembly includes at least one transfer container and branch conduit means for establishing between said primary container and said transfer container of said second collection assembly a fluid path which is closed from communication with the atmosphere.

11. A system according to claim 4 or 5

wherein said wall means is made of a radiant energy absorbing material and melts in response to exposure to a source of radiant energy sufficient to effectively sterilize said wall means.

12. A system according to claim 11

wherein said radiant energy is infrared energy.

13. A system according to claim 1 or 2 or 4 or 5

wherein said fluid path formed through said connector means presents a probability of non-sterility to said system which exceeds 10^{-3}.

14. A system according to claim 13

wherein said probability of non-sterility is at least 10^{-6}.

15. A blood collection system comprising,

a blood collection subassembly for collecting blood components from a donor,

an auxiliary subassembly separate from said blood collection subassembly for returning blood components to a donor, and

connector means communicating with said blood collection and said auxiliary subassemblies and operative for normally closing each of said subassemblies from communication with the atmosphere, each of said connector means including means for selectively mechanically coupling said connector means communicating with said blood collection subassembly with said connector means communicating with said auxiliary subassembly with a portion of each of said connector means in facing contact, thereby mechanically coupling said blood collection and auxiliary subassemblies together, said facing portions including means operative for melting to form a fluid flow path through said facing portions, thereby opening fluid communication between said blood collection and auxiliary subassemblies, only in response to exposure to an energy source sufficient to effectively sterilize said meltable means of said facing portions.

16. A system according to claim 15 and further including a third subassembly comprising a source of sterile saline, and connector means communicating with said third subassembly and said auxiliary conduit means and operative for normally closing each of said third and auxiliary subassemblies from communication with the atmosphere, each of said connector means including means for selectively mechanically coupling said connector means communicating with said third subassembly with said connector means communicating with said auxiliary subassembly with a portion of each of

said connector means in facing contact, thereby mechanically coupling said third and auxiliary subassemblies together, said facing portions including means operative for melting to form a fluid flow path through said facing portions, thereby opening fluid communication between said third and auxiliary subassemblies, only in response to exposure to an energy source sufficient to effectively sterilize said meltable means of said facing portions.

17. A system according to claim 15 or 16 wherein said meltable means of facing portions are further operative for fusing together about the periphery of said fluid path to hermetically seal said fluid path.

18. A system according to claim 17 wherein said fluid path formed through said connector means presents a probability of non-sterility to said system which exceeds 10^{-3}.

19. A system according to claim 18 wherein said probability of non-sterility is at least 10^{-6}.

20. A system according to claim 15 or 16 wherein said meltable means of said facing portions are made of a radiant energy absorbing material and melt in response to exposure to a source of radiant energy sufficient to effectively sterilize said meltable means of said facing portions.

21. An increased yield blood collection method comprising the steps of

collecting from a donor a quantity of whole blood in a first blood collection assembly which is closed from communication with the atmosphere,

separating within the closed first collection assembly the red cells and plasma from the whole blood therein collected,

retaining the plasma,

returning the red cells to the donor by means of a normally closed fluid path which can be opened only in response to exposure to an energy source sufficient to effectively sterilize the interior of the fluid path,

collecting from the donor another quantity of whole blood in a second blood collection assembly which is closed from communication with the atmosphere,

retaining the entirety of the quantity of whole blood collected in the second assembly for separation therein into its various therapeutic components.

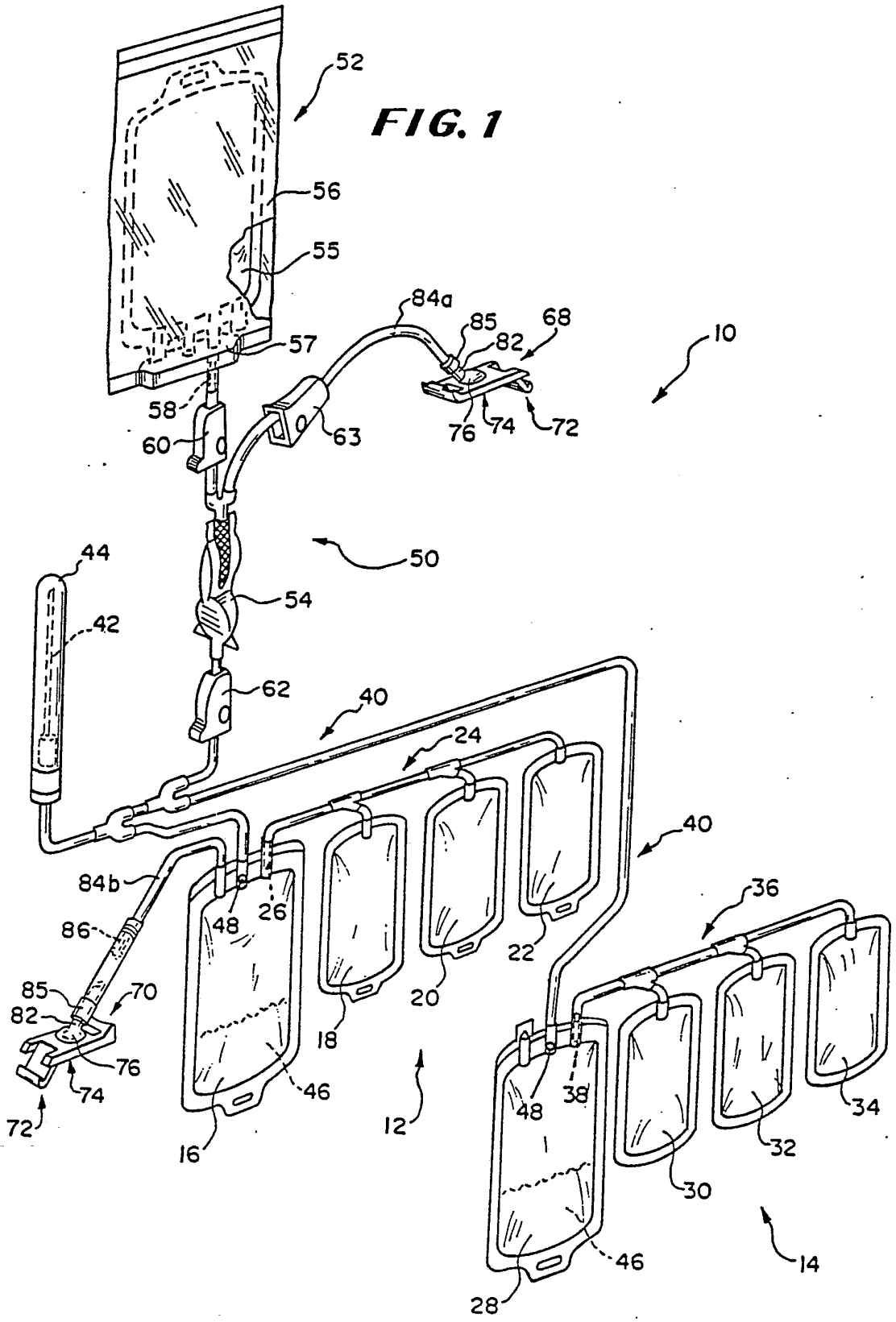
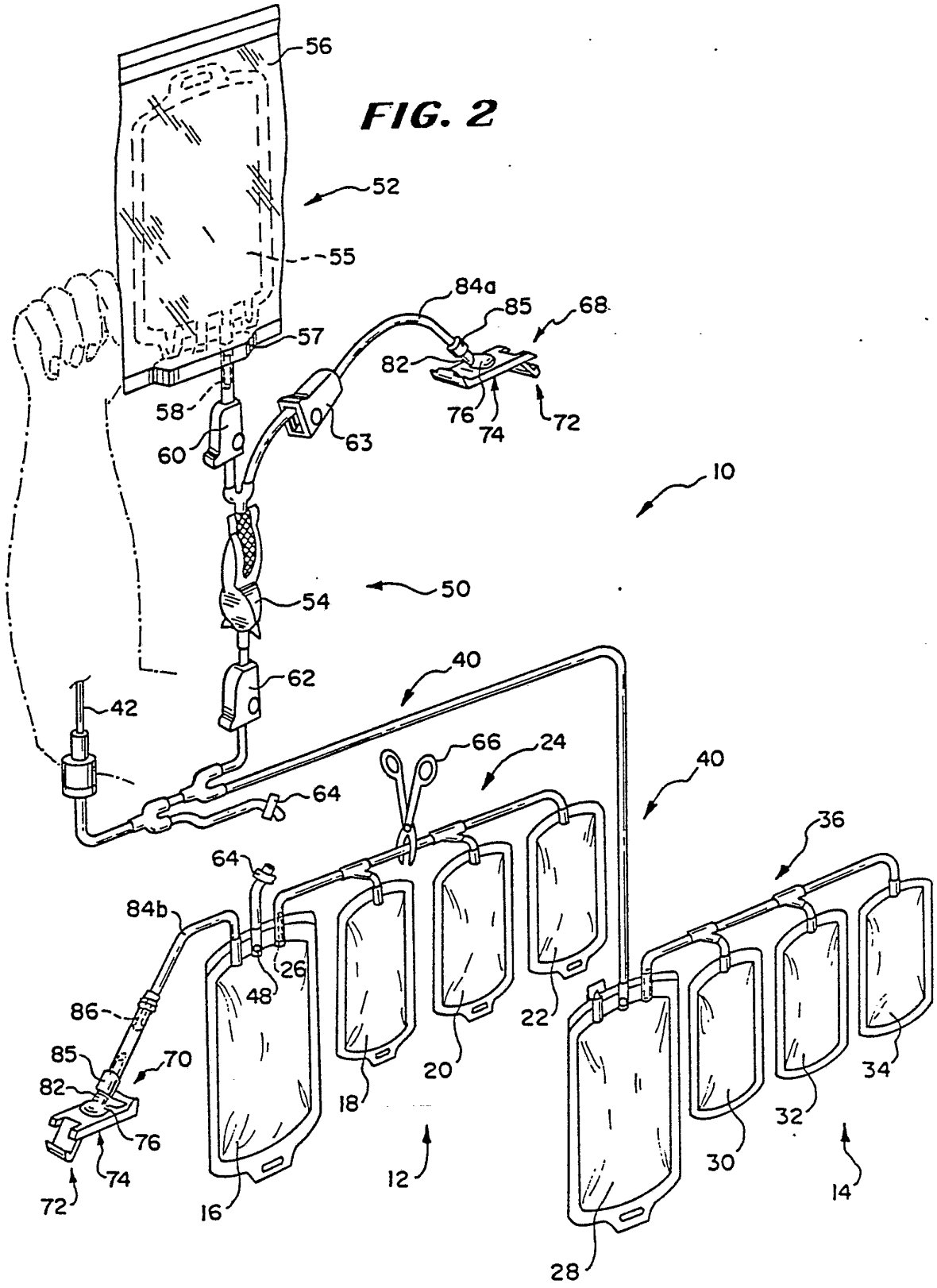


FIG. 1

FIG. 2



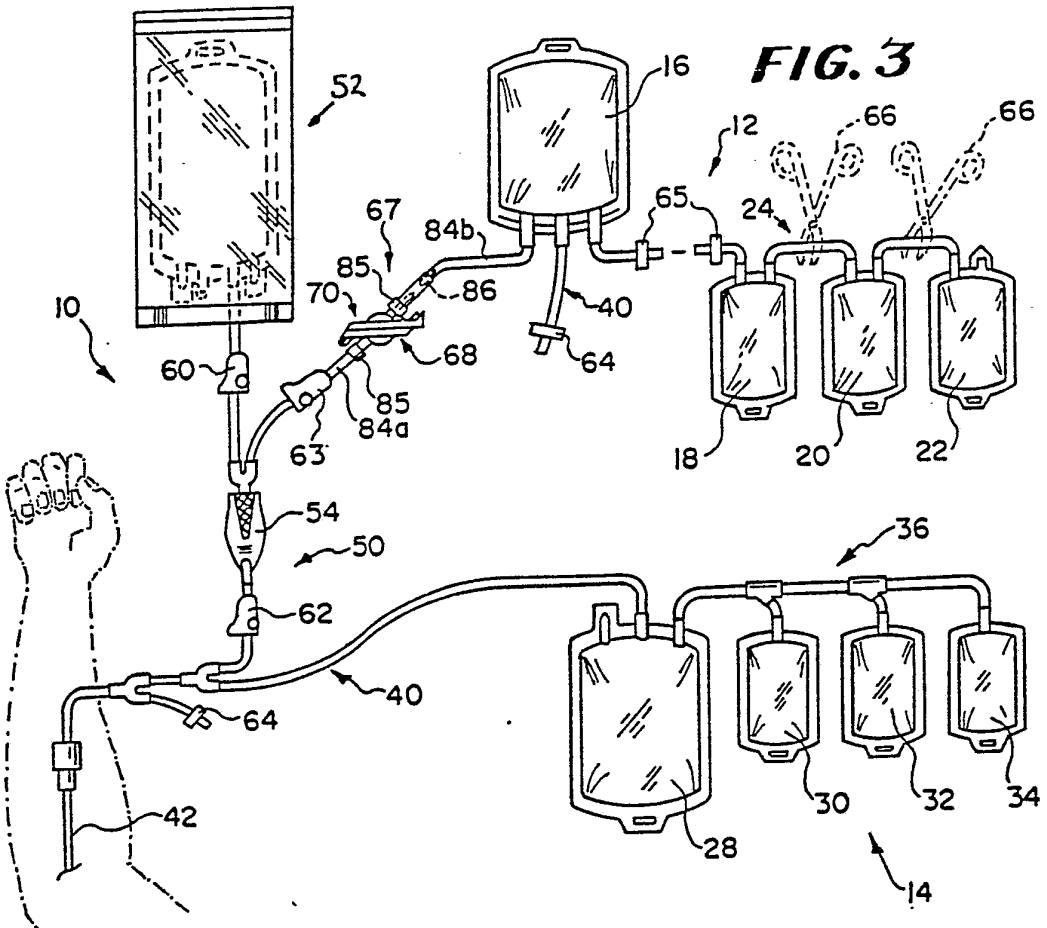


FIG. 3

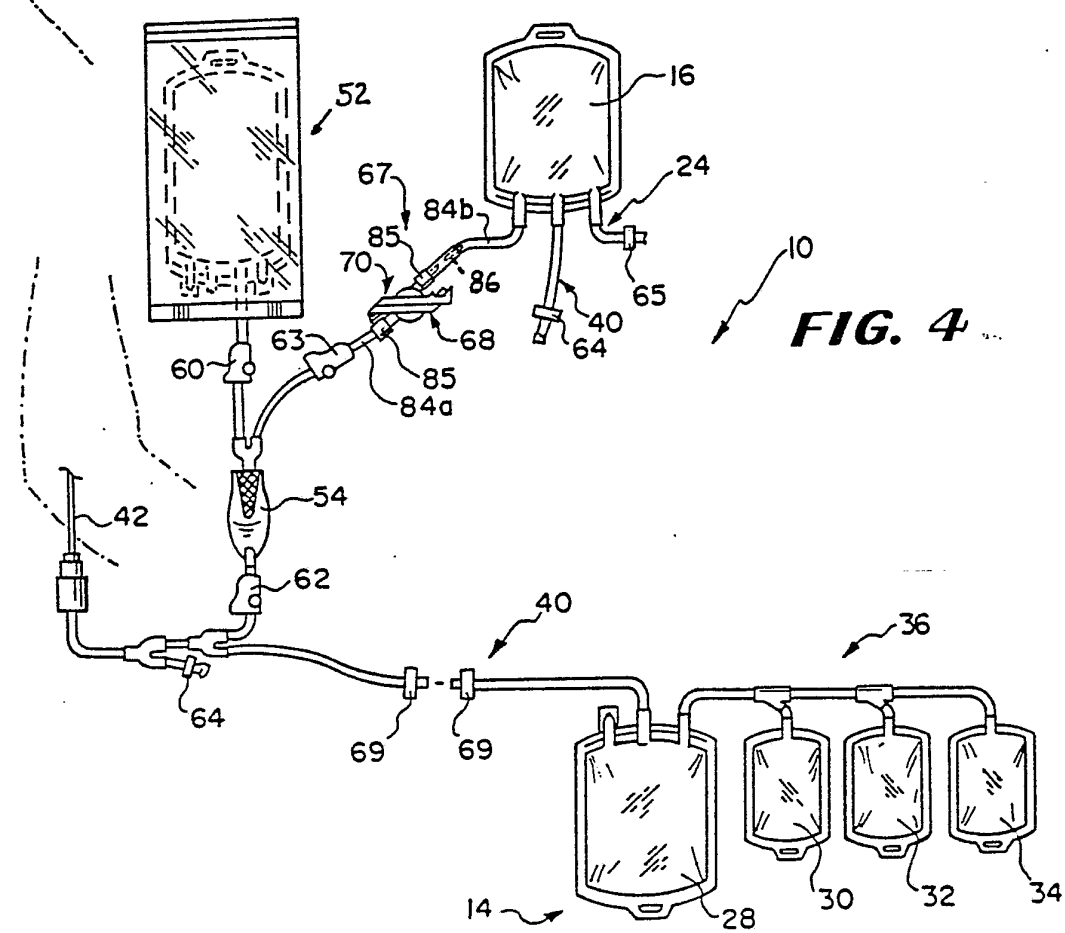


FIG. 4

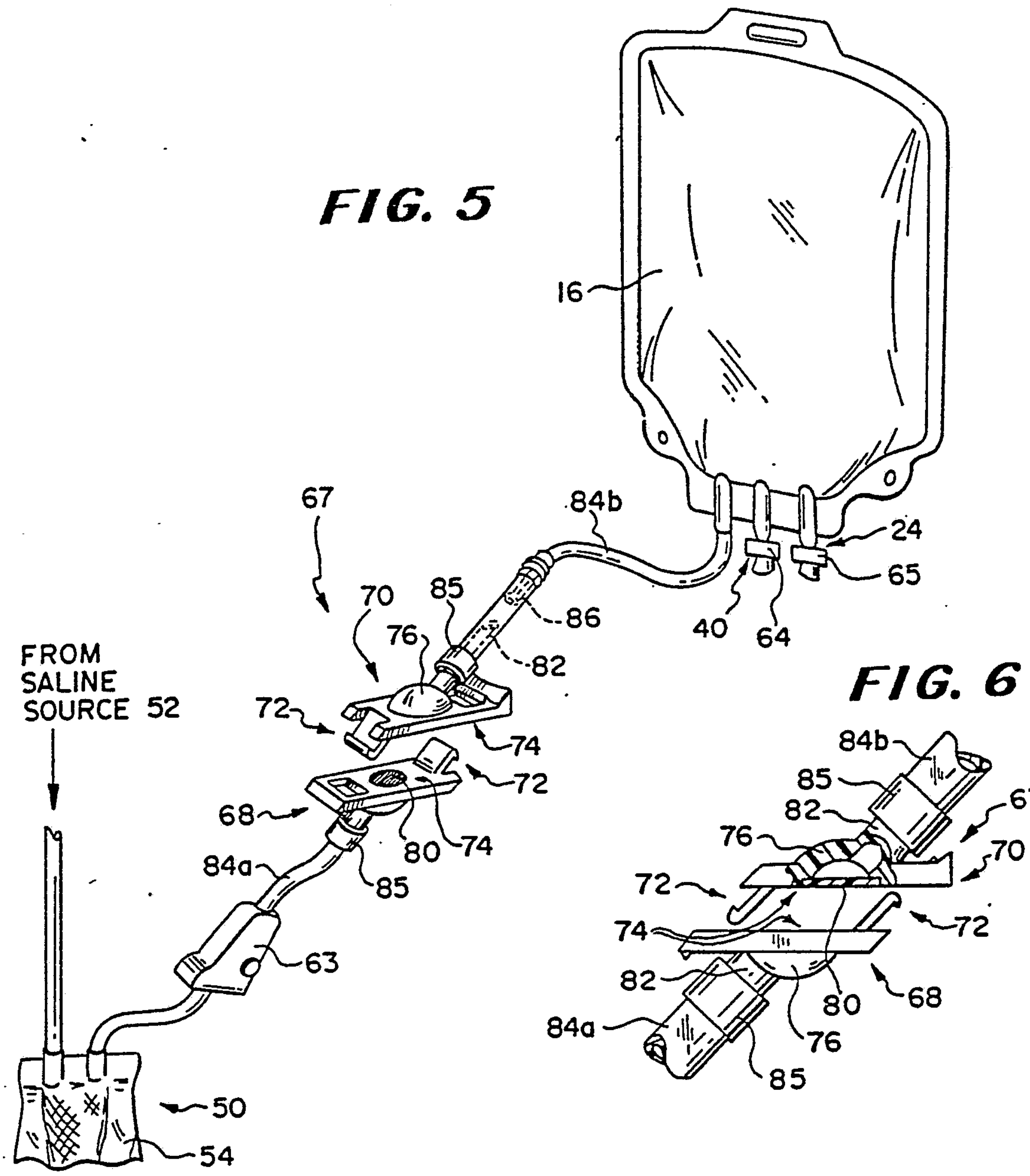


FIG. 5

FIG. 6

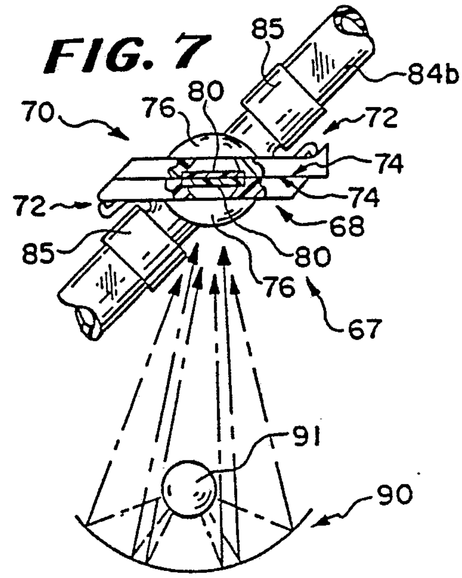


FIG. 7

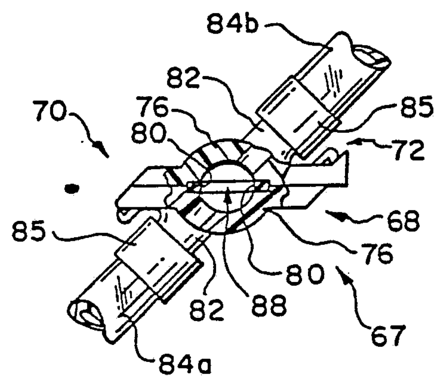


FIG. 8

FIG. 9

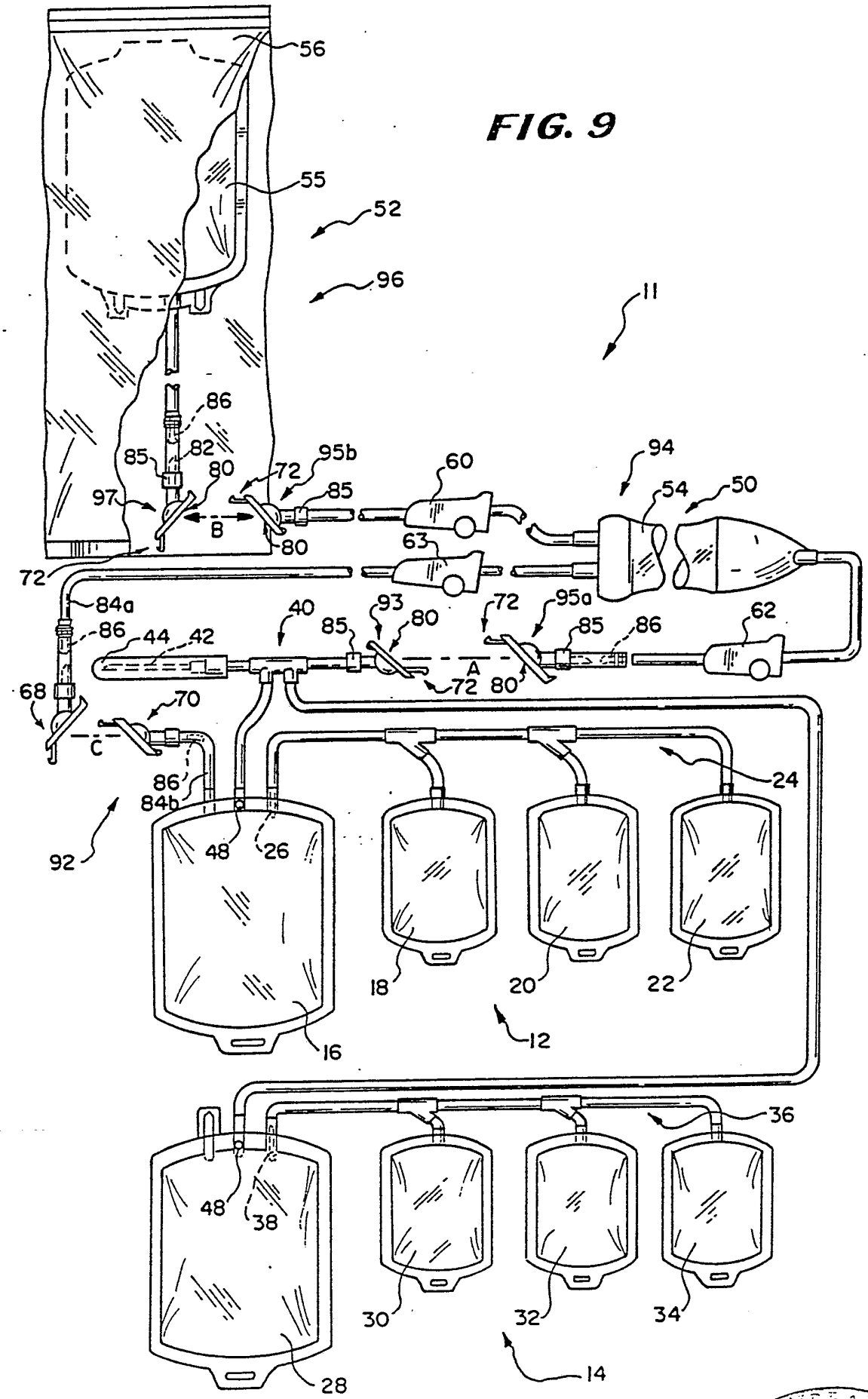
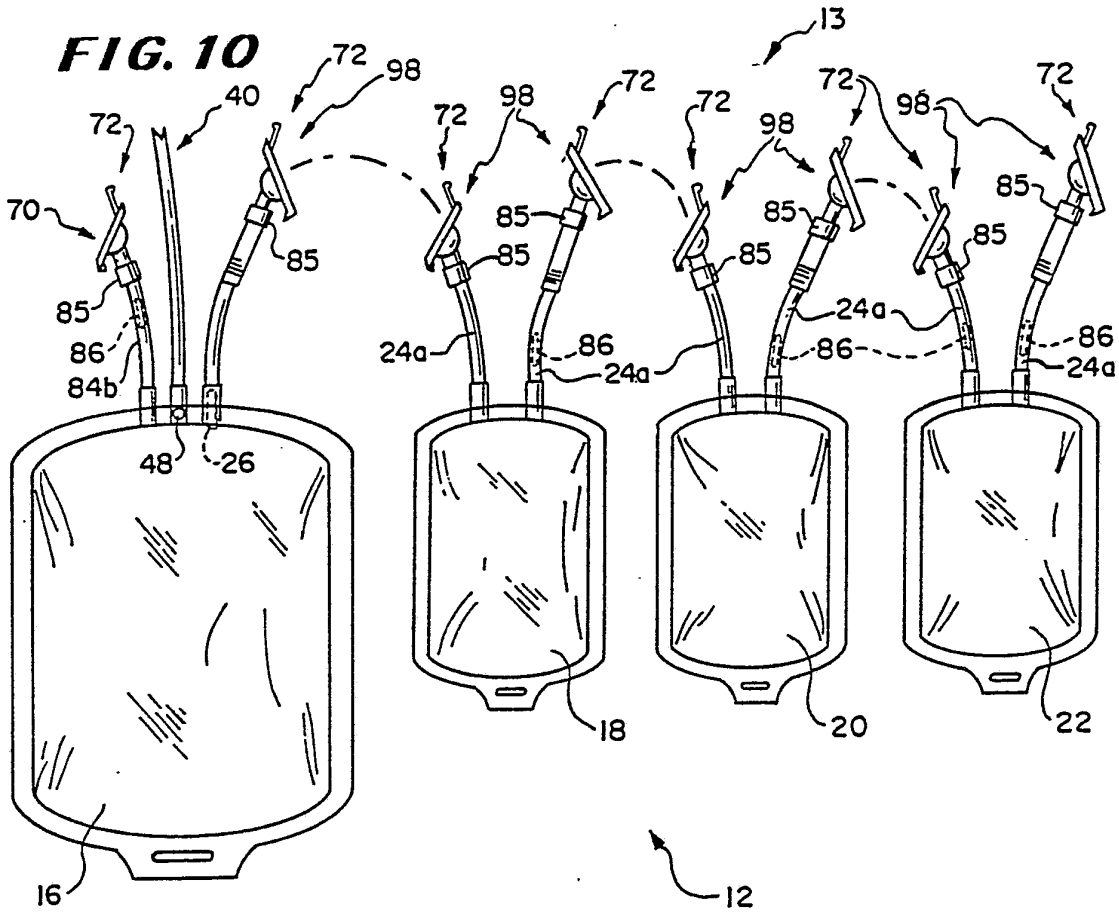


FIG. 10



INTERNATIONAL SEARCH REPORT

International Application No PCT/US82/01150

I. CLASSIFICATION OF SUBJECT MATTER (if several classification symbols apply, indicate all) [3]

According to International Patent Classification (IPC) or to both National Classification and IPC

US: 128/214R, 128/214D, 141/1; IPC: A61M 5/00, B65B 3/04

II. FIELDS SEARCHED

Minimum Documentation Searched [4]

Classification System	Classification Symbols
US	128/214R, 214D 141/1,98

Documentation Searched other than Minimum Documentation to the Extent that such Documents are Included in the Fields Searched [5]

III. DOCUMENTS CONSIDERED TO BE RELEVANT [14]

Category *	Citation of Document, [16] with indication, where appropriate, of the relevant passages [17]	Relevant to Claim No. [18]
Y	US, A, 3,945,380 Published 23 March 1976 (Dabney et. al.)	1-21
Y	US, A, 4,157,723 Published 12 June 1979 (Granzow et. al.)	1-21
Y	US, A, 4,222,379 Published 16 September 1980 (Smith) note column 5, lines 55-59	1-14,21
Y	US, A, 4,265,280 Published 05 May 1981 (Ammann et. al.)	1-21
P,Y	US, A, 4,332,122 01 June 1982 (Williams)	1-14

* Special categories of cited documents: [15]

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

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

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

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

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

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

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

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

"&" document member of the same patent family

IV. CERTIFICATION

Date of the Actual Completion of the International Search [2]	Date of Mailing of this International Search Report [2]
19 November 1982	10 DEC 1982
International Searching Authority [1] ISA/US	Signature of Authorized Officer [20]

FURTHER INFORMATION CONTINUED FROM THE SECOND SHEET

V. ☐ OBSERVATIONS WHERE CERTAIN CLAIMS WERE FOUND UNSEARCHABLE [10]

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

1. ☐ Claim numbers ....., because they relate to subject matter [12] not required to be searched by this Authority, namely:

2. ☐ Claim numbers ....., because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out [13], specifically:

VI. ☒ OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING [11]

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

I. Blood collection system: claims 1-20
II. Blood collection method: claim 21

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

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

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

4. ☒ As all searchable claims could be searched without effort justifying an additional fee, the International Searching Authority did not invite payment of any additional fee.

Remark on Protest

☐ The additional search fees were accompanied by applicant's protest.

☐ No protest accompanied the payment of additional search fees.