

CLAIMS

1. A device for sealing a vessel, in particular a cartridge (7) or a test-tube for accommodating a freeze-dried pharmaceutical product (S), wherein the vessel (1) comprises at its opening end (3) an opening edge (4) and an adjoining longitudinal portion (5) with an evenly formed inner cross section, including
- a front plunger (2) to be positioned inside the vessel (1) at the longitudinal portion (5),
- characterized in that the front plunger (2) is configured to be positioned in the vessel (1) in a sealing state, in which the front plunger (2) is fully inserted in the vessel (1), or in an exchange state, in which the front plunger (2) is inserted partly in the vessel (1) and partly protrudes over the opening edge (4) of the vessel (1), wherein the front plunger (2) comprises
- sealing means that are configured to seal the inside of the vessel (1) against the outside when the front plunger (2) is positioned in the sealing state, and
- one or more communicating grooves (2i) that are configured to place the inside and outside of the vessel (1) in communication with each other when the front plunger (2) is positioned in the exchange state.
2. The device according to claim 1, wherein the sealing means include at least one sealing rib – first sealing rib (2b) – whose outer form is adapted to the form of the inner cross section of the longitudinal portion (5).

3. The device according to claim 2, wherein the inner cross section of the longitudinal portion (5) has a circular form, and wherein the first sealing rib (2b) has an outer diameter that is larger than the inner diameter of the longitudinal portion (5), and that is configured to elastically contract when the front plunger (2) is positioned inside the vessel (1) so as to
5 form a tight seal with the inner surface of the longitudinal portion (5).

4. The device according to claim 2 or 3, wherein the first sealing rib (2b) is dimensioned in such a way that the front plunger (2), when an underpressure of predefined strength is applied to the outer environment of the vessel (1), is caused to move inside the
10 vessel (1) toward its opening end (3).

5. The device according to any of claims 2 to 4, wherein an inclined surface (2h) extending in a circumferential direction of the first sealing rib (2b) is formed at a rear end portion of the first sealing rib (2b), wherein the diameter of the surface gradually expands
15 as it moves from the rear end side toward the front end side.

6. The device according to any of claims 2 to 5, wherein the communicating grooves (2i) are formed in an outer circumferential surface of the front plunger (2) extending from the inner end side (2d) of the front plunger (2) up to the first sealing rib (2b), in particular
20 up to the center of the first sealing rib (2b) in the direction of a center axis (O) of the front plunger (2).

7. The device according to claim 2 or 6, wherein the sealing means include a positioning rib (2a) whose outer diameter is substantially the same as the inner diameter of the longitudinal portion (5) of the vessel (1), and that is positioned further to the inner end side (2d) of the front plunger (2) than the first sealing rib (2b), so as to remain inside the vessel (1) when the front plunger (2) is positioned in the exchange state.

8. The device according to any of claims 1 to 7, wherein the communicating grooves (2i) are formed at intervals in the circumferential direction of the front plunger (2).

9. The device according to any of claims 1 to 8, for use in a dual chamber combined container-syringe, comprising

a cartridge (7), in which the front plunger (2), a middle plunger (10), and an end plunger (11) are positioned in this sequence from the opening end,

a diluent (L), which is sealed inside the cartridge (7) between the end plunger (11) and the middle plunger (10), and

a freeze-dried pharmaceutical product (S), which is sealed inside the cartridge (7) between the middle plunger (10) and the front plunger (2).

10. A method of manufacturing a sealed vessel, in particular a cartridge (7) or a test-tube, containing a freeze-dried pharmaceutical product (S), wherein the vessel (1) comprises at its opening end (3) an opening edge (4) and an adjoining longitudinal portion (5) with an evenly formed inner cross section, at least comprising:

a drug solution (M) provisioning step in which a drug solution (M) to be freeze-dried is inserted into the vessel (1);

a drug solution (M) sealing step in which the drug solution (M) is sealed together with internal air (A) by positioning a front plunger (2) inside the vessel (1) at the longitudinal portion (5), and

a freeze-drying step in which the drug solution (M) is freeze-dried so as to form the freeze-dried pharmaceutical product (S),

characterized in that the freeze-drying step includes:

surrounding atmosphere cooling processing in which a surrounding atmosphere which surrounds the vessel (1) is cooled, such that the drug solution (M) inside the vessel (1) gets frozen;

pressure reduction processing in which, after the surrounding atmosphere has been cooled, the pressure of the surrounding atmosphere is reduced to below the pressure of the internal air (A), thereby causing the front plunger (2) to move toward the opening end (3) of the vessel (1) and to rest in an exchange state, in which the front plunger (2) is inserted partly in the vessel (1) and partly protrudes over the opening edge (4) of the vessel (1), such that one or more communicating grooves (2i) provided at the front plunger (2) define a duct between the inside and the outside of the vessel (1) through which solvent content can be removed by sublimation for enabling freeze-drying of the drug solution (M).

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11. The method according to claim 10, further comprising:

a diluent (L) provisioning step and a diluent (L) sealing step, both carried out

before the drug solution (M) provisioning step, in which a diluent (L) is inserted into the vessel (1) and sealed inside the vessel (1) between the bottom of the vessel (1) or an end plunger (11) that has been inserted into the vessel (1) and a middle plunger (10).

- 5 12. The method according to claim 11, wherein in the diluent (L) sealing step:
the diluent (L) is filled on top of the end plunger (11) inside the vessel (1); and
the diluent (L) is sealed by inserting the middle plunger (10) into the vessel (1) so
that air does not become contained between the end plunger (11) and the middle plunger
(10).

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13. The method according to claim 11 or 12, further comprising:
after having terminated the diluent (L) sealing step, sterilizing the diluent (L) by
means of autoclaving.

- 15 14. The method according to any of claims 11 to 13, wherein the freeze-drying step
further includes:
after having terminated the pressure reduction processing, substitution processing in
which, by substituting the surrounding atmosphere that surrounds the vessel (1) with an
inert gas, such as a nitrogen gas, the inside of the vessel (1) is filled via the exposed
20 communicating grooves (2i) with the inert gas.

15. The method according to any of claims 11 to 14, wherein the freeze-drying step

further includes:

sealing processing in which the front plunger (2) is pushed into a sealing state, in which the front plunger (2) is fully inserted in the vessel (1), wherein the sealing processing may further include:

- 5 causing the front plunger (2) to move toward the rear end side of the vessel (1) by applying to the outside of the vessel (1) a pressure higher than the pressure of the inert gas contained within the vessel (1).

16. A method of manufacturing a dual chamber combined container-syringe (6) in which, in a cartridge (7) in which a front stopper (2), a middle stopper (10), and an end stopper (11) have been inserted in this sequence from the distal end side, a diluents (L) is sealed between the end stopper (11) and the middle stopper (10), and a freeze-dried pharmaceutical product (S) is sealed between the middle stopper (10) and the front stopper (2), comprising:

- 15 a diluent sealing step in which the diluents (L) is sealed inside the cartridge (7) by the end stopper (11) and the middle stopper (10);

an injection drug solution sealing step in which an injection drug solution (M) before freeze-drying is sealed together with internal air (A) inside the cartridge (7) by the middle stopper (10) and the front stopper (2); and

- 20 a freeze-drying step in which the injection drug solution (M) is freeze-dried so as to form the freeze-dried pharmaceutical product (S), wherein

the freeze-drying step includes:

surrounding atmosphere cooling processing in which a surrounding atmosphere which surrounds the cartridge (7) is cooled;

pressure reduction processing in which, after the surrounding atmosphere has been cooled, by then reducing the pressure of the surrounding atmosphere to below the pressure of the internal air (A), the front stopper (2) is placed in the cartridge (7) in a half stoppering state; and

sealing processing in which the front stopper (2) in the half stoppering state is pushed inside the cartridge (7).

10 17. A front stopper that is used in the method of manufacturing a dual chamber combined container-syringe (7) according to claim 16, comprising:

a sealing rib (2b) whose outer diameter is larger than the inner diameter of the cartridge (7), and that elastically contracts when the sealing rib (2b) is inserted inside the cartridge (7) so as to form a tight seal with an inner circumferential surface of the cartridge (7);

15 a positioning rib (2a) that is positioned further to the rear end side than the sealing rib (2b) and whose outer diameter is substantially the same as the inner diameter of the cartridge (7); and

20 a communicating groove (2i) that is formed in an outer circumferential surface of the front stopper (2), that extends from the positioning rib (2a) to the sealing rib (2b), and that, when the front stopper (2) is placed in the cartridge (7) in the half stoppering state, places the inside and outside of the cartridge (7) in communication with each other.

CLAIMS

1. A device for sealing a vessel, in particular a cartridge or a test-tube for accommodating a freeze-dried pharmaceutical product , including

a front plunger to be positioned inside the vessel at a longitudinal portion,

5 wherein the front plunger is configured to be positioned in the vessel in a sealing state, in which the front plunger is fully inserted in the vessel, or in an exchange state, in which the front plunger is inserted partly in the vessel and partly protrudes over an opening edge of the vessel, wherein the front plunger comprises

sealing means that are configured to seal the inside of the vessel against the outside

10 when the front plunger is positioned in the sealing state, and

one or more communicating grooves that are configured to place the inside and outside of the vessel in communication with each other when the front plunger is positioned in the exchange state, wherein the one or more communicating grooves are formed in an outer circumferential surface of the front plunger extending from an inner end side of the front
.5 plunger into a first sealing rib of the front plunger.

2. The device according to claim 1, wherein the sealing means include at least one sealing rib – the first sealing rib – whose outer form is adapted to the form of the inner cross section of the longitudinal portion.

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3. The device according to claim 2, wherein the inner cross section of the longitudinal portion has a circular form, and wherein the first sealing rib has an outer diameter that is larger than the inner diameter of the longitudinal portion, and that is configured to elastically contract when the front plunger is positioned inside the vessel so as to form a tight seal with
25 the inner surface of the longitudinal portion.

4. The device according to claim 2 or 3, wherein the first sealing rib is dimensioned in such a way that the front plunger is movable inside the vessel toward its opening end by applying an underpressure of predefined strength to the outer environment of the vessel .

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5. The device according to any of claims 2 to 4, wherein an inclined surface extending in a circumferential direction of the first sealing rib is formed at a rear end portion of the first sealing rib, wherein the diameter of the inclined surface is configured to gradually expand during its movement from the rear end side toward the front end side.

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6. The device according to any of claims 2 to 5, wherein the one or more communicating grooves extend to the center of the first sealing rib in the direction of a center axis of the front plunger .

5 7. The device according to claim 2 or 6, wherein the sealing means include a positioning rib whose outer diameter is substantially the same as the inner diameter of the longitudinal portion of the vessel, and that is positioned further to the inner end side of the front plunger than the first sealing rib, so as to remain inside the vessel when the front plunger is positioned in the exchange state.

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8. The device according to any of claims 1 to 7, wherein the communicating grooves are formed at intervals in the circumferential direction of the front plunger.

9. The device according to any of claims 1 to 8, for use in a dual chamber combined
25 container-syringe, comprising

the cartridge, in which the front plunger, a middle plunger, and an end plunger are positioned in this sequence from the opening end,

a diluent, which is sealed inside the cartridge between the end plunger and the middle plunger, and

5 a freeze-dried pharmaceutical product, which is sealed inside the cartridge between the middle plunger and the front plunger.

10. A method of manufacturing a sealed vessel, in particular a cartridge or a test-tube, containing a freeze-dried pharmaceutical product, wherein the vessel comprises at its opening
10 end an opening edge and an adjoining longitudinal portion with an evenly formed inner cross section, at least comprising:

a drug solution provisioning step in which a drug solution to be freeze-dried is inserted into the vessel;

a drug solution sealing step in which the drug solution is sealed together with internal
15 air by positioning a front plunger inside the vessel at the longitudinal portion; and

a freeze-drying step in which the drug solution is freeze-dried so as to form the freeze-dried pharmaceutical product,

wherein the freeze-drying step includes:

surrounding atmosphere cooling processing in which a surrounding atmosphere which
20 surrounds the vessel is cooled, such that the drug solution inside the vessel gets frozen;

pressure reduction processing in which, after the surrounding atmosphere has been cooled, the pressure of the surrounding atmosphere is reduced to below the pressure of the internal air, thereby causing the front plunger to move toward the opening end of the vessel and to rest in an exchange state, in which the front plunger is inserted partly in the vessel and
25 partly protrudes over the opening edge of the vessel, such that one or more communicating

grooves provided at the front plunger and formed in an outer circumferential surface of the front plunger extending from an inner end side of the front plunger into a first sealing rib thereof define a duct between the inside and the outside of the vessel through which solvent content can be removed by sublimation for enabling freeze-drying of the drug solution.

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11. The method according to claim 10, further comprising:

a diluent provisioning step and a diluent sealing step, both carried out before the drug solution provisioning step, in which a diluent is inserted into the vessel and sealed inside the vessel between the bottom of the vessel or an end plunger that has been inserted into the

10 vessel and a middle plunger.

12. The method according to claim 11, wherein in the diluent sealing step:

the diluent is filled on top of the end plunger inside the vessel; and

the diluent is sealed by inserting the middle plunger into the vessel so that air does not

5 become contained between the end plunger and the middle plunger.

13. The method according to claim 11 or 12, further comprising:

after having terminated the diluent sealing step, sterilizing the diluent by means of autoclaving.

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14. The method according to any of claims 11 to 13, wherein the freeze-drying step further includes:

after having terminated the pressure reduction processing, substitution processing in which, by substituting the surrounding atmosphere that surrounds the vessel with an inert gas,

25 such as a nitrogen gas, the inside of the vessel is filled via the exposed communicating

grooves with the inert gas.

15. The method according to any of claims 11 to 14, wherein the freeze-drying step further includes:

5 sealing processing in which the front plunger is pushed into a sealing state, in which the front plunger is fully inserted in the vessel, wherein the sealing processing further includes:

causing the front plunger to move toward the rear end side of the vessel by applying to the outside of the vessel a pressure higher than the pressure of the inert gas contained within
10 the vessel.

16. A method of manufacturing a dual chamber combined container-syringe in which, in a cartridge in which a front plunger, a middle plunger, and an end plunger have been inserted in this sequence from the distal end side, a diluents is sealed between the end plunger and the
5 middle plunger, and a freeze-dried pharmaceutical product is sealed between the middle plunger and the front plunger, comprising:

a diluent sealing step in which the diluents is sealed inside the cartridge by the end plunger and the middle plunger;

an injection drug solution sealing step in which an injection drug solution before
20 freeze-drying is sealed together with internal air inside the cartridge by the middle plunger and the front plunger; and

a freeze-drying step in which the injection drug solution is freeze-dried so as to form the freeze-dried pharmaceutical product, wherein

the freeze-drying step includes:

25 surrounding atmosphere cooling processing in which a surrounding atmosphere

which surrounds the cartridge is cooled;

pressure reduction processing in which, after the surrounding atmosphere has been cooled, by then reducing the pressure of the surrounding atmosphere to below the pressure of the internal air, the front plunger is placed in the cartridge in a half stoppering state in which one or more communicating grooves provided at the front plunger and formed in an outer circumferential surface of the front plunger extending from an inner end side of the front plunger into a first sealing rib thereof define a duct between the inside and the outside of the vessel through which solvent content can be removed by sublimation for enabling freeze-drying of the drug solution; and

sealing processing in which the front plunger in the half stoppering state is pushed inside the cartridge.

17. A front plunger that is used in the method of manufacturing a dual chamber combined container-syringe according to claim 16, comprising:

a sealing rib whose outer diameter is larger than the inner diameter of the cartridge, and that elastically contracts when the sealing rib is inserted inside the cartridge so as to form a tight seal with an inner circumferential surface of the cartridge;

a positioning rib that is positioned further to the rear end side than the sealing rib and whose outer diameter is substantially the same as the inner diameter of the cartridge; and

a communicating groove that is formed in an outer circumferential surface of the front plunger, that extends from the positioning rib into the sealing rib, and that, when the front plunger is placed in the cartridge in the half stoppering state, places the inside and outside of the cartridge in communication with each other.