

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
27 April 2006 (27.04.2006)

PCT

(10) International Publication Number
WO 2006/043295 A1

(51) International Patent Classification: **B65D 47/20**,
47/18

(21) International Application Number:
PCT/IT2005/000170

(22) International Filing Date: 25 March 2005 (25.03.2005)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
RM2004A000524 22 October 2004 (22.10.2004) IT

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(81) Designated States (unless otherwise indicated, for every
kind of national protection available): AE, AG, AL, AM,
AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN,
CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI,
GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE,
KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD,
MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG,
PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY,
TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU,
ZA, ZM, ZW.

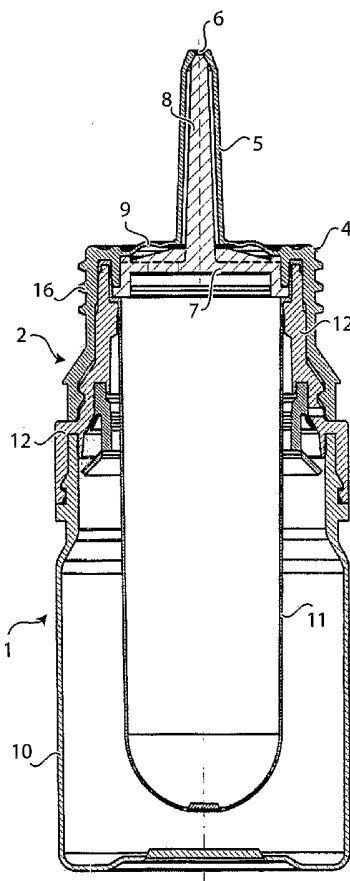
(84) Designated States (unless otherwise indicated, for every
kind of regional protection available): ARIPO (BW, GH,
GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM,
ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM),
European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI,
FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO,
SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN,
GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

— with international search report

[Continued on next page]

(54) Title: MULTIDOSE DISPENSER FOR STERILE LIQUID PREPARATIONS



(57) Abstract: A dispenser designed for storing liquid products in sterile conditions and for dispensing such products drop by drop, which enables maintaining the sterility of the product even after first opening the bottle, without the need to include preservatives in the liquid product. The dispenser comprises a container body (1) and a dropper assembly (2), which in turn comprises a closure element of the container body (1) ending with an elongated dropper nozzle (5) provided with a central port (6) and a pin plug (7) cooperating with the dropper nozzle (5) to intercept the outflow of a liquid preparation contained in the bottle. The pin plug (7) is placed inside the dropper nozzle (5) in a fixed position with respect to the container body (1), and the dropper nozzle (5) is able to move outward from the pin plug (7) in order to open the port (6) as a result of a mechanical pressure applied to the exterior of the container body (1).



For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

MULTIDOSE DISPENSER FOR STERILE LIQUID PREPARATIONS

DESCRIPTION

The present invention concerns a multidose bottle for dispensing
5 liquid preparations without preservatives. More specifically, the invention concerns a container specially designed for the sterile conservation of liquid products and their distribution in the form of drops, the sterility being maintained also after the first opening of the container, without the need to include preserving agents in the liquid product.

10 Many products, particularly but not exclusively in the medical field, are obtained and used in liquid form, such as solutions or mixtures of one or more liquid components with one or more dissolved solids. For their proper application, these liquids must be dispensed in the form of drops at the time of use. The most common example is that of liquid pharmaceutical products, both for
15 systemic administration (oral drops) and more frequently for topical administration, such as on the nasal or oral mucosa, in the auricle of the ear and, above all, in the conjunctival sac. Topical ophthalmic products, such as eye-drops and artificial tears, also have the peculiarity that, besides needing to be administered in the form of drops, they must also be applied by the users on
20 their own visual apparatus, and thus normally require the use of droppers with sufficiently elongated nozzles to facilitate as much as possible the actual application of the medication onto the surface of the cornea.

Other examples of liquid products that may require storage in vials or bottles and distribution in the form of drops are particular detergents or addi-
25 tives, also outside the pharmaceutical field, such as in the field of cosmetics or foodstuffs. These fields also have the problem of properly storing liquid products in sterile conditions and without altering their quality from one use to the next. Particular applications in these fields may also need a drop by drop dispensing of the product which may be as uniform and easily controllable as
30 possible.

The conventional way of preventing or combating the microbial growth in liquid products to be used several times over after the first opening of the

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relative container consists of adding suitable preserving agents, antioxidants and antibacterial agents in the liquid product itself. The choice and concentration of the agents used must in any case be such to guarantee the necessary sterility within the envisaged conditions and expiry date of the product life, and
5 at the same time must not alter the intrinsic characteristics of the liquid product.

More specifically, with reference to products for ophthalmic use that are packaged in multidose bottles of flexible material, the initial sterilization of the product takes place during the bottling phase, after which the bottle is
10 sealed and packaged, and arrives in the consumer's hands in sterile form. When the bottle is first opened, the product is still in a sterile condition, also without the use of preserving agents. On first use, by gently squeezing the bottle some liquid is forced out and made to pass through the dropper nozzle to reach the user. When the gentle pressure exerted on the bottle ceases, the
15 bottle stops distributing the liquid product. However, due to the elasticity of the material used, as soon as the pressure on the bottle ceases, the bottle returns to its original shape and reintegrates the volume of liquid used by sucking in air from the outside environment through its spout. This air is potentially polluted and could contaminate the remaining liquid in the bottle by starting an
20 oxidative process on the volume of product left inside. This contaminating activity exerted by the outside air is normally prevented by using preservatives or antioxidants: without these, the pharmaceutical product could only be used once because the remaining liquid would become irreparably altered and unusable. All this would be considerably worsened if, during product applica-
25 tion, the dropper came into contact with the user's body, which may potentially be contaminating.

Unless an alternative administration method is used – something which can only be economically justifiable in certain cases – namely the use of single dose packages containing a quantity of product for just one application,
30 which do not require any preservatives, in all other cases the use of preservatives and antioxidants in multidose bottles containing sterile preparations is made essential in view of a number of features that the product has to main-

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tain over time, and especially after its container is first opened. These features include the capacity to maintain the liquid in sterile conditions after the bottle is first opened, and also when non-sterile air is sucked back in to replace the liquid used and, in addition, in the case of accidental contact between the dropper and parts of the user's body that may be polluting. Such features also include the capacity to resist oxidation due to contact with the outside air that increasingly replaces the volume of liquid used, and this throughout the useful life of the product once the bottle is first opened.

The addition of preservatives to liquid products for ophthalmic use, although admitted in pharmacology and commonly accepted, is not devoid of a series of drawbacks, however. These include, in particular, the possibility of causing burning sensations or inflammatory or allergic reactions as well as, above all, the proven cytotoxicity of these products. For example, it is well-known that some preservatives used for ophthalmic products have a toxic effect on the goblet cells of the cornea, so that their prolonged use could cause more problems than the ones they can actually help to overcome.

One possible strategy to avoid using preservatives in multidose bottles of liquid products is to provide one or more antibacterial filters on the liquid pathway towards the exit point in the bottle. In particular, filters with openings or pores of about 0.2 micron in diameter are provided, which mechanically prevent any micro-organisms from getting into the bottle while not preventing the flow of liquid out. An example of this solution is described in the international patent application No. WO 90/05110 (Eye Research Institute of Retina Foundation), where a flexible plastic multidose bottle equipped with a dropper tip containing a pair of filters transversally placed with respect to the liquid flow direction. The filter closest to the bottle body is hydrophilic and has the characteristic of being easily wettable in order to facilitate the outward flow of the liquid product, while the filter located more downstream along the liquid path is of the hydrophobic or water-repellent kind so as not to retain the medicinal solution inside it after dispensing it. This results in preventing bacterial growth on the external surface of the filter assembly. It is obvious that, despite the adoption of an antibacterial filter, the external channel of the bottle lying

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downstream of the filter, including the dropper tip, is still exposed to contamination by the external environment.

A similar solution envisaging a bottle for liquid products to be dispensed drop by drop without the use of preservatives and featuring an antibacterial filter placed inside the dropper nozzle is disclosed in U.S. patent No. 5,105,993 (La Haye Laboratories), which also describes the presence of another filter placed on a venting port in the bottle. The said port is intended to allow air to enter the flexible bottle to replace the volume of liquid used.

Still in the specific filed of pharmaceutical products for topical use, U.S. patent No. 5,232,687 (Ursapharm) proposes adopting another, alternative or complementary, device in order to guarantee the sterility of a liquid product for topical administration without resorting to preservatives: the use of a solid substance with a germicide action like silver. The device proposed in this connection is not actually a drop dispenser, but a small reciprocating pump that supplies dosed quantities of liquid product in spray form. At each stroke of the pump a pre-fixed quantity of liquid passes into a dispensing chamber and, in order to exit into the outside environment, it must then come into close contact with a silver-based element with germicide functions. The pump device is airtight and does not allow any air to come into the product container to replace the outflowing liquid. This safeguards against any possibility of contamination from the outside environment. It is evident that such a solution is not very economical, also due to the need to construct a completely airtight device of such solidity to withstand the creation of a depression inside the product container. Moreover, the type of liquid dispensing obtained is not actually in drop form but in jet form, and is not really suitable for applying products to the eye.

Another commercially available device for supplying liquid pharmaceutical products in drop form not requiring the use of preservatives is described in U.S. patent No. 6,336,571 (Laboratoires Théa). In this case the main aim is considered to be that of being able to evenly control the flow of dosed product, with a proper formation of drops. To this end the patent proposes using a container with flexible bellow-shaped walls, that must necessar-

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ily be protected by an external rigid shell, that is removable in order to allow access to the bellow-shaped flask containing the liquid. Inside the rigid collar on which the bellow-shaped container is housed there is a pad made of porous material that creates a head loss sufficient to make the product come out in the form of drops through the dropper nozzle, by manually squeezing the bellow-shaped container. Here too, the necessary aseptic conditions are provided by an antibacterial filter placed along the product outflow path downstream of the porous pad but upstream of the dropper nozzle. In this case, too, the inside channel of the dropper nozzle is exposed to bacterial contamination from the external environment.

The aforesaid device was considered improvable by the patent-holders themselves, above all as regards construction complexity and production costs, as described in the later U.S. patent application No. 2004/0074925, of the same owner. In this document, the flexible bellow-shaped container and external shell assembly is replaced by a simple flexible single-walled container structured such that outside air can be sucked into the container once liquid outflow has finished, when the flexible container returns to its original shape after being squeezed. In the newly-packaged unused bottle, the entry of outside air is prevented by a frangible internal partition that remains closed until the product is first used. Thereafter, for the remaining period of the product life, the aseptic conditions are guaranteed by an antibacterial filter located along the product outflow path as in the previous version. The document describes this filter as being partially hydrophilic, to enable the liquid to pass through during administration, and partially hydrophobic, to enable air to come into the container once liquid outflow ceases.

A further solution for manufacturing multidose dispenser bottles for liquid products without preservatives is described in European patent application EP-A-1319606 (Nihon Tenganyaku Co. and Taisei Kako Co.), which concerns a double-walled container with an external flexible wall and an internal collapsible one, in which the manually exerted pressure on the external container is transmitted to the internal wall thereby forcing the liquid out during administration. Then, due to a vent hole on the external container, the latter

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can elastically return to its original shape by sucking air into the gap between the external wall and internal collapsible wall. This air does not come into contact with the product enclosed inside the internal container, thus preventing any possible contamination to the product itself.

5 The product flows out of the bottle through a check valve that does not allow the liquid to come back into the internal container. Downstream of this check valve the outflowing liquid still passes through a filter before leaving the container. In this case, too, the device includes a space between the check valve and the dropper tip on which the filter is located, in which some stagnant
10 liquid remains that is not excluded from contact with the outside air, even if the presence of the filter further downstream should at least prevent micro-organisms from entering the bottle spout.

 In view of the foregoing, it is evident that a device for dispensing products drop by drop, that should do without the addition of preservatives in
15 the product, must be able to prevent the entry of contaminating air inside the dropper nozzle representing the terminal element of the dispenser device. The said element normally ends with a more or less pronounced tip that facilitates product outflow. After use, there is the need to avoid the inside of the dropper being unprotected and wet with the product, which would inevitably mean a
20 contamination of the internal duct of the dropper nozzle itself. Normally, an external cap provides for closure of the bottle. Said cap mechanically closes the tip of the dropper nozzle through suitable protuberances or internal projections. However, when this happens (and provided that it happens, since it is not an automatic event), air has already entered the dropper nozzle because,
25 by returning to its original shape, the bottle sucks in outside air to replace the volume of liquid used in the administration.

 The known devices envisaging the presence of check valves on the liquid outflow duct still have sections downstream of the check valve – which may particularly include the dropper nozzle – where stagnant liquid remains
30 after administration and where contaminating air can enter from the outside. An object of the present invention is, thus, to provide a stable kind of closing mechanism operating on the dropper nozzle tip, which is operated automati-

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cally in a safe and continuative manner, without requiring any external action or the use of a potentially contaminating closing device (external cap).

To this end, according to a first aspect of the present invention, there is proposed to create a check valve directly on the bottle dropper nozzle tip.

5 This valve is configured with a truncated cone-shaped pin plug having a shape complementary to that of the nozzle, wherein, however, the valve element with the plugging function is fixed with respect to the bottle body, and the element that functions as the relative housing, i.e. the nozzle, is mobile. Actually, in the lower part of the nozzle tip, where the latter is inserted into the product con-

10 tainer in an airtight and fixed manner, there is provided an annular membrane expansion chamber that is sufficiently flexible to allow the dropper nozzle to extend forward with respect to the fixed plug when the pressure on the liquid contained in the bottle is increased by squeezing the bottle itself. The slight advancement of the nozzle with respect to the fixed plug opens up a

15 sufficient gap to enable the liquid to pass through to be dosed in drops from the nozzle tip. As soon as the externally applied pressure ceases, the annular membrane contracts again automatically causing the nozzle to draw back with respect to the fixed pin plug. In this way, as will be made clearer further on, the closure of the dropper after administration is automatic and, above all, it

20 occurs right at the tip of the dropper nozzle, without leaving any liquid residues within the intermediate space inside the dropper.

Therefore, the present invention specifically provides a dispenser for liquid preparations without preservatives, comprising a container body and a dropper assembly, which in turn comprises a container body closure element

25 ending with an elongated dropper nozzle provided with a central port, and a pin plug of a complementary shape to the said dropper nozzle and cooperating with it to intercept the outflow of a liquid preparation contained in said dispenser, the pin plug being located inside the dropper nozzle in a fixed position with respect to the container body, and said dropper nozzle being dis-

30 placeable outward from said pin plug in order to open up the port of the dropper assembly as a result of a mechanical pressure applied to the exterior of the container body.

According to a preferred solution, this movement of the dropper nozzle with respect to the fixed pin plug is obtained by the distension of an elastic annular membrane housed in the dropper nozzle and such to establish an expansion annular chamber that dilates due to the pressure exerted on the exterior of the container body. In order to obtain the required elasticity of the membrane while at the same time creating a device that can be manufactured at reasonable cost, said closure element of the container body ending with a dropper nozzle is made up of a suitable polymeric material workable by molding, and particularly a polyethylene.

As noted, the preferred shape for the dropper nozzle and the corresponding pin plug according to the present invention is a truncated cone shape, not only because the elongated shape of the dropper facilitates product administration in the eye, if the considered preparation is an ophthalmic product for topical application, but also because closure through the cooperation of two truncated cone-shaped coaxial surfaces is the easiest and most reliable form of blockage.

According to some preferred embodiments of the present invention, the container body of the bottle is of the double-wall type with a cavity in between, with an elastic external body and an internal collapsible body inside it, that contains the liquid preparation and decreases in volume as the liquid flows out of the dispenser. This type of construction provides the necessary solidity to the bottle, whose external body protects the internal collapsible container, and at the same time allows a gradual transfer of the external manual pressure applied to the bottle to the internal container, through the cavity between the two walls. This avoids any excessive dosage dispensing or spraying of the product.

Preferably, the said internal and external bodies of the dispenser are connected rigidly and in airtight manner to the closure element of the container, particularly via the interposition of a ring nut, to the closure device of the container body terminating with the dropper nozzle. Each of said inner and outer container is made of with a polymeric material suitable for the mechanical characteristics it must have. In particular, the internal container may be

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made of a thin polyethylene material so that it can collapse as it empties, without sucking in air from the outside. After dispensing the liquid dose, the volume of liquid product leaving the bottle is replaced by a corresponding volume of air sucked in from the outside, but this air fills the cavity between
5 the two walls and does not come into contact with the liquid contained inside the bottle. To enable the air to come into the cavity, the external body of the container has a port that may also be fitted with a suitable valve.

The dispenser according to the present invention is also completed by an external closure capsule which engages the described dropper assembly
10 to create a seal. This closing device preferably consists of a screw cap that can protect the dropper nozzle tip and also a knurled overcap outside the screw cap but connected to it. The combination of screw cap and overcap creates a safety closure system that prevents accidental opening of the bottle, like the kind of devices normally used on pharmaceutical bottles to avoid any
15 improper use by children (child-proof devices). In addition, the capsule envisages a frangible part only on first opening the bottle – a tamper-evident device also acting as a guarantee seal.

The specific features of the present invention, as well as its advantages and corresponding operating modalities, will be more evident further on
20 with reference to a specific embodiment of the invention, illustrated merely for exemplary purposes in the attached drawings, wherein:

Figure 1 shows a longitudinal cross-section of a multidose dispenser for liquid preparations according to the present invention, particularly designed for dispensing pharmaceutical products drop by drop without using preserva-
25 tives, and complete with all its closure elements;

Figure 2 shows a longitudinal cross-section of the same bottle of Figure 1, without the external closure capsule;

Figure 3 shows a longitudinal cross-section of the dropper nozzle of the aforesaid bottle;

30 Figure 4 shows a longitudinal cross-section of the corresponding pin plug element for closing the dropper nozzle;

Figure 5 is a perspective view of the said pin plug element shown in

Figure 4;

Figure 6 shows a longitudinal cross-section of the ring nut connecting the internal container of the dispenser to the external body, and onto which the dropper nozzle is fixed;

5 Figure 7 is a perspective view of the said ring nut shown in Figure 6;

Figure 8 shows a longitudinal cross-section of the cap that constitutes an element of the bottle closure capsule shown in Figure 1;

Figure 9 is a perspective view of the said cap shown in Figure 8;

10 Figure 10 shows a longitudinal cross-section of the overcap constituting an element of the bottle closure capsule shown in Figure 1;

Figure 11 is a perspective view of the said overcap shown in Figure 10; and

15 Figures 12 a), b), c) and d) schematically show the functioning of the multidose dispenser bottle shown in the above Figures, with a schematic longitudinal cross-section representation of four different operative phases of the bottle.

20 As shown in Figures 1 and 2, the illustrated embodiment of the dispenser for liquid products according to the present invention is composed of a container body (1) that is closed off at the top with a dropper assembly (2) and completed with an external closure capsule (3). The dropper assembly (2), which is also shown in more detail in Figures 3, 4 and 5, in turn includes a closure element (4), shown specifically in Figure 3, and consists of a single piece of moulded plastic material. This ends with a dropper nozzle (5) of a truncated cone shape, that has a central port (6) for channelling the drops of
25 the liquid contained in the bottle.

30 The second fundamental element of the dropper assembly (2) is the pin plug (7), which is shown specifically in Figures 4 and 5, and which includes a truncated cone-shaped pin (8) complementary to the dropper nozzle (5), that fits into the latter to completely plug the port (6) of the dropper nozzle (5) without any loss of liquid. The opening and closing of this assembly, which creates a check valve for the liquid product dispensed, is obtained by the outward movement of the dropper nozzle (5) with respect to the pin plug (7), which is

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firmly anchored to the bottle body and is thus fixed. On the other hand, the dropper nozzle (5) is connected to the closure element (4), of which it forms the terminal element, through an elastic annular membrane (9), and can thus slightly move forward (by some tenths of a millimetre, in the case of a dropper
5 bottle for ophthalmic use), as will be shown in detail below, opening up the port (6) for the passage of the product in the form of drops.

Going back to Figures 1 and 2, the container body (1) of the bottle according to the present invention is of the double-wall type with an air cavity in between, and consists of an external elastic cylindrical body (10) and an
10 internal collapsible body (11), also cylindrical but of a smaller diameter, which is the actual container of the liquid product. Both the internal (11) and external (10) bodies are attached to one another by means of a cylindrical ring, specifically shown in Figures 6 and 7. After filling up with the liquid product, the container body (1) is then attached – via the ring (12) – to the dropper assembly
15 (2), with the pin plug (7) and closure element (4), in order to obtain the complete dispenser device shown in Figure 2. All this takes place according to the standard sterilisation procedures.

When closed and in a resting state, the dispenser is as shown schematically in Figure 12 a): the port (6) of the dropper is closed by the pin (8) of
20 the plug (7). For use as an eye-drop dispenser, the dispenser is held upside-down as shown in Figure 12 b) so that the dropper nozzle (5) points to the user's conjunctival sac, and then the external body (10) of the container (1) is gently squeezed, as shown in Figure 12 c).

This pressure squeezes the flexible external container (10) and is
25 transmitted, via the air cavity, to the internal collapsible container (11). The increased pressure in the internal container (11) then causes a dilation in the expansion chamber formed by the elastic annular membrane (9), and the dropper nozzle (5) moves slightly outward with respect to the pin plug (7), which remains firmly fixed to the container body (1). This opens up a port
30 between the pin (8) and the dropper nozzle (5), which allows the outflow of the drops of product (13). When the user stops squeezing the external body (10), the pressure also ceases in the expansion chamber of the dropper (5) and

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immediately, due to the elasticity of the material used for the annular membrane (9), the dropper nozzle (5) withdraws by some tenths of a millimetre and its internal walls come into contact with the internal closing pin (8), thus safely and securely sealing the bottle, as shown in Figure 12 d). It is important to
5 note that the closure of the valve composed of both the dropper nozzle (5) and pin plug (7) occurs exactly at the tip of the dropper nozzle (5), thus avoiding any possible liquid remaining in the nozzle and preventing any contaminating elements from entering the dispenser. Since the internal body (11) of the container (1) is manufactured using thin material and is collapsible, and air is
10 sucked into the cavity between the internal body (11) and external body (10) of the container (1), the internal body (11) remains collapsed and no air comes into contact with the liquid product contained in the dispenser.

To complete the package and insulate the dropper from the external environment, the dispenser according to the present invention is equipped
15 with an external closure capsule (3) (visible in Figure 1) which, in the form illustrated, consists of two superimposed and combining elements. These elements are shown individually in Figures 8-10 and consist of a screw cap (14), whose internal thread (15) engages the thread (16) on the neck of the closure element (4) (see Figure 3), and also an externally knurled overcap
20 (17) which, by fitting over the screw cap (14), creates a secure child-proof closure device. The overcap (17) also includes a collar (18) that is broken and removed on first opening the dispenser and acts as a guarantee seal (tamper-evident device). An unbroken collar demonstrates that the dispenser is still sealed and has not been tampered with.

25 As may be deduced by the aforesaid description, the dispenser according to the present invention can be used in the same way as with other normal dropper bottles for repeated administrations of the product and does not require any specific procedure for its use, but guarantees an immediate and automatic closure of the container when the user stops using the product.
30 This type of stable, safe, sterile and automatic closure occurs at the tip of the dropper nozzle, where the product drops out, and thus guarantees the complete sterility of the product, its proper storage without any oxidative phenom-

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ena, and its availability for repeated administrations up to the complete emptying of the bottle contents.

Moreover, the device is easy to use also by the most inexperienced or elderly users and requires no strange preparatory movements before administering the liquid product; the dispenser is also easy to open and close.

Finally, the structure of the proposed device is such that it is not excessively complex and is easy to produce from a manufacturing standpoint. It also offers the possibility of being tested during production in order to reduce the number of rejects to negligible levels during the product filling phase in sterile conditions.

The present invention has been disclosed with particular reference to some specific embodiments thereof, but it should be understood that modifications and changes may be made by the persons skilled in the art without departing from the scope of the invention as defined in the appended claims.

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CLAIMS

1. A dispenser for liquid preparations without preservatives, comprising a container body (1) and a dropper assembly (2), which in turn comprises
5 a container body closure element (4) ending with an elongated dropper nozzle (5) provided with a central port (6) and a pin plug (7) of a complementary shape to the said dropper nozzle (5) and cooperating with it to intercept the outflow of a liquid preparation contained in said dispenser, the pin plug (7) being located inside the dropper nozzle (5) in a fixed position with respect to
10 the container body (1), and the said dropper nozzle (5) being displaceable outward from said pin plug (7) in order to open up the port (6) of the said dropper assembly (2) as a result of a mechanical pressure applied to the exterior of the container body (1).

2. A dispenser according to claim 1, wherein the outward movement
15 of said dropper nozzle (5) with respect to said fixed pin plug (7) is obtained by distension of an elastic annular membrane (9) connected to the dropper nozzle (5) and such to establish an annular expansion chamber that dilates due to a pressure exerted on the exterior of said container body (1).

3. A dispenser according to claims 1 or 2, wherein the said container
20 body closure element (4) ending with a dropper nozzle (5) is made of polymeric material.

4. A dispenser according to any one of claims 1-3, wherein said dropper nozzle (5) and said pin plug (7) are of a truncated cone shape.

5. A dispenser according to any one of claims 1-4, wherein said container
25 body (1) is a double-walled container with a cavity in between the two walls.

6. A dispenser according to claim 5, wherein said container body (1) comprises an elastic external body (10) and a collapsible internal body (11) enclosed within it, suitable to contain therein the liquid preparation and to
30 decrease in volume as said liquid preparation flows out of the dispenser.

7. A dispenser according to claim 6, wherein both said external body (10) and said internal body (11) of the container body (1) are connected rigidly

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and in airtight manner to said closure element (4) of the container body (1) ending with said dropper nozzle (5).

8. A dispenser according to claim 7, wherein the connection of said external body (10) and said internal body (11) of the container body (1) to the
5 said closure element (4) is by means of the interposition of a ring nut (12).

9. A dispenser according to any one claims 6-8, wherein said elastic external body (10) and said collapsible internal body (11) of the container (1) are each made of a suitable polymeric material.

10. A dispenser according to any one of claims 5-9, wherein said
10 external body (10) of the container (1) is provided with a port for allowing outside air to enter the cavity between the two walls of the container (1).

11. A dispenser according to any one of claims 1-10, also including an external closure capsule (3) that engages the said dropper assembly (2).

12. A dispenser according to claim 11, wherein said external closure
15 capsule (3) includes a screw cap (14) suitable to protect the said dropper nozzle (5) and also a knurled overcap (17) that fits over the screw cap (14) and is connected to it.

13. A dispenser according to claim 12, wherein the co-operation of said screw cap (14) and said overcap (17) creates a safety closure system
20 preventing children from opening the bottle (child-proof device).

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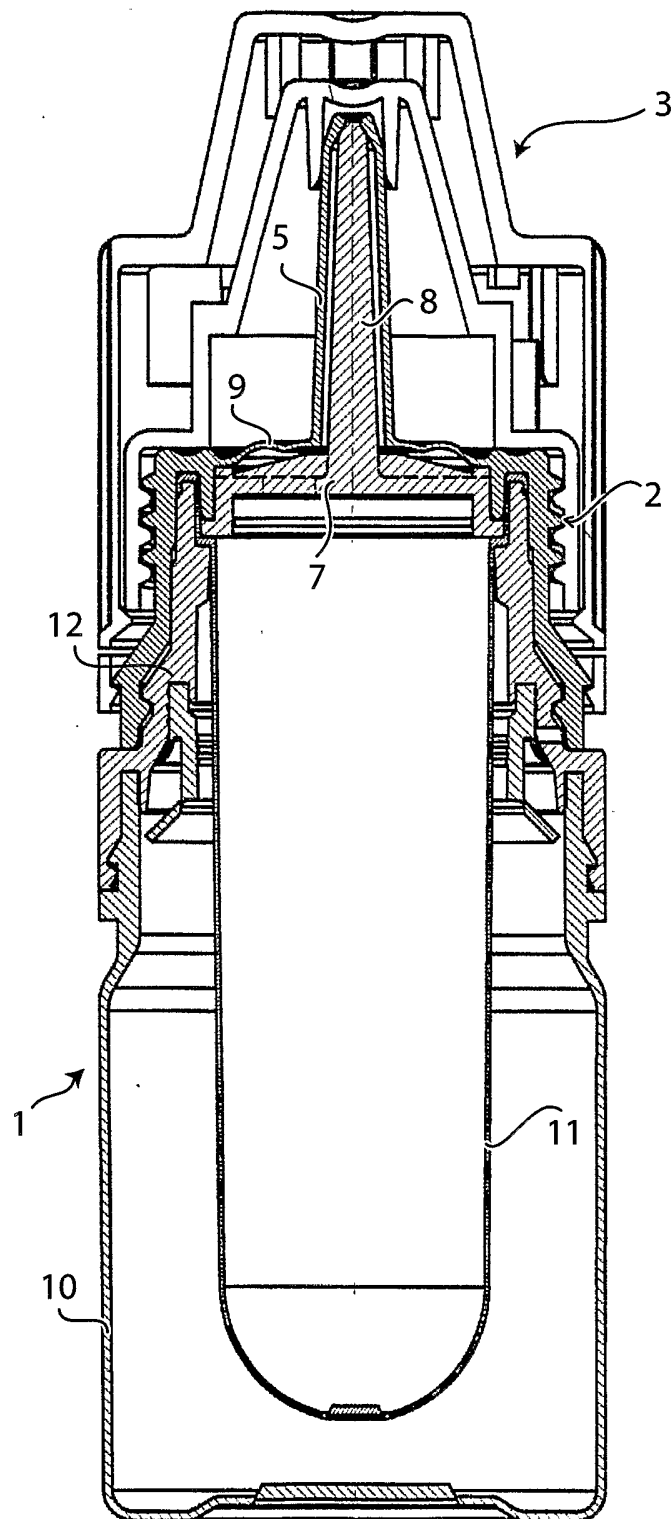


Fig. 1

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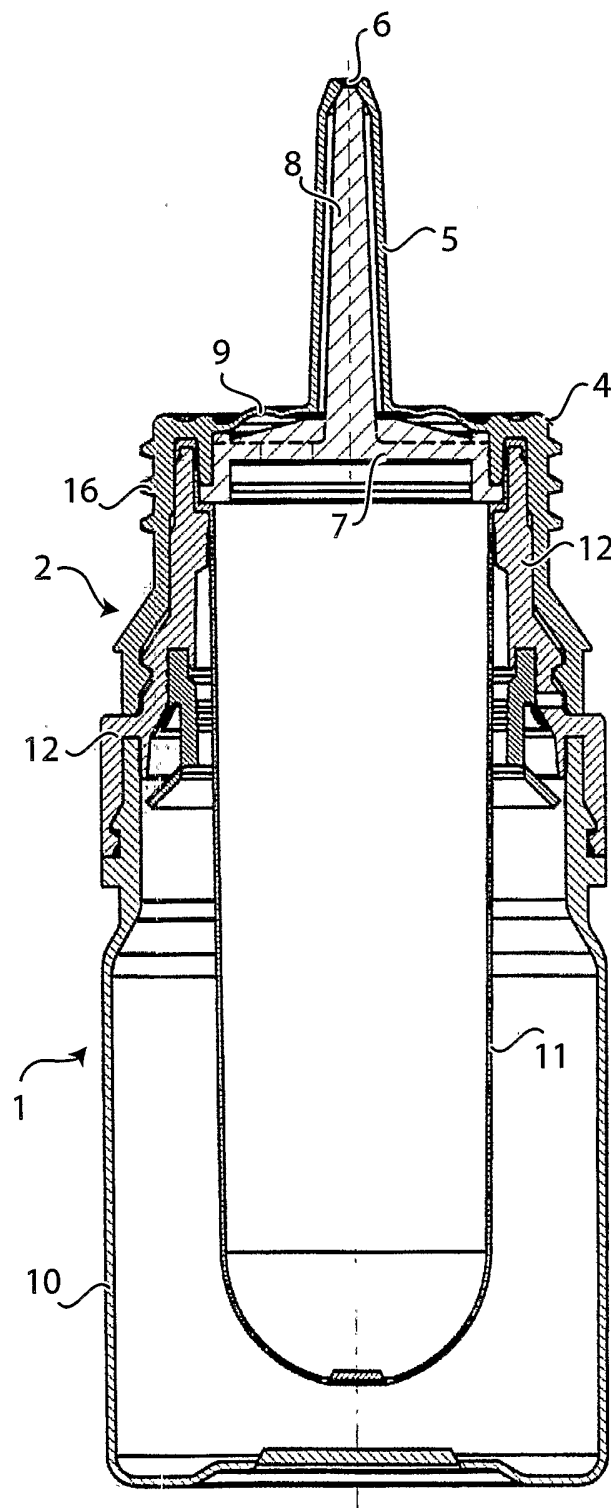


Fig. 2

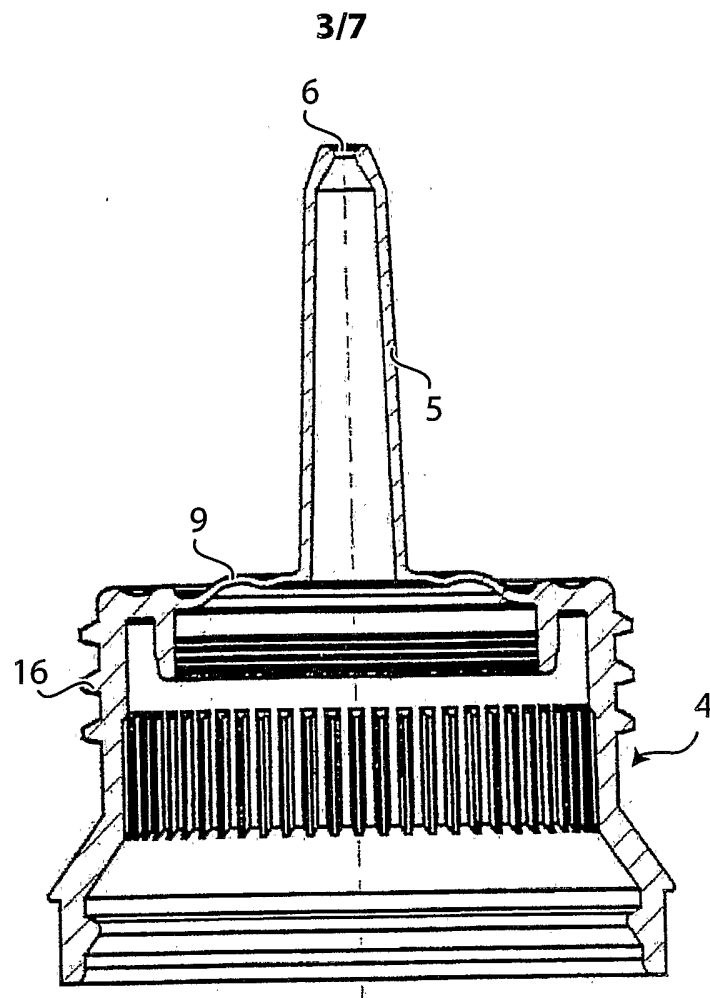


Fig. 3

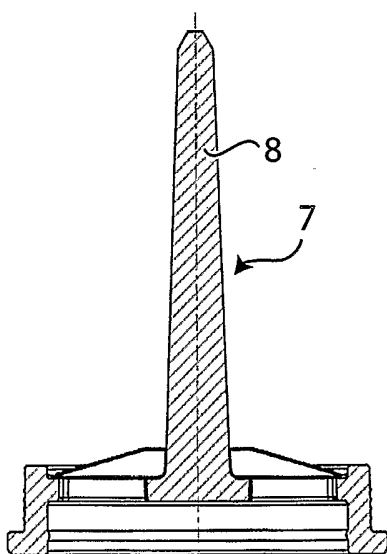


Fig. 4

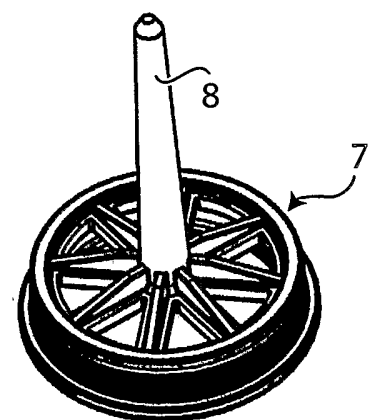


Fig. 5

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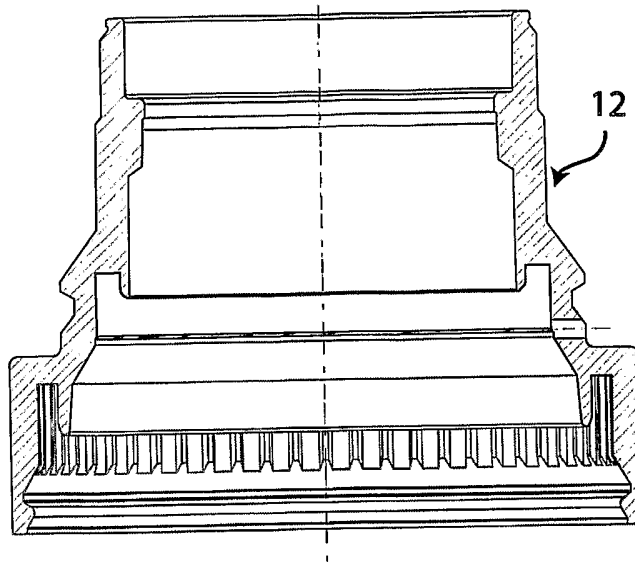


Fig. 6

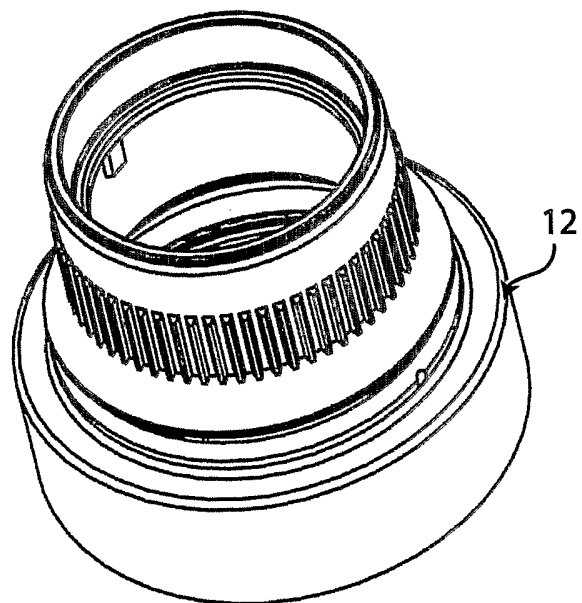


Fig. 7

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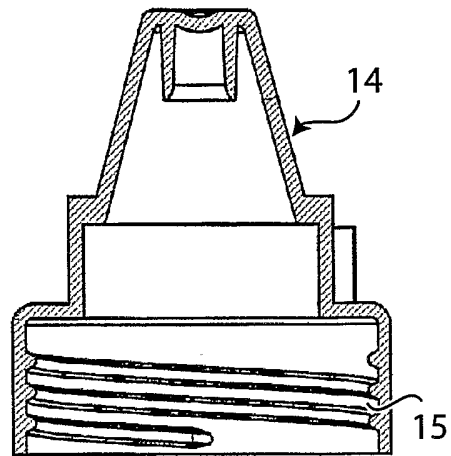


Fig. 8

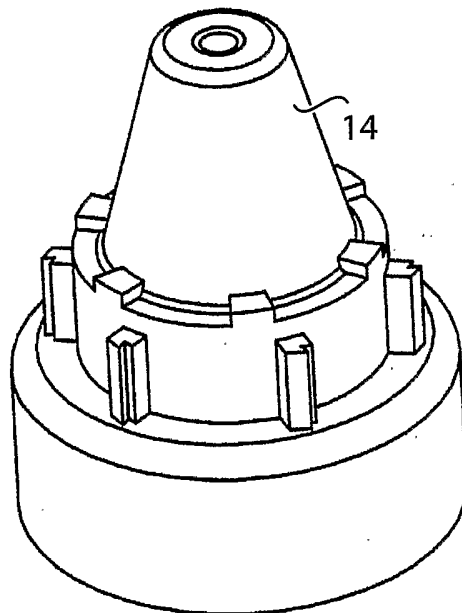


Fig. 9

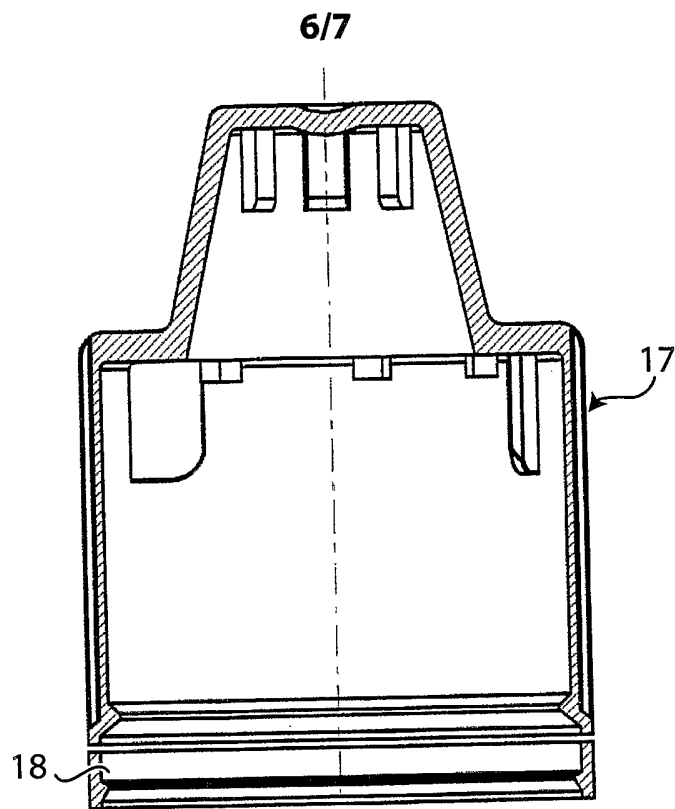


Fig. 10

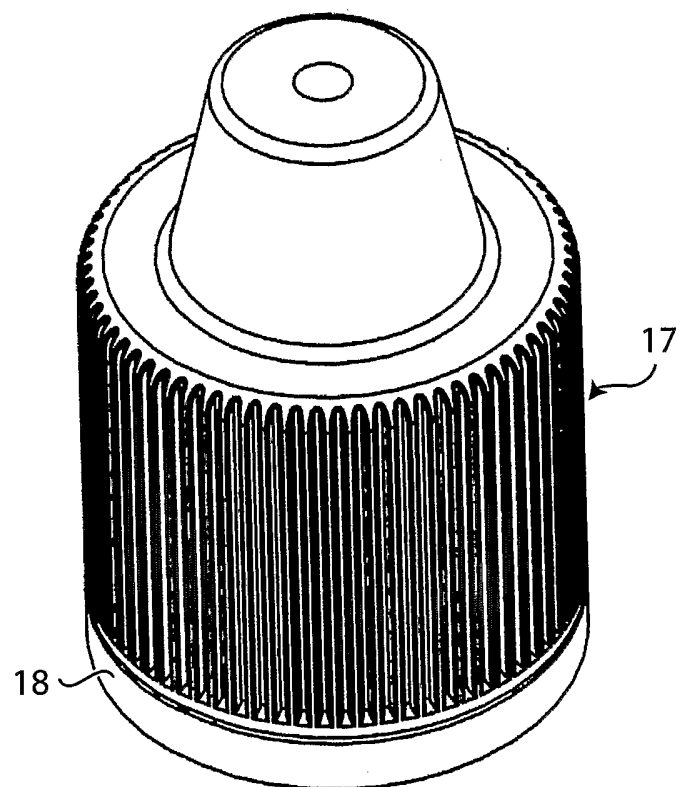
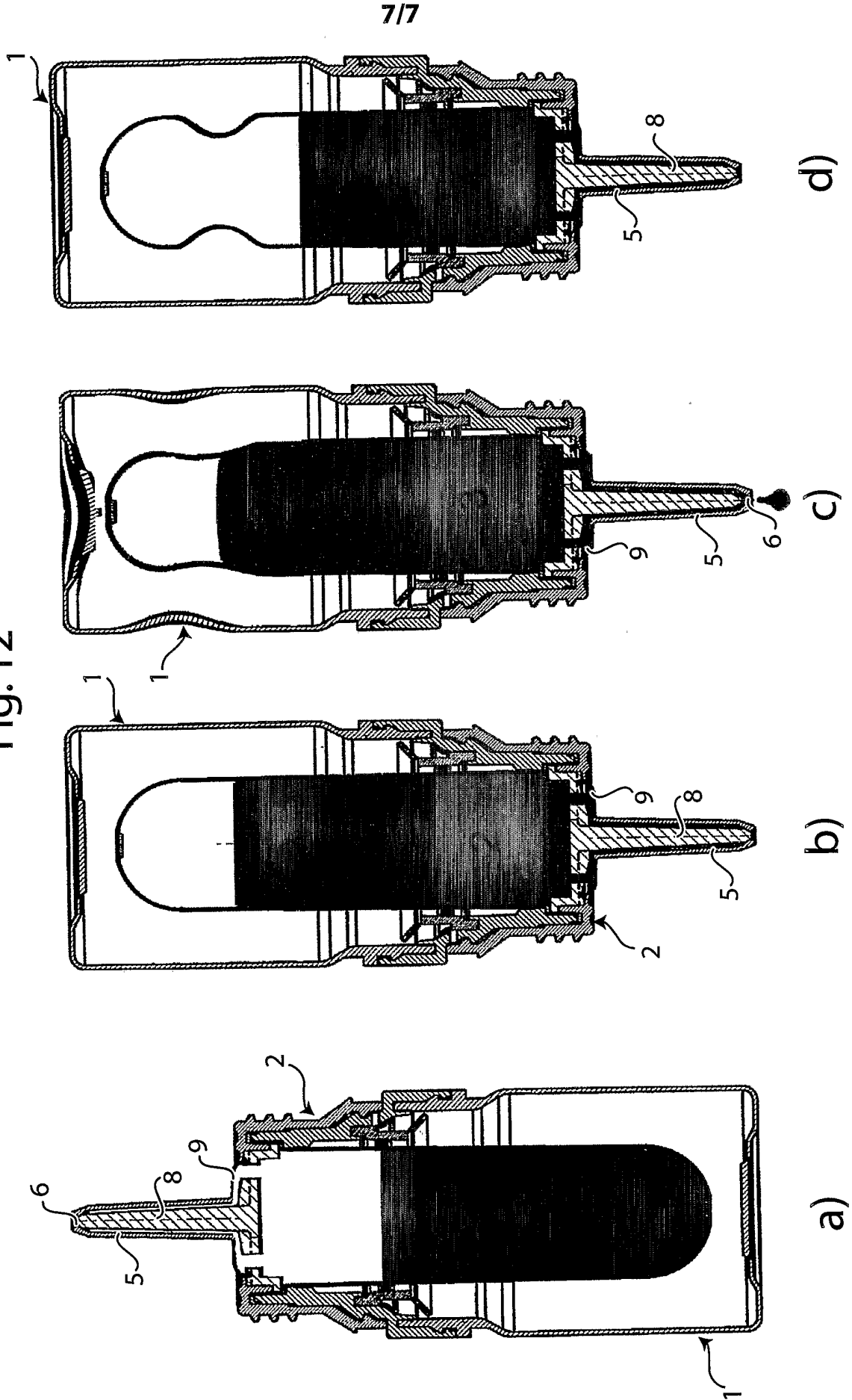


Fig. 11

Fig.12



INTERNATIONAL SEARCH REPORT

 International Application No
 PCT/IT2005/000170

 A. CLASSIFICATION OF SUBJECT MATTER
 IPC 7 B65D47/20 B65D47/18

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

 Minimum documentation searched (classification system followed by classification symbols)
 IPC 7 B65D

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, PAJ

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 4 420 100 A (MUELLER ET AL) 13 December 1983 (1983-12-13)	1-5
Y	column 1, line 55 - column 3, line 47; figures 1-4	6-11
X	----- US 4 739 906 A (LOTURCO ET AL) 26 April 1988 (1988-04-26) column 1, line 10 - line 17 column 3, line 7 - column 5, line 10; figures 4,5	1-4,11
X	----- PATENT ABSTRACTS OF JAPAN vol. 2002, no. 05, 3 May 2002 (2002-05-03) & JP 2002 002755 A (KITANO SEISAKU KK), 9 January 2002 (2002-01-09) abstract; figures 3,4 ----- -/--	1-4

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

° Special categories of cited documents :

"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 when the document is taken alone

"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

Date of the actual completion of the international search

14 July 2005

Date of mailing of the international search report

17 10. 2005

Name and mailing address of the ISA

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Authorized officer

Bevilacqua, V

INTERNATIONAL SEARCH REPORT

International Application No

PCT/IT2005/000170

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 5 033 647 A (SMITH ET AL) 23 July 1991 (1991-07-23) column 3, line 27 - line 59; figures 3,4 -----	6-11

INTERNATIONAL SEARCH REPORT

International application No.
PCT/IT2005/000170

Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos.:
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, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

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

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ 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 claims Nos.:

1-11

Remark on Protest

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

☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-11

A dispenser for liquid preparations without preservatives, comprising a container body and a dropper assembly, which in turn comprises a container body closure element ending with an elongated dropper nozzle provided with a central port and a pin plug of a complementary shape to the said dropper nozzle and cooperating with it to intercept the outflow of a liquid preparation contained in said dispenser, the pin plug being located inside the dropper nozzle in a fixed position with respect to the container body, and the said dropper nozzle being displaceable outward from said pin plug in order to open up the port of the said dropper assembly as a result of a mechanical pressure applied to the exterior of the container body
wherein

said container body comprises an elastic external body and a collapsible internal body enclosed within it, suitable to contain therein the liquid preparation and to decrease in volume as said liquid preparation flows out of the dispenser.

2. claims: 12,13

A dispenser for liquid preparations without preservatives, comprising a container body and a dropper assembly, which in turn comprises a container body closure element ending with an elongated dropper nozzle provided with a central port and a pin plug of a complementary shape to the said dropper nozzle and cooperating with it to intercept the outflow of a liquid preparation contained in said dispenser, the pin plug being located inside the dropper nozzle in a fixed position with respect to the container body, and the said dropper nozzle being displaceable outward from said pin plug in order to open up the port of the said dropper assembly as a result of a mechanical pressure applied to the exterior of the container body
wherein

the dispenser features an external closure capsule including a screw cap and a knurled overcap that fits over the screw cap and is connected to it

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/IT2005/000170

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
US 4420100	A	13-12-1983	NONE	
US 4739906	A	26-04-1988	CA 1278279 C DE 3782200 D1 DE 3782200 T2 EP 0253495 A2 ES 2036208 T3	27-12-1990 19-11-1992 06-05-1993 20-01-1988 16-05-1993
JP 2002002755	A	09-01-2002	JP 3492600 B2	03-02-2004
US 5033647	A	23-07-1991	AU 7573391 A IE 910773 A1 IL 97444 A NZ 237337 A PT 96980 A WO 9113812 A1 ZA 9101677 A	10-10-1991 11-09-1991 27-02-1994 25-11-1992 31-05-1993 19-09-1991 27-11-1991