(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
16 July 2015 (16.07.2015)

WIPO | PCT

(10) International Publication Number
WO 2015/105895 A1

(51) International Patent Classification:
A61M 15/00 (2006.01)

(21) International Application Number:
PCT/US2015/010506

(22) International Filing Date:
7 January 2015 (07.01.2015)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
14/150,268 8 January 2014 (08.01.2014) US
14/518,487 20 October 2014 (20.10.2014) US

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

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

Published:

— *with international search report (Art. 21(3))*

— *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments (Rule 48.2(h))*

(54) Title: DRY-POWDER INHALATION DEVICE

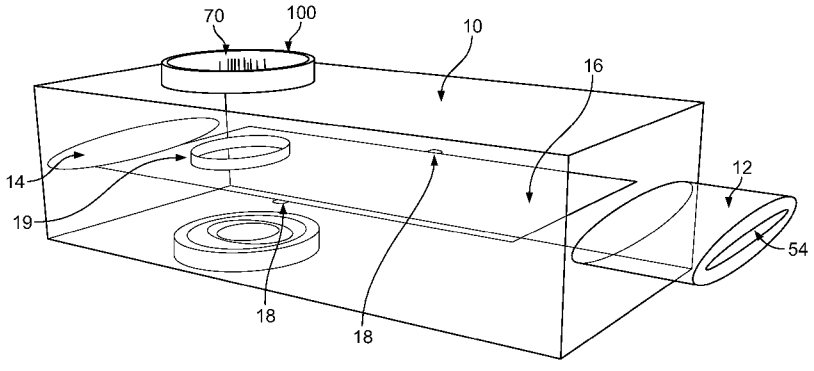


Figure 9

(57) Abstract: A dry-powder inhalation device including a casing having at least one push button located on an external portion thereof, the push button including at least one pin structure, an air inlet located at a first terminus of the casing; a powder delivery port located at a second terminus of the casing and is positioned distal to the air inlet; and an elongated support panel located within an interior of the casing and being fitted within the casing so as to partially rotate therein about a single axis. The support panel has at least one compartment containing dry-powder located proximal to the first terminus, and the at least one pin structure is located proximal to the air inlet and arranged above the dry-powder compartment. The compartment with a dry-powder includes a blister structure encasing the dry-powder, whereby airflow through the device causes the elongated support panel to partially rotate repeatedly within the casing, thereby striking the plurality of needle-like structures and releasing the dry-powder in the airflow.

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DRY-POWDER INHALATION DEVICE

FIELD OF THE INVENTION

[001] The present invention relates to improvements to dry-powder inhalers for the treatment of respiratory diseases and systemic drug delivery via deep lung access.

BACKGROUND OF THE INVENTION

[002] Numerous drugs, medications and other substances are inhaled into the lungs for rapid absorption in the blood stream and systemic delivery, or alternatively for therapeutic treatment locally. Inhaled drugs are typically either in aerosolized or powder form. In either case, the delivered agent should have a particle or droplet nuclei size that is 5 microns or less in order to reach the terminal ramifications of the respiratory tree.

[003] Such small particles are, however, thermodynamically unstable due to their high surface area to volume ratio, which provides significant excess surface free energy and encourages particles to agglomerate. Agglomeration of the particles, and adherence of the particles to the internal surfaces of the inhaler, result in delivery of particles that are too large in size, delivery of a lower dose due to particles adhering to the interior surfaces of the inhaler, and poor flow and non-uniform dispersion resulting in the delivery of a varying dosage. In addition, as noted above, many dry-powder formulations employ larger excipient particles to promote flow properties of the drug. However, separation of the drug from the excipient, as well as the presence of agglomeration, can require additional inspiratory effort, which, again, can impact the stable dispersion of the powder within the air stream of the patient. Unstable dispersions may inhibit the drug from reaching its preferred deposit/destination site and can prematurely deposit undue amounts of the drug elsewhere.

[004] Further, the hygroscopic nature of many dry-powder drugs may also require that the device be cleansed (and dried) at periodic intervals.

[005] U.S. Patent Application Publication No. 2013/0042864, filed October 3, 2012, which is hereby incorporated herein by reference in its entirety, describes a dry-powder inhaler including a casing having an air inlet located at a first terminus, a powder delivery port located at a second terminus and positioned distal to the air inlet, and an elongated assembly located within the interior of the casing. A first assembly terminus is located proximally to

the air inlet, and a second assembly terminus is located proximally to the powder delivery port. The elongated assembly is fitted within the casing such that the assembly partially rotates within the casing about a single axis, and said elongated assembly comprises at least one compartment containing a dry-powder and located proximally to the second assembly terminus. The dry-powder compartment includes a porous structure encasing the dry-powder; whereby airflow through the device causes the assembly to partially rotate or pivot within the casing about a single axis, and dry-powder is thereby released from the compartment and becomes entrained in the airflow.

[006] However, it is important to provide a single use (disposable) dry-powder inhalation device that facilitates the dispersion of active drug powder and delivers a consistent dose to the lung for respiratory disease treatment or the deep lung for systemic drug delivery. Many inhalation devices, such as described in U.S. Patent Application Publication No. 2013/0042864, require a mesh to be arranged over the dry-powder compartment and an additional film to be placed over the mesh in order to hermetically seal the compartment from air and prevent loss of the drug by movement or transport. Unfortunately, the process of filling the compartment, placing the mesh over the compartment and placing the film over the mesh is expensive and slow. Furthermore, the film is attached by glue or press, and must be pulled from over the cavity before use. However, pulling the film will twist the thin elongated assembly and disrupt its delicate rotating operation. Furthermore, developing an appropriate removable system and assembling it as an integrated part of the inhalation device is expensive and will require careful, complicated operating instructions.

[007] Therefore, a need exists for improved disposable, single dose, dry-powder inhalation device that facilitates the dispersion of active drug powder and delivers a consistent dose to the lung, and that does not utilize mesh, cover film, glue or other means to seal the dry powder compartment.

[008] In addition, a need exists for an improved single dose disposable dry-powder inhalation device that facilitates the dispersion of active drug powder and delivers a consistent dose to the lung the inhaler, but that does not require pushing, pulling or twisting of the inhalation device or of any of its components in order to withdraw the active drug powder from the dry-powder compartment.

SUMMARY OF THE INVENTION

[009] Accordingly, it is the object of the present invention to provide an improved dry-powder inhalation device which obviates the need to use a mesh and film to cover the dry-powder compartment. Without the mesh and the film, the improved dry-powder inhaler has a greatly reduced cost of packaging and assembly, as well as, cost of operation and development.

[010] It is an object of the present invention to provide an improved dry-powder inhalation device in which the dry-powder compartment is covered with a simple blister-type cover that protects the drug from moisture and light. Such blister-type covers may be composed of a material, for example, aluminum, aluminum foil or other suitable material, which may be easily punctured or ruptured.

[011] It is another object of the present invention to simplify the assembly of typical dry-powder inhalation devices, such that filling of the dry-powder compartment with the active drug powder and covering/sealing of the filled dry-powder compartment can be done inexpensively and quickly, while still being done hermetically.

[012] It is a further object of the present invention to simplify the withdrawal of the active drug powder from the dry-powder compartment by eliminating the need for a mesh and a mesh cover, as in the above-mentioned dry-powder inhalation devices. The uncovering or opening of the herein described dry-powder compartment and withdrawal of the active drug powder does not cause twisting or pulling and improper operation of the inhaler.

[013] In accordance with these and other objects of the invention, the invention relates to a dry-powder inhalation device whose dry-powder compartment is covered with a puncturable covering, such as thin aluminum foil or other known blister-pack type coverings, and sealed as known in the art. In addition, a region on an interior portion of the casing includes one or more fins, pins, edges, or other type of sharp or pointed needle- or pin-like structures. This region is arranged over or proximal to, and in alignment with, the puncturable covering of the dry-powder compartment, and is arranged such that, when the user inhales, the pin-like structures puncture the covering of the dry-powder compartment, causing the dry-powder compartment to be opened and the active drug powder within it to be withdrawn therefrom for inhalation by the user.

[014] The punctured compartment produces the same effect as does a mesh used in the prior art, i.e., providing the powder dry powder on demand. It is important to note that, in contrast to the prior art mesh and sealant, in which the inhaler film must be resistant to moisture, the arrangement of the present invention protects the air inlet and outlet opening from air and moisture. In other embodiments, a removable film may be added in order to maintain the inhaler's sterile conditions.

[015] For example, the invention can be adapted for use with known dry-powder inhalation devices, such as disclosed in US Patent Application Publication No. 2013/0042864, by placing such pin-like structures at the upper or lower surface of the casing and placing the covered dry-powder compartment on the elongated support panel that rotates within the casing. When the elongated support panel rotates towards the top surface of the casing, the covered dry-powder compartment is forced against the pin-like structures. Once the puncturable covering of the dry-powder compartment at the end of the elongated support panel strikes against the pin-like structures at the upper or lower surface of the casing, the needle- or pin-like structures puncture the puncturable covering the dry-powder compartment, thereby releasing the dry-powder from the compartment.

[016] Alternatively, the invention can be adapted for use with known dry-powder inhalation devices, such as disclosed in US Patent Application Publication No. 2013/0042864, in an alternative manner, by placing such pin-like structures on the top or bottom surface of the elongated support panel that rotates within the casing and at the end thereof. When the elongated support panel rotates towards the top or bottom surface of the casing, it strikes the covering of the dry-powder filled compartment that is situated on the upper or lower surface of the casing. Once the pin-like structures at the end of the elongated support panel strike the puncturable covering, the needle- or pin-like structures puncture the puncturable covering the dry-powder compartment, thereby releasing the dry-powder from the compartment.

[017] In certain embodiments of the present invention, the cover of the drug compartment is punctured just prior to inhalation by the user pressing a retractable button, which allows the needle- or pin-like structures to be extended and then retracted. The retraction of the arrangement of the needle- or pin-like structures avoids potential vibration interference, i.e., where the needles or pins stay at the same extended position and continue to touch the drug compartment cover with each vibration of the elongated support panel.

[018] In certain embodiments, the arrangement provides a drug compartment on only the upper or lower side of the elongated support panel, while the other side is not punctured and simply supports holding the drug compartment to be punctured. That is, the platform is rigid on the opposing side of the drug compartment and may not be punctured. In some embodiments, the pins may be on the side of the elongated support panel having the drug compartment.

[019] Modern improved inhalation devices use multi-dose blisters for drug delivery, mainly for diseases associated with the respiratory system. Some advantages of these inhalation devices are delivery of dose consistency and compliance. Some inhalation devices, such as those from MicroDose Therapeutx, Inc., claim potential control of exhaling into the device, piezo-electric mechanism for efficient delivery, and counting and protecting the user from taking repeated dose. However, the complexity of these devices and their validation is costly, and these devices are still not fool-proof delivery systems. In addition, the delivered drug amount is limited.

[020] The single disposable inhaler described herein allows those controls without the requirement of a complex electric and/or chip to be developed for the drug. A simple package arrangement and day printing on the container does the trick. The production costs are low. Following its use, the patient can dispose of the inhaler. No cleaning or resting and cartridge refilling of the device is required.

BRIEF DESCRIPTION OF THE DRAWINGS

[021] The subject matter regarded as the invention is particularly pointed out and distinctly claimed in the concluding portion of this specification. The invention, however, both as to organization and method of operation, together with objects, features, and advantages thereof, may best be understood by reference to the following detailed descriptions when read with the accompanying drawings in which:

[022] Fig. 1 shows a perspective view of a first embodiment of the inhalation device;

[023] Fig. 2 shows an exploded perspective view of an embodied inhalation device wherein the dry-powder compartment and needle-like structure are illustrated;

[024] Fig. 3a shows a cross-sectional view of an embodied inhalation device wherein the dry-powder compartment and needle-like structure are illustrated;

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[025] Fig. 3b shows a cross-sectional view of an alternate embodied inhalation device of Fig. 3a wherein the dry-powder compartment and a plurality of needle-like structures are illustrated;

[026] Fig. 4a shows a cross-sectional view of an embodied inhalation device, wherein the support panel is not blocking the airflow through said device;

[027] Figs. 4b and 4c show cross-sectional views of an embodied inhalation device wherein the ends of the support panel proximal and distal to the inlet, respectively, may block the airflow through the device;

[028] Fig. 4d shows a further cross-sectional view of an embodied inhalation device, showing some of the powder emerging from the punctured dry-powder compartment of the device after the cover of the dry-powder compartment has been punctured by the needle-like structures;

[029] Fig. 5 shows an exploded perspective view of an alternate embodied inhalation device wherein the dry-powder compartment and needle-like structure are illustrated;

[030] Fig. 6a shows a cross-sectional view of the alternate embodied inhalation device wherein the dry-powder compartment and needle-like structure are illustrated;

[031] Fig. 6b shows a cross-sectional view of an alternate embodied inhalation device of Fig. 6a wherein two dry-powder compartments and two needle-like structures are illustrated;

[032] Figs. 7a and 7b show cross-sectional views of an alternate embodied inhalation device wherein the dry-powder compartment and needle-like structure are illustrated;

[033] Figs. 7c and 7d show cross-sectional views of an alternate embodied inhalation device wherein the dry-powder compartment and needle-like structure are illustrated;

[034] Figs. 8a and 8b show cross-sectional views of an alternate embodied inhalation device wherein the dry-powder compartment and needle-like structure are illustrated;

[035] Figs. 8c and 8d show cross-sectional views of an alternate embodied inhalation device wherein the dry-powder compartment and needle-like structure are illustrated;

[036] Fig. 9 shows a perspective view of an alternate embodied inhalation device wherein the dry-powder compartment, the needle-like structure(s), and the push button(s) are illustrated;

[037] Figs. 10a and 10b are illustrations of several views of a push button according to aspects of certain embodiments of the present invention;

[038] It will be appreciated that for simplicity and clarity of illustration, elements shown in the figures have not necessarily been drawn to scale. For example, the dimensions of some of the elements may be exaggerated relative to other elements for clarity. Further, where considered appropriate, reference numerals may be repeated among the figures to indicate corresponding or analogous elements.

DETAILED DESCRIPTION OF THE INVENTION

[039] In the following detailed description, numerous specific details are set forth in order to provide a thorough understanding of the invention. However, it will be understood by those of ordinary skill in the art that the present invention may be practiced without these specific details. In other instances, well-known methods, procedures, components have not been described in detail so as not to obscure the present invention.

[040] This invention, *inter alia*, takes advantage of flow energy of inspired air to disperse neat or formulated micronized particles packaged in a dosage form. The present invention provides a novel inhaler device, in which a principle mode of operation of the device is the production of a beating action within the device, which facilitates, or causes, the release of a dry-powder drug contained in a blistered compartment located within the device.

[041] The devices, kits and/or methods of the present invention may be particularly suitable to dispense dry-powder substances to in-vivo subjects, including animal and, typically, human subjects. The dry-powder substance may include one or more active pharmaceutical constituents as well as biocompatible additives that form the desired formulation or blend.

[042] As used herein, the term "dry-powder" is used interchangeably with "dry-powder formulation" and means the dry-powder can comprise one or a plurality of constituents or ingredients with one or a plurality of (average) particulate size ranges.

[043] In some embodiments, individual dispensable quantities of dry-powder formulations can be a single ingredient or a plurality of ingredients, whether active or inactive. The inactive ingredients can include additives added to enhance flowability or to facilitate aerosolization delivery to the desired systemic target. The dry-powder drug formulations can include active particulate sizes that vary.

[044] In some embodiments, the dry-powder may comprise any therapeutic agent such as, for example, a drug or vaccine.

[045] In some embodiments, any drug or drugs that may be administered by inhalation and that are either a solid or may be incorporated in a solid carrier are envisioned for incorporation within the inhalers, kits and/or methods of this invention. In some embodiments, the drug will be a drug for the treatment of a respiratory disease or condition. In some embodiments, such drugs may comprise bronchodilators, corticosteroids and drugs for the prophylaxis of asthma. Other drugs such as anorectics, anti-depressants, anti-hypertensive agents, anti-neoplastic agents, anti-cholinergic agents, dopaminergic agents, amyloid plaque treatment, protein and prion protein mis-folding, neurodegeneration, narcotic analgesics, beta-adrenergic blocking agents, prostoglandins, sympathomimetics, tranquilizers, steroids, vitamins and/or hormones may be employed. Exemplary drugs include: Salbutamol, Terbutaline, Rimiterol, Fentanyl, Fenoterol, Pirbuterol, Reproterol, Adrenaline, Isoprenaline, Ociprenaline, Ipratropium, Beclomethasone, Betamethasone, Budesonide, Disodium Cromoglycate and analogs, Nedocromil Sodium, Ergotamine, Salmeterol, Fluticasone, Formoterol, Insulin, Atropine, Prednisolone, Benzphetamine, Chlorphentermine, Amitriptyline, Imipramine, Cloridine, Actinomycin C, Bromocriptine, Buprenorphine, Propranolol, Lacicortone, Hydrocortisone, Fluocinolone, Triamcinclone, Dinoprost, Xylometazoline, Diazepam, Lorazepam, Folic acid, Nicotinamide, Clenbuterol, Bitolterol, Ethinyloestradiol and Levenorgestrel. Drugs may be formulated as a free base, one or more pharmaceutically acceptable salts or a mixture thereof.

[046] The dry-powder formulation can also include desired excipients. Examples of excipients include lactose and trehalose. Other types of excipients can also be employed, such as, but not limited to, sugars which are approved by the United States Food and Drug Administration ("FDA") as cryoprotectants (e.g., mannitol) or as solubility enhancers (e.g., cyclodextrine) or other generally recognized as safe ("GRAS") excipients.

[047] Examples of diseases, conditions or disorders that may be treated or prevented with the inhalers, kits and/or methods of the invention include, but are not limited to, asthma, COPD (chronic obstructive pulmonary disease), viral or bacterial infections, influenza, allergies, and other respiratory ailments, as well as, diabetes, other related insulin resistance disorders and neurodegeneration. The dry-powder inhalant administration may be used to deliver locally acting agents such as antimicrobials, protease inhibitors, and nucleic

acids/oligionucleotides as well as systemic agents such as peptides like leuprolide and proteins such as insulin.

[048] For example, inhaler-based delivery of antimicrobial agents such as antitubercular compounds, proteins such as insulin for diabetes therapy or other insulin-resistance related disorders, peptides such as leuprolide acetate for treatment of prostate cancer and/or endometriosis and nucleic acids or ogligonucleotides for cystic fibrosis gene therapy may be performed. See e.g. Wolff et al., Generation of Aerosolized Drugs, J. Aerosol. Med. pp. 89-106 (1994). See also U.S. Patent Application Publication No. 2001/0053761, entitled "Method for Administering ASPB28-Human Insulin", and U.S. Patent Application Publication No. 2001/0007853, entitled "Method for Administering Monomeric Insulin Analogs", the contents of which are hereby incorporated herein by reference in their entirety.

[049] Typical dose amounts of the unitized dry-powder mixture dispersed in the inhaler will vary depending on the patient size, the systemic target, and the particular drug. Typical doses that can be delivered by the inhaler range from 10 μg to 10 mg. Some additional exemplary dry-powder drugs include, but are not limited to, albuterol, fluticasone, beclamethasone, cromolyn, terbutaline, fenoterol, β-agonists (including long-acting β-agonists), salmeterol, formoterol, cortico-steroids and glucocorticoids.

[050] In certain embodiments, the administered bolus or dose can be formulated with an increase in concentration (an increased percentage of active constituents) over conventional blends. Further, the dry-powder formulations may be configured as a smaller administrable dose compared to the conventional doses. For example, each administrable dry-powder dose may be on the order of less than about 60-70% of that of conventional doses. In certain particular embodiments, using the active dispersal systems provided by certain embodiments of the dry-powder inhaler configurations of the instant invention, the adult dose may be reduced to under about 15 mg, such as between about 10 μg to 10 mg. The active constituent(s) concentration may be between about 5-10%. In other embodiments, active constituent concentrations can be in the range of between about 10-20%, 20-25%, or even larger, up to the case where only pure drug is delivered.

[051] In certain particular embodiments, during dose dispensing, the dry-powder in a particular dose receptacle may be formulated as an active pharmaceutical constituent(s) substantially without additives (such as excipients). As used herein, "substantially without

additives" means that the dry-powder is in a substantially pure active formulation with only minimal amounts of other non-biopharmacological active ingredients. The term "minimal amounts" means that the non-active ingredients may be present, but are present in greatly reduced amounts, relative to the active ingredient(s), such that they comprise less than about 10%, and preferably less than about 5%, of the dispensed dry-powder formulation, and, in certain embodiments, the non-active ingredients are present in only trace amounts.

[052] In some embodiments, the therapeutic agent can be a biologic, which includes, but is not limited to, proteins, polypeptides, carbohydrates, polynucleotides, and nucleic acids. In some embodiments, the protein can be an antibody, which can be polyclonal or monoclonal. In some embodiments, the therapeutic can be a low molecular weight molecule. In addition, the therapeutic agents can be selected from a variety of known pharmaceuticals such as, but are not limited to: analgesics, anesthetics, analeptics, adrenergic agents, adrenergic blocking agents, adrenolytics, adrenocorticoids, adrenomimetics, anticholinergic agents, anticholinesterases, anticonvulsants, alkylating agents, alkaloids, allosteric inhibitors, anabolic steroids, antacids, anti-diarrheals, antidotes, anti-folics, antipyretics, anti-rheumatic agents, psychotherapeutic agents, neural blocking agents, anti-inflammatory agents, drugs that treat diseases associated with amyloidosis and peptide and protein mis-folding, such as prion (mad cow disease), Alzheimer's and Parkinson's diseases, anti-helmintics, anti-arrhythmic agents, antibiotics, anticoagulants, antidepressants, anti-diabetic agents, anti-epileptics, antifungals, antihistamines, antihypertensive agents, anti-muscarinic agents, anti-mycobacterial agents, anti-malarials, antiseptics, antineoplastic agents, antiprotozoal agents, immunosuppressants, immunostimulants, antithyroid agents, antiviral agents, anxiolytic sedatives, bone and skeleton agents, astringents, beta-adrenoceptor blocking agents, cardiovascular agents, chemotherapy agents, corticosteroids, cough suppressants, diagnostic agents, diagnostic imaging agents, diuretics, dopaminergics, enzymes and enzyme cofactors, gastrointestinal agents, growth factors, hematopoietic or thrombopoietic factors, hemostatics, hematological agents, hemoglobin modifiers, hormones, hypnotics, immunological agents, anti-hyperlipidemic and other lipid regulating agents, muscarinics, muscle relaxants, parasympathomimetics, parathyroid hormone, calcitonin, prostaglandins, radio pharmaceuticals, sedatives, sex hormones, anti-allergic agents, stimulants, steroids, sympathomimetics, thyroid agents, therapeutic factors acting on bone and skeleton, vasodilators, vaccines, vitamins, and xanthines. Anti-neoplastic, or anti-cancer agents,

include but are not limited to, paclitaxel and derivative compounds, and other anti-neoplastics selected from the group consisting of alkaloids, anti-metabolites, enzyme inhibitors, alkylating agents and antibiotics.

[053] Exemplary proteins, include therapeutic proteins or peptides, or carrier proteins or peptides, including GCSF, GMCSF, LHRH, VEGF, hGH, lysozyme, alpha-lactoglobulin, basic fibroblast growth factor (bFGF), asparaginase, tPA, urokin-VEGF, chymotrypsin, trypsin, streptokinase, interferon, carbonic anhydrase, ovalbumin, glucagon, ACTH, oxytocin, phosphorylase b, secretin, vasopressin, levothyroxine, phatase, beta-galactosidase, parathyroid hormone, calcitonin, fibrinogen, polyaminoacids (e.g., DNAse, alphal antitrypsin, polylysine, polyarginine), angiogenesis inhibitors or pro-immunoglobulins (e.g., antibodies), somatostatin and analogs thereof, casein, collagen, soy protein, and cytokines (e.g., interferon, interleukin and others), immunoglobulins, Exemplary hormones and hormone modulators include proinsulin, C-peptide of insulin, a mixture of insulin and C-peptide of insulin, hybrid insulin cocrystals, growth hormone, parathyroid hormone, luteinizing hormone-releasing hormone (LH-RH), adrenocorticotropic hormone (ACTH), amylin, oxytocin, luteinizing hormone, (D-Tryp6)-LHRH, nafarelin acetate, leuprolide acetate, follicle stimulating hormone, glucagon, prostaglandins, steroids, estradiols, dexamethazone, testosterone, and other factors acting on the genital organs and their derivatives, analogs and congeners.

[054] Exemplary hematopoietic or thrombopoietic factors include, among others, erythropoietin, granulocyte colony stimulating factor (G-CSF), granulocyte-macrophage stimulating factor (GM-CSF) and macrophage colony stimulating factor (M-CSF), leukocyte proliferation factor preparation, thrombopoietin, platelet proliferation stimulating factor, megakaryocyte proliferation (stimulating) factor, and factor VIII.

[055] Exemplary therapeutic factors acting on bone and skeleton and agents for treating osteoporosis include calcium, alendronate, bone GLa peptide, parathyroid hormone and its active fragments, histone H4-related bone formation and proliferation peptide and their muteins, derivatives and analogs thereof.

[056] Exemplary enzymes and enzyme cofactors include: pancrease, L-asparaginase, hyaluronidase, chymotrypsin, trypsin, tPA, streptokinase, urokinase, pancreatin, collagenase,

trypsinogen, chymotrypsinogen, plasminogen, streptokinase, adenyl cyclase, and superoxide dismutase (SOD).

[057] Exemplary vaccines include Hepatitis B, Influenza, MMR (measles, mumps, and rubella), and Polio vaccines and others.

[058] Exemplary growth factors include nerve growth factors (NGF, NGF-2/NT-3), epidermal growth factor (EGF), fibroblast growth factor (FGF), insulin-like growth factor (IGF), transforming growth factor (TGF), platelet-derived cell growth factor (PDGF), hepatocyte growth factor (HGF) and so on.

[059] Exemplary agents acting on the cardiovascular system include factors that control blood pressure, arteriosclerosis, etc., such as endothelins, endothelin inhibitors, endothelin antagonists, endothelin producing enzyme inhibitors vasopressin, renin, angiotensin I, angiotensin II, angiotensin III, angiotensin I inhibitor, angiotensin II receptor antagonist, atrial naturiuretic peptide (ANP), antiarrythmic peptide and so on.

[060] Exemplary factors acting on the central and peripheral nervous systems include opioid peptides (e.g. enkephalins, endorphins), neurotropic factor (NTF), calcitonin gene-related peptide (CGRP), thyroid hormone releasing hormone (TRH), salts and derivatives of TRH, neurotensin and so on.

[061] Exemplary chemotherapeutic agents, such as paclitaxel, mytomycin C, BCNU, and doxorubicin.

[062] Exemplary agents acting on the respiratory system include factors associated with asthmatic responses, e.g., albuterol, fluticazone, ipratropium bromide, beclamethasone, and other beta-agonists and steroids.

[063] Exemplary steroids include, but are not limited to, beclomethasone (including beclomethasone dipropionate), fluticasone (including fluticasone propionate), budesonide, estradiol, fludrocortisone, flucinonide, triamcinolone (including triamcinolone acetonide), and flunisolide. Exemplary beta-agonists include, but are not limited to, salmeterol xinafoate, formoterol fumarate, levo-albuterol, bambuterol, and tulobuterol.

[064] Exemplary anti-fungal agents include, but are not limited to, itraconazole, fluconazole, and amphotericin B.

[065] Numerous combinations of active agents may be desired including, for example, a combination of a steroid and a beta-agonist, e.g., fluticasone propionate and salmeterol, budesonide and formoterol, etc.

[066] The inhalers of this invention are dry-powder inhaler devices, comprising a casing, such as, for example, a rectangular or tubular shaped box or enclosure. In certain embodiments, the casing includes an elongated longitudinal axis, and includes a first terminus and a second terminus opposite the first terminus. The casing further includes an air inlet located at the first terminus of the casing and a powder delivery port located at the second terminus of the casing, said powder delivery port being located distal to the air inlet.

[067] The term "casing" refers to, *inter alia*, the container comprising the various elements of the device as described herein. The casing may be of any appropriate material, including, in some embodiments, any plastic or other appropriate synthetic material, which may be prepared to conform to the desired structure and will contain or comprise the elements described herein. In some embodiments, the casing may comprise a Polycarbonate or HDPE.

[068] The casing will include two openings placed at opposite ends of the casing. One such opening is the air inlet, which inlet is sufficient in size to facilitate air entry and exit therefrom. Another opening in the casing is a powder delivery port, which powder delivery port is positioned at an opposite end of the casing from that of the air inlet.

[069] The powder delivery port is an opening, and is, generally, larger in size, in terms of overall area, than the size of the air inlet.

[070] Referring now to Fig. 1a, the inlet **14** is positioned at one terminus of casing **10**, whereas the powder delivery port **54** is at the opposite end or terminus of casing **10**.

[071] The casings of this invention may be prepared by any means and may include, for example, designs which include two halves of the casing, which may be hermetically and permanently sealed, or in some embodiments, the casing may be of a single piece, for example, as prepared by molding or other conventional means.

[072] In some embodiments, the inhaler devices of this invention are suitable for inhalation delivery by mouth, or nasal delivery. According to one aspect, and in one embodiment, the powder delivery port **54** is partially enclosed by or attached to a mouthpiece **12** (see, e.g.,

Figs. 1, 2, 5 and 9), or in some embodiments, the delivery port **54** is partially enclosed by or attached to a nosepiece, which enables inhalation delivery via the mouth or nose.

[073] In some embodiments, such choice between nasal or mouth delivery will reflect a consideration of the target area for delivery in the nasopharynx and other regions of the respiratory tree, or the particle size for delivery, or the age of the subject to which the inhaled powder is being administered, or a combination thereof.

[074] In some embodiments, the air inlet **14** is positioned to be off center relative to a horizontal (i.e., longitudinal) axis, a vertical axis or a combination thereof of a side of the casing **10** containing the air inlet **14**. For example, referring to Figs. 4a-d, it is noted that the air inlet **14** is located in a lower half of side **56** relative to the longitudinal axis. Similarly, the air inlet **14** is located off-center relative to a vertical midline axis.

[075] Referring to Fig. 2, the casing **10** of the dry-powder inhaler devices of the present invention further include an elongated support panel **16** located within an interior cavity of the casing **10**. The elongated support panel **16** resembles an elongated plate, and includes a first terminus and a second terminus opposite the first terminus. In some embodiments, the first terminus is located proximally to the air inlet **14**, and the second terminus is located proximally to the powder delivery port **54**. In certain embodiments, the elongated support panel **16** is fitted, or arranged, within the casing **10** such that the elongated support panel **16** partially rotates, angles or pivots, within the casing **10** about a single axis, shown as pivot axis **18**.

[076] In some embodiments, the casing **10**, the support panel **16**, or a combination thereof is substantially rectangular. In some embodiments, the casing **10**, the support panel **16**, or a combination thereof is substantially cuboidal, or in some embodiments, the casing **10**, the support panel **16**, or a combination thereof is substantially columnar, or in some embodiments, the casing **10**, the support panel **16**, or a combination thereof is substantially oval, in shape.

[077] Referring to Figs. 3a and 3b, the longitudinal axis of the support panel **16** is preferably oriented in parallel to the longitudinal axis of the casing **10**.

[078] In some embodiments, a typical size range for the casing **10** of the present invention is between 5 cm and 15 cm in length, and with height and width dimensions in the 0.5 cm - 2 cm range. The length and width of support panel **16** are set to closer fit the inner dimensions

of this casing **10**. It should be noted that the size of the casing **10** is not a limitation on the device.

[079] Referring now to Figs. 2, 3a and 3b, in some embodiments of the invention, the elongated support panel **16** comprises at least one compartment **19**, located proximally to the second terminus of the support panel **16**, near the powder delivery port **54** when positioned within the casing **10** as herein described. In alternative embodiments, the compartment **19** is located proximally to the first terminus of the support panel **16**, near the air inlet **14**. In some embodiments, support panel **16** will comprise the same material as that of the compartment **19**, which may be formed of aluminum or some other suitable material, or in some embodiments, support panel **16** will comprise a different material than that of the compartment **19**. In some embodiments, the compartment **19** is contiguous in structure with that of support panel **16**, for example it has an indent for containing the medicament. In some embodiments, the compartment **19** is bonded, welded or otherwise attached to support panel **16**.

[080] In some embodiments, the at least one compartment **19** is a cavity that is filled with dry-powder medicament in an appropriate atmosphere and then sealed, e.g., by any suitable means as known in the art, such as is known in the field of packaging. In some embodiments, the dry-powder compartment **19** is covered and sealed by covering **60**, such as aluminum or other known blister-pack type coverings, and sealed as known in the art. Cover **60** of compartment **19** keeps the powdered medicament dry and uncontaminated. In certain embodiments, cover **60** is capable of being punctured or ruptured by sharp device or object, to thereby allow the dry-powder **52** contained within compartment **19** to be released therefrom.

[081] In certain embodiments, the casing **10** includes at least one sharp or pointed device **70** located on an internal surface thereof, proximal to the second terminus of the casing and near the powder delivery port **54**, or proximal to the first terminus of the casing near the air inlet **14**. In preferred embodiments, as shown in Fig. 2, 3a and 3b, the at least one sharp or pointed device **70** is a region of needle- or pin-like structures **70** that may include one or more fins, pins, needles, edges, or other type of sharp or pointed needle- or pin-like structures that extend from the casing **10** in a direction transverse (i.e., perpendicular) to a longitudinal

axis of the casing **10**. In preferred embodiments, the region of needle- or pin-like structures **70** is suitable for puncturing or rupturing the blister sealed compartment **19**.

[082] In some embodiments of the present invention, as shown in Fig. 3a, there is only one needle-like structure **70**. In other embodiments, as shown in Fig. 3b, there are two or more (i.e., a plurality) of needle-like structures **70**. In other embodiments of the present invention, a region, such as protruding surface, of casing **10** includes a series, comb or bristle of needle-like structures **70** (see, for example, Fig. 3b). In this embodiment, the shape of the comb of needle-like structures **70** may substantially replicate or mimic the shape of the cover **60** over compartment **19** such that, as the support panel **16** rotates and the cover **60** strikes the structures **70**, the series of needle-like structures **70** may produce a series of puncture holes, or pores, over substantially the entire surface area of the cover **60**.

[083] In preferred embodiments, the cover **60** may be fabricated from any suitable material as known in the art, such as, from an aluminum material, for example, aluminum or aluminum foil, aluminized foil, although the cover **60** may be fabricated from any suitable material that seals compartment **19** and is easily punctured or ruptured by the needle- or pin-like structures **70**.

[084] The support panel **16** located within the casing **10** is elongated and has a length sufficient that each terminus can abut or strike an interior surface of the casing **10** when rotated, angled or pivoted. Indeed, the support panel **16** is positioned within the casing **10** such that a first terminus of the support panel **16** is located proximally to the air inlet **14** while a second terminus of said support panel **16** is located proximally to said powder delivery port **54**, such that a long axis of the support panel **16** is oriented in parallel to a longitudinal axis of the casing **10**. In preferred embodiments, airflow through the device (i.e., air flowing from air inlets **14** towards powder delivery port **54** upon user inspiration) causes said elongated support panel **16** to partially rotate or pivot within said casing **10** about pivot axis **18** such that the second and/or first terminus of said support panel **16** will strike the interior surface of the casing **10**, on the upper and lower internal surfaces thereof.

[085] The principle of operation of an embodied device of the present invention is depicted in Figs. 4a-d. A number of different possible states of the support panel **16** within the casing **10** are shown, as the support panel **16** partially rotates back and forth about pivot axis **18** due to an inhalation action, at the powder delivery port **54**, which may be facilitated by the

incorporation of a mouthpiece at its end. Fig. 4a shows a state in which the support panel is not blocking the airflow through the casing **10**. Without being bound by theory, it is shown that the off-center positioning of the air inlet **14** creates turbulence in the area **20** between the inlet **14** and the portion **22** of the support panel **16** proximal to the air inlet **14**. According to this aspect, the support panel **16** is tipped by the turbulence into one of the states shown in Figs. 4b and 4c. Referring now to Fig. 4b, the support panel end **22** proximal to the air inlet **14** lowers, raising the support panel end **24** distal to the air inlet **14**, resulting in some blocking of the airflow through the device. In one mechanism, the airflow (shown as "A"; Figs. 4b and 2c) causes the support panel **16** to partially rotate, angle, pivot or rock in the direction shown by the arrow marked "R" (Figs. 4b and 4c), which, in turn, causes the support panel **16** to partially rotate in an opposing direction, or flip to the configuration shown in Fig. 4c. Such partial rotation or flipping, may cycle (i.e., repeat), i.e. the airflow ("A") may cause the support panel **16** to flip back to its former state.

[086] In some embodiments, such partial rotation, rocking or flipping of the support panel **16** within the casing **10** is accomplished due to a unique fitting of a lateral extension of the support panel **16**, for example pivot axis **18** in Fig. 2, which is pivotally mounted within an appropriate housing, for example, **15** in Fig. 1b. In some embodiments, such casing **10** may also comprise a slit or rounded hole through a side wall thereof, into which such lateral extension may insert. Any other modification of the support panel **16** to allow for positioning of the support panel within the casing **10** and facilitating partial rotation of the support panel **16** may be considered as operable within this invention.

[087] For example, in some embodiments of the present invention, the lateral extension of pivot axis **18** may be located at a mid-point (e.g., center) of support panel **16** such that, for example, there is equal distance between pivot axis 18 and the first and second termini of support panel **16** (e.g., the length of support panel **16** between pivot axis **18** and the first terminus is approximately equal to the length of support panel **16** between pivot axis **18** and the second terminus). In other embodiments of the present invention, the lateral extension of pivot axis **18** may not be at a center of support panel **16** (see, e.g., Figs. 7c-d and 8c-d). In some embodiments, as depicted in Figs. 7c-d and 8c-d, pivot axis **18** may be located proximal to the second terminus of support panel **16** such that the length of support panel **16** between pivot axis **18** and the first terminus is greater than the length of support panel **16**

between pivot axis **18** and the second terminus. In other embodiments the opposite is true, and pivot axis **18** is located proximal to the first terminus of support panel **16**.

[088] In preferred embodiments, a user's breathing action typically causes airflow through the device (i.e., air flowing from air inlets **14** towards powder delivery port **54** upon user inspiration), which causes said elongated support panel **16** to partially rotate or pivot within casing **10** about pivot axis **18** several times per second, in an up-and-down motion, thereby beating compartment **19** against casing **10**. In preferred embodiments, due to the alignment of compartment **19** and the region of pin-like structures **70**, the beating action of support panel **16** during inspiration causes the cover **60** covering compartment **19** to repeatedly strike the region of pin-like structures **70** provided on an internal surface of the casing **10**, whereupon the needle-like structures **70** puncture or rupture the cover **60**. As depicted in Fig. 4d, this repeated beating of compartment **19** against structures **70** causes the rupturing of cover **60**, which allows the dry-powder drug or medicament within compartment **19** to be released therefrom and into the air flow space, from where it is inhaled into the user's throat and lung space.

[089] Following repeat partial rotations, resulting in beating of the dry-powder containing compartment **19** distal to the air inlet **14** against one or more pin-like structures **70** provided on an internal surface of the casing **10**, the powder **36** contained within the compartment **19** emerges as free powder **52** into the airflow, which is drawn towards the powder delivery port **54** with mouthpiece **12**. Without being bound by theory, as this free powder **52** emerges, it is disaggregated as a result of the sieving action of the holes or pores created in the cover **60** of compartment **19** by the action of the needle-like structures **70**. In one embodiment, such hole-size for disaggregation to achieve dry-powder particles in the 1-5 micron diameter range is in the 10 micron to 70 micron range.

[090] In certain embodiments, the pins, fins, edges, or needles **70** of the region puncture the cover **60**, thereby or making holes therein or rendering the cover **60** porous.

[091] In certain embodiments, the needles-like structures **70** are sized such as to create pores in the cover **60** of a size sufficiently large to enable the exit of the particles of dry-powder. In some embodiments, the pores have a pore size ranging from about 20 to 50 microns, which in some embodiments, is ideally sized for the release of a dry-powder drug having a diameter of about 1-5 microns. For a 3 micron diameter particle, for example, the

pore size may range from between about 6 microns and 150 microns, or in some embodiments, between about 10 microns and 80 microns or in some embodiments between about 20 microns and 60 microns.

[092] In some embodiments, according to this aspect, dry-powder exit from the inhaler device of this invention is facilitated by the beating action, or abutment of the support panel against an interior surface of the casing **10**, which results in powder egress from the holes or pores created in the cover **60** by the needle- or pin-like structures **70**.

[093] In other embodiments, the interior surface of the casing **10** may include two or more regions of needle-like structures **70**. For example, casing **10** may include one region of needle-like structures **70** on a top interior surface thereof and one region of needle-like structures **70** on a bottom interior surface thereof. Additionally, in this embodiment, the inhaler may include two or more covered compartments **19**. In this embodiment, one covered compartment **19** is located on an upper surface of support panel **16** and aligned with the region of needle-like structures **70** located on the upper interior surface of casing **10**, and one covered compartment **19** is located on the bottom surface of support panel **16** and aligned with the region of needle-like structures **70** located on the bottom interior surface of casing **10**.

[094] In the embodiments described above, the one or more region of needle-like structure(s) **70** is located on an interior surface of the casing **10**, and the one or more covered compartment(s) **19** is located on support panel **16**.

[095] In other embodiments, support panel **16** may include the needle-like structures **70**, and the interior surface of the casing **10** may include the dry-powder compartment **19**. For example, it is possible to have one or more regions of needle-like structures **70** located on support panel **16** and the dry-powder compartment **19** located on an interior surface of casing **10** and aligned with the region of needle-like structures **70**. For example, in certain embodiments, such as illustrated in Fig. 4a, support panel **16** may include a region of needle-like structures **70** protruding vertically upwards from a top surface of support panel **16**, and aligned with a blistered compartments **19** extending vertically downwards from a top interior surface of casing **10**.

[096] However, in other embodiments, such as illustrated in Fig. 6b, support panel **16** may include one region of needle-like structures **70** on a top surface of support panel **16** and one

region of needle-like structures **70** on a bottom surface of support panel **16**. Additionally, in this embodiment, the inhaler may include two or more covered compartments **19**. One covered compartment **19** located on a bottom interior surface of casing **10** and aligned with the region of needle-like structures **70** located on the bottom surface of support panel **16**, and one covered compartment **19** located on the top interior surface of casing **10** and aligned with the region of needle-like structures **70** located on the top surface of support panel **16**.

[097] Referring now to Figs. 7a to 7b, in certain embodiments of the present invention compartment **19** is located proximal to the first terminus near air inlet **14** on an interior surface of casing **10**, and support panel **16** may include one or more regions of needle-like structures **70** on a top surface of support panel **16**. In certain embodiments, as illustrated in Fig 7a, the inhaler may include one covered compartment **19** on a top, interior surface of casing **10** extending vertically downwards toward support panel **16**, and support panel **16** may include at least one needle-like structure **70** on a top surface of support panel **16** extending vertically upwards towards compartment **19** and cover **60**. It is also contemplated that compartment **19** may be located on a bottom interior surface of casing **10**, and the at least one needle-like structure **70** may be located on a bottom surface of support panel **16**.

[098] Referring now to Figs. 7c and 7d, pivot axis **18** may also be located, rather than at a mid-point of support panel **16** (as shown in Figs. 7a and 7b), proximal to the second terminus near drug delivery port **54**. In this embodiment, the length of support panel **16** between pivot axis **18** and the first terminus is greater than the length of support panel **16** between pivot axis **18** and the second terminus. In this way, the length of support panel **16** is greater near air inlet **14**, thereby allowing for more effective rotation of support panel **16** as air is inspired by a user.

[099] Referring now to Fig. 8a, compartment **19** having cover **60** may be located on a top surface of support panel **16** proximal to the first terminus near air inlet **14**, and at least one needle-like structure **70** is located on a top interior surface of casing **10** proximal to the first terminus near air inlet **14**. In this embodiment, compartment **19** covered by cover **60** is provided on the top surface of support panel **16** and is aligned with the at least one needle-like structure **70**, which extends vertically downward from the top interior surface of casing **10**. As depicted in Fig. 8a, pivot axis **18** is located at a mid-point, or approximate center point, of support panel **16**.

[0100] Referring now to Fig. 8b, compartment **19** covered by cover **60** may be located on each of the top and bottom surfaces of support panel **16** proximal to the first terminus near the air inlet **14**. In this embodiment, at least one needle-like structure **70** is located on each of the top and bottom interior surfaces of casing **10**, and each is aligned with the respective covered compartment **19** located on the top or bottom surface of support panel **16**. As depicted in Fig. 8b, pivot axis **18** is located at a mid-point, or approximate center point, of support panel **16**.

[0101] Referring now to Fig. 8c, compartment **19** having cover **60** may also be located on a top surface of support panel **16** proximal to the first terminus near air inlet **14**, and at least one needle-like structure **70** may be located on a top interior surface of casing **10** proximal to the first terminus near air inlet **14**. In this embodiment, compartment **19** covered by cover **60** is provided on the top surface of support panel **16** and is aligned with the at least one needle-like structure **70**, which extends vertically downward from the top interior surface of casing **10**. As depicted in Fig. 8c, pivot axis **18** may be located proximal to the second terminus of support panel **16**, thereby creating a greater length of support panel **16** between pivot axis **18** and the first terminus, and a shorter length of support panel **16** between pivot axis **18** and the second terminus. The greater length of support panel **16** between pivot axis **18** and the first terminus allows for more effective rotation of support panel **16** as air is inspired by a user.

[0102] Referring now to Fig. 8d, compartment **19** covered by cover **60** may be located on each of the top and bottom surfaces of support panel **16** proximal to the first terminus near the air inlet **14**. In this embodiment, at least one needle-like structure is located on each of the top and bottom interior surfaces of casing **10**, and each is aligned with the respective compartment **19** located on the top and bottom surfaces of support panel **16**. As depicted in Fig. 8d, pivot axis **18** is located proximal to the second terminus of support panel **16**, thereby creating a greater length of support panel **16** between pivot axis **18** and the first terminus, and a shorter length of support panel **16** between pivot axis **18** and the second terminus. The greater length of support panel **16** between pivot axis **18** and the first terminus allows for more effective rotation of support panel **16** as air is inspired by a user.

[0103] Fig. 9 depicts an alternate embodied inhalation device according to certain aspects of the present invention. The embodiment of the inhalation device illustrated in Fig. 9 is similar to the embodiments of the inhalation devices discussed above in that it includes, *inter*

alia, a casing **10**, an air inlet positioned at one terminus of casing **10**, and a powder delivery port **54** partially enclosed by or attached to a mouth piece **12** positioned at another terminus of casing **10**, an elongated support panel **16** having a pivot axis **18** and a dry-powder compartment **19**, and at least one region of needle-like structure(s) **70**.

[0104] While not specifically depicted in Fig. 9, air inlet **14** may be positioned off center relative to a horizontal (i.e., longitudinal) axis, a vertical axis or a combination thereof of a side of the casing **10** containing the air inlet **14** (see Figs. 4a-d). Similarly, the air inlet **14** may be located off-center relative to a vertical midline axis.

[0105] Support panel **16** is located within an interior cavity of casing **10** and resembles an elongated plate, although other shapes are contemplated. Support panel **16** includes a first terminus and a second terminus opposite the first terminus. In some embodiments, the first terminus is located proximally to the air inlet **14**, and the second terminus is located proximally to the powder delivery port **54**. In certain embodiments, the elongated support panel **16** is fitted, or arranged, within casing **10** such that the elongated support panel **16** partially rotates, angles or pivots, within casing **10** about a single axis, shown as pivot axis **18**.

[0106] In the embodiment depicted in Fig. 9, pivot axis **18** includes at least two lateral extensions and is located at a mid-point or approximate center of support panel **16**. However, pivot axis **18** may be located at any point along a longitudinal axis of support panel **16**, such as discussed above with reference to, *inter alia*, Figs. 7c-d and 8c-d. For example, in some embodiments, pivot axis **18** may be located proximal to the second terminus of support panel **16**, thereby creating a greater length of support panel **16** between pivot axis **18** and the first terminus, and a shorter length of support panel **16** between pivot axis **18** and the second terminus. It is contemplated that pivot axis **18** may also be located proximal to the first terminus.

[0107] In the embodiment depicted in Fig. 9, elongated support panel **16** comprises at least one compartment **19** located proximally to the first terminus of the support panel **16**, near air inlet **14** when positioned within the casing **10** as herein described. Positioning the dry-powder compartment **19** near air inlet **14** (e.g., away from drug delivery port **54** and mouthpiece **12**) increases the distance that the dry-powder therapeutic must travel, thereby allowing the dry-powder to accelerate as it traverses the interior cavity of the inhaler and

enters the mouth and lungs. In alternative embodiments, the compartment **19** may be located proximally to the second terminus of the support panel **16**, near the drug delivery port **54**.

[0108] In some embodiments, compartment **19** is contiguous in structure with that of support panel **16**, for example support panel **16** has an indent, forming compartment **19** for containing the medicament. In some embodiments, compartment **19** is bonded, welded or otherwise attached to support panel **16**. In preferred embodiments, compartment **19** is covered and sealed by covering **60**, such as aluminum or other known blister-pack type coverings, and sealed as known in the art and as discussed above. In certain embodiments, cover **60** is capable of being punctured or ruptured by a sharp device or object (e.g., needle-like structure(s) **70**), to thereby allow the dry-powder drug or medicament contained within compartment **19** to be released therefrom.

[0109] In certain embodiments, casing **10** includes at least one sharp or pointed device **70** located on an internal surface thereof, proximal to the first terminus of casing **10** near air inlet **14**, or proximal to the second terminus of casing **10** near drug delivery port **54**. In preferred embodiments, as shown in Fig. 9 and discussed above, the at least one sharp or pointed device **70** is a region of needle- or pin-like structures **70** that may include one or more fins, pins, needles, edges, or other type of sharp or pointed needle- or pin-like structures extending in a direction transverse (e.g., perpendicular) to a longitudinal axis of casing **10**. In preferred embodiments, the region of needle- or pin-like structures **70** is suitable for puncturing or rupturing the cover **60** that seals compartment **19**.

[0110] It is contemplated, however, that having the needle- or pin-like structures **70** constantly exposed within the interior cavity of the casing may hinder the operation of the inhalation device. For example, the needles may hinder the free rotation of the elongated support panel about its axis during inspiration. In another example, the needles may hinder the release of the dry-powder from the dry-powder compartment. Also, there may be vibration interference in the release of the drug or medicament from the covered compartment **19** because the needles stay at the same extended position and continue to touch the drug compartment cover **60** with each vibration of the elongated support panel **16**. Accordingly, in certain embodiments of the present invention it is desirable that the needles be configured to extend into and retract from the interior cavity of the casing, such that the user extends the needle- or pin-like structures **70** to puncture the cover **60** of the drug

compartment **19**, and then retracts them, just prior to inhalation. In this way, the needles may still operate to puncture the dry-powder compartment while avoiding the issues associated therewith.

[0111] In some embodiments, such as depicted in Fig. 9, casing **10** includes at least one push button **100** to actuate the needle- or pin-like structures **70**, although it is contemplated that casing **10** may include two or more (e.g., a plurality) of push buttons **100**. Push buttons **100** are discussed in more detail below with reference to Figs. 10a-b.

[0112] In preferred embodiments, push button **100** is configured to communicate with the interior cavity of casing **10** in such a way that an object, specifically one or more needle- or pin-like structures **70**, may pass unhindered from push button **100** into the interior cavity of casing **10**, and vice versa. As discussed in more detail below, in some embodiments a region of needle-like structures **70** may pass unhindered from push button **100** into the interior cavity of casing **10**. In certain embodiments, push button **100** may be constructed, as known in the art, such as by including a spring, such that compressing push button **100** extends the region of needle-like structures into the interior cavity, and releasing the push button **100** retracts the region of needle-like structures from the interior cavity.

[0113] As shown in Fig. 9, certain embodiments of the present invention may include, without limitation, two push buttons **100**. In these embodiments, casing **10** may include a first push bottom located on a first external surface thereof and a second push button located on a second external surface opposing the first external surface (as depicted in Fig. 9). In one embodiment, both the first push button **100**, located, for example, on a top surface of casing **10**, and the second push button **100**, located, for example, on a bottom surface of casing **10**, include the needle-like structures **70**, and both push buttons **100** operate to puncture compartment **19**.

[0114] In another embodiment, only the first push button **100**, located, for example, on a top surface of casing **10**, includes one or more needle- or pin-like structures **70**, while the second push button **100**, located, for example, on a bottom surface of casing **10**, does not include the needle-like structures. Of course, the first push button **100** which includes one or more needle- or pin-like structures **70** may be located on a bottom surface of casing **10**, while the second push button **100** which does not include the needle-like structures **70** may be located on a top surface of casing **10**. (It should be understood, in these embodiments, that the

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location on casing **10** where push button **100** is be situated should be opposite to where on the surface of the support panel **16** the compartment **19** containing the drug or medicament is situated.) In this embodiment, only the first push button **100** operates to puncture compartment **19**, while the second push button **100** is configured as a support button.

[0115] In some embodiments push button(s) **100** may be contiguous in structure with that of casing **10**. In other embodiments, push button(s) **100** may be embedded, bonded, welded or otherwise attached to an external surface of casing **10**. Attachment points other than an external surface of casing **10** are contemplated. In preferred embodiments, push button **100** is aligned with compartment **19** on support panel **16** such that the beating action of support panel **16** during inspiration causes the cover **60** covering dry-powder compartment **19** to strike in the approximate area of push button **100**.

[0116] Reference is now made to Figs. 10a and 10b, which are illustrations of several views of a push button **100** according to aspects of certain embodiments of the present invention. Fig. 10a is a top view of push button **100** in an undepressed (left) and depressed (right) configuration. Fig. 10b is a bottom view of push bottom **100** in an undepressed (left) and depressed (right) configuration. In most embodiments, push button **100** includes a housing **101**, a top panel **102**, and a (e.g., internal) spring mechanism (not shown).

[0117] Housing **101** of push button **100** may be any desired shape (e.g., cylindrical) and may include an outer periphery, an inner periphery, a top opening, a bottom opening, as well as having a height and a width, thereby enclosing a volume. In preferred embodiments, bottom opening **103** of housing **101** is configured to communicate with the interior cavity of casing **10** in such a way that an object may pass unhindered from housing **101** through opening **103** into the interior cavity of casing **10**, and vice versa. For example, a region of needle-like structures **70** may pass unhindered from push button **100** into the interior cavity of casing **10**.

[0118] In preferred embodiments, the volume of housing **101** of push button **100** is sufficient to encompass or enclose (either partially or completely) at least one region of needle-like structures **70** when push button **100** is in an undepressed state (see left side of Figs. 10a and 10b). In some embodiments, the needle-like structures **70** are entirely enclosed within housing **101**, and no portion of the needle-like structures **70** extends into the interior cavity of casing **10** when push button **100** is in an undepressed state. In other embodiments, at least a portion of the needle-like structures **70** extends out of housing **101** into the interior

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cavity of casing **10** when push button **100** is in an undepressed state. In preferred embodiments, housing **101**, including at least one region of needle-like structures **70** contained therein, is aligned with dry-powder compartment **19** on support panel **16** such that the beating action of support panel **16** during inspiration causes dry-powder compartment **19** to strike the region of needle-like structures **70**, whereupon the needle-like structures **70** puncture or rupture cover **60** covering dry-powder compartment **19**.

[0119] In certain embodiments, top panel **102** of push button **100** includes a top surface and a bottom surface and is sufficiently sized to fit within the inner periphery of housing **101**. In preferred embodiments, top panel **102** may be substantially flat, although alternative embodiments wherein top panel **102** is not substantially flat are contemplated. Top panel **102** may be configured as a depressible button, such that a user may press on a top surface of top panel **102** and depress top panel **102** into housing **101**. The user may then release top panel **102** to allow top panel **102** to return to an undepressed position.

[0120] In preferred embodiments, push button **100** includes a (e.g., internal) spring mechanism configured to extend at least one region of needle-like structures **70** therefrom when depressed and retract the at least one region of needle-like structures **70** therein when released. The spring mechanism may be attached to a bottom surface of top panel **102** inside housing **101** to facilitate or assist the depress-ability of top panel **102**. For example, in certain embodiments the spring mechanism may be attached to an outer peripheral area, and a region of needle-like structures **70** may be attached at a central area, on the bottom surface of top panel **102**.

[0121] In this way, a user may depress push button **100** by applying a downward force on the top surface of top panel **102**, causing the spring mechanism to compress and moving the region of needle-like structures **70** in a downwards motion. The downwards motion of the region of needle-like structures **70** may expose the region of needle-like structures **70** to the interior cavity of casing **10** (see the right sides of Figs. 10a and 10b). The user may release the downward force on the top surface of top panel **102** of push button **100**, causing the spring mechanism to expand and retract the region of needle-like structures **70** back into push button **100** in an upwards motion. The upwards motion of the region of needle-like structures **70** may retract the region of needle-like structures **70** from the interior cavity of casing **10** (see left sides of Figs. 10a and 10b).

[0122] For example, in certain embodiments, and without limitation, casing **10** of the inhalation device of the present invention may have a width perpendicular to the longitudinal axis of approximately 0.6-0.8 cm. Housing **101** may have a height parallel to the width of casing **10** of approximately 0.5 cm, and the spring mechanism may be housed within the volume of housing **101** and also have a height of approximately 0.5 cm. Additionally, each needle (e.g., pin, nail, etc.) of the region of needle-like structures **70** may have a height of approximately 0.5 cm. In operation, a user may compress the spring mechanism from approximately 0.5 cm to approximately 0.2 cm thereby exposing approximately 0.3 cm of each needle to the interior cavity of casing **10**.

[0123] Certain embodiments of the present invention may include a method of administering an inhalable therapeutic agent to a subject comprising the steps of providing a therapeutic agent inhaler device including a casing having an air inlet, a delivery port opposing the air inlet, an elongated support panel located within an interior cavity of the casing and having at least one covered compartment containing the therapeutic agent, and at least one push button mechanism comprising at least one needle structure, and puncturing the covered compartment with the at least one needle structure by operating (e.g., pressing and/or compressing) the at least one push button to extend the at least one needle into the interior of the casing and through the cover of the at least one compartment, whereby drawing air through the casing causes the elongated support panel to partially rotate about a single axis within the casing thereby releasing the therapeutic agent into the air flowing through the casing.

[0124] The method according to this embodiment of the present invention may further include releasing the at least one push button thereby retracting the at least one needle from the interior of the casing. The covered compartment may be located near the air inlet or near the drug delivery port, although the covered compartment is always in alignment with the at least one needle to allow puncturing of the covered compartment. Accordingly, the push button (which in preferred embodiments houses the at least one needle) is typically located in alignment with the covered compartment, although alternative embodiments are contemplated. In certain embodiments, and as discussed above, the single axis may be located on the elongated support panel at an approximate mid-point (e.g., center), at a position near the air inlet, or at a position near the drug delivery port. In certain embodiments, the at least one needle is a region comprising a plurality of needles.

[0125] As discussed above, the airflow through the device causes the support panel **16** to repeatedly rotate between the two states. Each time this occurs, the support panel end **24**, comprising the needle- or pin-like structures **70** distal or proximal to the air inlet **14**, beats against an internal surface **26** of the casing **10** containing the dry-powder containing compartment **19**, causing the dry-powder compartment **19** to be punctured or ruptured by the needle- or pin-like structures **70** aligned with the cover **60**, thereby causing the dry-powder drug within the compartment **19** to be released gradually from compartment **19**.

[0126] The inhalers, kits and/or methods of the present invention, *inter alia*, are well suited to deliver two or more inhaled dry-powder drugs simultaneously while storing them separately.

[0127] From a chemical perspective, the co-storage of two or more drugs within the same physical compartment can be problematic as the two drugs may interact, especially if they have different pHs. From a regulatory standpoint, it may be necessary to prove that there is no such interaction over a long time period, and this can add significant expense to the regulatory approvals process.

[0128] In some embodiments, according this aspect of the invention, a technical challenge in the inhaler industry involving the storage of two or more drugs, which is potentially problematic for both chemical and regulatory reasons, is obviated by certain embodiments of this invention.

[0129] The assemblies of this invention may comprise, in some embodiments, one or more compartments, with each compartment comprising a dry-powder. In some embodiments, when the assemblies comprise more than one compartment, each compartment may comprise the same or different dry-powders.

[0130] In some embodiments, the support panel comprises two or three compartments containing a dry-powder. According to this aspect of the invention, and in some embodiments, the two or three compartments comprise two or three different dry-powders.

[0131] In some embodiments, the support panel comprises a compartment containing at least one or two partitions, which partitions create separate chambers in the compartment. According to this aspect of the invention, and in some embodiments, the separate chambers may contain different dry-powders.

[0132] In some embodiments, when the support panel **16** comprises two or more chambers or compartments **19**, the support panel **16** may strike the protruding surface at a region between the two chambers or compartments **19**, or in some embodiments, the interior surface may comprise multiple protruding surfaces such that each chamber or compartment will strike the interior surface at a region containing a protruding surface.

[0133] For example, in certain embodiments, each blistered compartment **19** on support panel **16** is aligned with a corresponding region of needle-like structures **70**, or comb of needle-like structures **70**.

[0134] In some embodiments, the present invention provides for a method of dispensing dry-powder from an inhaler, comprising facilitating airflow through a dry-powder inhaler device including any single or combined embodiments described herein, to cause the support panel to partially rotate within the casing about a single axis causing the covered compartment **19** to strike one or more needle- or pin-like structures **70**, thereby puncturing the cover **60**, releasing dry-powder from the compartment **19** to become entrained in the airflow, and dispensing dry-powder from the inhaler. Fig. 2 depicts an embodiment whereby a principle mode of operation of an embodied device of this invention results in the dispensing of a dry-powder from an inhaler of this invention, which represents an aspect of the methods of this invention.

[0135] In certain embodiments, the inhaler devices of this invention may be single use devices, which are preloaded with a desired dry-powder agent, at a desired dosage.

[0136] In some embodiments, according to this aspect, care is taken to ensure appropriate dry-powder containment within the blistered compartments of the inhaler devices of the present invention, prior to or between uses of the inhaler device.

[0137] It will be evident to those skilled in the art that the invention is not limited to the details of the foregoing illustrative embodiments and that the present invention may be embodied in other specific forms without departing from the spirit or essential attributes thereof.

[0138] The embodiments presented herein are, therefore, to be considered in all respects as illustrative and not restrictive of the scope of the invention, and the skilled artisan will appreciate the appropriate equivalents thereto, which are to be considered as part of this invention.

CLAIMS

1. An inhaler device comprising:

a casing having at least one pin structure located on an interior portion thereof;

an air inlet located at a first terminus of the casing;

a powder delivery port located at a second terminus of the casing and positioned distal to the air inlet; and

an elongated support panel comprising a first terminus and a second terminus at opposite ends thereof and at least one compartment containing an inhalable medicament located proximal to the first terminus and covered by a cover that is configured to be punctured by the at least one pin structure,

the support panel being rotatably mounted within an interior of the casing such that the first terminus is located proximal to the air inlet, the second terminus is located proximal to the powder delivery port, and the support panel partially rotates within the casing about a single axis upon flowing of air through the casing;

wherein the partial rotation of the elongated support panel within the casing causes the at least one compartment to strike the at least one pin structure, such that the at least one pin structure punctures the cover and allows the medicament contained within the at least one compartment to become released into the air flowing through the casing.

2. The inhaler device according to claim 1, wherein the further comprises at least one push button mechanism located on an external portion thereof, the push button mechanism comprising the least one pin structure.

3. The inhaler device according to claim 2, wherein the push button mechanism is configured to extend the at least one pin structure into the interior of the casing when a force is applied and is configured to retract the at least one pin structure from the interior of the casing when the force is released.

4. The inhaler device according to claim 2, wherein the push button mechanism comprises a housing, a top panel, and a bottom opening, the bottom opening configured to communicate with the interior of the casing.

5. The inhaler device according to claim 1, wherein at least one compartment is situated on an upper surface of the elongated support panel, and the at least one pin structure is situated on an upper interior side of the casing.

6. The inhaler device according to claim 1, wherein at least one compartment is situated on a lower surface of the elongated support panel, and the at least one pin structure is situated on a lower interior side of the casing.

7. The inhaler device according to claim 1, wherein the single axis of the support panel is located at a center of the support panel.

8. The inhaler device according to claim 1, wherein the single axis of the support panel is located proximal to the air inlet or proximal to the powder delivery port.

9. The inhaler device according to claim 1, wherein the compartment cover is made of aluminum or aluminum foil.

10. The inhaler device according to claim 1, wherein the compartment containing the inhalable medicament is hermetically sealed.

11. The inhaler device according to claim 1, wherein the casing, the elongated support panel, or a combination thereof is substantially rectangular.

12. The inhaler device according to claim 1, wherein the support panel comprises at least two compartments containing an inhalable medicament.

13. The inhaler device according to claim 12, wherein the two or more compartments each houses a different inhalable medicament.

14. The inhaler device according to claim 1, wherein the compartment containing the inhalable medicament comprises at least one partition, creating at least two separate chambers in the compartment.

15. The inhaler device according to claim 14, wherein each of the at least two separate chambers houses a different inhalable medicament.

16. The inhaler device according to claim 1, wherein the inhalable medicament is a therapeutic agent in the form of a dry-powder.

17. The inhaler device according to claim 16, wherein the therapeutic agent is a drug or a vaccine.

18. An inhaler device comprising:

a casing having an air inlet, a powder delivery port located opposite the air inlet, and at least one pin structure on an interior of the casing; and

an elongated support panel located within the interior of the casing and having at least one covered compartment containing a dry-powder medicament;

wherein the elongated support panel is configured to partially rotate about a single axis within the casing upon air flowing through the device, the partial rotation causing the covered compartment to strike the at least one pin structure, thereby puncturing a cover of the covered compartment and releasing the dry-powder into the air flowing through the device.

19. The inhaler device according to claim 18, wherein the casing further comprises at least one push button mechanism comprising the at least one pin structure.

20. The inhaler device according to claim 19, wherein the push button mechanism comprises a housing, a top panel, and a bottom opening, the bottom opening configured to communicate with the interior of the casing.

21. The inhaler device according to claim 19, wherein the push button mechanism is configured to extend the at least one pin structure into the interior of the casing when a force is applied thereto and retract the at least one pin structure from the interior of the casing when the force is released therefrom.

22. The inhaler device according to claim 21, wherein upon air flowing through the device, the partial rotation of the elongated support panel causes the covered compartment to strike the at least one pin structure once extended.

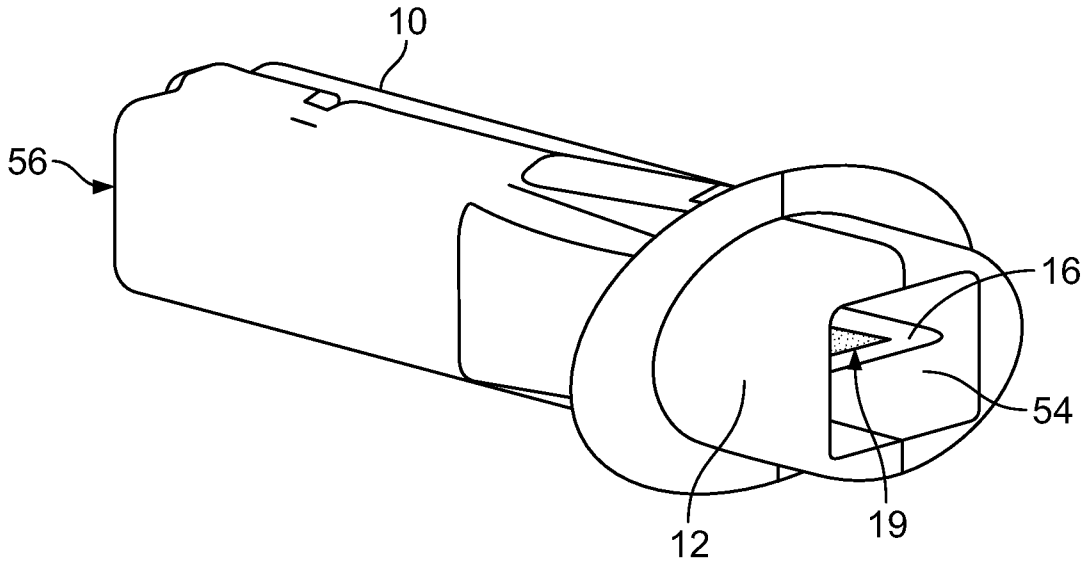


Figure 1

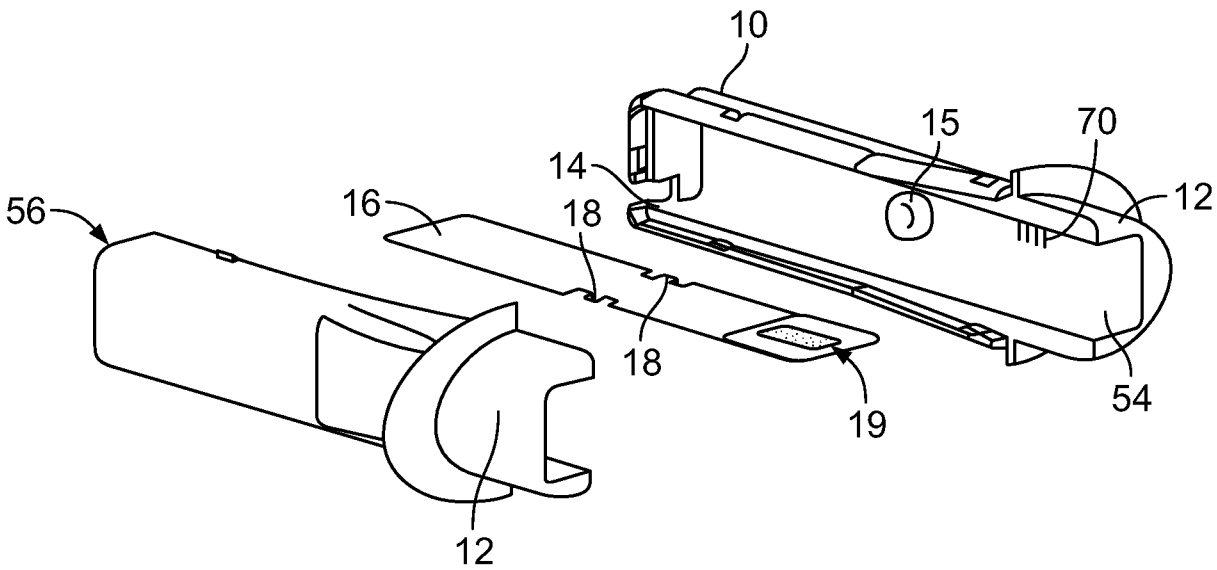


Figure 2

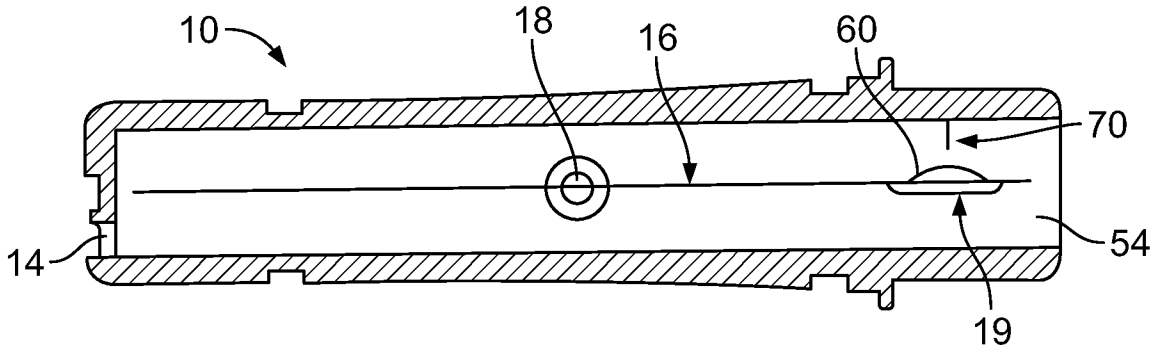


Figure 3a

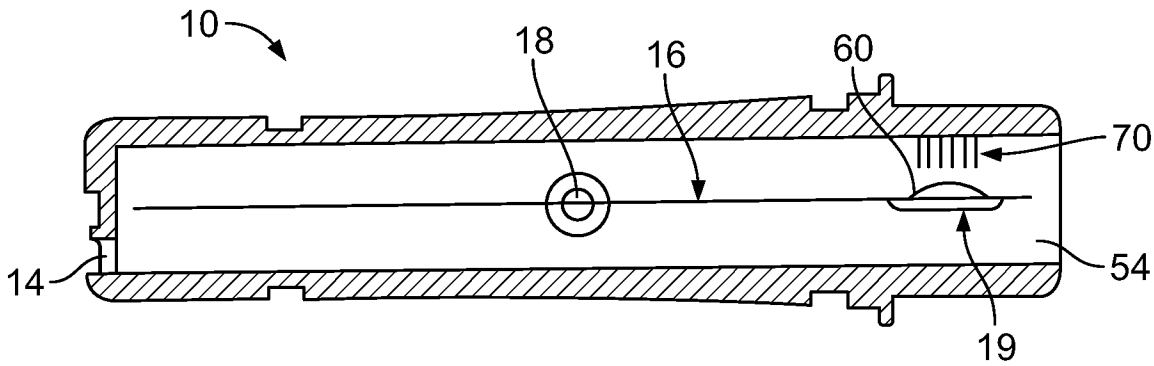


Figure 3b

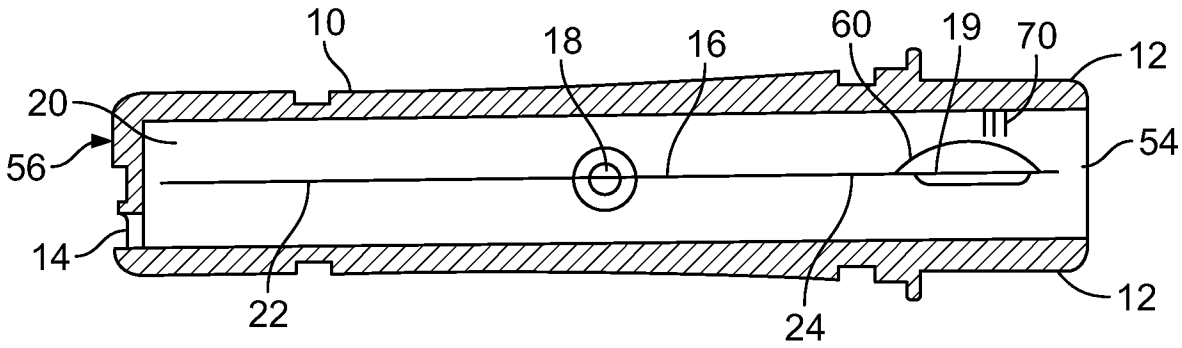


Figure 4a

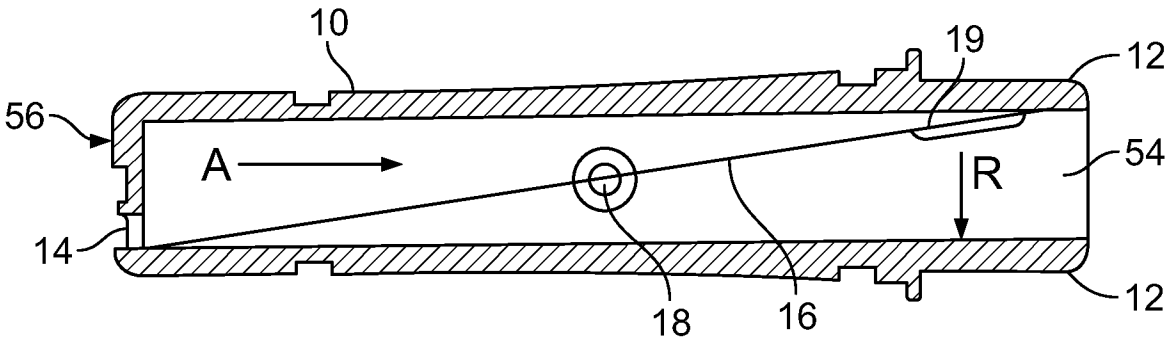


Figure 4b

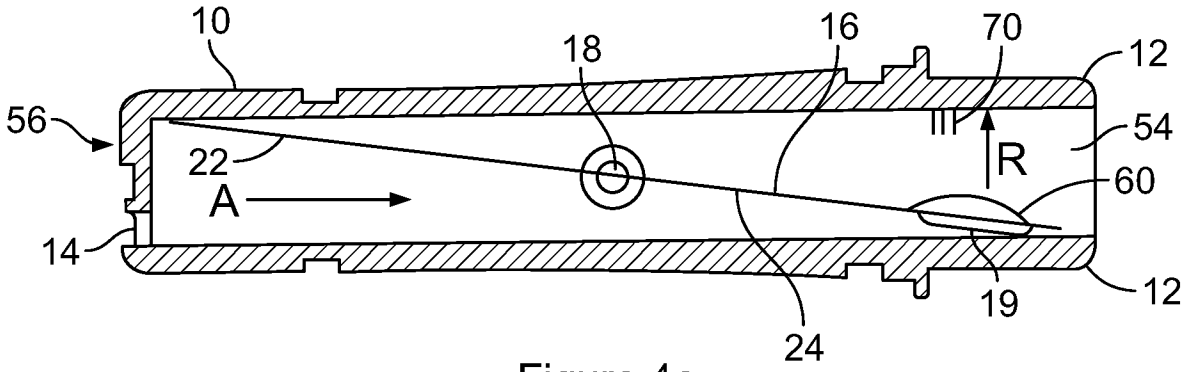


Figure 4c

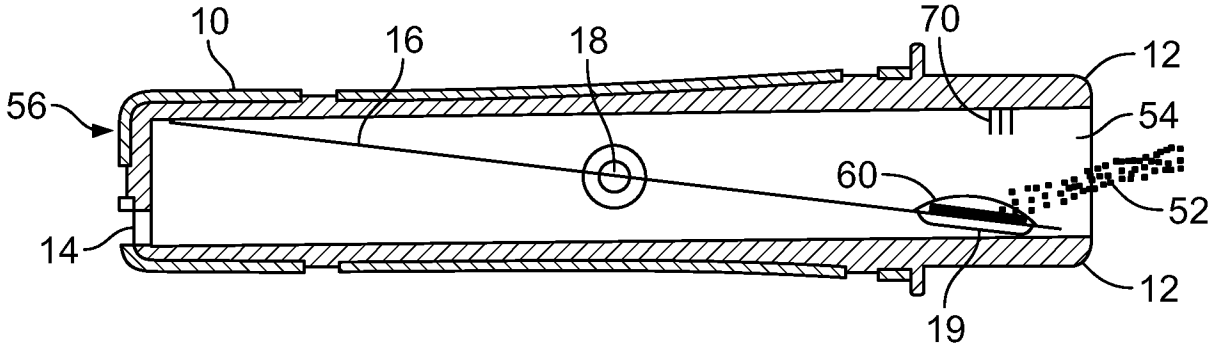


Figure 4d

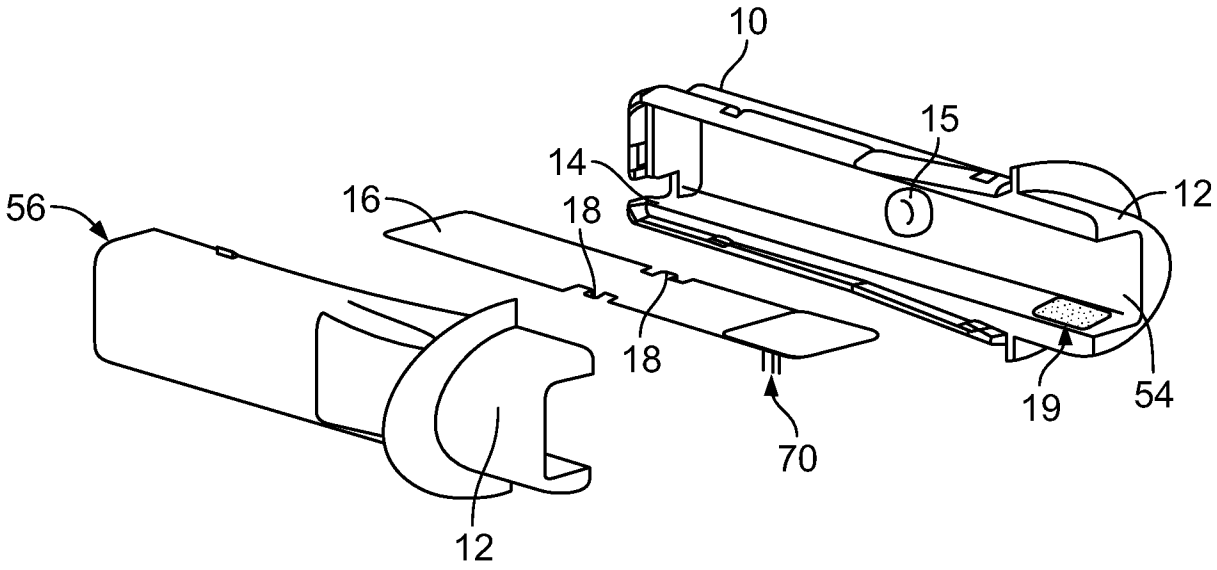


Figure 5

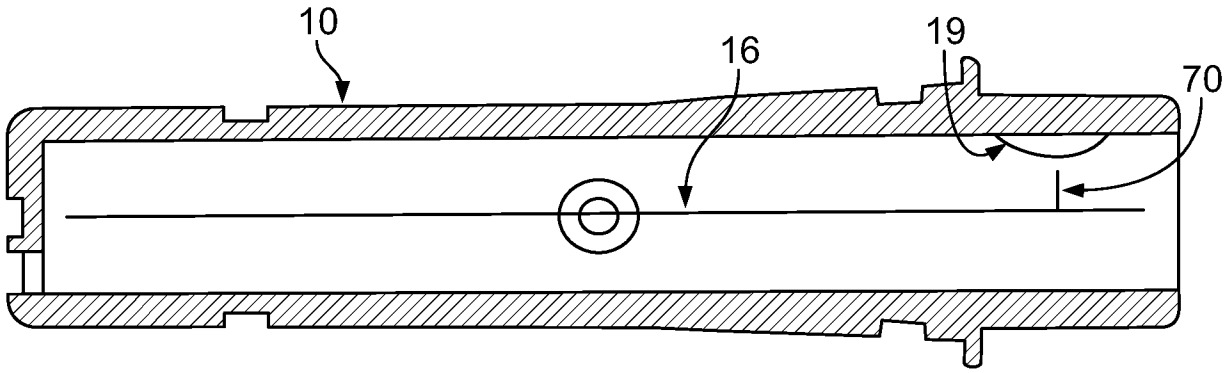


Figure 6a

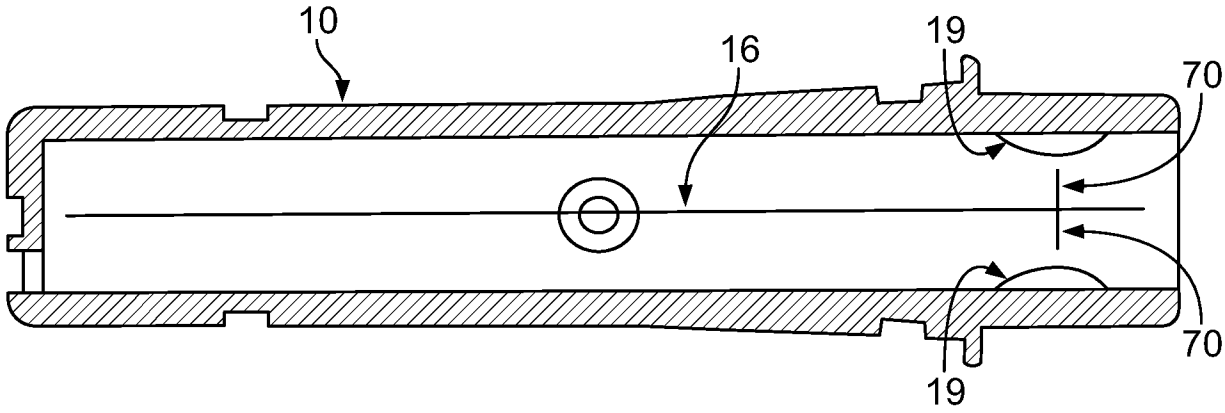


Figure 6b

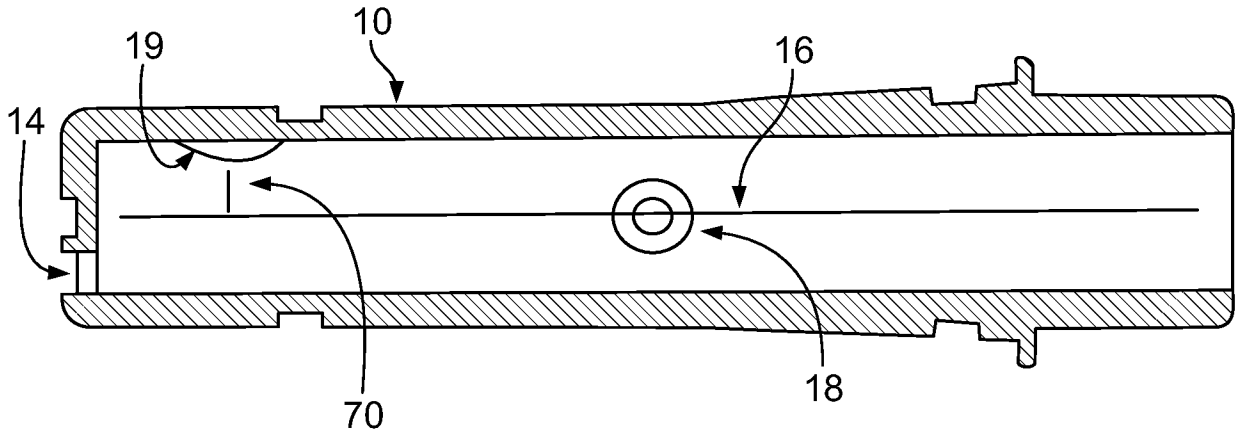


Figure 7a

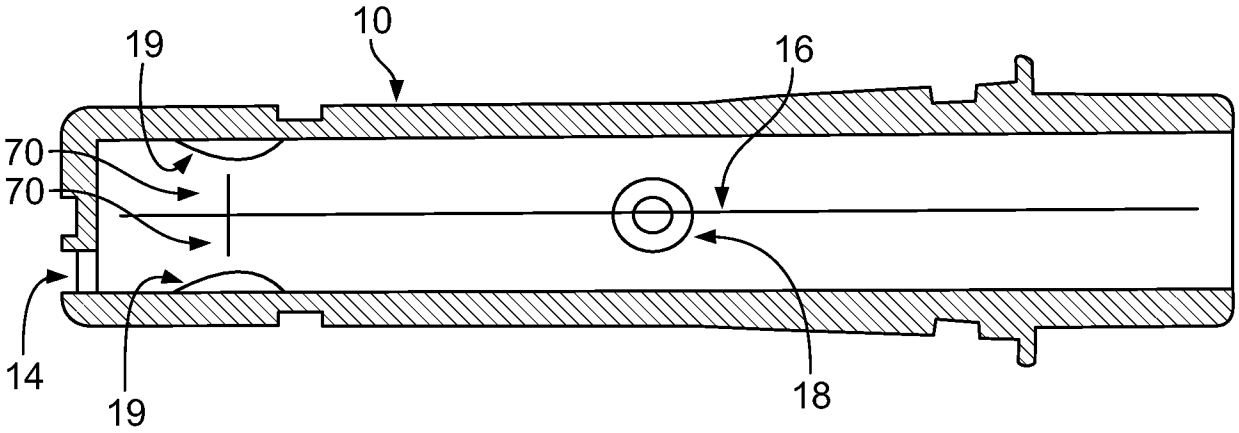


Figure 7b

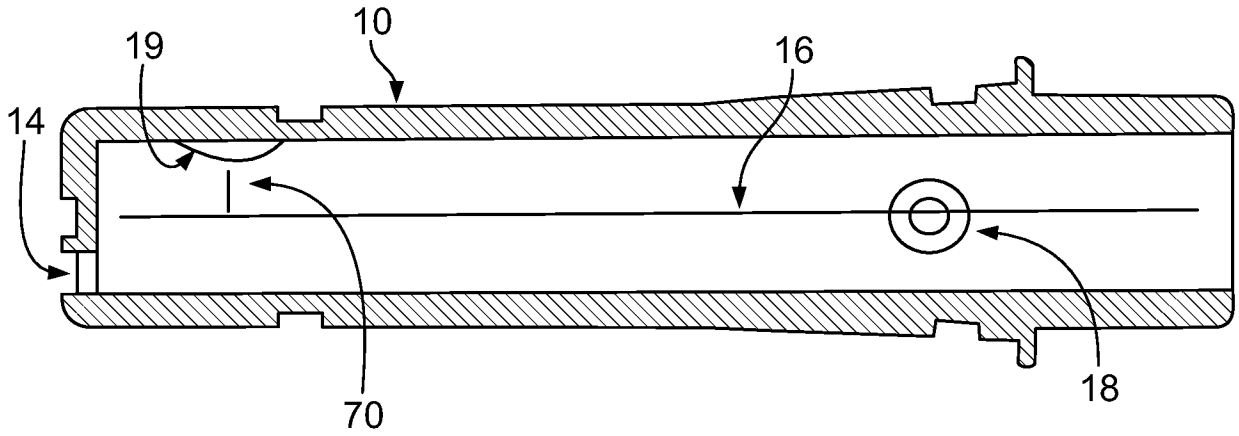


Figure 7c

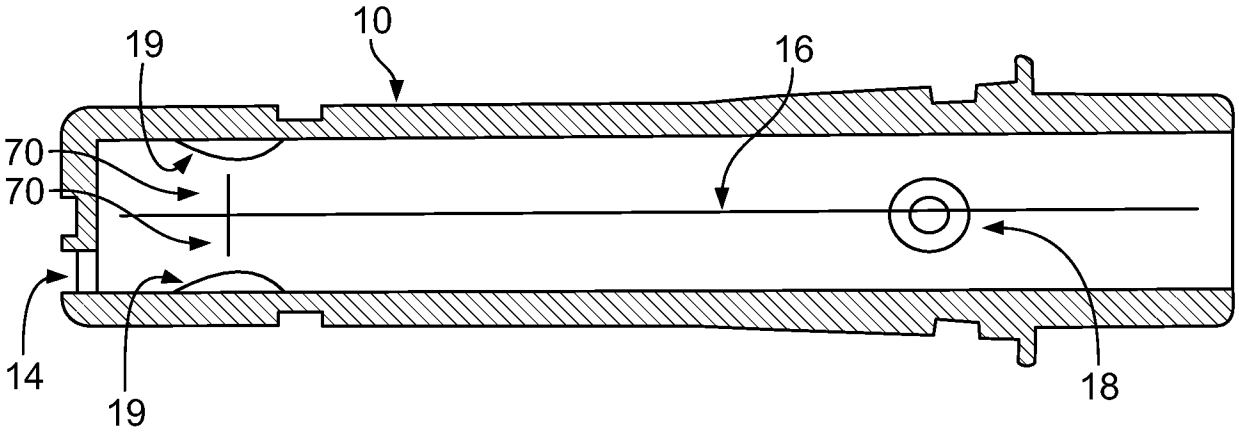


Figure 7d

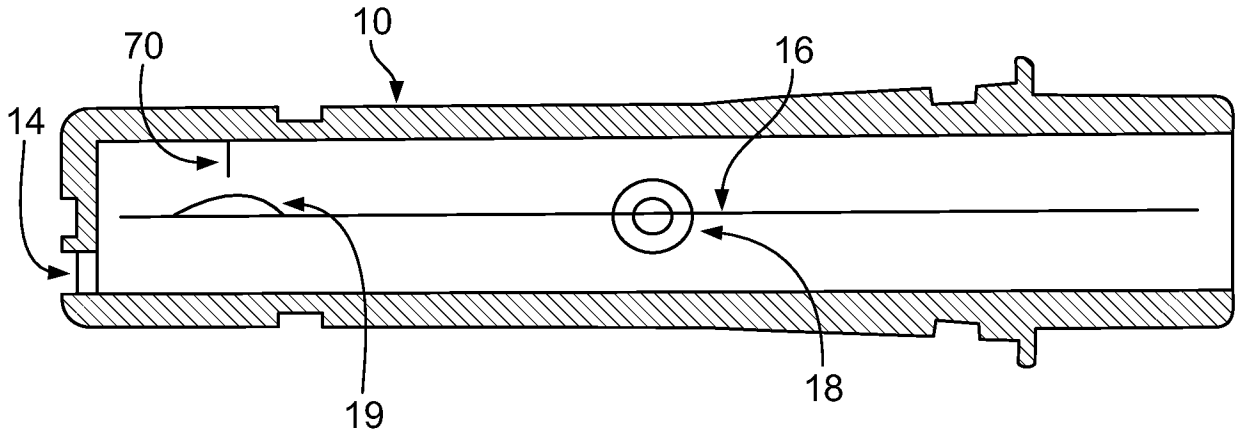


Figure 8a

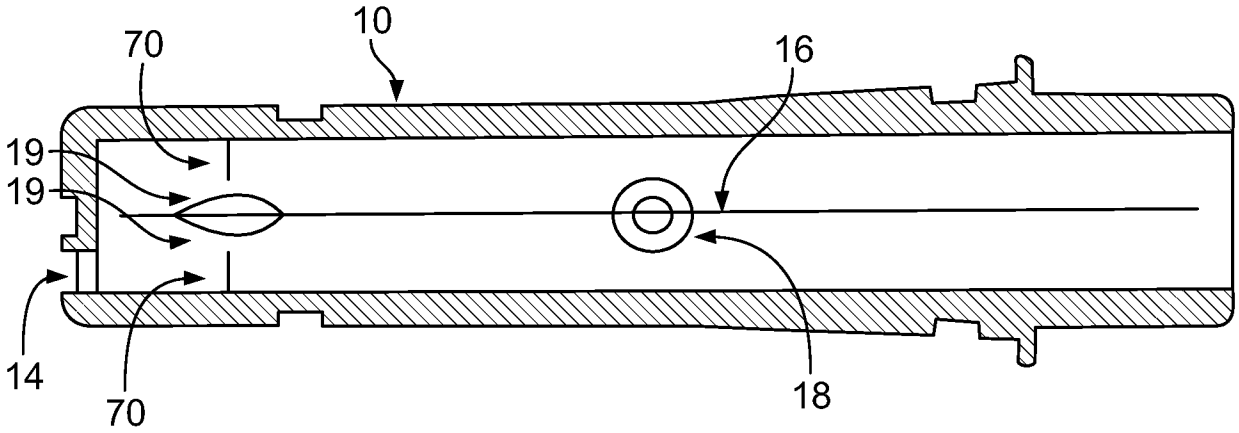


Figure 8b

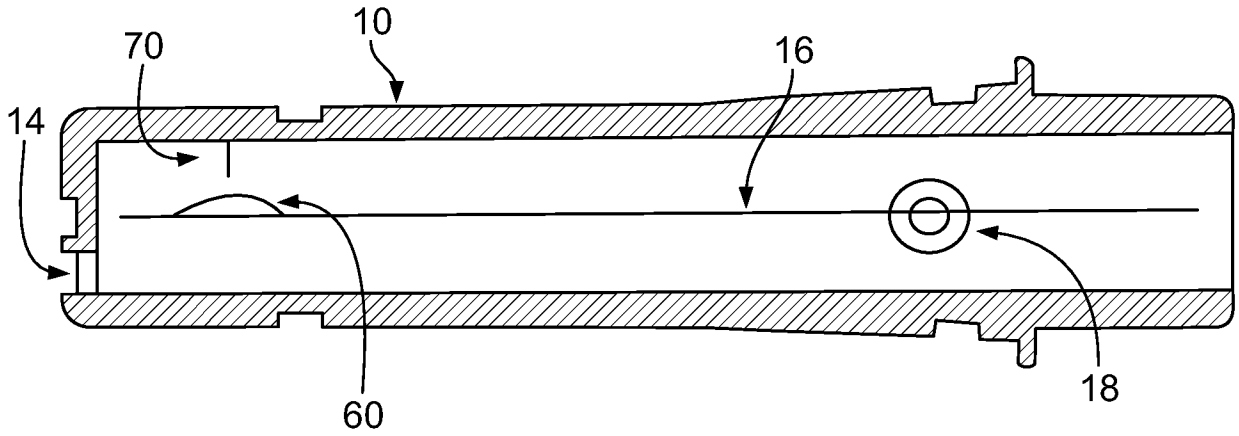


Figure 8c

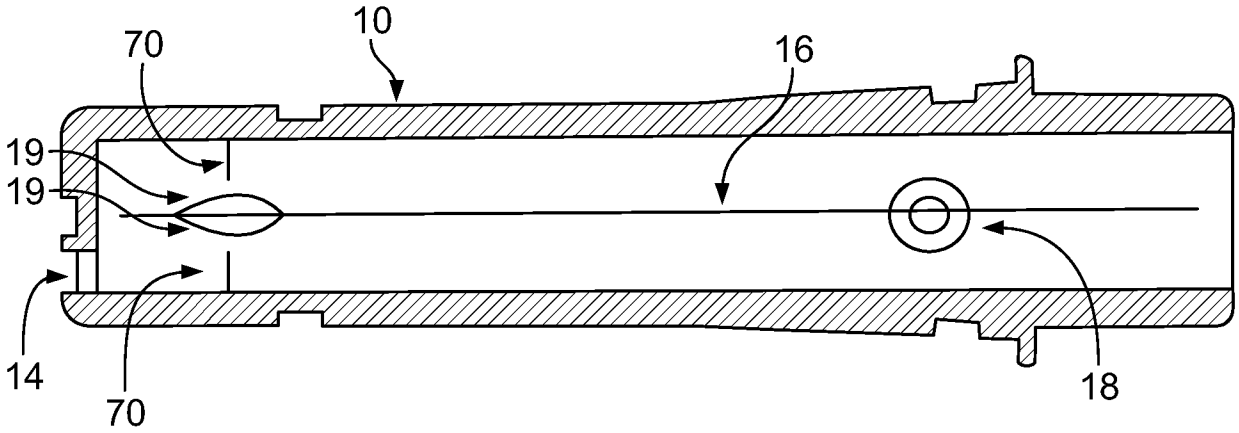


Figure 8d

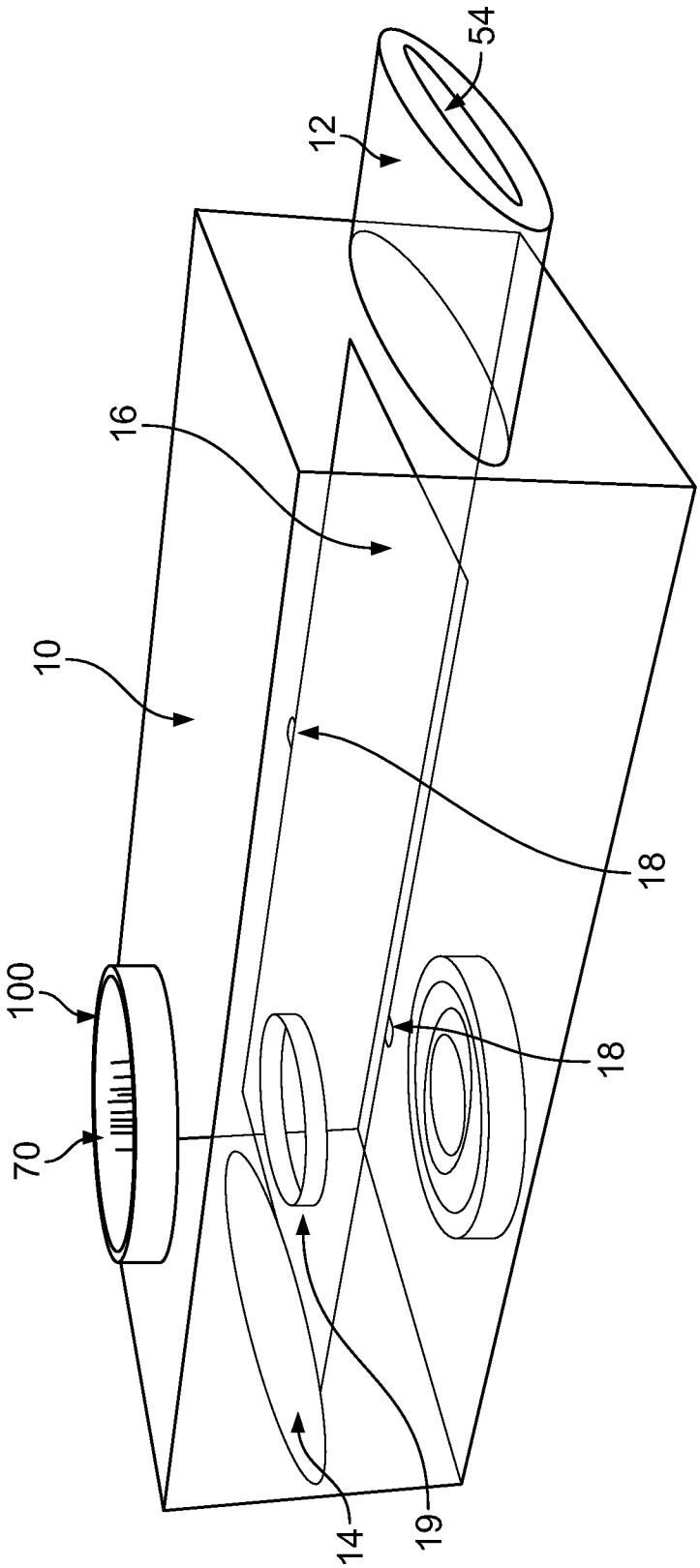


Figure 9

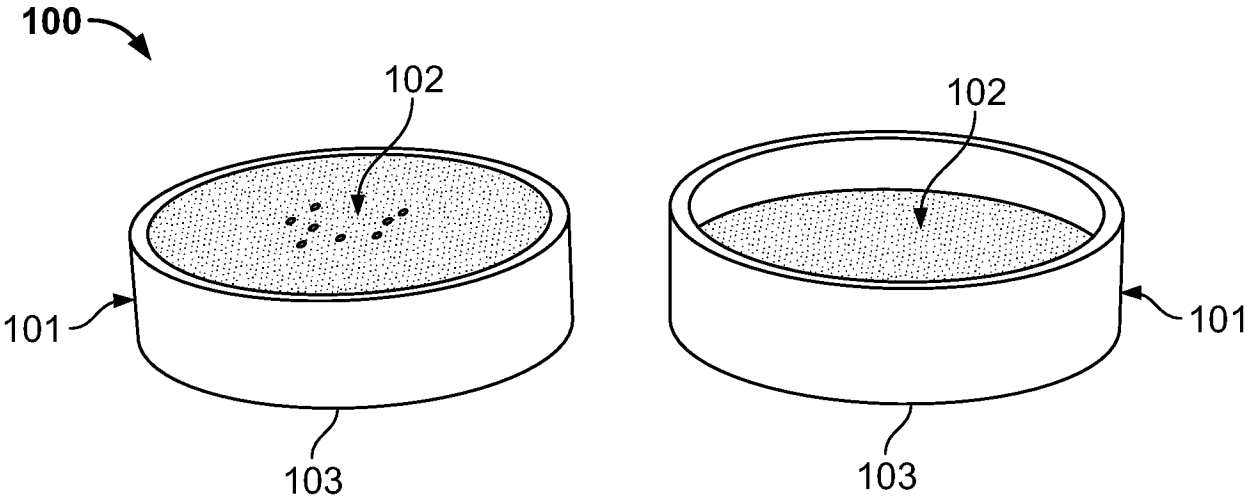


Figure 10a

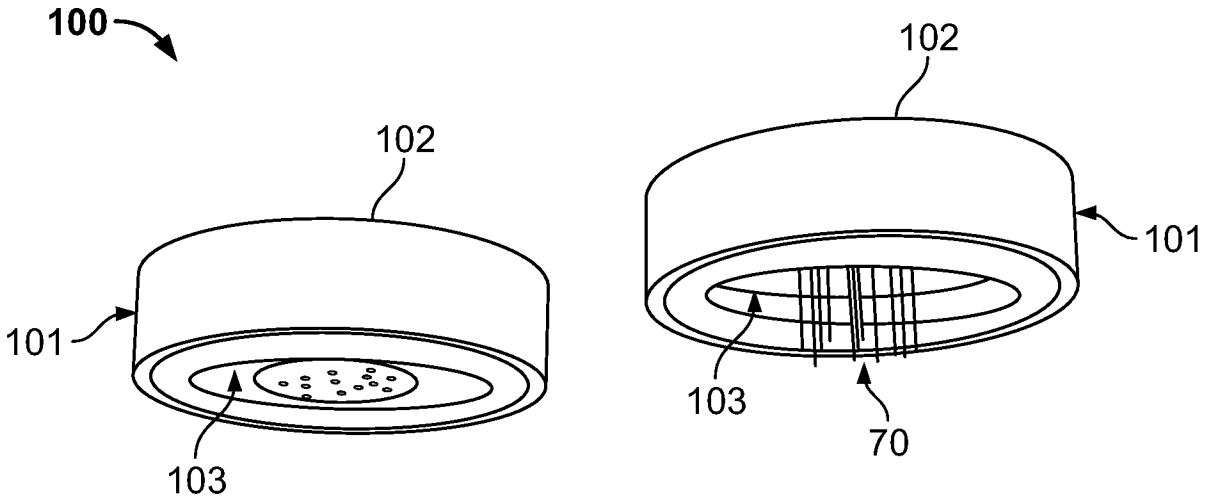


Figure 10b

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2015/010506

A. CLASSIFICATION OF SUBJECT MATTER
IPC(8) - A61M 15/00 (2015.01)
CPC - A61M 15/0028 (2015.01)
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC(8) - A61M 13/00, 15/00, 16/00 (2015.01)
CPC - A61M 3/00, 15/00, 15/0028, 16/00 (2015.01) (keyword delimited)

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
USPC - 30/358, 366; 128/208, 266, 203.15, 203.21

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
Orbit, Google Patents, Google Scholar
Search terms used: inhaler, needle, pin, puncture, rotate, rotation, powder

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2011/0220106 A1 (GANEM et al) 15 September 2011 (15.09.2011) entire document	1-22
A	US 2004/0154618 A1 (EDWARDS et al) 12 August 2004 (12.08.2004) entre document	1-22
A	US 3,991,761 A (COCOZZA) 16 November 1976 (16.11.1976) entire document	1-22
A,P	US 2014/0150787 A1 (CIVITAS THERAPEUTICS, INC) 05 June 2014 (05.06.2014) entire document	1-22

☐ Further documents are listed in the continuation of Box C. ☐

* Special categories of cited documents:
"A" document defining the general state of the art which is not considered to be of particular relevance
"E" earlier application or patent but published on or after the international filing date
"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
10 March 2015	07 MAY 2015
Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US, Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-3201	Authorized officer: Blaine R. Copenheaver PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774