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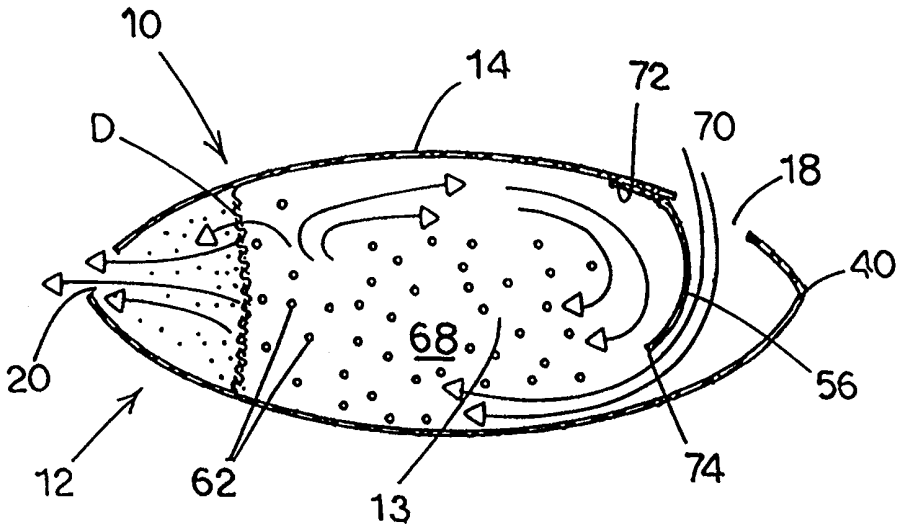

(57) Abstract

This invention is an inhaler apparatus (10) having a housing (12) with a first wall (14), a second wall (16), defining an air inlet (18), and an air outlet (20). The first and second walls define an internal housing volume (13), having portions which are movable relative to each other so as to expand the internal housing volume from a non–inhalation state, wherein the internal housing volume has a first volume, to an inhalation state, wherein the internal housing volume has a second volume, the second volume being larger relative to the first volume. An airflow chamber (68) is defined within the housing between the air inlet, and the air outlet when the housing is in the inhalation state. A medicament (62) is contained between the first and second walls, which is exposed to airflow within the airflow chamber when the housing is in the inhalation state.

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Description

UNIT DOSE INHALER APPARATUS AND METHOD OF DELIVERY USING SAME

Technical Field

The present invention relates generally to inhaler apparatuses, and more particularly, to compact, environmentally friendly, inexpensive dry powder unit dose inhalers.

Background Art

As appreciated by those of skill in the art, it is often beneficial to administer therapeutic or diagnostic agents (herein referred to variously as "medicaments", "medications", or "drugs") to the lungs or through the lungs of a patient. For certain medical conditions, topical administration of medication to the lung is often the preferred way to provide relief to the patient. For example, in the case of an acute asthma attack, direct "rescue" administration of medications such as albuterol directly to the smooth muscle of a patient's lungs provides for immediate relief of bronchial inflammation.

Systemic delivery or administration of medicament by inhalation to the blood stream via the alveolar blood vessels, may also provide advantages over standard oral or intravenous systemic delivery regimes. For example, in comparison with oral dosing, systemic delivery via the lung can increase bioavailability of some medications by avoiding metabolic inactivation of the medicament in the gut or liver. Respiratory delivery to the blood stream also avoids the potential risk of disease transmission from using intravenous delivery devices such as hypodermic needles.

Many devices exist in the art which are useful for delivering medicaments via the inhaled route, including propellant based metered dose inhalers (MDIs). Due to environmental concerns over ozone depletion, MDIs

using chlorofluorocarbons as propellants are being phased out in favor of more environmentally friendly powder inhalers.

Dry powder inhalers, which lack any propellants whatsoever, are viewed as one solution to the alleged problem caused by ozone depleting propellants. Dry powder inhalers are of three basic varieties: Reservoir based Dry Powder Inhalers (RDPIs); Multi-unit dose Dry Powder Inhalers (MDPIs); and Unit dose Dry Powder Inhalers (UDPIs). RDPIs meter doses in the device out of a powder reservoir to provide multiple doses of medication, while MDPIs contain multiple premeasured, individually packaged doses of drugs. UDPIs, in comparison, contain a single dose of medicament.

Despite the desirability of drug delivery via inhalation and the preferability of dry powder inhalers, it is often difficult to obtain a patient's full compliance with prescribed instructions for an inhaled medicament, and reasons for non-compliance may vary. Patients may fail to fully comply with prescribed dosing because of awkwardness of the size or shape of their inhaler. The dry powder inhalers currently known in the art, for the most part, tend to be bulky and, therefore, awkward to carry on one's person. The awkwardness of carrying such devices contributes to a patient's failure to have the inhaler available during daily activities. For some individuals in need of "rescue" applications of medication, such as patients with severe asthma or athletes experiencing exercise-induced asthma attacks, this can be a significant disadvantage to inhaler design. Bulky, cumbersome inhalers are ill-suited for such purposes.

Another reason patients might not comply with prescribed dosing is that they may perceive a social stigma from using their inhalers in public. In some cases, patients may feel embarrassed or self-conscious about using a cumbersome inhaler in public places and therefore, may not carry and/or use the inhaler as prescribed by their doctors.

A still further reason for patients not using inhalers may include the patient's inability to afford the devices at all due to limited financial

resources. Complexity of a device adds to its cost, and the more expensive a device is, the less accessible it may be to all potential users.

UDPIs are generally speaking less complex, more compact and less expensive than RDPIs and MDPIs. Moreover, RDPIs and MDPIs are not ideally suited for delivering therapies only needing a single application, especially where disposability after use is a desirable feature. Prior art UDPIs, unfortunately, in some instances remain relatively bulky and awkward and may be made from environmentally unfriendly, non-biodegradable materials, such as certain plastics.

Examples of prior art UDPIs include that disclosed in U.S. Patent No. 5,645,051 to Schultz, which describes a plastic and metal unit dose dry powder inhaler having a motor driven impeller. PCT Patent Publication No. WO 97/05918 to Asking discloses a UDPI having a dry powder dose sandwiched between two peelable cover strips. The cover strips are pulled from the device, thus internally exposing the drug in a flow path. PCT Publication No. 96/222802 assigned to Directhaler discloses a straw-like UDPI having a dose contained within the straw and which is sealed by removable end caps.

Despite the existence of various prior art unit dose dry powder inhalers, there remains much room for improvement in the art. Specifically, there exists a long-felt need for a UDPI apparatus and method of use wherein the inhaler apparatus is inexpensive, disposable, environmentally friendly, simple, compact and easily carried and used by a patient, so as to increase patient compliance, and yield improved drug delivery.

Disclosure of the Invention

In accordance with the present invention, a unit dose inhaler apparatus and method of use are described. The inhaler apparatus comprises a flexible housing having first and second walls. The housing defines an air inlet and an air outlet and an internal housing volume. The housing is preferably deformable or expandable so as to expand the

housing volume from a non-inhalation state having a first housing volume, to an inhalation state having a second housing volume. The second housing volume is greater than the first housing volume. An air flow chamber is defined within the housing between the air inlet and the air outlet when the housing is in its inhalation state.

A medicament dose, which may be a therapeutic or diagnostic agent, is positioned within the housing between the first and second walls. The medicament is sealed from the outside environment in the non-inhalation state. This sealed arrangement prohibits the medicament from falling out of the device, and also prevents air and moisture ingress into the device, thus preserving the sterility and stability of the medicament dose.

In use, the housing volume is expanded to its inhalation state, increasing the distance between at least portions of the interior surfaces of the first and second walls. The movement of the walls exposes the medicament contained in the housing within the air flow chamber. A patient inhales through the air outlet and entrains the medicament in an inhalation stream. The medicament flows through the inhalation stream, where it may pass directly to the air outlet and into the patient's lungs. Alternatively, the dosage may first be deagglomerated before passing to the air outlet and into the patient's lungs, for instance, by impacting on various surfaces in the device, or through vibrational effects provided by components within the device.

The UDPI of the present application may further include one or more one-way valves to allow airflow from the device to the patient's lungs, but prevent the user from exhaling through the device, so as to blow the drug out of the device.

A wide variety of mechanisms may be used to seal the medicament within the device, to deagglomerate the powdered drug upon inhalation, or to act as a valve, as is described in more detail below.

Accordingly, it is an object of this invention to provide a novel UDPI apparatus and method of using the same.

It is another object of this invention to provide a UDPI apparatus that is small, compact and easily carried.

It is a further object of this invention to provide a UDPI apparatus that is expandable and has a larger internal volume when it is in an inhalation state than it has when it is in a non-inhalation state.

It is a still further object of this invention to provide a UDPI apparatus that is inexpensive to manufacture.

It is a still further object of this invention to provide a unit dose inhaler device which may be disposed of with minimal environmental impact.

It is a still further object of the present invention to provide a UDPI where the medicament contained therein is preserved in a sealed fashion until ready to use.

It is a still further objection of the present invention to provide a UDPI with a deagglomeration mechanism to break up dry powder agglomerates to provide a greater percentage of powder particles within the respirable range.

It is a still further object of the present invention to provide a UDPI apparatus which a user may inhale through but may not exhale through so as to prevent loss of medicament prior to it being delivered to the lung.

Lastly, it is an object of the present invention to provide a UDPI apparatus and method of use that facilitates patient compliance with prescribed instructions for the medicament within the inhaler by being easy to use.

Some of the objects of the invention having been stated hereinabove, other objects will become evident as the description proceeds, when taken in connection with the accompanying drawings as best described hereinbelow.

Brief Description of the Drawings

Figure 1 of the drawings is a perspective view of an assembled inhaler apparatus of the present invention in an inhalation state;

Figure 2 of the drawings is a perspective view of an assembled inhaler apparatus of the present invention in a non-inhalation state;

Figure 3 of the drawings is an interior plan view of an unassembled inhaler apparatus of the present invention;

Figures 3A, 3B and 3C of the drawings are enlarged, isolated cross-sectional views of alternative structures for confining medicament in an inhaler apparatus of the present invention;

Figure 4 of the drawings is an exterior plan view of an unassembled inhaler apparatus of the present invention;

Figure 5 of the drawings is a top plan view of an assembled inhaler apparatus of the present invention in a non-inhalation state;

Figure 6 of the drawings is a top plan view of the inhaler apparatus of the present invention in an inhalation state;

Figure 7 of the drawings is a cross-sectional side view of the inhaler apparatus of the present invention in an inhalation state wherein filter flap **56** is shown in one manner of attachment;

Figure 8 of the drawings is a cross-sectional side view of the inhaler apparatus of the present invention in an inhalation state wherein filter flap **56** is shown in an alternative manner of attachment;

Figures 9A and 9B of the drawings are cross-sectional views of an alternative embodiment of an inhaler apparatus of the present invention;

Figure 10 of the drawings is a cross-sectional view of an inhaler apparatus of Figures 9A and 9B with a series of deagglomerators; and

Figures 11A and 11B of the drawings are cross-sectional views of another alternative embodiment of an inhaler apparatus of the present invention.

Detailed Description of the Invention

In accordance with the present invention, a UDPI apparatus and method of use are disclosed wherein the UDPI can be activated by

inhalation by the user. No propellent, other than the force of the user inhaling the medicament, is required to operate the present unit dose inhaler apparatus. Preferably, the unit dose inhaler apparatus comprises a paper material, such as a 14-16 point solid bleached sulfate (SBS) laminated with 00035 foil or TYVEK®, manufactured by DuPont, that is capable of being dye cut according to the structures described hereinbelow. Thus, the unit dose inhaler apparatus of the instant invention can be discarded after the unit dose is taken by the patient. It is envisioned, however, in accordance with this invention that any other suitable material or materials could be used for construction of the present unit dose inhaler apparatus.

Referring now to the drawings, wherein like reference symbols refer to like parts throughout, the unit dose inhaler apparatus of the present invention is referred to generally as **10**. Referring particularly to Figures 1 through 4, inhaler apparatus **10** comprises a flexible housing, generally referred to as **12**. Housing **12** includes an integral first wall **14** and an integral second wall **16** and possesses an internal housing volume **13** (not shown in Figures 1-4). As will be described hereinbelow with respect to additional or alternative embodiments, the walls of other embodiments of the inhaler apparatus of this invention can be separate but abutting with various configurations of the housing.

As best seen in Figure 1, housing **12** further comprises an air inlet port **18**, which, preferably takes the form of a pair of spaced-apart but proximate air inlet ports on first wall **14** of housing **12**. Housing **12** also comprises a mouthpiece or air outlet port **20** defined by portions of both first wall **14** and second wall **16** and substantially on the opposite side of housing **12** from air inlet port **18**.

As best seen in Figures 3 and 4, first wall **14** of housing **12** further comprises a series of flaps and folds by which first wall **14** is connected to

second wall **16** and by which expandability is imparted to the internal housing volume **13** of housing **12**. First wall **14** comprises a pair of outer side flaps **22** extending laterally therefrom with side flaps **22** being foldably attached along lower folds **24** to side walls **26**, which are formed between lower folds **24** and medial side wall folds **28**. Upper side walls **30** are formed between medial side wall folds **28** and upper folds **32**.

Distal tabs **34** are formed along a distal edge of first wall **14** and are foldable along fold **36**. Between distal tabs **34** is formed an arcuate segment **38**. Primary fold **40** is defined along proximal edges of walls **14** and **16** and forms a connection between walls **14** and **16** of housing **12**. Lateral arcuate edges **42** extend away from primary fold **40** in an arcuate path along the periphery of second wall **16**. Projections **44** are defined between arcuate lateral edges **42** of second wall **16** and arcuate segment **46**. Thus, arcuate segment **46** is defined along the distal edge of second wall **16** of housing **12** and lies between projections **44**. As best seen in Figure 4, instructional indicia **64** can be placed on first wall **14**.

Second wall **16** of housing **12** has an interior surface **48**. First wall **14** of housing **12** defines an interior surface **52**. As shown in Figure 3, valve flap or filter flap **56** is attached on interior surface **52** of first wall **14**, such that filter flap **56** covers air inlet port **18**.

Continuing with particular reference to Figure 3, second wall **16** of housing **12** further comprises interior surface **48**. First wall **14** of housing **12** further comprises interior surface **52**. Interior surfaces **48** and **52** are designed to contain, in various ways, a medicament dose **62**. In one embodiment of the present invention and as shown in Figure 3A, medicament dose **62** can be positioned between interior surfaces **48** and **52** without the use of a separate cover layer (the significance of which is described below with reference to the second and third embodiments) when, during assembly, first wall **14** is folded over second wall **16** (along

primary fold **40**), such that internal surfaces **48** and **52** face each other. Interior surfaces, **52** and **48**, respectively, can, by virtue of an adhesive **A** encircling dose **62**, form a dose or medicament holder **58** (Figure 5), which defines an internal holder volume **60** for containing dose **62**. In a second embodiment and as shown in Figure 3B, medicament holder **58** is formed by a single holder cover portion **54** which is adhesively bonded by adhesive **A** to interior surface **48**, with dose **62** sandwiched therebetween. In a third embodiment and as shown in Figure 3C, medicament holder **58** is formed between a first holder cover portion **50** and a second holder cover portion **54** which are bonded together by adhesive **A** with dose **62** sandwiched therebetween.

The first of the three embodiments described above may be assembled by first metering a quantity of a medicament into interior surface **52** of first wall **14**. A pressure-sensitive and biologically safe adhesive **A** is then spread around medicament **62**. The adhesive is preferably a natural rubber base, pressure-sensitive adhesive preferably having the property of not sticking to anything but its own substrate and to itself after it dries. Booth, K.N. ed. *Industrial Packing Adhesives*, Blackey: Glasgow, 1990. Outer side flaps **22** of first wall **14** are then folded along medial side wall folds **28**, and tabs **34** are folded along folds **36**. The preferred natural rubber adhesive is then placed along the surfaces of side flaps **22** and tabs **34** that face second wall **16**. Second wall **16** is then folded along primary fold **40** and moved into contact with side flaps **22** and tabs **34**. Second wall **16** is moved in such a manner so as to ensure that arcuate segments **38** and **46** are adequately aligned to form air inlet port **20**. Suitable pressure is then applied to second wall **16** so that the pressure-sensitive adhesive **A** on the abutting surfaces of side edges **22**, tabs **34**, and around medicament **62** adequately adheres between first and second walls **14**, **16**. So arranged, adhesive **A** surrounding medicament **62** confines the medicament **62** to the

space between the interior surfaces **52** and **48** of the first and second walls **14** and **16** to form medicament holder **58**.

In the second embodiment (Figure 3B) of the present invention mentioned above, single medicament cover portion **50** can be used within inhaler **10**. Cover portion **50** may be made of any suitable material, a metal or plastic foil being most preferred. In this second embodiment, and as seen in Figures 3-5, the single medicament holder cover portion **50** can be mounted with adhesive **A** on interior surface **52** generally in a medial position. As would be understood, mounting could also be made on the interior surface **48** of second wall **16** without departing from the scope of the present invention. Medicament dose **62** is then loaded onto cover portion **50** and a suitable adhesive is then spread around medicament **62** about the periphery of cover portion **54**. The device is assembled as described above in the discussion of the first embodiment, thus forming an adhesive bond between interior surface **48** of second wall **16** and the peripheral edge of cover portion **50**. So constructed, medicament holder **58** is formed between cover portion **50** and interior surface **48**.

In the third embodiment (Figure 3C) described above, medicament holder **58** is formed from a pair of cover portions **50** and **54** which when sealed together to form an envelope for containing medicament **62**. The envelope for medicament holder **58** may be formed by positioning first holder cover portion **50** on interior surface **52** of first wall **14**, and second holder cover portion **54** on interior surface **48** of second wall **16**. A suitable adhesive is then applied to the periphery of one of the cover portions, and the inhaler is assembled, as described above. When assembled, medicament cover portions **50** and **54** of second and first walls **16** and **14**, respectively, overlap for sealing medicament **62** within an internal volume **60** within medicament holder **58**.

In this third embodiment, medicament holder **58** may also be made as a discrete unit, separately from the rest of the inhaler apparatus. In this alternative, medicament holder **58** is fabricated by metering the selected medicament onto a first cover portion. A second cover portion is placed over the deposited medicament and the cover portions are sealed together using heat, adhesive or any other suitable means known to those skilled in the art to form holder **58**. The assembled medicament holder **58** may then be adhered with inhaler **10** on either interior surface **52** or **48**, and assembly completed as described herein.

In a still further embodiment (not shown), medicament holder **58** can be defined by the internal volume of housing **12**. In this embodiment, cover slips are used to seal air inlet port and air outlet port **18** and **20**, respectively, thus sealing medicament **62** within housing **12**.

Techniques for metering particulate medicaments are well known to those of ordinary skill. Suitable techniques include measuring volumes or weights of medicament directly onto surface **48**, or cover portion **54**, such as by vacuum tube; evaporation from suspension or solution, or by electrostatic deposition. In addition to metering particulate medicaments into medicament holder **58**, medicaments may also be placed on or into a suitable carrier such as beads, meshes, fibrous materials of films, as discussed for example in U.S. Patent Nos. 5,619,984 and 5,647,347, both of which are hereby incorporated by reference. These alternate substrates may be positioned in the internal housing volume as would be recognized by those of ordinary skill, to achieve substantially the same function and result in substantially the same was described above.

Medicament **62** may comprise any diagnostic or therapeutic agent that is suitable for inhalation. Generally, particles suitable for respiration have an aerodynamic diameter of between 0.5 and 10 micrometers. 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, ketoifen or nedocromil; antiinfectives, e.g., cephalosporins, penicillins, streptomycin, sulphonamides, tetracyclines and pentamidine; antihistamines, e.g., methapyrilene; anti-inflammatories, e.g., beclomethasone dipropionate, fluticasone propionate, flunisolilde, budesonide, rofleponide, mometasone furoate or triamcinolone acetonide; antitussives, e.g., noscapine; bronchodilators, e.g., albuterol, salmeterol, ephedrine, adrenaline, fenoterol, formoterol, isoprenaline, metaproterenol, phenylephrine, phenylpropanolamine, pirbuterol, reproterol, rimiterol, terbutaline, isoetharine, tulobuterol, orciprenaline, or (-)-4-amino-3,5-dichloro- -[[[6-2-(2-pyridinyl)ethoxy)]hexyl] methyl] benzenemethanol; diuretics, e.g., amiloride; anticholinergics, e.g., ipratropium, tiotroprium, 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 glucagon; vaccines; diagnostics; and gene therapy agents. 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 optimize the activity and/or stability of the medicament.

Preferred medicaments are selected from albuterol, salmeterol, fluticasone propionate and beclomethasone dipropionate and salts or solvates thereof, e.g., the sulphate of albuterol and the xinafoate of salmeterol.

Medicaments can also be delivered in combinations. Preferred formulations containing combinations of active ingredients contain salbutamol (e.g., as the free base or the sulphate salt) or salmeterol (e.g.,

as the xinafoate salt) in combination with an anti-inflammatory steroid such as a beclomethasone ester (e.g., the dipropionate) or a fluticasone ester (e.g., the propionate).

Combinations of medicaments may be premixed compounds delivered in a single medicament holder. Alternatively, combinations may be single compounds individually packaged in separated medicament holders, with combinations of such different medicaments being presented in the same device.

Indeed, it is envisioned in accordance with this invention that any suitable therapeutic or diagnostic agent can be included as medicament **62** within medicament holder **58** or the present UDPI apparatus. The medicament may be a pure drug, or drug mixed with an excipient, for example, lactose.

Operation and Use of the Unit Dose Inhaler Apparatus

Referring now to Figures 5 through 8, the preferred method of operation and use of inhaler apparatus **10** is described. In Figure 5, a ready-to-use inhaler apparatus **10** is presented wherein the internal housing volume **13** of housing **12** can be minimal, even zero, in a non-inhalation state. Medicament holder **58** having an internal volume **60**, and including medicament **62** within its internal volume **60**, is presented in phantom as it is contained within the interior of apparatus **10**. Apparatus **10** can further comprise instructional indicia **64** which advise the user as to the direction in which the user must push medial side wall folds **28** to place inhaler apparatus **10** in its operable position. In use then, as best seen in Figure 6, the user pushes inwardly along the direction of arrows **66**, and after placing air outlet port **20** next to his or her mouth, then inhales through air outlet portion **20**. Applying pressure in the direction of arrow **66** deforms and expands housing **12** and internal housing volume **13** from the non-

inhalation state of Figure 5 to the inhalation state of Figures 6 through 8. An air flow chamber **68** is simultaneously formed within housing **12** between air inlet ports **18** and air outlet port **20**. Air flow can be created between air inlet ports **18** and air outlet port **20** by inhalation by the user as illustrated by air flow arrows **70**. Expansion of housing **12** to an inhalation state preferably pulls medicament holder cover portion **54**, which is mounted on the interior surface **52** of first wall **14**, away from medicament holder portion **50**, which is mounted on the interior surface **48** of second wall **16**. Thus, the expansion of housing **12** to the inhalation state pushes walls **14** and **16** away from each other to break the seal between medicament holder portion **50** and medicament holder cover portion **54**, thereby opening medicament holder **58**. Medicament **62** contained within internal holder volume **60** of medicament holder **58** is thus exposed to air flow chamber **68** and the air flow along arrows **70** once the user inhales through air outlet port **20** to create the air flow represented by arrows **70**. Medicament **62** then flows along air flow depicted by arrows **70** into the mouth and ultimately into the lungs of the user, where medicament **62** is delivered to the desired location within the lung. Preferably, then, medicament **62** is exposed to air flow within air chamber **68** simultaneously with the expansion of housing volume **13** of housing **12**.

In use then, as best seen in Figure 6, the user pushes inwardly along the direction of arrows **66** to laterally compress housing **12** to deform and expand housing **12** and internal housing volume **13** from the non-inhalation state of Figure 5 to the inhalation state of Figures 6 through 8. An air flow chamber **68** is simultaneously formed within housing **12** between air inlet ports **18** and air outlet port **20**. Air flow can be created through air inlet ports **18** and air outlet port **20** by inhalation by the user as illustrated by air flow arrows **70**. At the same time, expansion of housing **12** to an inhalation

state releases the sealed medicament **62** from medicament holder **58** within the air flow chamber **68**.

In embodiments using one or more cover portions, this expansion pulls medicament holder cover portion **54**, which is mounted on the interior surface **52** of first wall **14**, away from opposing second wall **16** or, if two cover portions are included in inhaler apparatus **10**, away from medicament holder portion **50** which is mounted on the interior surface **48** of second wall **16**. The expansion of housing **12** to the inhalation state breaks the adhesive seal holding medicament holder **58** together and releases the contents thereof within the air flow chamber **68**. It will be recognized that the seal between cover portion **54** and either second wall **16** or cover portion **50** must be such that the layers can be peeled apart to expose the drug in the device. Alternatively, though, exposure of the medicament may be provided by using tearable cover portion materials. In such an instance, the shear force exerted on the cover portion(s) as it (they) are pulled by the housing walls during the transition to the inhalation state ruptures at least one of the cover portions to expose the contents thereof, as described below.

In the alternative embodiment where drug is maintained loosely in the interior volume of inhaler apparatus **10** and the ports are covered by port seals, the seals are first removed, inhaler apparatus **10** is expanded as described above and the patient delivers the medicament content of inhaler apparatus **10** by placing the air outlet port or mouthpiece **20** against his or her lips and inhaling.

Referring now particularly to Figures 7 and 8, cross-sectional views present the operation of the invention in more detail. Particularly, the operation of valve or filter flap **56** is depicted. In Figure 7, flap **56** comprises a non-porous material, such as foil or plastic film, and is attached to first wall **14** on the opposite side of air inlet port **18** from primary fold **40**. Thus, filter

flap **56** includes an attached end **72** and a free end **74**. At rest, free end **74** rests against first wall **14** and prevents entry of undesirable contaminants into the interior of inhaler apparatus **10**. During use, however, free end **74** of filter flap **56** proceeds toward air outlet port **20** as air flow proceeds along arrows **70** through air flow chamber **68**. As free end **74** moves in this manner, filter flap **56** extends substantially vertically into the interior of inhaler apparatus **10**, which prevents some portion of medicament **62** from spilling from inhaler apparatus **10** via air inlet ports **18** or from being blown from the device should the user erroneously exhale through the device. This feature facilitates the consumption of the predetermined unit dose of medicament **62** provided in inhaler apparatus **10**.

In Figure 8, an alternative configuration is shown wherein filter flap **56** comprises a porous filter material. Thus filter flap **56** is attached to first wall **14**, around its periphery, including its ends **72**, **74**. The pores of filter flap **56** are of a sufficiently small diameter to preclude entry into the interior of apparatus **10** of unwanted particulate contaminants, while at the same time allowing for air to flow through apparatus **10** along the path described by arrows **70**. Additionally, the pores of filter flap **56** may be of a sufficiently small diameter to preclude the loss of medicament **62** through air inlet port **18**. Thus, the provision of filter flap **56** facilitates the administration of an appropriate unit dose to the patient using inhaler apparatus **10** in that substantially all of medicament **62** passes out of inhaler apparatus **10** through air outlet port **20** along the air path described by arrows **70** and into the patient's lungs.

As described with reference to Figures 7 and 8, filter flap **56** may serve several functions. Flap **56** can permit the passage of air through air inlet ports **18** so that medicament within inhaler apparatus **10** can be inhaled. When a porous material is used, flap **56** prevents the entry of undesirable particles into the interior of housing **12**. When a non-porous

material is used, flap **56** prevents a person using inhaler apparatus **10** from exhaling through the air outlet and blowing the dose out of the air flow chamber through the air inlet ports prior to inhaling the dose into his or her lungs. It will be appreciated by those of ordinary skill, that a variety of other mechanisms for preventing medicament from being blown through air inlet port **18** may also be used, such as a one-way valve, a duck bill valve, etc. Likewise, such a mechanism may be positioned at various points within housing **12**. In the preferred embodiment described above it is positioned at air inlet port **18**. However, a valve mechanism could also be positioned in a more proximal position, such as between the medicament **62** and air outlet port or mouthpiece **20**.

As will be appreciated by those of skill in the art, and as shown in Figures 3, 5, 6, 7 and 8, inhaler apparatus **10** can optionally include additional features to suitably deagglomerate the micronized or particulate drug when the inhaler is used in the manner described above. For instance, the deagglomerating mechanisms include any known to those of ordinary skill, and include, without limitation the following: inhaler apparatus **10** may be fitted with deagglomerator **D**, shown in one embodiment as a mesh screen, which is positioned between medicament **62** and mouthpiece **20** upon which medicament **62** impacts upon inhalation to break up agglomerated drug particles and increasing fine particle mass. Alternatively, inhaler apparatus **10** may include angled abutment surfaces for creating a tortuous walled pathway through which medicament **62** passes and impacts against during inhalation to achieve the same results. Further still, the selected cover portion **50** or **54** on which the drug is positioned, may be made of a suitable material and affixed to the selected interior surface of housing **12** in such a manner that the selected cover portion vibrates upon inhalation, again assisting in deagglomeration.

Additional Embodiments

It is envisioned according to this invention that the inhaler apparatus described above can also be presented in different housing configurations. For instance and as shown in Figures 9A and 9B, inhaler apparatus **100** has a housing **102**, which can be tubular, having a proximal end **104**, a distal end **106** and a central bore **108** extending therebetween. In such an embodiment, an air inlet **110** is defined in housing **102** within the region of distal end **106** and air outlet **112** is defined within the region of proximal end **104**. A first wall **120** and a second wall **130** are positioned within central bore **108** and are movable along the internal length of central bore **108**. Medicament **M** can be maintained on or packed in beads between deagglomeration screens **140** and **142**. In the non-inhalation state, walls **120** and **130** are located between the air ports **110** and **112**. A seal can be present between the inner length of housing **102** and peripheral edges of walls **120** and **130** to prevent medicament **M** from movement. In this non-inhalation state, the internal volume of housing **102** between walls **120** and **130** is minimal and no air flow chamber is yet formed between air inlet **110** and air outlet **112**.

To prepare such an embodiment for use, walls **120** and **130** are drawn to their inhalation state by pulling them away from each other and toward opposite ends of housing **102** as shown in Figure 9B. String **S** can be used to accomplish such movement of walls **120** and **130** by a user pulling the strings. By this movement, the internal housing volume is increased and, as walls **120** and **130** are drawn past air outlet **112** and air inlet **110**, respectively, an air flow chamber is formed within central bore **108** between air inlet **110** and air outlet **112**. Suitable means, such as inwardly directed lips **122** may be suitably placed at central bore **108** to prevent walls **120** and **130** from being withdrawn from the bore completely.

For use in the inhalation state, the user inhales through air outlet **112** to cause an air flow within central bore **108**. Particles of medicament **M** are entrained in the air flow and the drug can be carried to the lungs of the user.

An additional embodiment of an inhaler apparatus according to the present invention is shown in Figure 10 wherein inhaler apparatus **150** is illustrated and is very similar to inhaler apparatus **100** of Figures 9A and 9B. Inhaler apparatus **150**, however, differs by including a series of additional, spaced-apart deagglomerators **D1**, **D2** and **D3**, which are illustrated in a preferred embodiment as screens. Deagglomerators **D1**, **D2** and **D3** are attached to string **S** which, in this embodiment, extends through one end of housing **102** and to deagglomerator screen **140**. Upon moving the device from the non-inhalation state to the inhalation state, deagglomerators **D1**, **D2** and **D3** are moved from a stacked arrangement against screen **140** and the positions depicted in Figure 10, to aide in further breaking up agglomerated powder particles.

In still another alternative embodiment and as shown in Figures 11A and 11B, inhalation apparatus **200** comprises a housing **202** having an expandable and collapsible accordion-like length. A first wall **210** is at one end of the housing, and a second wall **220** is at the opposite end. An air inlet port **230** and an air outlet port **240** are formed in opposite ends of housing **202**, in walls **210** and **220** or in the length of the housing. A medicament dose **M** is positioned medially in the length of the housing between the ends, as medicament **M** is attached to a substrate **X** which in Figures 11A and 11B takes the form of a mesh.

In the non-inhalation state, this accodian embodiment is collapsed, compressed into a compact, low profile package. In this non-inhalation state, the internal volume is minimal, as walls **210** and **220** are in close proximity to each other, and medicament **M** is positioned therebetween. Air

inlet port **230** and air outlet port **240** are suitably covered to prevent an air flow chamber from being formed therebetween.

To prepare this accordian embodiment of Figure 11A for use in its inhalation state, air inlet and outlet ports **230** and **240** are unsealed, and walls **210** and **220** are drawn away from each other by pulling tabs **T** thus expanding housing **202**. Upon expansion, as seen in Figure 11B, the internal housing volume is increased and an airflow chamber is created within housing **202**. The user then may inhale through air outlet port **240**, entrain medicament **M** in the inhalation stream and deliver medicament **M** to his or her lungs.

As will be appreciated by those of ordinary skill, medicament **M** may be suitably packaged in these additional embodiments in the same fashion described for all other embodiments: a medicament holder may be formed between the first and second walls themselves, may comprise a single cover portion layer and one wall, or may comprise two cover portions sealed to form an envelope.

The medicament may also be carried by substrates. Examples of substrates include mesh substrates loaded with drug and fixed within the housing between the walls; or beads loaded with drug and positioned between containment screens within the device.

Unidirectional flow valves and deagglomerators can also be incorporated within such alternative devices as described above. Deagglomerators can be fitted into the alternative housings which would act to break up larger particulate agglomerates. For instance, one or more screens may be placed within the bore of the tubular embodiment or the baffles embodiment, also between the movable walls. The screens may be linked to each other at slight distances by one or more strings or leaders to form a tow line, such as that depicted in Figure 10. One end of the tow line is anchored at a location within the housing, and the other to the wall toward

the proximal end of the device. When the proximal-most wall is drawn toward its inhalation state, the screen(s) also move proximally. The leader(s) making up the tow line distances the screens at intervals along the air chamber path as the device is configured to its inhalation state. In use, the user inhales into the outlet port, draws the medicament into the air flow stream, where the medicament impacts the successive deagglomeration screens, assisting any particle agglomerates to break up prior to exiting the air outlet port.

Based on the foregoing detailed description, it is apparent to one having ordinary skill in the art that an inhaler apparatus of this invention is small and compact and is therefore easily carried upon the person of a user. Given the preferred construction of paper and foil, an inhaler apparatus of this invention is also inexpensive to manufacture and can be discarded after its unit dose is consumed. An inhaler apparatus of this invention is also easy to use, thus addressing the problem of patient compliance with prescribed instructions associated with delivery of the medicament. Patient compliance is also facilitated in that inhaler apparatus **10** is easily carried on the patient's person.

It is also seen that a method for preparing medicament for inhalation as well as a method for delivering medicament by inhalation are provided.

It will be understood that various details of the invention may be changed without departing from the scope of the invention. Furthermore, the foregoing description is for the purpose of illustration only, and not for the purpose of limitation, as the invention is defined by the claims set forth below.

This 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 herein. They may take the form of

product, composition, process or use claims and may include, by way of example and without limitation, one or more of the following claims.

CLAIMS

What is claimed is:

1. An inhaler apparatus comprising:

(a) a housing;

(b) first and second walls defining an air inlet and an air outlet, said housing and said first and second walls defining an internal housing volume, said first and second walls being at least partially movable relative to each other so as to expand said internal housing volume from a non-inhalation state, wherein said internal housing volume has a first volume, to an inhalation state, wherein said internal housing volume has a second volume, said second volume being larger than said first volume, and said housing defining an air flow chamber between said air inlet and said air outlet when said housing is in said inhalation state; and

(c) medicament contained between said first and second walls, said medicament being exposed within said air flow chamber when said housing is in said inhalation state.

2. The inhaler apparatus of claim 1, further comprising a medicament holder positioned within said housing between said first and second walls and defining an internal volume, said medicament positioned within said internal volume of said medicament holder.

3. The inhaler apparatus of claim 2, wherein said medicament holder comprises said first and second walls.

4. The inhaler apparatus of claim 2, wherein said medicament holder comprises at least one cover portion attached to at least said first wall of said housing.

5. The inhaler apparatus of claim 4, wherein said cover portion is constructed of foil.

6. The inhaler apparatus of claim 2, wherein said medicament holder comprises two, opposing cover portions and wherein one of said two cover portions is attached to said first wall of said housing and the other of said two cover portions is attached to said second wall of said housing.

7. The inhaler apparatus of claim 1, wherein said housing is substantially planar in said non-inhalation state and substantially non-planar in said inhalation state.

8. The inhaler apparatus of claim 1, wherein said housing is constructed of paper.

9. The inhaler apparatus of claim 1, wherein said medicament comprises one or more therapeutic or diagnostic agents or combination thereof.

10. The inhaler apparatus of claim 9, wherein said medicament is contained within a single medicament holder.

11. The inhaler apparatus of claim 9, wherein said medicament comprises two separate agents each contained within separate medicament holders.

12. The inhaler apparatus of claim 9, wherein said agent comprises a dry powder medicament.

13. The inhaler apparatus of claim 1, wherein said medicament is selected from the group consisting of analgesic, anginal preparation, antiallergic, anti-infective, antihistamine, anti-inflammatory, antitussive, bronchodilator, corticosteroid, diuretic, anticholinergic, hormone, xanthine, therapeutic protein or peptide, vaccine, diagnostic agent or gene therapy agent.

14. The inhaler apparatus of claim 13, wherein medicament is selected from the group consisting of codeine, dihydromorphine, ergotamine, fentanyl, morphine, diltiazem, cromoglycate, ketotifen, nedocromil, cephalosporins, penicillins, streptomycin, sulphonamides,

tetracyclines, pentamidine, methapyrilene, beclomethasone dipropionate, fluticasone propionate, flunisolide, budesonide, rofleponide, mometsasone furoate, triamcinolone acetonide, noscapine, albuterol, salmeterol, ephedrine, adrenaline, fenoterol, formoterol, isoprenaline, metaproterenol, phenylephrine, phenylpropanolamine, pirbuterol, reproterol, rimiterol, terbutaline, isoetharine, tulobuterol, orciprenaline, (-)-4-amino-3,5-dichloro- -[[[6-[2-(2-pyridinyl)ethoxy]-hexyl]methyl] benzenemethanol, amiloride, ipratropium, tiotroprium, atropine or oxitropium, cortisone, hydrocortisone or prednisolone, aminophylloine, choline theophyllinate, lysine theophyllinate or theophylline, insulin or glucagon, or salts, esters, or solvates thereof, alone or in combination.

15. The inhaler apparatus of claim 1, wherein said medicament is releasably retained on a substrate.

16. The inhaler apparatus of claim 15, wherein said substrate is selected from the group consisting of spheres, meshes, fibers or films.

17. The inhaler apparatus of claim 1, further comprising a valve carried by said housing, said valve allowing unidirectional air flow through said housing.

18. The inhaler apparatus of claim 17, wherein said valve allows unidirectional air flow from said air inlet to said air outlet.

19. The inhaler apparatus of claim 1, further comprising a deagglomerator within said housing between said air inlet and air outlet.

20. The inhaler apparatus of claim 19, wherein said deagglomerator is positioned between said medicament and said air outlet when said housing is in said inhalation state.

21. The inhaler apparatus of claim 1, wherein said housing is tubular with said first and second walls movably positioned within said tubular housing such that in said inhalation state, said first and second walls

are spaced-apart from one another with each of said first and second walls positioned substantially at opposite ends of said tubular housing.

22. The inhaler apparatus of claim 21, wherein said tubular housing is collapsible between the opposite ends of said tubular housing.

23. The inhalar apparatus of claim 1, wherein said housing and said first and second walls are integral.

24. An inhaler apparatus comprising of:

(a) a flexible housing having first and second walls, said housing defining an air inlet and an air outlet and an internal housing volume, said housing being compressible from a non-inhalation state wherein said housing is substantially planar to an inhalation state wherein said housing is substantially non-planar to expand said housing volume wherein an air flow chamber is defined within said housing between said air inlet and said air outlet in said inhalation state of said housing; and

(b) a medicament holder for containing medicament in a sealed manner when said medicament holder is in a closed position, said medicament holder having an internal holder volume and said medicament holder being positioned within said housing between said first and second walls, said medicament holder further comprising first and second cover portions attached, respectively, to inner sides of first and second walls of said housing such that compression of said housing to expand said housing volume pulls apart said first and second cover portions to open said medicament holder from its closed position;

whereby said medicament holder is closed when said housing is in said substantially planar, non-inhalation state and said medicament holder

is open with its holder volume exposed to said air flow chamber when said housing is in said substantially non-planar, inhalation state.

25. A method for delivering medicament for inhalation, said method comprising the steps of:

(a) providing an inhaler apparatus comprising:

(i) a housing having first and second walls defining an air inlet and an air outlet, said housing and said first and second walls defining an internal housing volume, said first and second walls being at least partially movable relative to each other so as to expand said internal housing volume from a non-inhalation state, wherein said internal housing volume has a first volume, to an inhalation state, wherein said internal housing volume has a second volume, said second volume being larger than said first volume, and said housing defining an air flow chamber between said air inlet and said air outlet when said housing is in said inhalation state; and

(ii) medicament contained between said first and second walls, said medicament being exposed within said air flow chamber when said housing is in said inhalation state;

(b) moving said first and second walls to said inhalation state to thereby expose said medicament to said air flow chamber; and

(c) creating an air flow through said air flow chamber from said air inlet to said air outlet to deliver said medicament from said inhaler apparatus through said air outlet.

26. The method of claim 25, wherein said first and second walls of said housing of said inhaler are moved to expose said medicament to said air flow chamber by compressing said housing to expand said housing volume.

27. The method of claim 25, wherein a user inhales from said air outlet of said inhaler apparatus to create said air flow through said air flow chamber and further comprising the step of said user subsequently inhaling said medicament.

28. The method of claim 25, further comprising the step of deagglomerating said medicament by use of a deagglomerator within said housing.

29. A method of preparing medicament for inhalation within an inhaler apparatus, said method comprising the steps of:

(a) expanding an internal housing volume of an inhaler apparatus to form an air flow chamber within said inhaler apparatus; and

(b) exposing previously unexposed medicament within said housing volume of said inhaler apparatus to said air flow chamber whereby said medicament is prepared for inhalation and wherein said step of paragraph (a) causes and occurs substantially simultaneously with exposure of said medicament to said air flow chamber.

30. The method of claim 29, further comprising the initial step of maintaining said medicament in a sealed medicament holder within said housing volume of said inhaler apparatus and wherein said medicament holder is opened by expansion of said housing volume for exposure of said medicament to said air flow chamber.

31. A method of delivering a medicament to a user by inhalation, said method comprising the steps of preparing medicament for inhalation

according to the steps of claim 29 and further comprising the last step of a user inhaling said medicament through an air outlet of said inhaler apparatus.

32. An inhaler apparatus comprising:

(a) a flexible housing having first and second walls, said housing defining an air inlet and an air outlet and an internal housing volume, said housing being deformable so as to expand said housing volume from a non-inhalation state wherein said housing is substantially planar to an inhalation state wherein said housing is substantially non-planar and wherein an air flow chamber is defined within said housing between said air inlet and said air outlet; and

(b) a medicament holder for containing medicament in a sealed manner when said medicament holder is in a closed position, said medicament holder having an internal holder volume and said medicament holder being positioned within said housing between said first and second walls, said medicament holder further having at least one cover portion attached to at least said first wall of said housing such that said cover portion is pulled by expansion of said housing volume to said inhalation state to open said medicament holder from its closed position;

whereby said medicament holder is closed when said housing volume is in said substantially planar, non-inhalation state and said medicament holder is open with its internal holder volume exposed to said air flow chamber when said housing volume is in said substantially non-planar, inhalation state.

33. The inhaler apparatus of claim 32, wherein said medicament holder comprises two, opposing cover portions and wherein one of said two cover portions is attached to said first wall of said housing and the other of said two cover portions is attached to said second wall of said housing.

34. The inhaler apparatus of claim 32, wherein said housing is constructed of paper and said cover portion is constructed of foil.

35. A method for delivering medicament for inhalation, said method comprising the steps of:

(a) providing an inhaler apparatus comprising:

(i) a flexible housing having first and second walls, said housing defining an air inlet and an air outlet and an internal housing volume, said housing being deformable so as to expand said housing volume from a non-inhalation state wherein said housing is substantially planar to an inhalation state wherein said housing is substantially non-planar and wherein an air flow chamber is defined within said housing between said air inlet and said air outlet; and

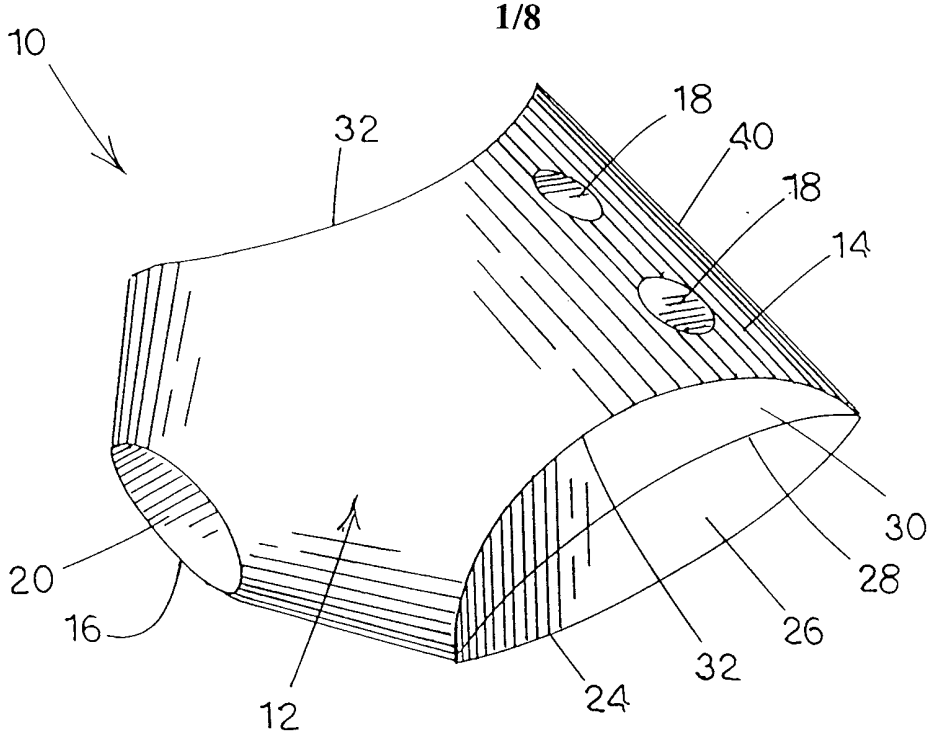
(ii) a medicament holder having an internal holder volume containing medicament, said medicament holder positioned within said housing between said first and second walls and said medicament holder having at least one cover portion attached to at least said first wall of said housing;

(b) deforming said housing to expand said housing volume and thereby open said medicament holder and expose said medicament to said air flow chamber; and

(c) creating an air flow through said air flow chamber from said air inlet to said air outlet to deliver said medicament from said inhaler apparatus through said air outlet.

36. The method of claim 35, wherein said housing of said inhaler apparatus is deformed by compressing said housing to expand said housing volume.

37. The method of claim 36, wherein a user inhales from said air inlet of said inhaler apparatus to create said air flow through said air flow chamber and further comprising the step of said user subsequently inhaling said medicament.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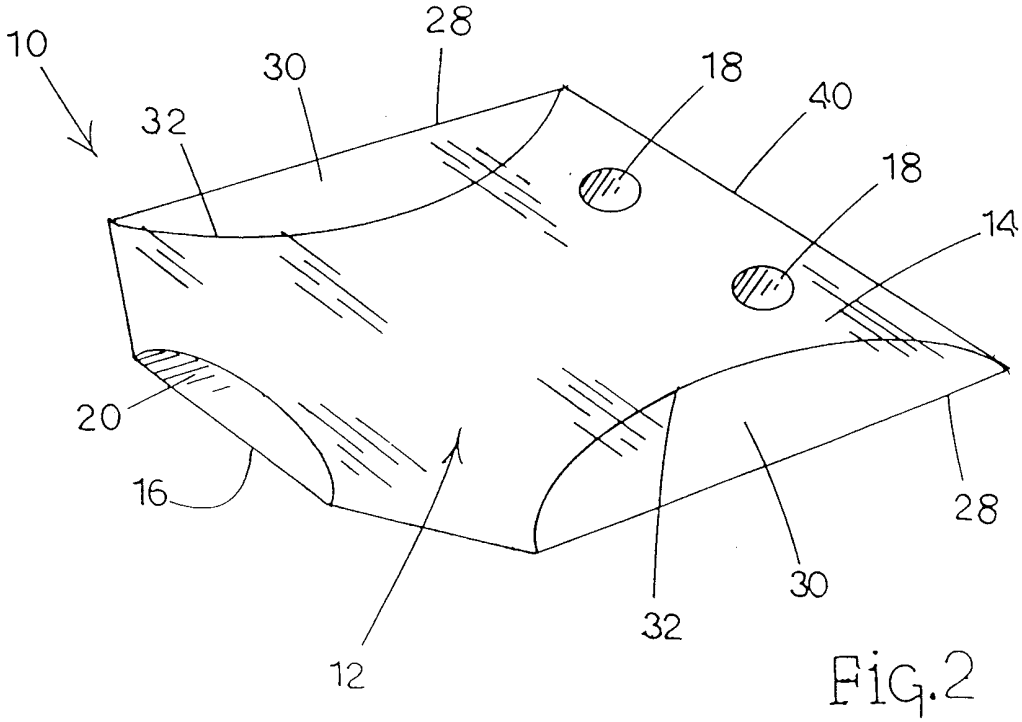
32
26

Fig.1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30
28

Fig.2

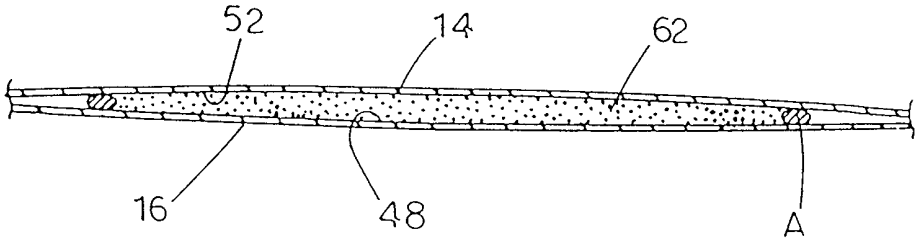


FIG.3A

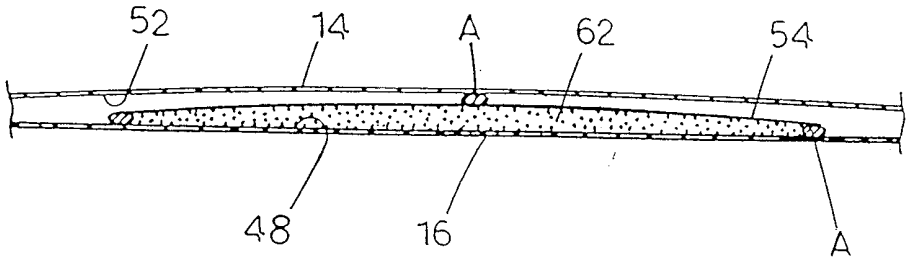


FIG.3B

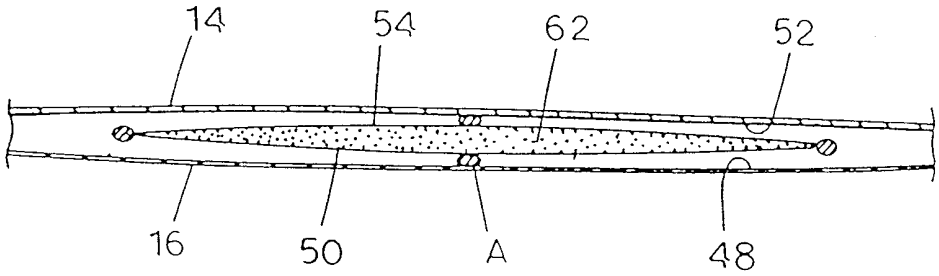
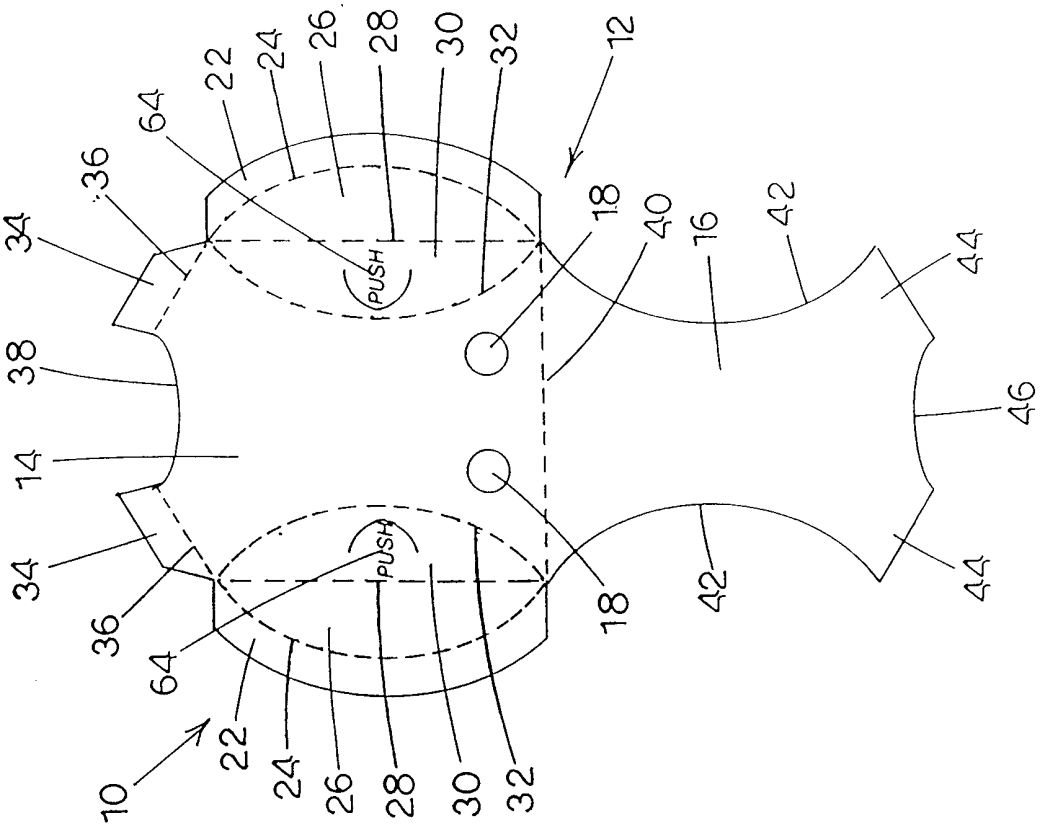


FIG.3C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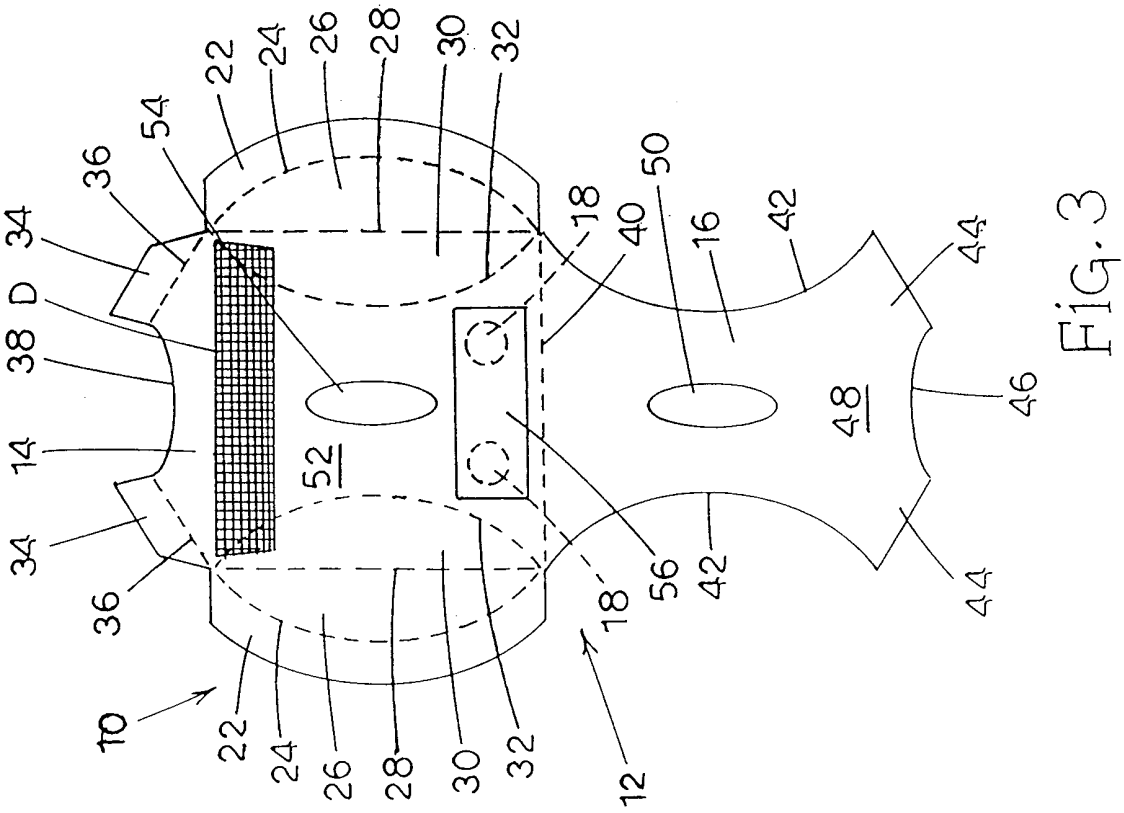
22
24
26
28
30
32
64
36
34
38
14
PUSH
18
40
16
42
44
46
10

FIG. 4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26
28
30
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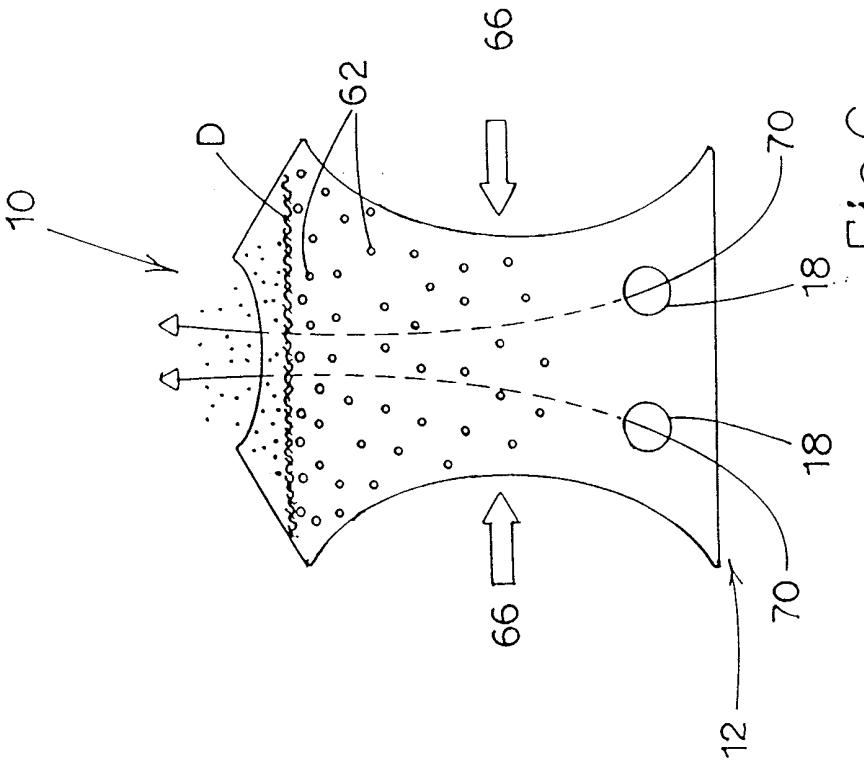
56
10
12

FIG. 3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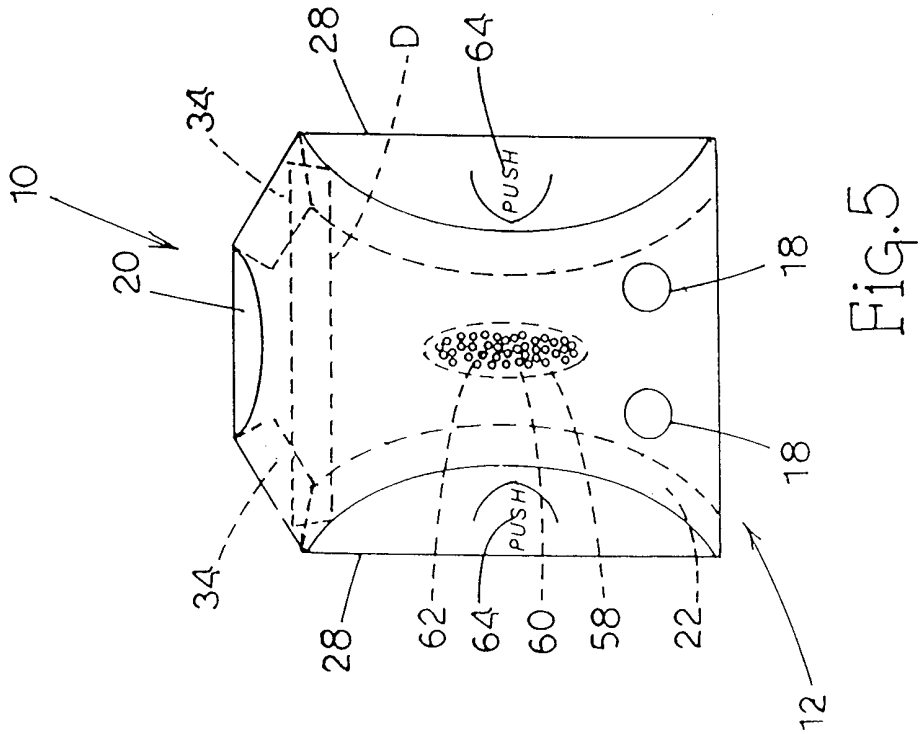
18
18
70
66
12

FIG.6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D
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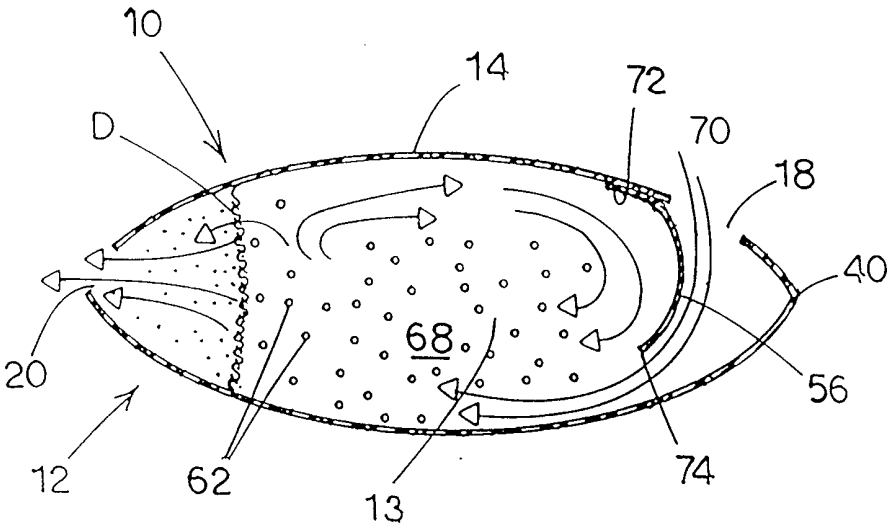
34
10
PUSH
20
18
18
PUSH
34
28
62
64
60
58
22
12

FIG.5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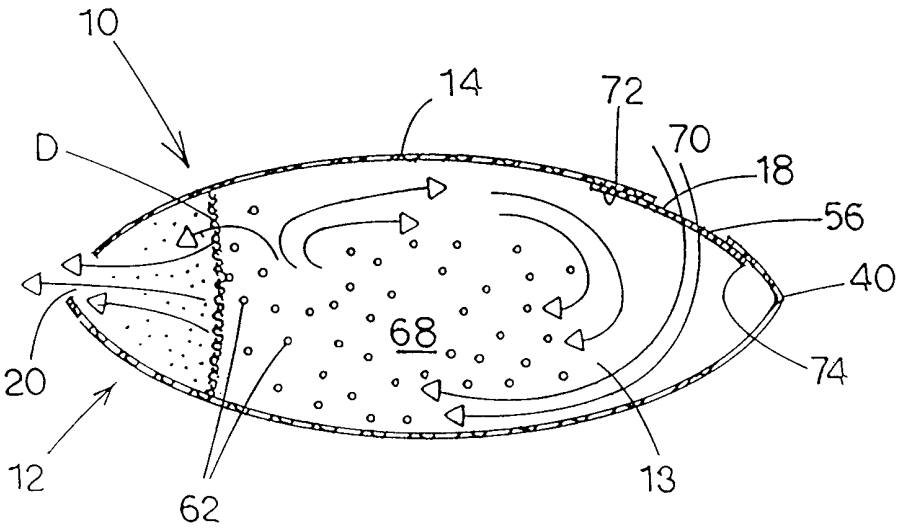
13
74

Fig.7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D
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62
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Fig.8

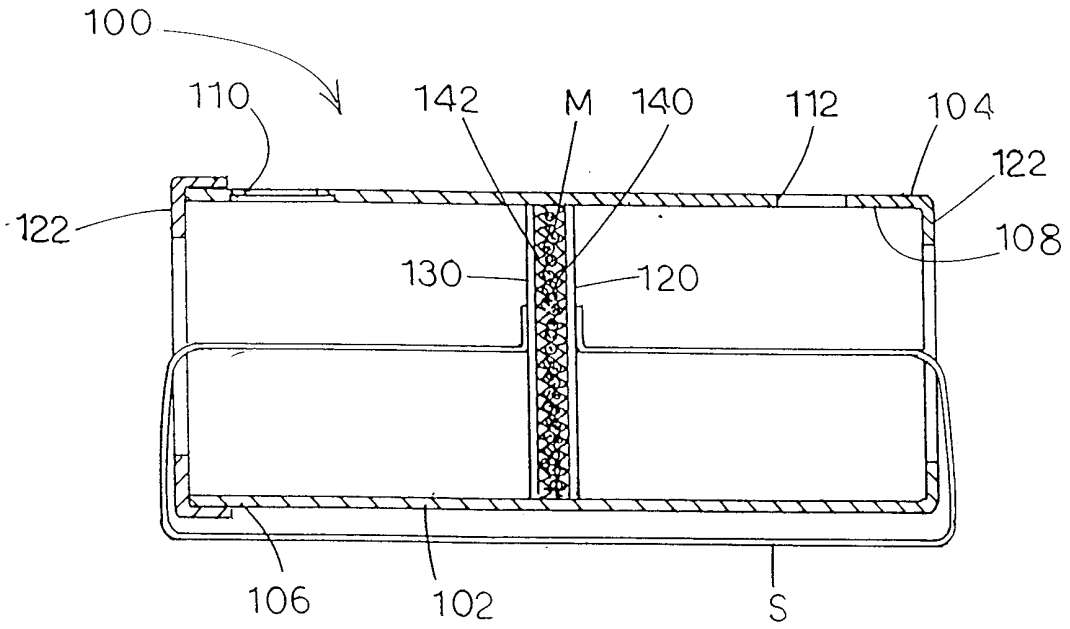
100
110
142
M
140
112
104
122
122
108
130
120
106
102
S

FIG. 9A

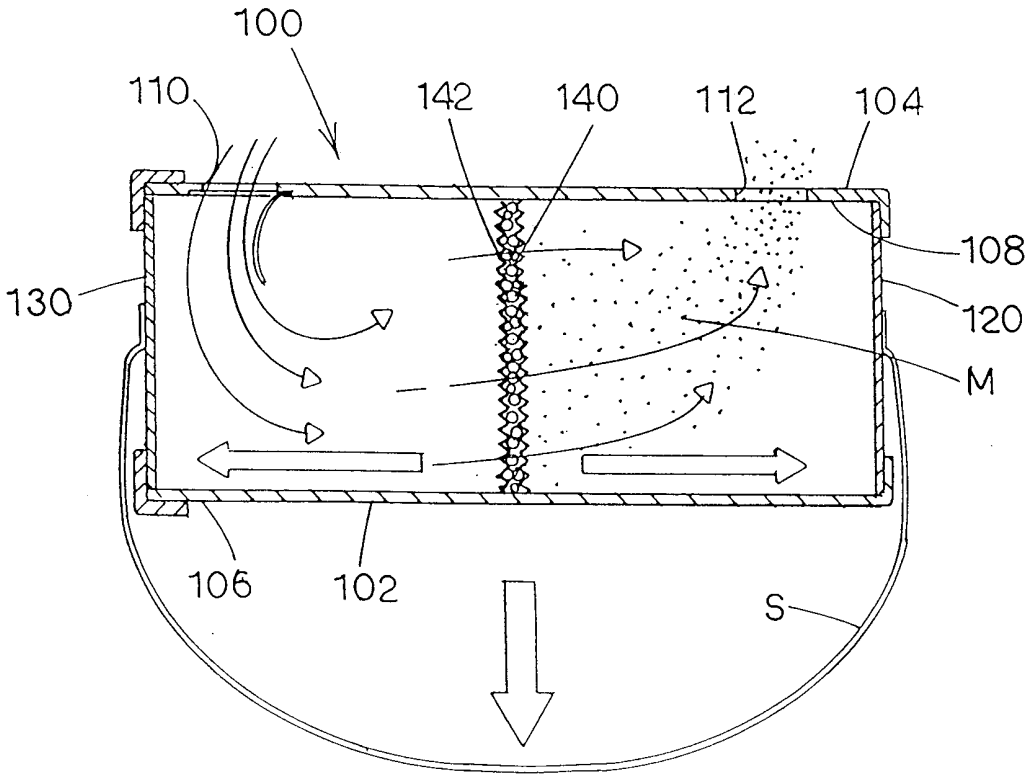
100
110
142
140
112
104
108
130
120
M
106
102
S

FIG. 9B

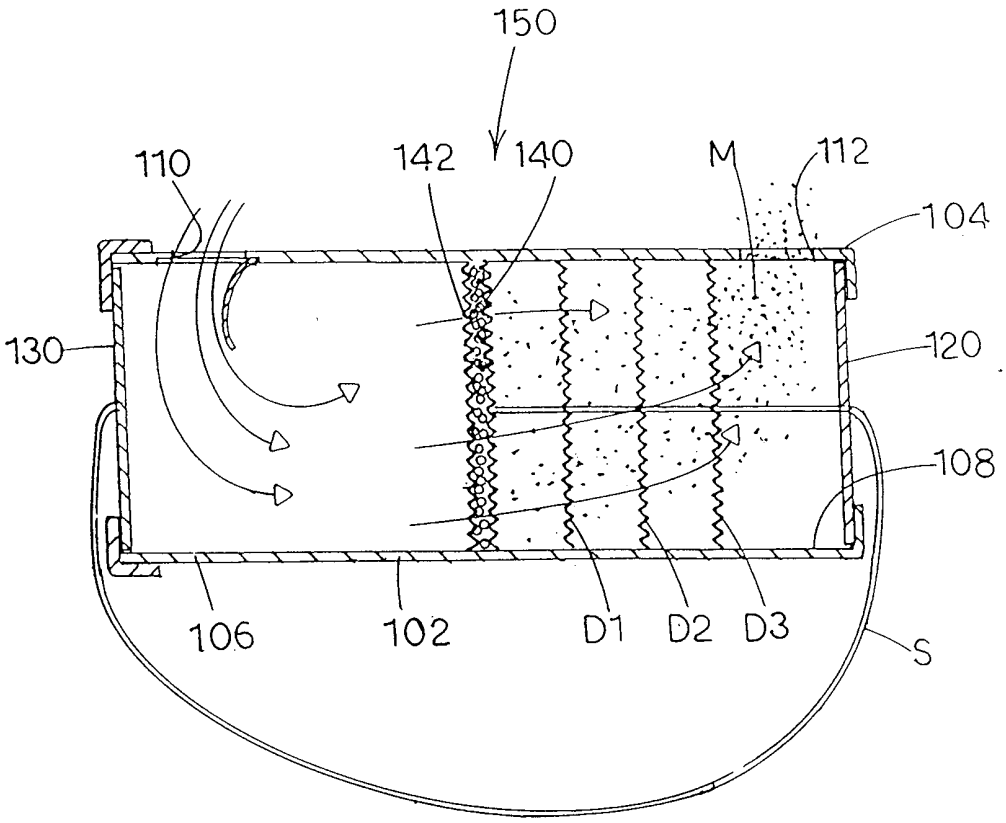

FIG.10

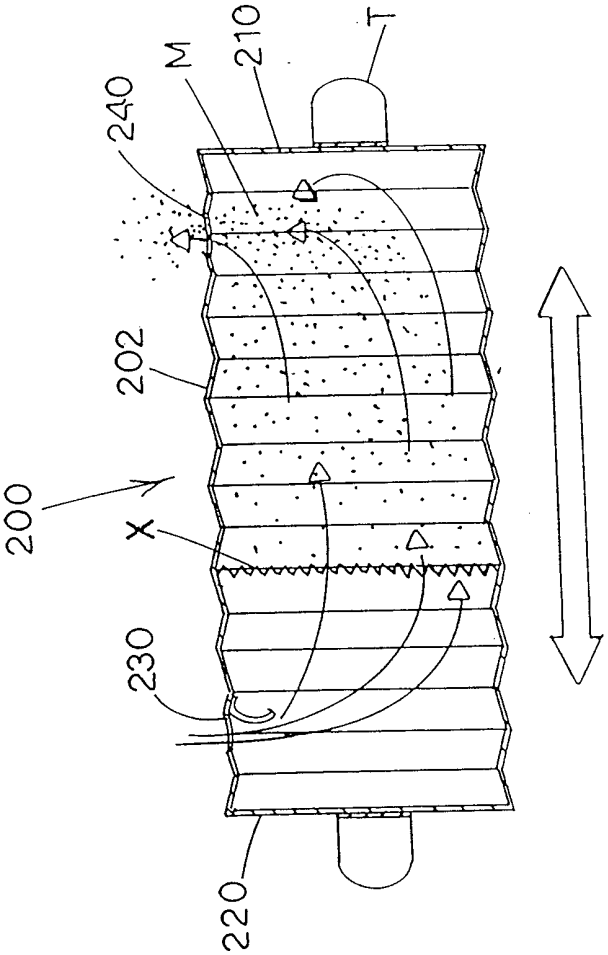

FIG. 11B

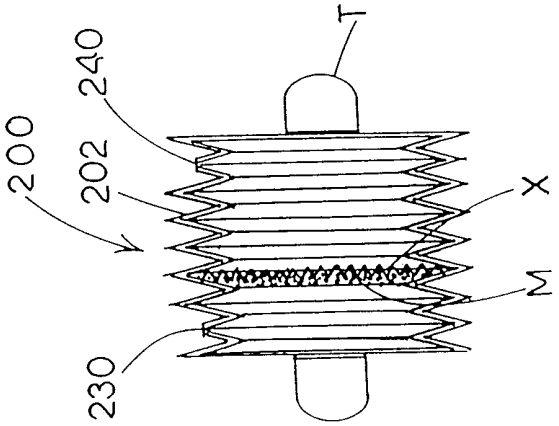

FIG. 11A

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US99/09413

A. CLASSIFICATION OF SUBJECT MATTER

IPC(6) :A61M 15/00, 16/00; B05D 7/14; B65D 83/06
US CL :128/203.12, 203.15; 604/58
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)

U.S. : 128/203.12, 203.15, 203.28; 222/636; 604/58

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 practicable, search terms used)

APS
Search Terms: powder, inhaler, flexible

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X --- Y	US 3949751 A (BIRCH et al.) 13 April 1976, Figs 1 and 2, and col. 2 line 16 to col. 4 line 64.	1-6, 8-18, 21-27, 29-34 --- 7, 19-20, 28
Y	US 5582162 A (PETERSSON) 10 December 1996, Fig. 1 elements (37)(38), and col. 3 line 64 to col. 4 line 13.	19-20, 28
Y	US 4508116 A (DUNCAN et al.) 02 April 1985, last three sentences of Abstract.	7

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

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"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

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

"P" document published prior to the international filing date but later than the priority date claimed

"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
20 JULY 1999	19 AUG 1999
Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3230	Authorized officer JOSEPH F. WEISS, JR. Telephone No. (703) 305-0323