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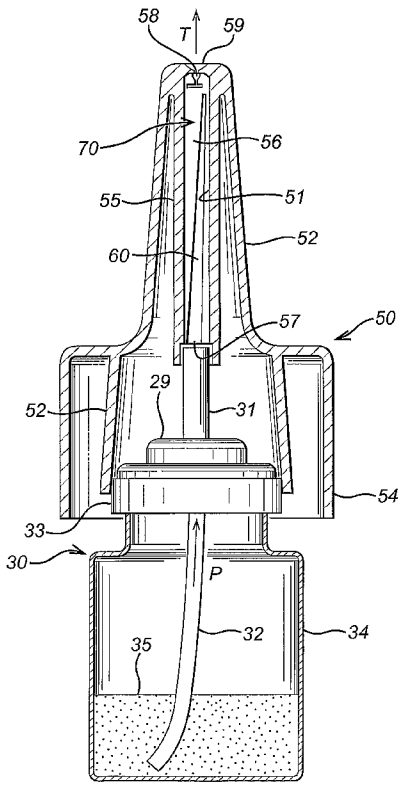
(54) Title: NOZZLE FOR A NASAL INHALER



(57) Abstract: There is provided a nasal dispensing nozzle (70) for use with a fluid medicament discharge pump device (30) having a discharge outlet (31) for discharge of pumped fluid medicament (35), the nasal dispensing nozzle comprising a body (56) defining a fluid flow channel (60), - an inlet port (57) defining an inlet to said channel, said inlet port shaped for receipt of said discharge outlet to enable delivery of said pumped fluid medicament to the channel; and an outlet port (58) defining an outlet from the channel. The channel is shaped to impart acceleration and angular momentum to the pumped fluid medicament. The body is comprised of a mating assembly of like component parts and suitably, defines a cylindrical form.

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Nozzle for a nasal inhaler

The present invention relates to a nozzle for use with a fluid dispensing device for nasal administration of medicament.

It is well known to provide a medicament dispenser device in which a fluid medicament formulation is dispensed as a spray via a nozzle to the nasal cavity of a user. In general, the fluid is delivered to the nozzle upon the application of user force to a fluid pumping mechanism. Such nasal dispensers may be arranged to dispense a single dose or may alternatively be arranged with a fluid reservoir from which individual metered doses may be pumped. A general example of such a pump action nasal inhaler device is shown and described in US Patent 4,946,069.

It is a problem with such pump action nasal spray devices that the characteristics of the spray are to an extent dependent upon the manner of actuation by the user. If the user actuates the device in a slow or lethargic manner then the dispensing of the fluid may be less spray-like than required for effective delivery to the nasal cavity. If the rate of discharge is too low full atomisation may not occur and the spray undesirably comprises of relatively large droplets of fluid. In extreme cases, no spray is produced and the fluid simply dribbles out from the tip of the nozzle.

To improve spray characteristics, it is known to be advantageous to provide a feature to the nozzle which causes acceleration and swirling of the fluid prior to its dispensing from the nozzle as a spray. Conventionally, the inner part of the nozzle provides a housing that defines an acceleration chamber and a separate shaped insert is provided to the chamber. The insert is shaped to cause the fluid to spin or swirl prior to it being dispensed from the tip and generally takes the form of a multi-bladed propeller-shaped swirl insert.

The Applicant has appreciated that the use of a separate swirl insert can give rise to certain manufacturing challenges. In particular, the performance of the swirl insert depends to an extent upon the accuracy of its fitting within the acceleration chamber. Variation in manufacturing tolerances in the shape and sizing of both the housing defining the acceleration chamber and the swirl insert can affect swirl performance as can variation in the fitting / location of the swirl insert within the chamber. Potential issues relating to manufacturing tolerances are only exacerbated by the small size of the swirl insert, which is typically sized to have a diameter of 2-3 millimetres. The Applicant has therefore realized the desirability of forming the housing and swirl insert as a composite part.

The Applicant has however, further appreciated that different challenges exist in forming the acceleration chamber and swirl insert as a single composite part. For mass production, moulding is the preferred manufacturing process, but the complex shaping of the inner (swirl) features of such a single composite part preclude the use of moulding as a manufacturing method. In essence, the problem is that it is impossible (or at least exceptionally difficult) to create a suitable mass production tool for moulding a single part that has the required inner acceleration / swirl features.

As a solution, the Applicant has therefore devised a composite part that may impart acceleration and swirl characteristics to a fluid wherein the composite part is defined by a mating assembly of like component parts. In particular, the composite part may be formed from two like mating halves or alternatively, from three like mating thirds, wherein each component part is shaped with both acceleration and swirl creating features. Preferably, the overall composite part defines an essentially cylindrical form such that each mating half of the two-part form defines a 180° segment of the cylinder or alternatively, each mating third of the three-part form defines a 120° segment of the cylinder.

It is an object of this invention to provide a nozzle for use in a fluid dispensing device that provides effective spraying from the nozzle.

It is a further object of this invention to provide a nozzle for use in a fluid dispensing device that on manufacture does not require the bringing together of separate acceleration chamber housing and swirl insert parts.

Applicant's co-pending PCT patent application no. WO 2004/094068 describes a nasal dispensing nozzle comprising a body defining a fluid flow channel; an inlet port defining an inlet to said channel, the inlet port shaped for receipt of said discharge outlet to enable delivery of said pumped fluid medicament to the channel; and an outlet port defining an outlet from said channel, the outlet port shaped for insertion into the nasal cavity of a user to enable delivery of the pumped fluid medicament thereto. A screw thread path is provided to the channel between the inlet and said outlet to impart angular momentum to the pumped fluid medicament.

According to one aspect of the present invention there is provided a nasal dispensing nozzle for use with a fluid medicament discharge pump device having a discharge outlet for discharge of pumped fluid medicament, the nasal dispensing nozzle comprising

a body defining a fluid flow channel;

an inlet port defining an inlet to said channel, said inlet port shaped for receipt of said discharge outlet to enable delivery of said pumped fluid medicament to the channel; and

an outlet port defining an outlet from the channel,

wherein the channel is shaped to impart acceleration and angular momentum to the pumped fluid medicament, and wherein the body is comprised of a mating assembly of like component parts.

The term acceleration herein is used to have its conventional meaning of speeding up. The term angular momentum is meant to encompass the terms spin and/or swirl and may occur in either a clockwise or anti-clockwise sense. In the nozzle herein, the pumped fluid medicament experiences acceleration and spin / swirl as a result of its experience of being pumped through the channel (from the inlet to the outlet).

The present invention provides a nozzle for use with a nasal dispensing device for use in dispensing fluid form medicament to the nasal cavity of a user. The nozzle generally forms a component (either separable or integral) of a fluid medicament dispensing device, and the present invention therefore also provides a fluid medicament dispensing device incorporating the nozzle herein.

The nozzle is suitable for use with a fluid medicament discharge pump device having a discharge outlet for discharge of pumped fluid medicament. The fluid medicament discharge pump is generally comprised within a fluid medicament dispensing device as an integral or separable part thereof.

The nasal dispensing nozzle comprises a body defining a fluid flow channel. In use, the channel acts to guide the flow of fluid form medicament through the nozzle for dispensing therefrom. Embodiments are envisaged which comprise plural fluid flow channels (e.g. from two to five, preferably from two to three fluid flow channels). Each fluid flow channel is suitably defined as an enclosed volume (i.e. space) within the body.

The exterior of the body is generally shaped for engagement with a suitable fluid medicament discharge pump device (e.g. incorporated within a fluid medicament dispensing device).

The body is provided with an inlet port defining an inlet to the fluid flow channel. The inlet port is shaped for receipt of the discharge outlet of a fluid discharge pump device to enable delivery of pumped fluid medicament to the channel.

The body is also provided with an outlet port defining an outlet from the fluid flow channel for dispensing there from. The outlet port, which generally takes the form of a tip to the nozzle may be shaped for insertion into the nasal cavity of a user to enable delivery of the pumped fluid medicament thereto.

Suitably, the exterior of the body is shaped to define an overall cylindrical profile (i.e. it is in the form of a cylinder). Thus, the nasal dispensing device with which it is to be used suitably defines a cavity of corresponding cylindrical inner profile for receipt of the body of the nozzle.

The fluid flow channel is shaped to impart acceleration and angular momentum to the pumped fluid medicament.

Suitably, the fluid flow channel defines a screw path. That is to say, it has the general (i.e. helical) form of a screw, which may follow either a clockwise or anti-clockwise screw path direction. The path generally comprises from half to five complete (i.e. 360°) screw turns, which a fluid will experience as it travels from the inlet to the outlet.

The screw path generally extends in symmetric fashion about a defined screw axis. Suitably, the screw axis corresponds to the pumping axis defined by the pump of the fluid discharge device. Suitably, the fluid flow channel defined by the body of the nozzle is also symmetric about the screw axis. Suitably, the body of the nozzle further has an overall form that is symmetric about the screw axis, for example defining a cylindrical form about the screw axis.

The body may define a single screw path. In other aspects however, multiple screw paths are defined, wherein generally each is arranged about a single (i.e. common) screw axis and in complementary fashion to the other. Typically, from two to five, particularly from two to three threaded screw paths are defined. The number of screw paths may correspond to the number of like component parts of the mating assembly that defines the body.

Preferably, the flow path of the fluid flow channel is arranged decrease in cross-sectional area from the entrance thereto (i.e. at the inlet) to the exit thereto (i.e. at the outlet). The volume available to the fluid pumped there through progressively decreases and acceleration of the flow of the fluid therefore results. The decrease in cross-sectional area from entrance to exit may be achieved by progressively reducing the effective diameter of the fluid flow channel. In one aspect, the decrease in cross-sectional area is achieved by tapering the fluid flow channel.

The body of the nozzle herein is comprised of a mating assembly of like component parts. The body thus, comprises a composite part formed when the component parts thereof are brought together in mating fashion as an assembly. Each like component part is shaped to define part of the fluid flow channel and to provide both acceleration and angular momentum imparting features to that channel.

By like component parts it is meant that each component part has a similar overall form such that an assembly may be formed. The component parts are in one aspect, configured as mirror images, one of the other.

Suitably, the mating assembly that defines the body is formed from two mating halves or alternatively, from three mating thirds.

Preferably, the mating assembly that defines the body defines an essentially cylindrical form such that each mating half of the two-part form defines a 180° segment of the cylinder or alternatively, each mating third of the three-part form

defines a 120° segment of the cylinder. Corresponding four (90°) and five (72°) part assemblies may also be envisaged, although it will be appreciated that increasing the number of component parts increases the complexity of assembly of the overall composite part.

Preferably, each like component part is amenable to manufacture by a moulding process such as an injection moulding process. Preferably, each like component part is comprised of a polymeric material that may be readily moulded. Moulding tools suitable for the manufacture of the like component parts form another aspect of the invention described herein.

Suitably, the body further defines a shaped outlet locating upstream of the fluid flow channel. Thus, the spinning and/or swirling fluid is delivered to the shaped outlet prior to its delivery in use, to the nasal cavity of the user. The shaped outlet is suitably arranged to define a tapered (e.g. fanned out) profile.

In one aspect, the outlet (e.g. shaped outlet) of the dispensing nozzle is provided with a reversible stopper. The stopper acts such as to prevent drain back of delivered fluid from the dispensing nozzle (in particular, from the area at the tip of the nozzle and generally adjacent to the dispensing outlet). The stopper is reversibly mountable to the nozzle (e.g. at the tip) and may have any suitable shape including disc shaped, wherein the disc may be flat, or in aspects have a convex or concave form.

It will be appreciated that the stopper is generally shaped for effective sealing engagement with the outlet of the dispensing nozzle (i.e. that area proximal to the dispensing orifice) and therefore that the shaping of the stopper may be arranged to inversely mirror that of the nozzle outlet.

The stopper may be formed from any suitable material including those with plastic properties, particularly those with resilient properties. Stoppers made from synthetic and naturally occurring polymers including rubber are herein envisaged.

According to another aspect of the present invention there is provided a housing assembly for reversible receipt of a fluid medicament discharge device for spraying a fluid medicament into a nasal cavity, the housing assembly comprising a housing defining a cavity; and engageable with said housing, a dispensing nozzle as described herein.

There is thus, also provided a fluid medicament dispensing device comprising a housing assembly as described above and received thereby, a fluid medicament discharge pump device.

In use, a fluid discharge device typically houses in the cavity, and in combination the housing assembly and fluid discharge device comprise a fluid dispensing device. Alternative embodiments are envisaged in which the fluid discharge device is either integral with or reversibly removable from the housing assembly of the fluid dispensing device.

The fluid discharge device typically has a hollow casing defining a reservoir for containing a volume of fluid and a pump having a suction inlet extending within the hollow casing, the pump having a discharge outlet extending from a first end of the hollow casing for co-operation with the dispensing nozzle to enable pumped delivery of fluid from the reservoir to the dispensing nozzle.

It will be appreciated that in general operation of the fluid discharge device relative movement between the hollow casing and the pump acts such as to pump fluid from the fluid reservoir into the dispensing nozzle for dispensing therefrom. The fluid reservoir typically contains several doses of fluid form medicament.

In aspects, the pumping is metered. For example, each pumping action results in delivery of a single dose of fluid from the reservoir to the nozzle.

Suitably for metered delivery, the pump includes a plunger, which is slideable in a metering chamber located within the hollow casing, the metering chamber being sized to accommodate a single dose of fluid.

Suitably, the pump comprises a pre-compression pump. Typically, such pre-compression pumps are used with a bottle (glass or plastic) capable of holding 8-50ml of a formulation. Each spray will typically deliver 50-100µl of such a formulation and the device is therefore capable of providing at least 100 metered doses.

The fluid medicament dispensing device may further comprise a protective end cap having an inner surface for engagement with the housing. The end cap is moveable from a first position in which it covers the nozzle to a second position in which the nozzle is uncovered.

In one aspect, a stopper locates on the end cap such that when the end cap is in the first (i.e. protective) position the stopper engages the nozzle to seal the nozzle orifice and thereby prevent drain back. In the second (i.e. in-use position) the stopper is disengaged from the nozzle such that the nozzle orifice is no longer sealed.

The stopper may form an integral part of the end cap or alternatively, the stopper may mount to the end cap. Any suitable method of mounting is envisaged including adhesive, snap-fit and weld mounting.

In general, the stopper locates in the inner part of the end cap. In one aspect, the inner part of the end cap is provided with annular walls defining a cavity for receipt of the stopper as an insert thereto. The stopper insert may be simply be mechanically inserted or it may be adhesively or otherwise fixed.

Suitable stopper insert forms may be formed in a variety of ways. In one aspect, a rubber disc-shaped stopper is stamped from a sheet of rubber. In another aspect, a disc-shaped stopper is moulded (e.g. by an injection moulding process). In a further aspect, the protective end cap is moulded and the stopper is then moulded within the formed end cap (i.e. a 'two shot' moulding process).

The hollow casing of the fluid medicament dispensing device may take any suitable form. Suitably, several lugs are formed on the hollow casing for engagement with complementary projections formed on the inner surface of the end cap, each of the lugs being arranged to extend through a longitudinally extending slot formed in the side wall of the body.

In one aspect, the hollow casing may have at least one outwardly extending detent for engagement with a complementary recess formed in the inner surface of the end cap so as to releasable hold the end cap in position on the body. Each detent may extend through a respective longitudinally extending slot in the body for engagement with the respective recess formed in the end cap.

According to a still further aspect of the present invention there is provided a kit of parts comprising a housing assembly as described above and a fluid discharge device receivable thereby. It is also envisaged that the housing assembly could be supplied as a separate item, into which a user or pharmacist later fits a suitable fluid discharge device.

It will be appreciated that whilst the present invention has been particularly described in terms of a nozzle suitable for delivery of fluid medicament to a nasal cavity, that variations of the invention are possible to enable delivery into other body cavities (e.g. the ear or eye).

The invention will now be described further with reference to the accompanying drawing in which:-

Figure 1 is a cross-sectional view of a dispensing nozzle herein in engaging contact with a fluid medicament discharge pump device;

Figure 2 shows a perspective view of one like mating half of a first nozzle herein;

Figure 3a shows a perspective view of the first nozzle herein formed by bringing together two like mating halves of the type as shown in Figure 2;

Figure 3b shows a perspective view of the first nozzle of Figure 3a as inverted to show the features of its lower end;

Figure 4 shows a cross-sectional view of the first nozzle of Figure 3a wherein for each like mating half thereof the cross-section is taken about plane X-X' of Figure 2;

Figure 5 shows a side view of details of the top part of the like mating half of Figure 2;

Figure 6 shows a perspective view of one like mating third of a second nozzle herein;

Figure 7a shows a perspective view of the second nozzle herein formed by bringing together three like mating thirds of the type as shown in Figure 6;

Figure 7b shows a perspective view of the second nozzle of Figure 7a as tilted to show the features of its lower end;

Figure 8 shows a cross-sectional view of the second nozzle of Figure 7a wherein for each like mating third thereof the cross-section is taken about plane Y-Y' of Figure 6; and

Figure 9 shows a side view of details of the top part of the like mating third of Figure 6.

Referring now to the detail of the drawings, at Figure 1 there is shown a dispensing nozzle housing 50 in engaging contact with a fluid medicament discharge pump device 30.

The fluid medicament discharge device 30 is of standard form and comprises a container 34 for storing the fluid form medicament 35 to be dispensed and a compression pump 29 having a suction inlet 32 located within the container 30 and a discharge outlet 31 for transferring fluid from the pump 29 to the nozzle housing 50. The compression pump 29 is actuable along a pumping axis designated 'P' in response to force applied to the container 34 to move it towards the nozzle housing 50 so as to compress the pump 29.

The nozzle housing 50 is provided with first cylindrical sleeve 52 for receiving collar 33 provided to the neck of the container 30. The nozzle housing 50 is also provided with a second cylindrical sleeve 54 concentric with the first cylindrical sleeve 52 and shaped for engagement with a second housing (not shown) for housing the fluid medicament discharge device 30.

Smooth cylindrical inner wall 55 of the nozzle housing 50 defines a cylindrical cavity 51 for receipt of cylindrical nozzle assembly 70 comprising body 56 that defines a progressively narrowing fluid flow channel 60 having a channel inlet 57 and tapering channel outlet 58. The tapering outlet 58 communicates with shaped outlet 59 of the cylindrical sleeve 52. It will also be seen that the channel inlet 57 communicates with the discharge outlet 31 of the fluid discharge pump device 30, which is in abutting contact therewith.

In use, the fluid medicament 35 is pumped from the container 34 via suction inlet 32 to discharge outlet 31 and thence, into the fluid flow channel 60 via the channel inlet

57. The inner structure of the body 56, which defines the fluid flow channel 60 will be better understood by reference to the later drawings of suitable nozzle assemblies 70, but for now it is noted that channel 60 defines a screw path having a screw thread axis 'T' such that pumped fluid medicament derives angular momentum there from before being dispensed from the dispensing outlet 58. The screw thread axis 'T' is arranged to be co-axial with pumping axis 'P'. Further, the aforementioned progressive narrowing of channel 60 imparts acceleration to the fluid medicament as it is pumped there through.

The characteristics of nozzles suitable for use with the fluid medicament dispensing device of Figure 1 may be better understood by reference to Figures 2 to 5 and 6 to 9.

In more detail, Figures 2 to 5 show aspects of a first nozzle herein comprised of an assembly 170 of like mating body halves 156a, 156b. The assembly 170 has an overall cylindrical form such as would make it suitable for receipt by the cylindrical cavity 51 of the nozzle housing 50 of Figure 1. Each mating body half 156a, 156b defines one half of a tapering, and hence progressively narrowing, fluid flow channel 160 having a channel inlet 157 and also a tapering channel outlet 158. In further detail, the fluid flow channel 160 may be seen to feed into inner chamber 162, which in turn feeds into chimney 164 that opens out into tapered dispensing outlet 158.

Referring now to the cross-sectional view of Figure 4, the fluid flow channel 160 may be appreciated to define a screw path having a screw thread axis 'T' such as to impact angular momentum to fluid that is pumped from the channel inlet 157 via inner chamber 162 and chimney 164 to the dispensing outlet 158. The particular shape and form of inner chamber 162 may be seen by reference to Figure 4.

The Applicant has appreciated that the dispensing performance of the first nozzle of Figures 2 to 5 may be fine tuned by varying certain structural parameters thereof. In particular and as best seen in Figure 4, first radius (r_i) and second radius (r_c) of the

screw thread form dispensing channel 160 may be varied. Additionally and as best seen in Figure 5, the height (h) of inner chamber 162 and the radius (r_o) of the chimney feed 164 to the tapering channel outlet 158 may be varied.

Turning now to Figures 6 to 9, there are shown aspects of a second nozzle herein comprised of an assembly 270 of like mating body thirds 256a, 256b, 256c. Again, the assembly 270 has an overall cylindrical form such as would make it suitable for receipt by the cylindrical cavity 51 of the nozzle housing 50 of Figure 1. Each mating body third 156a, 156b, 256c defines one third of a tapering, and hence progressively narrowing, fluid flow channel 260 having a channel inlet 257 and also a tapering channel outlet 258. In further detail, the fluid flow channel 260 may be seen to feed into inner chamber 262, which in turn feeds into chimney 264 that opens out into tapered dispensing outlet 258.

Referring now to the cross-sectional view of Figure 8, the fluid flow channel 260 may be appreciated to define a screw path having a screw thread axis 'T' such as to impact angular momentum to fluid that is pumped from the channel inlet 257 via inner chamber 262 and chimney 264 to the dispensing outlet 258. The particular shape and form of inner chamber 262 may be seen by reference to Figure 4.

As for the first nozzle, the Applicant has appreciated that the dispensing performance of the second nozzle of Figures 6 to 9 may be fine tuned by varying certain corresponding structural parameters thereof. In particular and as best seen in Figure 8, first radius (r_{ii}) and second radius (r_{cc}) of the screw thread form dispensing channel 260 may be varied. Additionally and as best seen in Figure 9, the height (h2) of inner chamber 262 and the radius (r_{oo}) of the chimney feed 264 to the tapering channel outlet 258 may be varied.

Administration of medicament may be indicated for the treatment of mild, moderate or severe acute or chronic symptoms or for prophylactic treatment. It will be appreciated that the precise dose administered will depend on the age and condition

of the patient, the particular medicament used and the frequency of administration and will ultimately be at the discretion of the attendant physician. When combinations of medicaments are employed the dose of each component of the combination will in general be that employed for each component when used alone.

The fluid dispensing device herein is particularly suitable for dispensing a fluid medicament formulation. The container therefore contains a fluid medicament formulation e.g. formulated either as a solution formulation or as a suspension formulation comprising a suspension of active medicament particles in an inert suspending formulation.

Appropriate medicaments may thus be selected from, for example, analgesics, e.g., codeine, dihydromorphine, ergotamine, fentanyl or morphine; anginal preparations, e.g., diltiazem; antiallergics, e.g., cromoglycate (eg as the sodium salt), ketotifen or nedocromil (eg as the sodium salt); antiinfectives e.g., cephalosporins, penicillins, streptomycin, sulphonamides, tetracyclines and pentamidine; antihistamines, e.g., methapyrilene; anti- inflammatories, e.g., beclomethasone (eg as the dipropionate ester), fluticasone (eg as the propionate ester), flunisolide, budesonide, rofleponide, mometasone (eg as the furoate ester), ciclesonide, triamcinolone (eg as the acetonide), 6α, 9α-difluoro-11β-hydroxy-16α-methyl-3-oxo-17α-propionyloxy-androsta-1,4-diene-17β-carbothioic acid S-(2-oxo-tetrahydro-furan-3-yl) ester or 6α, 9α-Difluoro-17α-[(2-furanylcarbonyl)oxy]-11β-hydroxy-16α-methyl-3-oxo-androsta-1,4-diene-17β-carbothioic acid S-fluoromethyl ester; antitussives, e.g., noscapine; bronchodilators, e.g., albuterol (eg as free base or sulphate), salmeterol (eg as xinafoate), ephedrine, adrenaline, fenoterol (eg as hydrobromide), formoterol (eg as fumarate), isoprenaline, metaproterenol, phenylephrine, phenylpropanolamine, pirbuterol (eg as acetate), reproterol (eg as hydrochloride), rimiterol, terbutaline (eg as sulphate), isoetharine, tulobuterol or 4-hydroxy-7-[2-[[2-[[3-(2-phenylethoxy)propyl]sulfonyl]ethyl]amino]ethyl-2(3H)-benzothiazolone; PDE4 inhibitors eg cilomilast or roflumilast; leukotriene antagonists eg montelukast, pranlukast and zafirlukast; [adenosine 2a agonists, eg 2R,3R,4S,5R)-2-[6-Amino-2-

(1S-hydroxymethyl-2-phenyl-ethylamino)-purin-9-yl]-5-(2-ethyl-2H-tetrazol-5-yl)-tetrahydro-furan-3,4-diol (e.g. as maleate)]*; [α4 integrin inhibitors eg (2S)-3-[4-({[4-(aminocarbonyl)-1-piperidinyl]carbonyl}oxy)phenyl]-2-[((2S)-4-methyl-2-{[2-(2-methylphenoxy) acetyl]amino}pentanoyl)amino] propanoic acid (e.g as free acid or potassium salt)]*, diuretics, e.g., amiloride; anticholinergics, e.g., ipratropium (eg as bromide), tiotropium, atropine or oxitropium; hormones, e.g., cortisone, hydrocortisone or prednisolone; xanthines, e.g., aminophylline, choline theophyllinate, lysine theophyllinate or theophylline; therapeutic proteins and peptides, e.g., insulin or glucagons. It will be clear to a person skilled in the art that, where appropriate, the medicaments may be used in the form of salts, (e.g., as alkali metal or amine salts or as acid addition salts) or as esters (e.g., lower alkyl esters) or as solvates (e.g., hydrates) to optimise the activity and/or stability of the medicament and/or to minimise the solubility of the medicament in the propellant.

Preferably, the medicament is an anti-inflammatory compound for the treatment of inflammatory disorders or diseases such as asthma and rhinitis.

In one aspect, the medicament is a glucocorticoid compound, which has anti-inflammatory properties. One suitable glucocorticoid compound has the chemical name: 6α, 9α-Difluoro-17α-(1-oxopropoxy)-11β-hydroxy-16α-methyl-3-oxo-androsta-1,4-diene-17β-carbothioic acid *S*-fluoromethyl ester (fluticasone propionate). Another suitable glucocorticoid compound has the chemical name: 6α, 9α-difluoro-17α-[(2-furanylcarbonyl)oxy]-11β-hydroxy-16α-methyl-3-oxo-androsta-1,4-diene-17β-carbothioic acid *S*-fluoromethyl ester. A further suitable glucocorticoid compound has the chemical name: 6α,9α-Difluoro-11β-hydroxy-16α-methyl-17α-[(4-methyl-1,3-thiazole-5-carbonyl)oxy]-3-oxo-androsta-1,4-diene-17β-carbothioic acid *S*-fluoromethyl ester.

Other suitable anti-inflammatory compounds include NSAIDs e.g. PDE4 inhibitors, leukotriene antagonists, iNOS inhibitors, tryptase and elastase inhibitors, beta-2 integrin antagonists and adenosine 2a agonists.

The medicament is suitably in particulate form. The particulate medicament suitably has a mass mean diameter (MMD) of less than 20μm, preferably between 0.5-10μm, especially between 1-5μm. If particle size reduction is necessary, this may be achieved by techniques such as micronisation, wet bead milling and/or microfluidisation.

Suitable medicament particles may be produced by conventional techniques, for example by micronisation, milling or sieving. Additionally, medicament and/or excipient powders may be engineered with particular densities, size ranges, or characteristics. Particles may comprise active agents, surfactants, wall forming materials, or other components considered desirable by those of ordinary skill.

In one aspect, the fluid medicament formulation is formulated as a medicament suspension formulation comprising a suspension of active medicament particles in an inert suspending formulation, optionally containing other pharmaceutically acceptable additive components.

The inert suspending formulation is typically aqueous and comprises one or more excipients. By the term "excipient", herein, is meant substantially inert materials that are non-toxic and do not interact with other components of a composition in a deleterious manner including, but not limited to, pharmaceutical grades of carbohydrates, organic and inorganic salts, polymers, amino acids, phospholipids, wetting agents, emulsifiers, surfactants, poloxamers, pluronics, and ion exchange resins, thixotropic agents and combinations thereof.

Suitable carbohydrates include monosaccharides including fructose; disaccharides, such as, but not limited to lactose, and combinations and derivatives thereof;

polysaccharides, such as, but not limited to, cellulose and combinations and derivatives thereof; oligosaccharides, such as, but not limited to, dextrins, and combinations and derivatives thereof; polyols, such as but not limited to sorbitol, and combinations and derivatives thereof.

Suitable organic and inorganic salts include sodium or calcium phosphates, magnesium stearate, and combinations and derivatives thereof.

Suitable polymers include natural biodegradable protein polymers, including, but not limited to, gelatin and combinations and derivatives thereof; natural biodegradable polysaccharide polymers, including, but not limited to, chitin and starch, crosslinked starch and combinations and derivatives thereof; semisynthetic biodegradable polymers, including, but not limited to, derivatives of chitosan; and synthetic biodegradable polymers, including, but not limited to, polyethylene glycols (PEG), polylactic acid (PLA), synthetic polymers including but not limited to polyvinyl alcohol and combinations and derivatives thereof;

Suitable amino acids include non-polar amino acids, such as leucine and combinations and derivatives thereof. Suitable phospholipids include lecithins and combinations and derivatives thereof.

Suitable wetting agents, surfactants and/or emulsifiers include gum acacia, cholesterol, fatty acids including combinations and derivatives thereof. Suitable poloxamers and/or Pluronics include poloxamer 188, Pluronic® F-108, and combinations and derivations thereof. Suitable ion exchange resins include amberlite IR120 and combinations and derivatives thereof;

Preferred suspension formulations herein comprise an aqueous suspension of particulate medicament and one or more additional components selected from the group consisting of suspending agents, preservatives, wetting agents, viscosity enhancing agents and isotonicity adjusting agents.

Suitable suspending agents include carboxymethylcellulose, veegum, tragacanth, bentonite, methylcellulose and polyethylene glycols.

Particular suspending agents are those sold under the trade name Miglyol by Condea Chemie GmbH wich comprise ester oils of saturated coconut and plam oil-derived caprylic and capric fatty acids and glycerin or propylene glycol. Particular examples include Miglyol 810, Miglyol 812 (caprylic / capric trigltceride); Miglyol 818 (caprylic / capric / linoleic triglyceride); Miglyol 829 (caprylic / capric / succinic triglyceride); and Miglyol 840 (propylene glycol dicaprylate / dicaprate).

Suitable preservatives include quaternary ammonium compounds (e.g. benzalkonium chloride, benzethonium chloride, cetrimide and cetylpyridinium chloride), mercurial agents (e.g. phenylmercuric nitrate, phenylmercuric acetate and thimerosal), alcoholic agents (e.g. chlorobutanol, phenylethyl alcohol and benzyl alcohol), antibacterial esters (e.g. esters of para-hydroxybenzoic acid), chelating agents such as disodium edetate (EDTA) and other anti-microbial agents such as chlorhexidine, chlorocresol, sorbic acid and its salts and polymyxin.

Suitable wetting agents function to wet the particles of medicament to facilitate dispersion thereof in the aqueous phase of the composition. Examples of wetting agents that can be used are fatty alcohols, esters and ethers. Preferably, the wetting agent is a hydrophilic, non-ionic surfactant, most preferably polyoxyethylene (20) sorbitan monooleate (supplied as the branded product Polysorbate 80).

Suitable viscosity enhancing agents include carboxymethylcellulose, veegum, tragacanth, bentonite, hydroxypropylmethylcellulose, hydroxypropylcellulose, hydroxyethylcellulose, poloxamers (eg. poloxamer 407), polyethylene glycols, alginates xanthym gums, carageenans and carbopols.

Suitable isotonicity adjusting agents act such as to achieve isotonicity with body fluids (e.g. fluids of the nasal cavity), resulting in reduced levels of irritancy

associated with many nasal formulations. Examples of suitable isotonicity adjusting agents are sodium chloride, dextrose and calcium chloride.

Suitable thixotropic agents include that sold under the trade name Avicel RC951 NF, which comprises a mixture of carboxymethylcellulose sodium salt (8.3% to 13.8%) and microcrystalline cellulose. Thixotropic agents tend to make the formulation more viscous when static, but to become less viscous when kinetic energy is applied (e.g. on shaking the container).

In another aspect, the fluid medicament formulation is formulated as a solution medicament formulation. The formulation may be an aqueous, or in particular embodiments, a non-aqueous formulation. Suitable solution formulations may comprise a solubilising agent such as a surfactant.

Suitable surfactants include α-[4-(1,1,3,3-tetramethylbutyl)phenyl]-ω-hydroxypoly(oxy-1,2-ethanediyl) polymers including those of the Triton series e.g. Triton X-100, Triton X-114 and Triton X-305 in which the X number is broadly indicative of the average number of ethoxy repeating units in the polymer (typically around 7-70, particularly around 7-30 especially around 7-10) and 4-(1,1,3,3-tetramethylbutyl)phenol polymers with formaldehyde and oxirane such as those having a relative molecular weight of 3500-5000 especially 4000-4700, particularly Tyloxapol. The surfactant is typically employed in a concentration of around 0.5-10%, preferably around 2-5% w/w based on weight of formulation.

Suitable solution formulations may also comprise hydroxyl containing organic co-solvating agents include glycols such as polyethylene glycols (eg PEG 200) and propylene glycol; sugars such as dextrose; and ethanol. Dextrose and polyethylene glycol (eg PEG 200) are preferred, particularly dextrose. Propylene glycol is preferably used in an amount of no more than 20%, especially no more than 10% and is most preferably avoided altogether. Ethanol is preferably avoided. The hydroxyl containing organic co-solvating agents are typically employed at a

concentration of 0.1-20% e.g. 0.5-10%, e.g. around 1-5% w/w based on weight of formulation.

Suitable solution formulations may also comprise solublising agents such as polysorbate, glycerine, benzyl alcohol, polyoxyethylene castor oils derivatives, polyethylene glycol and polyoxyethylene alkyl ethers (e.g. Cremophors, Brij). Other solubilising agents are those sold under the trade name Miglyol by Condea Chemie GmbH wich comprise ester oils of saturated coconut and plam oil-derived caprylic and capric fatty acids and glycerin or propylene glycol.

One non-aqueous solution formulation is based upon Miglyol (trade name) either used neat to solubilise the medicament substance, or as a mixture with propylene glycol and/or polyethylene glycol.

Suitable suspension or solution formulations may be stabilised (e.g. using hydrochloric acid or sodium hydroxide) by appropriate selection of pH. Typically, the pH will be adjusted to between 4.5 and 7.5, preferably between 5.0 and 7.0, especially around 6 to 6.5.

The fluid medicament formulation herein suitably has a viscosity of from 10 to 2000 mPa.s (10 to 2000 centipoise), particularly from 20 to 1000 mPa.s (20 to 1000 centipoise), such as from 50 to 1000 mPa.s (50 to 1000 centipoise) at 25°C.

The viscosity of the inert suspending formulation herein is measured by any suitable method.

The dispensing device herein is suitable for dispensing fluid medicament formulations for the treatment of inflammatory and/or allergic conditions of the nasal passages such as rhinitis e.g. seasonal and perennial rhinitis as well as other local inflammatory conditions such as asthma, COPD and dermatitis.

A suitable dosing regime would be for the patient to inhale slowly through the nose subsequent to the nasal cavity being cleared. During inhalation the formulation

would be applied to one nostril while the other is manually compressed. This procedure would then be repeated for the other nostril. Typically, one or two inhalations per nostril would be administered by the above procedure up to three times each day, ideally once daily. Each dose, for example, may deliver 5μg, 50μg, 100μg, 200μg or 250μg of active medicament. The precise dosage is either known or readily ascertainable by those skilled in the art.

It will be understood that the present disclosure is for the purpose of illustration only and the invention extends to modifications, variations and improvements thereto.

The application of which this description and claims form part may be used as a basis for priority in respect of any subsequent application. The claims of such subsequent application may be directed to any feature or combination of features described therein. They may take the form of product, method or use claims and may include, by way of example and without limitation, one or more of the following claims:

Claims

1. A nasal dispensing nozzle for use with a fluid medicament discharge pump device having a discharge outlet for discharge of pumped fluid medicament, the nasal dispensing nozzle comprising

a body defining a fluid flow channel;

an inlet port defining an inlet to said channel, said inlet port shaped for receipt of said discharge outlet to enable delivery of said pumped fluid medicament to the channel; and

an outlet port defining an outlet from the channel,

wherein the channel is shaped to impart acceleration and angular momentum to the pumped fluid medicament, and wherein the body is comprised of a mating assembly of like component parts.

2. A dispensing nozzle according to claim 1 comprising a single fluid flow channel.

3. A dispensing nozzle according to claim 1 comprising from two to three fluid flow channels.

4. A dispensing nozzle according to any of claims 1 to 3, wherein the body is in the form of a cylinder.

5. A dispensing nozzle according to any of claims 1 to 4, wherein the or each fluid flow channel defines a screw path.

6. A dispensing nozzle according to claim 5, wherein said screw path is symmetric about a screw axis.

7. A dispensing nozzle according to claim 6, wherein the body is symmetric about said screw axis.

8. A dispensing nozzle according to either of claims 6 or 7, wherein the screw axis corresponds to the pumping axis of the fluid medicament discharge device.

9. A dispensing nozzle according to any of claims 5 to 8, wherein from two to three screw paths are defined.

10. A dispensing nozzle according to any of claims 5 to 9, wherein the number of screw paths corresponds to the number of like component parts of said mating assembly.

11. A dispensing nozzle according to any of claims 1 to 10, wherein the cross-sectional area of the or each fluid flow channel decreases from said inlet to said outlet thereof.

12. A dispensing nozzle according to any of claims 1 to 11, wherein the like component parts are configured as mirror images, one of the other.

13. A dispensing nozzle according to any of claims 1 to 12, wherein the mating assembly is comprised of two mating halves.

14. A dispensing nozzle according to claim 13, wherein the body is in the form of a cylinder such that each mating half defines a 180° segment of the cylinder.

15. A dispensing nozzle according to any of claims 1 to 12, wherein the mating assembly is comprised of three mating thirds.

16. A dispensing nozzle according to claim 15, wherein the body is in the form of a cylinder such that each mating third defines a 120° segment of the cylinder.

17. A dispensing nozzle according to any of claims 1 to 16, wherein each like component part is formable by a moulding process.

18. A dispensing nozzle according to any of claims 1 to 17, wherein each like component part comprises a polymeric material.

19. A dispensing nozzle according to any of claims 1 to 18, wherein the body defines a shaped outlet port locating upstream of the fluid flow channel.

20. A dispensing nozzle according to claim 19, wherein said shaped outlet port defines a tapering profile.

21. A dispensing nozzle according to any of claims 1 to 20, wherein the outlet port is provided with a reversible stopper.

22. A nozzle housing assembly for reversible receipt of a fluid medicament discharge pump device for spraying a fluid medicament into a nasal cavity, the nozzle housing assembly comprising a nozzle housing defining a cavity; and engageable with said nozzle housing, a dispensing nozzle according to any of claims 1 to 21.

23. A nozzle housing assembly according to claim 22, wherein said cavity is shaped for receipt of a cylindrical nozzle.

24. A fluid medicament dispensing device comprising a nozzle housing assembly according to claim 23 and received thereby, a fluid medicament discharge pump device.

25. A fluid medicament dispensing device according to claim 24, wherein the fluid medicament discharge pump device comprises a hollow casing defining a reservoir for containing a volume of fluid medicament and a pump having a suction inlet extending within the hollow casing, the pump having a discharge outlet extending from a first end of the hollow casing for co-operation with the dispensing nozzle to enable pumped delivery of fluid from the reservoir to the dispensing nozzle.

26. A fluid medicament dispensing device according to either of claims 24 or 25, wherein said reservoir contains a volume of fluid medicament formulation.

27. A fluid medicament dispensing device as claimed in claim 26, wherein said fluid medicament formulation is in the form of a solution formulation.

28. A fluid medicament dispensing device as claimed in claim 27, wherein said fluid medicament formulation is in the form of a suspension formulation.

29. A fluid medicament dispensing device as claimed in any of claims 26 to 28, wherein the fluid medicament formulation comprises an anti-inflammatory medicament compound.

30. A fluid medicament dispensing device as claimed in claim 29, wherein said medicament compound is a glucocorticoid compound.

31. A fluid medicament dispensing device as claimed in claim 30, wherein said glucocorticoid compound is selected from the group consisting of 6α, 9α-Difluoro-17α-(1-oxopropoxy)-11β-hydroxy-16α-methyl-3-oxo-androsta-1,4-diene-17β-carbothioic acid *S*-fluoromethyl ester; 6α, 9α-difluoro-17α-[(2-furanylcarbonyl)oxy]-11β-hydroxy-16α-methyl-3-oxo-androsta-1,4-diene-17β-carbothioic acid *S*-fluoromethyl ester; and 6α,9α-Difluoro-11β-hydroxy-16α-methyl-17α-[(4-methyl-1,3-

thiazole-5-carbonyl)oxy]-3-oxo-androsta-1,4-diene-17β-carbothioic acid *S*-fluoromethyl ester.

32. A fluid medicament dispensing device as claimed in claim 29, wherein said medicament compound is selected from the group consisting of PDE4 inhibitors, leukotriene antagonists, iNOS inhibitors, tryptase and elastase inhibitors, beta-2 integrin antagonists and adenosine 2a agonists.

33. A kit of parts comprising a nozzle housing assembly according to either of claims 21 or 22 and a fluid medicament discharge pump device receivable thereby.

FIG. 1

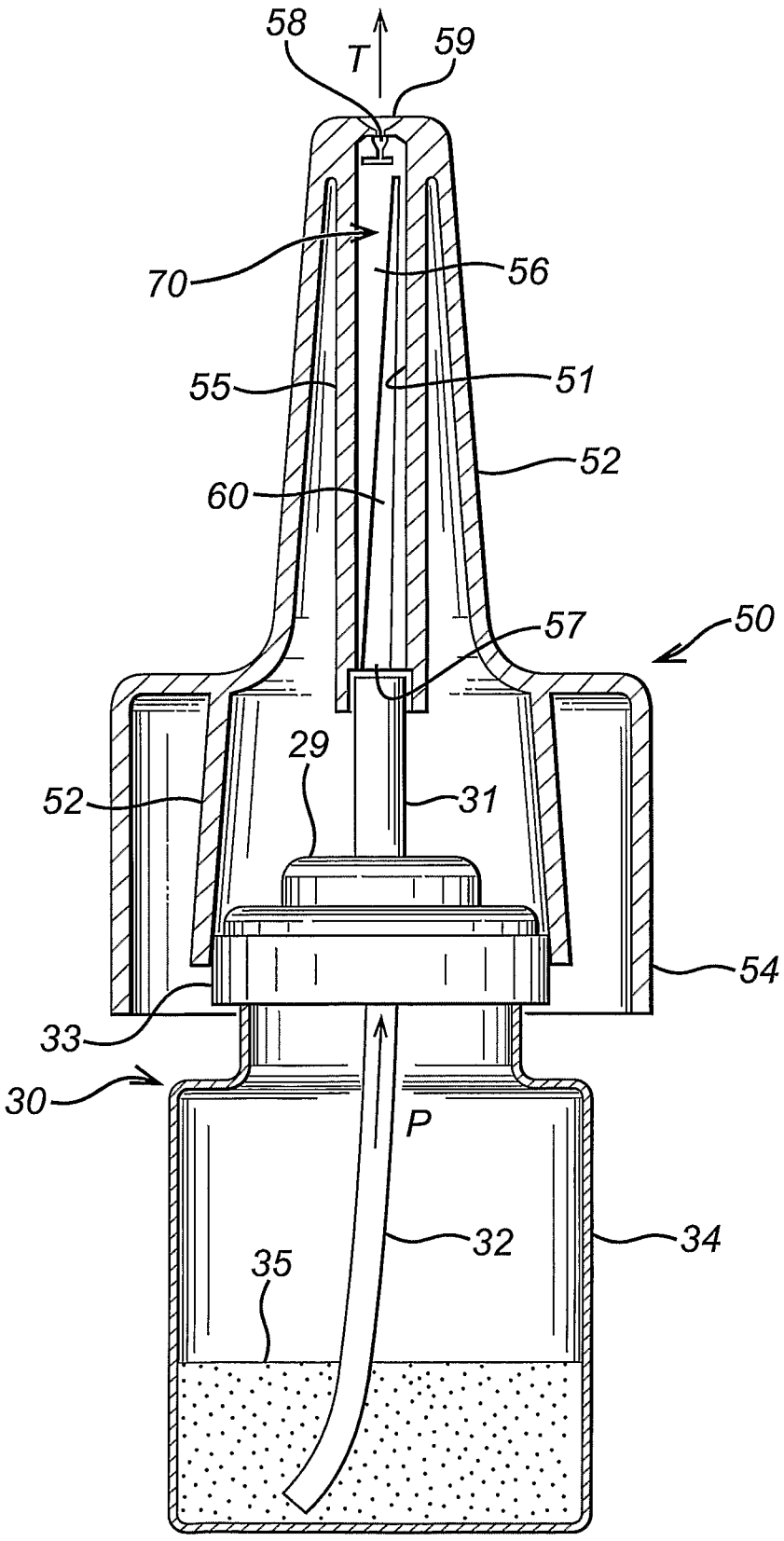


FIG. 2

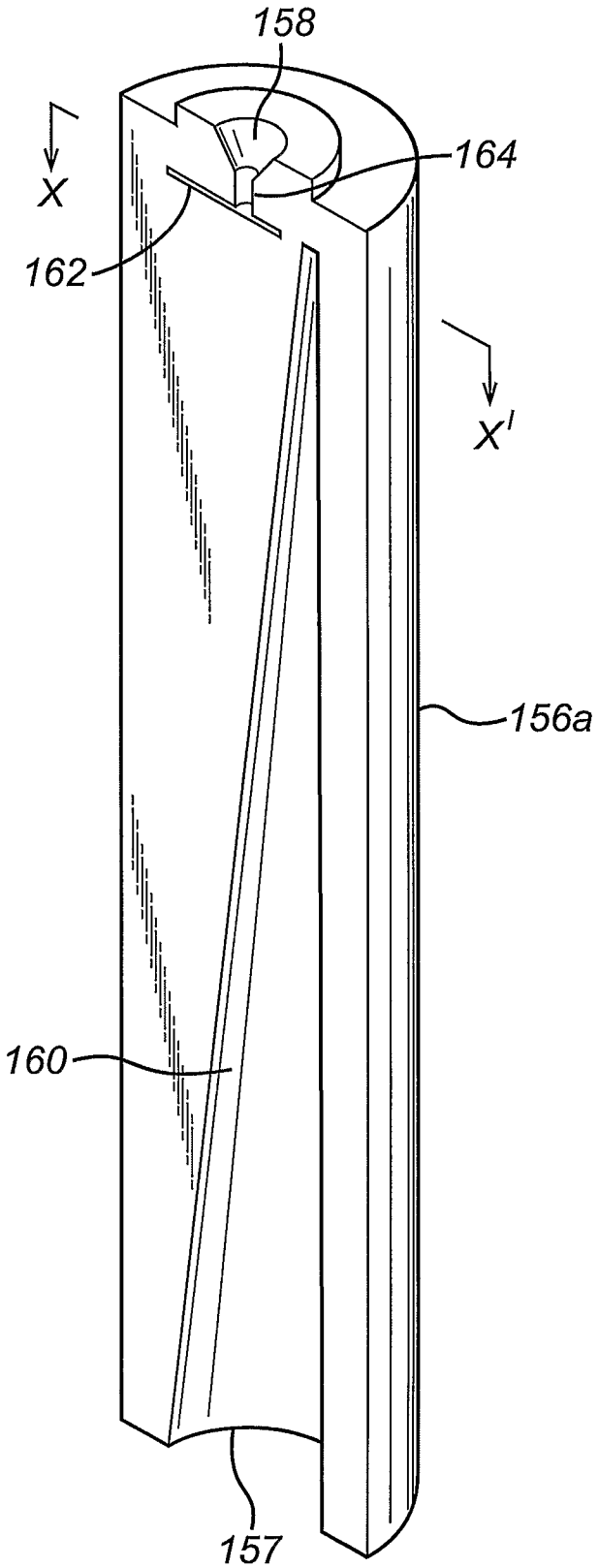


FIG. 3a

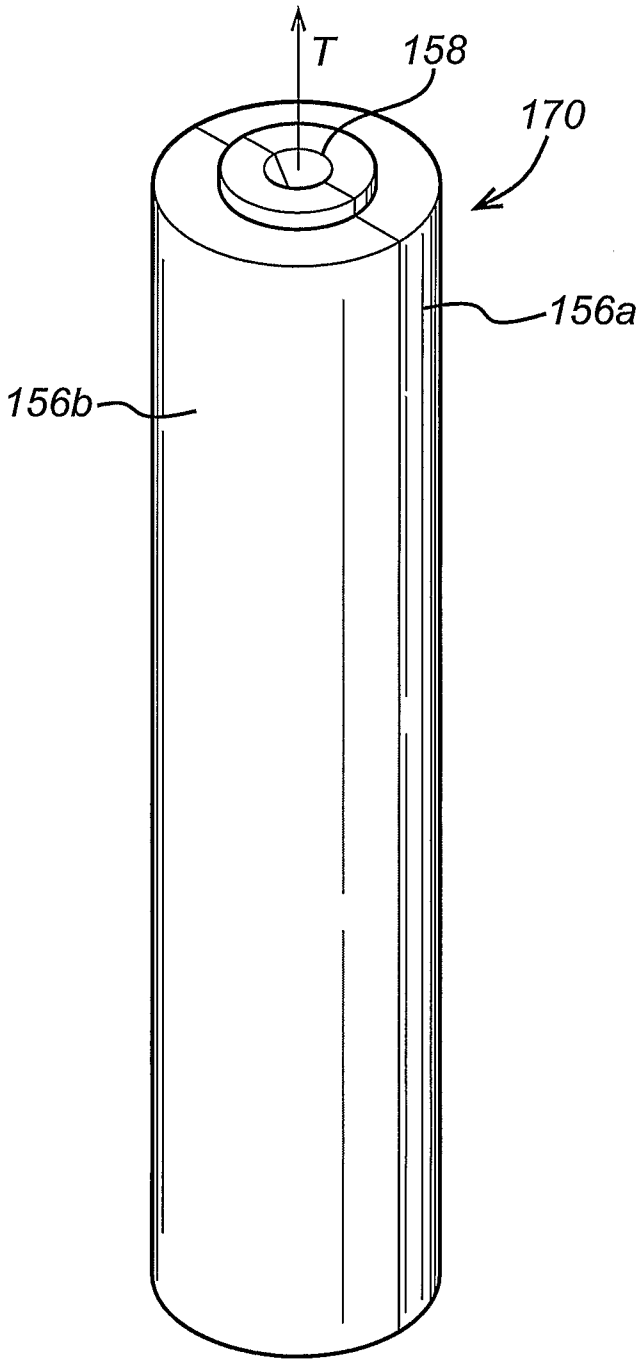


FIG. 3b

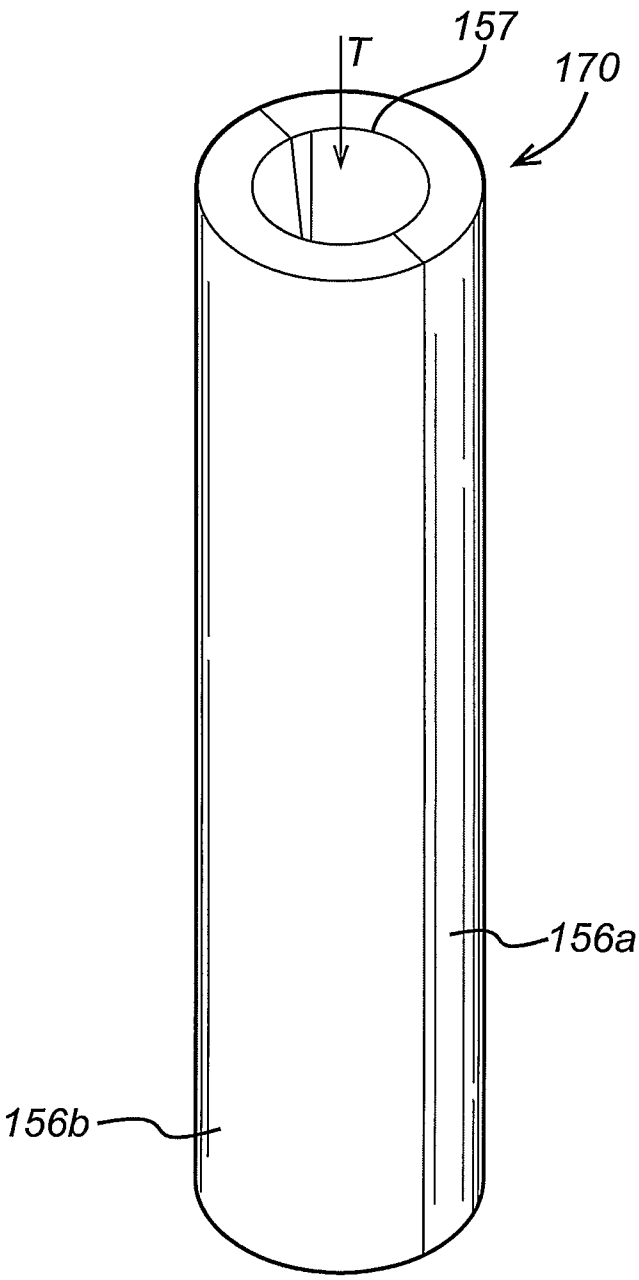


FIG. 4

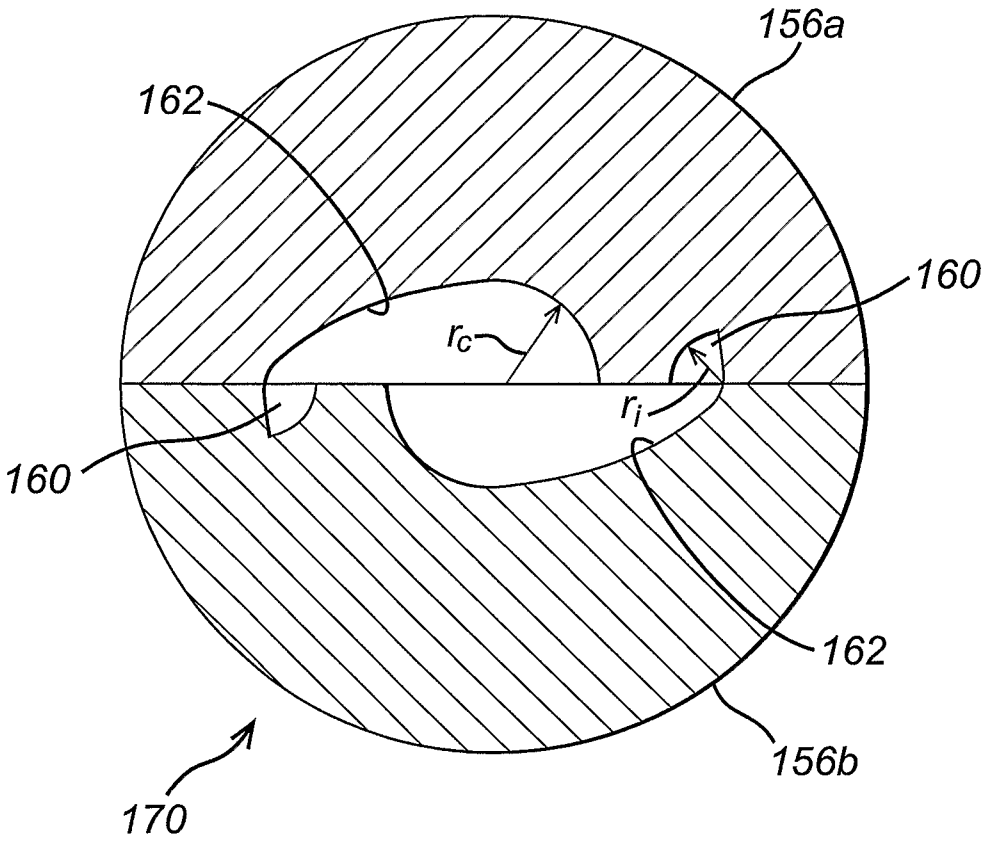


FIG. 5

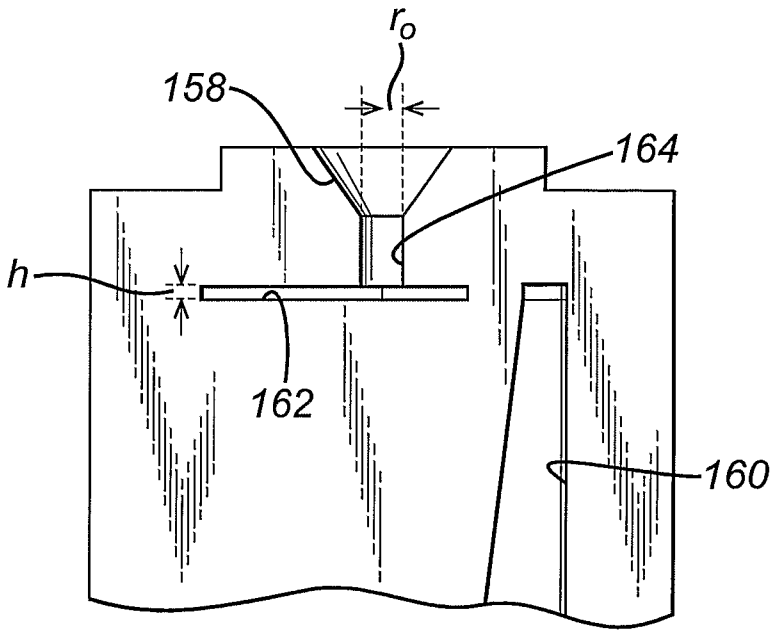


FIG. 6

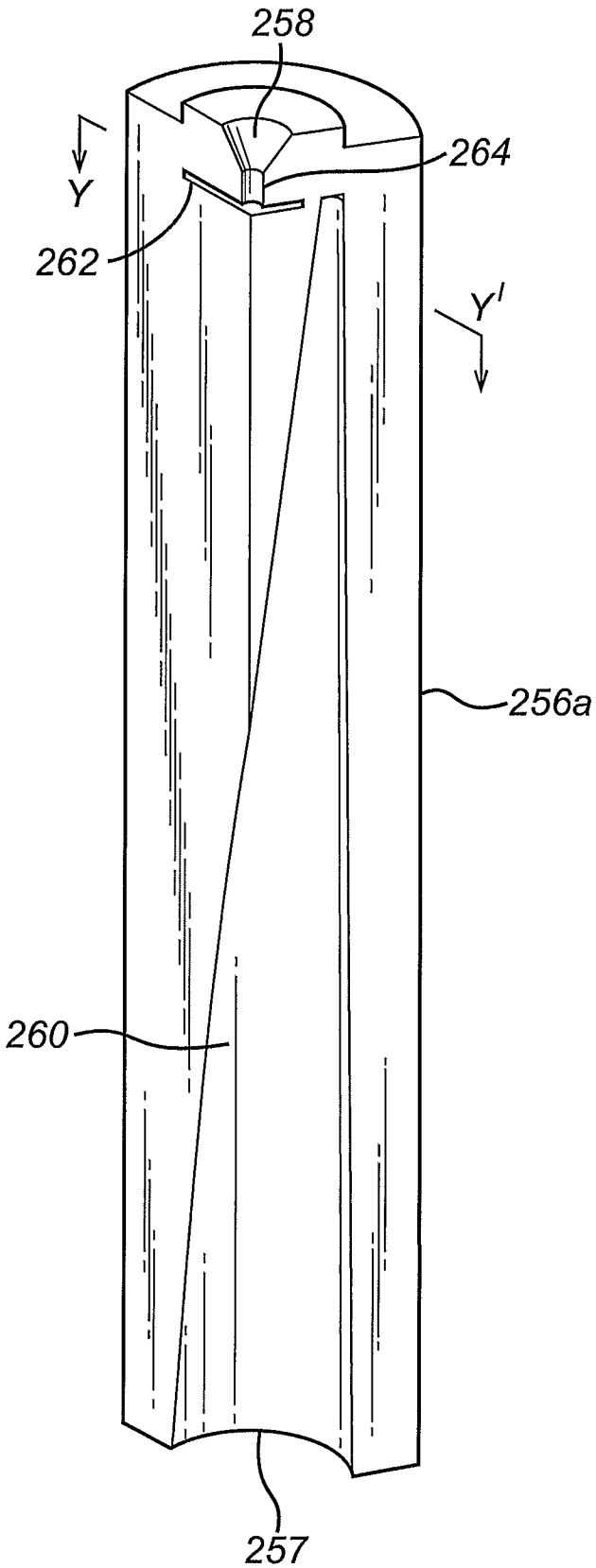


FIG. 7a

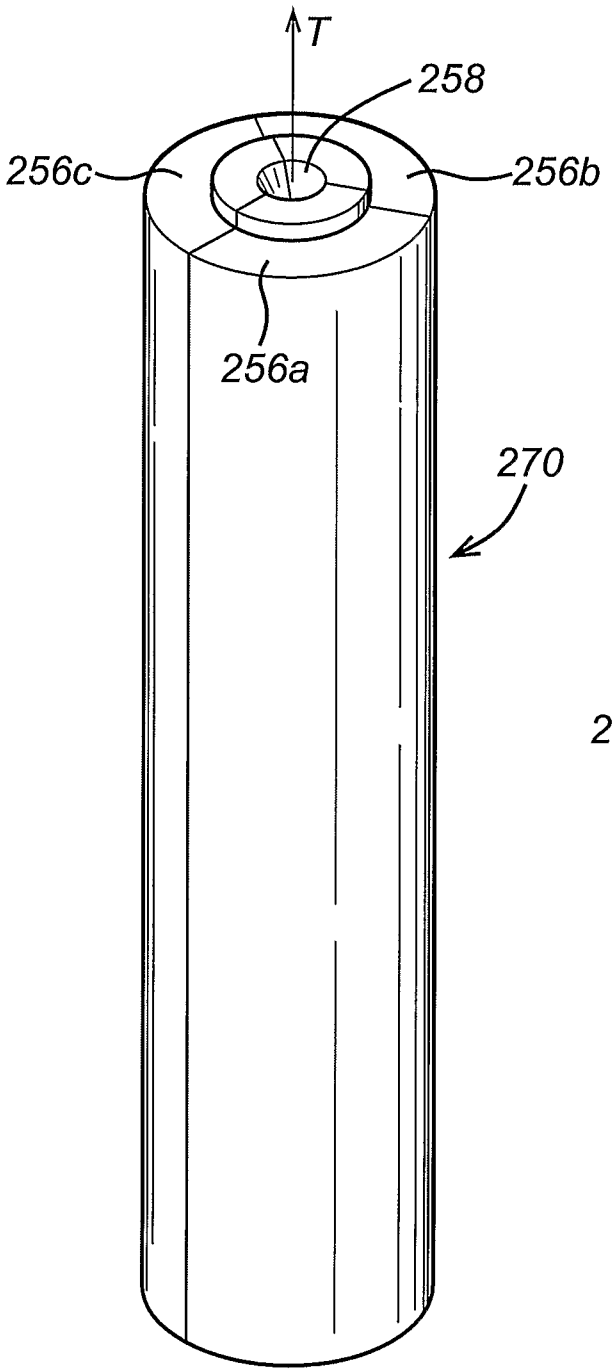


FIG. 7b

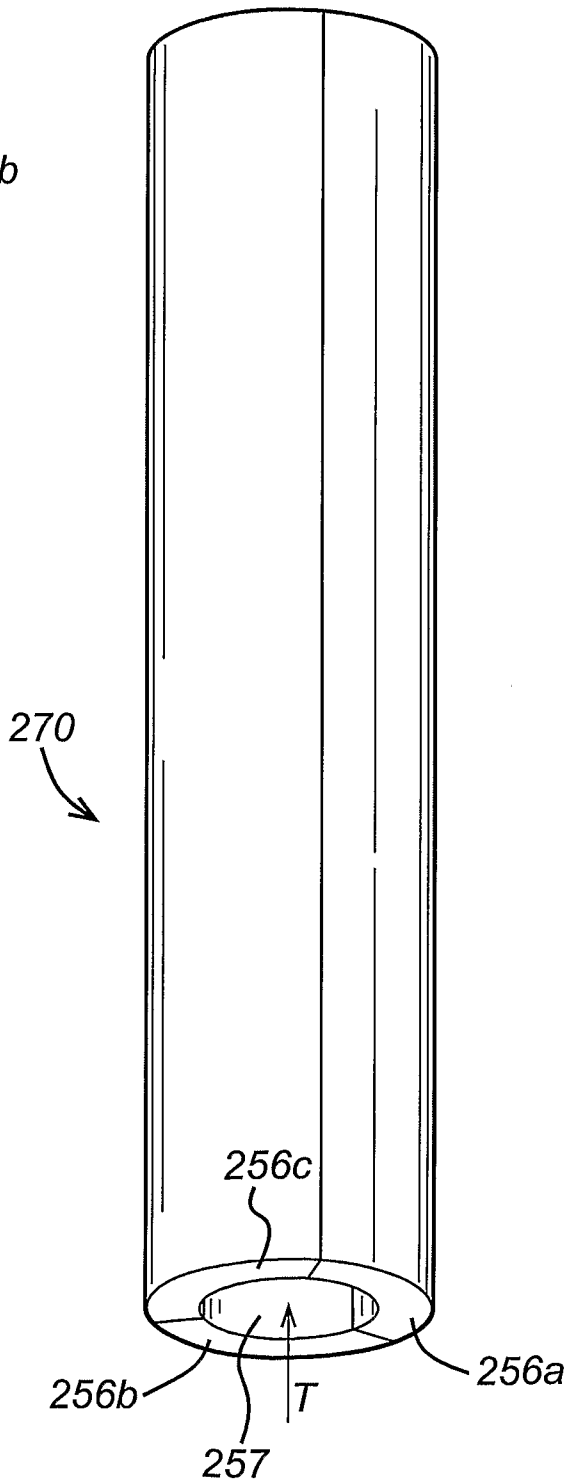
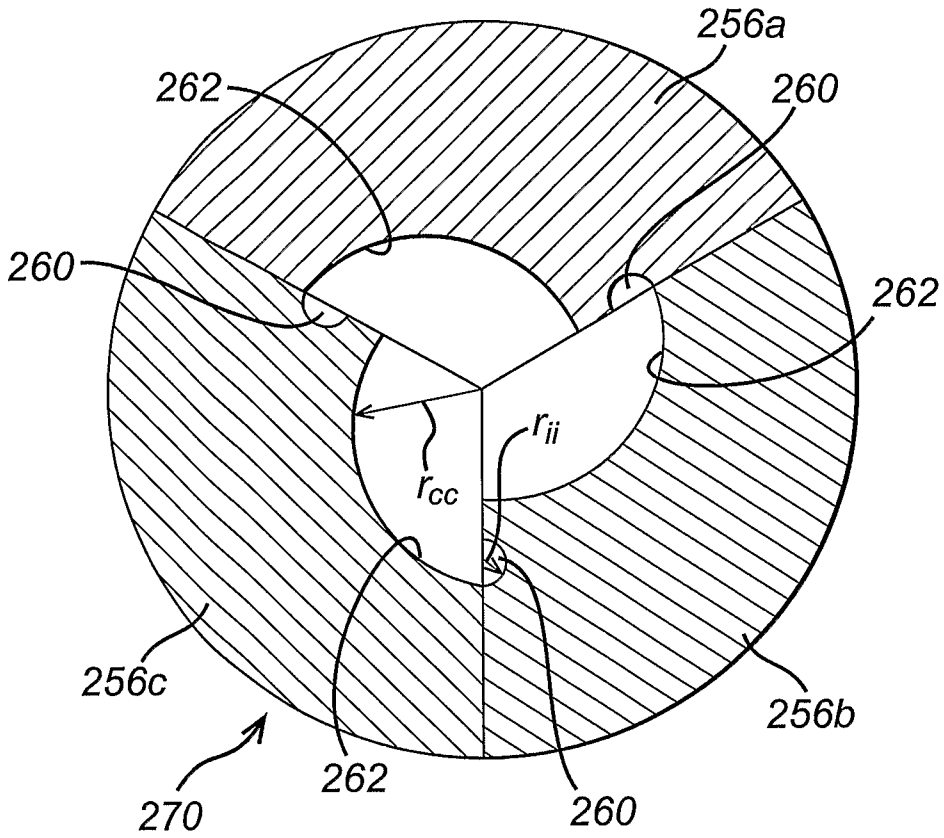


FIG. 8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r_{cc}
256c
256b
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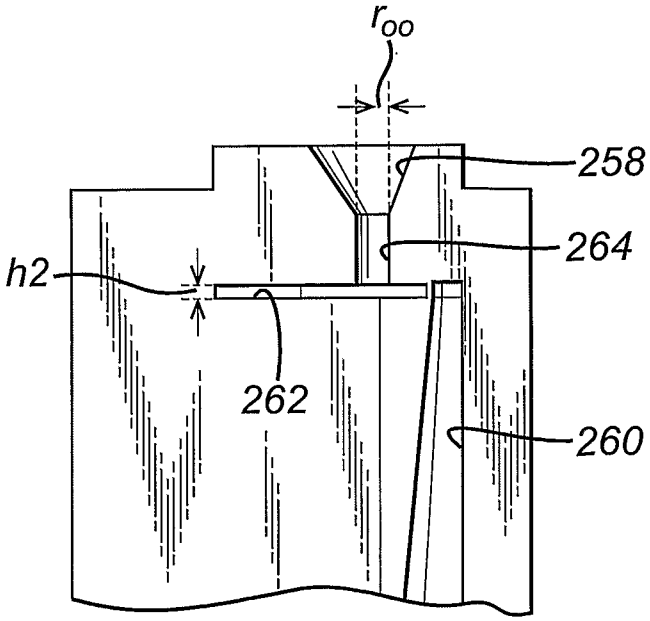
260

FIG. 9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INTERNATIONAL SEARCH REPORT

International application No
PCT/GB2006/002792

A. CLASSIFICATION OF SUBJECT MATTER
INV. B05B1/34 A61M15/08 A61M11/06

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)
B05B 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 2004/094068 A (GLAXO GROUP LIMITED; MORRISON, ROBIN, LAW) 4 November 2004 (2004-11-04) cited in the application	1-9,11, 17-21
A	the whole document	22-33
X	US 6 503 362 B1 (BARTELS FRANK ET AL) 7 January 2003 (2003-01-07)	1-4, 12-15, 17-20, 22-33
	column 1, lines 18-23 - lines 50-54 column 2, lines 62-65 column 7, lines 6-56 column 13, line 16 - column 14, line 62 column 15, lines 22-28; figures 13,19	
	-/--	

[X] Further documents are listed in the continuation of Box C. [X] See patent family annex.

* Special categories of cited documents :

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"O" document referring to an oral disclosure, use, exhibition or other means

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"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
9 October 2006	19/10/2006
Name and mailing address of the ISA/ 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	Authorized officer Azaïzia, Mourad

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INTERNATIONAL SEARCH REPORT

International application No
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C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

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Information on patent family members

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