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(54) **A DEVICE AND A PROCESS FOR ASEPTIC MIXING OF LIQUID PRODUCTS**

VORRICHTUNG UND VERFAHREN ZUM ASEPTISCHEN VERMISCHEN VON FLÜSSIGKEITEN

DISPOSITIF ET PROCEDE DE MELANGE ASEPTIQUE DE PRODUITS LIQUIDES

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## Description

[0001] The present invention relates to an apparatus and a method for aseptically mixing liquid products. The invention particularly relates to an apparatus and a method for mixing aseptically three or more liquid products for pharmaceutical or nutritive use. Even more particularly, the invention relates to an apparatus and to method for mixing aseptically liquid products for inclusion in a preparation for administering nutrient parenterally, particularly intravenously. The invention also relates to a connection device and to a system for mixing aseptically three or more liquid products.

[0002] Nutrients are very often administered parenterally to patients who are unable to ingest nutrients in the normal way, for some reason or another. The nutrient supply is comprised primarily of three main types of nutrient, namely carbohydrates, amino acids and fat. However, in order to achieve a good nutrient status it is necessary to supply a patient with approximately fifty different nutrients in total on a daily basis. The carbohydrates and amino acids are supplied in the form of solutions, and the fat in the form of an emulsion. These preparations also contain other necessary nutrients, such as electrolytes, trace elements and water-soluble and fat-soluble vitamins. However, it is not normally possible to prepare storage mixtures which contain all three liquid components, since such mixtures will not have sufficient storage stability. Unsuitable reaction products are formed as a result of different reaction processes, at times these reaction products can be harmful to a patient when administered parenterally. For instance, carbohydrates and amino acids may form Maillard reaction products, which can cause toxic secondary effects. The Maillard reaction products often give the solution a yellowish colour, which is undesirable and in many cases unacceptable to the national health authorities. Other components are liable to render fat emulsions unstable and cause the emulsions to break down and form large fat particles, i.e. creaming, or a complete separation of the fat phase.

[0003] Attempts to avoid the problems have been made by administering the three components to the patient separately and by combining the components at a point located only a short distance from the infusion location, with the aid of a branch tube. This method is complicated, however, and it is difficult to meter the individual components in their correct dosages.

[0004] It is also possible to mix the three components in desired proportions immediately prior to their administration and then to infuse the supply immediately before any undesirable reactions are able to occur. In this case, however, it is very often necessary to mix the components in a completely aseptic manner without having access to sterilized locations and without the assistance of personnel who have been especially trained for this purpose. The task of mixing these solutions in a manner which is correct both physically and

chemically while preventing microbial contamination at the same time has been found to present a serious problem to hospital personnel. Among other things, there has been developed and used hitherto an apparatus which is designed for mixing together two liquid products aseptically. This apparatus has been used to mix aseptically a fat emulsion with a ready mix of amino acids and carbohydrates in aqueous solution. Stock mixtures of amino acids and carbohydrates are not really suitable, however, for the reasons aforementioned. No apparatus has been available which will enable three or more liquid products to be mixed aseptically. This drawback is eliminated by means of the present invention.

[0005] The present invention provides an apparatus in accordance with claim 1 for mixing three liquid products aseptically.

[0006] According to the invention, there is also provided a connection device in accordance with claim 2 for mixing together three or more liquid products.

[0007] The invention also relates to a method in accordance with claim 4, using said device for mixing three or more liquid products aseptically.

[0008] According to one preferred embodiment of the method, at least the product in the last container is pre-packed at a pressure beneath atmospheric pressure and the first product container is caused to communicate with the surrounding atmosphere through the medium of a sterilizing filter, so that the products will be driven or drawn successively through the series of product containers under the influence of the outer atmospheric pressure and mixed mutually together and are finally collected in the last product container as a final mixture. Preferably, all products are packed in their respective containers at a pressure beneath atmospheric pressure.

[0009] The invention also relates to a system in accordance with claim 3 for producing an aseptic mixture of three or more liquid products.

[0010] The invention will now be described in more detail with reference to the accompanying drawings, in which Figure 1 is a sectioned view of the first pointed connection device according to the invention; Figure 2 is a side view of the connection device shown in Figure 1; Figure 3 is a sectioned view of the second pointed connection device according to the invention; Figure 4 is a side view of the second connection device; Figure 5 illustrates an additional, intermediate connection device used in accordance with one embodiment of the invention; and Figure 6 illustrates schematically the construction of the inventive system.

[0011] Figs. 1 and 2 illustrate the first connection device, generally referenced 1, which includes a pointed part 2 and two mutually separate and generally parallel through-passing passageways 3 and 4. One end of the first passageway 3 opens at 5 into the pointed end 2, while the other end of the first passageway communicates at 6 with the surrounding atmosphere through a

sterilizing filter 7. The Figure shows the sterilizing filter 7 mounted in a chamber 8 and held in position by a cover member 9 provided with openings 10 in communication with the surrounding atmosphere. The sterilizing filter may, of course, be arranged in other ways.

[0012] The second passageway 4 also opens at one end into the pointed part 2, at 11, while the other end of the second passageway 4 is connected at 12 to a connection line (not shown) by means of a connection 13.

[0013] Figs. 3 and 4 illustrate the second connection device, generally referenced 21, which includes a first pointed part 22 and a second pointed part 23, said pointed parts normally extending in mutually opposite directions, although this is not strictly necessary. The second connection device 21 includes two mutually separate and generally parallel passageways 24 and 25. One end of the first passageway 24 opens at 26 into the first pointed part 22, while the other end of said passageway is connected at 27 to a connection line (not shown) from the first connection device 1, by means of a connection 28.

[0014] A first end of the second passageway 25 also opens into the first pointed part 22, at 29, and the other end of the passageway opens out adjacent the second pointed part 23, at 30.

[0015] Figure 5 is a sectional view of an intermediate, pointed connection device, generally referenced 41, which is used in the embodiment of the invention in which four or more liquids are to be mixed together. This intermediate connection device includes a pointed part 42 and two mutually separate and generally parallel through-passing passageways 43 and 44. One end 45 and 46 of respective passageways 43 and 44 opens into the pointed end-part 42, while the other ends 47 and 48 of respective passageways connect with connections 49 and 50 for coupling the intermediate connection device in the connection line (not shown) between the first and the second connection devices 1 and 21.

[0016] It will be understood that several intermediate connection devices 41 may be coupled sequentially in the connection line, one such intermediate connection device being required for each additional liquid product to be mixed in accordance with the invention, over and above the first-mentioned three products.

[0017] The pointed ends of the connection devices illustrated in Figures 1-5 and the passageways contained therein shall be protected against mechanical damage and primarily against microbial contamination, by means of protective hoods or caps placed over respective points. These protective hoods will preferably be airtight and may also include a means which is destroyed when the hood is removed, so that the hood cannot subsequently be replaced without it being evident that the hood has been removed (tamper-proof). The design of such protective hoods and such safety devices lies within the competence of one of normal skill in this art. The protective hood shall not be removed from its respective point until immediately prior to insert-

ing the point through the penetrable product container closure means. The protective hoods have not been shown in the drawings, for the sake of clarity.

[0018] Figure 6 is a schematic illustration of an inventive system for mixing three liquid products aseptically. The first product 51 is contained in the first product container 52, and the second product 53 is contained in the second product container 54. The third product 55 is contained in a product container 56 whose empty volume 57 is sufficiently large to accommodate the products 51 and 53 arriving from the containers 52 and 54 respectively.

[0019] The three containers 52, 54 and 56 are closed by means of penetrable closure means 58, 59 and 60 respectively. These closure means may be of a conventional kind, consisting in a rubber membrane which closes the container opening and which is held in place by a metal capsule. This capsule contains in the central region of the closure an opening which exposes the rubber membrane so as to enable said membrane to be pierced by a pointed connection device. The opening in the metal capsule can be protected from damage and from bacterial contamination during storage and transportation with the aid of a metal or plastic protective covering. It will be obvious to those skilled in this art that other penetrable closure means are conceivable.

[0020] Figure 6 shows schematically a first pointed connection device 1 according to Figures 1 and 2 inserted through the penetrable closure means 58 of the container 52. The passageways 3 and 4 of the connection device 1 connect at one end with the interior of the container 52 at the pointed end 2 of the device. The other end of the passageway 3 communicates with the surrounding atmosphere through a sterilizing filter at 6, while the other end of the passageway 4 connects at 12 to a connection line 61 extending to a second connection device 21 of the kind illustrated in Figures 3 and 4.

[0021] The pointed end 22 of the connection device 21 is inserted into the container 54 through the penetrable closure means 59, while the pointed end 23 of said connection device 21 is inserted into the container 56 through the penetrable closure means 60. The orifice 27 of the first passageway 24 of said connection device connects with the connection line 61 extending from the first container 52. The second passageway 25 connects the interior of the second container 54 with the interior of the third container 56. Thus, there is obtained an open connection from the surrounding atmosphere through the sterilizing filter 7 (Figure 1) and successively through the containers to the third, and in the illustrated case the last container 56. Thus, when subjected to the influence of a suitable driving force, liquid product 51 is able to flow from the container 52 and through the container 54 while mixing with the liquid product 53 contained therein, and finally into the conductor 56 in which all three products are mixed together to form a final mixture.

[0022] When four or more liquid products are to be

mixed together, one or more intermediate connection devices of the kind shown in Figure 5 are coupled in the connection line 61 with the aid of their two connectors 49 and 50. The pointed part 42 of this connection device, which includes the passageways 43 and 44, is then inserted through a penetrable closure means of a product container of similar type to the containers 52 and 54.

**[0023]** The last container 56 in line which accommodates the final mixture of said liquid products, including the product 55, shall have a volumetric capacity sufficient to accommodate the final mixture. The final container 56 will thus have a significant empty volume 57 prior to the mixture components having been transferred to this final container. This empty volume shall be under a vacuum or a pressure beneath atmospheric pressure. It is this subpressure that generates the driving force in the mixing process, as will be described in more detail below.

**[0024]** The products contained in the containers 52 and 54, and also in any other additional container arranged upstream of the final container 56 will also preferably be contained under a vacuum or a subpressure. However, subpressure conditions are not necessary in the case of these containers, and the containers may be under atmospheric pressure or a moderate overpressure. When an overpressure or subpressure prevails in one or more containers, with the exception of the last container, this overpressure must be equalized through the sterilizing filter. In order to achieve this, it is necessary for the pointed ends of the connection devices to lie above the surfaces of the liquid in respective containers. The products are often packed under some suitable protective gas, such as nitrogen, and not under air, in order to prevent the oxidation of sensitive components.

**[0025]** The connection line 61 extending between the two connection devices 1 and 21 may have the form of a hose connection between the connectors 13 and 28 of respective connection devices, optionally with additional, intermediate connection devices 41 coupled in the connection line. However, it is preferred that the connection line 61 and the two connection devices 1 and 21 are permanently connected together in the manufacture of the mixing apparatus, such as to form a unit. This combination of connection devices and connection line can then be combined with a suitable container holding device which functions to hold the three product containers 52, 54 and 56 and their respective connections and connecting line in the form of a unit. Such a unit can be handled more easily in the mixing process than separate product containers.

**[0026]** The inventive method of aseptically mixing three liquid products is carried out in the following manner:

**[0027]** The two connection devices 1 and 21 will have been connected together by means of the connecting line 61 and all pointed parts 2, 22 and 23 of respective

connection devices will have been covered with protective hoods (not shown) which are impervious to air and bacteria and therewith prevent air and bacteria from entering the passageways 3, 4 and 24, 25 of respective devices 1 and 21, as before described. The protective hood is now removed from the pointed part 2 of the connection device 1 and the point is inserted through the penetrable closure means 58 of the product container 52. If the product 51 in the container 52 is under subpressure, the interior of the container will now assume atmospheric pressure by virtue of ambient air being able to flow into the device 1, through the sterilizing filter 7 and the passageway 3.

**[0028]** The protective hood covering the pointed part 22 of the connection device 21 must not be removed before the subpressure in the container 52 has been equalized. This is important in ensuring aseptic conditions in the container 52. If the hood covering the point 22 is removed prematurely while a subpressure still prevails in the container 52, unfiltered air will be sucked in through the passageway 24 and the connection line 61 and enter the container 52 and therewith contaminate the container contents 51.

**[0029]** When the subpressure in the container 52 has been equalized, the hood covering the point 22 of the connection device 21 is removed and the point is inserted through the penetrable closure means 59 of the container 54. The subpressure prevailing in this container is thereafter equalized by air that flows into the connection device 1 through the sterilized filter 7 and from there into the product container 52, while displacing part of its content 51 into the container 54. The hood covering the point 23 of the connection device 21 may not be removed before the pressure has been equalized. This is important in preventing unfiltered air from flowing into the product container 54 through the passageway 25 and contaminating the content 53 of said container.

**[0030]** When the subpressure in the container 54 has been equalized, the hood is removed from the point 23 of the connection device 21 and said point is inserted through the penetrable closure means 60 of the last container 56 in line. The subpressure prevailing in the mixing chamber 57 in the container 56 will now draw in product 53 from the container 54 by suction, at the same time as the product 51 from the container 52 will pass through the container 54 and enter the final container 56, in which the three products are mixed. The subpressure prevailing in the final container 56 will also be equalized by air drawn by suction through the sterilizing filter 7 and passing through the containers 52 and 54 and the connection line 61.

**[0031]** When four or more liquid products are to be mixed together, the mixing process is analogous with that described above. The containers are connected successively by means of the pointed connection devices, it being ensured that the subpressure in a connected container has been equalized before removing

the protective hood from the point of the next following connection device and a liquid connection is established with the next following container.

[0032] As mentioned earlier, it is only necessary for a subpressure to prevail in the final container. This subpressure must be of sufficient magnitude to drive the remaining liquid products into the final container. The pressure in the preceding containers may initially be atmospheric pressure, whereby there is no danger of non-filtered air being sucked into the containers. Notwithstanding, it is preferable to remove the protective hood from a respective point on a connection device immediately prior to the point being inserted through the penetrable closure means of the container concerned. This gives added assurance against non-filtered air coming into contact with anyone of the products and contaminating the same.

[0033] When the mixing of the products has been completed and the pressure in the final container 56 has been equalized, the container can be removed from the connection device 21 and the finished mixture administered in a conventional manner, for instance by infusion or by injection. For added safety, it is recommended that the mixture is administered as quickly as possible after being produced, in order to reduce the risk of reactions taking place between the component products, these reactions possibly giving rise to undesirable reaction products. Furthermore, the finished mixture will preferably be stored in a dark and cool environment, until it can be administered.

[0034] Naturally, it is necessary to carry out the mixing process under hygienically and unimpeachable conditions. Thus, the penetrable closure means will preferably be washed with a disinfectant, e.g. alcohol, prior to inserting the point of a connection device therethrough. The actual connection devices and associated connecting line will preferably be disposable, i.e. intended for one-time use only and stored in a sterilized package prior to use, for instance a package that has been sterilized by ionizing radiation. The simple method and apparatus provided by the invention enable the products to be mixed by hospital personnel who have no particular training in this regard without any appreciable risk of bacterial contamination.

[0035] The components of the inventive apparatus may be made of a material that is normally used within known techniques for the aseptic handling of liquids. The product containers are conveniently conventional glass or plastic bottles intended for injection or infusion preparations. The pointed connection devices are conveniently made of a metal and/or plastic material conventionally used in this field. It is important that the materials can be sterilized, for instance by autoclaving or with the aid of gas or radiation. Since the components will preferably be intended for one-time use only, the cost of the components is also important. A skilled person who has knowledge of the invention will find no difficulty in choosing suitable materials and determining

the construction of the components in detail.

[0036] The present invention thus provides a simple technical solution to the problem of mixing three or more liquid products under aseptic conditions without risk of contamination. This is of particular value when, e.g., mixing all of the nutrients required for a complete intravenous nutrient supply.

## Claims

1. An apparatus for mixing three or more liquid products together aseptically, characterized by

a) a first pointed connection device (1) for insertion through a penetrable closure means (58) of a first product container (52), wherein the connection device includes two separate, generally parallel through-going passageways (3, 4) of which the first one (3) opens at one end into the pointed part (2) of the connection device (1) and at the other end communicates with the surrounding atmosphere through a sterilizing filter (7), and wherein the second passageway (4) also opens at one end into the pointed part (2) of the connection device (1) and is connected to a connection line at its other end; and

b) a second, double-pointed connection device (21) wherein a first pointed part (22) of said device is arranged for insertion through a penetrable closure member (59) of a second product container (54) and includes two separate, generally parallel through-penetrating passageways (24, 25) of which a first passageway (24) opens at one end into the first pointed part (22) and the other end of said passageway (24) is connected to the connection line (28) extending from the first connection device (1), and wherein the second passageway (25) also opens at one end into the first pointed part (22) and at the connection device (20), this second pointed part (23) being arranged for insertion through a penetrable closure means (60) of a final product container (56) in which a mixture of all products is collected, and furthermore, when four or more liquid products are to be mixed;

c) one or more additional, intermediate, pointed connection devices (41), each having a hollow point (42) for insertion through a penetrable closure means of an intermediate liquid product container, wherein each said point (42) includes two separate, generally parallel passageways (43, 49) which both open into the pointed end (42) of the connection device and which are connected at their other open ends

to a respective connecting line extending from a preceding or to a subsequent connection device.

2. A connection device (21) for mixing three or more liquid products, characterized by a first, hollow pointed part (22) which is arranged to pierce a penetrable closure means of a liquid product container, wherein the pointed part (22) includes two separate, generally parallel, through-going passageways (24, 25), both of which open into the end of the pointed part (22), wherein the first passageway (24) is connected to a connecting line (28) for the supply of liquid product or product mixture to be mixed with the liquid product in said container, and wherein the second passageway (25) opens into the end of a second pointed part (23) which is arranged to pierce a penetrable closure means of a final container for an additional liquid product with which the other liquid products are to be mixed finally to form a final mixture.
3. A system for aseptically mixing three or more liquid products together, characterized in that the system includes
  - a) a container (52) which contains a first liquid product (51) which is enclosed in the container with the aid of a penetrable closure means (58);
  - b) a first, pointed connection device (1) which includes a first through-going passageway (3) which opens at one end (5) into the pointed part (2) of the connection device and is connected with the ambient atmosphere at its other end through the medium of a sterilizing filter (7), and which also includes a second, through-going passageway (4) which is generally parallel with the first passageway (3) and separate therefrom, wherein one end of the second passageway opens into the pointed part (2) of the connection device and the other end (12) is connected to a connection line (13), wherein the pointed part (2) of the first connection device (1) is inserted through the penetrable closure means (58) of the first container (52) to achieve fluid connection therewith;
  - c) a container (54) which contains a second liquid product (53) which is enclosed in the container by means of a penetrable closure means (59);
  - d) a second double-pointed connection device (21) which includes a first through-going passageway (24) which opens at one end (26) into the first pointed part (22) of the connection

device and is connected at its other end (27) to the connection line (28) extending from the first connection device (1), and also includes a second through-going passageway (25) which is generally parallel with the first passageway (24) and opens at one (29) end into the first pointed part (22) of the connection device (21) and opens at its other end (30) into the second pointed part (23) of said connection device (21), wherein the first pointed part (22) is inserted through the penetrable closure means (59) of the second product container (54) to achieve fluid connection therewith; and

e) a final product container (56) in which the product is contained at a pressure below atmospheric pressure and which includes a penetrable closure means (60) through which the second pointed part (23) of the second connection device (21) is inserted to achieve fluid connection with said product container (56), wherein the volumetric capacity of the container is sufficient to accommodate the mixture of liquid products; and furthermore, when four or more liquid products are to be mixed;

f) one or more additional, intermediate pointed connection devices, (41) each having a hollow pointed part (42) for insertion through a penetrable closure means of an intermediate liquid product container, wherein each said pointed part (42) includes two separate, generally parallel passageways (43, 44) which both open into the pointed part (42) of the connection device (41) and whose other end-openings (47, 48) are each connected to a respective connecting line (49, 50) extending from a preceding or to a subsequent connection device, and wherein the pointed part (42) of each of said intermediate connection devices (41) is inserted through a penetrable closure means of an additional, intermediate liquid product container to provide a liquid connection with said product container.

4. A method for aseptically mixing three or more liquid products, characterized in that each of the products is contained in an individual product container (52, 54, 56), wherein the containers are connected together in series and product or product mixture from each of the containers, beginning with the first container (52) in the series, is caused to flow successively under aseptic conditions to the next container in line and there to mix with the product in said container, until a final mixture of all products has been collected in the last container (56) in the series, the last and second last containers being connected by the connecting device according to

claim 2.

5. A method according to claim 4, characterized in that at least the product (55) in the last product container (56) in line is prepacked in the container at a pressure below atmospheric pressure; and in that the first product container (52) is placed in communication with the surrounding atmosphere via a sterilizing filter (7), such that the products will be driven through the series of product containers through the influence of the surrounding atmospheric pressure while mutually mixing the contents of the containers, said products being collected finally as a final mixture in the last product container (56) in line.
6. A method according to claim 4 or 5, characterized in that the first product container (52) is first connected to the connecting line (61) extending to the second container (54) and to the surrounding atmosphere, and the first container (52) is brought to atmospheric pressure while the connecting line (61) to said second container (54) is closed, whereafter the connecting line (61) to the second container (54) is opened after the pressure in the first container (52) has assumed atmospheric pressure, and the second container (54) is brought to atmospheric pressure while the connecting line to the third container is held closed, whereafter the connecting line to the following container is opened when the second container has assumed atmospheric pressure and said following container is brought to atmospheric pressure, wherein the process is repeated successively for each of the product containers in the series down to the last product container (56) in line, wherein the atmospheric pressure prevailing in the preceding product containers to the final product container in line so as to obtain a final product mixture in said container.
7. A method according to any one of claims 4-6, characterized by mixing together three liquid products.

#### Patentansprüche

1. Vorrichtung zum aseptischen Zusammenmischen von drei oder mehr flüssigen Produkten, **gekennzeichnet durch**

a) eine erste spitze Verbindungsvorrichtung (1) zum Einführen durch eine durchstoßbare Verschlußeinrichtung (58) eines ersten Produktbehälters (52), wobei die Verbindungsvorrichtung zwei getrennte, allgemein parallele, durchgehende Durchführungen (3, 4) aufweist, von denen sich die erste (3) an ihrem einen Ende in den spitzen Teil (2) der Verbindungsvorrichtung (1) öffnet und an dem anderen Ende durch ein

Sterilisierfilter (7) mit der umgebenden Atmosphäre kommuniziert, und wobei die zweite Durchführung (4) sich ebenfalls an dem einen Ende in den spitzen Teil (2) der Verbindungsvorrichtung (1) öffnet und an ihrem anderen Ende mit einer Verbindungsleitung verbunden ist; und

b) eine zweite, mit Doppelspitze versehene Verbindungsvorrichtung (21), wobei ein erster spitzer Teil (22) der Vorrichtung zum Einführen durch ein durchstoßbares Verschlußelement (59) eines zweiten Produktbehälters (54) ausgebildet ist und zwei getrennte, allgemein parallele, durchgehende Durchführungen (24, 25) aufweist, von denen sich eine erste Durchführung (24) an dem einen Ende in den ersten spitzen Teil (22) öffnet und das andere Ende der Durchführung (24) mit der Verbindungsleitung (28) verbunden ist, die sich von der ersten Verbindungsvorrichtung (1) wegstreckt, und wobei sich die zweite Durchführung (25) ebenfalls an einem Ende in den ersten spitzen Teil (22) öffnet und sich an dem anderen Ende in den zweiten spitzen Teil der Verbindungsvorrichtung (21) öffnet, wobei dieser zweite spitze Teil (23) zum Einführen durch eine durchstoßbare Verschlußeinrichtung (60) eines abschließenden Produktbehälters (56) ausgebildet ist, in dem eine Mischung aus allen Produkten gesammelt wird; und

c) ferner, wenn vier oder mehr flüssige Produkte gemischt werden sollen, durch eine oder mehrere zusätzliche, zwischengeordnete, spitze Verbindungsvorrichtungen (41), die jeweils eine hohle Spitze (42) zum Einführen durch eine durchstoßbare Verschlußeinrichtung eines zwischengeordneten Behälters für flüssiges Produkt aufweisen, wobei jede Spitze (42) zwei getrennte, allgemein parallele Durchführungen (43, 49) aufweist, die sich beide in das spitze Ende (42) der Verbindungsvorrichtung öffnen und die an ihren anderen offenen Enden mit einer jeweiligen Verbindungsleitung verbunden sind, die sich von einer vorausgehenden bzw. zu einer nachfolgenden Verbindungsvorrichtung erstreckt.

2. Verbindungsvorrichtung (21) zum Mischen von drei oder mehr flüssigen Produkten,

#### **gekennzeichnet durch**

einen ersten hohlen spitzen Teil (22), der zum Durchstoßen einer durchstoßbaren Verschlußeinrichtung eines Behälters für flüssiges Produkt ausgebildet ist, wobei der spitze Teil (22) zwei getrennte, allgemein parallele, durchgehende Durchführungen (24, 25) aufweist, die sich beide in das Ende des spitzen Teils (22) öffnen, wobei die erste Durchführung (24) mit einer Verbindungs-

leitung (28) verbunden ist für die Zufuhr von flüssigem Produkt oder Produktmischung zur Mischung mit dem flüssigen Produkt in dem Behälter, und wobei die zweite Durchföhrung (25) sich in das Ende eines zweiten spitzen Teils (23) öföfnet, der zum Durchstoßen einer durchstoßbaren Verschlufleinrichtung eines abschließenden Behälters für ein zusätzliches flüssiges Produkt ausgebildet ist, mit dem die anderen flüssigen Produkte letztendlich zur Bildung einer abschließenden Mischung gemischt werden sollen.

3. System zum aseptischen Zusammenmischen von drei oder mehr flüssigen Produkten, **dadurch gekennzeichnet**, daß das System folgendes aufweist:

a) einen Behälter (52), der ein erstes flüssiges Produkt (51) enthält, das in den Behälter mit Hilfe einer durchstoßbaren Verschlufleinrichtung eingeschlossen ist;

b) eine erste spitze Verbindungsvorrichtung (1), die eine erste durchgehende Durchföhrung (3) aufweist, die sich an ihrem einen Ende (5) in den spitzen Teil (2) der Verbindungsvorrichtung öföfnet und an ihrem anderen Ende unter Zwischenschaltung eines Sterilisierfilters (7) mit der umgebenden Atmosphäre verbunden ist, und die ferner eine zweite durchgehende Durchföhrung (4) aufweist, die allgemein parallel zu der ersten Durchföhrung (3) sowie von dieser getrennt ausgebildet ist, wobei sich das eine Ende der zweiten Durchföhrung in den spitzen Teil (2) der Verbindungsvorrichtung öföfnet und das andere Ende (12) mit einer Verbindungsleitung (13) verbunden ist, wobei der spitze Teil (2) der ersten Verbindungsvorrichtung (1) durch die durchstoßbare Verschlufleinrichtung (58) des ersten Behälters (52) hindurch eingeföhrt wird, um eine Fluidverbindung mit diesem herzustellen;

(c) einen Behälter (54), der ein zweites flüssiges Produkt (53) enthält, das mittels einer durchstoßbaren Verschlufleinrichtung (59) in dem Behälter eingeschlossen ist;

(d) eine zweite, mit Doppelspitze versehene Verbindungseinrichtung (21), die eine erste durchgehende Durchföhrung (24) aufweist, die sich an ihrem einen Ende (26) in den ersten spitzen Teil (22) der Verbindungsvorrichtung öföfnet und an ihrem anderen Ende (27) mit der sich von der ersten Verbindungsvorrichtung (1) wegerstreckenden Verbindungsleitung (28) verbunden ist, und die ferner eine zweite durchgehende Durchföhrung (25) aufweist, die allgemein parallel zu der ersten Durchföhrung (24) ist und sich an ihrem einen Ende (29) in den ersten spitzen Teil (22) der Verbindungs-

vorrichtung (21) öföfnet und sich an ihrem anderen Ende (30) in den zweiten spitzen Teil (23) der Verbindungsvorrichtung (21) öföfnet, wobei der erste spitze Teil (22) durch die durchstoßbare Verschlufleinrichtung (59) des zweiten Produktbehälters (54) hindurch einföhbar ist, um eine Fluidverbindung mit diesem herzustellen; und

(e) einen abschließenden Produktbehälter (56), in dem das Produkt mit einem unter dem Atmosphärendruck liegenden Druck enthalten ist und der eine durchstoßbare Verschlufleinrichtung (60) aufweist, durch die der zweite spitze Teil (23) der zweiten Verbindungseinrichtung (21) hindurch eingeföhrt wird, um eine Fluidverbindung mit dem Produktbehälter (56) herzustellen, wobei die Volumenkapazität des Behälters zum Aufnehmen der Mischung der flüssigen Produkte ausreichend ist; und

(f) ferner, wenn vier oder mehr flüssige Produkte gemischt werden sollen, eine oder mehrere zusätzliche, zwischengeordnete spitze Verbindungsvorrichtungen (41), deren jede einen hohlen spitzen Teil (42) zum Einföhren durch eine durchstoßbare Verschlufleinrichtung eines zwischengeordneten Behälters für flüssiges Produkt aufweist, wobei jeder spitze Teil (42) zwei getrennte, allgemein parallele Durchföhrungen (43, 44) aufweist, die sich beide in den spitzen Teil (42) der Verbindungsvorrichtung (41) öföfnen und deren am anderen Ende befindlichen Öföfnungen (47, 48) mit einer jeweiligen Verbindungsleitung (49, 50) verbunden sind, die sich von einer vorausgehenden bzw. zu einer nachfolgenden Verbindungsvorrichtung erstrecken, und wobei der spitze Teil (42) jeder der zwischengeordneten Verbindungsvorrichtungen (41) durch eine durchstoßbare Verschlufleinrichtung eines weiteren, zwischengeordneten Behälters für flüssiges Produkt hindurch eingeföhrt wird, um eine Flüssigkeitsverbindung mit dem Produktbehälter herzustellen.

4. Verfahren zum aseptischen Mischen von drei oder mehr flüssigen Produkten, **dadurch gekennzeichnet**, daß jedes der Produkte in einem einzelnen Produktbehälter (52, 54, 56) enthalten ist, wobei die Behälter in Reihe miteinander verbunden werden und Produkt oder Produktmischung von jedem der Behälter beginnend mit dem ersten Behälter (52) in der Reihe dazu veranlaßt wird, nacheinander unter aseptischen Bedingungen zu dem nächsten Behälter in der Reihe zu fließen und sich dort mit dem Produkt in dem Behälter zu mischen, bis eine abschließende Mischung von allen Produkten in dem letzten Behälter (56) in der Reihe angesam-

melt ist, wobei der letzte sowie der vorletzte Behälter durch die Verbindungsvorrichtung gemäß Anspruch 2 verbunden sind.

5. Verfahren nach Anspruch 4,  
**dadurch gekennzeichnet**,  
daß wenigstens das Produkt (55) in dem letzten Produktbehälter (56) in der Reihe vorab unter einem unter dem Atmosphärendruck liegenden Druck in den Behälter eingebracht wird; und daß der erste Produktbehälter (52) über ein Sterilisierfilter (7) mit der umgebenden Atmosphäre in Verbindung gebracht wird, so daß die Produkte unter dem Einfluß des umgebenden Atmosphärendrucks unter gleichzeitiger gegenseitiger Mischung des Inhalts der Behälter durch die Reihe von Produktbehältern getrieben werden, wobei die Produkte schließlich als abschließende Mischung in dem letzten Produktbehälter (56) in der Reihe gesammelt werden.
6. Verfahren nach Anspruch 4 oder 5,  
**dadurch gekennzeichnet**,  
daß der erste Produktbehälter (52) zuerst mit der Verbindungsleitung (61), die sich zu dem zweiten Behälter (54) erstreckt, und der umgebenden Atmosphäre verbunden wird, und der erste Behälter (52) auf Atmosphärendruck gebracht wird, während die Verbindungsleitung (61) zu dem zweiten Behälter (54) geschlossen ist, wonach die Verbindungsleitung (61) zu dem zweiten Behälter (54) geöffnet wird, nachdem der Druck in dem ersten Behälter (52) Atmosphärendruck angenommen hat, und daß der zweite Behälter (54) auf Atmosphärendruck gebracht wird, während die Verbindungsleitung zu dem dritten Behälter geschlossen gehalten wird, wonach die Verbindungsleitung zu dem nachfolgenden Behälter geöffnet wird, wenn der zweite Behälter Atmosphärendruck angenommen hat, und der nachfolgende Behälter auf Atmosphärendruck gebracht wird, wobei der Prozeß nacheinander für jeden der Produktbehälter in der Reihe bis zu dem letzten Produktbehälter (56) in der Reihe wiederholt wird, wobei der in den vorausgehenden Produktbehältern bis zu dem abschließenden Produktbehälter in der Reihe vorherrschende Atmosphärendruck derart ist, daß eine abschließende Produktmischung in dem Behälter erzielt wird.
7. Verfahren nach einem der Ansprüche 4 bis 6,  
**dadurch gekennzeichnet**,  
daß drei flüssige Produkte zusammengemischt werden.

#### Revendications

1. Un appareil pour mélanger trois produits liquides ou

plus conjointement de façon aseptique, caractérisé par :

- a) un premier dispositif de liaison à pointe (1) pour l'insertion au travers d'un moyen de fermeture apte à être pénétré (58) d'un premier récipient de produit (52) dans lequel le dispositif de liaison comprend deux passages traversants séparés généralement parallèles (3,4) dont le premier (3) débouche dans une extrémité dans la partie en pointe (2) du dispositif de liaison (1) et dont l'autre extrémité communique avec l'atmosphère environnante au moyen d'un filtre de stérilisation (7) et dans lequel le deuxième passage (4) débouche également à une extrémité dans la partie en pointe (2) du dispositif de liaison (1) et est relié à une conduite de liaison à son autre extrémité et,
- b) un deuxième dispositif de liaison à double pointe (21) dans lequel une première partie en pointe (22) dudit dispositif est agencée pour l'insertion au travers d'un élément de fermeture apte à être pénétré (59) d'un deuxième récipient de produit (54) et comprend deux passages traversants séparés généralement parallèles (24, 25) dont un premier passage (24) débouche à une extrémité dans la première partie en pointe (22) et l'autre extrémité dudit passage (24) est reliée à la conduite de liaison (28) s'étendant à partir du premier dispositif de liaison (1) et dans lequel le deuxième passage (25) débouche également à une extrémité dans la première partie en pointe (22) et au dispositif de liaison (20), cette deuxième partie en pointe (23) étant agencée pour être insérée au travers d'un moyen de fermeture apte à être pénétré (60) d'un récipient de produit final (56) dans lequel un mélange de tous les produits est recueilli, et, en outre lorsque quatre produits liquides ou plus doivent être mélangés ;
- c) un ou plusieurs dispositifs de liaison en pointe additionnels, intermédiaires (41) ayant chacun une pointe creuse (42) pour l'insertion au travers d'un moyen de fermeture apte à être pénétré d'un récipient de produit liquide intermédiaire dans lequel chaque dite pointe (42) comporte deux passages séparés généralement parallèles (43, 49) qui tous deux débouchent dans l'extrémité en pointe (42) du dispositif de liaison et qui sont reliés à leurs autres extrémités ouvertes à une conduite de liaison respective s'étendant à partir d'un dispositif de liaison précédent ou subséquent.

2. Un dispositif de liaison (21) pour mélanger trois produits liquides ou plus, caractérisé par une première partie en pointe creuse (22) qui est agencée pour

percer un moyen de fermeture apte à être pénétré d'un récipient de produit liquide, dans lequel la partie en pointe (22) comprend deux passages traversants séparés généralement parallèles (24, 25) dont tous deux débouchent dans l'extrémité de la partie en pointe (22), dans lequel le premier passage (24) est relié à une conduite de liaison (28) pour l'alimentation du produit liquide ou du mélange de produit devant être mélangé avec le produit liquide dans ledit récipient et dans lequel le deuxième passage (25) débouche dans l'extrémité d'une deuxième partie en pointe (23) qui est agencée pour percer un moyen de fermeture apte à être pénétré d'un récipient final pour un produit liquide supplémentaire avec lequel les autres produits liquides doivent être mélangés finalement pour former un mélange final.

3. Un système pour mélanger de façon aseptique trois ou plusieurs produits liquides conjointement, caractérisé en ce que le système comprend :

- a) un récipient (52) qui renferme un premier produit liquide (51) qui est enfermé dans le récipient avec l'aide d'un moyen de fermeture apte à être pénétré (58) ;
- b) un premier dispositif de liaison à pointe (1) qui comprend un premier passage traversant (3) qui débouche à une extrémité (5) dans la partie en pointe (2) du dispositif de liaison et est relié à l'atmosphère ambiante à son autre extrémité par l'intermédiaire du milieu d'un filtre de stérilisation (7) et qui comprend également un deuxième passage traversant (4) qui est généralement parallèle au premier passage (3) et séparé de celui-ci, dans lequel une extrémité du deuxième passage débouche dans la partie en pointe (2) du dispositif de liaison et l'autre extrémité (12) est reliée à une conduite de liaison (13), dans lequel la partie en pointe (2) du premier dispositif de liaison (1) est insérée au travers du moyen de fermeture apte à être pénétré (58) du premier récipient (52) pour obtenir une liaison fluïdique avec celui-ci ;
- c) un récipient (54) qui renferme un deuxième produit liquide (53) qui est enfermé dans le récipient au moyen d'un moyen de fermeture apte à être pénétré (59) ;
- d) un deuxième dispositif de liaison à pointe double (21) qui comprend un premier passage traversant (24) qui débouche à une extrémité (26) dans la première partie en pointe (22) du dispositif de liaison et est relié à son autre extrémité (27) à la conduite de liaison (28) s'étendant à partir du premier dispositif de liaison (1) et comprend également un deuxième passage traversant (25) qui est généralement parallèle au premier passage

(24) et débouche à une extrémité (29) dans la première partie en pointe (22) du dispositif de liaison (21) et débouche à son autre extrémité (30) dans la deuxième partie en pointe (23) dudit dispositif de liaison (21), dans lequel la première partie en pointe (22) est insérée au travers du moyen de fermeture apte à être pénétré (59) du deuxième récipient de produit (54) pour obtenir une liaison fluïdique avec celui-ci ; et

e) un récipient de produit final (56) dans lequel le produit est contenu à une pression en dessous de la pression atmosphérique et qui comprend un moyen de fermeture apte à être pénétré (60) au travers duquel la deuxième partie en pointe (23) du deuxième dispositif de liaison (21) est insérée pour obtenir une liaison fluïdique avec ledit récipient de produit (56), dans lequel la capacité volumétrique du récipient est suffisante pour recevoir le mélange des produits liquides et en outre, lorsque quatre produits liquides ou plus doivent être mélangés ;

f) un ou plusieurs dispositifs de liaison à pointe intermédiaires supplémentaires (41) ayant chacun une partie en pointe creuse (42) pour l'insertion au travers d'un moyen de fermeture apte à être pénétré d'un récipient de produit liquide intermédiaire, dans lequel chaque dite partie en pointe (42) comporte deux passages séparés généralement parallèles (43, 44) qui tous deux débouchent dans la partie en pointe (42) du dispositif de liaison (41) et dont les autres ouvertures d'extrémité (47, 48) sont chacune reliées à une conduite de liaison respective (49, 50) s'étendant à partir d'un dispositif de liaison précédent ou subséquent et dans lequel la partie en pointe (42) de chacun desdits dispositifs de liaison intermédiaires (41) est insérée au travers d'un moyen de fermeture apte à être pénétré d'un récipient de produit liquide intermédiaire supplémentaire pour fournir une liaison liquide avec ledit récipient de produit.

4. Un procédé pour mélanger de façon aseptique trois produits liquides ou plus, caractérisé en ce que chacun des produits est contenu dans un récipient de produit individuel (52, 54, 56) dans lequel les récipients sont reliés conjointement en série et le produit ou le mélange de produits à partir de chacun des récipients en commençant avec le premier récipient (52) dans la série, est amené à s'écouler successivement sous des conditions aseptiques au récipient suivant en ligne et là pour être mélangé avec le produit dans ledit récipient jusqu'à ce qu'un mélange final de tous les produits ait été recueilli dans le dernier récipient (56) dans la série, le der-

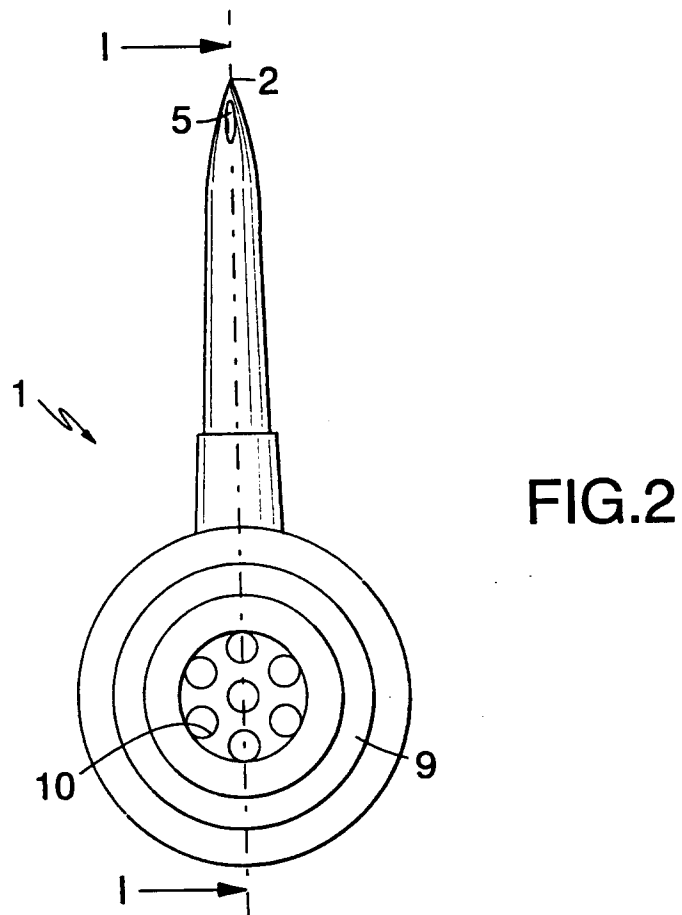
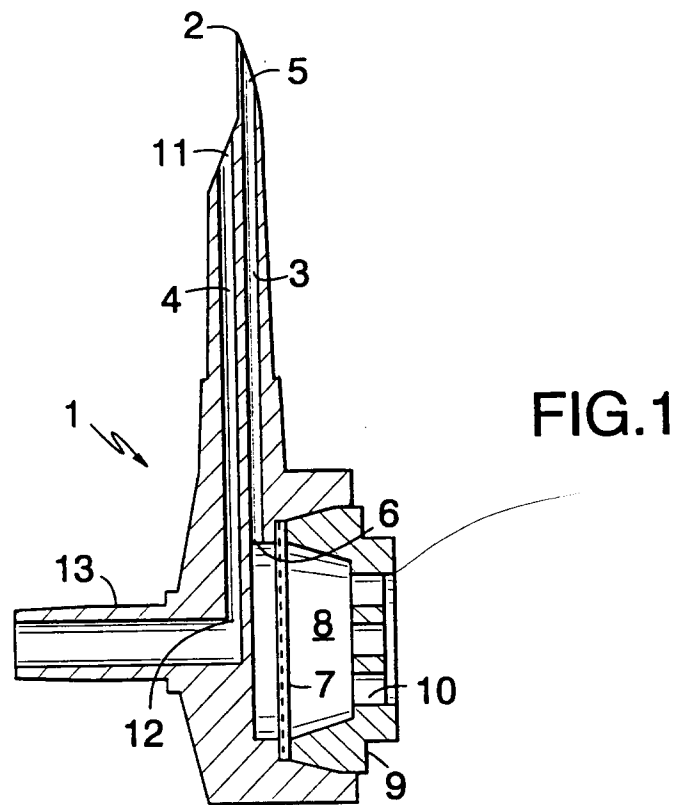
nier et le deuxième dernier récipient étant reliés par le dispositif de liaison selon la revendication 2.

5. Un procédé selon la revendication 4, caractérisé en ce que, au moins le produit (55), dans le dernier récipient de produit (56) en ligne est pré-conditionné dans le récipient à une pression en dessous de la pression atmosphérique et en ce que le premier récipient de produit (52) est placé en communication avec l'atmosphère environnante par l'intermédiaire d'un filtre de stérilisation (7), si bien que les produits sont entraînés au travers des séries de récipients de produit par l'influence de la pression atmosphérique environnante tout en mélangeant mutuellement les contenus des récipients, lesdits produits étant finalement recueillis comme un mélange final dans le dernier récipient de produit (56) en ligne.
 

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10  
15
6. Un procédé selon la revendication 4 ou 5, caractérisé en ce que le premier récipient de produit (52) est tout d'abord relié à la conduite de liaison (61) s'étendant au deuxième récipient (54) et à l'atmosphère environnante et le premier récipient (52) est amené à la pression atmosphérique tandis que la conduite de liaison (61) audit deuxième récipient (54) est fermée, après quoi la conduite de liaison (61) au deuxième récipient (54) est ouverte après que la pression dans le premier récipient (52) se soit établie à la pression atmosphérique et le deuxième récipient (54) est amené à la pression atmosphérique tandis que la conduite de liaison au troisième récipient est maintenue fermée, après quoi la conduite de liaison au récipient suivant est ouverte quand le deuxième récipient s'est établi à la pression atmosphérique et ledit récipient suivant est amené à la pression atmosphérique, dans lequel le procédé est répété successivement pour chacun des récipients de produit dans les séries jusqu'au dernier récipient de produit (56) en ligne, dans lequel la pression atmosphérique prévaut dans les récipients de produit précédents au récipient de produit final en ligne afin d'obtenir un mélange de produit final dans ledit récipient.
 

20  
25  
30  
35  
40  
45
7. Un procédé selon l'une quelconque des revendications 4 à 6, caractérisé par le mélange de trois produits liquides conjointement.
 

50  
55



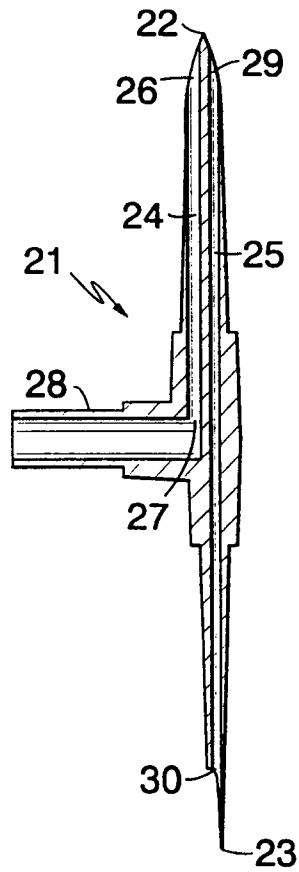


FIG. 3

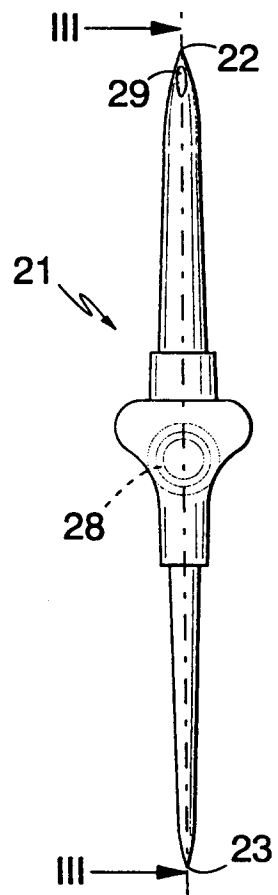


FIG. 4

