

(19) World Intellectual Property Organization  
International Bureau



(43) International Publication Date  
19 October 2006 (19.10.2006)

PCT

(10) International Publication Number  
**WO 2006/108563 A1**

(51) International Patent Classification:

A61M 11/02 (2006.01) B05B 11/06 (2006.01)  
A61M 15/00 (2006.01) B05B 7/14 (2006.01)

(21) International Application Number:

PCT/EP2006/003165

(22) International Filing Date: 7 April 2006 (07.04.2006)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:

10 2005 016 230.4 8 April 2005 (08.04.2005) DE

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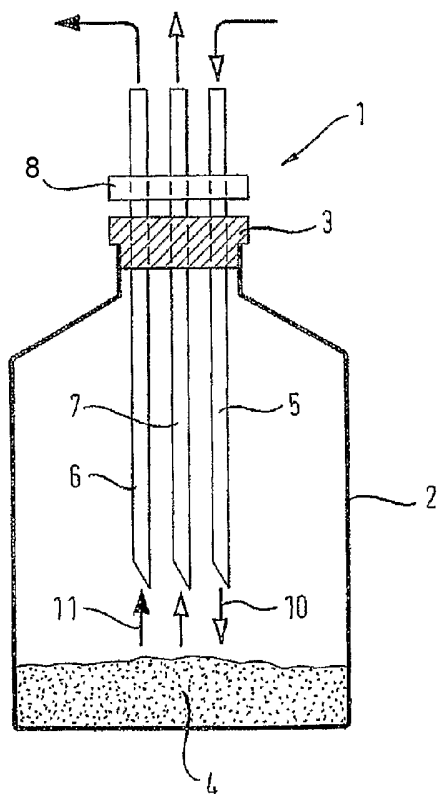
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(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID,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

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

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(54) Title: DEVICE FOR DRY NEBULIZATION



(57) Abstract: The present invention relates to a device (1) for dry nebulization of nebulizable material (4) which is contained in a gas-tight container (2), with a gas-tight container seal (3) and with a gas admission line (5) whose first end can be connected to a carrier gas source and whose second end can be guided through the seal, with a dry mist discharge line (6) which can be guided through the seal and is used for discharging a carrier gas dry mist of the nebulizable material generated in the container, and an excess discharge line (7) which can be guided through the seal and is used for discharging at least an excess of carrier gas in the container. According to a further aspect, the invention relates to a corresponding device comprising the gas-tight container seal (3) through which the gas admission line (5), dry mist discharge line (6) and excess discharge line (7) are guided. The invention additionally relates to systems comprising the device (1) and the gas-tight container (2), the use of the device for nebulization of a powdered pharmaceutical preparation, in particular a lung surfactant preparation. The device according to the invention permits aseptic dry nebulization, in particular of powdered pharmaceutical preparations, directly from the product container.



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

**Published:**

— *with international search report*

## Device for dry nebulization

### Field of the invention

The present invention relates to a device for dry nebulization of nebulizable material, in particular powdered pharmaceutical preparations. The present invention relates in particular to devices for direct dry nebulization of pharmaceutical preparations from the product bottle.

### Background of the invention

Critically ill patients requiring mechanical ventilation often suffer from pulmonary infections and diseases which have to be treated by medication. Ideally, they are treated by direct administration of the medication into the lungs. In spontaneously ventilating patients too, a wide variety of pulmonary diseases are advantageously treated by direct administration of the medication into the lungs.

This requires the production of small particles which are able to access the lungs and alveoli. This is achieved using nebulizers. There are two main types of nebulizers, namely liquid nebulizers and dry nebulizers. In liquid nebulizers, the medicament in liquid form is nebulized into fine aerosol droplets which are able to reach as far as the lungs and alveoli. In dry nebulizers, solid and preferably powdered pharmaceutical preparations in very finely dispersed form are converted into a gas-carried state and transported into the lungs.

The medicines to be administered directly into the lungs with dry nebulizers must be as free as possible of microorganisms, in order to exclude the possibility of pulmonary infections right from the outset. This is a serious problem both in dry nebulizers for intermittent operation, as are described for example in WO 01/62323, DE-A-42 11 475 and DE-A-36 12 473, and also in dry nebulizers for continuous operation, as are disclosed for example in US 1,599,959 and US 5,186,166. This is because the powdered pharmaceutical preparation supplied in sterile aseptic medicine bottles has in most cases to be poured into dry nebulizers of this kind. This involves a considerable risk of contamination. An added factor is the danger of air moisture getting into the pharmaceutical preparation that is to be nebulized. This can lead to formation of lumps, that is to say agglomeration of the primary particles of the powdered pharmaceutical preparation.

US 2,693,805 describes a dry nebulizer comprising a container whose open end is sealed with a rubber stopper. This stopper has two holes. Extending through one of these holes

- 2 -

there is a tube whose end outside the container is connected to a pressure bulb made of rubber. Inside the container, this tube is provided with a baffle plate. A tube that can be connected to a mouthpiece or to a face mask is guided through the second hole of the rubber stopper. When using the dry nebulizer from US 2,693,805, the patient places his lips round the mouthpiece or puts the face mask on and squeezes the pressure bulb at specific intervals and then releases it again. In this way, the powdered material situated in the container is nebulized and can be inhaled by the patient through the mouthpiece or face mask.

The system in US 2,693,805 has serious disadvantages, however. First, it involves filling the medication, for example finely powdered penicillin, into the container. As has been described above, this is associated with considerable risk of contamination. US 2,693,805 makes no mention of the possibility of fitting such a dry nebulizer directly onto the product bottle. A more serious problem is that the squeezing and release of the pressure bulb does not allow all of the nebulizable material contained in the container to be nebulized and converted into an inhalable state. The residual amount of nebulizable material that can be expected to remain in the container is therefore considerable. This is a serious disadvantage especially in cases where expensive pharmaceutical preparations are to be nebulized.

Against the background of this prior art, the inventors have set themselves the object of developing a dry nebulizer with which the nebulizable material located in the container can be nebulized almost completely. It was also an object of the inventors to make available a dry nebulizer with which pharmaceutical preparations can be nebulized directly from the product bottle and the risk of contamination of the nebulizable material, in particular of powdered pharmaceutical preparations, can thus be minimized.

#### Summary of the invention

The object formulated above is achieved by the device having the features of Claim 1 and Claim 5, the use of such a device according to Claim 21, the method for nebulization according to Claim 26, and the systems having the features of Claims 27 and 28. Advantageous embodiments of the invention are the subject of the respective dependent claims.

#### Detailed description of the invention

Within the meaning of the present invention, dry nebulization of nebulizable material is

- 3 -

understood as its dispersion and conversion into a carrier gas dry mist of the nebulizable material. Carrier gas dry mist of the nebulizable material is understood here as carrier gas in which nebulizable material is contained in the carrier-gas-borne state.

The present invention relates in principle to two variants of the device according to the invention for dry nebulization according to Claims 1 and 5. Where the present description refers to the device for dry nebulization, this in principle signifies both variants of the device according to the invention, unless otherwise stated in the particular context.

The first variant is configured such that the second end of the gas admission line, the dry mist discharge line and the excess discharge line can be guided through the gas-tight seal of a gas-tight container which contains nebulizable material. In this case, the container seal is preferably made of an elastic, pierceable material. For example, the gas-tight container, onto whose seal the first variant of the device according to the invention can be connected, can be a DIN or ISO infusion bottle or a vial with a rubber stopper or flanged cap. It is particularly preferably an infusion bottle with a capacity of approximately 100 ml. The nebulizable material is already contained in the corresponding gas-tight container, preferably in a sterile and aseptic form. In this variant of the device according to the invention, said device, preferably the gas admission line, the dry mist discharge line and the excess discharge line, is provided with one or more spikes for piercing the gas-tight container seal. The spike or spikes preferably have a diameter of 1 to 20 mm, preferably 1 to 10 mm, particularly preferably 1 to 5 mm. The shape of the spike or spikes is not specially restricted here, as long as piercing of the gas-tight container seal is possible. For example, the spikes are tapered towards the bottom or beveled, in order to permit clean penetration of the gas-tight seal when the latter is pierced. It is particularly preferable that these spikes comply with the current DIN and ISO standards, i.e. that they are tapered or beveled, for example. These standards are, for example, DIN EN ISO 8536, DIN 13097, DIN 58362 and DIN EN ISO 1135.

According to a second variant of the device according to the invention, said device is already integrated in the gas-tight container seal, and this seal is then connected in a gas-tight manner to the gas-tight container in which nebulizable material is already contained or into which nebulizable material has previously been filled. Connection of this variant of the device according to the invention, which comprises a gas-tight container seal, can be effected by screwing or fitting the container seal onto the container, provided that a substantially gas-tight connection to the container is guaranteed. The gas-tight container seal can, for example, be a screw-on cap, rubber stopper or clip-on cap.

- 4 -

The gas admission line of the device according to the invention for dry nebulization should be configured in such a way that, with the device connected to the gas-tight container which contains nebulizable material, and at the selected initial pressure and volumetric flow rate of the carrier gas conveyed from the carrier gas source and through the gas admission line, the flow of gas to the dry mist discharge line is guaranteed, thus permitting the discharge of the carrier gas dry mist of the nebulizable material generated in the container. For this purpose, the gas admission line can have one opening, preferably more than one opening, on that part situated inside the gas-tight container during use of the device for dry nebulization. In the case of a plurality of openings, provision is preferably made for a large number of said openings, these particularly preferably being spaced apart from one another at uniform intervals around the circumference of the gas admission line. In particular, the openings are arranged at uniform intervals along the free length of the gas admission line in the container. The shape of the opening or openings in the gas discharge line is not specially restricted and, for example, round or slit-shaped openings are included within the scope of the invention. In the case of openings with a substantially round cross section, a diameter of 0.05 to 3 mm, preferably of 0.3 to 1.5 mm, is preferred.

The gas admission line can be stationary or can also be designed to be movable. With the aid of a movable gas admission line, the nebulizable material in the gas-tight container can be converted particularly efficiently and uniformly to the carrier-gas-borne state. The gas admission line can be movable by means of a rotary or reciprocating motion, for example. During the operation of the device according to the invention, the driving action can be effected by a stream of gas, for example the carrier gas stream, or in another way that is well known in the technical field, for example with an electric motor. Suitable measures for moving the gas admission line will be immediately apparent to the skilled person.

With the device according to the invention connected to the gas admission line, the initial pressure of the carrier gas source is between 100 mbar and 5 bar, for example. It typically lies between 0.5 bar and 2.5 bar. Here, initial pressure signifies the overpressure in relation to the environment or in relation to the pressure inside the device according to the invention when it is in use. The arrangement and geometry of the component parts of the device according to the invention are preferably such that the volumetric flow rate of carrier gas is between 100 ml/min and 100 l/min during operation.

The dry mist discharge line is used for discharging a carrier gas dry mist of the nebulizable material that has been generated in the gas-tight container. For this purpose, the dry mist discharge line preferably has an opening, or more preferably a plurality of openings. The

- 5 -

opening or openings are arranged in such a way that they are situated inside the gas-tight container when the device according to the invention is connected to the container. The specific design of the dry mist discharge line, for example the total cross-sectional surface area and arrangement of the opening or openings, is in this case dependent on the shape of the gas-tight container in which the nebulizable material is contained, and on the amount of carrier gas dry mist that is to be discharged, and the average person of skill in the art will choose the most suitable design on the basis of his specialist knowledge. The total cross-sectional surface area of the opening or openings can be between 1 and 500 mm<sup>2</sup>, for example. It typically lies between 5 and 60 mm<sup>2</sup>.

The nebulizable material can be powdered pharmaceutical preparations, in particular preparations which comprise a lung surfactant or predominantly consist of the latter. Such pharmaceutical preparations tend to undergo agglomeration, among other reasons because of residual moisture. Within the meaning of the present application, agglomeration is understood as meaning when primary particles of the nebulizable material join to form larger agglomerates consisting of a plurality of primary particles. The device according to the invention can be used for dry nebulization of powdered pharmaceutical preparations, in particular lung surfactants, which are intended to be administered to patients by inhalation. When using the device according to the invention for inhaled administration of nebulizable material, it is advantageous if the MMAD (mass median aerodynamic diameter) of the particles of the nebulizable material in the carrier gas dry mist is set in such a way that the particles which leave the dry mist discharge line in the carrier-gas-borne state are most of them able, or preferably all able, to reach the lungs. The corresponding MMAD lies in the range of 1 to 5 µm, in particular 1 to 3 µm. According to a preferred embodiment, during operation of the device according to the invention when it is connected to the gas-tight container, the opening or openings of the dry mist discharge line are arranged at a sufficient distance from the nebulizable material, which is situated for example on the bottom of the gas-tight container. In this way, it is possible to minimize the risk of particles being discharged that are unsuitably large for the particular area of application.

For the purpose of achieving a desired MMAD range of the particles in the carrier gas dry mist, it is also possible to use means for deagglomeration of the nebulizable material, which means are provided in the dry mist discharge line according to a preferred embodiment. Such a means for deagglomeration can, for example, be a flow constriction point, in particular a nozzle. Cross sections of the nozzle are typically 0.01 mm<sup>2</sup> to 4 mm<sup>2</sup>. The dry mist discharge line can have one or several flow constriction points. Other suitable means for deagglomeration are flow reversal points in the dry mist discharge line, for

- 6 -

example bends, meanders and helical formations. Further means for deagglomeration are, for example, baffle plates, screens or filters. In the case of screens or filters, the mesh width or pore width is typically between 1  $\mu\text{m}$  and 0.5 mm. Finally, the means for deagglomeration can also include turbines or propellers with a typical blade diameter of 3 to 15 mm. Combinations of the above-described components can also be used as the means for deagglomeration.

According to a preferred embodiment, the opening or openings of the dry mist discharge line at the same time constitute the means for deagglomeration. In this case, the openings of the dry mist discharge line are advantageously of such a size that only particles of the carrier gas dry mist that have a size within a desired range are able to pass through them. For powdered pharmaceutical preparations intended to be administered by inhalation, this desired particle size range is preferably an MMAD of 1 to 5  $\mu\text{m}$ , in order to ensure that the particles can access the lungs. In the case of a circular opening or openings of the dry mist discharge line, typical diameters are between 0.2 to 2 mm, preferably 0.5 to 1 mm, and their diameter is very particularly preferably about 1 mm.

The excess discharge line of the device according to the invention is used for discharging at least an excess of carrier gas in the container. The excess discharge line permits the use of a greater volumetric flow rate of carrier gas than can be carried off in the form of a carrier gas dry mist through the dry mist discharge line. The excess discharge line thus allows the nebulizable material present in the gas-tight container to be nebulized completely or at least almost completely. This was not really possible with corresponding devices from the prior art, for example as described in US 2,693,805.

When using the device according to the invention for dry nebulization of nebulizable material in the gas-tight container together with excess carrier gas, it is not possible to entirely rule out the possibility of a small amount of nebulized material also passing into the excess discharge line. This danger can be minimized by suitable arrangement of the excess discharge line in relation to the dry mist discharge line and the gas admission line, taking into account the flow conditions in the container during operation of the device according to the invention.

Suitable measures can be easily taken by the skilled person within the context of his specialist knowledge. According to a particularly preferred embodiment, the excess discharge line has a device for separating the nebulizable material. Particularly suitable separating devices are filters. Commercially available membrane filters or deep-bed filters can be used, for example. The pore width of these filters is preferably 0.1 to 10  $\mu\text{m}$ ,

- 7 -

particularly preferably 0.5 to 3  $\mu\text{m}$ . The separating device is ideally chosen such that it offers the least possible flow resistance to the stream of excess carrier gas and at the same time reliably prevents nebulized material from being carried off through the excess discharge line and thus lost. Consequently, it is immediately apparent to the skilled person that the filter material and the filter surface area must be chosen as a function of the volumetric flow rate of the excess carrier gas and the properties of the nebulizable material, in particular its particle size in the carrier-gas-borne state. The filter material and the filter surface are suitably chosen by the skilled person on this basis. The filter surface area is typically in the range of from below 1  $\text{cm}^2$  to as much as 10  $\text{cm}^2$ . Because of their good material stability, sintered plastic filters (trade name Porex®) are particularly advantageous. According to a particularly preferred embodiment, the separating device of the excess discharge line is arranged in relation to the gas admission line in such a way that separated nebulizable material can be blown off from the carrier gas stream conveyed through the gas admission line, so as to avoid clogging of the separating device, for example the filter. The use of filters as separating device is also particularly advantageous in that a contamination of the interior of the gas-tight container, and of the nebulizable material contained in it, can be very effectively suppressed.

In the device according to the invention for dry nebulization, the gas admission line, dry mist discharge line and excess discharge line are not particularly restricted in terms of the way they are arranged with respect to one another. According to a preferred embodiment, however, they are connected to one another, preferably by means of a plate, in particular a grip plate. According to a further preferred embodiment, they are located within a common line.

There are no particular restrictions in terms of the cross-sectional shape of the gas admission line, dry mist discharge line and excess discharge line. Round or oval cross sections are possible, for example. Particularly if the gas admission line, dry mist discharge line and excess discharge line are situated within a common line and this common line has a circular cross section, it is possible to use irregular cross sections. This is illustrated in Fig. 2b.

The dry nebulization of the nebulizable material and thus its conversion to the carrier-gas-borne state can be further enhanced by a device for agitating the nebulizable material. When using the device according to the invention connected to the gas-tight container, this device preferably encloses the container in such a way that it encloses at least that area of the container that contains nebulizable material. A vibrator device is alternatively used for this purpose. Mechanical agitator devices are preferably used. According to a

- 8 -

particularly preferred embodiment, an ultrasonic agitator device is used. The agitator device improves the conversion of the nebulizable material to the carrier-gas-borne state by means of energy being input. The device for agitating the nebulizable material permits further improved utilization of the nebulizable material, ensures a continuous rate of dry nebulization and minimizes the residual amount of nebulizable material in the gas-tight container.

There is no particular restriction on the materials used for producing the device according to the invention. For example, it is possible to use glass, and also commercially available plastics which have been processed, for example, by injection moulding. Such plastics are used in particular in devices according to the invention which are disposed of after one use. Aluminium and stainless steel alloys can also be used. Anodized aluminium is particularly advantageous if the nebulizable material is a lung surfactant based on recombinant surfactant protein C (rSP-C surfactant), because the powder of this material has only a slight surface adherence to anodized aluminium.

The device according to the invention can be suitable for repeated use or for disposal after one use. Devices for repeated use should preferably be produced in such a way that they can be cleaned prior to the next use. To make such cleaning easier, such a device is preferably made from sterilizable materials. The sterilizing can be carried out, for example, by ethylene oxide, radiation, steam or dry heat. In the case of disposal after one use, the device according to the invention is preferably designed as a discardable article complying with the regulations governing medical products.

The device according to the invention, when operatively connected to the gas-tight container which contains nebulizable material, can be used for acute treatment in spontaneously ventilating patients. For this purpose, the dry mist discharge line can be provided, at its end outside the container, with a breathing mask, a spacer (inhalation auxiliary), a mouthpiece or an attachment piece for nasal administration.

In the treatment of spontaneously ventilating patients, the first end of the gas admission line is preferably connected to a carrier gas source which is under pressure.

In use on ventilated patients, the device according to the invention, connected to the gas-tight container containing nebulizable material, is built into the respirator. It is preferably joined to the side port of the respirator or the intensive care ventilation apparatus. The connection to the respirator can be made via an attachment piece. This attachment piece can be a ventilation tube adapter which is preferably connected to the respirator by a valve

- 9 -

and a circuit triggered by the ventilation apparatus. During operation of a respirator into which the device according to the invention is built while connected to the gas-tight container holding nebulizable material, i.e. during operation of a respirator with a built-in system according to Claim 27 or 28, the stream of the carrier gas is set in such a way that the desired transport of carrier-gas-borne nebulized material into the dry mist discharge line is achieved. When the system according to the invention is used in respirators, the carrier gases used can be ventilation gases, such as air, oxygen and other commercially available ventilation gases.

The system according to the invention, consisting of the device for dry nebulization and of the gas-tight container with nebulizable material contained in it, can also be used to apply such material, for example pharmaceutical preparations for topical application or cosmetics, onto the body or tissue surfaces. In this case, the dry mist discharge line is preferably connected to a spray gun. In this area of use of the system according to the invention, any desired carrier gases can be used, as long as these are not toxic.

The nebulizable material is preferably a pharmaceutical preparation. This pharmaceutical preparation is advantageously powdered, for example a micronized powder. According to a preferred embodiment, the pharmaceutical preparation comprises a surfactant or is essentially composed of a surfactant. An example of such a surfactant is Surfaxin (KL4 surfactant). The surfactant is particularly preferably a lung surfactant. A lung surfactant is a substance mixture which is contained in the lungs of all vertebrates. It has surface-active properties and reduces the surface tension in the alveolar region of the lungs to such an extent that collapse of the pulmonary alveoli is avoided during exhalation. Essential components in the lung surfactant are proteins, designated by SP-A, SP-B and SP-C. The lung surfactant contained in the nebulizable material is particularly advantageously a recombinant lung surfactant, such as is described in WO 95/32992. This is a mutant of human SP-C (also designated as rSP-C). The most preferred lung surfactant is Venticute® (INN: lusupultide, also designated as rSP-C (FF/I)). rSP-C (FF/I) is described in WO 95/32992. In addition to the described surfactant based on the recombinant surfactant protein C (rSP-C), the pharmaceutical preparation can contain a further lung surfactant based on proteins SP-A and SP-B. Moreover, it may also contain phospholipids and other additives familiar to the skilled person.

Particularly preferably, the pharmaceutical preparation is or comprises a powdered lung surfactant preparation which is produced as described in EP-B-877 602. In the process in EP-B-877 602, an organic solution or suspension containing lung surfactant and possibly other constituents is subjected to spray drying. Venticute® is the most preferred lung

- 10 -

surfactant in this context.

Accordingly, the dry nebulization in particular of powdered pharmaceutical preparations containing such lung surfactants, in particular Venticute®, is a particularly preferred use of the device according to the invention for dry nebulization.

Lung surfactants are suitable for the prevention and early treatment of acute lung diseases. This use is described in WO 01/76619. Diseases to be treated by lung surfactant are, for example, asthma, pulmonary fibrosis, pneumonias, bronchitis, chronic obstructive pulmonary disease (COPD) and various respiratory distress syndromes (RDS), such as adult respiratory distress syndrome (ARDS), and infant respiratory distress syndrome (IRDS) seen in children and in particular in premature babies. The use of the device according to the invention for dry nebulization and of the system according to the invention for dry nebulization of Venticute® for treatment of ARDS is a particularly preferred area of use.

The basic structure of the device according to the invention for dry nebulization is described below with reference to the drawings.

#### Description of the drawings

Fig. 1 shows a schematic side view of a system according to the invention, comprising the device according to the invention and the gas-tight container with nebulizable material contained therein;

Figs 2a and 2b show a schematic cross-sectional view of a common line within which the gas admission line, the dry mist discharge line and the excess discharge line are arranged.

Fig. 1 shows in detail a system comprising the device 1 for dry nebulization of the nebulizable material 4, which is contained in the gas-tight container 2 with the gas-tight container seal 3. The device 1 has already been guided through the gas-tight container seal 3. The device has a gas admission line 5, a dry mist discharge line 6 and an excess discharge line 7, each of them provided with beveled spikes which have been pushed through and pierced the container seal 3. The gas admission line 5, dry mist discharge line 6 and excess discharge line 7 are connected to a plate 8. A stream of carrier gas, identified by an open arrow 10, is guided through the gas admission line 5 towards and into the nebulizable material contained in the container. In this way, a carrier gas dry mist

- 11 -

of the nebulizable material is generated. A stream of this carrier gas dry mist is conveyed through the dry mist discharge line 6. This stream of the carrier gas dry mist is identified by solid arrows 11. Excess carrier gas, which may possibly contain small amounts of nebulizable material, is led off through the excess discharge line.

According to a preferred embodiment, the gas admission line 5, the dry mist discharge line 6 and the excess discharge line 7 lie within a common line 9. Examples of arrangements are depicted in Figures 2a and 2b. In Fig. 2a, the admission and discharge lines 5, 6, 7 are present in the form of channels of different diameter inside a line 9 made of solid material. In Fig. 2b, by contrast, the lines 5, 6, 7 are formed by dividing walls in the inside of a substantially tubular line 9.

**Patent Claims**

1. Device (1) for dry nebulization of nebulizable material (4) which is contained in a gas-tight container (2) with a gas-tight container seal (3), comprising:

a gas admission line (5) whose first end can be connected to a carrier gas source and whose second end can be guided through the seal,

a dry mist discharge line (6) which can be guided through the seal and is used for discharging a carrier gas dry mist of the nebulizable material generated in the container, and

an excess discharge line (7) which can be guided through the seal and is used for discharging at least an excess of carrier gas in the container.

2. Device according to Claim 1, characterized in that the device (1), preferably the gas admission line (5), the dry mist discharge line (6) and the excess discharge line (7), has one or more spikes for piercing the gas-tight container seal (3).

3. Device according to Claim 2, characterized in that the spike or spikes have a diameter of 1 – 20 mm.

4. Device according to one of the preceding claims, characterized in that the gas admission line (5), the dry mist discharge line (6) and the excess discharge line (7) are connected to one another, preferably by means of a grip plate (8).

5. Device (1) for dry nebulization of nebulizable material (4) contained in a gas-tight container (2), comprising:

a gas-tight container seal (3),

a gas admission line (5) whose first end can be connected to a carrier gas source and whose second end is guided through the seal,

a dry mist discharge line (6) which is guided through the seal and is used for discharging a carrier gas dry mist of the nebulizable material generated in the container, and

- 13 -

an excess discharge line (7) which is guided through the seal and is used for discharging at least an excess of carrier gas in the container.

6. Device (1) according to one of the preceding claims, characterized in that the gas admission line (5), the dry mist discharge line (6) and the excess discharge line are present within a common line (9) and are preferably provided with a common spike.
7. Device according to one of the preceding claims, characterized in that the device (1), connected to the container (2), protrudes at least 2 mm into the container.
8. Device according to one of the preceding claims, characterized in that the gas admission line (5) has, at its second end, more than one opening, preferably a multiplicity of openings, in particular spaced apart at uniform intervals around the circumference of the gas admission line.
9. Device according to Claim 8, characterized in that the openings are preferably arranged at uniform intervals along the free length of the gas admission line in the container.
10. Device according to Claim 8 or 9, characterized in that the openings have a substantially round cross section with a diameter of 0.05 – 3 mm, preferably 0.3 – 1.5 mm.
11. Device according to Claim 8 or 9, characterized in that the openings have a slit-shaped configuration.
12. Device according to one of the preceding claims, characterized in that the dry mist discharge line (6) has one or more openings arranged in such a way that they are situated inside the container when the device is connected to the container.
13. Device according to Claim 12, characterized in that the total cross-sectional surface area of the openings of the dry mist discharge line (6) is from 1 mm<sup>2</sup> to 500 mm<sup>2</sup>, preferably 5 mm<sup>2</sup> to 60 mm<sup>2</sup>.
14. Device according to Claim 12 or 13, characterized in that the opening(s) is/are arranged in such a way that they are spaced apart from the nebulizable material in

- 14 -

the state of connection to the container.

15. Device according to one of the preceding claims, characterized in that the dry mist discharge line (6) has means for deagglomeration of the nebulizable material in the carrier gas dry mist.
16. Device according to Claim 15, characterized in that the means for deagglomeration is a flow constriction point and/or a flow reversal point, preferably a bend or a meander or a helical formation, and/or turbines or propellers and/or one or more baffle plates and/or screens or filters.
17. Device according to one of the preceding claims, characterized in that, when the device is connected to the container, the end of the dry mist discharge line (6) directed away from the container is connected to a breathing mask, a spacer, a mouthpiece, or a connector piece for an intensive-care ventilation apparatus.
18. Device according to Claim 17, characterized in that the connector piece is a ventilation tube adapter preferably connected to a valve and to a circuit triggered by the ventilation apparatus.
19. Device according to one of the preceding claims, characterized in that the excess discharge line (7) has a filter for the nebulizable material.
20. Device according to Claim 19, characterized in that the filter is a sintered plastic filter.
21. Use of the device according to one of the preceding claims for nebulization of the nebulizable material (4) contained in the gas-tight container, said nebulizable material being a pharmaceutical preparation.
22. Use according to Claim 21, in which the pharmaceutical preparation is in powder form.
23. Use according to Claim 21 or 22, in which the pharmaceutical preparation comprises a lung surfactant.
24. Use according to Claim 23, in which the lung surfactant is a surfactant based on recombinant surfactant protein C.

- 15 -

25. Use according to Claim 24, in which the surfactant based on recombinant surfactant protein C is lusupultide.
26. Method for nebulization of a nebulizable material contained in a gas-tight container with a gas-tight seal, comprising:
  - (i) connecting the device (1) according to Claims 1 – 4, and 6 – 20, unless referred back to Claim 5, to the container (2) by guiding the second end of the gas admission line (5), of the dry mist discharge line (6) and of the excess discharge line (7) through the gas-tight container seal (3), and
  - (ii) connecting the first end of the gas admission line (5) to a carrier gas source.
27. System comprising the device (1) according to Claims 1 – 4, and 6 – 20, unless referred back to Claim 5, and a gas-tight container (2) with a gas-tight container seal (3), in which the gas-tight container (2) contains nebulizable material (4).
28. System comprising the device (1) according to Claim 5, and Claims 6 – 20, unless referred back to Claims 1 – 4, and a gas-tight container (2), in which the gas-tight container (2) contains nebulizable material (4).
29. System according to Claim 27 or 28, in which the gas-tight container (2) is a commercially available DIN or ISO bottle, preferably a DIN or ISO vial for infusion or injection purposes or for lyophilization.

Fig. 1

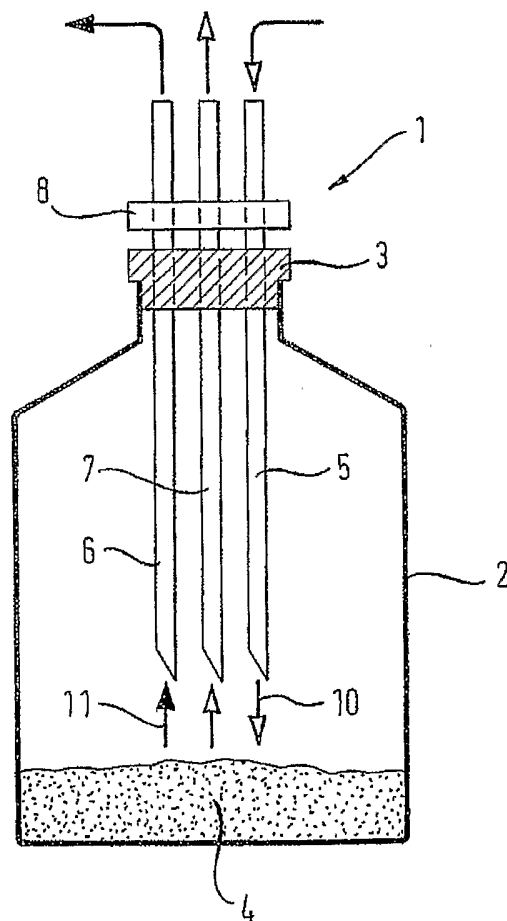


Fig. 2a

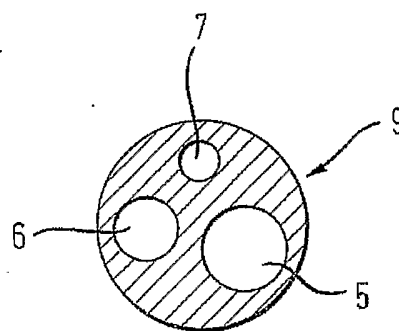
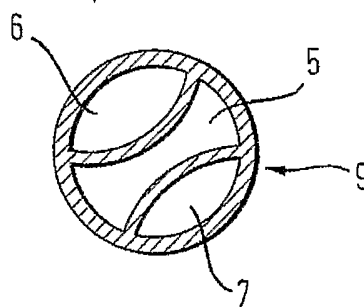


Fig. 2b



# INTERNATIONAL SEARCH REPORT

International application No  
PCT/EP2006/003165

## A. CLASSIFICATION OF SUBJECT MATTER

INV. A61M11/02 A61M15/00 B05B11/06 B05B7/14

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

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

A61M B05B

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

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

EPO-Internal, PAJ, WPI Data

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category* | Citation of document, with indication, where appropriate, of the relevant passages                                                 | Relevant to claim No.            |
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☒ Further documents are listed in the continuation of Box C.

☒ See patent family annex.

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- \*A\* document defining the general state of the art which is not considered to be of particular relevance
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- \*P\* document published prior to the international filing date but later than the priority date claimed

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- \*Z\* document member of the same patent family

Date of the actual completion of the international search

18 July 2006

Date of mailing of the international search report

01/08/2006

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## INTERNATIONAL SEARCH REPORT

International application No  
PCT/EP2006/003165

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

| Category* | Citation of document, with indication, where appropriate, of the relevant passages                                                                                         | Relevant to claim No.  |
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Information on patent family members

International application No

PCT/EP2006/003165

| Patent document<br>cited in search report | Publication<br>date | Patent family<br>member(s) | Publication<br>date                                                                                                                                                                                                             |
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