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(54) Airtight container for storing a liquid, and in particular a medicament, and aseptic process for filing said container

(57) The airtight container (1) for storing a liquid comprises a rigid vial (2) with at least one filling hole (2c), a first cap (3) that can be easily punctured with a syringe or the like for emptying the vial (2), and an external filling pipe (5) for filling the vial (2) through the filling hole (2c). Said filling pipe (5) airtightly seals the filling hole (2c) of the vial (2), and is temporarily opened during the filling process.

The container is particularly suitable for storing prior to use a liquid such as a medicament (vaccines or the like) under sterile conditions.

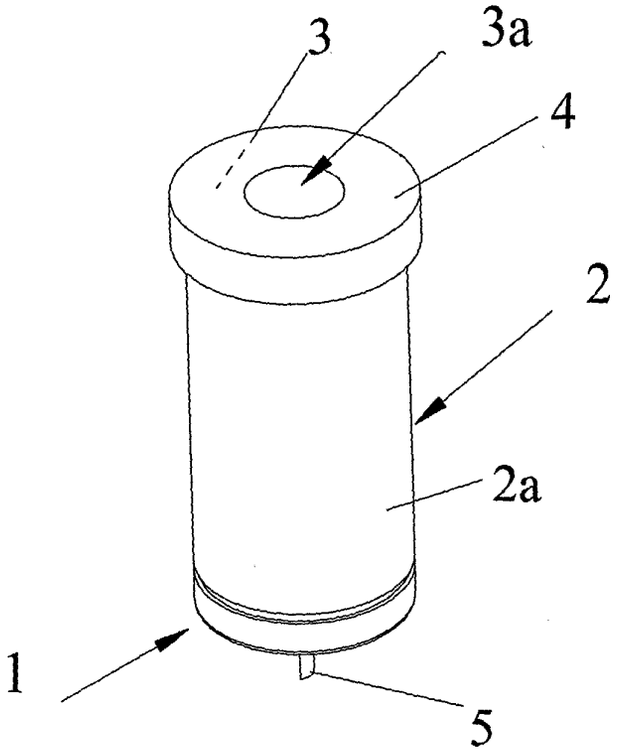

FIG 1

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Description

Field of the invention

[0001] The present invention generally relates to an airtight container that is being used for storing a liquid under sterile conditions, and that comprises a cap which is designed to be manually punctured, for example by using a needle or a syringe, in order to empty the container. A preferred application of the invention is a small-sized airtight container that is being used in the pharmaceutical field for storing a medicament such as vaccines or the like.

Prior Art

[0002] In the pharmaceutical field, liquid medicaments, such as vaccines, are usually stored, prior to use, in small-sized airtight containers constituted by a rigid vial that is typically made of glass or plastic, and that is airtight sealed by a cap. The cap is typically made of vulcanized rubber or similar resilient material that neither contaminates nor affects the medicament, and that can be manually punctured by using a sharp element such as a syringe or a needle, in order to empty the vial.

[0003] A major technical problem in this technical field is to avoid the contamination of the liquid (medicament or the like) stored inside the container, and thus to guarantee the sterility of the inside of the container during the filling process and also after the filling process.

[0004] According to one first known aseptic filling procedure, the vial and the cap are sterilized separately, then the vial is filled with the medicament or the like, and the cap is assembled to the vial in order to seal the medicament in the vial. One major drawback of this first filling procedure is that it is difficult to maintain the sterility of the cap and vial during the assembly step. In addition, it is difficult to maintain the sterility of the vial and cap during transportation and storage prior filling.

[0005] In an attempt to overcome said risk of contamination of the vial and cap, it has been proposed in the past to use a second aseptic filling procedure wherein: in a first step, the cap is assembled to the vial so as to hermetically seal the vial ; in a second step the vial and the cap are sterilized, for example by gamma irradiation or the like ; in a third step, the vial is filled with the medicament by using a sterile syringe or like injection element that is temporarily inserted through the cap.

[0006] A first major drawback associated with this second aseptic filling procedure is that when the injection member (syringe, needle or the like) is temporarily inserted through the cap, and then withdrawn, a tiny hole is being formed in the cap.

[0007] The hole resulting from the insertion of the needle or the like shrinks somewhat due to the resiliency of the cap. In practise, the tiny hole that is formed in the cap is small enough to keep the medicament from leaking out, but is typically not small enough to prevent air or other gases from passing through the hole and into the vial. In addition, a resilient material such as vulcanized rubber is infusible. It is thus not possible to fuse such material in situ, for example with a suitable laser, in order to hermetically close the said tiny hole formed in the cap. Finally, when the aforesaid second filling procedure is being used, because of this tiny hole resulting from the insertion of the needle or the like, there is still a high risk of spoiling and/or contamination of the medicament stored in the vial.

[0008] A second major drawback associated with the aforesaid second filling procedure is that the exhaust of the air contained in the vial during the filling step is difficult, because of the very small diameter of the needle used for filling the vial ; said exhaust of air typically involves the use of an additional duct acting as a vent, and it is in practise difficult to correctly measure out the medicament introduced in the vial.

[0009] In US patent N° 6,604,561, it is further disclosed a heat resealable cap comprising a first base portion formed of vulcanized rubber or like material known for providing a stable environment for the medicament contained in the vial, and a second heat resealable portion overlying the base portion. In particular, the second heat resealable portion is made of low-density polyethylene or like material, that can be manually punctured by a needle or similar. The aforesaid second filling procedure is used for filling the vial with the liquid medicament, and once the needle or the like is being withdrawn, the penetrated region of the cap is fused by laser or direct heat sealing, in order to hermetically seal the needle hole in the cap. The use of said composite cap (heat resealable portion/ vulcanized rubber base portion) disclosed in US patent N° 6,604,561 solves the problem of contamination due to the formation of the needle hole in the cap after filling.

[0010] The use of the composite heat resealable cap disclosed in US patent N° 6,604,561 does not however solve the aforesaid major second drawback linked to the exhaust of air during filling. In particular, referring for example to figure 3 of US patent N° 6,604, 561, an additional venting needle or syringe (referenced "142") has to be used for venting the vial during the filling step.

[0011] Furthermore, the use of the composite heat resealable cap disclosed in US patent N° 6,604,561 involves at least one additional drawback. There is a risk that part of the liquid contained in the vial passes trough the needle hole made in the vulcanized rubber base portion or the like, and detrimentally comes into contact with the upper heat sealable portion of the cap, which heat sealable portion of the cap is not compatible with the liquid. The risk is higher when the vial is turned upside down, or when the vial and cap are slightly deformed by a small negative internal pressure.

Objective of the invention

[0012] It is an objective of the invention to propose a

new technical solution for storing a liquid under sterile conditions, and in particular a medicament, in a container, which solution enables to maintain the sterility of the inside of the container, and overcomes all the aforesaid drawbacks of the prior art.

Summary of the invention

[0013] This objective is achieved by the new airtight container of claim 1 and by the aseptic filling process of claim 11.

[0014] A major advantage of the invention is to avoid a perforation of the cap for filling the container. According to the invention, the filling of the container is performed through the filling pipe of the container, once said filling pipe has been temporarily opened ; the invention thus overcomes all the drawbacks of the prior art that were associated to the formation of the hole in the cap after filling, and to the closing of said hole.

[0015] Furthermore, according to the invention, the cap is being punctured only when emptying the vial ; the structure of the cap can thus be very simple and the cap can be made from any material that is compatible with the liquid and that can be manually punctured. In particular, said material does not need to be resealable.

[0016] Another advantage of the invention is that in practise the filling pipe can easily have a diameter that is large enough for enabling an easy exhaust of the air contained in the vial, during the filling step.

[0017] According to a further advantage of the invention, the equipment used for filling the vial or the equipment used for closing the filling pipe comes into contact with the filling pipe only, and does necessarily penetrate inside the vial.

[0018] Other characteristics and advantages of the invention will become readily apparent in view of the following detailed description of several preferred embodiments of the invention and the accompanying drawings, which description and drawings are given by way of non-exhaustive and non-limiting examples of the invention.

Brief description of the drawings

[0019]

- Figure 1 is a perspective view of an empty container of the invention, prior to the filling step ;
- Figure 2 is a perspective view of an half of the container of figure 1 showing the inside of the container;
- Figure 3 is a cross-sectional view of the bottom part of the container prior to the filling step, and shows a first embodiment for the fixing means of the filling pipe ;
- Figure 4 is a cross-sectional view of the bottom part of the container prior to the filling step, and shows a second embodiment for the fixing means of the filling pipe;
- Figure 5 is a cross sectional view of the distal end of a filling pipe closed by a cap ;
- Figure 6 is a cross-section view of the distal end of a filling pipe closed by a clip ;
- Figures 7 to 10 schematically shows the successive steps for filling the container of figure 2 with a liquid, and
- Figure 11 is a perspective view of the final container filled with the liquid.

Detailed description

[0020] Figures 1 and 2 show an empty container 1 of the invention, prior aseptic filling with a liquid, such as for example a medicament or the like.

[0021] Said container 1 comprises :

- a rigid vial 2 constituted by a cylindrical sidewall 2a and a bottom wall 2b, said bottom wall 2b having a small central filling hole 2c,
- a cap 3 in the form of a rubber vulcanized element which is slidably received in the open end of the vial 2 (opposite to the bottom end 2b) ; such a cap 3 is also commonly referred as a "stopper" ;
- a locking ring 4, for example made of aluminium or plastic, that is crimped in place onto the vial 2 in order to lockably connect and airtight seal the cap 3 to the vial 2;
- an add-on external filling pipe 5 which is fixed at one end on the bottom wall 2b of the vial 2.

[0022] The vial 2 can be made of any sterilizable and inert material that is compatible with the liquid that has to be stored. The vial 2 can be for example made of glass or plastic.

[0023] The cap 3 can be made of any sterilizable material that is compatible with the liquid, and that can be easily and manually punctured with a needle, a syringe or the like. The invention is not limited to a rubber vulcanized cap.

[0024] The filling pipe 5 defines an internal fluid passage 6 (figure 3) having an open proximal end 6a, and is airtightly fixed to the bottom end 2b of the vial 2 by any suitable means, in such a way that the open proximal end 6a of the fluid passage 6 communicates with the bottom filling hole 2c of the vial 2. It is important for the seal between the filling pipe 5 and the vial 2 to be airtight, in order to avoid any risk of contamination of the inside of the vial 2.

[0025] In the particular embodiment of figure 3, the filling pipe 5 has a proximal end 5a in the form of a "T", and is locked onto the vial 2 by an additional locking cap 7 which squeezes the proximal end 5a of the filing pipe against the external face of the bottom end 2b of the vial 2. Said fixing means does not limit the scope of the invention, and can be replaced by any other suitable airtight fixing means. In particular, the proximal end 5a of the filling pipe 5 could be inserted and airtightly fixed through the bottom filling hole 2c of the vial 2 (as shown

on figure 2). Figure 4 shows another variant for airtightly fixing the filling pipe 5 on the vial 2. In another variant, the filling pipe 5 could be welded on the vial.

[0026] The filling pipe 5 is made of any sterilizable material that is compatible with the liquid that will be stored inside the vial 2. The pipe is preferably flexible and is for example made of any biocompatible polymer and more particularly any biocompatible elastomer.

[0027] As shown in the particular embodiment of figure 3 or figure 4, the distal end 5b of the filling pipe is airtightly closed. The filling pipe 5 thus airtightly seals the filling hole 2c of the vial 2, in order to avoid the accidental penetration of any contaminant (solid, liquid or gaz) inside the vial 2.

[0028] More particularly, in the embodiment of figure 3 or 4, the opening of the distal end 5b of the filling pipe (during the filling step) can be performed by simply pinching the distal end 5b of the pipe 5, so as to create an internal fluid passage 6 on the whole length of the filling pipe. When the pinching pressure is released, the distal end 5b of the filling pipe 5 comes back to its closed state, as illustrated on figure 3 or figure 4.

[0029] The process for the aseptic filling of the container 1 with a liquid, such as a medicament, comprises the following steps.

(a) The empty container 1 of figure 1 or figure 2 is sterilized by using any well-known sterilization process and for example by using gamma radiations.

(b) The distal end 5b of the filling pipe of the sterilized empty container 1 is temporarily opened by two jaws 11 (figure 7) that pinch the filling pipe ; advantageously, the opening system (jaws 11) does not penetrate inside of the vial 2 . Then a sterile filling nozzle 10 is inserted inside said opened distal end 5b ; advantageously, the filling nozzle 10 does not penetrate inside the vial 2, but is inserted only inside the filling pipe 5.

(c) The liquid is injected inside the vial 2 through the filling pipe 5 and through the bottom filling hole 2c. In order to enable the exhaust of the air contained in the vial 2 during this filling step, the external diameter of the filling nozzle 10 has to be smaller than the internal diameter of the filling pipe 5.

(d) The filling nozzle 10 is removed from the filling pipe 5 and the distal end 5b of the filling pipe is hermetically closed (figure 8), by releasing the pressure exerted by the jaws 11.

(e) The filling pipe 5 is definitely closed.

[0030] The final closing step (e) can be performed in different ways. For example the filling pipe 5 is pressed in order to airtightly close the pipe 5, and the distal end 5b of the pipe 5 is thermally sealed (by laser or by using any thermal source for fusing the distal end of the pipe). Then the filling pipe 5 is preferably fold up as depicted on figure 9. This can be achieved by a mechanical action eventually combined with a local heating of the pipe in order to locally soften the pipe 5. Advantageously, all the equipments used for definitely closing the filling pipe (step e) do not come into contact with the inside of the vial 2

[0031] Finally, in a preferred embodiment of the invention (figures 10 and 11), a cap 12 is definitely fixed onto the bottom end 2b of the vial 2, said bottom cap 12 defining with the vial 2 an housing 12a for the pipe 5. The pipe 5 is this no longer accessible. The cap 12 protects the filling pipe 5, and avoids any risk of detrimental manipulation thereof. The cap 12 also forms a stable and aesthetic base for the container 1.

[0032] According to the invention, thanks to the use of the external filling pipe 5, there is advantageously no need to perforate the vial 2 or the cap 3 during the filling process. There is thus no risk of contamination of the inside of the vial by particles or the like coming from the vial, the cap or from any equipment used during the aseptic filling process.

[0033] It should be also noted that during the filling step (c) and the closing steps (d) and (e), the liquid is advantageously not subjected to any pressure variations or to any thermal variations. There is thus not modification of the properties of said liquid.

[0034] It is important for the invention that the filling pipe 5 is airtightly closed, prior the filling step (b), so as to preclude the penetration of any contaminant inside the vial during the process. But the invention is not limited to the particular filling pipe shown in figures 3 and 4.

[0035] In another variant shown on figure 5, the distal end 5b of the filling pipe 5 is airtightly closed by a removable cap 8.

[0036] In another variant shown on figure 6, the distal end 5b of the filling pipe 5 is airtightly closed by a removable clip 9.

[0037] In another variant (not shown), the distal end 5b of the filling pipe 5 could be thermally fused so as to be hermetically closed, and the opening of the pipe (step (b)) could be performed by cutting the closed end the pipe 5 (for example by using a laser or any mechanical cutting means).

[0038] The final container 1' containing the liquid is shown on figure 11. The emptying of the container 1' is performed by puncturing the cap 3 (in the area 3a that is not surrounded by the locking ring 4) with a needle or syringe, and by sucking through the cap 3 the liquid contained inside the vial 2.

Claims

1. An airtight container (1) for storing a liquid, wherein said container comprises a rigid vial (2) with at least one filling hole (2c), a first cap (3) that can be easily punctured for emptying the vial (2), and an external filling pipe (5) for filling the vial (2) through the filling hole (2c), and wherein said filling pipe (5) airtightly seals the filling hole (2c) of the vial (2).

2. The container of claim 1 wherein the filling pipe (5) can be opened by exerting a pressure on the pipe.

3. The container of claim 1 wherein the filling pipe (5) is airtightly sealed by a second removable cap (8).

4. The container of claim 1 wherein the filling pipe (5) is airtightly sealed by removable clip (9).

5. The container of claim 1 wherein the first cap (3) is made of vulcanized rubber.

6. The container of claim 1 wherein the filling pipe (5) is flexible.

7. The container of claim 1 wherein the filling pipe (5) is fixed on the bottom end (2b) of the vial (2), said bottom end (2b) being opposite to the first cap (3), and comprising said filing hole (2c).

8. A container according to any one of claims 1 to 7, wherein the vial (2) is containing a liquid, and the filling pipe (5) is definitely airtightly sealed.

9. The container of claim 8 further comprising a housing cap (12) that is definitely assembled to the vial (2), and that forms an housing (12a) for the filling pipe (5).

10. The container of claim 8 or claim 9 wherein the liquid is a medicament, and in particular a vaccine.

11. Aseptic process for filling a container (1) according to anyone of claims 1 to 7 with a liquid, said process comprising the following steps :

- sterilizing the empty container (1),
- temporarily opening the filling pipe (5) and introducing the liquid inside the vial (2) through the filling pipe (5),
- definitely and airtightly sealing the filling pipe (5).

12. The process of claim 11 wherein a cap (12) is definitely assembled to the vial (2), said cap (12) forming a protective housing (12a) for the filling pipe (5).

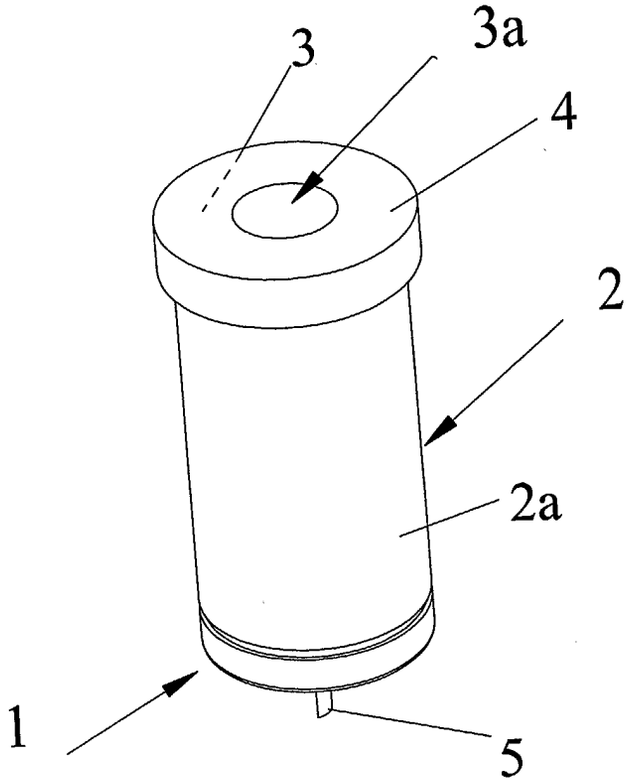

FIG 1

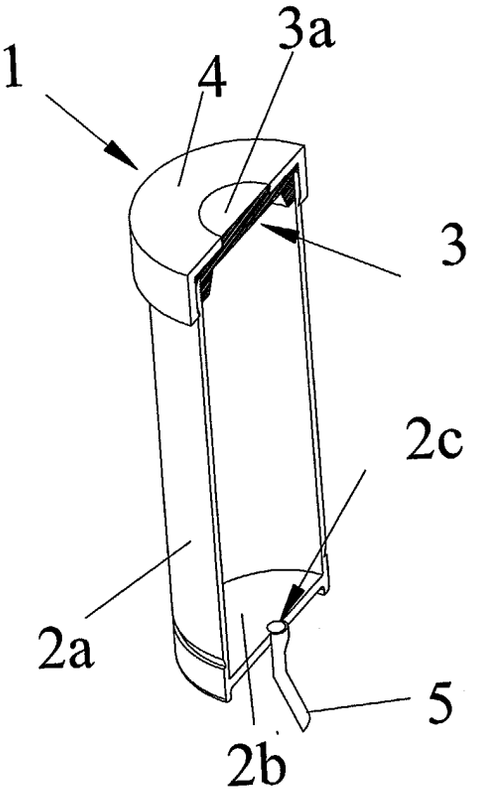

FIG 2

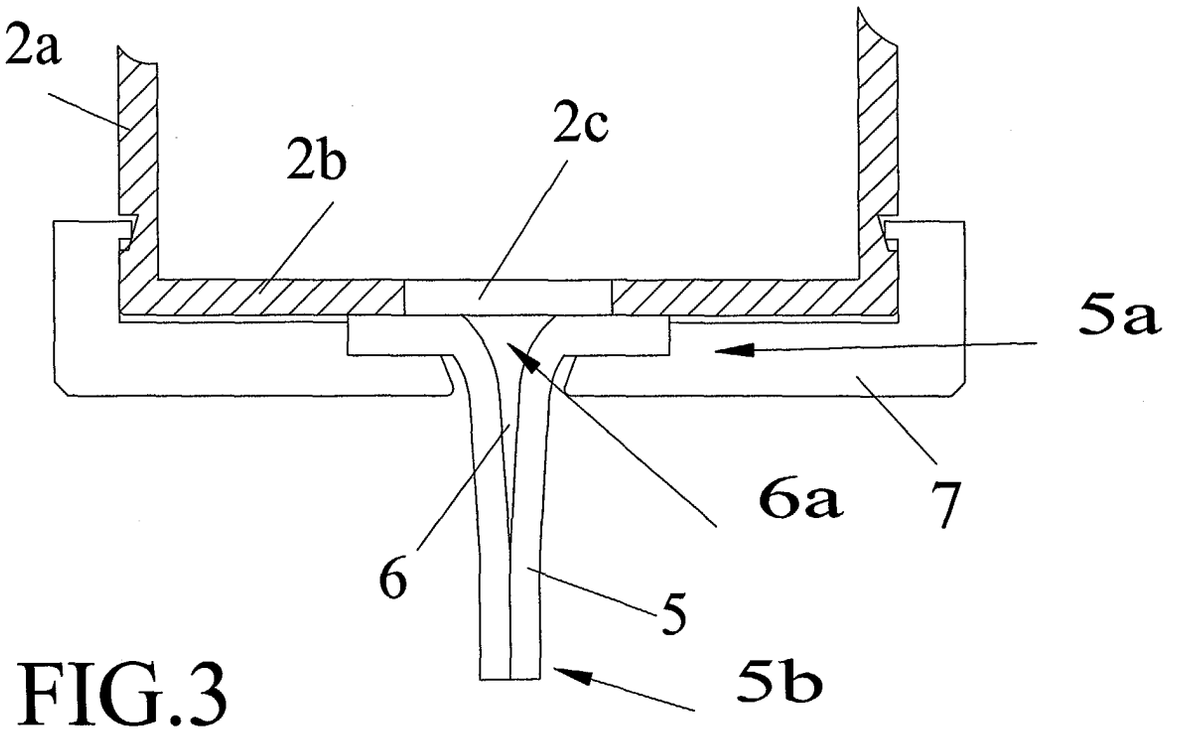

FIG.3

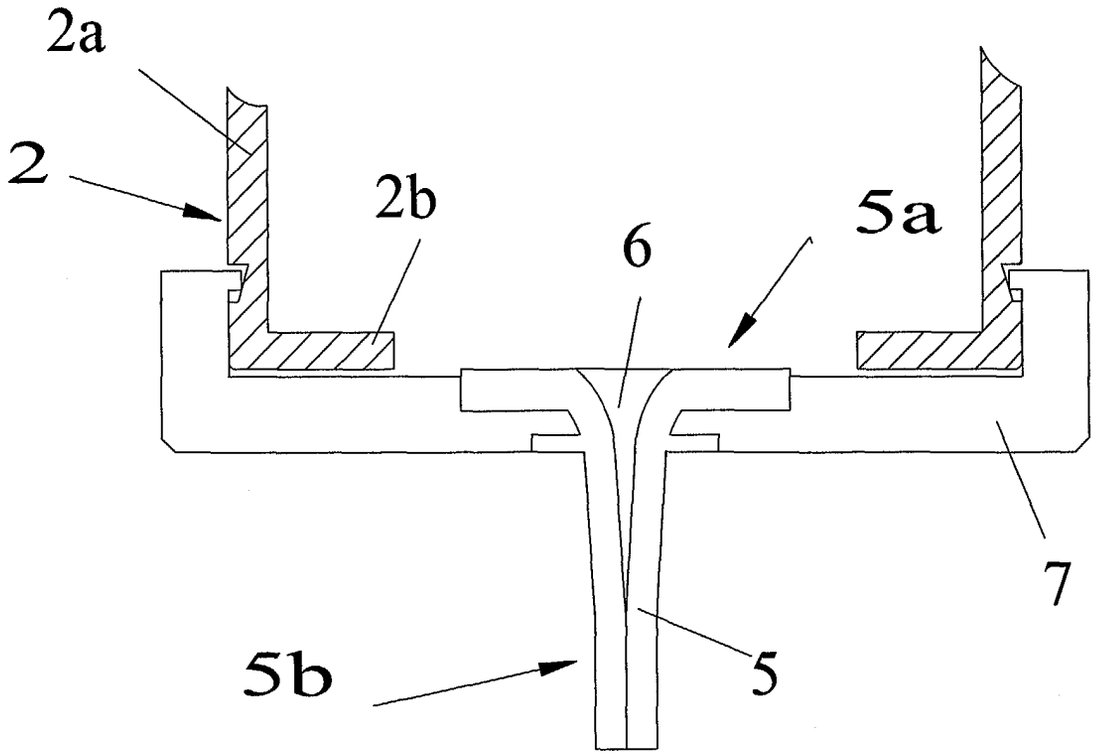

FIG.4

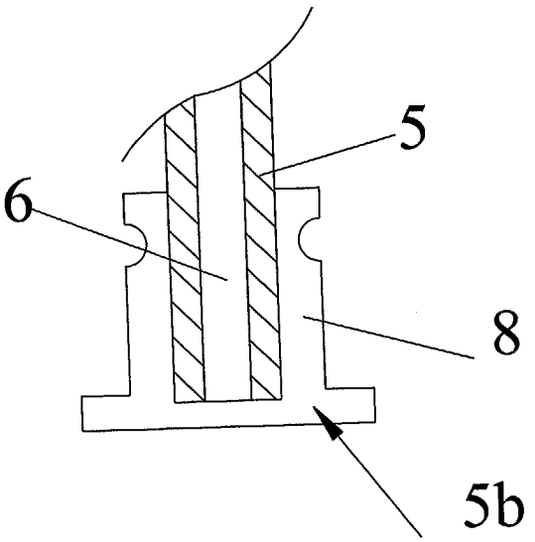

FIG.5

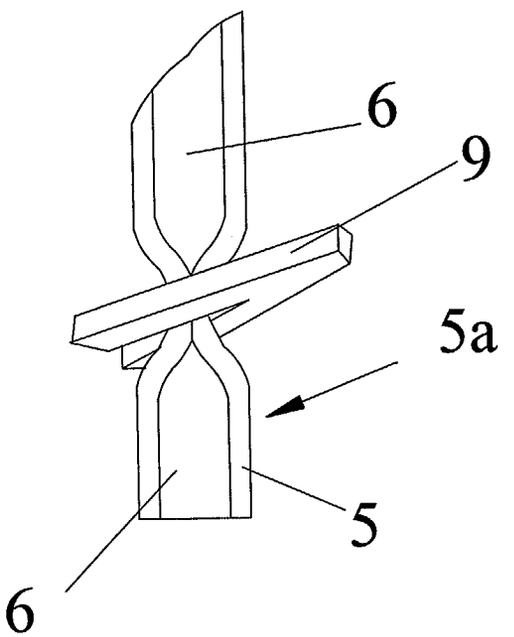

FIG.6

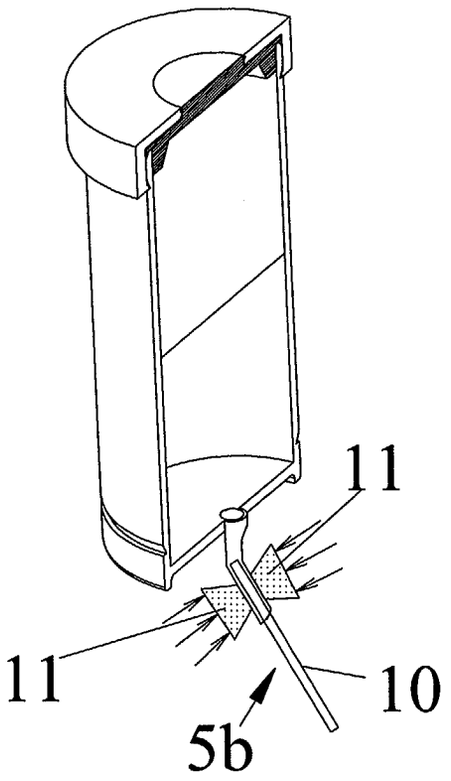

FIG.7

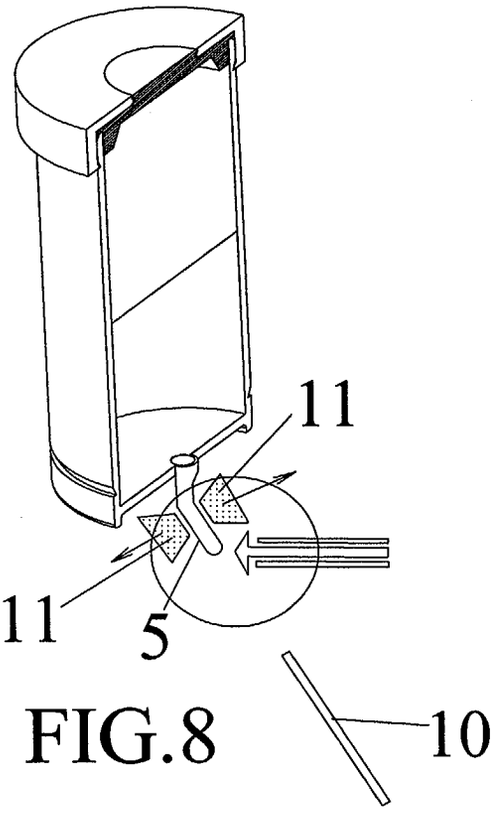

FIG.8

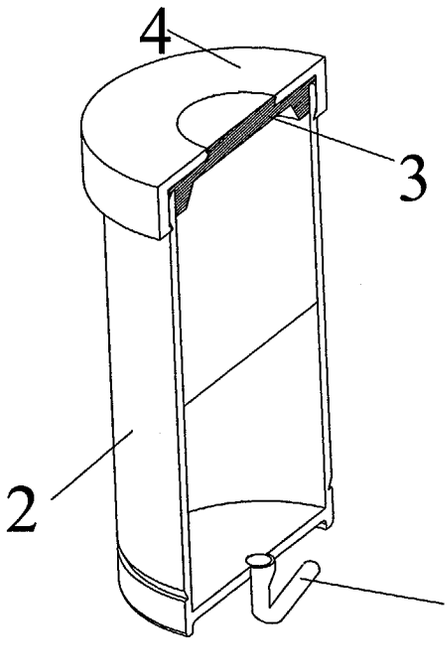

FIG.9

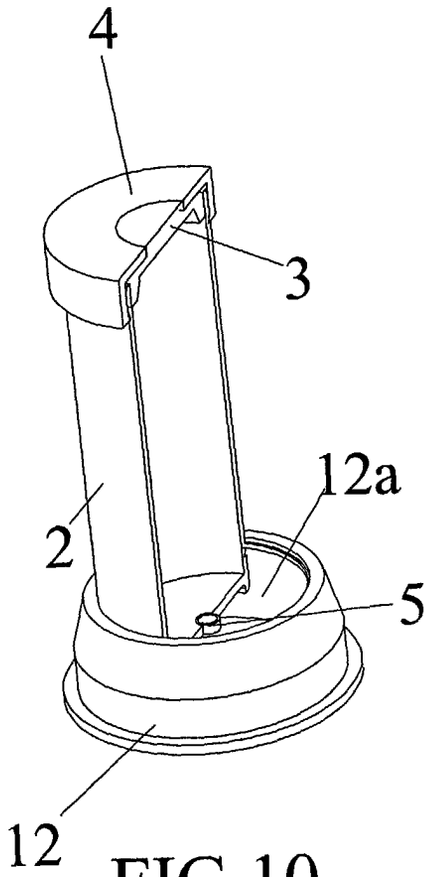

FIG.10

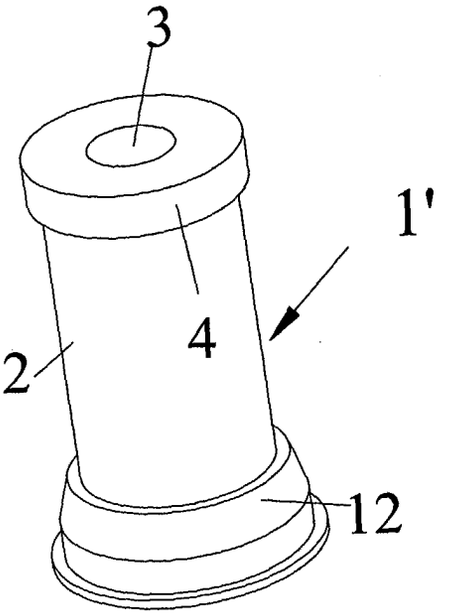

FIG.11

European Patent Office

EUROPEAN SEARCH REPORT

Application Number
EP 04 37 0016

DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int.Cl.7)
X	US 6 364 168 B1 (CHOI ROBERT ET AL) 2 April 2002 (2002-04-02) * column 3, line 20 - line 33 * * column 3, line 54 - line 63; figures * -----	1-12	A61J1/00 F16K7/02
X A	WO 95/13786 A (REINA GIUSEPPE) 26 May 1995 (1995-05-26) * page 3, line 6 - page 4, line 7; figures * -----	1-6,11,12 7-10	
A	EP 0 320 938 A (KOKEN KK) 21 June 1989 (1989-06-21) * column 2, line 6 - line 23; figures * -----	1,11	
A	US 274 447 A (WILLIAM KENNISH) 20 March 1883 (1883-03-20) * the whole document * -----	1-12	
A	US 1 579 996 A (OWEN BANES GLENN) 6 April 1926 (1926-04-06) * page 1, line 50 - line 62; figures * -----	1-12	

TECHNICAL FIELDS SEARCHED (Int.Cl.7)

A61J
A61M
F16K

The present search report has been drawn up for all claims

Place of search	Date of completion of the search	Examiner
The Hague	10 November 2004	Cametz, C

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Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 6364168 B1	02-04-2002	US 6032831 A	07-03-2000
		US 6070767 A	06-06-2000
		AU 743809 B2	07-02-2002
		AU 5105899 A	07-02-2000
		CA 2302210 A1	27-01-2000
		EP 1017618 A1	12-07-2000
		JP 2003530270 T	14-10-2003
		WO 0003946 A1	27-01-2000
		AU 8500098 A	07-02-2000
		WO 0003945 A1	27-01-2000
WO 9513786 A	26-05-1995	IT TS930008 A1	19-05-1995
		AT 171064 T	15-10-1998
		AU 1118795 A	06-06-1995
		DE 69413388 D1	22-10-1998
		EP 0683658 A1	29-11-1995
		WO 9513786 A1	26-05-1995
EP 0320938 A	21-06-1989	JP 1095937 U	26-06-1989
		JP 4012986 Y2	27-03-1992
		EP 0320938 A2	21-06-1989
US 274447 A		NONE	
US 1579996 A	06-04-1926	NONE	

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