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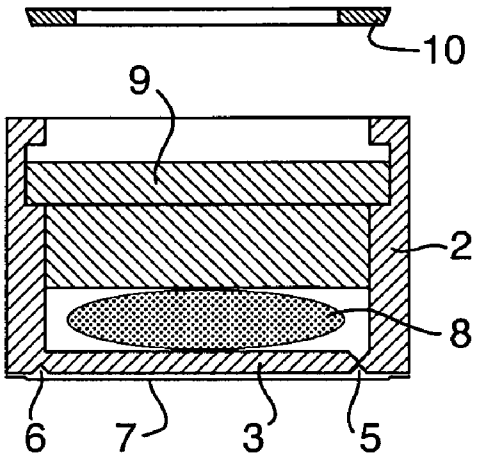
(54) Title: A PRE-FILLED CONTAINER INSERT FOR MIXING TWO OR MORE INGREDIENTS FOR USE IN A PHARMACEUTICAL CONTAINER SYSTEM

Fig.1e.



(57) Abstract: The present invention relates to pharmaceutical container systems (21), and to pre-filled container inserts (17) for use therein, for mixing two or more ingredients (8) of a pharmaceutical product. The pre-filled container insert (17) of one embodiment comprises a moulded container casing (1) having walls (2), a bottom (3) and an open top (4) for receiving a solid component (8), a resilient stopper (9) for sealing the open top (4) of the moulded container casing (1), and a bottom disc (3) formed by a weakening rim (5) in the bottom periphery of the moulded container casing (1). The bottom disc (3) is openable to allow mixing of the pre-filled solid component (8) with a diluents fluid of the pharmaceutical container system (21) by introducing a spike (20) through the resilient stopper (9) applying a pushing force on the bottom disc (3), by which force the weakening rim (5) is broken and the container (17) is opened. The pre-filled container insert (17) of a further embodiment comprises a moulded container casing (1) having walls (2), a bottom (3) and an open top (4) for receiving an inner open cylinder (30) and a solid component (8), a resilient stopper (9) for sealing the open top (4) of the moulded container casing (1), and a bottom disc (3) formed by a weakening rim (5) in the bottom periphery of the moulded container casing (1). The bottom disc (3) is openable to allow mixing of the pre- filled solid component (8) with a diluents fluid of the pharmaceutical container system (21) by applying a pushing force onto the top of the moulded container compressing the casing (1) and forcing the inner cylinder (30) to push on the bottom disc (3), by which force the weakening rim (5) is broken and the container insert (17) is opened.

WO 2010/019096 A1

A pre-filled container insert for mixing two or more ingredients for use in a pharmaceutical container system

Technical Field

The present invention relates to a pharmaceutical multi-chamber container system for mixing two or more ingredients of a pharmaceutical product, and more particularly to a pre-filled container insert to be used with such a system.

Background of the Invention

Solid active pharmaceutical ingredients (API) or formulated products generally have better shelf-life, i.e. degrade at a slower rate than solutions (or dispersions/emulsions) of the same compound. Therefore, it is commonplace to use dry powder, for example to freeze-dry or spray-dry pharmaceutical products to extend shelf-life of a pharmaceutical product to practical length, typically at least 18-24 months. At time of use, such a solid product must be dissolved in a suitable solvent before it can be administered to the patient, usually via oral or parenteral routes or by nasal delivery. The dissolution of the solid in a solvent is typically made via transfer of the solvent from a vial or bag using a syringe. Although such a process is a standard procedure amongst hospital staff, it does take training and skill to do it in a safe and efficient manner without risk of needle-stick injury or compromising product sterility and thereby patient safety.

Patent abstract of Japan, JP2000037441A relates to an infusion container system having a solid drug storing part connected to a liquid solution container. A fluid communication channel is established between the two containers by pressing the solid medicine storing part to the solution container side and a partitioning member is opened and moved from a seal part. After making the solid drug storage container and the solution container open for free passage the solid drug dissolves in the liquid solution by shaking the whole transfusion container. The solution is now ready to be administered to a patient and a puncture needle is introduced into an infusion solution take off connection provided in the top of the solid drug storage container. A drawback with this device is that it requires a complicated construction of the solid drug storing part comprising several parts and which will involve

a number of production steps. A further drawback is that two steps need to be carried out before the solution can be administered to a patient, namely first allow for mixing of the two ingredients and then introducing a needle to connect for example an infusion set.

The Object of the Invention

It is an object of the present invention, in preferred embodiments at least, to provide a container system in which mixing of two or more ingredients of a pharmaceutical product, e.g. a solid and solvent or two different liquids, is made using a simple, effective and intuitive procedure with minimum risks for hospital staff and patients.

It is a further object of the present invention, in preferred embodiments at least, to provide a robust concept to be used in connection with blow-fill-seal (BFS) equipment having a construction involving few parts as well as few production steps.

Summary of the Invention

In accordance with the present invention, from a first broad aspect at least, there is provided a pre-filled container insert for use in a pharmaceutical container system for mixing two or more ingredients of a pharmaceutical product. The pre-filled container insert comprises;

- a moulded container casing having walls, bottom and an open top for receiving a solid component,
- a resilient stopper for sealing the open top of the moulded container casing,
- a bottom disc formed by a weakening rim in the bottom periphery of the moulded container casing, wherein the bottom disc is openable to allow mixing of the pre-filled solid component with a diluents fluid of the pharmaceutical container system by introducing a spike through the resilient stopper applying a pushing force on the bottom disc, by which force the weakening rim is broken and the container insert is opened.

In accordance with the present invention, from a further broad aspect at least, there is provided a pre-filled container insert for use in a pharmaceutical container system for

mixing two or more ingredients of a pharmaceutical product. The pre-filled container insert comprises;

- a moulded container casing having walls, bottom and an open top for receiving an inner open cylinder and a solid component,
- a resilient stopper for sealing the open top of the moulded container casing,
- a bottom disc formed by a weakening rim in the bottom periphery of the moulded container casing, wherein the bottom disc is openable to allow mixing of the pre-filled solid component with a diluents fluid of the pharmaceutical container system by applying a pushing force onto the top of the moulded container, thereby compressing the casing and forcing the inner cylinder towards the bottom disc, by which force the weakening rim is broken and the container insert is opened.

An advantage of preferred embodiments of the present invention is that there is provided a pre-filled container insert that is constructed from a minimum of parts and at the same time has efficient and robust construction. A further advantage of preferred embodiments of the present invention is that there is provided a pre-filled container insert that easily can be opened to provide mixing of contents in the insert and the liquids container. A still further advantage is that the pre-filled container insert is manufactured as a separate device and can be incorporated into different types of blow-fill-seal containers forming a pharmaceutical multi-chamber container system. Yet another advantage is that the separate device can be aseptically filled, sealed and processed (e.g. terminally sterilised) under controlled conditions before the next unit operation of actually mounting the device into the diluents container.

According to preferred embodiments of the invention, the weakening rim in the bottom disc is arranged around the periphery of the bottom of the container casing forming a hinged disc such that the bottom disc remains connected to the container casing when the weakening rim is broken and the container is opened.

In this way the bottom disc is prevented from falling out into the diluents container after opening of the pre-filled container insert.

According to preferred embodiments of the invention, the resilient stopper is secured in place by a clamp ring to hermetically seal the top opening.

The clamp ring locks and fixes the resilient stopper in the open top of the container casing and the moulded casing is hermetically sealed.

According to preferred embodiments of the invention, the bottom disc is covered by a moisture barrier foil.

According to preferred embodiments of the invention, the resilient stopper is covered by a moisture barrier foil.

By covering the container insert with a moisture barrier foil, both on the bottom side or on the resilient top side, the pre-filled content has a maximum of protection from the outside environment, i.e. light, moisture and/or oxygen.

According to preferred embodiments of the invention, the pre-filled container insert is aseptically mounted into the top of a BFS-container forming a multi-chamber pharmaceutical container system.

According to preferred embodiments of the invention, the moulded container casing has pleated sidewalls forming a bellows container insert.

By forming the container casing as a bellows container an easily deformable casing is formed in one single piece.

According to preferred embodiments of the invention, the pre-filled container insert is capable of use with one or more delivery systems, such as a nasal delivery system. Preferably the pre-filled container insert is connectable to or within, or otherwise can be incorporated with, for example, a standard nasal delivery mechanism such as a nasal spray.

According to preferred embodiments of the invention, there is provided a pharmaceutical container system for mixing two or more ingredients of a pharmaceutical product, comprising

- a first container comprising a diluents liquid,
- a second container insert aseptically mounted into the top of the first container, the second container comprising
- a moulded container casing for receiving a solid component,
- a resilient stopper for sealing the open top of the moulded container casing,
- a bottom disc formed by a weakening rim in the bottom periphery of the moulded container casing, wherein the bottom disc is openable to allow mixing of the pre-filled solid component with a diluents fluid of the pharmaceutical container system by introducing a spike through the resilient stopper applying a pushing force on the bottom disc, by which force the weakening rim is broken and the container insert is opened.

According to preferred embodiments of the invention, there is provided a pharmaceutical container system for mixing two or more ingredients of a pharmaceutical product comprising

- a first container comprising a diluents liquid,
- a second container insert aseptically mounted into the top of the first container, the second container comprising
- a moulded container casing having walls, bottom and an open top for receiving an inner open cylinder and a solid component,
- a resilient stopper for sealing the open top of the moulded container casing,
- a bottom disc formed by a weakening rim in the bottom periphery of the moulded container casing, wherein the bottom disc is openable to allow mixing of the pre-filled

solid component with a diluents fluid of the pharmaceutical container system by applying a pushing force onto the top of the moulded container, thereby compressing the casing and forcing the inner cylinder towards the bottom disc, by which force the weakening rim is broken and the container insert is opened.

A standard procedure for a nurse preparing an intra-venous (IV)-container is to visually inspect, and in some procedures to spike, the IV-container before starting infusion. Therefore, using a pharmaceutical container system according to embodiments of the present invention, the standard working procedure is not changed. In preferred embodiments, by simply pushing the container top to allow mixing and then ensure the complete mixing operation by visual inspection, a simple an intuitive procedure is obtained. In addition, no separate mixing step using hypodermic needles are necessary, eliminating the risk of needle-stick injuries. Mixing is made without risk of microbial contamination since the solid and liquid chambers are both parts of the same hermetically sealed container. In other embodiments, similar steps are carried out but for preparing a nasal delivery device such as a nasal spray, which typically comprises a container, and a spray or other nasal delivery mechanism attached thereto.

Medicaments suitable for administration via a pharmaceutical multi-chamber container system for mixing two or more ingredients of a pharmaceutical product, and more particularly to be pre-filled with the container insert of the present invention include for example proton pump inhibitors, for example omeprazol, anticancer medicaments, antibiotics, immunotherapies, vaccines, antiviral medicaments, polypeptides and peptides, for example, peptide hormones and growth factors, polypeptide vaccines, enzymes endorphines, lipoproteins and polypeptides involved in the blood coagulation cascade.

Brief Description of the Drawings

The present invention will now be described, for exemplary purposes, in more detail by way of embodiments and with reference to the enclosed drawings, in which:

Figures 1a-1g illustrate schematically the manufacturing steps of a pre-filled container

insert in accordance with a preferred embodiment of the present invention, and,

Figures 2a and 2b schematically illustrate the opening procedure of the pre-filled container insert, and,

Figures 3a-3d show a pharmaceutical container system for mixing two or more ingredients of a pharmaceutical product, which system consists of a BFS-container filled with a diluents liquid and a pre-filled insert sealed to the container, and,

Figures 4a-4h illustrate schematically the manufacturing steps of a further pre-filled container insert in accordance with a preferred embodiment of the present invention, and,

Figures 5a-5c schematically illustrate the opening procedure of the pre-filled container insert of Figures 4a-4h, and;

Figures 6a-6d show a pharmaceutical container system for mixing two or more ingredients of a pharmaceutical product, which system consists of a BFS-container filled with a diluents liquid and a pre-filled insert sealed to the container.

Detailed Description of Preferred Embodiments

Figures 1a to 1g and 4a to 4h schematically illustrate how pre-filled container inserts can be manufactured. The container inserts, being manufactured separately e.g. by injection moulding can use any type thermoplastic material, e.g. high-barrier engineering plastics if necessary to impart high-barrier properties, e.g. with light, moisture or oxygen sensitive compounds.

Figure 1a shows the moulded container casing 1 having walls 2, bottom 3 and an open top 4 for receiving a medicament component. The container casing 1 which is made using e.g. injection moulding preferably has a cylindrical geometry and the bottom 3 has a suitable weakening rim 5 in the bottom periphery. The weakening rim 5 will make it possible to push open the bottom disc 3 to allow material transfer between the pre-filled insert and a liquid container. Preferably, a small portion of the weakening rim is kept thicker, functioning as a hinge 6 so as to prevent the bottom disc 3 to completely disengage from the solids container on opening.

To further augment the moisture or gas barrier of the container insert and thus to protect the content, a barrier foil 7, e.g. an aluminium foil can be used to cover the bottom disc 3, which can be seen in Figure 1b.

In Figure 1c the moulded container casing is pre-filled with a content 8, a powder or other suitable solid (or semi-solid) in a well-defined, clean environment (e.g. aseptic filling in isolator or other suitable uni directional air flow hood (UDF)). According to another aspect of this invention not shown in the drawings, the moulded container casing is pre-filled with a semi-solid content or a liquid, which is to be mixed with the diluents prior to infusion.

Figures 1d, 1e and 1f show how the container insert is hermetically closed using a resilient stopper 9, e.g. a standard rubber stopper or thermoplastic elastomer (TPE) part, which is mounted through the open top and secured by a clamp ring 10 to ensure a safe and tight fastening of the stopper 9. As shown in Figure 1g, a barrier foil 15, i.e. an aluminium foil, can be used to cover the resilient stopper 9 and clamp ring 10 to further augment the moisture or gas barrier of the pre-filled container insert 17. The open centre of the clamp ring 10 reveals a circular area of the resilient stopper where the spike (or a puncture needle) can be entered through the stopper. The pre-filled container insert 17 can be sterilised either in-line or in a separate step after filling/closing using standard methods such as e-beam or gamma irradiation. Such a sterile pre-filled container insert can then be transported to a suitable standard filling line for liquids to be mounted to a blow-fill-seal container or other suitable liquids plastic container. The container may comprise a component of a nasal delivery device, which preferably contains the appropriate liquid.

Figure 2a schematically illustrate how a spike 20 is pushed through the resilient stopper 9 of the pre-filled container insert and in 2b how the pushing force from the spike 20 breaks the weakened rim 5 in bottom periphery (as well as the barrier foil 7) and the content 8 of the pre-filled container insert is free to leave the container.

Figure 3a illustrates an embodiment of a pharmaceutical container system 21 wherein a pre-filled container insert 17 according to the present invention is mounted into the top of a blow-fill-seal container 22. In the embodiment of Figures 3a to 3d, the system 21 comprises means suitable for intravenous delivery of a medicament, but the system may comprise any other, suitable pharmaceutical system, such as a container (e.g. a bottle, vial or tube) for use with a nasal delivery mechanism, e.g. a spray or dropper that connects to the container. The pre-filled container insert 17 of the Figure 3a embodiment filled with a content 8 will be enclosed into the liquid blow-fill-seal container and the top portion of the pre-filled container is revealed to the user by opening a twist-off top 23 of the blow-fill-seal container 22, which is shown in Figure 3b. In a preferred embodiment, also shown in Figure 3b, a moisture barrier seal 15 covers the top, i.e. a resilient stopper 9 of the pre-filled container under the twist-off top 23. After the moisture barrier seal 15 has been removed the content 8 of the pre-filled container insert 17 is ready to be mixed with the diluents fluid in the blow-fill-seal container 22. Figure 3c shows how a spike 20 punctures the resilient stopper 9 and enters into the pre-filled container 17. The pushing force from the spike 20 acts on the bottom disc 3and the weakened rim 5 in the periphery of the disc breaks up. The disc 3 is prevented from falling out into the blow-fill-seal container 22 by a hinge 6 connecting the bottom disc to the wall 2 of the container insert. The content of the pre-filled container can now be mixed with the diluents fluid of the blow-fill-seal container by gentle shaking the container. In Figure 3d a bottom flap 25 is pulled up to allow hanging of the container system near a patient while administering the substance to the patient. According to another aspect of the present invention not shown in the drawings, the pre-filled container insert is welded into a flexible bag wall being filled with the diluents liquid.

Figure 4a shows another embodiment of the present invention. Like reference numerals are used to indicate components similar to those of the embodiment of Figures 1 to 3. The moulded container casing 1 has walls 2, bottom 3 and an open top 4 for receiving a medicament component. The container casing 1 which is made using e.g. injection moulding preferably has a cylindrical geometry and differs from the previous embodiment

in that the walls 2 are pleated such that the container casing has the form of a bellows. The bottom 3 has a suitable weakening rim 5 in the bottom periphery. Preferably, a small portion of the weakening rim is kept thicker, functioning as a hinge 6 so as to prevent the bottom disc 3 to completely disengage from the solids container on opening. To further augment the moisture or gas barrier of the container insert and thus to protect the content, a barrier foil 7, e.g. an aluminium foil can be used to cover the bottom disc 3, which can be seen in Figure 4b.

In Figure 4c an inner cylinder 30 is placed inside the moulded container casing and, as shown in Figure 4d, the inner cylinder placed within the container walls is then pre-filled with a content 8, a powder or other suitable solid (or semi-solid) in a well-defined, clean environment (e.g. aseptic filling in isolator or other suitable uni directional air flow hood (UDF)). According to another aspect of this invention not shown in the drawings, the inner cylinder with container is pre-filled with a semi-solid content or a liquid which is to be mixed with the diluents prior to infusion. The weakening rim 5 will make it possible to push open the bottom disc 3 using the inner cylinder 30 to allow material transfer between the pre-filled insert and a liquid container. The inner cylinder 30 is tapered and oriented in relation to the weakening rim so that the tapered end push first at the position directly opposite the hinge part of the weakening rim along the periphery.

Figures 4e and 4f show how the container insert is hermetically closed using a resilient stopper 9, e.g. a standard rubber stopper or thermoplastic elastomer (TPE) part, which is mounted through the open top and secured by a clamp ring 10 to ensure a safe and tight fastening of the stopper 9. As shown in Figure 4h, a barrier foil 15, i.e. an aluminium foil, can be used to cover the resilient stopper 9 and clamp ring 10 to further augment the moisture or gas barrier of the pre-filled container insert 17. Alternatively, the aluminium foil is replaced with a standard tamper-evident protective seal. The open centre of the clamp ring 10 reveals a circular area of the resilient stopper where the spike (or a puncture needle) can be entered through the stopper. The pre-filled container insert 17 can be sterilised either in-line (at filling) or in a separate step after filling/closing using standard

methods such as e-beam or gamma irradiation. Such a sterile pre-filled container insert can then be transported to a suitable standard filling line for liquids to be mounted to a blow-fill-seal container or other suitable liquids plastic container.

Figure 5a schematically illustrates how a pressing force is applied to the top of the bellows container insert 17 and how the pushing force compresses the walls 2 of the container insert. In Figure 5b the inner cylinder 30 presses on the bottom 3 and breaks the weakened rim 5 in bottom periphery (as well as the barrier foil 7) and the content 8 of the pre-filled container insert is free to leave the container and be mixed with a diluent fluid (not shown). In Figure 5c a spike 20 is introduced through the rubber stopper 9 to make the container ready for administration to a patient.

Figure 6a illustrates an embodiment of a pharmaceutical container system 21 wherein a pre-filled container insert 17 according to the present invention is mounted into the top of a blow-fill-seal container 22. As discussed above, the system may comprise any other, suitable pharmaceutical system, such as a container for use with a nasal delivery mechanism. The pre-filled container insert 17 filled with a content 8 will be enclosed into the liquid blow-fill-seal container and the top portion of the pre-filled container is revealed to the user by opening a twist-off top 23 of the blow-fill-seal container 22, which is shown in Figure 6b. In a preferred embodiment, also shown in Figure 6b, a moisture barrier seal 15 covers the top, i.e. a resilient stopper 9 of the pre-filled container under the twist-off top 23. After removal of the twist-off top the content 8 of the pre-filled container insert 17 is ready to be mixed with the diluents fluid in the blow-fill-seal container 22. Figure 6c shows how the walls 2 of the bellows insert are compressed. The pushing force makes the inner cylinder 30 to break the weakened rim 5 in the periphery of the bottom disc 3 and the rim breaks up. The disc 3 is prevented from falling out into the blow-fill-seal container 22 by a hinge 6 connecting the bottom disc to the wall 2 of the container insert. The content of the pre-filled container can now be mixed with the diluents fluid of the blow-fill-seal container by gentle shaking of the container. After visual inspection to ensure complete mixing of the contents and confirmation of the absence of particulates, the moisture barrier

seal (or tamper-evident seal) can be removed. A spike 20 (or puncture needle) may be introduced through the stopper 9 to make the container ready to be administered to a patient. According to another aspect of the present invention not shown in the drawings, the pre-filled container insert is welded into a flexible bag wall being filled with the diluents liquid.

To mix the content of the solid and liquid containers in the above intravenous examples, the user (typically a nurse) adopts a normal working procedure with intravenous, i.e. IV-infusions. A preferred use of a system in accordance with an embodiment of the present invention as illustrated in Figures 1 to 3 is described below in chronological order.

1) The nurse twists off the blow-fill seal container top and peels off the moisture barrier seal if there is one (and disinfects the rubber stopper top if that is standard procedure).
2) A sterile IV-administration set bag is opened.
3) The IV-spike of the administration set is inserted into the rubber stopper top, thereby piercing the rubber stopper. As the spike is fully inserted, the bottom disc of the solids chamber is pushed open by the spike, and the solids and liquids chambers are now communicating to enable mixing.
4) The contents of the solids and liquids chambers are mixed by gently rocking the container.
5) The nurse visually inspects the contents of the container to ensure full dissolution and absence of particulate matter.
6) The needle is attached to the patient after purging, and IV-infusion is ready to start.

A preferred use of a system in accordance with another embodiment of the present invention as illustrated in Figures 4 to 6 is described below in chronological order.

1) The nurse twists off the blow-fill seal container top.

2) The nurse compresses the bellows insert to make the pre-filled content fall into the diluents container and the solids and liquids chambers are now communicating to enable mixing.

3) The contents of the solids and liquids chambers are mixed by gently rocking the container.

4) The nurse peels off the moisture barrier (or protective) seal and disinfects the rubber stopper top if that is standard procedure

4) A sterile IV-administration set bag is opened. The IV-spike of the administration set is inserted into the rubber stopper top, thereby piercing the rubber stopper.

5) The nurse visually inspects the contents of the container to ensure full dissolution and absence of particulate matter.

6) The needle is attached to the patient after purging, and IV-infusion is ready to start.

In other embodiments, for example where the pre-filled insert is for use with, e.g., a nasal delivery device, some of the above steps may be carried out, but with the insert contained within, or otherwise associated with, a suitable container such as a nasal spray bottle or the like.

Further, it will be understood that the present invention is not limited to the described embodiments but can be modified in many different ways without departing from the scope of the appended claims.

CLAIMS

1. A pre-filled container insert for use in a pharmaceutical container system for mixing two or more ingredients of a pharmaceutical product, the pre-filled container insert comprising;
- a moulded container casing having walls, a bottom and an open top for receiving a solid component,
- a resilient stopper for sealing the open top of the moulded container casing,
- a bottom disc formed by a weakening rim in the bottom periphery of the moulded container casing, wherein the bottom disc is openable to allow mixing of the pre-filled solid component with a diluents fluid of the pharmaceutical container system by introducing a spike through the resilient stopper applying a pushing force on the bottom disc, by which force the weakening rim is broken and the container insert is opened.

2. A pre-filled container insert for use in a pharmaceutical container system for mixing two or more ingredients of a pharmaceutical product, the pre-filled container insert comprising;
- a moulded container casing having walls, a bottom and an open top for receiving an inner open cylinder and a solid component,
- a resilient stopper for sealing the open top of the moulded container casing,
- a bottom disc formed by a weakening rim in the bottom periphery of the moulded container casing, wherein the bottom disc is openable to allow mixing of the pre-filled solid component with a diluents fluid of the pharmaceutical container system by applying a pushing force onto the top of the moulded container, thereby compressing the casing and forcing the inner cylinder towards the bottom disc, by which force the weakening rim is broken and the container insert is opened.

3. A pre-filled container insert according to claim 2, wherein the moulded container casing has pleated sidewalls forming a bellows container insert.

4. A pre-filled container insert according to claim 1, 2 or 3, wherein the weakening rim in the bottom disc is arranged around the periphery of the bottom of the container casing forming a hinged disc such that the bottom disc remains connected to the container casing when the weakening rim is broken and the container is opened.

5. A pre-filled container insert according to any preceding claim, wherein the resilient stopper is secured in place by a clamp ring to hermetically seal the top opening.

6. A pre-filled container insert according to any preceding claim, wherein the bottom disc is covered by a moisture barrier foil.

7. A pre-filled container insert according to any preceding claim, wherein the resilient stopper is covered by a moisture barrier foil.

8. A pre-filled container insert according to any preceding claim, wherein the pre-filled container insert is aseptically mounted into the top of a Blow-Fill-Seal (BFS) container forming a multi-chamber pharmaceutical container system.

9. A pre-filled container insert according to any preceding claim, wherein the pre-filled container insert is aseptically mounted into a container, the container having a delivery mechanism capable of attachment thereto, such that there is provided a multi-chamber pharmaceutical delivery system.

10. A pre-filled container insert according to claim 9, wherein the delivery mechanism comprises a nasal delivery component, preferably a spray, dropper or the like.

11. A pharmaceutical container system for mixing two or more ingredients of a pharmaceutical product, comprising
- a first container comprising a diluents liquid,
- a second container insert aseptically mounted into the top of the first container, the second container comprising
- a moulded container casing for receiving a solid component,
- a resilient stopper for sealing the open top of the moulded container casing,
- a bottom disc formed by a weakening rim in the bottom periphery of the moulded container casing, wherein the bottom disc is openable to allow mixing of the pre-filled solid component with a diluents fluid of the pharmaceutical container system by introducing a spike through the resilient stopper applying a pushing force on the bottom disc, by which force the weakening rim is broken and the container is opened.

12. A pharmaceutical container system for mixing two or more ingredients of a pharmaceutical product, comprising
- a first container comprising a diluents liquid,
- a second container insert aseptically mounted into the top of the first container, the second container comprising
- a moulded container casing having walls, a bottom and an open top for receiving an inner open cylinder and a solid component,
- a resilient stopper for sealing the open top of the moulded container casing,
- a bottom disc formed by a weakening rim in the bottom periphery of the moulded container casing, wherein the bottom disc is openable to allow mixing of the pre-filled solid component with a diluents fluid of the pharmaceutical container system by applying a pushing force onto the top of the moulded container, thereby compressing the casing and forcing the inner cylinder towards the bottom disc, by which force the weakening rim is broken and the container insert is opened.

Fig.1a.

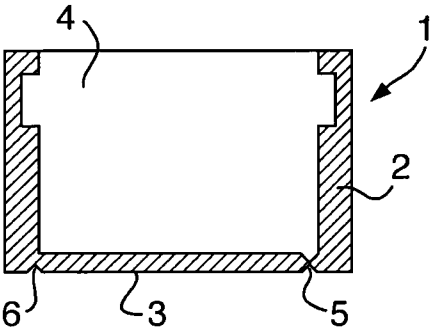


Fig.1b.

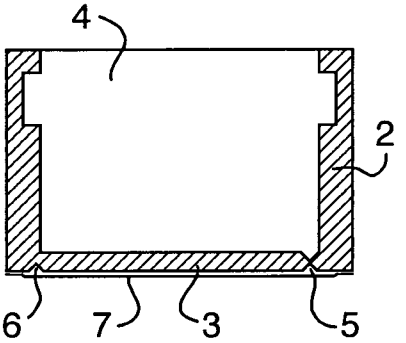


Fig.1c.

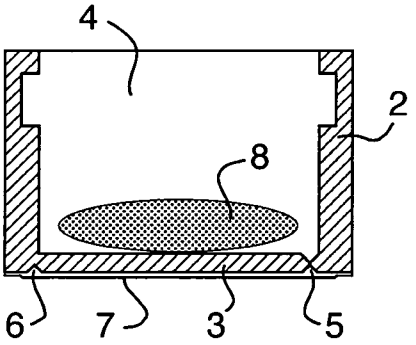


Fig.1d.

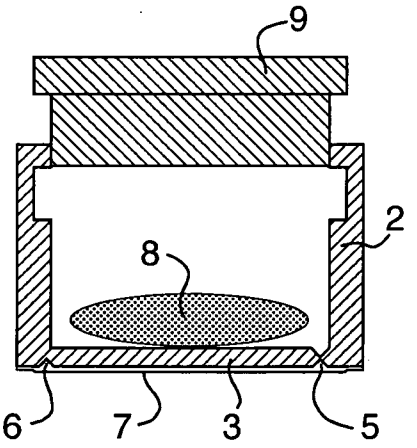


Fig.1e.

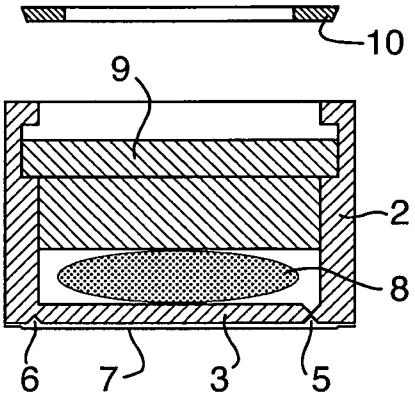


Fig.1f.

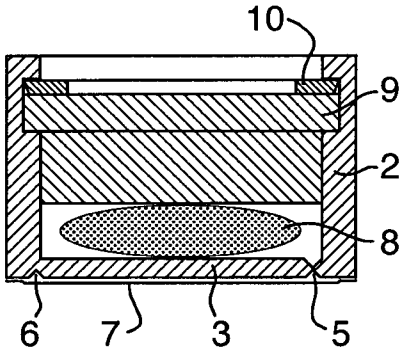


Fig.1g.

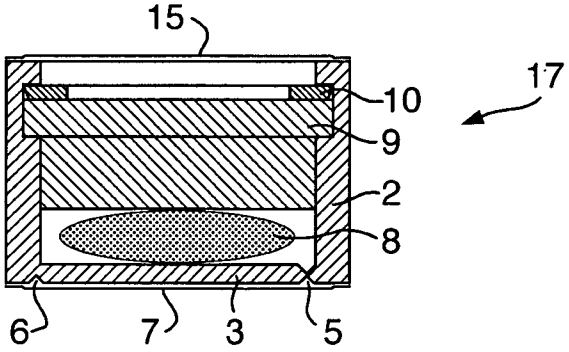


Fig.2a.

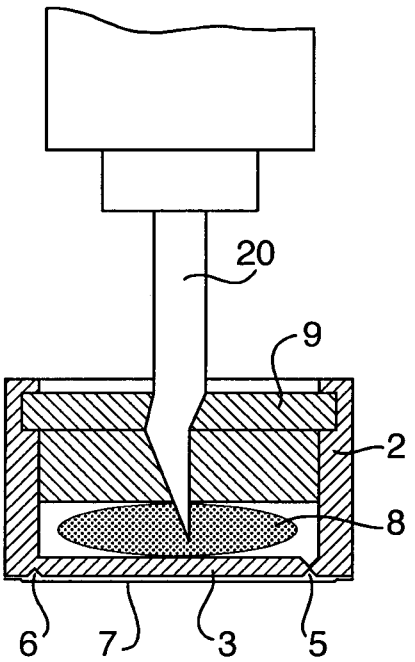


Fig.2b.

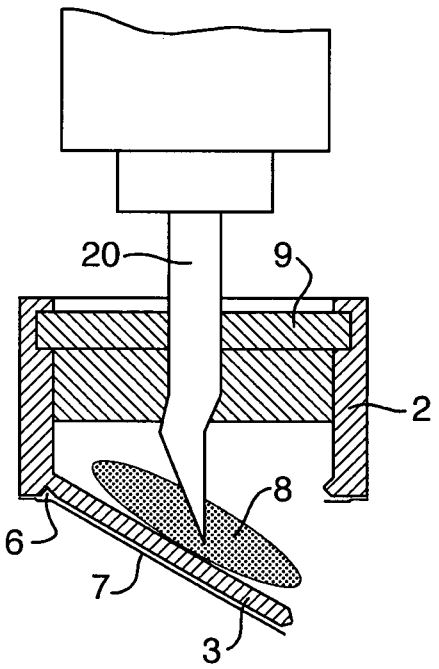


Fig.3a.

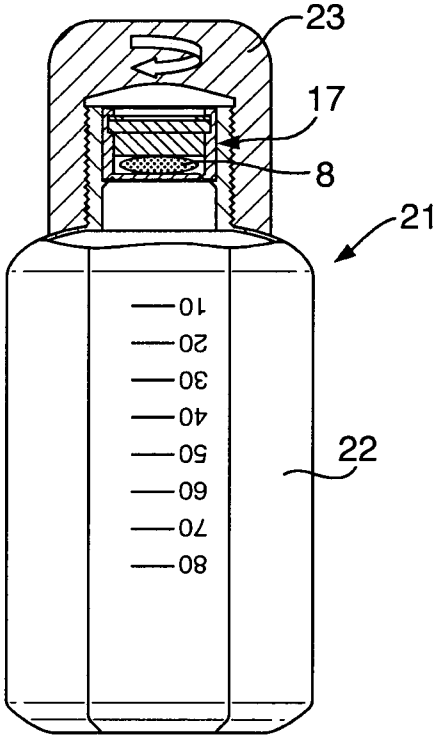


Fig.3b.

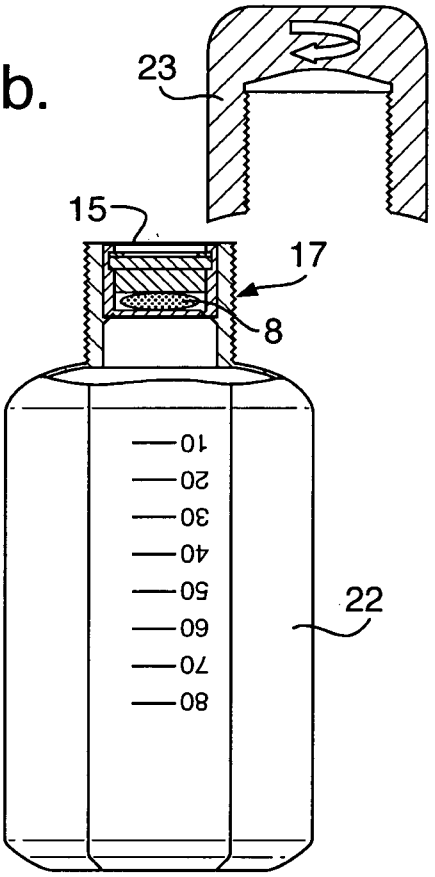


Fig.3c.

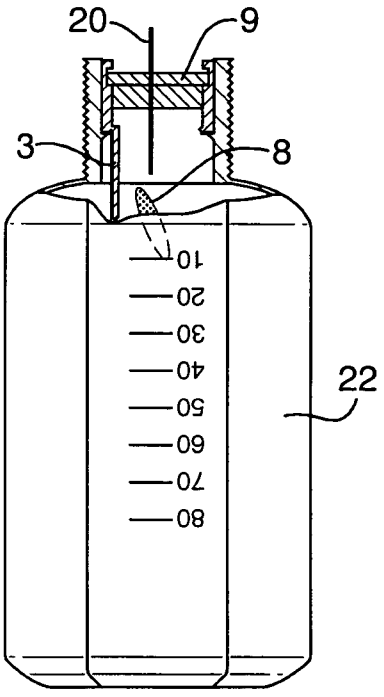


Fig.3d.

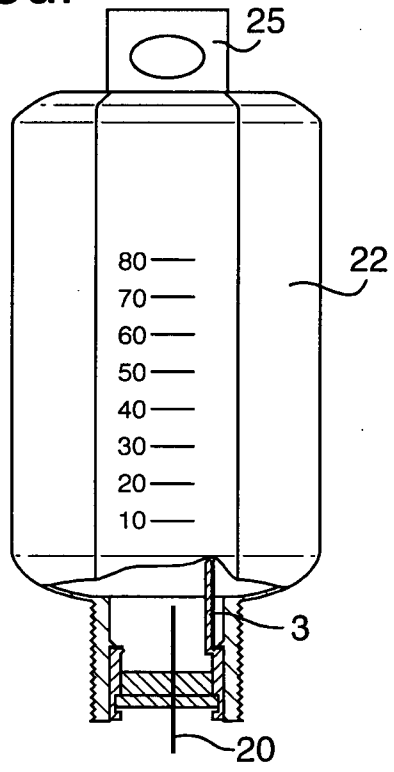


Fig.4a.

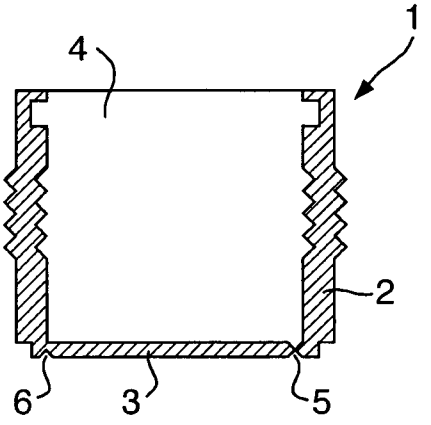


Fig.4b.

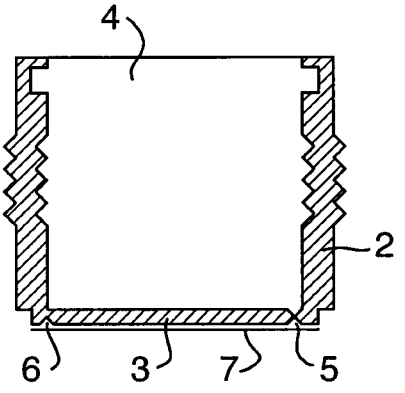


Fig.4c.

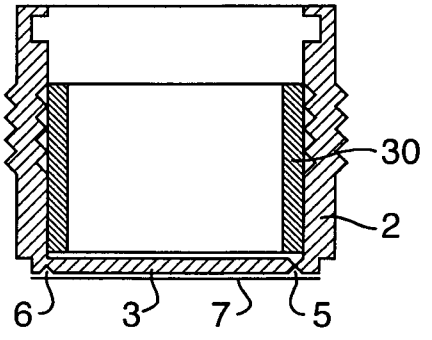


Fig.4d.

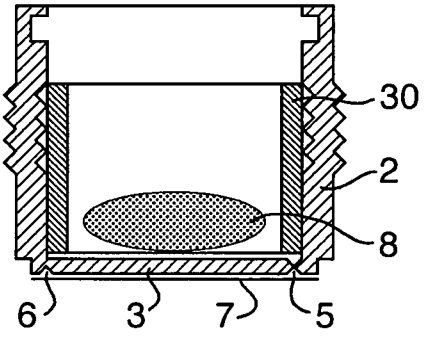


Fig.4e.

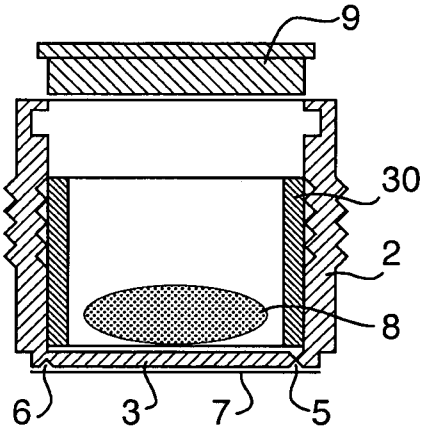


Fig.4f.

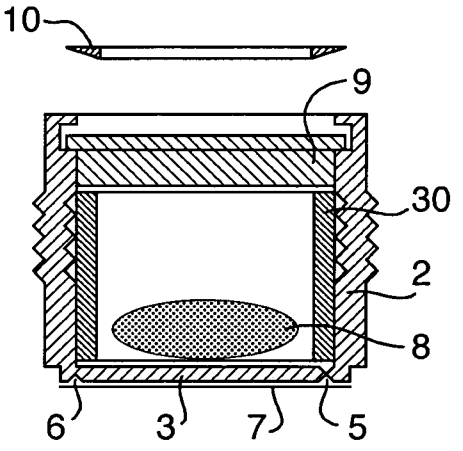


Fig.4g.

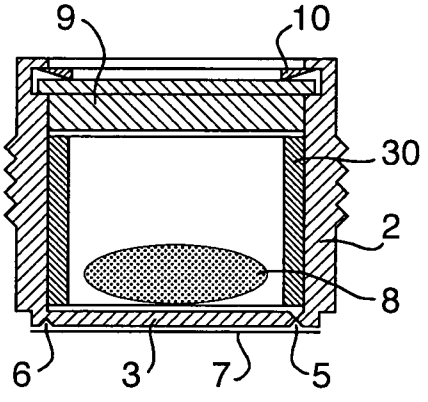


Fig.4h.

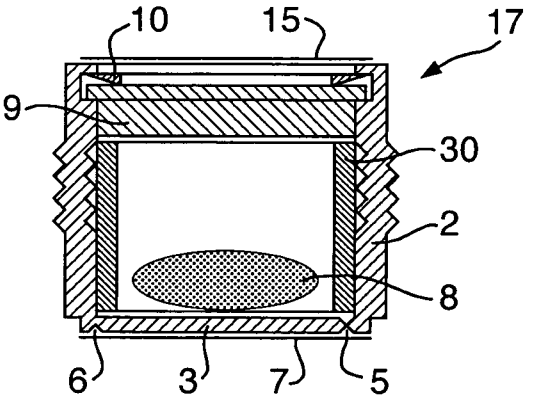


Fig.5a.

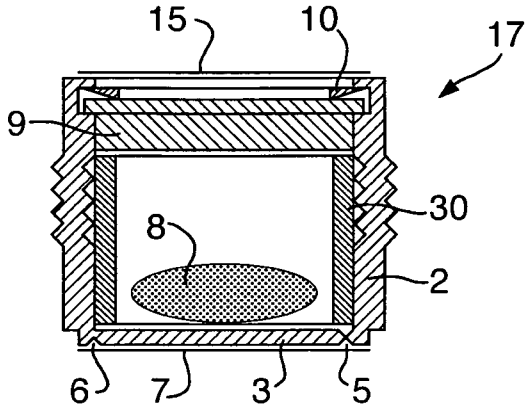


Fig.5b.

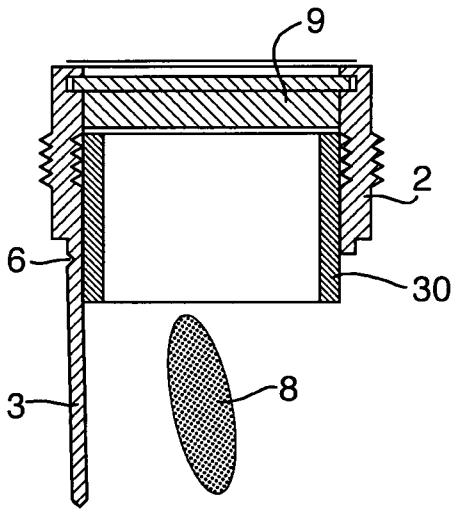


Fig.5c.

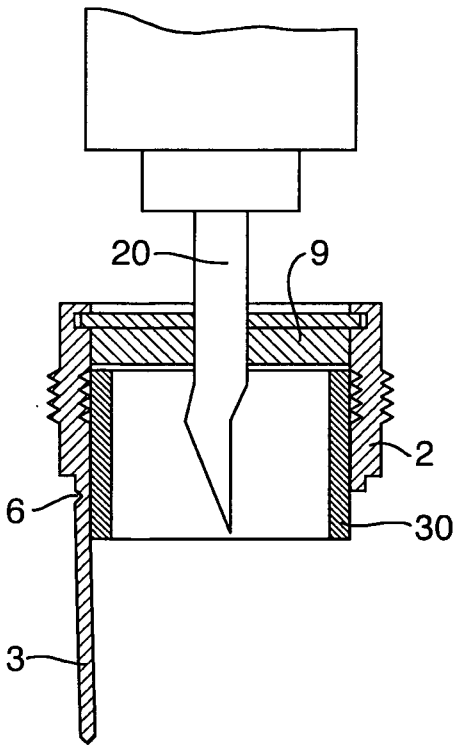


Fig.6a.

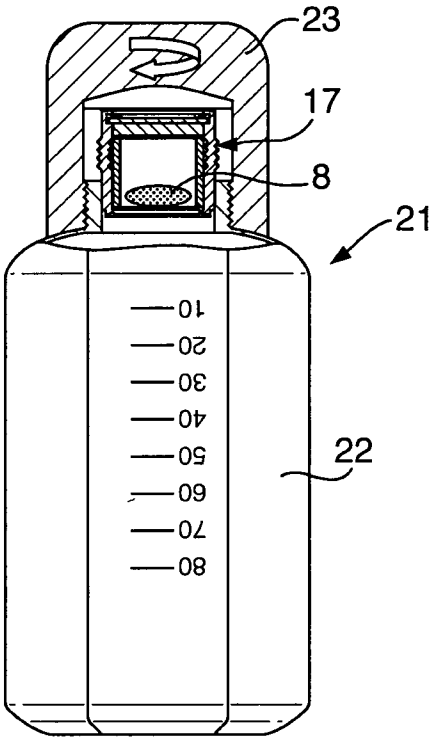


Fig.6b.

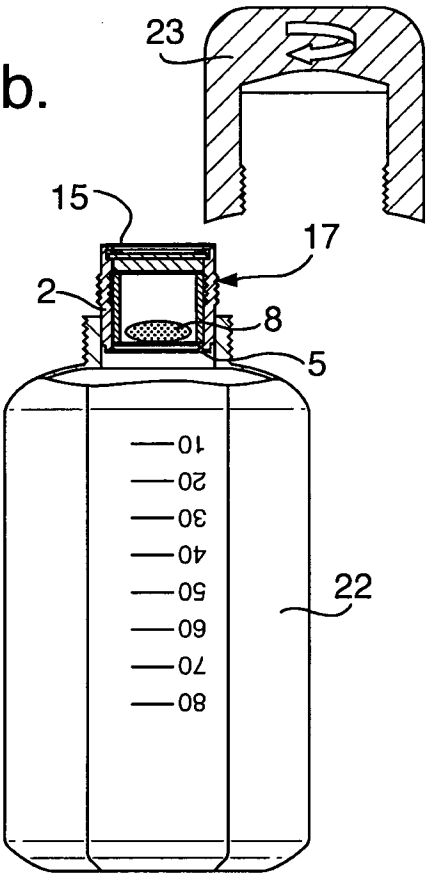


Fig.6c.

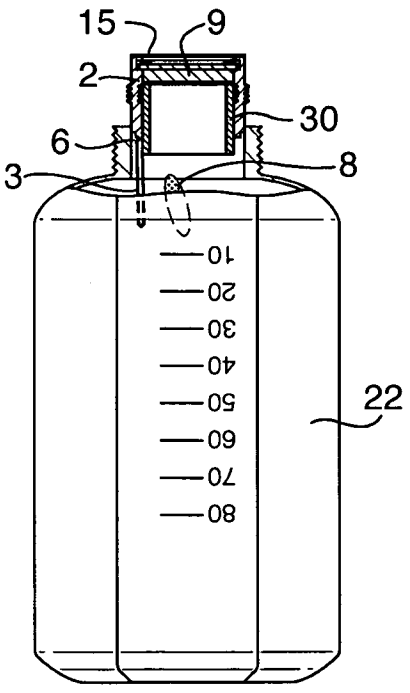
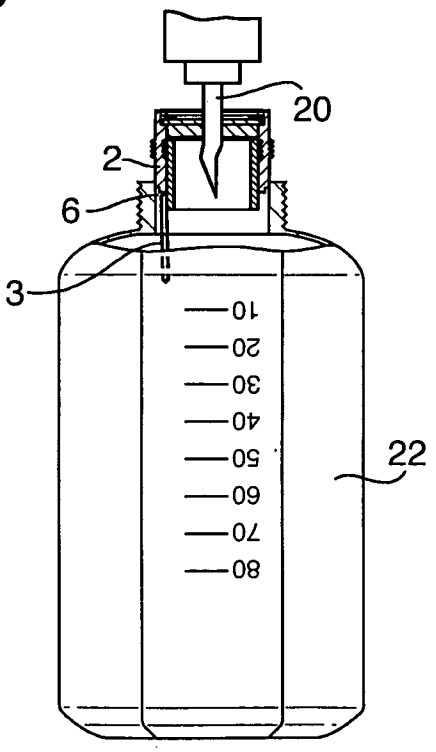


Fig.6d.



INTERNATIONAL SEARCH REPORT

International application No.
PCT/SE2009/050922

A. CLASSIFICATION OF SUBJECT MATTER

IPC: see extra sheet
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: B65B, B65D, A61M

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

SE,DK,FI,NO classes as above

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

EPO-INTERNAL, WPI DATA, PAJ

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 5322165 A (R.J. MELKER ET AL), 21 June 1995 (21.06.1995), column 1, line 56 - line 68	1,4-11
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X	EP 0561322 A1 (LAMEPLAST S.R.L.), 22 Sept 1993 (22.09.1993), column 2, line 57 - column 3, line 51, figures 1,2	2,4,12
Y		1,3,5-11
	--	
Y	EP 1842795 A1 (SORIA NATURAL, S.A.), 10 October 2007 (10.10.2007), paragraphs (0025)-(0026)	3-10
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Date of the actual completion of the international search	Date of mailing of the international search report
18 November 2009	18 -11- 2009
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INTERNATIONAL SEARCH REPORT

International application No.
PCT/SE2009/050922

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

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A	US 3220588 A (M. LIPARI), 30 November 1965 (30.11.1965), whole document	1-12
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International patent classification (IPC)

B65B 29/10 (2006.01)
B65D 25/08 (2006.01)

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US	3603484	A	07/09/1971	NONE		
US	20020066750	A1	06/06/2002	NONE		