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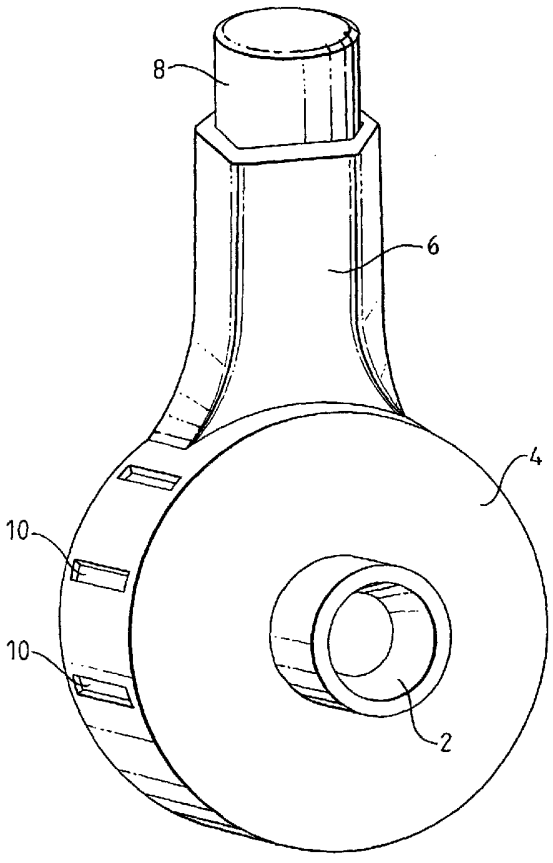
(54) Title: INHALERS



(57) Abstract: A metered dose inhaler for receiving a pressurised medicament canister (8) comprises a mouthpiece (2) and a cyclonic flow chamber (4) disposed between the canister and the mouthpiece (2). The flow chamber (4) is arranged so that upon inhalation by a user through the mouthpiece (2), a substantially planar cyclonic flow is generated in the flow chamber (4). The mouthpiece (2) is disposed generally centrally of this planar cyclonic flow.

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INHALERS

This invention relates to metered dose inhalers for delivering medicaments into the lungs of users.

Small, hand-held inhaler devices incorporating a pressurised canister of the required medicament have become a familiar and well used means of delivery directly into the lungs for drugs to treat a wide variety of conditions. As is well known the actual drug is expelled in a metered dose from the canister by depressing the hollow stem thereof into the body of the canister. The drug is typically carried by droplets of a volatile propellant which are inhaled by the user through their mouth.

It is well documented that this method of delivery is highly inefficient with only of the order of 10% of the dispersed dose actually reaching the user's lung. Of the remaining 90%, approximately 10% is deposited on the device itself or exhaled. The rest of the deficit (approximately 80% of the original dose) is accounted for by deposition of the droplets in the spray in the user's oral cavity and throat. This is a result of the high speed at which the droplets exiting the nozzle of the canister are travelling - typical anywhere between 50 m/s and 200 m/s. As the distance between the nozzle and the user's throat is only of the order of 50 mm, there is little attenuation of this speed, and little evaporation of the propellant from the drops which would reduce their momentum.

As well as being wasteful of the drug this deposition has a number of side effects. It can leave the user with a cold sensation in the throat due to subsequent evaporation of the propellant, as well as leaving an unpleasant taste in the mouth.

The sensation can also cause the user to cough, further reducing the amount of drug deposited in their

lungs. Some drugs when deposited in the mouth can give oral candidiasis or otherwise cause irritation of the throat. Moreover, some drugs such as inhalation corticosteroids can give systemic side effects if they are ingested instead.

There have been many proposals for overcoming the problems outlined above. One approach has been to suggest the use of a physical spacer between the pressurised canister and the point from which the user inhales. An example of such a proposal is shown in US 6435176.

The advantage of such arrangements is that the droplets travel a greater distance before entering the user's mouth which allows for a greater degree of evaporation of the propellant. The result of this is that the mean particle size entering the user's mouth is reduced which means that a greater proportion may be inhaled rather than striking the back of the throat.

Studies have borne out this advantage in terms of reduction in throat deposition. However, such spacers are by their nature bulky and cumbersome making them unsuitable to be carried at all times which it is often important for the users of such inhalers to do. They also tend to lead to high levels of the drug being deposited in the device without ever reaching the user.

Another approach has been to suggest arrangements in which air drawn into the device during inhalation is directed towards the spray exiting the canister. This is intended to encourage turbulent mixing and therefore greater evaporation and also to reduce the average velocity of the particles in the spray. An example of such a proposal is given in EP-A-0911048. However, these devices tend to suffer from the drawback in that they are relatively complicated and require several different parts which makes them uneconomic to mass-produce.

A yet further proposal is shown in WO 99/12596. In

this device the spray from the canister is introduced into a circular cavity and its momentum is used to drive a swirling vortex flow in the cavity to enhance evaporation and increase residence time. The user inhales the contents of the cavity diametrically opposite from where the spray is introduced.

None of the above proposals is entirely satisfactory and it is an aim of the present invention to provide an improved inhaler device. Thus when viewed from a first aspect there is provided a metered dose inhaler for receiving a pressurised medicament canister comprising a mouthpiece and a cyclonic flow chamber disposed between a pressurised canister received in use in the inhaler and the mouthpiece, the flow chamber being so arranged that upon inhalation by a user through the mouthpiece, a substantially planar cyclonic flow is generated in the flow chamber; wherein the mouthpiece is disposed generally centrally of said planar cyclonic flow.

Thus it will be seen by those skilled in the art that in accordance with the present invention, the spray exiting the pressurised canister is entrained into a cyclonic flow in the flow chamber and that the user draws off the particles entrained in air from the centre of the flow. The cyclonic flow is advantageous since it increases the residence time of the droplets in the inhaler and therefore allows for greater evaporation of propellant therefrom. As explained previously, this reduces the tendency of particles to be deposited at the back of the user's throat or in their mouth.

Furthermore, by drawing the inhaled particles from the centre of the cyclone, only the smaller particles, which are therefore easier to inhale will be drawn through the mouthpiece. Larger particles will circulate in larger diameter paths until sufficient propellant has evaporated that they move towards the centre of the flow and may therefore be inhaled through the mouthpiece.

The largest particles, those most undesirable for inhalation, are deposited around the inner peripheral edge of the chamber, by the centrifugal effect of the cyclone.

Effectively therefore the cyclone and centrally located mouthpiece act to filter out particles which are too big. The average size of the particles which may be inhaled through this filter will of course depend on the size and geometry of the flow chamber. Thus in accordance with the invention the proportion of droplets deposited in the throat and mouth may be significantly reduced.

Furthermore however, not only are larger particles advantageously prevented from reaching the user, those particles which are too large to be inhaled, but not so large as to be deposited centrifugally on the peripheral wall, are allowed to continue to circulate as they continue to reduce in size by evaporation of propellant. This means that these medium size particles are not necessarily wasted. It will be immediately apparent that any increase in the percentage of drug which is utilised will have clear benefits in terms either of the possibility of smaller canisters or of a longer useful life for traditional canisters.

It will be appreciated by those skilled in the art that by "cyclonic flow" is meant a fluid flow in which the air and entrained droplets generally form one main vortex in the chamber which is designed for this purpose. This is to be contrasted with flow in one or more vortices which is generally a turbulent phenomenon in which the vortices are substantially smaller than the flow considered. By a "substantially planar" cyclonic flow is meant a flow in which components of flow parallel to the axis of circulation are inconsequential in comparison to components normal to it, especially flow about the said axis.

The flow chamber preferably comprises a plurality

of circumferentially-spaced air inlets directed approximately tangentially in order to establish the required cyclonic flow when the user inhales through the mouthpiece. Clearly the size, number and spacing of these apertures will determine, for a given inhalation pressure differential, the characteristics of the cyclone, particularly its speed of circulation. The particular speed etc. required will of course depend on the particular application, but the dimensions of the inlets necessary to achieve this may be determined by the skilled person without difficulty, either empirically or using mathematical modelling techniques, well known *per se*, such as computational fluid dynamics.

The mode of introduction of the spray into the cyclonic flow may be chosen as required by the skilled person. For example, it may be arranged for the drug to be sprayed approximately tangentially to and in the same direction as the flow in order to ensure efficient entrainment. Alternatively the spray may be directed radially towards the flow in order to maximise the distance between the point at which it is introduced and the opposite wall of the chamber in a bid to reduce direct deposition onto the opposite wall.

In one set of preferred embodiments however the inhaler is arranged such that the spray enters the cyclonic chamber in the generally opposite direction to the cyclone's flow in the chamber, preferably substantially tangentially thereto. In accordance with this feature the impact of the circulating air in the chamber reduces the speed of the droplets in the spray. A reduction in the speed of the droplets is beneficial since it promotes evaporation and reduces the average speed of particles entering the user's mouth and throat. It also reduces deposition on the side wall of the chamber leading to a greater emitted dose from the device.

The Applicants have realised that for a given spray

velocity (typically between 50 and 200 metres per second) there is a trade-off in selecting the opposite velocity of the circulating air. Clearly a high opposite velocity will reduce direct deposition on the portion of the wall of the chamber opposite where the spray is introduced. On the other hand however, it will increase deposition around the side wall generally since the centrifugal effect will be enhanced. In preferred embodiments the cyclonic longitudinal velocity is arranged to be between approximately 1 m/s and 70 m/s, more preferably between 1 m/s and 10 m/s and most preferably approximately 2 m/s.

The Applicants have further appreciated that the shape of the spray exiting a standard pressurised canister is not optimised for spraying into a cyclone. For example, the spray tends to spread out at a greater angle than is ideal. In some preferred embodiments therefore means for shaping the flow of the spray is provided in its path. Such flow shaping means could take the form of a suitably shaped additional nozzle or one or more suitably shaped or positioned vanes. Preferably however, the flow shaping means comprises an impingement surface arranged to redirect the spray in a desired direction or range of directions.

Although flow shaping means may be provided in any design of inhaler in accordance with the invention, i.e. it is not essential that the spray is directed against the cyclonic air flow, the impingement surface is particularly suitable for use in designs where the spray is not directed against the flow, since the impingement surface will also have the effect of reducing the spray's velocity.

In fact in one preferred set of embodiments, the inhaler is arranged such that the spray is introduced into the cyclonic chamber towards the centre of the cyclone, with an impingement surface being provided which is arranged to direct the spray generally radially

thereof. This is advantageous since it achieves a reduction in spray velocity and an improvement in mixing of the spray with the cyclone without having to have a high circulating velocity. It may also give greater design freedom for the device and particularly allow a more compact device since the width of the inhaler is then governed only by the diameter of the cyclonic chamber. It will be appreciated by those skilled in the art that the precise shape of the cyclonic chamber is not essential, although a substantially circular chamber is considered most convenient.

In another set of particularly preferred embodiments, the inhaler comprises a plurality of nozzle outlets arranged to deliver the spray into the cyclonic chamber in a plurality of different directions. Such an arrangement effectively divides the spray into a plurality of smaller sprays. This has been found to aid dispersion of the droplets into the cyclonic air flow and to reduce their velocity. The greater spatial dispersion of the spray also enhances evaporation of the propellant by taking advantage of the greater availability of heat from the cyclonic chamber. The overall effect of this is that it decreases the amount of primary deposition - i.e. the proportion of the dose which is deposited on the walls of the chamber.

The nozzles are preferably equally spaced around an arc, most preferably substantially around 360 degrees.

The nozzles described above may be located at any position envisaged for a single nozzle, but preferably they are provided substantially on the axis of the flow chamber and are directed substantially radially. This allows efficient delivery of the sprays into the cyclonic flow, particularly when nozzles are provided all the way around the axis since the medicament may then be sprayed relatively evenly into all parts of the cyclonic flow at once.

Any number and size of nozzles may be provided to

suit the application, but it is presently preferred to provide at least four and more preferably at least six nozzles.

As has been previously explained, inhalers in accordance with the invention can filter out particles above a predetermined size so that only particles smaller than this can pass into the user's mouth and throat. The actual average size of particles which is desirable in a particular application will depend upon the medicament used and the condition being treated. For example, if it is required to get the medicament into the deep lung, a particle size of the order of 2 microns (2×10^{-6}m) or less is required. If, however, it is only required to get the medicament to the mid lung a particle size of the order of between 2 and 4 microns would be needed. Clearly the smaller the particle size that is needed, the greater the degree of filtration that must be achieved by the cyclonic chamber and this inevitably means that more of the drug will be deposited on the walls of the chamber. However, this is significantly more preferable than deposition on the back of the user's throat.

Certain preferred embodiments of the present invention will now be described, by way of example only, with reference to the accompanying drawings in which:

Figure 1 is a perspective view of a metered does inhaler in accordance with a first embodiment of the invention;

Figure 2 is a side cross-section through the inhaler of Fig. 1;

Figure 3 is a rear cross-section through the inhaler of Figure 1 at right angles to the view of Figure 2;

Figure 4 is a view similar to Figure 3 showing the flow of air;

Figure 5 is a side cross-section showing a second embodiment of the invention;

Figure 6 is a side cross-section showing a third embodiment;

Figure 7 is a cross-section of a fourth embodiment;

Figure 8 is a cross-section of a fifth embodiment of the invention; and

Figure 9 is an enlarged view of the nozzle moulding of Figure 8.

Turning firstly to Figure 1, there may be seen a metered dose inhaler comprising broadly a mouthpiece 2, a squat cylindrical chamber 4 and a radially extending canister holster 6. The mouthpiece 2 is arranged coaxially with the cyclonic chamber 4 and projects outwardly from it. The canister holster is sized and shaped to receive a standard pressurised medicament canister 8 capable of delivering metered doses of the medicament together with a propellant. A series of tangentially directed openings 10 are provided around the circumference of the cyclonic chamber 4. Further appreciation of the internal construction of the embodiment of Figure 1 may be achieved by considering the cross-sections in Figures 2 and 3.

As may been seen in Figure 2, in the base wall 12 of the canister holster 6 is a socket 14 which receives the nozzle tube 16 of the pressurised canister 8. The end of the nozzle 16 rests against an internal shoulder in the socket 14.

In use the user places his or her lips around the mouthpiece 2 and begins to inhale. The reduction in pressure inside the cyclonic chamber sucks in air through the tangential air inlets 10. The tangential inward flow of air causes a swirling body of air to be generated. It will be appreciated that as a result of the shape of the chamber 4, this cyclonic flow will be essentially planar - i.e. net momentum parallel to the axis of the chamber is less significant than azimuthal flow. The flow may be seen in Fig. 4.

The user will then depress the upper end of the

canister 8. Since the nozzle 16 is in abutment with the shoulder in the socket 14, the body of the canister 8 will be moved down, forcing the nozzle into the body to deliver a metered dose of drug in a spray of propellant droplets as is well known in the art. The droplets in the spray exit at an average velocity of approximately 200 metres per second into the cyclonic chamber 4. The flared shape of the lower end 14a of the nozzle socket helps to allow the spray to disperse laterally as much as possible to avoid an undesirably narrow spray shape. As the spray droplets meet the swirling air, their average speed is significantly reduced by the air's momentum. Most of the spray is therefore entrained into the circulating flow although inevitably a small proportion is deposited directly into the region of the chamber wall 4a opposite the nozzle 16. As well as reducing the speed of the droplets, the forced mixing with a moving body of air accelerates evaporation of the volatile propellant. This reduces the average size and mass of the droplets.

In spite of the above, the largest droplets in the spray have too great a mass to continue in the circulatory flow and these are deposited harmlessly onto the inner walls of the chamber 4. The smallest particles will migrate towards the centre of the circulating flow where they can be drawn through the mouthpiece 2 and into the user's lungs. Thus the cyclonic flow in the chamber 4 filters out all but the smallest particles. In addition to this, their speed is reduced by impact of the spray. The combination of these factors means that deposition of spray droplets in the oral cavity and at the back of the throat is significantly reduced compared to prior art devices, so that the vast majority of the droplets inhaled by the user through the mouthpiece of the inhaler reach the user's lungs.

Furthermore, the medium-sized particles in the

circulating flow in the chamber 4, i.e. those not so large as to be deposited on the chamber walls, but too large to circulate in the central region of the chamber where they can be drawn through the mouthpiece, will gradually reduce in size through evaporation of propellant as they travel round. Since the equilibrium orbit diameter for a particle is proportional to its mass, as propellant evaporates and it becomes smaller and lighter, it will migrate to ever decreasing orbits until it is circulating beneath the mouthpiece and can therefore be inhaled. This means that the proportion of drug wasted is reduced.

A second embodiment of the invention is shown in Figure 5. In this embodiment rather than the spray from the nozzle 16 being delivered directly into the cyclonic chamber 4', it is conveyed by a short horizontal channel 18 radially into the chamber 4' opposite the mouthpiece 2'. At the end of the channel 18 is a generally conical baffle 20, the surface of which forms an impingement surface 22.

Operation of the device shown in Figure 5 is the same as previously described except that the spray from the nozzle 16 is conveyed into the conical impingement surface 24 and so is dispersed laterally, in all directions, into the cyclonic air flow in the chamber. This helps to promote better mixing between the spray and the air flow and thus enhances evaporation of the propellant. Also, the change of direction of the spray caused by the baffle 20 helps to reduce the speed of the particles in the spray. This embodiment reduces the proportion of the drug which is deposited on the walls of the chamber, but not at the expense of greater oral and throat deposition since it still has the advantages of a reduction in speed of the particles and filtering out larger particles.

The embodiment of Figure 6 uses a similar principle to that of Figure 5, i.e. the spray is directed via a

channel 18' onto an impingement surface, 24 which in this embodiment has a "crown" shape with a central peak and peripheral raised rim, to be laterally dispersed into the circulating air flow in the chamber 4". The main difference over the embodiment of Figure 4 however is that the spray is introduced by the channel 18' into the same side as the mouthpiece 2", indeed coaxially with it, rather than the opposite side. This necessitates provision of the holster canister 6" on the same side of the chamber 4" as the mouthpiece 2" and lengthening of the mouthpiece 2". A series of radial spokes 26 support the channel 18' in the mouthpiece 2". It will be appreciated that in this embodiment there is no opportunity for droplets to travel directly from the channel to the mouthpiece. Furthermore, the longer mouthpiece gives an additional benefit in enhancing evaporation prior to passing into the user's mouth (as is known *per se*) which allows the threshold size of particle which is filtered out by the cyclone to be increased slightly. This arrangement may also allow a more compact design for the overall outer casing.

Figure 7. is a cross-section through a further embodiment of the invention. It will be seen that this embodiment is similar to that of Figs. 1 to 4 except that the axis of the canister holster 6''' is laterally offset from the centre of the cyclonic chamber 4'''. This means that rather than the spray being directed essentially radially towards the cyclonic flow of air in the chamber, it is directed essentially tangentially towards it. It will further be noted that the direction of the offset is such as to ensure the spray is travelling in substantially the opposite direction to the airflow. This maximises the impact between the spray and the air and therefore maximises the reduction in average particle velocity and the degree of mixing therebetween.

Figures 8 and 9 show a further embodiment of the

invention. This embodiment is similar to the embodiment of Figure 5 except that instead of the conical baffle 20, a moulding 28 (shown in greater detail in Fig. 9) having a plurality of nozzles 30 is formed at the end of the channel 18. The moulding 28 has a series of six nozzles 30 equally spaced around the moulding and therefore around the axis of the cyclone chamber 4'.

In use the particle/propellant mix ejected from the canister 8 will be sprayed from the nozzles 30 in the form of six small sprays into all parts of the cyclonic air flow. The reduction of the average particle speed by nozzle moulding 28 means that fewer particles have such a great speed that they are deposited on the inner walls of the cyclone chamber 4'. The greater spatial dispersion of the spray also enhances evaporation of propellant from the particles by better utilising the heat available in the cyclone chamber 4'. This helps to increase the fine particle dose.

Example 1

Tests were carried out on the embodiment shown in Fig. 7. The test device had a cyclonic chamber 4''' with a diameter of 35 millimetres and a depth (from front to rear) of 20 mm. The diameter of the mouthpiece 2 was 18 mm and the total area of the tangential air inlets (not shown in Fig. 7 but denoted by 10 in Figs. 1 and 2) was 24 mm^2.

Inhalation by a user was simulated by coupling the device to a standard Multiple Stage Liquid Impinger. A reduced pressure was applied to the mouthpiece 2 such as to give a flow rate of 30 litres per minute. It was found that a cyclone was set up in the cyclonic chamber having a maximum flow velocity of approximately 50 metres per second. A single dose of medicament was dispensed from a standard canister and the dose emitted from the mouthpiece 2 was measured. This emitted dose

was found to have a fine particle fraction of 77% - that is to say that 77% of the particles in the emitted dose were 5.8 microns or less. The dose was drawn into the simulated throat cavity from which a throat deposition percentage of just 2% was measured. This is clearly in stark contrast to known metered dose inhalers in which this proportion is of the order of 80%.

Example 2

A further test was carried out on the embodiment shown in Figs. 8 and 9. The test device had a cyclone chamber 4' which had a diameter of 50 mm and a depth of 20 mm. Six circumferentially spaced nozzles 30 were provided in the moulding 28, the diameter of each being 0.19 mm. A flow rate of solution from the canister of 90 litres per minutes was used. The inhalation parameters were as in Example 1. In this example a fine particle dose of 45% was achieved and an oropharyngeal deposition of 16% of the metered dose both of which represent considerable improvements over the prior art.

Claims:

1. A metered dose inhaler for receiving a pressurised medicament canister comprising a mouthpiece and a cyclonic flow chamber disposed between a pressurised canister received in use in the inhaler and the mouthpiece, the flow chamber being so arranged that upon inhalation by a user through the mouthpiece, a substantially planar cyclonic flow is generated in the flow chamber; wherein the mouthpiece is disposed generally centrally of said planar cyclonic flow.

2. An inhaler as claimed in claim 1 wherein the flow chamber comprises a plurality of circumferentially-spaced air inlets.

3. An inhaler as claimed in claim 2 wherein said inlets are directed approximately tangentially.

4. An inhaler as claimed in claim 1, 2 or 3 such that a spray from the canister enters the cyclonic chamber in a generally opposite direction to the cyclonic flow in the chamber.

5. An inhaler as claimed in claim 4 wherein the spray is arranged to enter the chamber substantially tangentially to said cyclonic flow.

6. An inhaler as claimed in any preceding claim comprising means for shaping the flow of spray from the canister.

7. An inhaler as claimed in claim 6 wherein the flow shaping means comprises an impingement surface arranged to redirect the spray in a desired direction or range of directions.

8. An inhaler as claimed in any of claims 1 to 3 arranged such that spray from the canister is introduced into the cyclonic chamber towards the centre of the cyclone, said inhaler comprising an impingement surface arranged to direct the spray generally radially thereof.

9. An inhaler as claimed in any of claims 1 to 3 comprising a plurality of nozzle outlets arranged to deliver spray from the canister into the cyclonic chamber in a plurality of different directions.

10. An inhaler as claimed in claim 9 wherein the nozzle outlets are equally spaced substantially around 360 degrees.

11. An inhaler as claimed in claim 9 or 10 wherein said nozzle outlets are provided substantially on the axis of the flow chamber and are directed substantially radially.

12. An inhaler as claimed in claim 9, 10 comprising at least four nozzle outlets.

13. An inhaler as claimed in any preceding claim wherein the cyclonic longitudinal velocity is arranged to be between approximately 1 metre per second and 70 metres per second, preferably between 1 m/s and 10 m/s and most preferably approximately 2 m/s.

AMENDED CLAIMS

[received by the International Bureau on 21 April 2004 (21.04.04);
original claim 1 replaced by new claim 1;
remaining claims unchanged (1 page)]

1. A metered dose inhaler for receiving a pressurised medicament canister comprising a mouthpiece and a cyclonic flow chamber disposed between a pressurised canister received in use in the inhaler and the mouthpiece, the flow chamber being so arranged that upon inhalation by a user through the mouthpiece, a substantially planar cyclonic flow is generated in the flow chamber; wherein the mouthpiece is disposed to draw generally centrally from said planar cyclonic flow.

2. An inhaler as claimed in claim 1 wherein the flow chamber comprises a plurality of circumferentially-spaced air inlets.

3. An inhaler as claimed in claim 2 wherein said inlets are directed approximately tangentially.

4. An inhaler as claimed in claim 1, 2 or 3 such that a spray from the canister enters the cyclonic chamber in a generally opposite direction to the cyclonic flow in the chamber.

5. An inhaler as claimed in claim 4 wherein the spray is arranged to enter the chamber substantially tangentially to said cyclonic flow.

6. An inhaler as claimed in any preceding claim comprising means for shaping the flow of spray from the canister.

7. An inhaler as claimed in claim 6 wherein the flow shaping means comprises an impingement surface arranged to redirect the spray in a desired direction or range of directions.

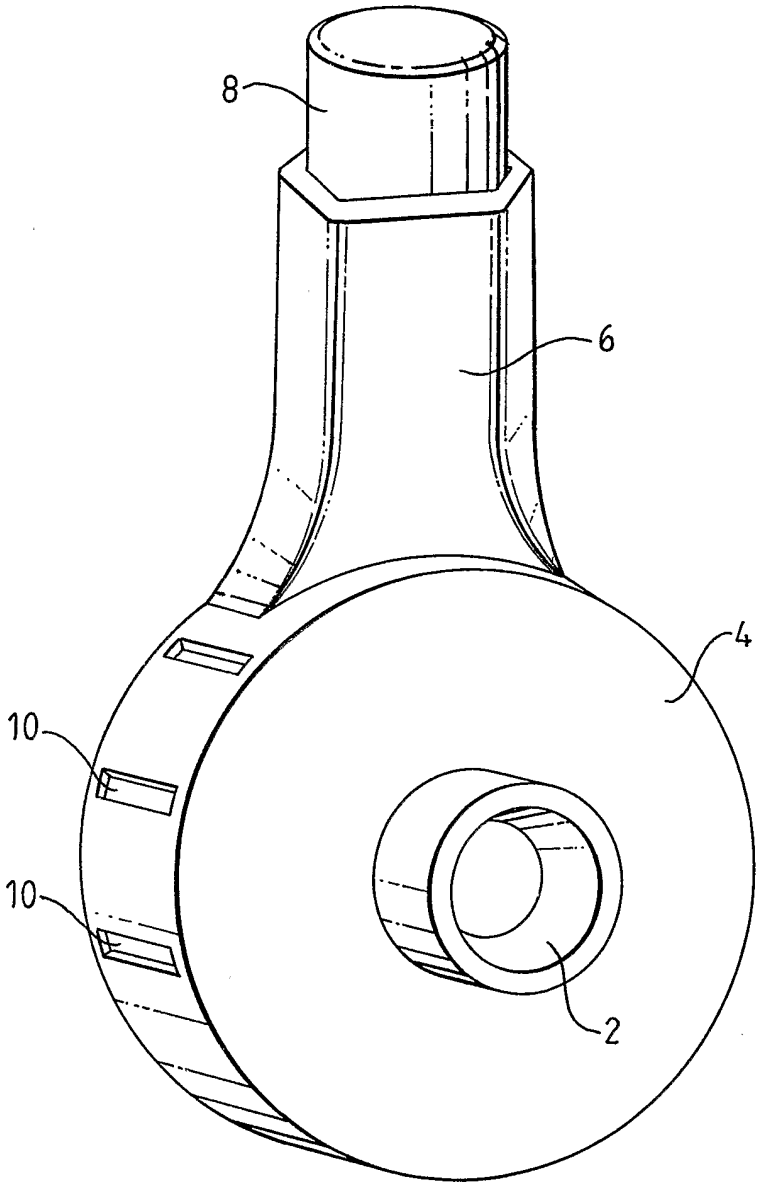

FIG. 1

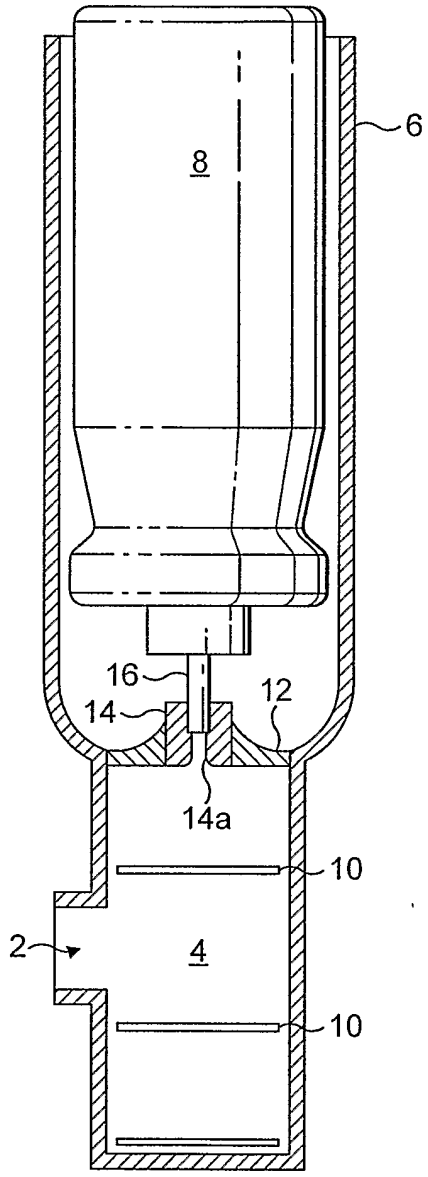

FIG. 2

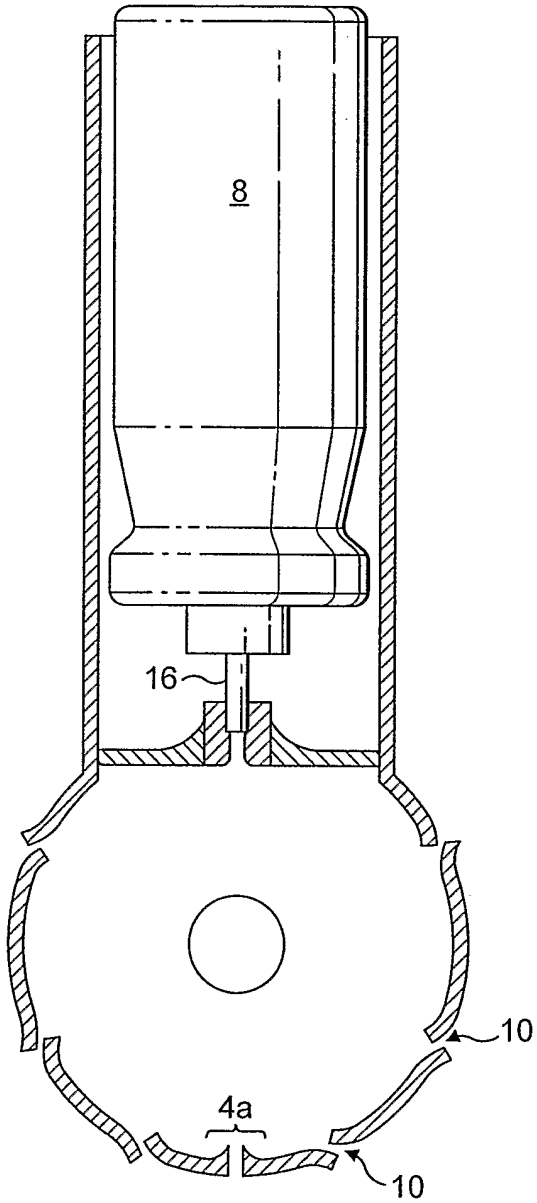

FIG. 3

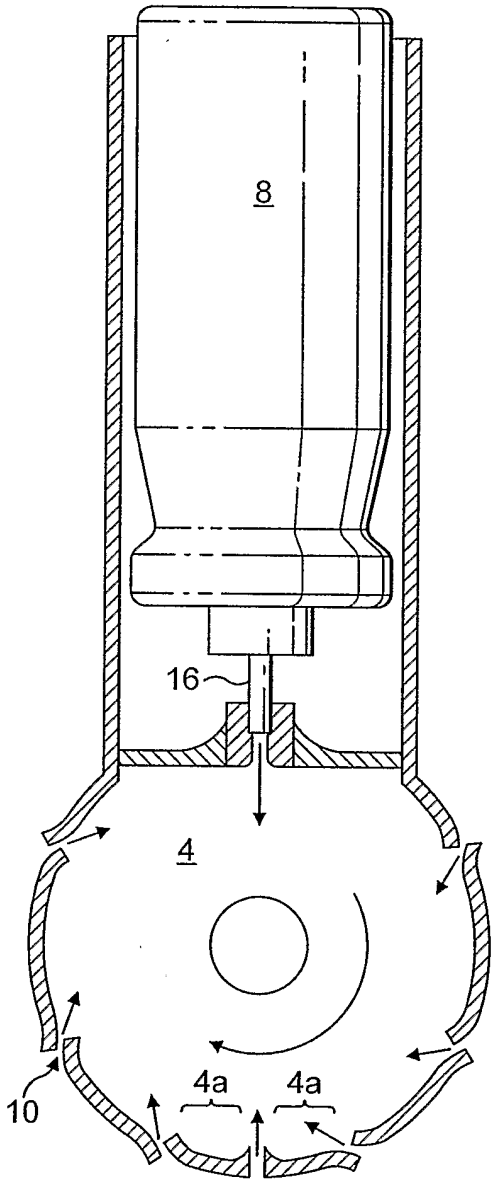

FIG. 4

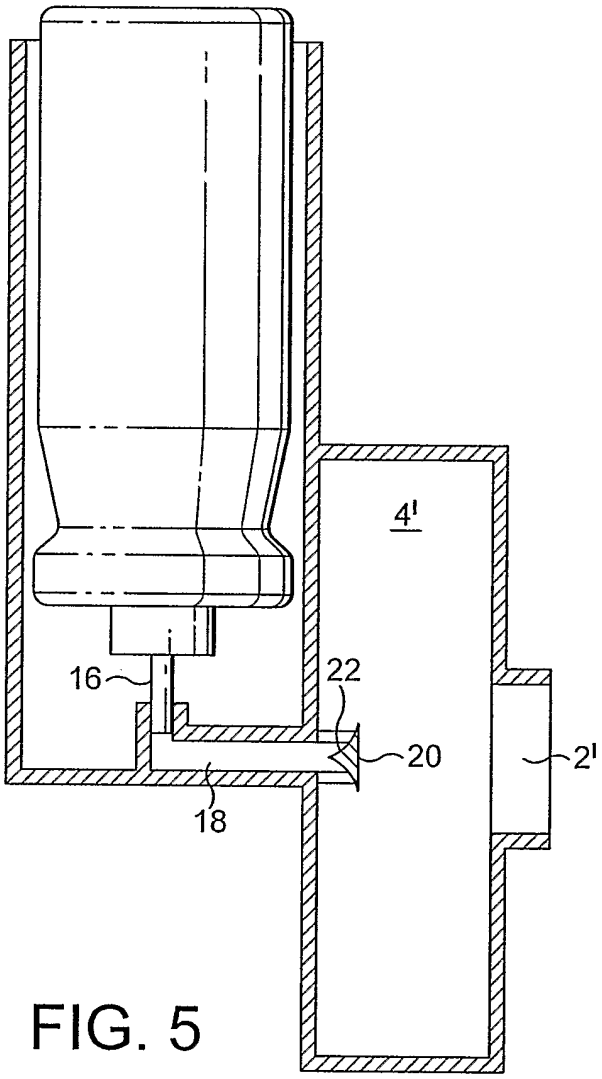

FIG. 5

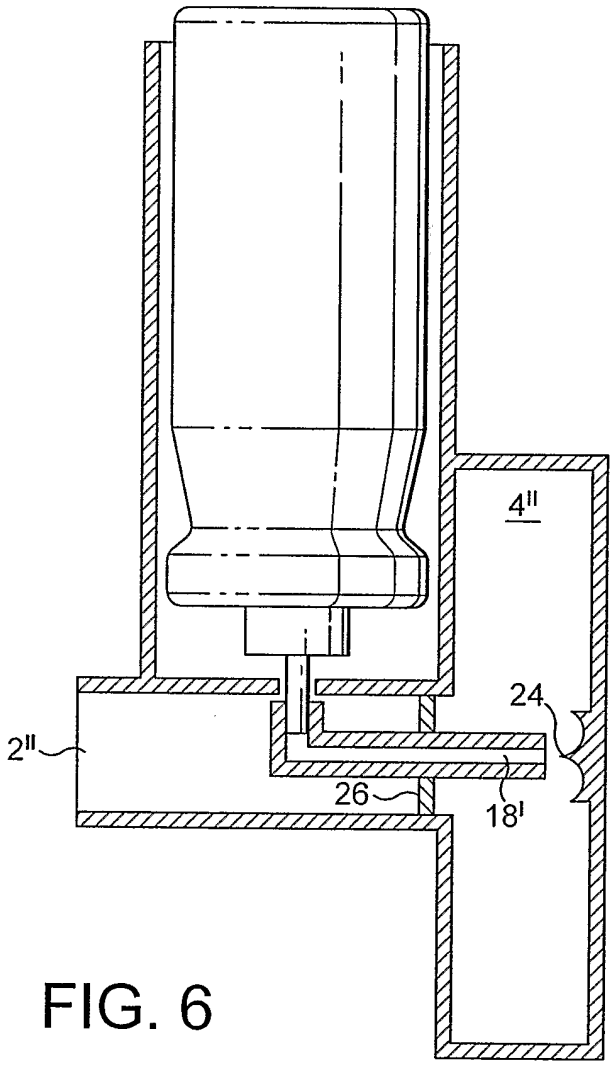

FIG. 6

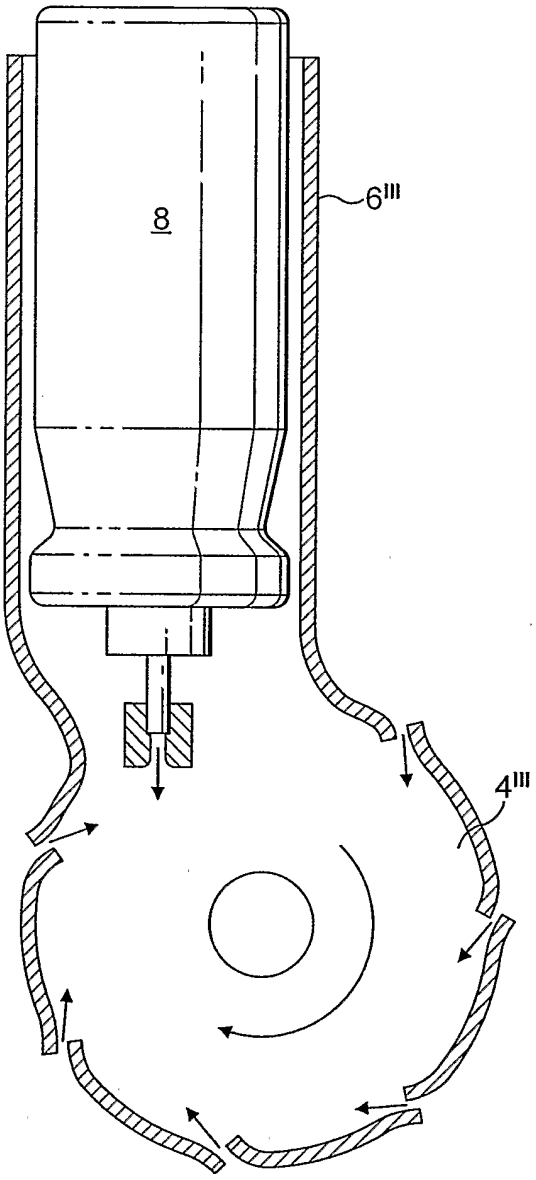

FIG. 7

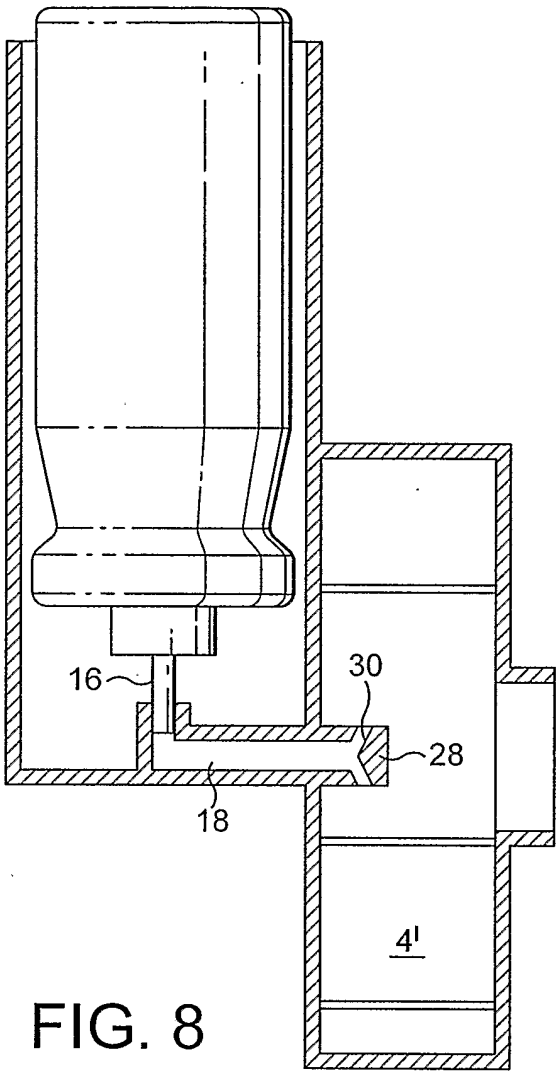

FIG. 8

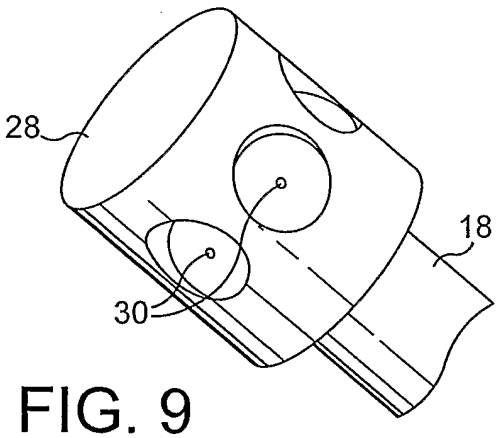

FIG. 9

INTERNATIONAL SEARCH REPORT

International Application No
PCT/GB 03/04748

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61M15/00

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

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A61M

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, WPI Data, PAJ

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 01 36033 A (SYSTEMIC PULMONARY DELIVERY LT) 25 May 2001 (2001-05-25) page 9, line 24 -page 13, line 32 figures	1-3,6,13
A		4,8
X	EP 1 010 438 A (BESPAK PLC) 21 June 2000 (2000-06-21) column 3, line 3 -column 5, line 16 figures 1-6	1,6,13
A	EP 0 839 544 A (BESPAK PLC) 6 May 1998 (1998-05-06) column 3, line 3 -column 4, line 33 figures	1-3

-/--

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

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Date of the actual completion of the international search	Date of mailing of the international search report
13 February 2004	25/02/2004

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Azaïzia, M

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INTERNATIONAL SEARCH REPORT

International Application No
PCT/GB 03/04748

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication,where appropriate, of the relevant passages	Relevant to claim No.
X	WO 98 26827 A (INNOVATA BIOMED LTD ;BRAITHWAITE PHILIP (GB)) 25 June 1998 (1998-06-25) page 13, line 24 -page 15, line 7 figures 9-9D	1,6-10, 12,13

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INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/GB 03/04748

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 0136033 A	25-05-2001	US 6367471 B1	09-04-2002
		AU 2749201 A	30-05-2001
		CA 2389535 A1	25-05-2001
		CN 1387447 T	25-12-2002
		EP 1225943 A2	31-07-2002
		JP 2003513763 T	15-04-2003
		NO 20022051 A	28-06-2002
		TR 200201176 T2	21-08-2002
		WO 0136033 A2	25-05-2001
EP 1010438 A	21-06-2000	GB 2344533 A	14-06-2000
		EP 1010438 A1	21-06-2000
		US 6336455 B1	08-01-2002
EP 0839544 A	06-05-1998	GB 2318737 A	06-05-1998
		DE 69723202 D1	07-08-2003
		EP 0839544 A2	06-05-1998
		US 6062214 A	16-05-2000
WO 9826827 A	25-06-1998	US 6347629 B1	19-02-2002
		AU 7735998 A	15-07-1998
		DE 69708327 D1	20-12-2001
		DE 69708327 T2	04-07-2002
		EP 0959926 A1	01-12-1999
		ES 2167800 T3	16-05-2002
		WO 9826827 A1	25-06-1998
		JP 2001506885 T	29-05-2001