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(54) **DUAL CHAMBER SYSTEM**

(57) The present invention relates to a dual chamber system for medicine. The dual chamber system comprises a first chamber defined by walls, and a second chamber defined by walls. The first chamber and the second chamber are separated and individually sealed by a plug, such as a first membrane or foil. The second chamber is configured to be moved at least partially into the first chamber, thereby rupturing the plug.

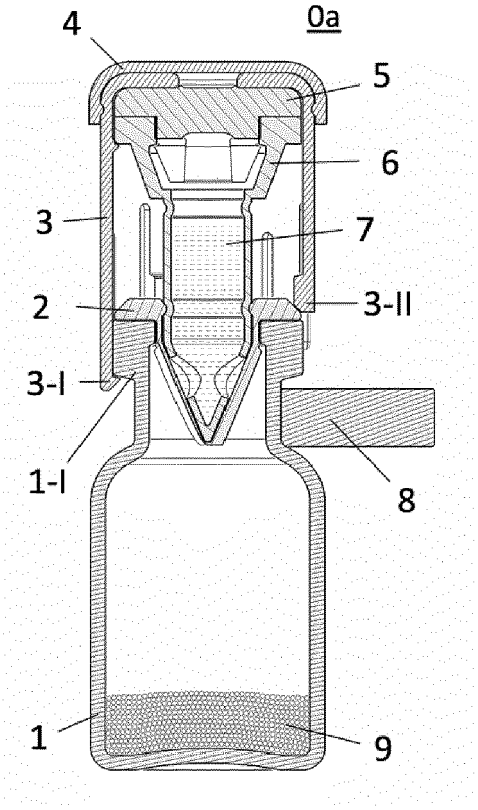

FIG. 1

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Description

Technical field of the invention

[0001] The present invention relates to dual chamber systems for medicine for parenteral administration.

Background of the invention

[0002] Despite numerous clever inventions, the act of reconstituting parenteral medicine is still primarily done by moving diluents from one container to the vial containing the medicine using a mixing syringe. One reason for the lack of widespread use of dual chamber systems is that these systems require major changes to the existing methods of manufacturing, assembly, filling, and operation of said systems. Such investments are expensive, and presumably less profitable than maintaining the status quo.

[0003] WO02/36065 discloses a bottle for two-component extemporaneous products, of the type that comprises: a container for a first component, which is provided with an upper mouth; a reservoir for containing a second component, which is inserted substantially coaxially in the mouth, is open upward and has a bottom constituted by a diaphragm; a perforator, which can be inserted in the reservoir and is adapted to pierce the diaphragm in order to mix the two components; and a removable cap for closing the container in an upward region. The cap comprises a lower annular portion that is fixed to the container and an upper cylindrical portion that cooperates with the perforator and is rigidly coupled to the annular portion at an intermediate weakened region suitable to act as sealing means, a downward pressure on the cylindrical portion being adapted to disengage it from the annular portion and to make the perforator slide in the reservoir in order to pierce the underlying diaphragm.

[0004] WO 2008/036889 discloses a storage and dispensing cap for a liquid receptacle having a cap body storage chamber for use with a receptacle such as a bottle, pouch, or intravenous bag that is used to store a liquid for use with a syringe that is inserted into the receptacle for drawing the liquid contents into the syringe. A liquid, powder or capsule in the cap body chamber is mixed into the liquid receptacle for use with the syringe. A sleeve penetrator is mounted inside said cap body chamber and is sized in length to permit rupture of the bottom floor of said cap body chamber when manually depressed for dispensing whatever material is placed inside said cap body chamber and sleeve penetrator into said syringe bottle. An open passage from the cap body to the inside of the receptacle is provided once the storage chamber is ruptured by manually depressing the penetrator to allow the syringe needle end to be inserted into the liquid receptacle.

[0005] It is an objective of the present invention to provide an improved dual chamber solution.

Description of the invention

[0006] One aspect relates to a dual chamber system for medicine, said dual chamber system comprising:

- a first chamber defined by walls; and
- a second chamber defined by walls;

wherein the first chamber and the second chamber are separated and
individually sealed by a plug, preferably a vial stopper, alternatively a membrane or foil; and wherein the second chamber is configured to be moved at least partially into the first chamber, thereby rupturing the plug.

[0007] Another aspect relates to a dual chamber system for medicine, said dual chamber system comprising:

- a first chamber defined by walls and configured as a vial;
- a vial stopper adapted for being mounted to the first chamber; and
- a second chamber defined by walls and adapted for being directly or indirectly mounted to the first chamber and/or to the vial stopper;

wherein said dual chamber system is configured to be in a preparatory state and in a ready to use state;
wherein in the preparatory state, the vial stopper is connected to the first chamber in a partially seated position;
wherein in the ready to use state, the vial stopper is adapted to seal said first chamber from said second chamber, and vice versa; wherein the vial stopper is connected to the first chamber in a fully seated position, and the second chamber is directly or indirectly mounted to the first chamber and/or to the vial stopper and configured to be moved at least partially into the first chamber when a downward force is applied onto the second chamber, e.g., by pushing and/or twisting the second chamber, thereby rupturing the vial stopper.

[0008] Yet another aspect relates to a dual chamber system for medicine, said dual chamber system comprising:

- a first chamber defined by walls and configured as a vial;
- a vial stopper adapted for being mounted to the first chamber; and
- a second chamber defined by walls and adapted for being directly or indirectly mounted to the first chamber and/or to the vial stopper;

wherein said dual chamber system is configured to be in a preparatory state, a ready to use state, and an

in-use state;

wherein in the preparatory state, the vial stopper is connected to the first chamber in a partially seated position;

wherein in the ready to use state, the vial stopper is adapted to seal said first chamber from said second chamber, and vice versa; wherein the vial stopper is connected to the first chamber in a fully seated position, and the second chamber is directly or indirectly mounted to the first chamber and/or to the vial stopper;

wherein in the in-use state, the second chamber is configured to be moved at least partially into the first chamber when a downward force is applied onto the second chamber, e.g., by pushing and/or twisting the second chamber, thereby rupturing the vial stopper.

[0009] In the present context, the term "rupturing" is to be understood broadly, also including terms such as cutting and breaking.

[0010] The inventors of the present invention have developed a dual chamber system constructed around the design of the medical vial, i.e., the first chamber may be configured as a traditional medical vial. Hence, the system utilizes existing industry infrastructure, technology investments, regulatory approvals, and medical acceptance associated with the medical vial and can thus ease the dissemination of dual chamber systems into the industry.

[0011] The solution comprises a second chamber adapted for containing or comprising one substance/-composition, which is installed onto (directly or indirectly) a first chamber containing or comprising another substance/composition. The two chambers are separated and individually sealed by a plug (e.g., a membrane or foil) to avoid premature mixing of the two substances/-compositions. The plug is preferably a vial stopper.

[0012] In one or more embodiments, a lower part of the plug is configured to be torn, by said second chamber, into one or more splinter/leafs/plates with a first free end, and a second end attached to an upper part of the plug, when a downward force is applied onto the second chamber, and the second chamber is moved at least partially into the first chamber.

[0013] In one or more embodiments, the plug is configured with one or more seams configured for providing weakened areas/lines within a lower part of said plug, thereby allowing said lower part to be torn, by said second chamber, into one or more splinter/leafs/plates with a first free end, and a second end attached to an upper part of the plug, when a downward force is applied onto the second chamber, and the second chamber is moved at least partially into the first chamber.

[0014] In one or more embodiments, at least some of said seams are positioned or formed on an outer face of said plug.

[0015] In one or more embodiments, at least some of said seams are positioned or formed on an inner face of said plug.

[0016] In one or more embodiments, one or more seams define a relatively weak spot at the center of the lower part of said plug, and wherein said weak spot is configured to rupture when a downward force is applied onto the second chamber, and the second chamber is moved at least partially into the first chamber.

[0017] In one or more embodiments, one or more seams define a relatively weak spot at the edge of the lower part of said plug, and wherein said weak spot is configured to rupture when a downward force is applied onto the second chamber, and the second chamber is moved at least partially into the first chamber.

[0018] Medicine is often delivered in solid form, as this increases their stability and shelf-life. However, medicine is preferably dosed in liquid form, as this allows for a more precise dosing than dry powder filling. To obtain both of these qualities, medicine is filled as liquid solution, and then converted to solid form through the lyophilization/-freeze-drying process: A lyophilization stopper, here the plug, is placed on top of the vial and/or slightly inside the neck of the vial, here the first chamber, after it is filled with the liquid medicine solution before entering the lyophilization chamber - a position referred to as "partially seated". The vial is then placed in the lyophilization chamber, and the temperature is reduced to freezing temperature, such as e.g., -50 to -80 degrees Celsius, thereby freezing the liquid medicine solution solid. The pressure is then reduced inside the lyophilization chamber, e.g., creating a near perfect vacuum. The floor of the lyophilization chamber is configured to heat the vial slowly, so that the frozen solvent sublimates into a gas. During this process, the solvent gas has to escape, which is why traditional lyophilization stoppers have cavities on their outer faces, which allows for the construction of channels/vents for the solvent gas to escape through when the stopper is partially placed in the vial. After freeze-drying, the lyophilization chamber is then usually backfilled with an inert gas, such as nitrogen, and e.g., creating a partial vacuum, such as e.g., 0.5-0.9 atmospheres, as this prevents oxygen from subsequently entering the vial, which would oxidize and ruin the medicine. Then, the floor within the lyophilization chamber is raised, or the roof is lowered, until the stopper/plug hits the roof, forcing the stopper/plug further down the neck of the vial until the flange of the stopper/plug meets the flange of the vial - reaching the so-called "fully seated" position - with the headspace of the vial now e.g., being filled with an inert gas, usually nitrogen - or e.g., constituting a near perfect vacuum in the case where backfilling does not take place. The vial is then removed from the lyophilization chamber, and the stopper/plug is sealed with a crimp cap (usually made of a metal such as aluminum) to ensure complete container closure integrity.

[0019] In one or more embodiments, the plug is configured for being connected to the first chamber in a partially seated position, and in a fully seated position.

[0020] In one or more embodiments, the second chamber comprises a second membrane or foil adapted for being penetrated by a needle or a spike. This configuration allows the user to extract the mixed substances/-compositions with a syringe or to connect the system to another system using a Closed System Transfer Device (CSTD).

[0021] In one or more embodiments, the second chamber comprises a seal adapted for being connected to a Luer taper system (such as Luer lock or a Luer slip). This configuration allows the user to extract the mixed substances/compositions with a needle-less syringe. The Luer taper is a standardized system of small-scale fluid fittings used for making leak-free connections between a male-taper fitting and its female mating part.

[0022] In one or more embodiments, the dual chamber system further comprises a lid or a cap adapted for covering the second membrane or foil or a seal prior to use, said lid or cap being removably fastened to the first and/or the second chamber.

[0023] In one or more embodiments, the dual chamber system further comprises a mechanism adapted for holding the first and second chambers in position relative to one another after the second chamber has been moved (e.g., by the user) at least partially into the first chamber.

[0024] In one or more embodiments, the mechanism comprises hooks/clips adapted for sliding past or being slid past by a collar/interface on an outer face of the first and/or second chamber's walls, wherein said hooks/clips is adapted for engaging with said collar/interface, if said first or second chamber are attempted forced apart.

[0025] In one or more embodiments, mechanism comprises a frame comprising a lower set of hooks/clips adapted for hindering removal of the frame from the vial, and an upper threaded part adapted for hindering removal of the second chamber from the frame, and wherein the second chamber is configured to rotate within said threaded part.

[0026] In one or more embodiments, the second chamber comprises a sharpened edge adapted for penetrating the plug. The plug may e.g., be a first membrane or foil.

[0027] In one or more embodiments, the first chamber comprises a first composition, and wherein the second chamber comprises a second composition adapted for being mixed with said first composition.

[0028] In one or more embodiments, the second chamber is positioned above and/or at least partially inside the first chamber.

[0029] In one or more embodiments, the dual chamber system further comprises a safety mechanism adapted for holding the first and second chambers in position relative to one another prior to use.

[0030] In one or more embodiments, the safety mechanism comprises a safety ring, a clamp, a tape, or the like adapted for blocking the relative movement of said first and second chambers. The safety mechanism may be releasably removed.

[0031] In one or more embodiments, the mechanism comprises a frame comprising a lower set of hooks/clips adapted for hindering removal of the frame from the vial, and an upper threaded part adapted for hindering removal of the second chamber from the frame, and wherein the second chamber is configured to rotate within said threaded part.

[0032] The dual chamber system may be configured to be compatible with existing types of vials - be it made of glass, plastic, or some other commonly utilized material - and in any ISO regulated vial size (≥1ml volume) and neck dimension (≥13mm Ø).

[0033] The dual chamber system may also be compatible with existing crimp caps used to ensure container closure integrity (CCI) between a stopper/plug and a vial flange.

[0034] In one or more embodiments, the dual chamber system is capable of holding any combination of liquids, solids (e.g., powder), gas, or plasma - hereunder self-partnering (e.g., two liquids).

[0035] In one or more embodiments, the second chamber is compatible with existing types of stoppers - both in terms of type (e.g., solid serum stopper or lyophilization stoppers with one or multiple cutouts), blowback (e.g., European, American, none) material (e.g., bromobutyl or chlorobutyl) and size (e.g., 13 mm or 20 mm diameter).

[0036] In one or more embodiments, the dual chamber system is compatible with existing types of tamper-evident caps - be it liftable, twistable, or tearable.

[0037] In one or more embodiments, the second chamber is compatible with press-fit/push-fit integrated stoppering/capping systems.

[0038] In one or more embodiments, the second chamber is compatible with Closed System Transfer Devices such as vial adapter systems.

[0039] In one or more embodiments, the dual chamber system is compatible with any future commonly utilized vial, substance, stopper, tamper-evident cap, and crimp cap seal - which due to potential changes in materials, sizes, manufacturing techniques, and/or operational procedures is not commonly utilized today.

[0040] In one or more embodiments, the dual chamber system is configured for receiving a downward force (e.g., by a user) on the top or upper part of the system, causing one or multiple sharp ends - hereunder a continuously sharp end - of a second chamber to rupture a plug in one or multiple areas and subsequently displacing the plug out of its way.

[0041] The dual chamber system may comprise a cover or frame having a minimum of one set of hooks/clips ensuring downwards movement of the innards of the system, while inhibiting upwards movement.

[0042] The cover or frame may comprise one or multiple hooks/clips per set.

[0043] In one or more embodiments, the second chamber comprises one opening in the top, and one or multiple openings in the bottom.

[0044] In one or more embodiments, when in the preparatory state, the second chamber is detached from the

first chamber and the vial stopper.

[0045] In one or more embodiments, the vial stopper is configured with one or more cavities on its outer face(s), said cavity or cavities being adapted for forming one or multiple channels/vents together with the first chamber, when the vial stopper is in its partially seated position in the preparatory state.

[0046] In one or more embodiments, the vial stopper is configured with one or more protrusions on its outer face(s), said protrusion(s) being adapted for forming channels/vents together with the first chamber, when the vial stopper is in its partially seated position in the preparatory state.

[0047] In one or more embodiments, in the in-use state, a lower part of the vial stopper is configured to be torn/-ruptured, by said second chamber, into one or more leafs/plates with a first free end, and a second end attached to an upper part of the vial stopper, when a downward force is applied onto the second chamber, and the second chamber is moved at least partially into the first chamber.

[0048] In one or more embodiments, a lower part of the second chamber is shaped with one or more edges adapted for penetrating said vial stopper during the in-use state and when a downward force is applied onto the second chamber, and the second chamber is moved at least partially into the first chamber.

[0049] In one or more embodiments, a lower part of the second chamber is shaped with a plurality of edges adapted for penetrating said vial stopper during the in-use state and when a downward force is applied onto the second chamber, and the second chamber is moved at least partially into the first chamber.

[0050] In one or more embodiments, the vial stopper is configured with one or more weakened areas/lines within a lower part of said vial stopper, thereby allowing said lower part to be torn/ruptured, in the in-use state, by said second chamber, into one or more splinter/leafs/plates with a first free end, and a second end attached to an upper part of the vial stopper, when a downward force is applied onto the second chamber, and the second chamber is moved at least partially into the first chamber. In some embodiments, at least some of said weakened areas/lines are positioned on an outer face of said vial stopper. Alternatively, or in combination, at least some of said weakened areas/lines are positioned on an inner face of said vial stopper. In one or more embodiments, at least some of said weakened areas/lines defines a relatively weak spot at the center of the lower part of said vial stopper. In one or more embodiments, at least some of said relatively weakened areas/lines defines a weakened area at the periphery of the lower part of said vial stopper.

[0051] In one or more embodiments, the dual chamber system further comprises a mechanism adapted for holding the second and first chambers in position relative to one another, in the in-use state, after the second chamber has been moved at least partially into the first chamber. The mechanism may comprise hooks/clips adapted for sliding past or being slid past by a collar/interface on an outer face of the first and/or second chamber's walls, wherein said hook/clip is adapted for engaging with said collar/interface, if said first or second chamber are attempted to be forced apart. In one or more embodiments, the mechanism comprises a frame comprising a lower set of clips adapted for hindering removal of the frame from the vial, and an upper set of clips adapted for hindering removal of the second chamber from the frame.

[0052] In one or more embodiments, the dual chamber system further comprises a padded holder during the preparatory state; wherein the padded holder is configured to seal the bottom of the second chamber and to support the second chamber during filling thereof.

[0053] In one or more embodiments, the dual chamber system further comprises a mechanism adapted for holding the second and first chambers in position relative to one another, in the in-use state, after the second chamber has been moved at least partially into the first chamber, wherein said mechanism comprises a lower set of hooks/clips adapted for hindering removal of the mechanism from the vial, wherein the padded holder comprises locking regions adapted for receiving said lower hooks/clips.

[0054] Another aspect relates to a first chamber and a corresponding vial stopper/plug in accordance with the present invention and/or to the use of such first chamber and vial stopper for a dual chamber system.

[0055] Yet another aspect relates to a vial stopper/plug, in accordance with the present invention and/or to the use of such vial stopper/plug for a dual chamber system.

[0056] Another aspect relates to a second chamber and a corresponding vial stopper/plug in accordance with the present invention and/or to the use of such second chamber and vial stopper for a dual chamber system.

[0057] As used in the specification and the appended claims, the singular forms "a", "an", and "the" include plural referents unless the context clearly dictates otherwise. Ranges may be expressed herein as from "about" or "approximately" one particular value and/or to "about" or "approximately" another particular value. When such a range is expressed, another embodiment includes from the one particular value and/or to the other particular value. Similarly, when values are expressed as approximations, by use of the antecedent "about", it will be understood that the particular value forms another embodiment.

[0058] It should be noted that embodiments and features described in the context of one of the aspects of the present invention also apply to the other aspects of the invention.

Brief description of the figures

[0059]

Figures 1-2 illustrate cross-sectional views of one embodiment in accordance with various embodiments of the present invention.

Figures 3-4 illustrate outside views of the embodiment shown in Figures 1-2.

Figures 5-6 illustrate cross-sectional views of one embodiment in accordance with various embodiments of the present invention.

Figures 7-8 illustrate outside views of the embodiment shown in Figures 5-6.

Figure 9 illustrates an example of a second chamber in accordance with various embodiments of the present invention.

Figures 10-11 illustrate an example of a plug, in accordance with various embodiments of the present invention for use with the second chamber of Figure 9.

Figure 12 illustrates an example of a second chamber in accordance with various embodiments of the present invention.

Figures 13-14 illustrate an example of a plug, in accordance with various embodiments of the present invention for use with the second chamber of Figure 12.

Figures 15-16 illustrate an example of a plug, in accordance with various embodiments of the present invention.

Figures 17-18 illustrate an example of a plug, in accordance with various embodiments of the present invention.

Figures 19-20 illustrate an example of the plug of Figures 15-16, placed on/in a first chamber in accordance with various embodiments of the present invention.

Figures 21-22 illustrate an example of the plug of Figures 17-18, placed on/in a first chamber in accordance with various embodiments of the present invention.

Figure 23-24 illustrate an example of a plug, in accordance with various embodiments of the present invention.

Figure 25 illustrates an example of the plug of Figures 23-24, placed on/in a first chamber in accordance with various embodiments of the present invention.

Figure 26 illustrates three examples A-C of a first chamber and a corresponding plug, in accordance with various embodiments of the present invention.

Figure 27 illustrates three examples A-C of a first chamber and a corresponding plug, in accordance with various embodiments of the present invention.

Figure 28 illustrates the lyophilization process in steps A-F for a medicine in a European blowback vial with a corresponding plug (plug from Figures 10-11).

Figure 29 illustrates the lyophilization process in steps A-E for a medicine in a European blowback vial with a corresponding plug (plug from Figures 15-16).

Figure 30 illustrates the lyophilization process in steps A-E for a medicine in a European blowback vial with a corresponding plug (plug from Figures 17-18).

Figure 31 illustrates the lyophilization process in steps A-D for a medicine in a European blowback vial with a corresponding plug (plug from Figures 23-24).

Figure 32 illustrates the lyophilization process in steps A-C for a medicine in a European blowback vial with a corresponding plug (plug not shown elsewhere).

Figure 33 illustrates an example of a three-splinter/-leaf/plate plug, in accordance with various embodiments of the present invention in four views.

Figure 34 illustrates three two-splinter/leaf/plate plug designs, in accordance with various embodiments of the present invention with two views each.

Figure 35 illustrates three examples of a second chamber in accordance with various embodiments of the present invention, viewed from behind.

Figure 36 illustrates three examples of a second chamber in accordance with various embodiments of the present invention, viewed from behind.

Figure 37 illustrates two examples of a plug with continuous seams/weaknesses.

Figure 38 illustrates two examples of a plug with continuously arching curvature.

Figure 39 illustrates outside views and cross-sectional views of one embodiment in accordance with various embodiments of the present invention.

Figure 40 illustrates outside views and cross-sectional views of one embodiment in accordance with various embodiments of the present invention.

Figure 41 illustrates outside views and cross-sectional views of one embodiment in accordance with various embodiments of the present invention.

Figure 42 illustrates outside views and cross-sectional views of one embodiment in accordance with various embodiments of the present invention.

Figure 43 illustrates top views of four different embodiments of plugs with varying numbers of weaknesses/seams.

Figure 44 illustrates two different embodiments of plugs with corresponding second chambers.

Figure 45 illustrates two different embodiments of plugs with corresponding second chambers.

Figure 46 illustrates a holder compatible for holding a plug and a second chamber (not shown).

Figure 47 illustrates a holder compatible for holding a plug, a second chamber (not shown) and a cover or frame (not shown).

Figure 48 illustrates a padded holder compatible for holding a second chamber (not shown) and illustrates a temporary seal for a second chamber (not shown).

Figure 49 illustrates a holder compatible for holding a plug and a second chamber (not shown).

Figure 50 illustrates a holder compatible for holding a plug, a second chamber (not shown) and a cover or frame (not shown).

Figure 51 illustrates a padded holder compatible for holding a second chamber (not shown) and illustrates a temporary seal for a second chamber (not shown).

Figure 52 illustrates a holder with grooves/locks compatible for holding a plug (not shown), a second chamber (not shown) and a cover or frame (not shown).

References

[0060]

0	Dual chamber system
1	First chamber/vial
1-I	Collar/outer interface
1-II	Neck/inner interface
1-II-EBL	European blowback lock
1-II-NB	Non-blowback interface
1-II-ABL	American blowback lock
2	Plug/vial stopper
2-I	Splinter/leaf/plate
2-II	Contact point
2-III	Flange
2-IV	First chamber interface
2-IV-EBL	European blowback lock
2-IV-NB	Non-blowback interface
2-IV-ABL	American blowback lock
2-V	Weakened line/area
2-VI	Lowest point on breaking area/initial breaking point
2-VII	Cavity
2-VIII	Vent spew
2-IX	Protrusion/Second chamber interface
3	Cover
3-I	Lower set of hooks/clips
3-II	Middle set of hooks/clips
3-III	Upper set of hooks/clips
3-IV	Cutout
4	Lid
4-I	Tap
4-II	Thread
5	Stopper/membrane
6	Second chamber
6-I	End
6-II	(Lower) opening
6-III	Maximum width
6-IV	(Upper) opening
6-V	Collar/flange
6-VI	Indentation/Plug interface
6-VII	Edge
6-VIII	Stopper/seal interface
6-IX	Frame/cover interface
6-X	Notch/Adapter/CSTD interface
6-XI	Notch/Press-fit cap interface
7	Second substance
8	Safety mechanism
9	First substance
10	Channel/vent
11	Crimp cap
12	Press-fit cap
13	Frame
13-I	Lower set of hooks/clips
13-II	Upper set of hooks/clips
13-III	Thread
14	O-ring
15	Seal/syringe connector
15-1	Slot
15-II	Tabbed hub
15-III	One-way valve
15-IV	Female fitting
15-V	Second chamber interface
15-VI	Thread
16	Holder
17	Holder with collar
18	Padded holder
19	Temporary seal
20	Holder with grooves/locks

20-I Groove/lock

a Breaking area and/or breaking means being on-center
b Breaking area and/or breaking means being off-center

Detailed description of the invention

[0061] The following is to be seen as non-limiting examples of embodiments of the present invention. References made to the Figures (denoted with lines), may only point to a single instance of each feature, leaving some duplicate features unreferenced.

[0062] Upon the time of use of the dual chamber system 0 (see e.g., Figure 1 - i.e., the system is in its ready to use state, also referred to as the closed state) according to the present invention, the user removes a safety ring 8 (a safety mechanism) and applies a downward force (e.g., by pushing and/or twisting) on the top or upper part of the system 0, activating said system (see e.g., Figure 2 - i.e., the system is in its in-use state, also referred to as the opened state). This action forces the sharp or blunt end 6-I of the second chamber 6 through one or multiple points in the plug 2 (here embodied as a vial stopper), thereby rupturing the vial stopper 2 in a way that ensures that no parts break off and fall into the first chamber 1. As the second chamber 6 continues downwards, it gradually tears or further cuts more of the bottom of the vial stopper 2, along a weakened line/breaking area 2-V (see e.g., Figures 10-11), displacing the resulting splinter(s)/leaf(s) 2-I in the process. When the system is fully depressed, the bottom part of the splintered/torn plug 2 is fully displaced, leaving a second substance 7 in the second chamber 6 free to fall into the first chamber 1 where a first substance 9 resides. The two substances 7, 9 can then be mixed, e.g., by swirling and/or inverting the system. By removing a tamper-evident lid 4 on top of a cover 3 (see e.g., Figures 5-6) or a frame 13 (see e.g., Figures 39-42), a portion of a stopper 5 (see e.g., Figures 39-40) or a seal 15 (see e.g., Figures 41-42) is exposed, and the operator can extract the mixed substance through the stopper 5 or seal 15 with a syringe or a Closed System Transfer Device (CSTD).

[0063] Referring to the numbering of the drawings, 1 refers to the first chamber e.g., made of glass, plastic, or some other material (preferably transparent) in which the first substance 9, such as a liquid, lyophilate, powder, suspension, or the like is contained. The first chamber 1 is sealed with the vial stopper 2, e.g., made of a soft and flexible material, such as rubber, plastic, or elastomeric polymer. The second chamber 6, e.g., made of plastic, glass, or some other material, is adapted for holding the second substance 7, such as a liquid, a powder, a gas, or the like, and is here shown mounted on the plug/vial stopper 2. The vial stopper 2 may in the preparatory state be mounted on the second chamber 6, prior to the initiation of a lyophilization process, but preferably, the second chamber 6 is mounted subsequently to such a process. The second chamber 6 may be configured with one or more indentations 6-VI (see e.g., Figure 9), which allows the vial stopper/plug 2 - if configured with a corresponding protrusion 2-IX (see e.g., Figure 28B) - to lock more easily thereto (e.g., both before and after activation of the dual chamber system). The opposite can also be true, with one or more protrusions on the second chamber 6 and one or more indentations on the plug 2. If no indentation or protrusion is present, the plug 2 may be installed onto the second chamber 6 with a sufficiently tight fit to ensure that no air can enter the second chamber 6.

[0064] The second chamber 6 may be provided with a blunt, or sharp end 6-I (see Figures 9 and 12, respectively), which, when the second chamber 6 is subjected to a downward force, is adapted to rupture one, or multiple, areas of the plug 2 and to displace parts of the plug 2.

[0065] The vial stopper's/plug's lower part (2-I + 2-V - see Figures 10-11 and Figures 13-14) may be constructed with one or multiple weakened lines/areas 2-V or have a uniform construction. In the former case, the weakened lines/areas 2-V can be formed on the inner face of the vial stopper 2 (as seen in Figures 13-14) and/or on the outer face of the vial stopper 2 (as seen in Figure 10). In the latter case, any part of the plug's lower end must be weak enough to be ruptured by the second chamber 6. One or multiple openings 6-II (see e.g., Figure 9) at the bottom of the second chamber 6 enables the contained substance 7 to flow out into the first chamber 1 when the system 0 is in its opened state, thereby allowing for mixing of the two substances 7, 9. The resulting mixed solution 7+9 can subsequently flow back up through said holes back into the second chamber 6 when the entire system is inverted (placed upside down), thereby allowing for extraction of the content, preferably by utilizing a syringe, or a Closed System Transfer Device (CSTD) if the mixed content 7+9 is to be used in another system, e.g., an infusion bag.

[0066] The first chamber 6 may be provided with an upper opening 6-IV (not shown but the position is indicated in Figures 9 and 12 with a dotted line), preferably compatible with a stopper 5 commonly used in medical vials today. The stopper shown in Figures 1-2 and Figures 5-6 is a serum stopper with a European blowback lock adapted for interfacing with a European blowback vial whose neck has the same dimensions as the neck of the shown second chamber 6. However, the second chamber 6 can alternatively be made to work with serum stoppers with an American blowback lock adapted for interfacing with American blowback vials, or a serum stopper without a blowback lock for use with non-blowback vials. A cover 3 ensures that the second chamber 6 is fastened to the vial stopper 2 and to the first chamber 1, while also making sure the second chamber 6 is inaccessible. The cover 3 and the second chamber 6 may be manufactured to varying heights of the second chamber 6 to accommodate different amounts and/or different types of substance 7 filled in the second chamber 6.

Besides the hole 3-IV (see e.g., Figure 6) on top of the cover 3, the cover 3 may be configured with one or multiple cutouts to enable easier deformation of the cover 3 when the system 0 is pressed down, with the added benefit of letting the operator view the condition of the second chamber's substance 7 prior to activating the mechanism.

[0067] The cover 3 shown in Figures 1-8 is equipped with three sets of clips 3-I, 3-II, 3-III that ensures that the cover 3 can be easily installed, but not easily removed. The upper set of clips 3-III clicks onto the underside of a collar/flange 6-V on the upper part of the second chamber 6. The middle 3-II and lower 3-I sets of clips click onto the underside of a collar 1-I present on the first chamber 1, with the lower set of clips 3-I being utilized in the closed position, and the middle set of clips 3-II being utilized in the opened position. The middle set of clips 3-II has the added benefit of resting on top of the plug 2 in the closed position, thereby preventing the plug 2 from sliding upwards due to a potential gas overpressure if the vial 1 (first chamber) is filled with an inert gas (usually nitrogen) after lyophilization without requiring a crimp cap or a press-fit cap. The embodiments have three clips per set 3-I, 3-II, 3-III (best illustrated in Figures 3-4 and Figures 7-8), but the cover 3 may be designed in other ways: E.g., in the case where the cover 3 has no cutouts besides the opening 3-IV on it's top, the clips in each set 3-I, 3-II, 3-III can revolve continuously around the inside of the cover 3, in effect constituting only a single clip. To save material, one could make gaps in the continuous clip, creating any suitable number of clips in each set. In the case the cover 3 has multiple cutouts across one or multiple sets of clips, each affected clip should consist of a minimum of two clips, preferably spaced as far apart as possible to ensure sufficient locking ability. The distance between clips of different sets should also be placed as far apart as possible. This asynchronous spacing between clips of different sets ensures optimal deformation of the cover 3 when the system 0 is pressed down. In the special case the cover 3 only has a single cutout across one or multiple continuous sets of clips, in effect creating only a single clip per set, the cutout part should not exceed that which is needed to ensure proper locking functionality of the remaining clip.

[0068] The cover 3 is preferably made of a relatively soft and flexible material, such as plastic, which allows the lower set of clips 3-I to deform outwards when hitting the outside wall of the first chamber 1 as a downward force is applied - without inhibiting the middle set of clip's 3-II ability to click onto the underside of the collar 1-I of the first chamber 1 when the system 0 is pressed down. The cover 3 may be configured to work with a tamper-evident lid 4 (see e.g., Figure 1), which preferably cannot be remounted once removed. The cover 3 shown is mounted between the underside of the collar 1-I of the first chamber 1 and on the upper side of a removable safety ring 8. The safety ring 8 could be a peel-off ring, as illustrated, a horseshoe ring/clamp, or something similar. The safety ring 8 is not required, but it is recommended, as it prevents the cover 3 - and by extension the second chamber 6 - from being pressed down involuntarily or in bad faith. An alternative to a safety ring would be to increase the height of the lower set of clips of the cover 3-1, so that they take up the same amount of space as the shown safety ring 8. Another alternative - which might be utilized in tandem with the prior alternative - would be to make the cover 3 slightly smaller, so that it would sit slightly tighter around the collar 1-I of the first chamber 1. This in turn would require additional force to initiate the downward motion of the second chamber 6, presumably preventing the mechanism from activating during freight or during a non-intentional force application.

[0069] In the embodiments shown in Figures 39-42, the cover 3 is replaced with a frame 13. Such a frame 13 is not designed for movement like the cover 3, but rather retains the same position regardless of whether the system is in its closed or opened position. The frame 13 is thus preferably more rigid than the cover 3. Two O-rings 14 may also be present, one on the frame 13 and one on the second chamber 6, to ensure sterility of the inside of the system 0. In the embodiments shown in Figures 39-40, the frame 13 is provided with two sets of clips, a lower set of clips 13-1 that hinders removal of the frame from the first chamber 1, and an upper set of clips 13-II that hinders removal of the second chamber 6 from the frame 13. Similarly, to that explained about the cover 3, the frame can be designed to have a continuous clip per set, or a large single clip per set as a result of a cut-out of a significant part of a continuous clip, as long as the remaining clip/non-cutout piece can retain sufficient locking ability. In the embodiments shown in Figures 41-42, the upper set of clips 13-II is interchanged with threads 13-III. If the second chamber 6 and the frame 13 is manufactured as a single piece, the safety mechanism 8 shown in the embodiments in Figures 39-42 can be substituted by a weakness in the construction approximately where the safety mechanism 8 is located in the current embodiments, so that an intended force is sufficient to have the second chamber 6 irreversibly break off from the frame 13.

[0070] In the embodiment shown in Figure 9, the lower end (area from the end 6-I up to maximum width 6-III) of the second chamber 6 is of the on-center design (a), configured as an arrowhead. In general, the arrowhead may have different shapes such as outward arching (bullet point arrowhead - see top illustration of Figure 35), linear (broadhead arrowhead - see middle illustration of Figure 35) and inwards arching (field point arrowhead - see bottom illustration of Figure 35). The arrowhead may also have varying numbers of edges, with one edge constituting a continuous, one-dimensional blade (see top illustration of Figure 35), two edges culminating in a point (see bottom left corner of Figure 44), three edges culminating in a point (see bottom right corner of Figure 44), all the way up to infinite edges for a cone shaped variant (see top illustration of Figure 9).

[0071] The embodiment shown in Figure 9 has two lower openings 6-II but can be designed with fewer or additional openings. The corresponding vial stopper/plug 2 shown in Figures 10-11 has a weak spot towards the center at the plug's lowest point 2-VI, where the seams of the different splinters/leafs 2-I meet. The plug 2 ruptures at this spot as the end 6-I of the second chamber 6 tears through when a downward force is applied. The plug 2 is then further torn apart in the seams 2-V between the splinters/leafs 2-I and displaced by the second chamber's edges 6-VII as more of the second chamber 6 is pressed down. This continues until the lower part of the second chamber 6 reaches it maximum width 6-III, fully displacing the splinters 2-I, all while the splinters 2-I are held together at the upper part (2-III + 2-IV) of the plug 2.

[0072] In the embodiment shown in Figure 12, the lower part (area from lowest point 6-I up to maximum width 6-III) of the second chamber 6 is of the off-center design (b), configured as a bevel. Like the arrowhead design, the bevel design has different variations, and is either a one/infinite edged continuous blade (Tuohy, see top illustration on Figure 36), a two-edged variant culminating in a point (Quincke, see middle illustration on Figure 36), or a two-edged variant culminating in a line (Chisel, see bottom illustration on Figure 36 - a custom bevel design not utilized in medical field today).

[0073] The embodiment shown in Figure 12 has two lower openings 6-II but can be designed with fewer or additional openings. The corresponding plug 2 shown in Figures 13-14 has a weakened area 2-V towards the periphery at the plug's lowest point 2-VI (the weakened area and the lowest point is on the inside of the plug, and thus merely indicated with dotted lines). The plug 2 is cut at this spot, as the end 6-I of the second chamber 6 tears through when a downward force is applied. After the initial cut, the cut is deepened along the weakened area 2-V, and the splinter 2-I displaced by the second chamber's edge 6-VII, as more of the second chamber 6 is pressed down. This continues until the lower part of second chamber 6 reaches it maximum width 6-III, fully displacing the splinter 2-I, all while the splinter 2-I is held together at the upper part (2-III + 2-IV) of the plug 2.

[0074] Figure 1 illustrates, in a cross-sectional view, the on-center design's (a) closed position, where the two chambers 1, 6 are separated and individually sealed by the plug 2. Figure 2 illustrates, in a cross-sectional view, the on-center design's (a) opened position, where the two chambers 1, 6 connect and upon which their substances 7, 9 can be mixed and the resulting mixed substance 7+9 extracted. Figures 3 and 4 illustrate the outside of the embodiments shown in Figures 1 and 2, respectively, in addition to being rotated 90 degrees counterclockwise.

[0075] Figures 5-8 illustrate the same as Figures 1-4, only for the off-center design (b).

[0076] Figures 9-11 illustrate a specific embodiment of the on-centered design (a); a second chamber 6 with a corresponding plug 2 in its closed and opened state.

[0077] Figures 12-14 illustrate a specific embodiment of the off-centered design (b); a second chamber 6 with a corresponding plug 2 in its closed and opened state.

[0078] Figures 15-25 show examples of vial stopper-vial combinations that are particularly suitable for use in a lyophilization process. A part of the dual chamber system is here shown in its preparatory state (left) and in its ready to use state (right). In the ready to use state, the second chamber 6 has been left out to provide a better view of the interaction between the vial 1 and the vial stopper 2. Figures 15-18 show vial stoppers 2 of both the on-centered design (a) and the off-centered design (b) with cavities 2-VII, which allows for larger vents 10 than what is possible when utilizing the plugs 2 shown in Figures 10-11 and Figures 13-14. Figures 19-22 shows the vial stoppers 2 in Figures 15-18 placed in vials 1 in the partial and fully seated positions. Figures 23-24 shows a vial stopper/plug 2 of the on-centered design (a) featuring vent spew protrusions 2-VIII. The vent spew 2-VIII is a byproduct of the compression molding technique used to manufacture rubber components and is usually trimmed away. However, in this case, the vent spew 2-VIII acts as scaffolding for the plug 2 when partially seated in the vial 1, raising the plug 2 sufficiently together with the vial 1 to create vents 10 necessary for lyophilization (see Figure 25), and being of negligible size so that it does not inhibit rupturing and displacement of the lower end of the plug 2 when the system 0 is activated. Even though one vent spew protrusion 2-VIII is sufficient to create vents 10 together with the vial 1, two or more protrusions with maximum spacing between them on the same horizontal plane is preferred, as this ensures more even lyophilization. The vent spew design can be made to work with the off-centered design (b), but its preferred embodiment is the on-centered design (a) for the abovementioned reasons.

[0079] Figure 26 illustrates three examples A-C of a first chamber 1 and a corresponding vial stopper 2 of the on-center design (a) (shown relatively larger than the first chamber 1 for a more detailed view) in accordance with various embodiments of the present invention. The weakness/seam(s) are formed on the inside of the vial stopper 2 and are as thus not shown. The first chambers 1 are shown with different vial neck designs 1-II: European blowback A (1-II-EBL), non-blowback C (1-II-NB), and American blowback B (1-II-ABL), respectively. The vial stoppers 2 show corresponding outer interfaces 2-I with the appropriate blowback locks for A and C (2-IV-EBL, 2-IV-ABL), and a lack of a blowback lock on the vial stopper 2 corresponding to the non-blowback vial B (2-IV-NB).

[0080] Figure 27 illustrates the same as Figure 26, only for the off-center design (b). This design has superior fastening ability in the partially seated position, as there is more contact with the first chamber 1, as illustrated by the contact points 2-II with corresponding blowback design (matching optional). It is worth noting that even though there seemingly is no room for an American blowback-like contact point protrusion 2-II to fit into a vial 1 in the fully seated position (see Figure 27 C), traditional lyophiliza-

tion stoppers are known to have "larger than vial" properties and still retain perfect sealing capabilities when fully seated in the vial.

[0081] Figures 28-32 show different vial stopper-vial combinations as well as examples of the individual steps within the preparatory state (A-C) and the ready to use state (D-F). All combinations are shown as European blowback types, as this is the most commonly used vial for use with lyophilized medicine. However, both American and non-blowback variants can be utilized, and a mix is also possible, as it is known that non-matching blowback combinations can ensure proper container closure integrity. Also note the "European" protrusion 2-IX on the inside of the plug 2 in the embodiments presented in Figures 28-32 for interfacing/engaging with the outside of the second chamber 6 (not shown) to match this style of vial (matching optional).

[0082] An important point regarding the present invention is the compatibility with existing aluminum crimp caps 11. This method is the standard way of ensuring container closure integrity today and works by first placing the aluminum cap 11 onto the lyophilized vial as it exits the lyophilization chamber, and then crimping the skirt of the aluminum cap around the collar of the vial 1-I to ensure complete container closure integrity.

[0083] In the embodiment illustrated in Figure 28, the vial stopper 2 is not designed to avoid displacement thereof during lyophilization, but rather designed to act as a lid on the vial 1, moving up and down and/or from side to side (without jumping out of the vial) as the pressure of the vapor sporadically creates the necessary channels/-vents 10 for the vapor to escape with nothing but the untorn splinters/leafs/plates 2-I acting as sporadic contact points 2-II to the vial 1. Having the weakness/seam(s) 2-V on the outside of the plug 2 as shown in Figures 10-11 might aid this design with the venting, as the seam(s) 2b-V may double as channels/vents 10, but this is not a requirement. It is worth noting that the roof in the lyophilization chamber may be lowered until it is slightly above the plug 2 so that said plug is prohibited from jumping out of the vial 1, but still have enough leeway to create sporadic channels/vents 10 for the vapor to escape.

[0084] In the embodiment illustrated in Figure 29, a European blowback type vial 1 is shown with a corresponding vial stopper 2 of the on-centered design (a) with multiple cavities as also shown in Figures 15-16. The vial in step B is rotated 45 degrees in relation to the other views (A, C-E) to illustrate the channels/vents 10.

[0085] In the embodiment illustrated in Figure 30, a European blowback vial 1 is shown with a corresponding vial stopper 2 of the off-centered design (b) with a single cavity as also shown in Figures 17-18.

[0086] In the embodiment illustrated in Figure 31, a European blowback vial 1 is shown with a corresponding vial stopper 2 of the on-centered design (a) with vent spews as also shown in Figures 23-24. Note the substitution of a crimp cap 11 with a press-fit cap 12, which removes the need for the crimping step (see step E in Figure 28 and step D in Figures 29-30), as the press-fit cap can be mounted onto the vial 1 in one single downward motion.

[0087] In the embodiment illustrated in Figure 32, a European blowback vial 1 is shown with a corresponding vial stopper 2 of the off-centered design (b) and with no cavities as also shown in Figures 13-14. Instead, its contact point(s) 2-II is lowered to give the sufficient height for a pre-mounted press-fit cap 12 to form a vent 10 with the vial 1 for vapor to escape through. This embodiment is especially beneficial, as it further reduces the number of steps in the fill-finish process when compared to the already condensed process presented in Figure 31, as the press-fit movement is done by the lyophilization shelf when the floor is raised/roof is lowered at the end of the lyophilization process, forcing the press-fit cap 12 around the collar of the vial 1-I and sealing it shut.

[0088] Figure 33 illustrates four views of a three-splinter/leaf/plate vial stopper 2 of the on-centered design (a) in closed position. The first two illustrations show the vial stopper 2 from a side view, whereas the latter two illustrations show the vial stopper 2 in perspective view.

[0089] Figure 34 illustrates three different two-splinter/leaf/plate vial stoppers 2 of the on-centered design (a), with a front view on the left-hand side, and a side view on the right-hand side - all in closed position, but with different curvature (convex, linear, and concave, respectively, when viewed from top to bottom).

[0090] Even though only some examples of splinters/leafs/plates, weaknesses, contact points, and blowback lock combinations are given, any reasonable combination of these features, and in varying numbers (e.g., 3 splinters, 3 weakened lines, 3 contact points, 3 blowback locks as is the case for Figure 33), are within the scope of the invention.

[0091] Figure 35 shows corresponding second chambers 6 to the vial stoppers 2 illustrated in Figure 34.

[0092] Figure 36 shows three different second chambers 6 of the off-centered (b) design. These can be used with any single splinter plug 2 of reasonable design and does not as such have corresponding plugs like the plug-second chamber combinations illustrated in Figures 34-35.

[0093] Figures 37-38 shows two special case plugs 2, with Figure 37 showing an example of a plug 2 with a single, continuous seam/weakness 2-V, and Figure 38 showing an example of a plug 2 with a continuously concavely/inwards arching splinter/leaf/plate 2-I.

[0094] Figures 39-42 illustrates advanced embodiments of a fully assembled system 0 in four different modes (from left to right): Inactive mode (freight/storage), Primed mode (safety mechanism removed), Active mode (first chamber pressed into second chamber), and Extraction mode (tamper-evident lid removed). The two first modes are subsets of the ready to use (closed) state, and the two latter modes are subsets of the in-use (opened) state.

[0095] Figure 39 illustrates a first advanced embodi-

ment of a fully assembled system, where the upper views are back views, and the lower views are cross-sectional views of said back. This design features a frame 13 as opposed to a cover 3, and also features a second chamber 6 capable of holding a larger volume of the second substance/composition 7 as opposed to that shown in e.g., Figures 1-2.

[0096] Figure 40 illustrates a second advanced embodiment of a fully assembled system with the same views as Figure 39. The stopper 5 is covered by a press-fit cap 12 similar to those illustrated in Figures 31-32. The second chamber is also fitted with a notch 6-X the same distance from the top of the system 0 as the vial collar 1-I is from the top of the vial 1, making it compatible with Closed System Transfer Devices such as e.g., an infusion bag vial adapter once the lid 4 is removed (a tear-off lid in this example).

[0097] Figure 41 illustrates a third advanced embodiment of a fully assembled system, with the upper views being front views, and the lower views being cross-sectional views of said front. This system is activated by a twisting force as opposed to a pushing force shown in the previous embodiments. In addition, the means of extracting the mixed solution is to be done with a needle-less syringe whereas the previous embodiments are designed to be used with a syringe outfitted with a needle or a CSTD outfitted with a spike. This is done by interchanging the stopper/membrane 5 with a seal 15, preferably made from plastic, which is fitted with a female fit 15-IV for a male syringe tip (not shown) to be inserted into. The seal 15 is also outfitted with a slot 15-I for the skirt of a Luer lock syringe (not shown) to vacate in when the male syringe tip is inside the female fit 15-IV of the seal 15. The slot 15-1 also features a tabbed hub 15-II for the skirt to thread onto, increasing the fastening ability. Thus, this embodiment makes the seal 15 compatible with both Luer lock and Luer slip syringes. The same tabbed hub 15-1 can be used to further fasten the lid 4 if the lid is fitted with protruding taps 4-I.

[0098] The seal 15 also features a one-way, self-closing valve 15-III such as a duckbill valve, a joker valve or a cross slit valve that closes off the inside of the second chamber 6 to the outside environment during freight and storage but is displaced when a syringe tip (not shown) is inserted into the female fit 15-IV, allowing for extraction of the mixed substance/composition 7+9 upon time of use. The seal 15 featured in this embodiment is installed onto the second chamber 6 by pressing it into position, forcing the second chamber interface 15-V to lock onto the European blowback notch 6-VIII present on the second chamber 6 similar to how a stopper/membrane 5 is installed onto the second chamber 6 in the previous embodiments of this application (also similar to how a serum stopper is installed onto a vial in the conventional way today). However, the seal 15 could be made to work with a threaded design, if corresponding threads are present inside the throat of the second chamber 6. The lid 4 can also be made to work to fasten to the seal 15 instead of the frame 13, so that the seal 15 and the lid 4 can be pre-mounted as one component before being installed onto the second chamber 6 and/or frame 13.

[0099] Figure 42 shows a fourth advanced embodiment of a fully assembled system with the same views as shown in Figure 41. This embodiment also features connectivity with a needle-less syringe, as the featured threading 15-VI allows a corresponding Luer lock syringe tip (not shown) to be screwed on after the lid 4 - which is fitted with corresponding threads 4-II - is removed. This design is incompatible with Luer slip syringe tips, as the seal does not feature a tapering fit as in Figure 41, and as such are dependent on threads to establish a secure connection - threads which a Luer slip syringe tip does not have.

[0100] Figures 39-42 are all shown with the on-center design (a). However, the embodiments could be made to work with the off-center design (b), with the embodiments shown in Figures 39-40 being directly interchangeable. The embodiments shown in Figures 41-42 would need to be outfitted with a device such as a buffer (not shown) that translate the horizontal twisting motion to a vertical pushing motion onto the second chamber 6, as the plug 2 of the off-centered design (b) is non-functioning with rotational activation.

[0101] Figure 43 illustrates four different embodiments of plugs 2 with varying numbers of breaking lines/areas 2-V formed on the inside of said plug. In general, these weaknesses may be formed on the inside and/or on the outside of the plug. In general, the thickness of the weakened area 2-V should preferably be in the range 0.1-1 mm to ensure sufficient protection from the outside environment, while still being weak enough to be ruptured and/or cut by the second chamber 6. The hardness of the plug should preferably be in the range 50-85 Shore A to ensure that the plug 2 is neither to soft (which results in no rupturing), nor to hard (which results in the plug 2 being torn apart in the intersection between the flange 2-III and the outer interface 2-IV). The choice of exact thickness within the presented range is influenced by the choice of exact hardness/stiffness within the presented range, and vice versa - along with the size of the plug 2 (e.g., 13mm vs 20mm diameter flange 2-III), the choice of material (e.g., bromobutyl vs chlorobutyl rubber) among other factors.

[0102] Figure 44 illustrates two different embodiments of inwards curving plugs 2 with corresponding second chambers 6. Inwards curving plugs 2 offer increased sealing capability for the second chamber 6, as the splinters/leafs/plates can flush/adjoin the lower opening(s) 6-II of the second chamber 6 - but at the expense of restricting the ways the second chamber 6 can be installed onto the plug 2 around the rotary X-axis (yaw). The second chamber 6 shown in the bottom left corner is a perspective view of the linear/broadhead arrowhead design shown in the middle illustration in Figure 35. The second chamber 6 shown in the bottom right corner is configured with two hook/clip interfaces 6-

IX, that inhibits the removal of the second chamber 6 from the frame 13 once mounted, with the bottom interface engaging in the system's 0 ready to use (closed) state, and the top interface engaging in the system's 0 in-use (opened) state.

[0103] Figure 45 illustrates two additional plug-second chamber pairings. The second chamber 6 shown in the bottom left corner features a threaded interface 6-IX instead of the hook/clip interface 6-IX shown in the embodiment at bottom right corner of Figure 44. These threads 6-IX, together with corresponding threads on the inside of the frame 13 (not shown), enables the user to activate the system 0 by a twisting force as opposed to a pushing force. The second chamber 6 shown in the bottom right corner features two set of notches, with the top notch 6-XI being intended for a press-fit cap to lock onto, and the lower notch 6-X being intended for a CSTD (not shown) such as a vial adapter to lock onto.

[0104] Figure 46 illustrates a cross-sectional view of a holder 16 suitable for holding a plug 2 and a second chamber 6, so that the second chamber 6 can be held upright during filling of the second substance/composition 7 in the case the second chamber 6 is to be filled and sealed separately for later assembly onto the first chamber 1. This solution is restricted to non-lyophilized fills in the first chamber 1, e.g., serum or dry powder fills as a vial 1 undergoing lyophilization needs to be stoppered inside the lyophilization chamber to maintain a complete/partial vacuum, and this is not possible in this configuration, as the plug 2 is in the holder 16 outside of the chamber.

[0105] Figure 47 illustrates a cross-sectional view of a holder 17 compatible for holding a plug 2, a second chamber 6, and a cover (3) or frame (13) and is designed to look like the neck of a vial, so that the lower set of hooks/clips on a cover 3 or a frame 13 can hook/clip onto the holder 17 like it would a vial collar 1-I. The shoulders/widened lower portion of the holder 17 is intended for increased grippability for when a plug, second chamber, cover/frame installation is to be forced apart from the holder 17 after filling of the second substance 7 for mounting onto a vial 1 containing the first substance 9 (not shown). It is worth noting that the force required to remove these components from the holder 17 should preferably exceed that which a human would reasonably be able to provide, as this would entail that a human would also be able to force these components apart from a vial 1.

[0106] Figure 48 illustrates cross-sectional views of a padded holder 18 (left illustration) and a temporary seal 19 (right illustration) both intended for use with a second chamber 6 (not shown). The padded holder 18 is intended to seal the bottom of the second chamber 6, and also position said chamber upright during filling in the instance the vial 1 is not available as a holder, as would be the case if the second chamber 6 is filled separately from the first chamber 1. An added benefit of a padded holder, is that it frees up a plug 2, so that a plug can be used with the vial 1 in the lyophilization process. A filled and sealed second chamber 6 still placed in the padded holder 18, can then be turned on its head, said padded holder removed, and a vial 1 with the lyophilized content can then be mounted "up-side-down" onto the inverted second chamber 6. Alternatively, if the plug 2 and second chamber 6 is of a small design (e.g., 13mm diameter opening 6-IV), surface tension should prevent the filled content on a second chamber 6 in a padded holder 18 from falling out if said second chamber is removed from said holder without being placed "up-side-down" - and as such a filled and sealed second chamber 6 can thus be installed onto a vial 1 without inverting said vial. A padded holder 18 can also be designed with the outside looking like a vial similar to the holder 17 shown in Figure 47. The design of the padding shown in 18, features a protrusion to interface with an indent in the second chamber 6 but could be made with an indentation or no protrusion/indentation to match a different interfacing design on the second chamber 6 (matching optional). Similarly, a temporary seal 19 can be placed in a non-padded holder 16, 17, and a second chamber 6 can then be placed into said holder 16, 17 and seal 19 to enable the second chamber 6 to stand upright during filling of the second substance/composition 7. When removing the second chamber 6, the temporary seal 19 will then have clicked onto said second chamber as a result of the second chamber interface 2-IX on the plug 2, and the plug interface 6-VI on the second chamber 6. Similar to that explained with the padded holder 18, the second chamber 6 can then be placed "up-side-down", and the temporary seal 19 removed when it is time to mount onto a filled vial 1 featuring a plug 2.

[0107] Figures 49-51 illustrates the same holders and seals as shown Figures 46-48, only adapted for the off-centered design (b).

[0108] It is worth noting that with the off-centered design (b), it is possible to fill a second chamber 6 that is pre-sealed with a stopper/membrane 5 or a seal 15 "up-side-down", due to its relatively large lower opening 6-II, and then mount a pre-filled vial 1 "up-side-down" onto said second chamber 6 - all without the need of any holder or temporary seal. Alternatively, if the second chamber 6 is sufficiently small (e.g., 13mm diameter upper opening 6-IV), said second chamber can be turned back to "normal" after filling of the second composition 7 through the lower opening 6-II, for mounting onto a vial 1 containing a first composition 9, as surface tension will prevent the second composition 7 from falling out of the second chamber 6. However, a padded holder or a temporary seal will still be necessary if there is sufficient time delay between filling of the second chamber 6 and the vial 1 (such as for storage and/or freight of a filled second chamber 6 for subsequent mounting onto a filled and sealed vial 1).

[0109] Figure 52 illustrates a holder 20 compatible for holding a plug, a second chamber, and a cover/frame similar to that of the collared holder 17 shown in Figure 47 and Figure 50, but with locking regions 20-I where the lower hooks/clips 3-I, 13-I of a cover/frame (not shown)

would engaged in the locked position (i.e., by slotting the lower set of hooks/clips of a cover/frame into the corresponding grooves of the holder 20 and turn said cover/-frame counter-clockwise), but would then be disengaged in the unlocked position (i.e., turning the cover/frame clockwise and lifting said cover/frame) for easy removal from the holder 20. This design can be made with fewer or additional grooves/locks 20-I, corresponding to different numbers of hooks/clips in the lower set of hooks/clips 3-I, 13-1 on a cover/frame (not shown). The grooves/locks 20-I can also be flipped horizontally, so that a clockwise movement engages the lock, and a counter-clockwise movement disengages said lock. The holder 20 can be made to work with a padded design, like the holder 18 shown in Figure 48 and Figure 51.

Claims

1. A dual chamber system (0) for medicine, said dual chamber system (0) comprising:

- a first chamber (1) defined by walls and configured as a vial;
- a vial stopper (2) adapted for being mounted to the first chamber (1); and
- a second chamber (6) defined by walls and adapted for being directly or indirectly mounted to the first chamber (1) and/or to the vial stopper (2);

wherein said dual chamber system is configured to be in a preparatory state, a ready to use state, and an in-use state;
wherein in the preparatory state, the vial stopper (2) is connected to the first chamber (1) in a partially seated position;
wherein in the ready to use state, the vial stopper (2) is adapted to seal said first chamber (1) from said second chamber (6), and vice versa;
wherein the vial stopper (2) is connected to the first chamber (1) in a fully seated position, and the second chamber (6) is directly or indirectly mounted to the first chamber (1) and/or to the vial stopper (2);
wherein in the in-use state, the second chamber (6) is configured to be moved at least partially into the first chamber (1) when a downward force is applied onto the second chamber (6), e.g., by pushing and/or twisting the second chamber (6), thereby rupturing the vial stopper (2).

2. The dual chamber system (0) according to claim 1, wherein in the preparatory state, the second chamber (6) is detached from the first chamber (1) and the vial stopper (2).

3. The dual chamber system (0) according to any one of the claims 1-2, wherein the vial stopper (2) is configured with one or more cavities (2-VII) on its outer face(s), said cavity or cavities (2-VII) being adapted for forming one or multiple channels/vents (10) together with the first chamber (1), when the vial stopper (2) is in its partially seated position in the preparatory state.

4. The dual chamber system (0) according to any one of the claims 1-2, wherein the vial stopper (2) is configured with one or more protrusions (2-VIII) on its outer face(s), said protrusion(s) (2-VIII) being adapted for forming channels/vents (10) together with the first chamber (1), when the vial stopper (2) is in its partially seated position in the preparatory state.

5. The dual chamber system (0) according to any one of the claims 1-4, wherein, in the in-use state, a lower part of the vial stopper (2) is configured to be torn/-ruptured, by said second chamber (6), into one or more leafs/plates (2-II) with a first free end, and a second end attached to an upper part of the vial stopper (2), when a downward force is applied onto the second chamber (6), and the second chamber (6) is moved at least partially into the first chamber (1).

6. The dual chamber system (0) according to any one of the claims 1-5, wherein a lower part of the second chamber (6) is shaped with one or more edges (6-VII) adapted for penetrating said vial stopper (2) during the in-use state and when a downward force is applied onto the second chamber (6), and the second chamber (6) is moved at least partially into the first chamber (1).

7. The dual chamber system (0) according to any one of the claims 1-5, wherein a lower part of the second chamber (6) is shaped with a plurality of edges (6-VII) adapted for penetrating said vial stopper (2) during the in-use state and when a downward force is applied onto the second chamber (6), and the second chamber (6) is moved at least partially into the first chamber (1).

8. The dual chamber system (0) according to any one of the claims 1-7, wherein the vial stopper (2) is configured with one or more weakened areas/lines (2-V) within a lower part of said vial stopper (2), thereby allowing said lower part to be torn/ruptured, in the in-use state, by said second chamber (6), into one or more splinter/leafs/plates (2-II) with a first free end, and a second end attached to an upper part of the vial stopper (2), when a downward force is applied onto the second chamber (6), and the second chamber (6) is moved at least partially into the first chamber (1).

9. The dual chamber system (0) according to claim 8, wherein at least some of said weakened areas/lines (2-V) are positioned on an outer face of said vial stopper (2).

10. The dual chamber system (0) according to any one of the claims 8-9, wherein at least some of said weakened areas/lines (2-V) are positioned on an inner face of said vial stopper (2).

11. The dual chamber system (0) according to any one of the claims 8-10, wherein at least some of said weakened areas/lines (2-V) defines a relatively weak spot at the center of the lower part of said vial stopper (2).

12. The dual chamber system (0) according to any one of the claims 8-10, wherein at least some of said weakened areas/lines (2-V) defines a relatively weakened area (2-V) at the periphery of the lower part of said vial stopper (2).

13. The dual chamber system (0) according to any one of the claims 1-12, further comprising a mechanism (3,3-I,3-II,3-III,13,13-I,13-II,13-III) adapted for holding the second (6) and first (1) chambers in position relative to one another, in the in-use state, after the second chamber (6) has been moved at least partially into the first chamber (1).

14. The dual chamber system (0) according to claim 13, wherein said mechanism (3,3-I,3-II,3-III,13,13-I,13-II) comprises hooks/clips adapted for sliding past or being slid past by a collar/interface (1-1,6-V) on an outer face of the first (1) and/or second (6) chamber's walls, wherein said hooks/clips is adapted for engaging with said collar/interface, if said first (1) or second (6) chamber are attempted forced apart.

15. The dual chamber system (0) according to claim 13, wherein said mechanism (13,13-I,13-II) comprises a frame (13) comprising a lower set of clips (13-I) adapted for hindering removal of the frame from the vial (1), and an upper set of clips (13-II) adapted for hindering removal of the second chamber (6) from the frame (13).

16. The dual chamber system (0) according to claim 13, wherein said mechanism (13,13-I,13-III) comprises a frame (13) comprising a lower set of hooks/clips (13-I) adapted for hindering removal of the frame from the vial (1), and an upper threaded part (13-III) adapted for hindering removal of the second chamber (6) from the frame (13), and wherein the second chamber (6) is configured to rotate within said threaded part (13-III).

17. The dual chamber system (0) according to any one of the claims 1-16, wherein the first chamber (1) comprises a first composition (9), and wherein the second chamber (6) comprises a second composition (7) adapted for being mixed with said first composition (9).

18. The dual chamber system (0) according to any one of the claims 1-17, further comprising a padded holder (18) during the preparatory state; wherein the padded holder (18) is configured to seal the bottom of the second chamber (6) and to support the second chamber (6) during filling thereof.

19. The dual chamber system (0) according to claim 18, further comprising a mechanism (3,3-I,3-II,3-III,13,13-I,13-II,13-III) adapted for holding the second (6) and first (1) chambers in position relative to one another, in the in-use state, after the second chamber (6) has been moved at least partially into the first chamber (1), wherein said mechanism (3,3-I,3-II,3-III,13,13-I,13-III) comprises a lower set of hooks/clips (3-I, 13-I) adapted for hindering removal of the mechanism from the vial (1), wherein the padded holder (18) comprises locking regions (20-I) adapted for receiving said lower hooks/clips (3-I, 13-I).

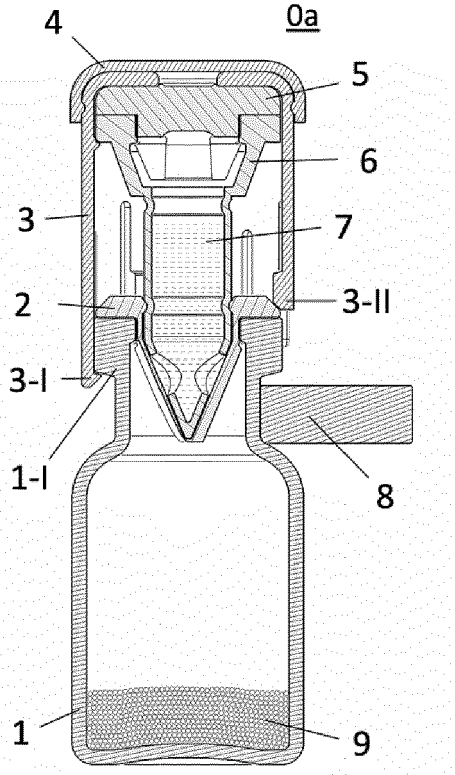


FIG. 1

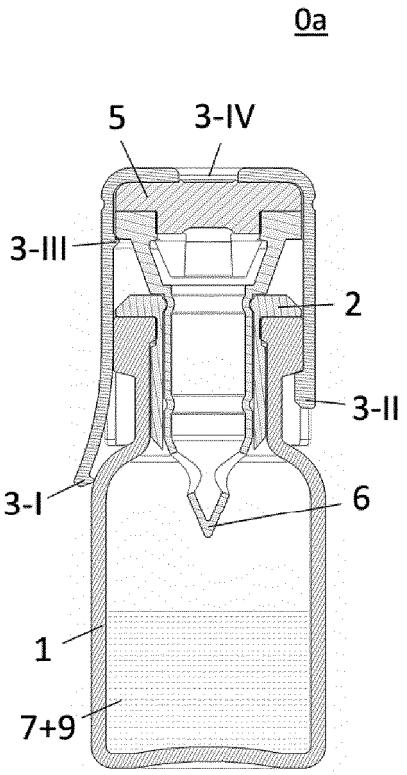


FIG. 2

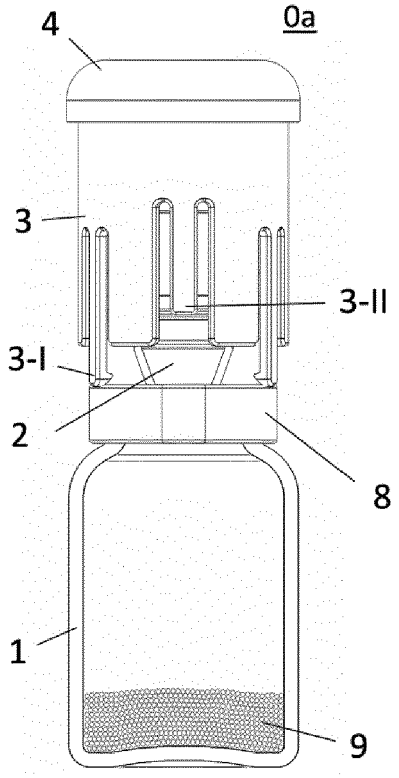


FIG. 3

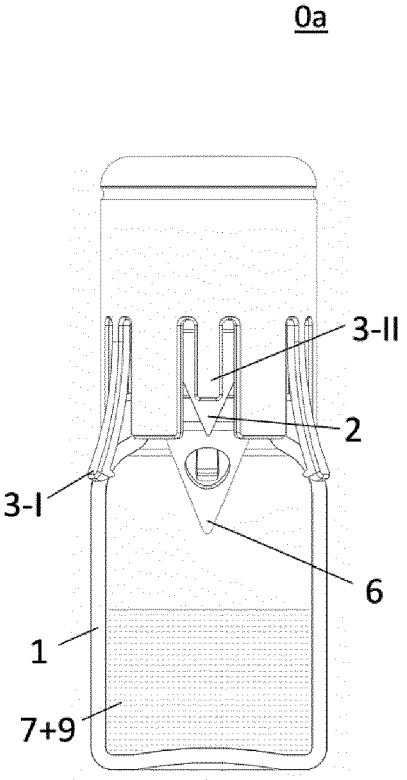


FIG. 4

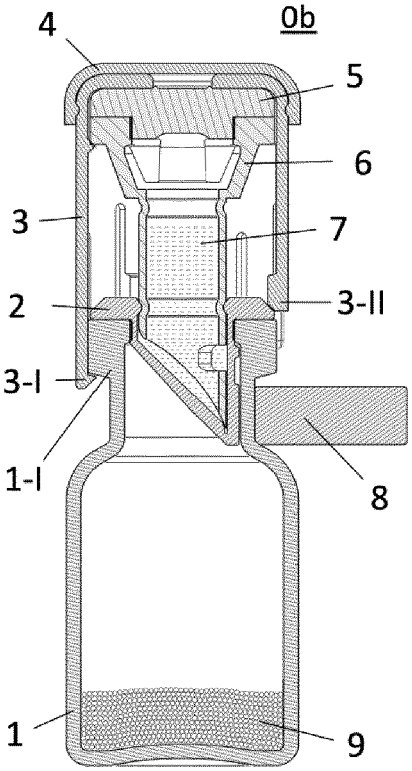


FIG. 5

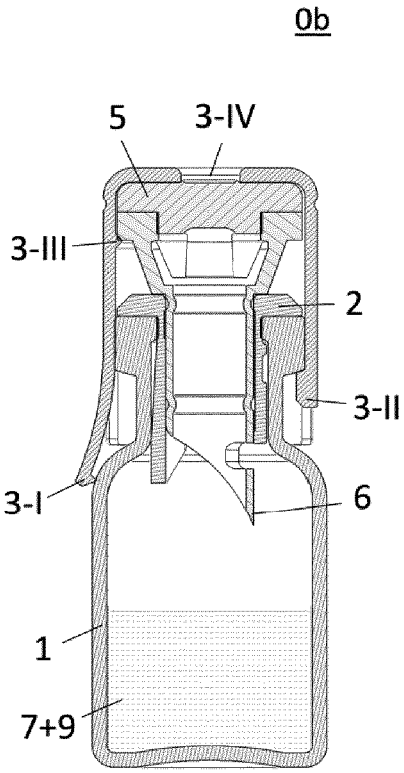


FIG. 6

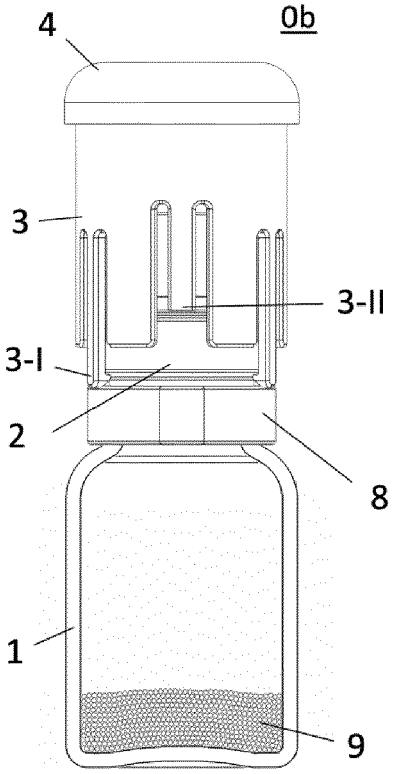


FIG. 7

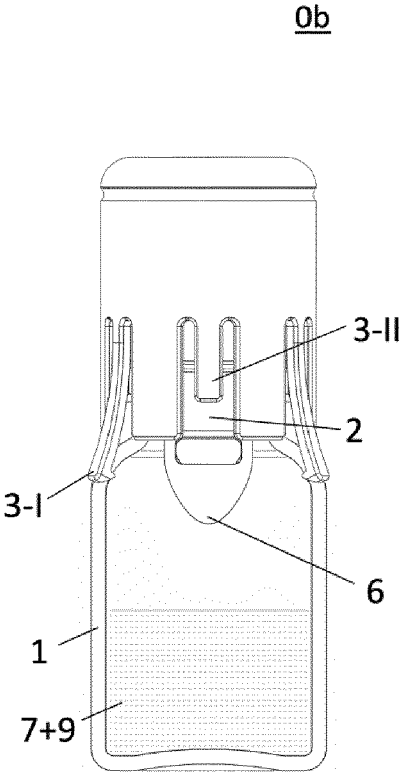


FIG. 8

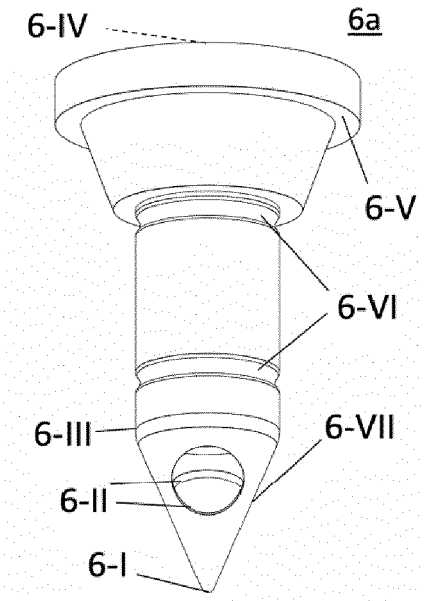


FIG. 9

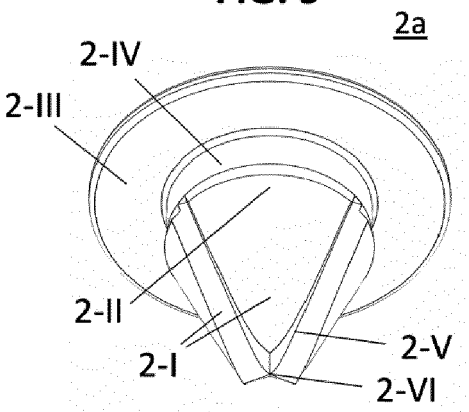


FIG. 10

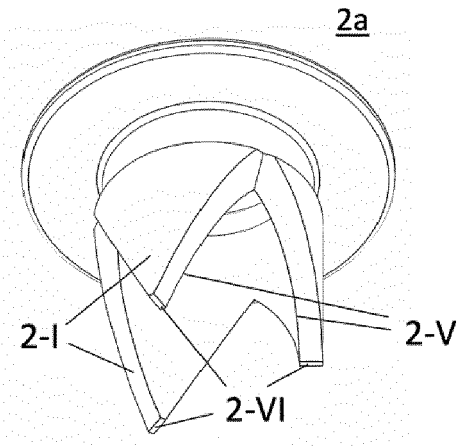


FIG. 11

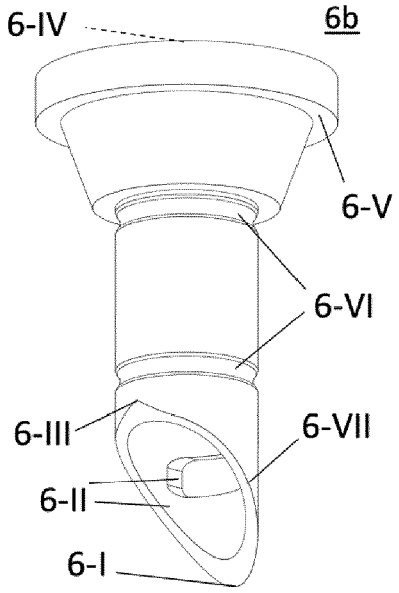


FIG. 12

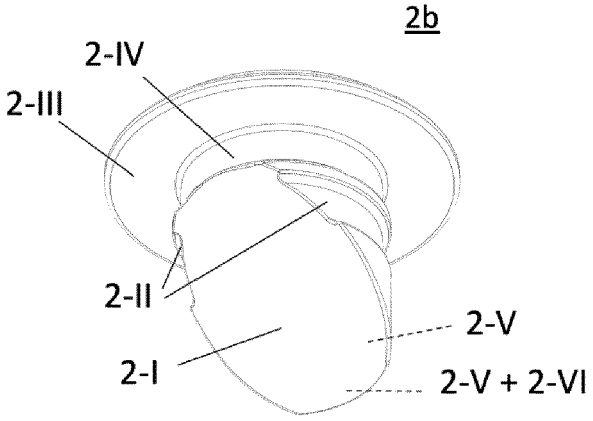


FIG. 13

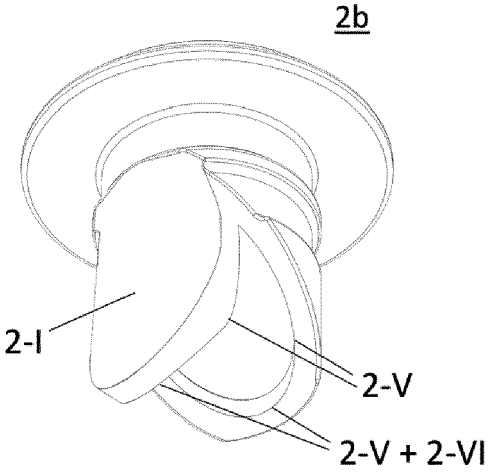


FIG. 14

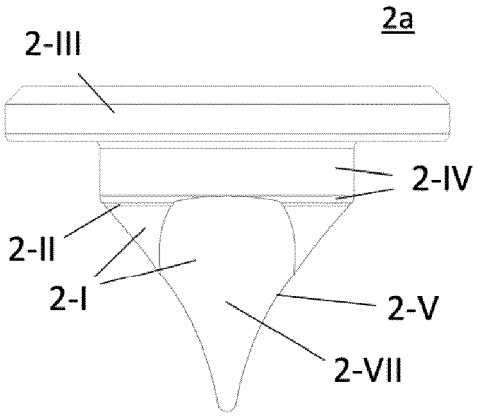


FIG. 15

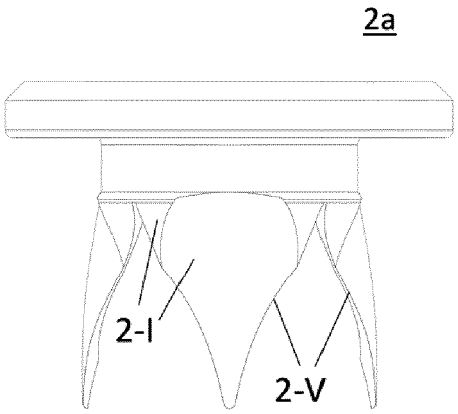


FIG. 16

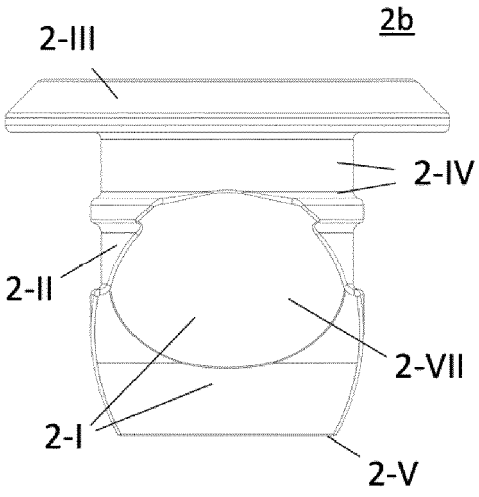


FIG. 17

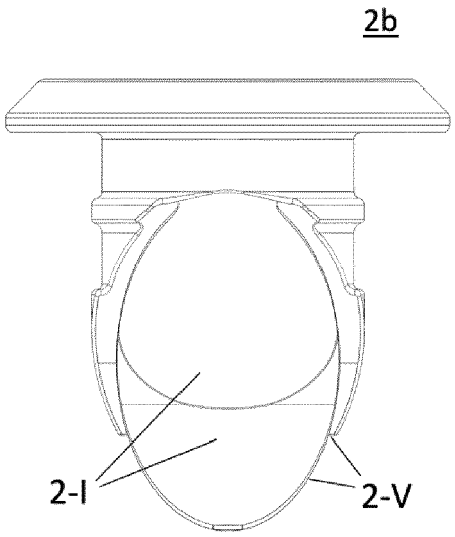


FIG. 18

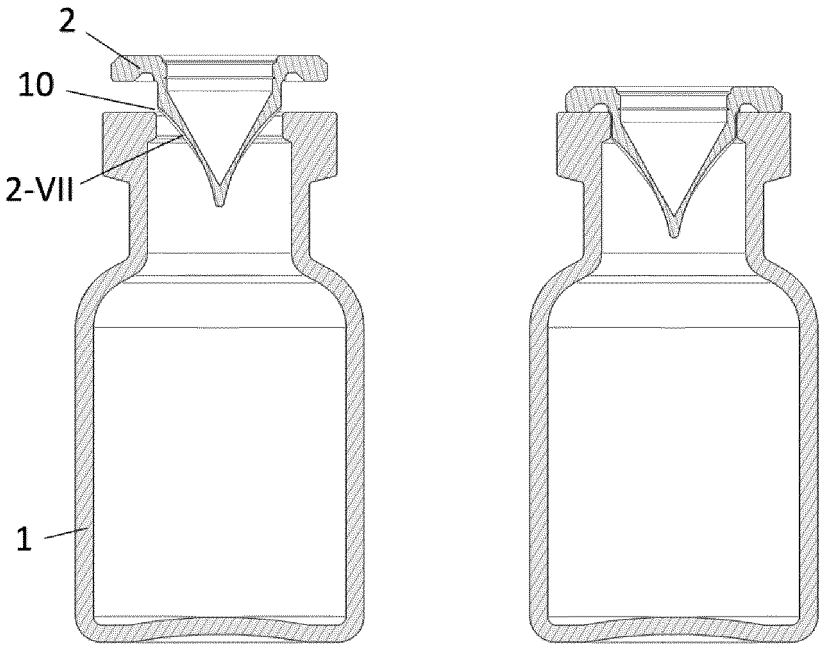


FIG. 19

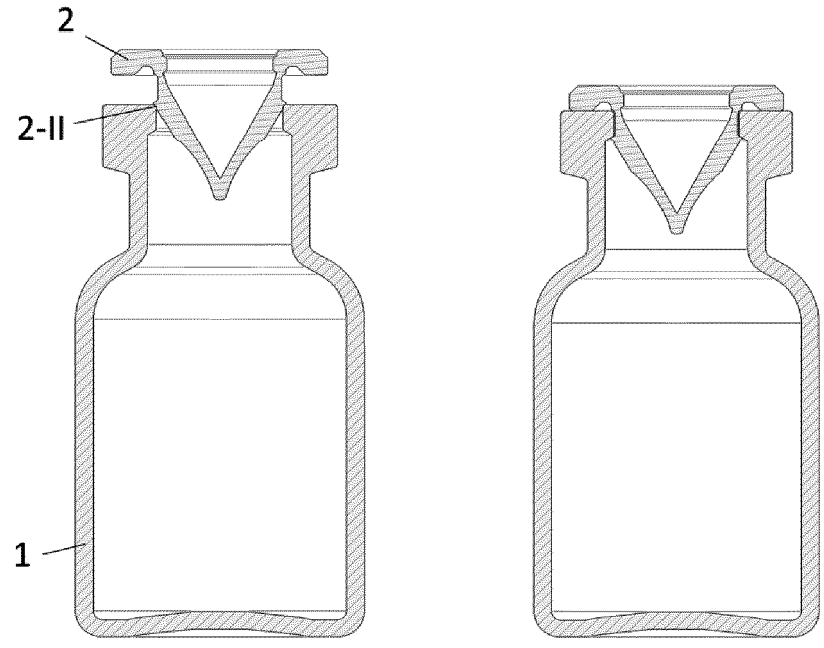


FIG. 20

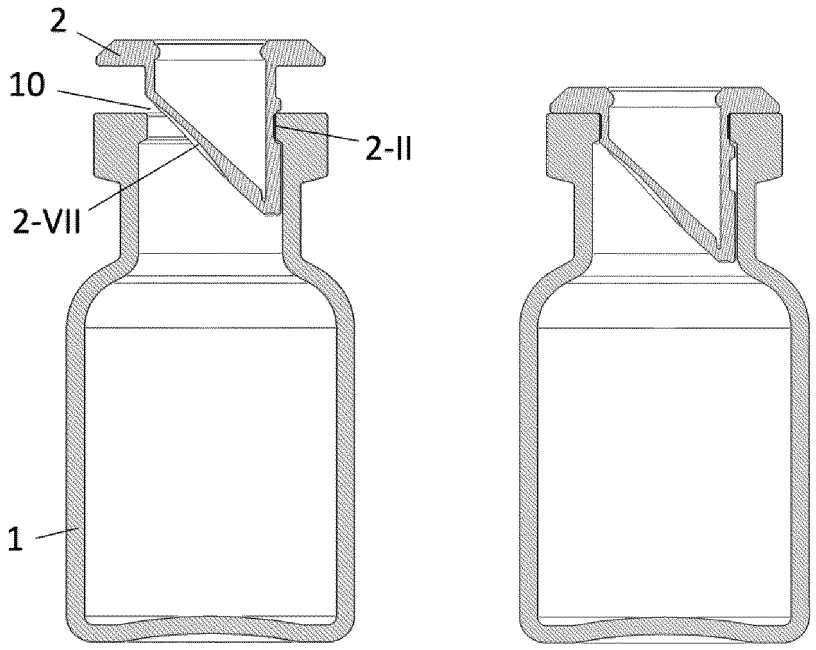


FIG. 21

FIG. 22

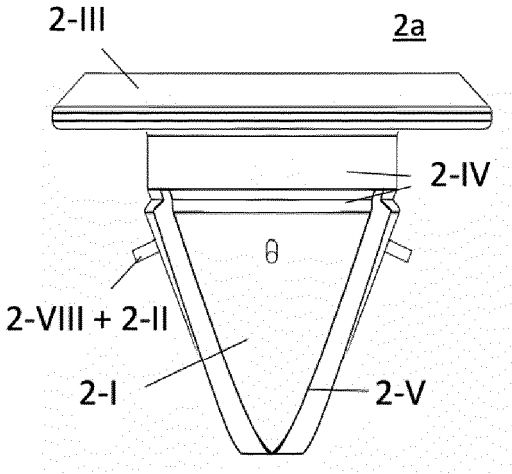


FIG. 23

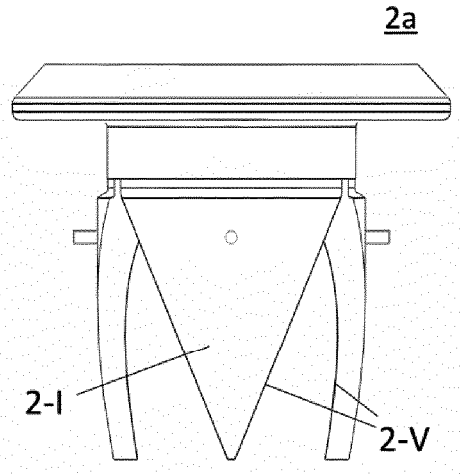


FIG. 24

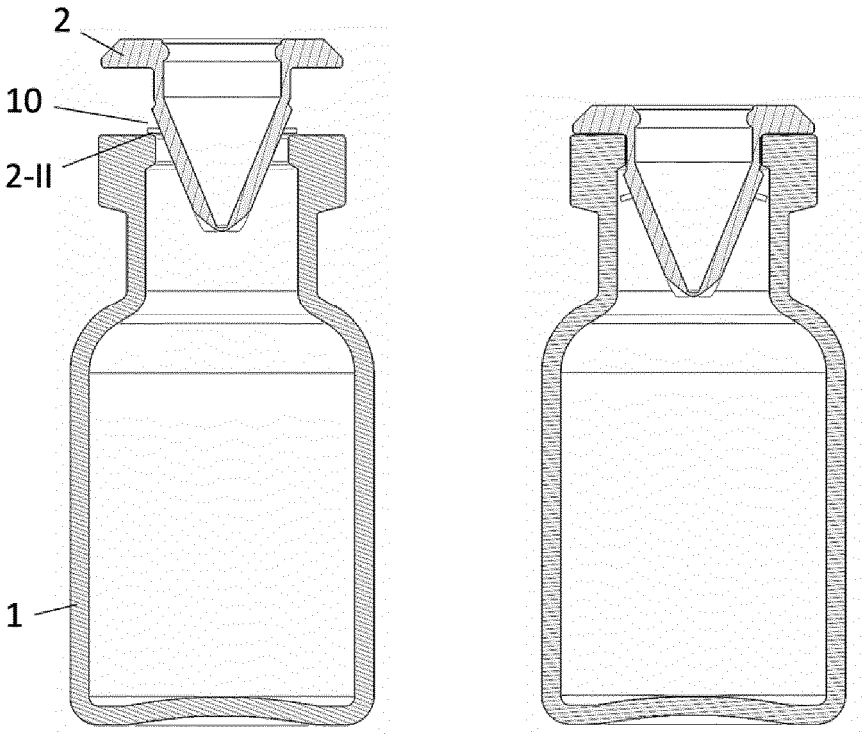


FIG. 25

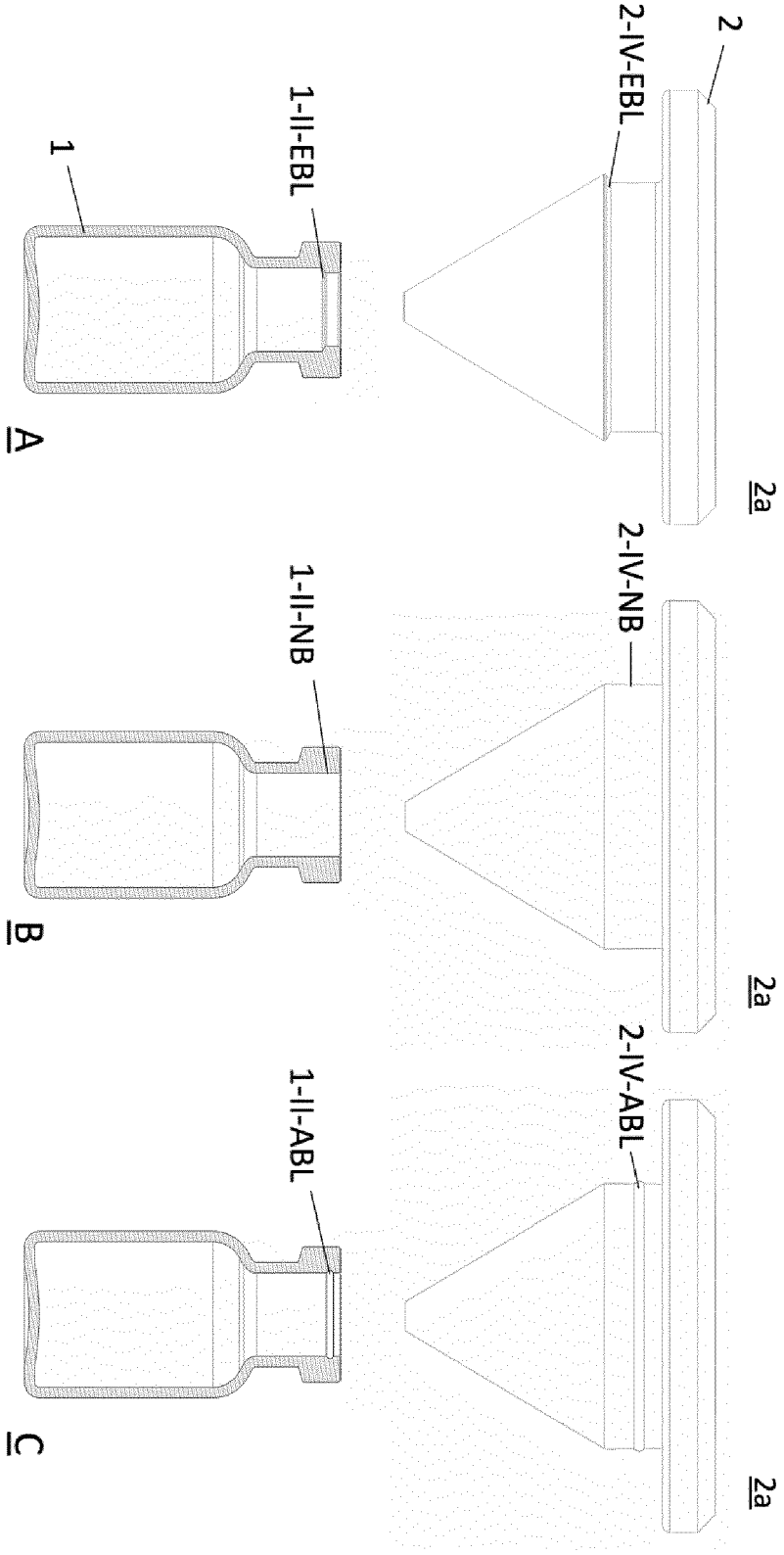


FIG. 26

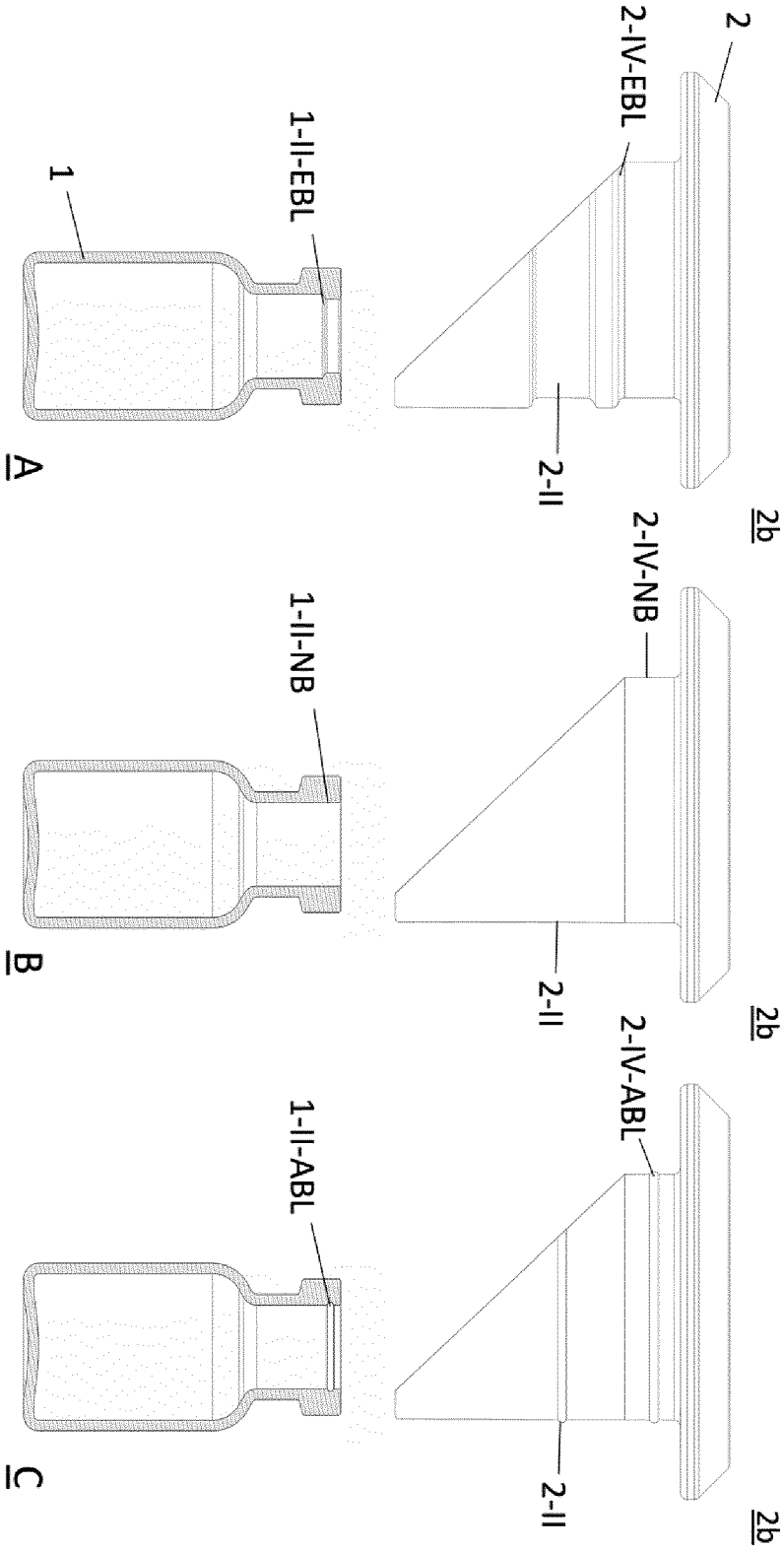

2
2-IV-EBL
1-II-EBL
1
2-II
2b
A
2-IV-NB
1-II-NB
2-II
2b
B
2-IV-ABL
1-II-ABL
2-II
2b
C

FIG. 27

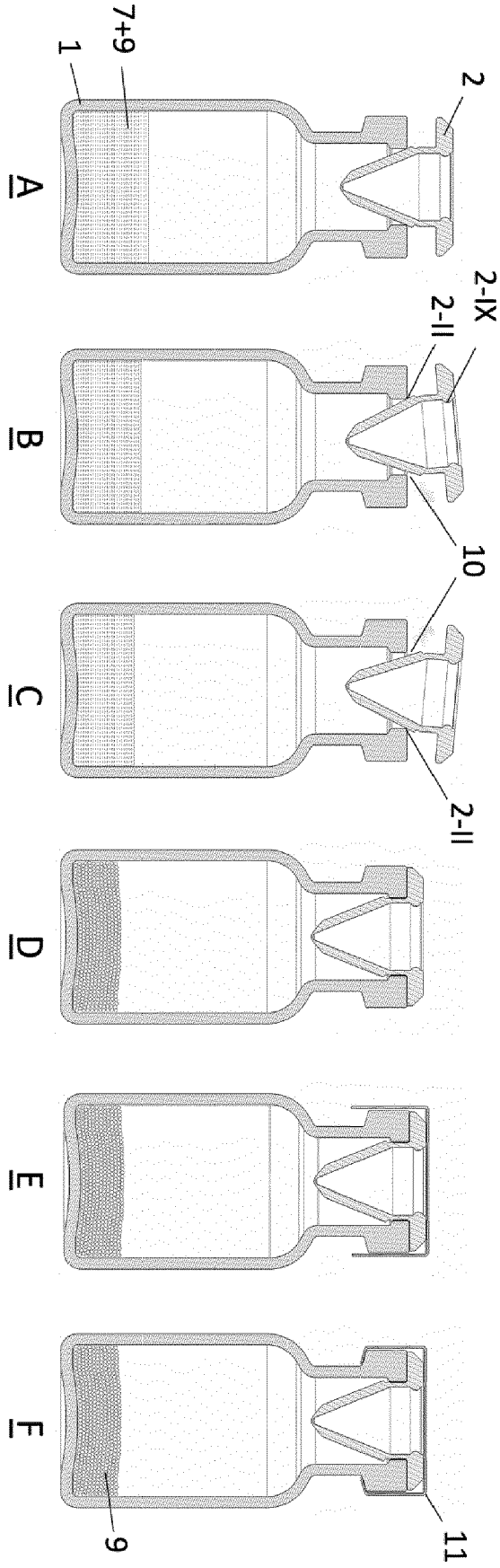


FIG. 28

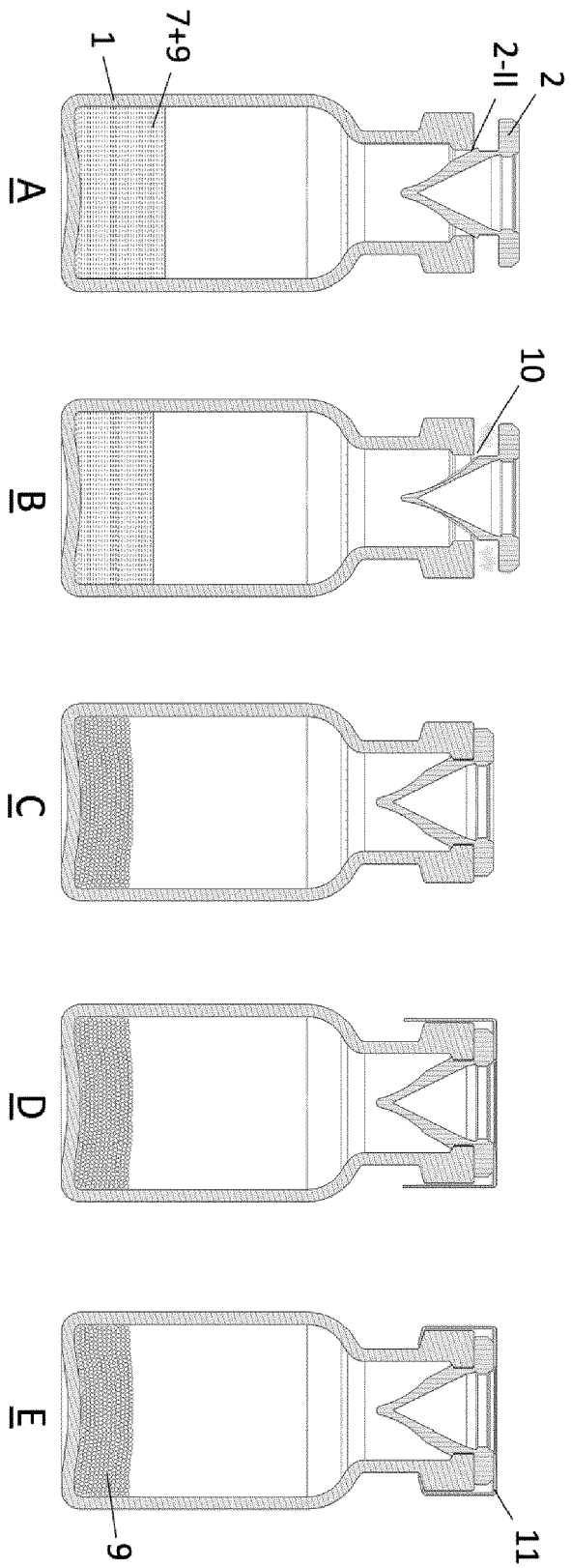


FIG. 29

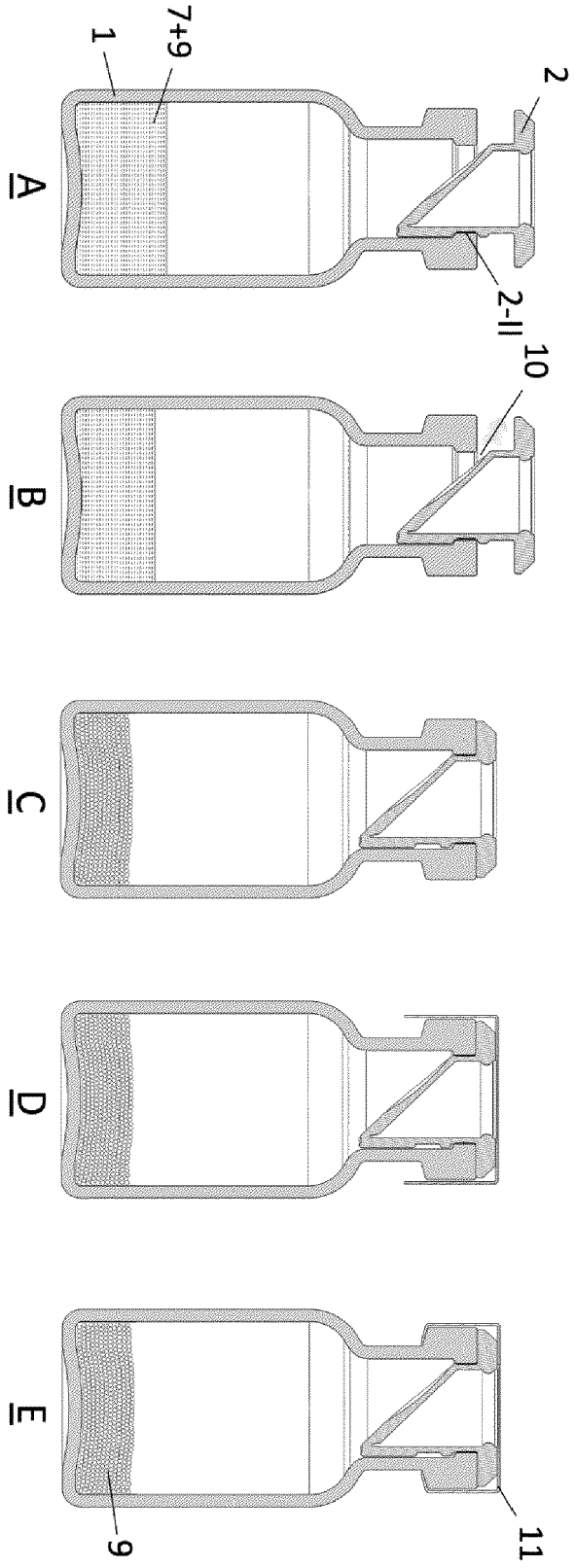


FIG. 30

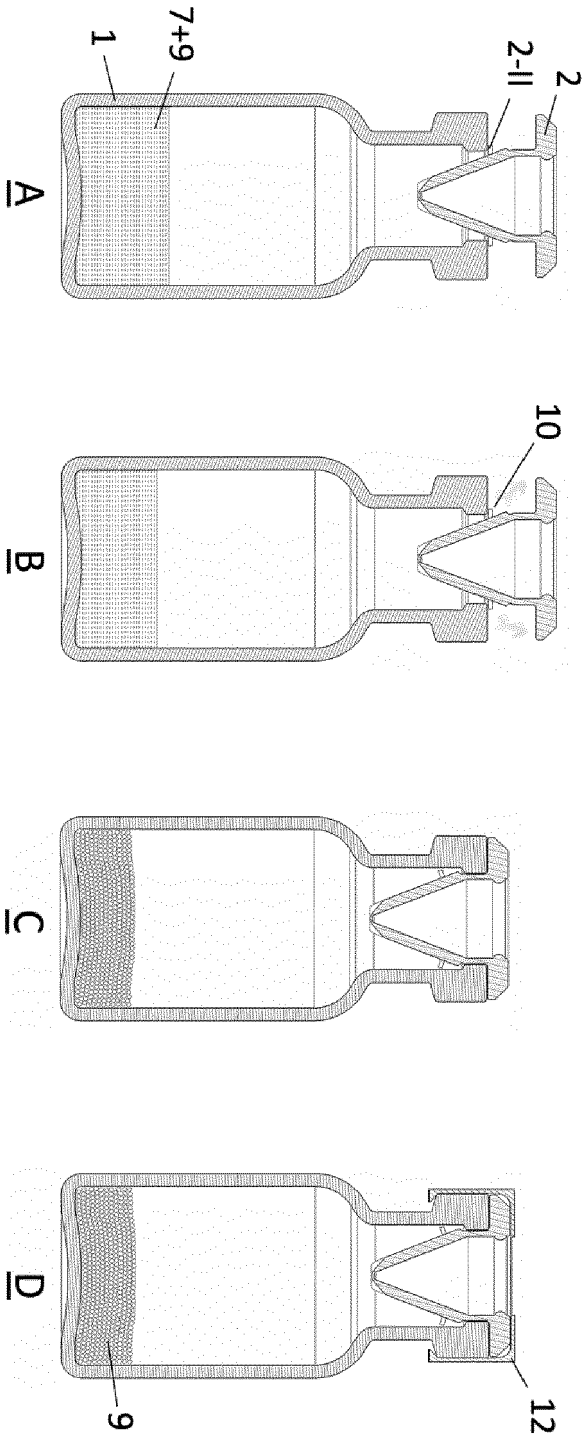


FIG. 31

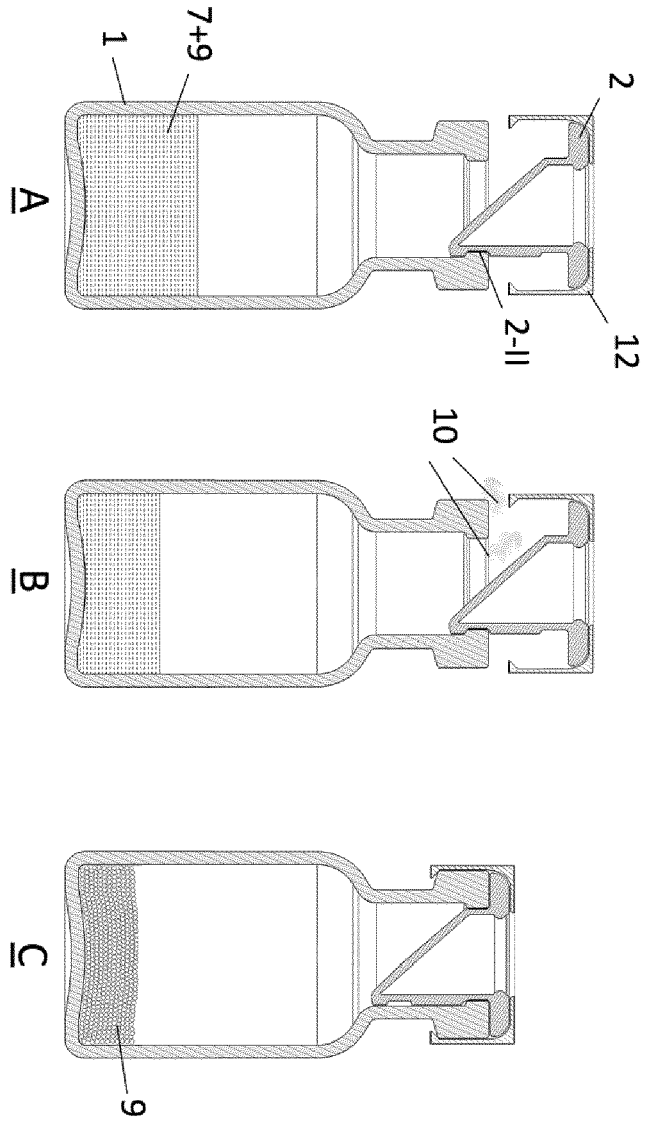


FIG. 32

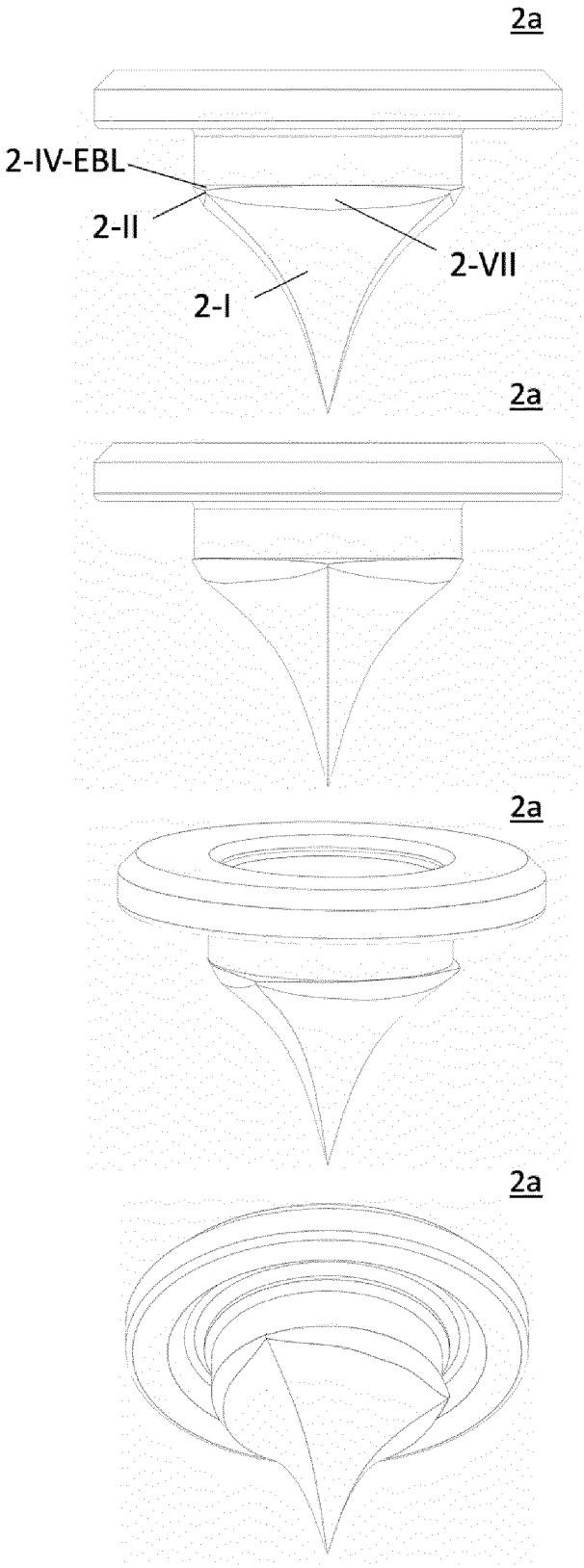


FIG. 33

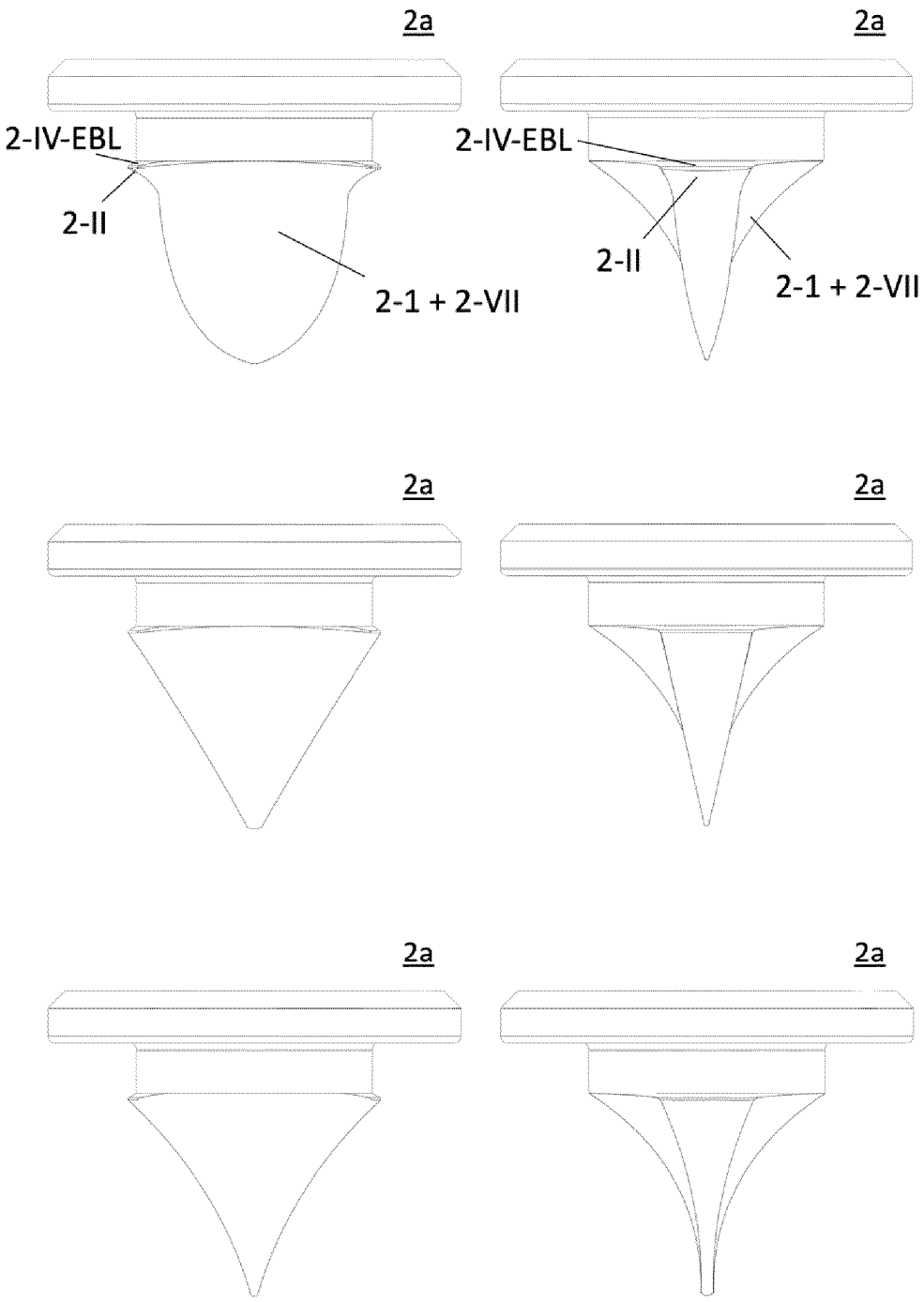


FIG. 34

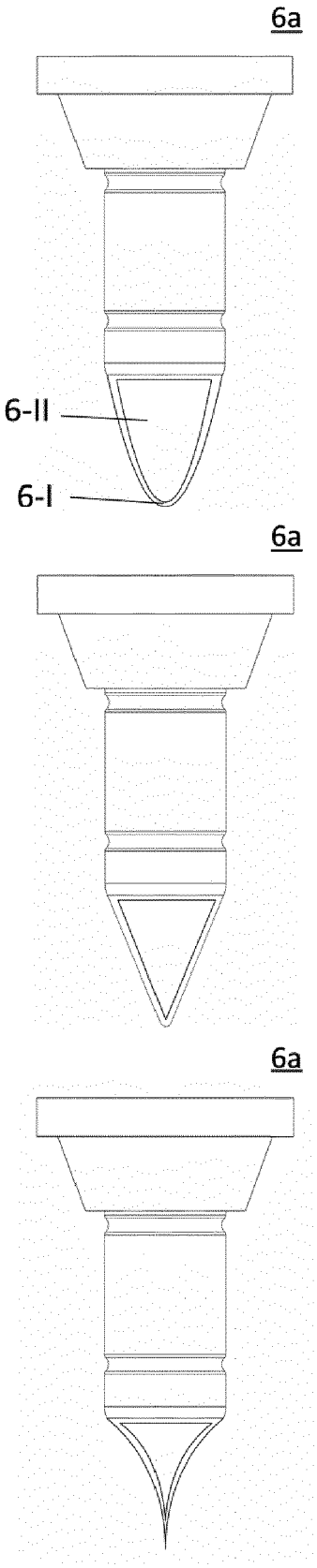


FIG. 35

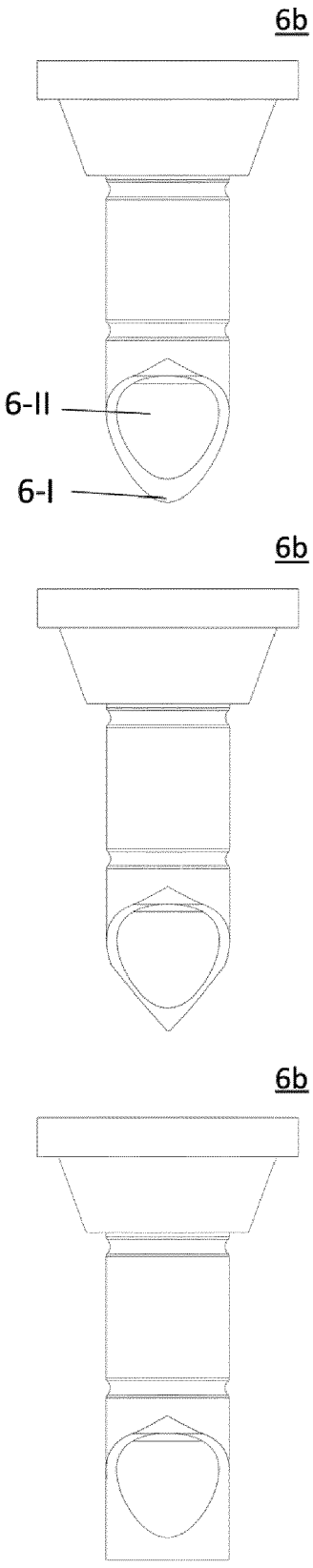


FIG. 36

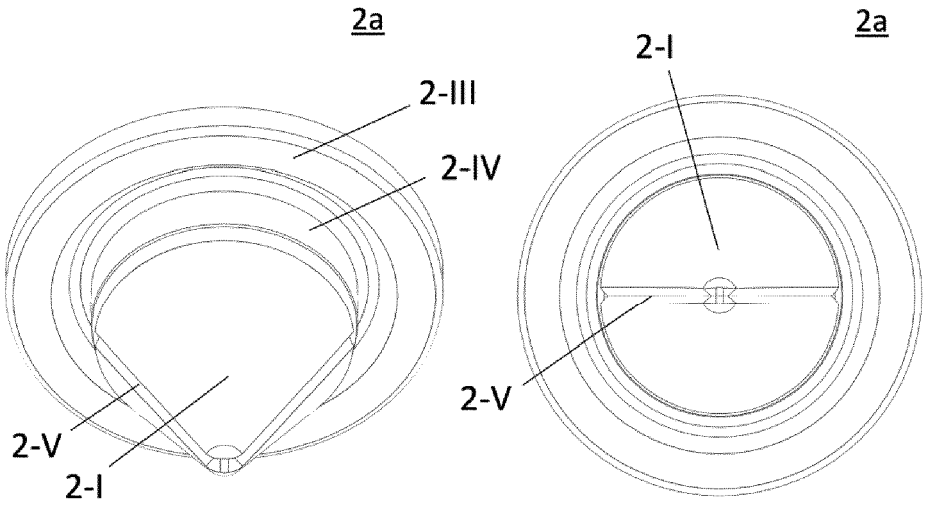


FIG. 37

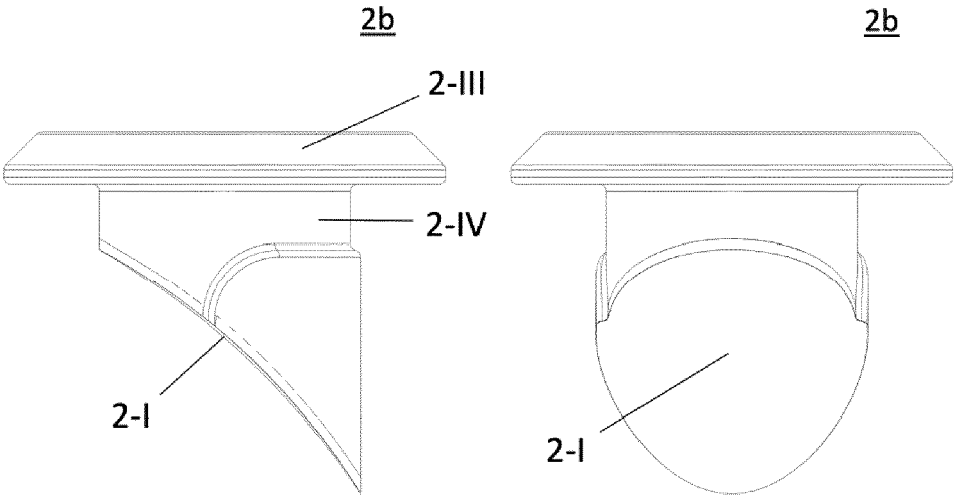


FIG. 38

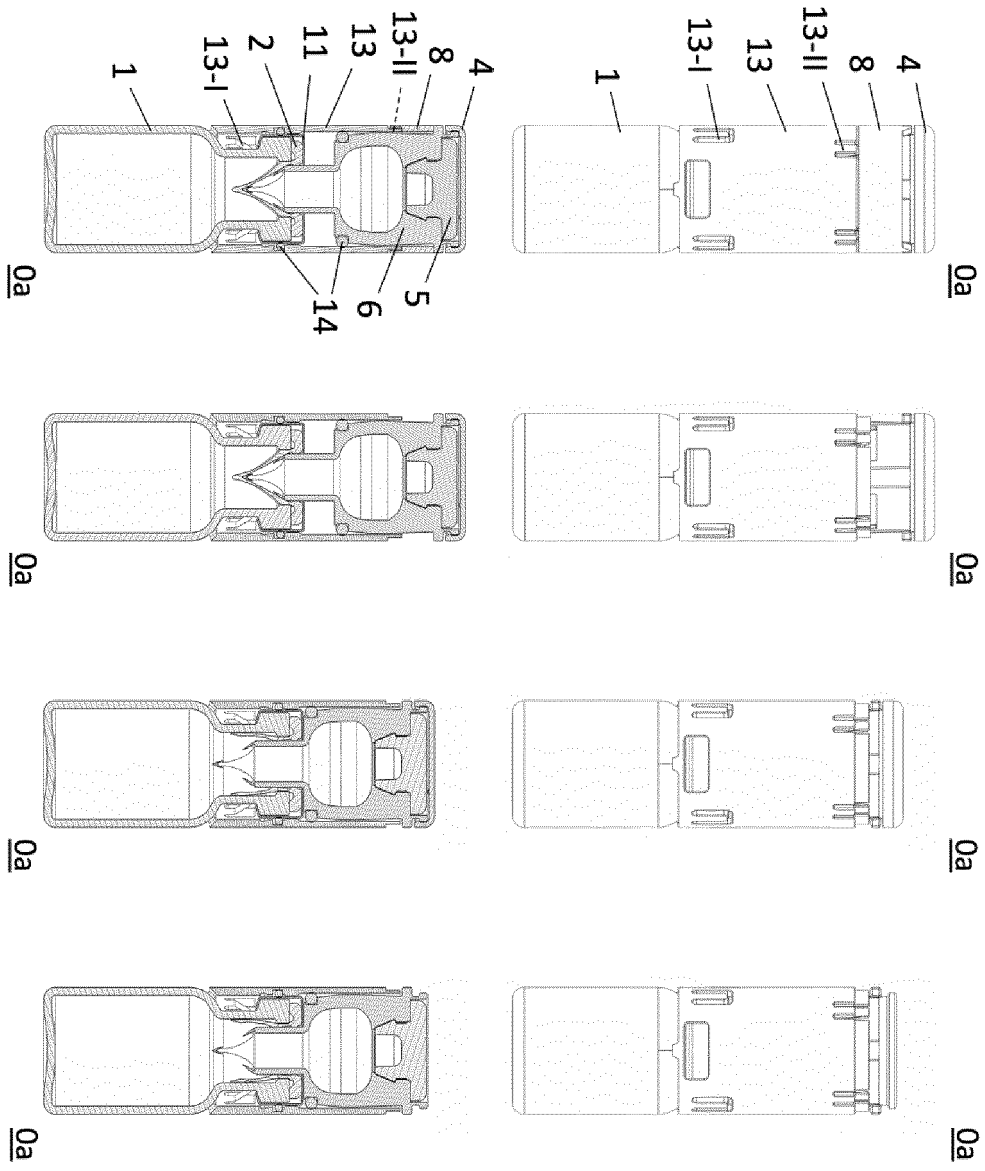


FIG. 39

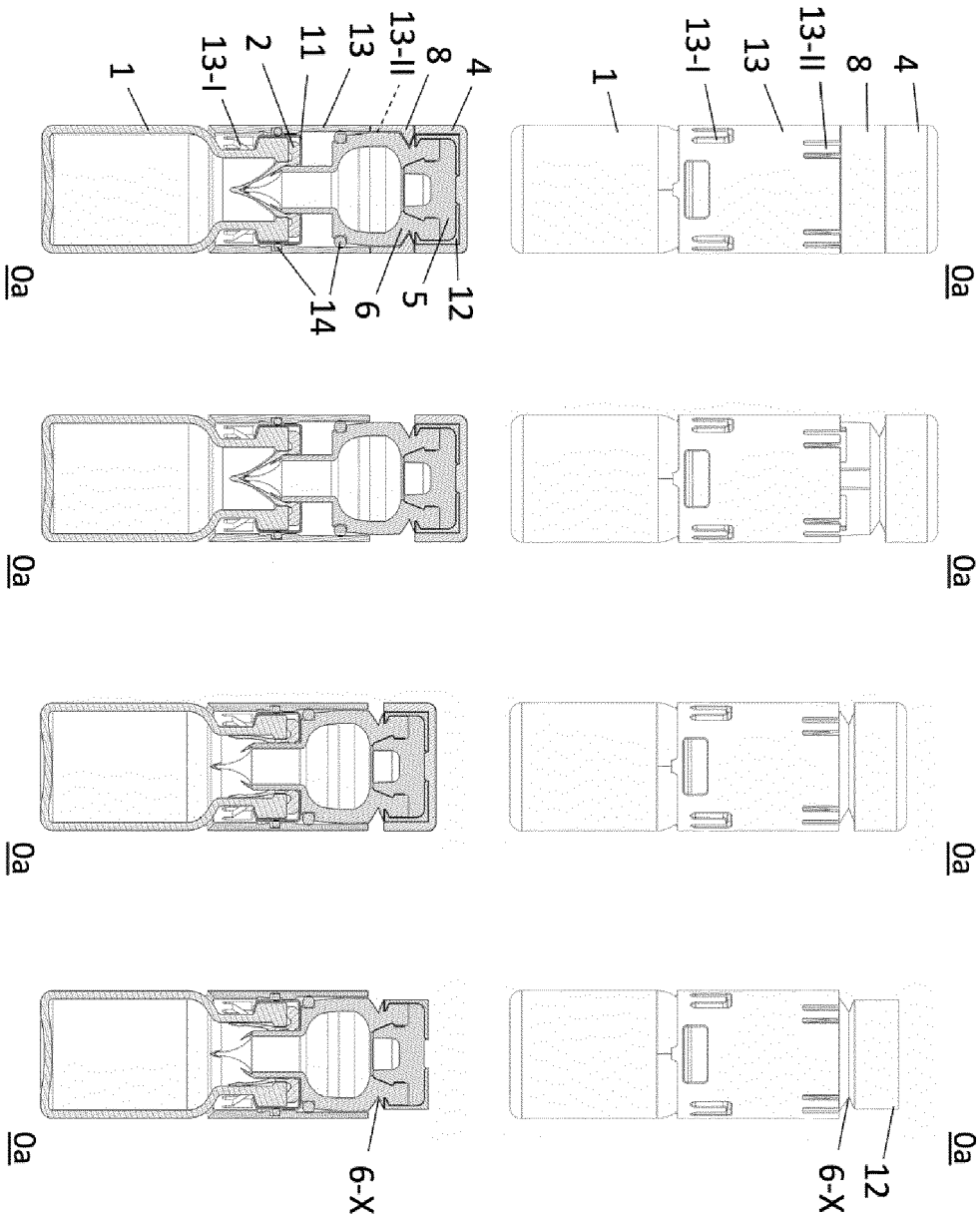
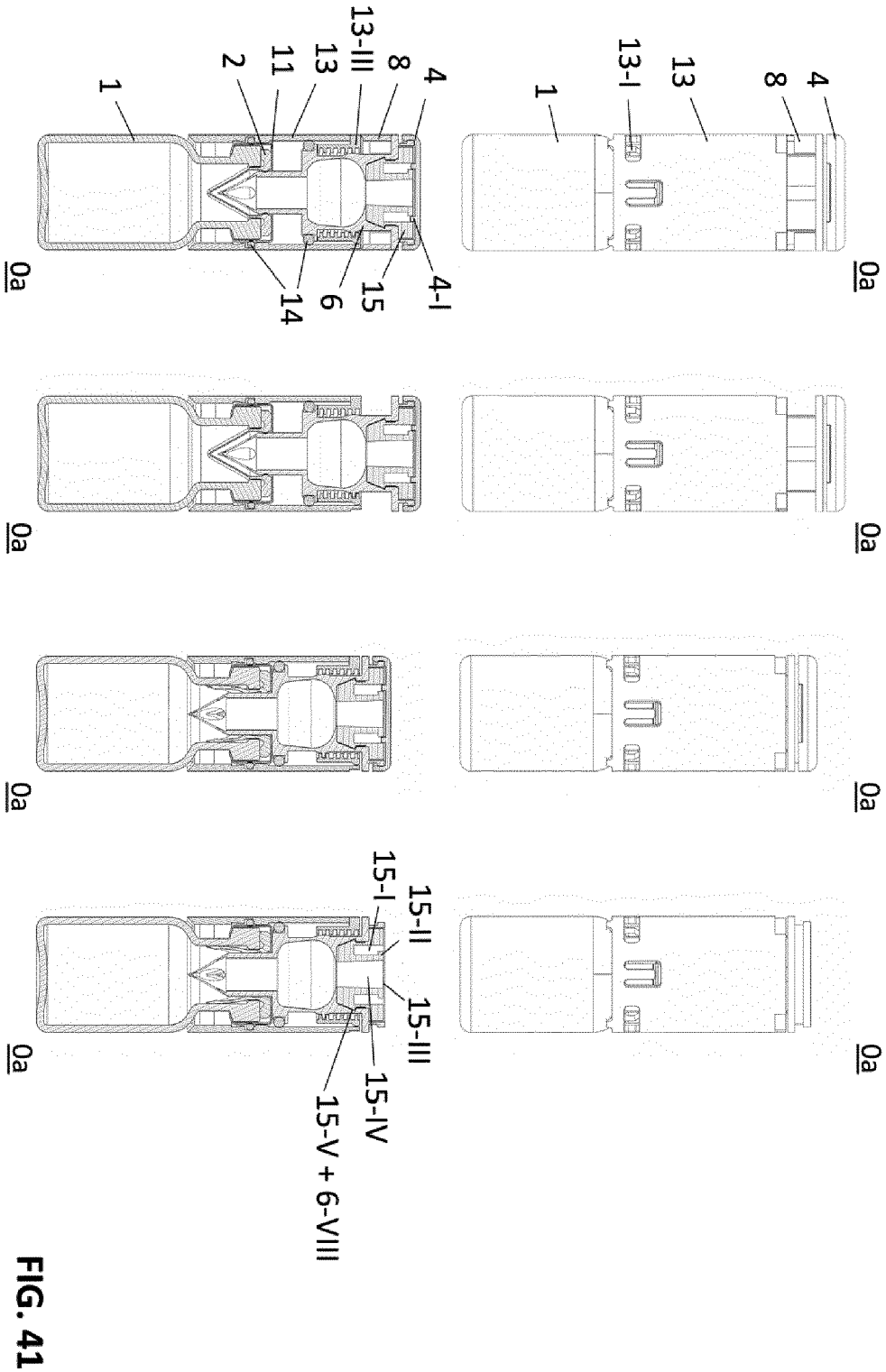


FIG. 40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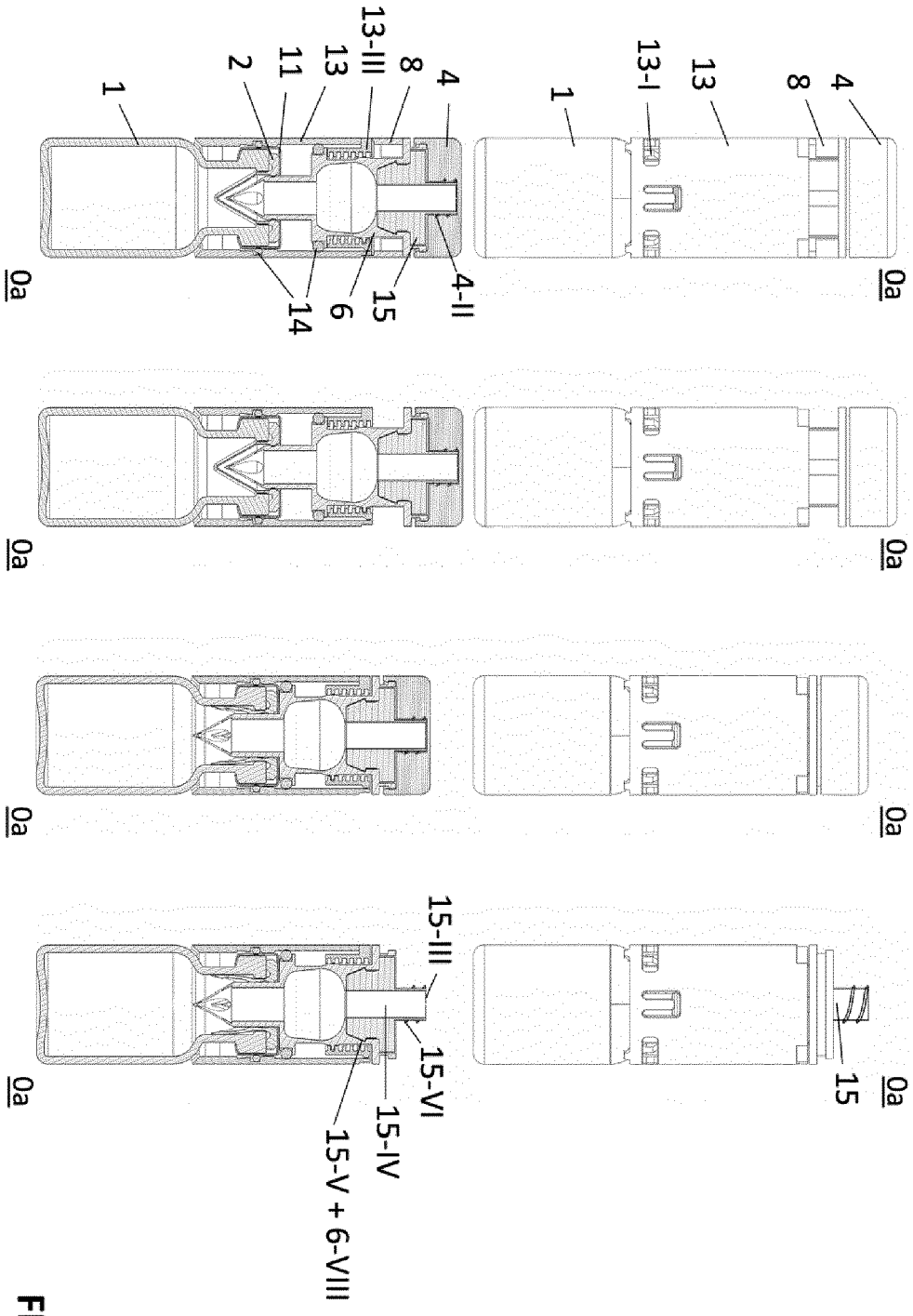
13
13-III
8
4
14
6
15
4-I
0a
1
13-I
13
8
4
0a
0a
0a
0a
15-I
15-II
15-III
15-IV
15-V + 6-VIII

FIG. 41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13-III
8
4
14
6
15
4-II
0a
1
13-I
13
8
4
0a
0a
0a
0a
15-III
15-VI
15-IV
15-V + 6-VIII
15
0a

FIG. 42

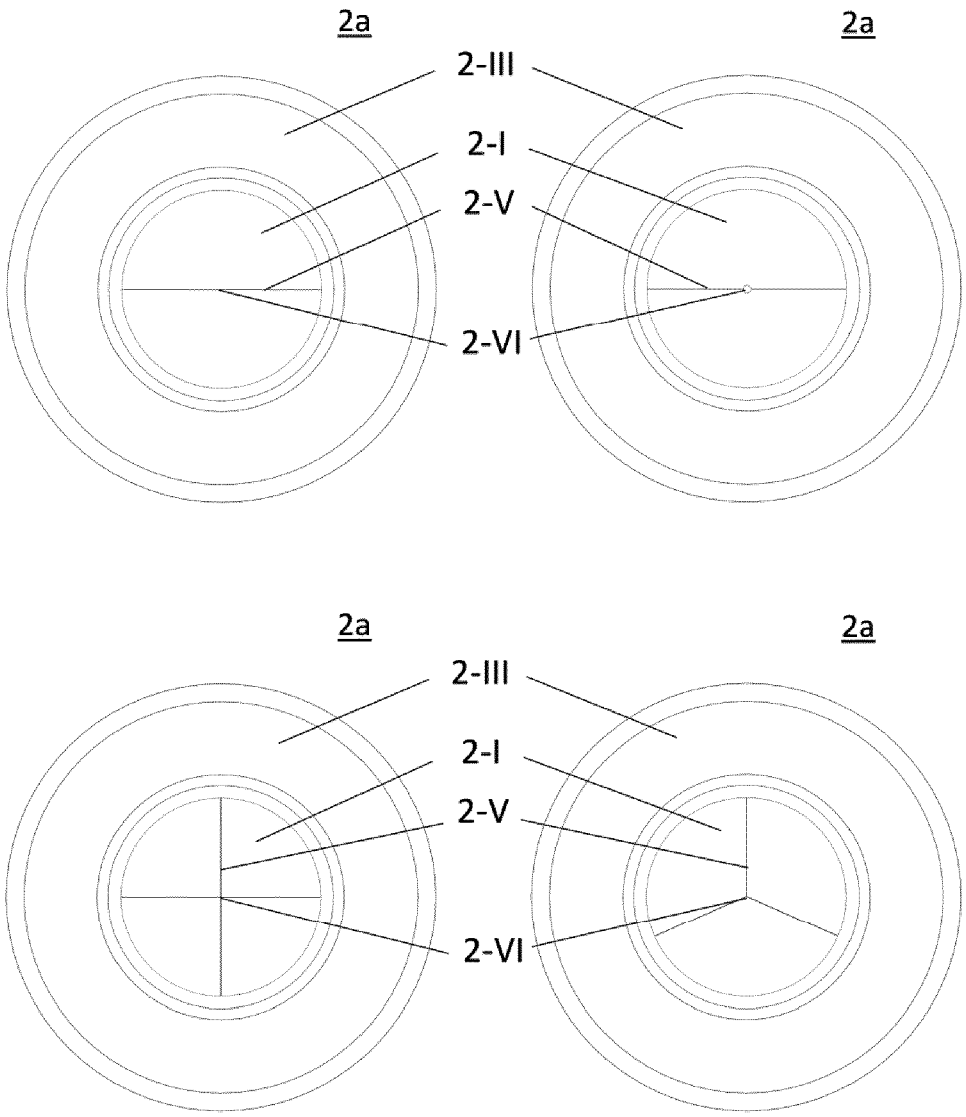


FIG. 43

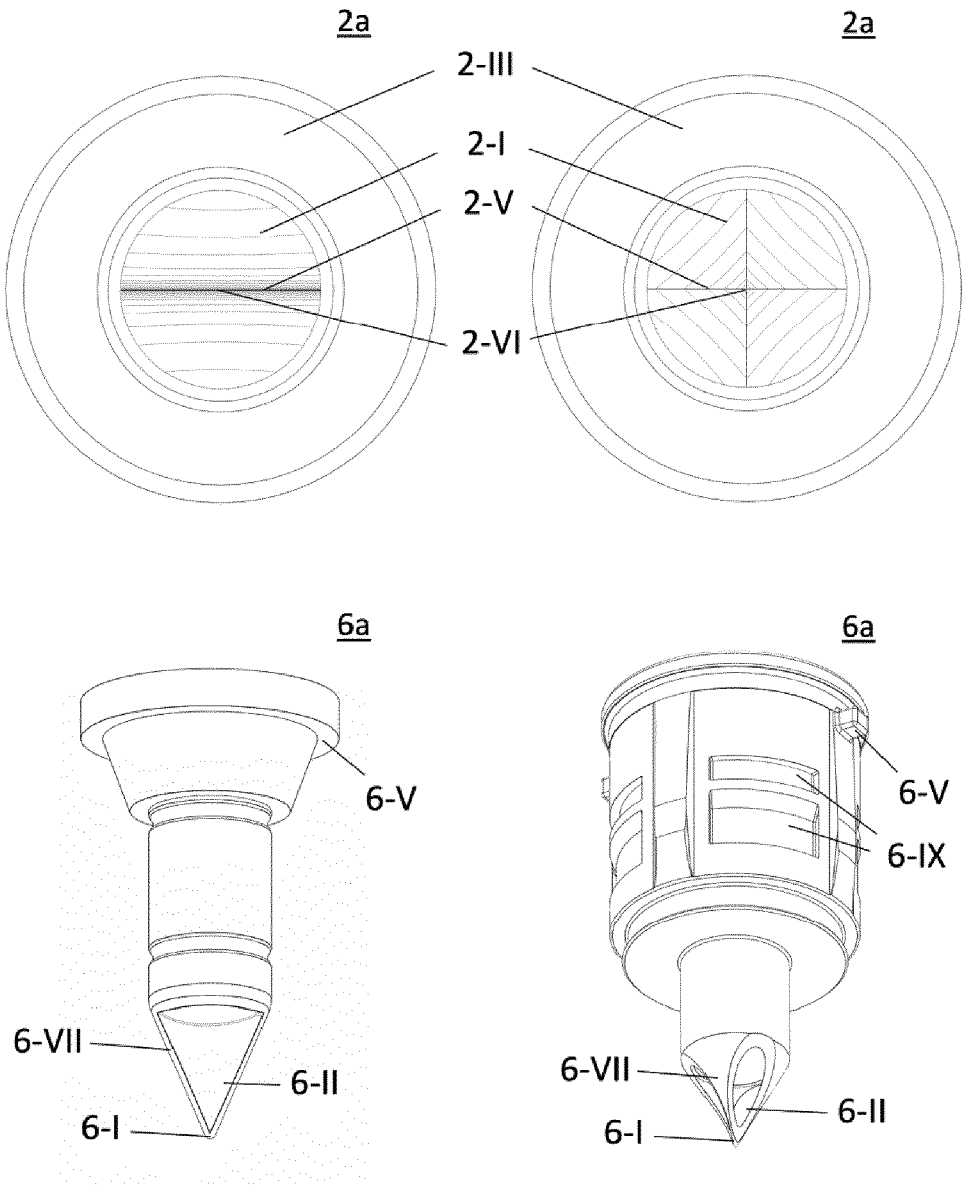
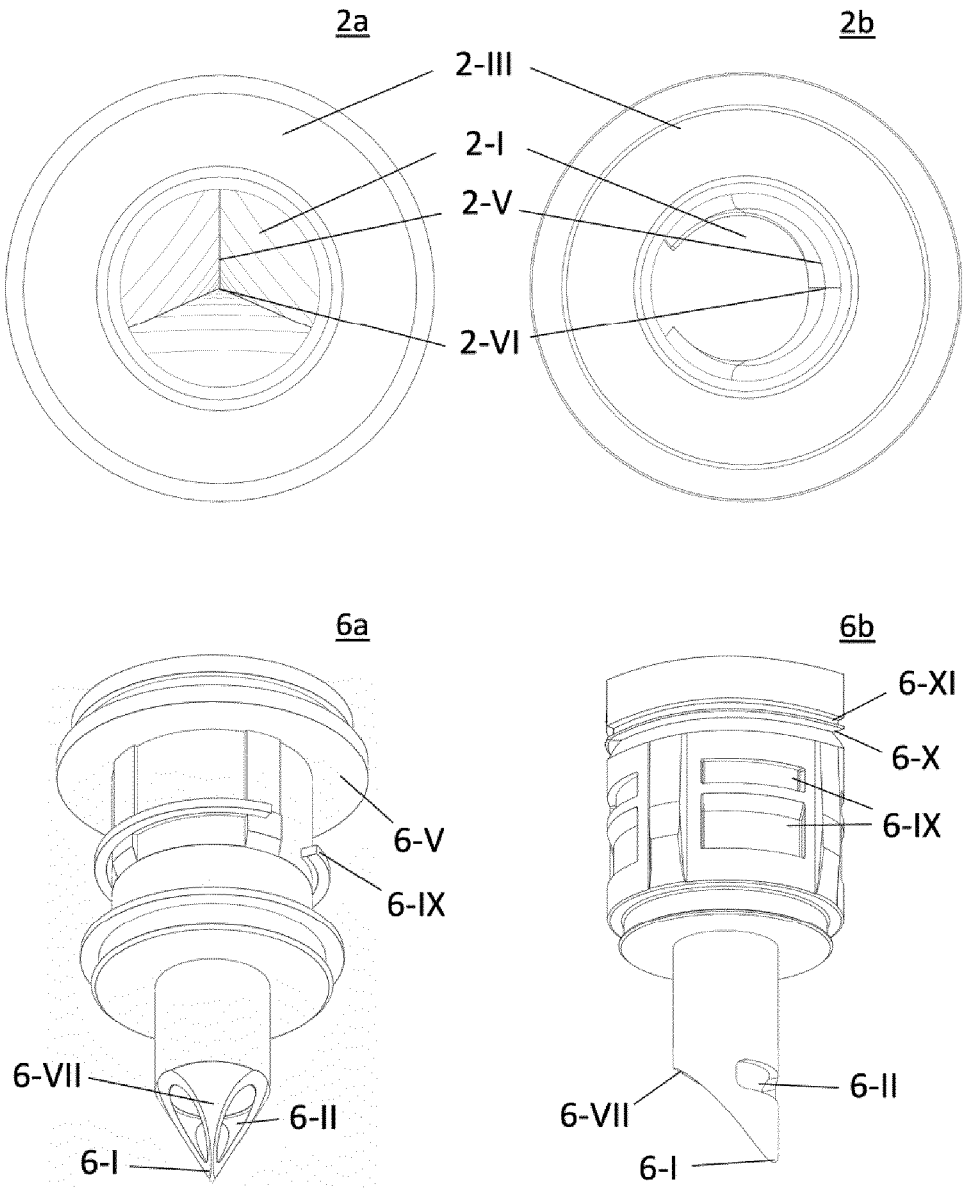


FIG. 44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2b
2-III
2-I
2-V
2-VI
6a
6b
6-V
6-IX
6-VII
6-II
6-I
6-XI
6-X
6-IX
6-VII
6-II
6-I

FIG. 45

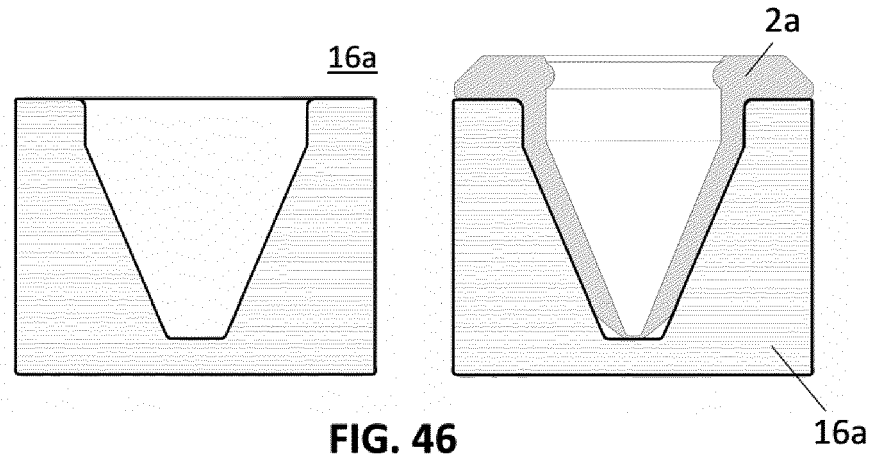

FIG. 46

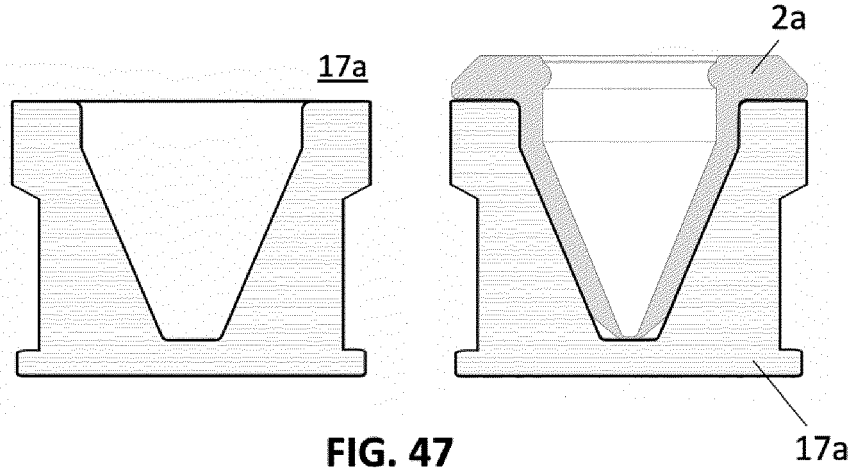

FIG. 47

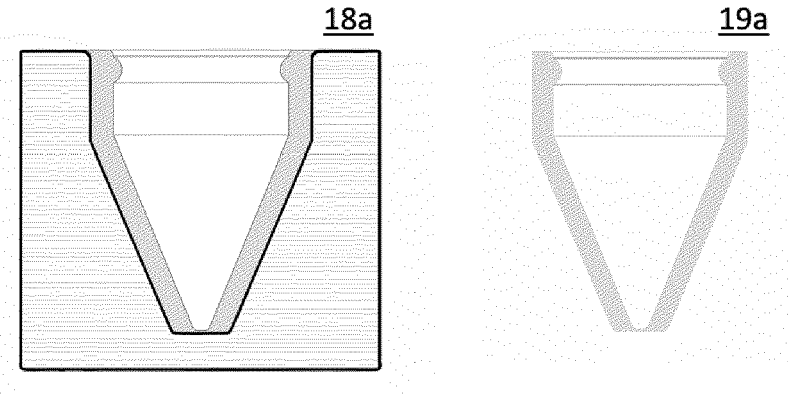

FIG. 48

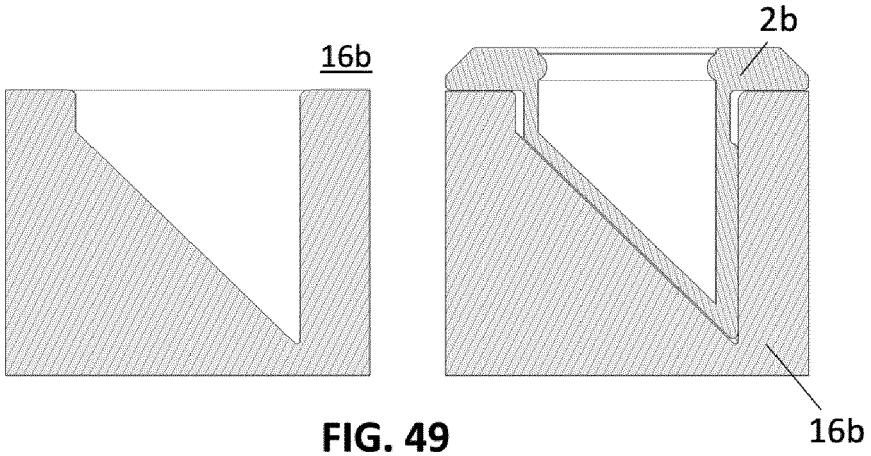

FIG. 49

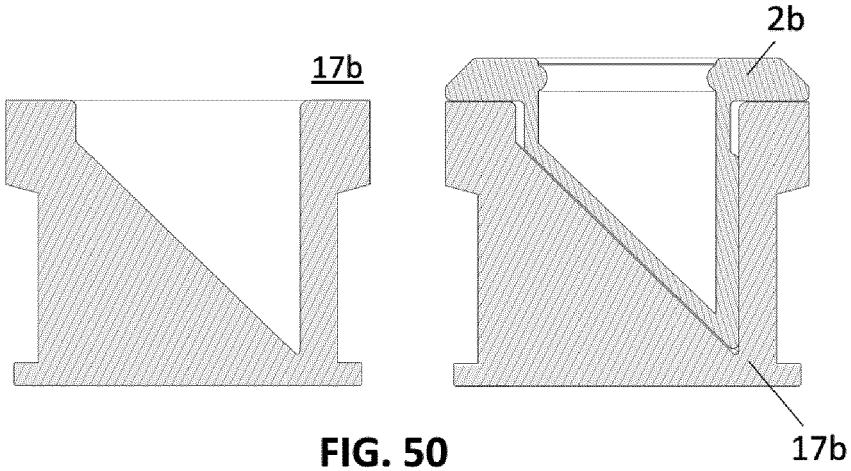

FIG. 50

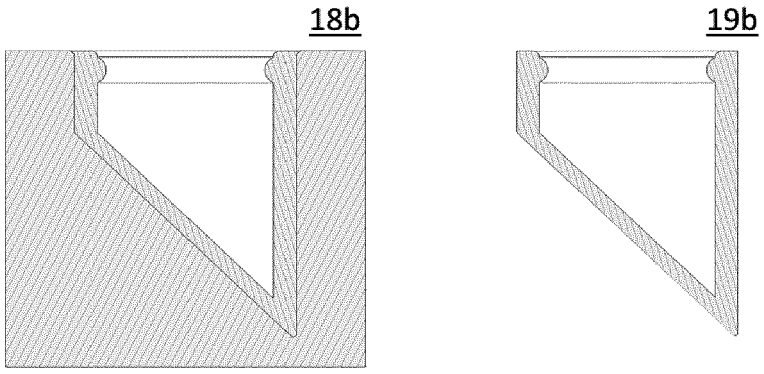

FIG. 51

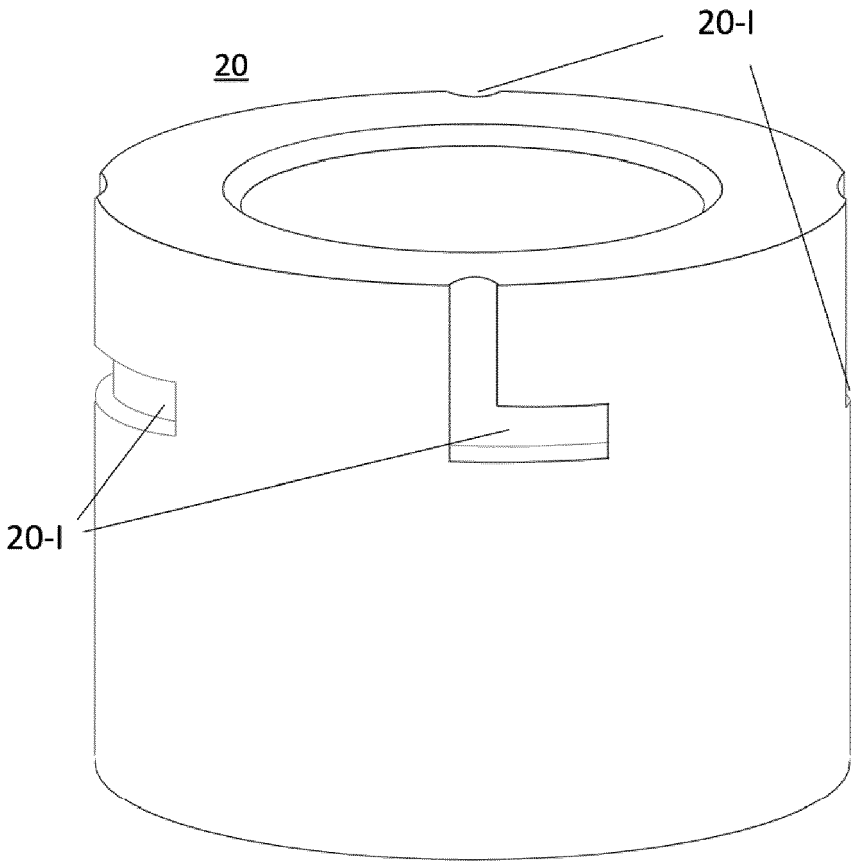

FIG. 52

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EUROPEAN SEARCH REPORT

Application Number
EP 23 19 6580

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X A	US 4 858 760 A (DI STURCO PAOLO [IT]) 22 August 1989 (1989-08-22) * column 1, line 64 - column 3, line 16; figure 1 *	1-6,8-13 7,14-19	INV. A61J1/20 B65D51/28
X A	US 2014/048507 A1 (BRAMBILLA FRANCESCO [IT] ET AL) 20 February 2014 (2014-02-20) * paragraphs [0023], [0024], [0042], [0004] - [0045]; figures 1-5 *	1-6, 13-17 7-12,18, 19	
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The present search report has been drawn up for all claims

Place of search	Date of completion of the search	Examiner
The Hague	9 February 2024	Birlanga Pérez, J

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