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(54) **INHALERS WITH AIRWAY DISKS HAVING DISCRETE AIRWAY CHANNELS AND RELATED DISKS AND METHODS**

INHALATOREN MIT ATEMWEGSSCHEIBEN MIT DISKRETEN ATEMWEGSKANÄLEN UND RELEVANTE SCHEIBEN UND VERFAHREN

INHALEURS AVEC DISQUES DE VOIE AÉRIENNE MUNIS DE CANAUX DE VOIE AÉRIENNE DISCRETS AINSI QUE DISQUES ET PROCÉDÉS ASSOCIÉS

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Description

Related Applications

[0001] This application claims the benefit of and priority to U.S. Provisional Application Serial No. 61/100,482, filed September 26, 2008, and U.S. Provisional Application Serial No. 61/148,520, filed January 30. 2009.

Field of the Invention

[0002] The present invention relates to inhalers, and may be particularly suitable for dry powder inhalers.

Background of the Invention

[0003] Generally described, known single and multiple dose Dry Powder Inhalers (DPIs) are an established alternative to pressurized metered dose inhalers (pMDIs). DPIs can use: (a) individual pre-measured doses in blisters containing the drug, which can be inserted into the device prior to dispensing; or (b) bulk powder reservoirs which are configured to administer successive quantities of the drug to the patient via a dispensing chamber which dispenses the proper dose. *See generally* Prime et al., Review of Dry Powder Inhalers, 26 Adv. Drug Delivery Rev., pp. 51-58 (1997); and Hickey et al., A new millennium for inhaler technology, 21 Pharm. Tech., n. 6, pp. 116-125(1997). Examples using dose container disks are disclosed in WO 02/053215, US 2007/235029 and WO 0134234.

[0004] In operation, DPI devices strive to administer a uniform aerosol dispersion amount in a desired physical form of the dry powder (such as a particulate size or sizes) into a patient's airway and direct it to desired internal deposit site(s).

[0005] Unfortunately, some dry powder inhalers can retain some amount of the drug within the device that may be delivered with another dose of the drug. This may be particularly prone to happen when a user actuates the inhaler but does not inhale the indexed dose of medicament.

[0006] There remains a need for alternative inhalers and/or dose containment devices that can be used to deliver medicaments.

Summary of Embodiments of the Invention

[0007] Embodiments of the invention provide dose container assemblies that can define individual airway channels for one or more dose containers that align with an inhalation port and capture dry powder from a respective dose container(s) to define apart of the inhalation path to the inhalation port for dispensing the dry powder to a user of the inhaler.

[0008] Some embodiments are directed to dry powder dose container assemblies that include: (a) a dose container disk having opposing upper and lower primary surfaces and a plurality of circumferentially spaced apart dose containers; and (b) at least one airway disk residing above or below the dose container disk. The at least one airway disk includes a plurality of circumferentially spaced apart airway channels. The dose containers can have dry powder sealed therein.

[0009] Embodiments of the invention are directed to dry powder dose container assemblies. The assemblies include: (a) a dose container disk having a plurality of circumferentially spaced apart dose containers, the dose containers having dry powder therein (typically a defined or metered amount); (b) an upper airway disk residing above the dose container disk; and (c) a lower airway disk residing below the dose container disk. The upper and the lower airway disks each include a plurality of circumferentially spaced apart channels and pairs of the lower airway disk channels and the upper airway disk channels are aligned with at least one corresponding dose container therebetween.

[0010] The dose container can be used in combination with an inhaler. The inhaler can include an inhaler body with an inhalation port and a piercing mechanism. In operation, a dose container is indexed to an inhalation position and the piercing mechanism is configured to travel through an airway disk aperture, pierce first and second sealant layers, enter, then stay or retract from the dose disk aperture while occluding the airway disk aperture, thereby allowing dry powder which falls from the dose container to reside captured in the airway channel.

[0011] In some embodiments, the dose container assembly includes both an upper and lower airway disks and each includes a respective plurality of short airway channels and a respective plurality of long airway channels, the short airway channels associated with the first row of dose container apertures and the long airway channels associated with the second row of dose container apertures. The short and long airway channels can be arranged to reside adjacent to each other and alternate circumferentially about the disk.

[0012] In some embodiments, pairs of upper and lower airway disk channels cooperate to define a curvilinear airflow path to inhibit undesired spillage of the dry powder from the inhaler (*e.g.*, provide a sink trap configuration).

[0013] Other embodiments are directed to dry powder inhalers. The inhalers includes an inhaler body with an inhalation port, a dose container assembly held in the inhaler body, a dose container openinig mechanism configured to open a dose container in a dispensing position in the inhaler, and an indexing mechanism configured to rotate the dose container assembly into the dispensing position.

[0014] The dose container assembly includes a dose container disk having a plurality of circumferentially spaced apart apertures with dry powder therein. The dose container assembly also includes a lower airway disk having a plurality of airway channels with upwardly extending sidewall residing under the dose container disk, each of the lower airway channels being in commu-

nication with at least one dose container aperture, whereby the lower airway disk channels define a plurality of spaced apart single-use or multi-use inhalation delivery paths that serially communicate with the inhalation port to thereby provide protection from inadvertent overdose.

[0015] The dose container assembly includes: (a) a dose container disk haying opposing upper and lower primary surfaces and a plurality of circumferentially spaced apart apertures with first and second sealant layers attached to the upper and lower primary surfaces of the dose container disk and defining respective floors and ceilings of the dose container apertures to form dose containers holding dry powder therein; (b) an upper airway disk residing above the dose container disk, the upper airway disk comprising a plurality of circumferentially spaced apart channels with downwardly extending sidewalls; and (c) a lower airway disk residing under the dose container disk, the lower airway disk comprising a plurality of circumferentially spaced apart channels with upwardly extending sidewalls. Pairs of the lower airway disk channels and the upper airway disk channels are aligned with at least one corresponding dose container therebetween.

[0016] Yet other embodiments are directed to methods of operating an inhaler. The methods include: (a) providing a dose container ring having staggered concentric dose container apertures sealed by upper and lower sealant layers residing over and under the apertures respectively to define sealed dose containers, the dose container ring attached to an airway channel disk having a plurality of circumferentially spaced apart airway channels, at least one for each dose container; (b) rotating the dose container ring and disk together to present a respective dose container and a corresponding airway channel to a dispensing position in the inhaler; (c) advancing a piercing mechanism to open both sealant layers and release dry powder from the dose container to the corresponding airway channel; (d) leaving the piercing mechanism in an extended position or at least partially retracting the piercing mechanism; (e) fully retracting the piercing mechanism from the airway disk aperture after the step of leaving; and (f) isolating the airway channel associated with the released dry powder from an inhalation flow path so that the channel is reused only once or is not used for any subsequent inhalation delivery.

[0017] Additional embodiments are directed to methods of fabricating a dose container assembly. The methods include: (a) providing a dose container disk having upper and lower primary surfaces with a plurality of circumferentially spaced apart apertures; (b) attaching a sealant layer to one of the upper or lower primary surfaces of the dose container disk; (c) filling the dose container disk apertures with dry powder; (d) attaching a sealant layer to the other primary surface of the dose container to provide sealed dose containers; (e) placing the dose container disk between upper and lower airway disks; (f) aligning the dose containers with circumferentially spaced apart airway channels on upper and lower airway disks so that each dose container is in communication with one of the airway channels in both the upper and lower disks; and (g) attaching the upper and lower airway disks to sandwich the dose container disk therebetween.

[0018] In some embodiments, the dose container assemblies can be configured to allow for operation irrespective of orientation and to capture the dose from a respective dose container whether the inhaler device is held right side-up or down so that the dry powder is retained in the respective airway path and the inhaler is thereby resistant to overdosing. In some embodiments; the inhalers can also provide overdose protection to inhibit dispensing accumulated doses released from different dose containers.

[0019] It is noted that aspects of the invention described with respect to one embodiment, may be incorporated in a different embodiment although not specifically described relative thereto. That is, all embodiments and/of features of any embodiment can be combined in any way and/or combination. Applicant reserves the right to change any originally filed claim or file any new claim accordingly, including the right to be able to amend any originally filed claim to depend from-and/or incorporate-any feature of any other claim although not originally claimed in that manner. These and other objects and/or aspects of the present invention are explained in detail in the specification set forth below.

Brief Description of the Figures

[0020]

Figure 1A is a front perspective view of an inhaler With a cover according to some embodiments of the present invention.

Figure 1B is a front perspective of the inhaler shown in **Figure 1A** with the cover in an open position according to some embodiments of the present invention.

Figure 2A is a top perspective view of an exemplary dose container assembly according to some embodiments of the present invention.

Figure 2B is an exploded view of the assembly shown in **Figure 2A**.

Figure 2C is a partial cutaway view of airway channels aligned with two dose containers according to some embodiments, of the present invention.

Figure 2D is a top perspective view of another exemplary dose container assembly according to some embodiments of the present invention.

Figure 2E is an exploded view of the dose container assembly shown in **Figure 2D** according to embodiments of the present invention.

Figure 2F is an exploded view of a dose container assembly with stacked dose disks according to embodiments of the present invention.

Figure 2G is a partial cutaway view of airway chan-

nels aligned with two concentric rows of staggered dose containers according to some embodiments of the present invention.

Figure 3A is a top perspective view of a dose container ring according to some embodiments of the present invention.

Figure 3B is a top perspective view of a dose container ring according to some other embodiments of the present invention.

Figure 3C is a partial cutaway view of a single dose container according to some embodiments of the present invention.

Figure 3D is a partial cutaway view of single dose container according to some embodiments of the present invention.

Figure 4A is a greatly enlarged top perspective view of a lower airway disk according to some embodiments of the present invention.

Figure 4B is a top view of lower airway disk according to some embodiments of the present invention.

Figure 4C is a bottom view of an exemplary lower airway disk.

Figure 5A is a greatly enlarged top perspective view of an upper airway disk according to some embodiments of the present invention.

Figure 5B is a greatly enlarged perspective view of an upper airway disk according to other embodiments of the present invention.

Figure 6 is a greatly enlarged partial view of the dose container assembly shown in **Figure 2A** according to embodiments of the present invention.

Figures 7A-7C are partial cutaway views of a dose container assembly in an inhaler cooperating with a piercing mechanism having a three-stage operation sequence according to some embodiments of the present invention.

Figure 8A is a bottom perspective partial cutaway view of an inhaler with a dose container assembly configured so that the outer ring of dose containers are aligned with airway channels in disks that have "sink traps to inhibit spillage according to some embodiments of the present invention.

Figure 8B is a side perspective view of the device shown in **Figure 8A** illustrating the inner row of dose containers are aligned with airway channels in disks that define "sink traps" to inhibit spillage according to some embodiments of the present invention.

Figure 9A is a top perspective view of a dose container assembly and piercing mechanism according to some embodiments of the present invention.

Figure 9B is a top view of the device shown in **Figure 9A**.

Figure 9C is a side view of the device shown in **Figure 9A.**

Figure 10 is a partial exploded view of the device shown in **Figure 9A** according to some embodiments of the present invention.

Figure 11 is a top assembled view of the portion of the device shown in **Figure 10**.

Figure 12 is a side section view taken along lines 12-12 of **Figure 11**, illustrating an outer ring actuation according to some embodiments of the present invention.

Figure 13 is a top assembled view of the portion of the device shown in **Figure 10**.

Figure 14 is a side section view taken along lines 14-14 of **Figure 13**, illustrating an inner ring actuation according to embodiments of the present invention.

Figure 15A is a top view of a dose container ring according to some embodiments of the present invention.

Figure 15B is a partial enlarged fragmentary view of the ring shown in **Figure 15A**.

Figure 16 is a side view of the ring shown in **Figure 15A**.

Figure 17A is a greatly enlarged partial cutaway view of an inhaler with discrete airway channels for each dose container and along airway path according to some embodiments of the present invention.

Figures 17B-17D are greatly enlarged partial cutaway side perspective views of an inhaler with a biasing mechanism according to embodiments of the present invention.

Figure 17E is a greatly enlarged cutaway view of an airflow path in an inhaler and secure airpath joint provided by a biasing mechanism such as that shown, for example, in **Figures 17B-17D** or **17F** and **17G** according to Embodiments of the present invention.

Figure 17F is a perspective partial cutaway view of an inhaler with an alternate biasing mechanism (shown inverted from normal orientation) according to embodiments of the present invention.

Figure 17G is an additional perspective view of the biasing mechanism shown in **Figure 17F**.

Figure 18A is a greatly enlarged partial cutaway view of an inhaler with discrete airway channels and a short airway path according to some embodiments of the present invention.

Figure 18B is a greatly enlarged partial cutaway view of the inhaler shown in Figure **18A** illustrating an indexing mechanism according to some embodiments of the present invention.

Figure 18C is a greatly enlarged partial cutaway view of an inhaler with discrete airway charnels and a short airway path according to some embodiments of the present invention.

Figure 18D is a greatly enlarged partial cutaway view of the inhaler shown in **Figure 18C** illustrating an indexing mechanism according to some embodiments of the present invention.

Figure 18E is an exploded side perspective view of components of the indexing mechanism shown in **Figures 18C** and **18D**.

Figure 18F is an enlarged side perspective view of some assembled components of the inhaler devices

shown in **Figure 18E.**

Figure 19A is an enlarged partial section view of an alternate piercing mechanism for the dose containers according to some embodiments of the present invention.

Figure 19B is an enlarged partial section view of a piercing mechanism similar to that shown in **Figure 19A** according to some embodiments of the present invention.

Figure 19C is a partial front schematic view of a piercing mechanism with a fluted piercer according to some embodiments of the present invention.

Figure 19D is an end view of the device shown in **Figure 19C.**

Figure 19E is a partial front schematic view of another fluted piercer configuration according to some embodiments of the present invention.

Figure 19F is an end view of an exemplary four lobe fluted piercer according to some embodiments of the present invention.

Figure 19G is a partial cutaway schematic illustration of an inhaler with a piercing configuration according to some embodiments of the present invention.

Figure 20 is an enlarged partial section view of an inhaler.having generally "U" shaped inhalation flow paths according to embodiments of the present invention.

Figure 21 is a flow chair of exemplary operations that can be used to operate an inhaler according to some embodiments of the present invention.

Figure 22 is a flow chart of operations that can be used to fabricate or assemble a dose container assembly according to some embodiments of the present invention.

Description of Embodiments of the Invention

[0021] The present invention will now be described more fully hereinafter with reference to the accompanying figures, in which embodiments of the invention are shown. This invention may, however, be embodied in many different forms and should not be construed as limited to the embodiments set forth herein. Like numbers refer to like elements throughout. In the figures, certain layers, components for features may be exaggerated for clarity, and broken lines illustrate optional features or operations unless specified otherwise. In addition, the sequence of operations (or steps) is not limited to the order presented in the figures and/or claims unless specifically indicated otherwise. In the drawings, the thickness of lines, layers, features, components and/or regions may be exaggerated for clarity and broken lines illustrate optional features or operations, unless specified otherwise. Features described with respect to one figure or embodiment can be associated with another embodiment of figure although not specifically described or shown as such.

[0022] It will be understood that when a feature, such as a layer, region or substrate, is referred to as being "on" another feature or element, it can be directly on the other feature or element or intervening features and/or elements may also be present. In contrast, when an element is referred to as being "directly on" another feature or element, there are no intervening elements present. It will also be understood that, when a feature or element is referred to as being "connected", "attached" or "coupled" to another feature or element, it can be directly connected, attached or coupled to the other element or intervening elements may be present. In contrast, when a feature or element is referred to as being "directly.connected", "directly attached" or "directly coupled" to another element, there are no intervening elements present. Although described or shown with respect to one embodiment, the features so, described or shown can apply to other embodiments.

[0023] The terminology used herein is for the purpose of describing particular embodiments only and is not intended to be limiting of the invention. As used herein, the singular forms "a", "an" and "the" are intended to include the plural forms as well, unless the context clearly indicates otherwise. If will be further understood that the terms "comprises" and/or "comprising," when used in this specification, specify the presence of stated features, steps, operations, elements, and/or components, but do not preclude the presence or addition of one or more other features, steps, operations, elements, components, and/or groups thereof. As used herein, the term "and/or" includes any and all combinations of one or more of the associated listed items.

[0024] Spatially relative terms, such as "under", "below", "lower", "oyer", "upper" and the like, may be used herein for ease of description to describe one element or feature's relationship to another element(s) or feature(s) as illustrated in the figures. It will be understood that the spatially relative terms are intended to encompass different orientations of the device in use or operation in addition to the orientation depicted in the figures. For example, if a device in the figures is inverted, elements described as "under" or "beneath" other elements or features would then be oriented "over" the other elements or features. Thus, the exemplary term "under" can encompass both an orientation of over and under. The device may be otherwise oriented (rotated 90 degrees or at other orientations) and the spatially relative descriptors used herein interpreted accordingly. Similarly, the terms "upwardly", "downwardly", "vertical", "horizontal" and the like are used herein for the purpose of explanation only unless specifically indicated otherwise.

[0025] It will be understood that although the terms "first" and "second" are used herein to describe various components, regions, layers and/or sections, these regions, layers and/or sections should not be limited by these terms. These terms are only used to distinguish one component region, layer or section from another component, region, layer or section. Thus, a first component, region, layer or section discussed below could

be termed a second component, region, layer or section, and *vice versa*, without departing from the teachings of the present invention. Like numbers refer to like elements throughout.

[0026] Unless otherwise defined, all terms (including technical and scientific terms) used herein have the same meaning as commonly understood by one of ordinary skill in the art to which this invention belongs. It will be further understood that terms, such as those defined in commonly used dictionaries, should be interpreted as having a meaning that is consistent with their meaning in the context of the specification and relevant art and should not be interpreted in an idealized or overly format sense unless expressly so defined-herein. Well-known functions or constructions may not be described in detail for brevity and/or clarity.

[0027] In the description of the present invention that follows, certain terms are employed to refer to the positional relationship of certain structures relative to other structures. As used herein, the term "front" or "forward" and derivatives thereof refer to the general or primary direction that the dry powder travels to be dispensed to a patient from a dry powder inhaler; this term is intended to be synonymous with the term "downstream," which is often used in manufacturing or material flow environments to indicate that certain material traveling or being acted upon is farther along in that process than other material. Conversely, the terms "rearward" and "upstream" and derivatives thereof refer to the direction opposite, respectively, the forward or downstream direction.

[0028] The term "deagglomeration" and its derivatives refer to flowing or processing dry powder in the inhaler airflow path to inhibit the dry powder from remaining or becoming agglomerated or cohesive during inspiration.

[0029] The inhalers and methods of the present invention may be particularly suitable for holding a partial or bolus dose or doses of one or more types of particulate dry powder substances that are formulated for *in vivo* inhalant dispersion (using an inhaler) to subjects, including, but not limited to, animal and, typically, human subjects. The inhalers can be used for nasal and/or oral (mouth) respiratory inhalation delivery, but are typically oral inhalers.

[0030] The terms "sealant", "sealant layer" and/or "sealant material" includes configurations that have at least one layer of at least one material and can be provided as a continuous layer that covers the entire upper surface and/or lower surface or may be provided as strips or pieces to cover portions of the device, *e.g.*, to reside over at least a target one or more of the dose container apertures. Thus, terms "sealant" and "sealant layer" includes single and multiple layer materials, typically comprising at least one foil layer. The sealant or sealant layer can be a thin multi-layer laminated sealant material with elastomeric and foil materials. The sealant layer can be selected to provide drug stability as they may contact the dry powder in the respective dose containers.

[0031] The sealed dose containers can be configured to inhibit oxygen and moisture penetration to provide a sufficient shelf life.

[0032] The term "primary surface" refers to a surface that has a greater area than another surface and the primary surface can be substantially planar or may be otherwise configured. For example, a primary surface can include protrusions or recessions, such as where some blister configurations are used. Thus, a disk can have upper and lower primary surfaces and a minor surface (*e.g.*, a wall with a thickness) that extends between and connects the two.

[0033] The dry powder substance may include one or more active pharmaceutical constituents as well as biocompatible additives that form the desired formulation or blend. As used herein, the term "dry powder" is used interchangeable with "dry powder formulation" and means that the dry powder can comprise one or a plurality of constituents, agents or ingredients with one or a plurality of (average) particulate size ranges. The term "low-density" dry powder means dry powders having a density of about 0.8 g/cm^3 or less. In particular embodiments, the low-density powder may have a density of about 0.5 g/cm^3 or less. The dry powder may be a dry powder with cohesive or agglomeration tendencies.

[0034] The term "filling" means providing a bolus or sub-bolus metered amount of dry powder. Thus, the respective dose container is not required to be volumetrically full.

[0035] In any event, individual dispensable quantities of dry powder formulations can comprise 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 target. The dry powder drug formulations can include active particulate sizes that vary. The device may be particularly suitable for dry powder formulations having particulates which are in the range of between about 0.5-50μm, typically in the range of between about 0.5μm - 20.0μm, and more typically in the range of between about 0.5μm -8.0μm. The dry powder formulation can also include flow-enhancing ingredients, which typically have particulate sizes that may be larger than the active ingredient particulate sizes. In certain embodiments, the flow-enhancing ingredients can include, excipients having particulate sizes on the order of about 50-100 μm. 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.

[0036] "Active agent" or "active ingredient" as described herein includes an ingredient, agent, drug, compound, or composition of matter or mixture, which provides some pharmacologic, often beneficial, effect. This includes foods, food supplements, nutrients, drugs, vac-

cines, vitamins, and other beneficial agents. As used herein, the terms further include any physiologically or pharmacologically active substance that produces a localized and/or systemic effect in a patient.

[0037] The active ingredient or agent that can be delivered includes antibiotics, antiviral agents, anepileptics, analgesics, anti-inflammatory agents and bronchodilators, and may be inorganic and/or organic compounds, including, without limitation, drugs which act on the peripheral nerves, adrenergic receptors, cholinergic receptors, the skeletal muscles, the cardiovascular system, smooth muscles, the blood circulatory system, synoptic sites, neuroeffector junctional sites, endocrine and hormone systems, the immunological system, the reproductive system, the skeletal system, autacoid systems, the alimentary and excretory systems, the histamine system, and the central nervous system. Suitable agents may be selected from, for example and without limitation, polysaccharides, steroids, hypnotics and sedatives, psychic energizers, tranquilizers, anticonvulsants, muscle relaxants, anti-Parkinson agents, analgesics, anti-inflammatories, muscle contractants, antimicrobials, antimalarials, hormonal agents including contraceptives, sympathomimetics, polypeptides and/or proteins (capable of eliciting physiological effects), diuretics, lipid regulating agents, antiandrogenic agents, antiparasitics, neoplastics, antineoplastics, hypoglycemics, nutritional agents and supplements, growth supplements, fats, antienteritis agents, electrolytes, vaccines and diagnostic agents.

[0038] The active agents may be naturally occurring molecules or they may be recombinantly produced, or they may be analogs of the naturally occurring or recombinantly produced active agents with one or more amino acids added or deleted. Further, the active agent may comprise live attenuated or killed viruses suitable for use as vaccines. Where the active agent is insulin, the term "insulin" includes natural extracted human insulin, recombinantly produced human insulin, insulin extracted from bovine and/or porcine and/or other sources, recombinantly produced porcine, bovine or other suitable donor/extraction insulin and mixtures of any of the above. The insulin may be neat (that is, in its substantially purified form), but may also include excipients as commercially formulated. Also included in the term "insulin" are insulin analogs where one or more of the amino acids of the naturally occurring or recombinantly produced insulin has been deleted or added.

[0039] It is to be understood that more than one active ingredient or agent may be incorporated into the aerosolized active agent formulation and that the use of the term "agent" or "ingredient" in no way excludes the use of two or more such agents. Indeed, some embodiments of the present invention contemplate administering combination drugs that may be mixed *in situ.*

[0040] Examples of diseases, conditions or disorders that may be treated according to embodiments of the invention include, but are not limited to, asthma, COPD (chronic obstructive pulmonary disease), viral or bacterial infections, influenza, allergies, cystic fibrosis, and other respiratory ailments as well as diabetes and other insulin resistance disorders. The dry powder inhalation 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. 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. 20010063761, entitled *Method for Administering ASPB28-Human-Insulin* and U.S. Patent Application Publication No. 20010007853, entitled *Method for Administering Monomeric Insulin Analogs*.

[0041] Typical dose amounts of the unitized dry powder mixture dispersed in the inhalers may vary depending on the patient size, the systemic target, and the particular drug(s). The dose.amounts and type of drug held by a dose container system may vary per dose container-or may be the same. In some embodiments, the dry powder dose amounts can be about 100 mg or less, typically less than 50 mg, and more typically between about 0.1 mg to about 30 mg.

[0042] In some embodiments, such as for pulmonary conditions (*i.e.*, asthma or COPD), the dry powder can be provided as about 5 mg total weight (the dose amount may be blended to provide this weight). A conventional exemplary dry powder dose amount for an average adult is less than about 50 mg, typically between about 10-30 mg and for an average adolescent pediatric subject is typically from about 5-10 mg. A typical dose concentration may be between about 1-5%. 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.

[0043] 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 10-25 mg 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 dispersal systems provided by certain embodiments of the DPI configurations of the instant invention, the adult dose may be reduced to under about 15 mg, such as between about 10μg-10mg, and more typically between about 50μg-10mg. The active constituent(s) concentration may be between about 5-10%. In other embodi-

ments, active constituent concentrations can be in the range of between about 10-20%, 20-25%, or even larger. In particular embodiments, such as for nasal inhalation, target dose amounts may be between about 12-100μg.

[0044] In certain particular embodiments, during inhalation, the dry powder in a particular drug compartment or blister may be formulated in high concentrations of 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.

[0045] In some embodiments, the unit dose amount of dry powder held in a respective drug compartment or dose container is less than about 10 mg, typically about 5 mg of blended drug and lactose or other additive (*e.g.*, 5 mg LAC), for treating pulmonary conditions such as asthma. Insulin may be provided in quantities of about 4 mg or less, typically about 3.6 mg of pure insulin. The dry powder may be inserted into a dose container/drug compartment in a "compressed" or partially compressed manner or may be provided as free flowing particulates.

[0046] Some embodiments of the invention are directed to inhalers that can deliver multiple different drugs for combination delivery. Thus, for example, in some embodiments, some or all of the dose containers may include two different drugs or different dose containers may contain different drugs configured for dispensing substantially concurrently.

[0047] The inhalers can be configured to provide any suitable number of doses, typically between about 30 - 120 doses, and more typically between about 30-60 doses. The inhalers can deliver one drug or a combination of drugs. In some embodiments, the inhalers can provide between about 30-60 doses of two different drugs (in the same or different unit amounts), for a total of between about 60-120 individual unit doses, respectively. The inhaler can provide between a 30 day to a 60 day (or even greater) supply of medicine. In some embodiments, the inhalers can be configured to hold about 60 doses of the same drug or drug combination, in the same or different unit amounts, which can be a 30 day supply (for a twice per day dosing) or a 60 day supply for single daily treatments.

[0048] Certain embodiments may be particularly suitable for dispensing medication to respiratory patients, diabetic patients, cystic fibrosis patients, or for treating pain. The inhalers may also be used to dispense narcotics, hormones and/or infertility treatments.

[0049] The dose container assembly and inhaler may be particularly suitable for dispensing medicament for the treatment of respiratory disorders. Appropriate medicaments may be selected from, for example, analgesic, e.g., codeine, dihydromorphine, ergotamine, fentanyl or morphine; anginal preparations, e.g., diltiazem; antiallergics, e.g., cromoglycate, ketotifen or nedocromil; antiinfectives e.g., cephalosporins, penicillins, streptomycin, sulphonamides, tetracyclines and pentamidine; antihistamines, e.g., methapyrilene; anti-inflammatories, e.g., beclomethasone dipropionate, fluticasone propionate, flunisolide, budesonide; rofleponide, mometasone furoate or triamcinolone acetonide; antitussives, e.g., noscapine; bronchodilators, e.g., albuterol, salmeterol, ephedrine, adrenaline, fenoterol, formoterol, isoprenaline, metaproterenol, phenylephrine, phenylpropanolamine, pirbuterol, reproterol, rimiterol, terbutaline, isoetharine, tulobuterol, or (-)-4-amino-3, 5-dichloro-α-[[6-[2-(2-pyridinyl) ethoxy] hexyl] methyl] benzenemethanol; diuretics, e.g., amiloride; anticholinergics, e.g., ipratropium, tiotropium, atropine or oxitropium; hormones, e.g., cortisone, hydrocortisone or prednisolone; xanthines, e.g., aminophylline, choline theophyllinate; lysine theophyllinate or theophylline; therapeutic proteins and peptides, *e.g.*, insulin or glucagon. It will be clear to a person of skill in the art that, where appropriate, the medicaments may be used in the form of salts, (*e.g.*, as alkali metal or amine salts or as acid addition salts) or as esters (*e.g.*, lower alkyl esters) of as solvates (e.g., hydrates) to optimize the activity and/or stability of the medicament.

[0050] Some particular embodiments of the dose container assembly and/or inhaler include medicaments that.are selected from the group consisting of: albuterol, salmeterol, fluticasone propionate and beclometasone dipropionate and salts or solvates thereof, *e.g.*, the sulphate of albuterol and the xinafoate of salmeterol. Medicaments can also be delivered in combinations. Examples of particular formulations containing combinations of active ingredients include those that contain salbutamol (*e.g.*, as the free base or the sulphate salt) or salmeterol (*e.g.*, as the xinafoate salt) in combination with an anti-inflammatory steroid such as a beclomethasone ester (*e.g.*, the dipropionate) or a fluticasone ester (*e.g.*, the propionate).

[0051] Turning now to the figures, **Figures 1A** and **1B** illustrate an example of a multi-dose inhaler **10** with a cover **11** and inhalation port **10p**. The cover **11** may extend over a top surface of the inhaler to extend down over an inhalation port **10p** of the mouthpiece **10m**, then extend rearward away from the mouthpiece **10m** over a bottom surface of the inhaler. However, this inhaler configuration is shown merely for completeness and embodiments of the invention are not limited to this inhaler configuration as other form factors, covers and inhalation port configurations may be used.

[0052] **Figure 2A** illustrates a dose container assembly **20** with a dose ring or disk **30** having a plurality of dose containers **30c.** As shown in **Figures 2B** and **2E,** in some embodiments, the dose ring or disk **30** can in-

clude a plurality of circumferentially spaced apart through apertures **30a** that form a portion of the dose containers **30c.** As shown in **Figure 2E**, the dose containers **30c** can be defined by dose container apertures **30a** and upper and lower sealants **36**, **37.**

[0053] As shown, the dose container assembly **20** includes a lower airway disk **40** and an upper airway disk **50**. In other embodiments, the dose container assembly **20** can include the dose container disk **30** and only one of the lower airway disk **40** or the upper airway disk **50**. In such a configuration, another type of airway can be used for the other side of the disk **30, such** as, but not limited to, a fixed or "global" upper or lower airway can be used with the individual airways provided by either an upper or lower airway disk **50, 40.** Also, it is contemplated that the upper and lower airway disks **50, 40** described herein can be reversed for normal operation (or inadvertently for atypical operation) so that the lower airway disk is the upper airway disk and the upper airway disk is the lower airway disk.

[0054] As shown in **Figures 2A** and **2B**, the lower and upper airway disks **40, 50**, respectively, include a plurality of circumferentially spaced apart airway channels **41, 51**, respectively. Typically, the disks **40, 50** include one channel **41, 51** for one dose container **30c**. However, in other embodiments, as shown, for example, in **Figure 2C**, a respective airway channel **51**, **41** from one or both of the disks **50', 40'** can be in communication with two or more different dose containers **30c**. This configuration will allow for (simultaneous) combination delivery of two or more different dry powders from two or more dose containers **30c** in communication with the associated one airway channel **51** or **41** and/or a respective airway channel pair. Thus, while embodiments of the invention are illustrated as releasing only a dose from a single dose container **30c** during one delivery, other embodiments allow the inhalers to dispense a combination drug so that two or more dose containers **30c** may use a respective airway channel **41, 51** for delivery.

[0055] It is also noted that the disk **30** can have a single dose container **30c** circumferentially spaced apart between aligned dual containers $\mathbf{30c_1}$, $\mathbf{30c_2}$. However, it is contemplated that in some embodiments, the dose disk **30** can be configured so that the dose disk **30** has radially spaced apart dual (or more) containers $\mathbf{30c_1}$, $\mathbf{30c_2}$ with a corresponding airway channel **41/51** (typically a channel pair) and does not require either the shorter channels **41, 51** or a single dose container **30c.** The dose containers can be arranged in concentric rows of aligned pairs (or more) of dose containers. In some embodiments, the combination delivery configuration can employ dose containers $\mathbf{30c_1}$, $\mathbf{30c_2}$ which can be configured to reside under or over a respective airway channel **41/51**, but the airway channel **41/51** can angularly extend from a dose container proximate the inner perimeter to a staggered dose container proximate the outer perimeter of the disk as shown in **Figure 2G**. However, the airway channel(s) can extend over or under two or more dose channels with non-staggered centerlines.

[0056] In other embodiments, as shown in **Figure 2F,** two or more dose disks **30** can be stacked and reside either sandwiched between the airway channel disks **40, 50** or can be used with a single airway disk **40/50** and the piercer can be configured to open two or more stacked dose disk containers to release the medicaments from two or more stacked dose containers and allow inhalation using one or both channels **41, 51.**

[0057] In other embodiments, the different dose containers in communication with the respective airway channel **51, 41** can allow one dose container $\mathbf{30c_1}$ to release dry powder to the airway channel **41** and/or **51**, then be used again later for another dose container $\mathbf{30c_2}$. Thus, embodiments of the invention allow for some or all airway channels **41, 51** to be used once or twice (although other configurations may allow for greater number of uses).

[0058] In some embodiments, the airway channels **41, 51** can define airways that are not able to release dry powder residing in a respective airway channel to a user once the inhaler is indexed again to another position so that the outer ring of dose containers are aligned with airway disks. The channels can be configured to have "sink traps" to inhibit spillage according to some embodiments of the present invention to provide overdose protection (unless the dual use configuration is used whereby only a single other dose may be released using that airway channel(s) as noted above).

[0059] Where two airway disks are used, *e.g.*, both the lower and upper disks **40, 50**, the inhaler device **10** can be configured to operate even when inverted and have the same overdose protection feature. Spillage of dry powder from the inhaler **10** as the dose container **30c** is opened can be influenced by gravity. For example, for a conventional obround or elliptical mouthpiece shape, there are two primary device orientations (right-side-up and upside-down), embodiments of the invention allow for operation of the inhaler device in both orientations. In the embodiment shown, for example, in **Figure 2A,** this can be accomplished by having an individual airway section for a respective dose container **30c** (or dose containers where combination drug delivery is desired) both above and below the target corresponding dose container(s) **30c**.

[0060] **Figures 2A, 2D** and **3A** illustrate that the dose container disk **30** can include 60 dose containers **30c** while **Figure 3B** illustrates that the dose container disk **30** can include 30 dose containers **30c**. Greater or lesser numbers of dose containers may be used.

[0061] **Figure 2E** illustrates that sealant layers **36, 37** may be configured as annular flat rings as shown can be used to seal the top and bottom surfaces of the dose disk **30.** The sealant layers **36, 37** can have the same or different material(s) and may include foil, polymer(s) and/or elastomer(s), or other suitable material or combinations of materials, including laminates. Typically, the sealant layers **36, 37** are thin flexible sealant layers comprising

foil.

[0062] The sealant layers **36, 37** (where used) may be provided as a substantially continuous ring as shown in **Figure 2E** or may be attached to the dose container disk **30** as individual strips or spots of sealant that can be placed over and under the apertures **30a**. In other embodiments, sealant layers may be provided on only one primary surface of the dose disk **30,** and the apertures **30a** may be closed on one side rather than have through apertures (not shown). In yet other embodiments, the dose disk **30** can have a blister configuration **130** (**Figure 17A**).

[0063] **Figures 2A, 2D, 3A** and **3B** also illustrate that the dose container disk **30** can include at least one indexing notch **34,** shown as a plurality of circumferentially spaced apart indexing notches **34**. A mating component on one of the other disks **40, 50** can be used to help orient the disks **30, 40, 50** relative to each other. For example, one of the airway disks **40, 50,** typically the lower disk **40,** may include an inner wall with an outwardly radially extending tab **45** (**Figures 4A, 6**) that aligns with and engages one of those notches **34** to position the channels **41, 51** in alignment with the dose containers **30c.** Other alignment means may be used, including, for example, the reverse of the notch and tab configuration described (*e.g.*, one or both airway disks **40, 50** can have a notch and the dose container disk **30** can include a tab or other component).

[0064] As shown in **Figures 2B**, **2D, 3A** and **3B,** the dose containers **30c** may be arranged so that they are circumferentially spaced apart in one or more rows. As shown in **Figure 3A**, the dose containers **30c** are arranged in staggered concentric rows, a front row **31** at a first radius from a center of the disk and a back row **32** at a second different radius. The dose containers **30c** can be arranged so that centerlines of the dose containers **30c** of the back row are circumferentially offset from the centerlines of the dose containers **30c** in the front row by a distance. As shown in **Figure 3A** dose containers **30c** on each respective row are spaced apart a distance "D" and the offset of the centerlines of those on the back row to those on the front row is "D/2". The dose container disk **30** can be a molded polymer, copolymer or blends and derivatives thereof, or may comprise metal, or combinations thereof, or other materials that are capable of providing sufficient moisture resistance.

[0065] The dose container disk **30** can have an outer diameter of between about 50-100 mm, typically about 65 mm and a thickness of between about 2-5 mm, typically about 3 mm. The disk **30** can comprise a cyclic olefin (COC) copolymer. The apertures **30a** can have a diameter of between about 2-5 mm, typically about 3 mm and the sidewalls **30w** of the dose containers **30c** may have an angle or draft of about 1-3 degrees per side, typically about 1.5 degrees, as shown in **Figure 3D,** to facilitate removal from a mold (where a molding process is used to form the disk **30**). The dose container **30** is configured to be able to protect the powder from moisture ingress, while providing a desired number of doses in a compact overall inhaler size. The individual dose container apertures **30a** are spaced apart from each other to allow sufficient seal area and material thickness for moisture protection of the powder.

[0066] Similar to the embodiment shown in **Figure 2E, Figure 3C** illustrates that the dose containers **30c** may be defined by apertures **30a** sealed by sealant layers **36, 37** over and under the apertures **30a.** As discussed above, the sealant layers **36, 37** can include foil, a polymer and/or elastomer, or other suitable materials or combinations of materials, including laminates. In a dry powder medicament inhaler **10**, the drug powder is stored in a closed, moisture-resistant space provided by the dose container **30c**.

[0067] Embodiments of the invention provide a dose container assembly **20** that can provide a suitable seal and facilitate attachment of the airway disks **40, 50** to hold the dose ring or disk 30 therebetween. As shown in **Figures 2D, 2E,** in some embodiments, the dose container disk **30** contains sealants **36, 37** which may be a continuous layer over the upper and lower (primary) surfaces of the dose disk **30** and the upper and lower airway disks **50, 40** can contact the respective sealant and abut the dose disk **20** to allow for a tight fit. The exemplary attachment features shown in **Figures 2A, 2E** and **6** can reduce air leakage by allowing a close fit of the airway disks **40, 50** to the dose ring **30**. The disks **40**, **50** can sandwich the dose ring **30** and the dose ring can act as the "stop" to set the depth of engagement of the assembly features on the airway disks **40, 50.** Embodiments of the invention provide a feature to index and/or orient the airway disks **40, 50** relative to the dose ring **30** as discussed above. In addition or alternatively, as shown in **Figures 2E** and **4A,** in some embodiments, relatively simple frictional engagement members, such as, but not limited to, "crush ribs" **47r**, on one or both of the airway disks **40**, **50** may be used to secure their attachment to each other as will be discussed further below.

[0068] **Figure 4A** illustrates an example of a lower airway disk **40**. As shown, the disk **40** defines a plurality of circumferentially spaced apart channels **41.** For the staggered concentric dose container configuration, the disk **40** can include alternating long and short airway channels **42, 43,** respectively. Each channel **41** includes opposing end portions **41a, 41b,** one (substantially or entirely) closed end portion **41a** typically positioned adjacent the dose container **30c** and one open end portion **41b**. The open end portion end portion **41b** can merge into and/or is positioned adjacent the exit port **10p** and/or mouthpiece **10m** (**Figures 7A-7C**) and/or a make-up air port or channel. The intake and flow can be in either direction and the open end **41b** can be configured to face either the inner or outer perimeter of the disk **40** (*e.g.*, be either positioned radially innermost or radially outermost on the disk **40**)**.** The channels **41** include upwardly extending sidewalls **41w** with adjacent pairs of the long and short channels sharing one of the sidewalls **41w**. Optionally,

as shown by feature **48** in **Figure 4A** aligned with some charnels, all or some of the channels **41** can include a small bleed hole **48** that allows air to enter but is sized to inhibit dry powder from exiting therefrom (the bleed holes **48** are shown only with a few of the channels **41** for ease of illustration).

[0069] **Figures 4A** and **4B** also illustrate that the disk **40** can include circumferentially spaced apart upwardly extending walls or tabs **47.** One of which can include the radially (outwardly) extending tab **45** discussed above. The disk **40** can also or alternatively optionally include circumferentially extending recesses which align with tabs on the upper airway disk **50** to sandwich the dose disk **30** therebetween. The tabs **47** can optionally include crush ribs **47r** that matably engage with tabs **57** on the upper airway disk **50** to hold the three piece dose disk assembly **20** together with sufficient force without requiring and additional attachment means.

[0070] **Figures 4C, 18D** and **20** illustrate that the disk **40** can also include dose indicia **44** so that a user can visually note what dose is being dispensed or a number of doses left in the inhaler. The dose indicia **44** can align with a dose reading aperture in the inhaler housing so that a user can visually assess the dose indicia/information that is visible to a user when a respective dose is indexed or is next to be indexed, to the dispensing position. Dose indicia **44** may also or alternatively be placed on the upper disk **50** and aligned with a dose reading aperture (**Figure 20**), or on both upper and lower airway disks **50**, **40**, respectively. **Figure 18D** illustrates that indicia 44 may be placed along the outer perimeter edge of the lower surface of the lower disk **40**, and numbered sequentially 1-60. In some embodiments, as shown in **Figure 20,** the indicia **44** numbering can serially progress to alternate between rows of the dose containers **30** where the dose containers are opened in sequence in alternate rows, *e.g.*, number 1 on the outer row, number 2 on the inner row, number 3 on the outer row (or vice versa) and so on. However, other dose numbering patterns may be used, depending on the opening sequence (and the number of doses on the disk). That is, this numbering may be appropriate where the inhaler is configured to open a dose container in one row, then open an adjacent dose container in the other row (*e.g.*, inner to outer ring or outer to inner ring of dose containers), and repeating this sequence serially, where two rows of dose containers are used. However, other embodiments may open all the inner dose containers or all the outer dose containers, then open the dose containers in the other row or use a different alternating pattern of opening the dose containers on the inner and outer rows, and the dose numbering indicia on the disk **40** and/or **50** can be presented accordingly.

[0071] **Figure 5A** illustrates an example of an upper airway disk **50**. In this embodiment, the upper airway disk **50** is shown inverted from its normal use position (and inverted relative to the orientation shown in **Figure 2A**). As shown, the disk **50** defines a plurality of circumferentially spaced apart channels **51**. For the staggered concentric dose container configuration, the disk **50** can include alternating long and short airway channels **52, 53,** respectively. Each channel **51** includes opposing end portions **51a, 51b,** the closed or substantially closed portion **51a** is typically positioned adjacent the dose container **30c.** The intake and flow can be in either direction and the open end **51b** can be configured to face either the inner or outer perimeter of the disk **50** (*e.g.*, be either positioned radially innermost or radially outermost). The other (open) end portion **51b** merges into and/or is positioned adjacent the exit flow path port **10p** and/or mouthpiece **10m** and/or make-up air port or channel. The channels **51** include downwardly expending sidewalls **51w** with adjacent pairs of the long and short channels sharing one of the sidewalls **51w**. Optionally, as shown by the broken line with respect to feature **48** in **Figure 5A**, one or all of the channels **51** can include a small, (air) bleed hole **48** (shown with only a few channels for ease of illustration) that allows air to enter but is sized to inhibit dry powder from exiting therefrom.

[0072] As also shown in **Figure 5A,** each channel **51** can include an aperture **55** that is configured to reside over (aligned with) a respective dose container **30c** with the upper sealant layer **36** of the dose container **30c** residing under the aperture **55**. The apertures **55** allow a piercing (*e.g.*, slicing or puncturing) mechanism to extend through the aperture and open the sealant layers **36, 37** (**Figure 3C**)**.** As shown in **Figure 5A**, the upper disk **50** can also include one or more of indexing ribs **58** and/or inner perimeter gear teeth **59** or other features that can index the disk within the inhaler to rotate the disk to provide the different dose container **30c** to a dispensing position and/or position a piercing mechanism over the target dose container for dispensing to open the dose container **30c.** In other embodiments, one or both of these rotating and positioning mechanisms (or different features) can be provided on the lower disk or the dose disk (not shown).

[0073] **Figure 5B** illustrates that the disk **50** can include three tabs **57** instead of four as shown in **Figure 5A** (the lower airway disk **40** can also include three tabs instead of four in this embodiment, *see* **Figures 4B, 4C**). One of the tabs **57** can have a vertically extending orientation rib **56**, shown on an inner perimeter surface of the tab **57**. The orientation rib **56** can be on the upper disk **50** and may be configured to cooperate with a piercing frame associated with the piercing mechanism fixed in the inhaler housing so that the orientation rib **56** aligns to the frame to set a correct initial position according to dose number (*e.g.*, 1) and prevents indexing past the number of doses in the disk assembly **20.** Stated differently, the orientation rib **56** cooperates with the inhaler housing or components attached thereto to set an initial position of the disk assembly **20** and may also be used to stop the disk assembly from rotating around more than once (*e.g.*, more than 360 degrees). In other embodiments, these functions can be provided by alternate features or com-

ponents such as the dose counter as described in co-assigned, co-pending U.S. Application US20100078021.

[0074] The indexing of the disk assembly **20** in the inhaler **10** can be about 6 degrees for every dose (about 6 degrees for each of 60 doses to arrive at a single rotation of 360 degrees to dispense the 60 doses).

[0075] **Figure 5B** also illustrates that the apertures **55** can be configured with a geometry that corresponds to the shape of the piercer **100**. The apertures **55** can be configured to closely surround the piercer **100** (**Figure 20**). The piercer **100** can be a fluted piercer. As shown, the aperture **55** has three lobes **551** to snugly matably receive a correspondingly shaped three lobe (fluted) piercer **111** (**Figures 19C/19D**). The fluted piercer can have other number of lobes, such as, for example four circumferentially spaced apart lobes **111'** as shown in **Figure 19F** and the aperture **55** can have a corresponding four lobe shape. The lobes **551** can be in a different orientation in the inner row versus the outer row, *e.g.*, rotated 180 degrees (see also, **Figure 20**).

[0076] **Figures 2A** and **6** illustrate the dose container assembly **20** integrally attached together. **Figures 2B, 4A**, and **5A** illustrate the exemplary disk components, **30, 40, 50**. The tabs **57** of the disk **50** fit into spaces **49** of the disk **40** and the tabs **47** of the disk **40** fit into spaces **59** of the disk **50** with the crush ribs **47r** (where used) firmly abutting the outer edges of tabs **57** to frictionally engage the components together with the dose disk **30** sandwiched therebetween with a flush fit via a relatively easy "press-fit" assembly method. The dose container disk **30** is aligned with the upper and lower airway disks via the (radially outward extending) tab **45** that engages one of the alignment notches **34** of the dose container ring **30** as discussed above. However, other alignment features or indicia may be used as well as other attachment configurations.

[0077] The upper and lower airway disks **50, 40** (where both are used) can be attached to the dose container disk **30** or the upper and lower disks **50, 40** can be attached together with the dose container disk **30** therebetween so as to reduce any gaps in the airway path defined thereby. The disk **30** can be a stop for attachment features on the airway disks **40, 50**. The disk **30** with the sealants **36**, **37** can have-substantially planar upper and lower primary surfaces without requiring any attachment features. The lower portion of the upper airway disk **50** and the upper portion of the lower airway disk **40** can snugly reside directly against the sealant **36, 37** on the respective opposing primary surfaces of the dose container disk **30** and/or against the primary surfaces of the dose disk **30** so that the attachment features/components are only on the upper and/or lower disks **50,40** allowing for a snug and sufficiently air-tight interface between the disks **30, 40, 50** without gaps created by tolerances in other build configurations. The press-fit attachment without use of adhesives while providing for the substantially air-tight interface can be advantageous and cost-effective. However, as noted above, other attachment configurations may be used, including, for example, ultrasonic welding, adhesive, laser weld, other friction fit and/or matable configurations, the use of seals (O-rings, gaskets and the like) between the connection regions of the walls of the airway channels facing the dose container **30c** and the sealant layers **36, 37** over and/or under the dose containers **30c** of the disk, including combinations thereof, and the like.

[0078] As shown in **Figures 7A-7C**, in operation, pairs of upper and lower aligned and radially extending channels **41, 51** can reside one over and one under a respective dose container **30c** and are in fluid communication via the opened dose container **30c** and aperture **30a.** That is, as shown in **Figure 7A**, a piercing mechanism **100** advances to pierce the upper and lower sealant layers **36, 37**, respectively (**Figures 2E, 3C**). The piercing mechanism **100** can be configured to extend and remain in the lower airway channel or may (partially or fully) retract before the dispensing after opening the lower sealant. Also, although shown as extending down to pierce the sealant layers, the piercing mechanism **100** can be configured to extend upward from the bottom. Either way, in some embodiments, the piercing mechanism **100** can be configured to occlude part of the aperture **30a** and/or aperture **55** in the upper (or lower disk).

[0079] As shown in **Figure 7B**, the piercing mechanism **100** can then partially or fully retract, or stay extended in the lower (or upper) airway channel, depending on the configuration of the mechanism, but is typically configured to plug and/or cooperate with a member that can plug the aperture **55** of the upper disk **50** (or lower disk **40** if piercing from the bottom) or otherwise occlude this passage **55** so that the piercing mechanism **100** and/or cooperating member substantially blocks, occludes (and/or seals) the aperture/opening **55** (**Figures 2A, 5A**). In this way, if the inhaler is inserted, powder is prevented from spilling out of the channel **51** because of the blockage provided by the piercing mechanism **100**. The airflow path **10f** may be any direction from above to below the dose container **30c** or vice versa. The airflow path **10f** that entrains the dry powder can extend from the inner perimeter to the outer perimeter or vice versa. **Figures 7B, 20** illustrate an exemplary aiflow path **10f** direction (shown by the arrow) to allow air to flow through in through the open end of the bottom channel **41b** on the outer perimeter of the disk assembly **20** up through the aperture **30a** and out the open end **51b** of the top channel **51** of the disk assembly **20** to the mouthpiece **10m.** It is also noted. that the exit or inlet open end portions of the channels **41b, 51b** may both face the inner perimeter rather than the outer perimeter of the disc assembly **20** as shown in **Figures 7A-7C** (*see, e.g.,* **Figure 17A**).

[0080] After dispensing, the piercing mechanism **100** is fully retracted as shown in **Figure 7C** and the dose container assembly **20** can be rotated to a dispensing position and/or the piercing mechanism **100** can be activated to open a different dose container **30c.** In operation, the dose container assembly **20** can be radially

pushed outward to seal or provide a snug exit flow path for the airway channel **41** and/or **51** against an exit flowpath member **10fm**, *e.g.*, that is or merges into the mouthpiece **10m.**

[0081] **Figure 17A** illustrates that a seal **129**, such as an O-ring may be used to provide a sufficiently air-tight path between the airflow exit path **10/** (or short path **10s** and/or mouthpiece **10m**) and the disk assembly **20**. Other disk to exit airpath seals or closure configurations may be used, examples of which are discussed below:

[0082] In some embodiments, partial retraction of the piercer **100** can inhibit or prevent powder from falling out of the airway channel when the inhaler **10** is used in the inverted position. As shown, for example, in **Figures 17A** and **17E,** to facilitate this operation, clearance between the piercer head **100h** and the access aperture **55** in the upper airway disk **50** can be small and/or snugly receive the piercer head **100h**. The piercer mechanism **100** can also be configured to operate with a high level of positional accuracy so that the piercer **100** aligns with and is able to cleanly enter the access aperture **55** of each dose container **30c** held by the disk **30** (on each row, typically alternating between rows). In some embodiments, air leakage at the joint **10j** (**Figures 17A, 17E**) between the fixed airway associated with the mouthpiece **10m** and the rotating disk subassembly **20** can be reduced or eliminated to allow for consistent dose delivery and that leakage, where present, is consistent dose to dose. As discussed with respect to **Figure 17A**, the use of a compliant seal (**129**) may allow this functionality. Also, the disk **20** can be biased toward the mouthpiece **10m** as discussed above (*e.g.*, pushed radially toward the joint **10j**/mouthpiece **10m**).

[0083] **Figures 17B-17E** illustrate an embodiment of the inhaler **10** that can bias the disk assembly **20** toward the mouthpiece **10m** using a lever assembly **80** that can facilitate an accurate, repeatable position of the disk assembly **20** for piercing, as well as control air leakage at the mouthpiece joint **10j**. With regard to air leakage, embodiments of the inhaler provide a tight connection that is temporally synchronized with the time of inhalation, while at other times, *e.g.*, during indexing of the disk assembly **20**, the inhaler can allow a looser fit which facilitates rotation of the disk assembly **20** in the inhaler **10**. In this embodiments, the mouthpiece **10m** resides on the outer perimeter of the disk assembly **20** with the exit ports of the disk assembly **20** also residing on the outer perimeter of the disk assembly. In other embodiments, the exit ports of the airway channels can be on the inner perimeter of the disk or otherwise configured or located.

[0084] As shown in **Figure 17B**, the lever assembly **80** includes a lever arm **81** that communicates with an upper surface of the upper airway disk **50** and extends down a distance to reside closely spaced to an outer perimeter of the disk assembly **20**. The lever assembly **80** also includes a finger **82** that resides above the disk assembly **20** and extends down toward the disk assembly **20**. In the embodiment shown, the lever assembly **80** also includes a loading post **84** that resides proximate an outer perimeter of the disk assembly **20**. The lever arm **81** includes a recess **83** that is configured to receive the finger **82**. As the finger **82** resides in the recess **83**, the post **84** post pushes the disk **20** radially inward to causes a tight joint **10j** at the time of inhalation (**Figure 17E**). The recess **83** can have an open perimeter shape and the finger **82** can slidably enter and exit therefrom. The lever arm **81** can define a ramp (inclined in the direction toward the recess **83**) that slidably engages the finger **82** and directs the finger **82** to move toward the recess **83**.

[0085] The lever assembly finger **82** is attached to lever **12n** (also labeled as **10/** in **Figure 1B**) and rotates with respect to the frame **12** in the inhaler housing, typically upon user actuation of the lever **12n**. When the lever **12n** is returned from "actuated" (dosing) position, the finger **82** is pulled out of the recess **83** so that the disk assembly **20** is free to rotate to index to a next dispensing position.

[0086] Typically during inhalation, the loading post **84** resides radially opposite (substantially diametrically opposed to) the mouthpiece **10m.** The lever arm **81** and post **84** do not rotate. This component is affixed to a frame **12** that is attached to the inhaler housing. The finger **82** rotates with respect to the frame **12** (and the lever arm **81**).

[0087] As shown in **Figure 17B**, the finger **82** does not contact the lever arm **81** during this portion of the stroke cycle of the lever assembly **80** to allow for free rotation during indexing. **Figure 17C** illustrates the finger **82** moving toward the recess **83. Figure 17D** illustrates the finger **82** in the recess **83** to bias the disk assembly **20** toward the exit flow path member **10fm**. At the moment of inhalation, the finger **82** is advanced to its fullest extent of travel. Indexing (rotation) of the disk assembly **20** occurs while the finger **82** is elsewhere in its travel path. Therefore, as shown by the arrows in **Figure 17D**, the lever assembly **80** can bias the disk assembly **20** while the finger **82** is at the far extent of travel to seal the joint **10j** at the proper time (inhalation), while allowing free movement during indexing (typically also unbiased the rest of the time).

[0088] It is recognized that, during manufacturing, there may be a tolerance-induced mismatch between the diameters of the dose disk 30 and the upper airway disk **50** of the disk assembly **20**. As shown in **Figure 17E**, inner or outer sidewall surfaces (shown as outer sidewall surfaces) of both of these disks, **30**, **50** contact the mouthpiece **10m** when the disk assembly **20** is biased against it. Thus, as shown in **Figure 17E** a small relief **10r** can be cut or otherwise formed into the proximate or abutting surface of the an exit flowpath member **10fm** (which may be the mouthpiece **10m**) at a location that coincides with the dose disk **30** to assure that the upper airway disk **50**, which has the greater amount of contact surface, is always the part to contact the mouthpiece or exit flowpath member **10fm** in communication with the mouthpiece **10m.**

[0089] **Figures 17F** and **17G** illustrate an alternate em-

bodiment of a biasing mechanism **180** that can bias the disk assembly **20** toward the mouthpiece **10m** during inhalation then releasing or disengaging to allow rotation of the disk assembly **20** for indexing. As discussed above, in some embodiments, the inhaler **10** can be configured to rotate the disk assembly **20** a defined angular rotation, such as about 6 degrees, to serially dispense or access dose containers alternately on inner and outer rows. This biasing mechanism **180** can be configured to operate with the lever **10*l*** similar to that discussed above with respect to the lever assembly **80** but may also be activated using other components or features.

[0090] As shown in **Figure 17F**, the biasing mechanism **180** can include a post **182** that resides proximate an inner perimeter of the dose container disk assembly **20**. The post **182** can reside in a circumferentially extending slot **182s** having an end portion that merges into a slot portion **183** that extends radially outward toward the inner perimeter of the dose disk assembly **20**. During and/or just prior to release of the medicament to a user for inhalation (*e.g.*, "dosing"), the post **182** travels in slot **182s** until it reaches slot portion **183** whereby the post pushes (typically indirectly) against the inner perimeter of the disk assembly **20** to bias the disk assembly **20** toward the mouthpiece **10m** (as shown by the arrow). The inhaler is shown upside down from normal orientation in **Figure 17F.**

[0091] **Figure 17G** illustrates that the post **182** can communicate with a stationary post **182b** on an indexing plate or frame **184**. In the embodiment shown, the biasing post **182** is configured to contact and push against post **182b** causing post **182b** to flex radially outward against the dose container assembly **20**. The two posts **182, 182b** can be configured to project toward each other, one upwardly and one downwardly, with the post **182b** typically residing closer to an inner perimeter of the dose disk assembly **20**.

[0092] The post **182** is typically attached to or in communication with the lever **10*l*** which is accessible by a user. However, the post **182** can be in communication with other mechanisms that cause the post **182** to move in the slot **182s** and bias the disk assembly **20** toward the mouthpiece **10m.**

[0093] As shown in **Figure 17G**, the indexing plate **184** can reside under gears **109g** that are associated with the indexer **109**. The rotatable gears **109g** can be held on mounts **110** on a frame member **109f** as shown in **18E**. Generally stated, the gears **109g** communicate with teeth **109t** on indexing post **109p** (that can be part of a ramp disk **209**, **Figure 18F**) and gear teeth **59a** on the disk assembly **20** (*e.g.*, as shown, on the lower disk **40**). Turning the indexing post **109p** turns gears **109g** which, in turn, indexes the disk assembly **20**. The other gear teeth **59b** (residing closer to the bottom of the inhaler housing) can communicate with indexing control arms **109r** as shown in **Figure 18D** which can help more precisely turn the dose container assembly a desired rotational amount. Note that **Figures 18D** and **18E** illustrate the inhaler in an inverted orientation from that of normal use. **Figure 18F** shows the inhaler in a "normal" use orientation with the dose disk assembly **20** below the piercer mechanism **100** as also shown, for example, in **Figure 18C**. The piercer **100** can be in communication with a ramp disk **209** with fin-like ramps **211** as shown in **Figure 18F.** In the embodiment shown, the ramp disk **209** cooperates with the piercers **100a, 100b** to push the respective piercer **100a** or **100b** into the respective dose containers **30c**. The post **182** is typically attached to the lever **10*l*** such as shown in **Figure 17F, 18E** and **18F** which is accessible by a user. However, the post **182** can be in communication with other mechanisms that cause the post to move in the slot **182s** and bias the disk assembly **20** toward the mouthpiece **10m.**

[0094] The indexing mechanism **109** shown in **Figures 17F** and **17G** is discussed further below with respect to **Figures 18C-18F**. However, other indexing configurations can be used.

[0095] **Figure 19A** illustrates one embodiment of a piercing mechanism **100** with a corkscrew piercer **110**. In operation the corkscrew moves up and down vertically straight, typically without rotation, to create a desired opening shape (e..g., circular) through the sealant layers **36, 37.** In other embodiments, the corkscrew may rotate during extension and/or dispensing. In the embodiment shown, the corkscrew piercer **110** can remain in the lower channel **41** while the dry powder is dispensed in the airflow path and the blockage of the aperture **30a** can be provided by a resilient member **120** that is mounted on the corkscrew **110** and moves up and down therewith. The piercing mechanism **100** can have a two stage operation, fully up (for indexing) and fully down. The most forward portion of the corkscrew can have a point with a configuration that creates a desired cutting configuration into the sealant (*e.g.*, foil). In some embodiments, the corkscrew piercer **110** can cut a shape with a tab into the sealant **36**, **37**, then fold the tab down to release the dry powder. Positioning the corkscrew piercer **110** in the channel **41** during dispensing may provide improved aerodynamics or shear or impaction flow turbulence for the dry powder. The resilient member **120** can comprise a foam block or other resilient member **120** (such as a hard or rigid member biased by a spring) that can be used to seal or plug the aperture **30a. Figure 19B** illustrates a similar corkscrew piercer **110** that is used with a disk assembly **20** having both upper and lower airway disks **50**, **40**. A resilient and/or flexible member **100p** such as a polymeric and/or elastomeric or foam plug can be used to occlude or seal the disk aperture **55**.

[0096] **Figures 19C** and **19D** illustrate a piercing mechanism **100** with a fluted solid piercer **111**. The flute may have a straight flute configuration or the flute can have a twist or partial twist along it length, *e.g.*, for a twist configuration, the maxima and minima of the lobes can change axially along the length of the flute. The flute can have a cross section with a plurality of lobes, typically three or four lobes, shown as three lobes in **Figure 19C**.

The fluted configuration may extend only a partial forward length and merge into a constant diameter segment that resides in and helps occlude or seal the aperture **55** as shown in **Figure 19E**. In other embodiments, the solid or fluted piercer configuration can merge into a cap or plug **100p** that resides over and/or in the aperture **55** (see, *e.g.*, **Figure 19C**). In some embodiments, the twisted flute **111** can remain in the dose container aperture **30** and/or lower disk **40** during dispensing which may facilitate turbulence and/or compaction in the airway.

[0097] **Figure 19D** illustrates that the fluted piercer **111** can rotate as it pierces the foil or other sealant material to form a round hole or may be extended straight without rotation. In other embodiments, the fluted piercer **111** can be extended or advanced without rotation to pierce the sealant layer(s) **36, 37. Figure 19E** illustrates that the fluted piercer **111**' can include a fluted forward portion **111f** with a length "L_1" that merges into a solid portion **112** that can have a substantially circular cross-section with a length "L_2". L_1 is typically longer than L_2. L_1 can have a length sufficient to allow the forward fluted portion **111f** to reside in the dose container aperture **30a** (typically just below the lower sealant line or in-line with or slightly above or below the lower surface of the disk **30**) and in or through the lower sealant **37** at the same time, with the solid portion engaging the airway disk aperture **55**.

[0098] **Figure 19G** illustrates a piercing mechanism **100** that can include a plug **100p** (similar to that shown in **Figure 19B** for the corkscrew configuration) that can occlude the passage **55**. The plug **100p** can be used with any piercer, including the corkscrew **110** (**Figure 19A**) or the solid fluted piercer **111** (**Figure 19B**) or other piercer configuration. The piercing head can remain in the lower channel **41** during dispensing as shown in **Figure 19E**, or the piercer may retract partially through a passage in the plug (not shown) while leaving the plug **100p** in position against and/or over the aperture or passage **55**.

[0099] In some embodiments, the fluted piercer **111** can be configured with lobes that twist along its length (**Figure 19D**). For example, the fluted piercer **111** can have about 60 degrees of twist along its length such that the lobes of the fluted piercer turn about its circumference. During a straight piercing stroke (straight into and through the sealant), the twisted fluted piercer **111** can make a fully round hole in the sealant **36** and/or **37**.

[0100] **Figure 20** illustrates substantially U-shaped airpaths that may be created by the disk assembly **20**. The "U" shape is created by the upper disk channel **51** and the lower disk channel **41** defining the long sides of the "U" which extend in a radial direction across the disk body. As shown, in this embodiment, the outer perimeter of the disk assembly **20** holds both the outlet and an inlet for the airflow path **10f.** The "U" shaped flow path (or, in some embodiment, a" partial "U" where only a one of the airflow disks **40**, **50** is used) can function as a powder deagglomerator. The particles impact the opposing wall of the airway disk channel **51** as they exit the dose container **30c** with sufficient force to deagglomerate the drug powder.

[0101] **Figure 20** also illustrates an example of dry powder particle trajectories **10d** entrained in air flow associated with the inspiratory airflow path **10f**. After the dry powder exits the dose container **30c** in the airflow path **10f**, the air flow and smaller, powder particles (**10f**) in the air are able to make the about 90 degree turn while heavier dry powder particles (**10d**) bounce off the inner wall **51w** of the upper airway disk channel **51** with increasingly shallow angles eventually going more or less straight out of the mouthpiece **10m.** The impact of the heavier dry powder against the walls **51w** helps deagglomerate the dry powder. Referring again to **Figure 5A**, in the dual row dose container **30** embodiments, the channels, **51** vary in length depending on if the dose container **30** is on the inner or outer row.

[0102] In some particular embodiments, the airway channels **41, 51** can include alternating short and long channels (see, *e.g.*, **Figure 5A**). The length of the long channel (the channels with the dose container on the inner perimeter where the outer perimeter is the exit location and vice versa if the inner perimeter is the exit location) can between about 5 mm to about 15 mm, typically about 10 mm, the length of the short channel can be between about 3-10 mm, typically about 5 mm, e.g., about 40-70% the length of the long channel. The depth (vertical height) of each channel **41, 51** can be the same or can, in some embodiments vary. Exemplary depths of the channels **41, 51** are between about 1 mm to about 3 mm, typically about 2 mm, but other depths can be used.

[0103] The inhaler **10** can include a user-accessible actuator such as a lever, knob, switch, slider, crank, pushbutton or other mechanical and/or electromechanical device that can index the dose ring or disk **30** to rotate the assembly **20** to place one or more dose containers **30c** (**Figure 2B**) in a dispensing position in an inhalation chamber in fluid communication with the inhalation port **10p** (**Figure 1B**) and/or cause a piercing mechanism **100** (**Figures 7A-7C**) to open a dose container **30c** in the front row, then the back row (or vice versa) to release medicament to an inhalation air flow path for inhalation by a user (as will be discussed further below). To release the powder for inhalation, the sealed dose container **30c** is opened and connected to an airway **41** and/or **51** which is in turn connected to an exit flowpath member **10fm** which can be the inhaler mouthpiece **10m** (*see*, *e.g.*, **Figures 7A-7C, 17A, 17E, 18A**) or can merge into the inhaler mouthpiece **10m** After the drug falls into the channel **41** or **51** (depending on which orientation the inhaler is in), this is a "used" channel and the drug therein is either delivered (if the user inhales properly and timely) or isolated (if the user does not inhale and closes the mouthpiece or otherwise causes the indexing of the disk assembly **20**), and the "used" channel is indexed with the opened dose container **30c** so that it cannot be used again or so that it is used again for only the other dose

container in the shared channel (as discussed with respect to **Figure 2C**). Any powder remaining in the opened dose container is separated from the airway when the next dose container is indexed into position.

[0104] In some embodiments, the portion of the airway provided by the airway channel **41** or **51** adjacent to each dose container **30c** is unique to that individual dose container **30c**. In this way, any spillage of powder into the airway will only be available to the mouthpiece and user as long as that dose container is indexed into connection with the primary (mouthpiece) airway. Indexing to the next dose container will also index the adjacent airway section out of connection with the active inhalation airway path, taking any spilled and/or accumulated powder with it.

[0105] **Figures 8A** and **8B** illustrate another embodiment of an inhaler **10**. In this embodiment, the upper airway channel **51** can be configured as a "sink trap" **51t** path that has a portion of the airflow path that rises and then turns down or vice versa. That is, as shown, the path **51t** can rise above the aperture **30a**, then turn to extend downwardly for a distance to provide additional spill resistance of the dry powder from the airway/inhaler. Similarly, the lower airway channel **41** can be configured to rise upward a distance downstream of the dose container aperture **30a** to form a "sink trap" **41t** path. In some embodiments, only one of the airway disks (*e.g*, the upper or the lower **50, 40**) have a sink trap path while in others, both disks **40, 50** have airway configurations with sink traps **41t**, **51t** at shown. The dose container assembly **20** has an aligned channel pair **41, 51** that are in fluid communication once the respective dose container is opened **30c** that reside under and over the respective dose container **30c** and have the sink trap configurations **41t**, **51t** to that cooperate to form a curvilinear airflow path (*e.g.*, a generally "S" shape, with the "S" layed on its side). The airflow path **10f** can extend either from the outer perimeter toward the inner perimeter or from the inner perimeter toward the outer perimeter.

[0106] As also shown in **Figures 8A and 8B**, in this embodiment, the piercing mechanism **100** can include two piercing members **100a, 100b**, one dedicated to opening the first row of dose containers **30c** and another for the second row of dose containers **30c**.

[0107] **Figures 9A-9C** and **10-14** illustrate an exemplary inhaler configuration with upper and lower airways forming a sink trap **51t, 41t** airflow path according to embodiments of the present invention. As shown, the piercing mechanism **100** can include the two piercing members **100a, 100b** mounted on a housing that slides over the dose container assembly **20'**. The dose container assembly **20'**. can rotate under the piercing mechanism **100** as a respective dose container(s) **30c** is indexed to a dispensing position. Similarly, the dose container assembly **20**' can rotate above the piercing mechanism if the piercing mechanism is below the dose container assembly **20, 20'**.

[0108] **Figures 10, 12** and **14** illustrate that the lower airway disk **40** can include two components, an upper member **40u** and a lower member **40*l*** that attach to define the curvilinear sink trap paths **41t**. Similarly, the upper airway disk **50** can include two components, an upper member **50u** and a lower member **50*l*** that attach to define the curvilinear sink trap paths **51t**. In particular embodiments, the dry powder can be provided as a pre-measured amount of dry powder **200** and sealed in the aperture **30a** between the sealant layers **36, 37**. As shown in **Figure 10**, the upper member **50u** can include a tab **150t** that engages a slot **150s** in the lower member **50*l*** of the airway disk **50** for alignment and/or attachment.

[0109] **Figure 12** illustrates a dose container **30c** on the outer row **31** being opened with the piercing member **100b** and the associated curvilinear airflow path **41t, 51t. Figure 14** illustrates the piercing member **100a** in position to open a dose container **30c** on the inner row **32** with the associated airflow path **41t, 51t.**

[0110] **Figures 15A, 15B** and **16** illustrate an example of a dose container disk or ring **30** with two rows of apertures **30a** used for dose containers **30c.** The dose container disk **30** can be relatively thin, such as about 2-4 mm thick. The dose container apertures **30a** can be configured so that the inner row **32** is at least about 2 mm from the outer row **31** and so that the inner and outer rows of dose containers are spaced inward from the respective perimeters by about 2 mm. This spacing can provide sufficient moisture permeability resistance and/or oxygen resistance.

[0111] **Figure 17A** illustrates on embodiment of an inhaler **10** with a long exit air path **10*l*** compared to the shorter flow path in **Figure 18A.** In this embodiment, the airway disks can orient the channels **41, 51** so that the open ends **41b, 51b** face and open to the inside of the disk rather than the outside. **Figure 17A** also illustrates that the dose container disk **30** can be configured with blisters **130.**

[0112] **Figure 17A** also illustrates that the piercing mechanism **100** can comprise a rotating piercer head **102** configured to pierce a dose container **30c** on the inner row, then rotate to pierce the adjacent one **30c** on the outer row.

[0113] **Figure 18A** illustrates that the inhaler **10** can be configured with a piercing mechanism **100** that moves radially to open a dose container **30c** in one row then move radially inward or radially outward to open a dose container **30c** in the other row. The dose container assembly **20** and/or one or more of the airway disks **40, 50** and dose container disk **30** can also be configured to axially or otherwise bias (together or individually) with a wall or walls of an exit airflow path to provide a sufficiently tight seal, such as discussed above. **Figures 18A, 18B** also illustrate that the inhaler **10** can include an indexing mechanism **109** that cooperates with the gear teeth **59** on the inner perimeter of the upper disk **50**. Other indexing mechanism may be used to rotate the assembly **20** to place the different dose containers **30c** in the dispensing position.

[0114] **Figure 18C** illustrates that the inhaler **10** can be configured with a piercing mechanism **100** that has two piercers **100a, 100b**, one that pierces dose containers on the inner row and the other that pierces/opens dose containers on the outer row. Typically, the piercing mechanism **100** is configured so that a dose container on the outer or inner row is pierced, then a dose container on the opposite row is pierced. The piercers **100a, 100b** can reciprocate up and down to open the respective dose container. The dose container assembly **20** and/or one or more of the airway disks **40, 50** and dose container disk **30** can also be configured to axially or otherwise bias (together or individually) with a wall or walls of an exit airflow path to provide a sufficiently tight seal.

[0115] **Figures 18C-18E** also illustrate that the inhaler **10** can include an indexing mechanism **109** with gears **109g** that cooperate with an indexing post **109p** and the disk assembly **20** gear teeth **59a** can reside on the inner perimeter of the lower disk **40. Figure 18D** is shown inverted from the normal use orientation shown in **Figure 18C. Figure 18C-18E** also show that the lower airway disk **40** can include two proximately stacked layers of gear teeth **59a, 59b**, one of which **59a** cooperates with the post **109p** and associated indexing gears **109g** and the other of which **59b** can provide more precise positioning using arms **109r** as shown in **Figure 18D.** Other indexing mechanisms may be used to rotate the assembly **20** to place the different dose containers **30c** in the dispensing position. The dual piercers **100a, 100b** can cooperate with ramp surfaces on ramp disk **209**. The ramp disk **209** can have circumferentially offset fins **211** on two concentric rows that force the respective piercers down in response to contact with the fins. Additional description of the indexer and dual piercer are provided in co-pending, co-assigned U.S. Patent Application US20100078021.

[0116] In some embodiments, the mouthpiece port **10p** and an air inlet port (not shown) may be spaced apart about a distance of between about 12-127 mm (about 0.5-5 inches). The inhaler **10** may have a relatively short air intake airpath (measured from where an air intake is disposed to the inhalation port **10p**), such as between about 12-25.4 mm such as shown in **Figures 7A-7C, 18A** and **18C**, or a longer air path such as shown in **Figure 17A**, typically between about 50-127 mm (about 2-5 inches). The shorter air path can be defined to include a short tubular air path extending between the dry powder release location and the inhalation mouthpiece with a turbulence promoter segment that inhibits agglomeration that merges into the inhaler mouthpiece (not shown). The longer air path may extend across a major portion or substantially all of a width or length of the inhaler body. The inner surfaces/shape of the flow path can be polygonal to facilitate a cyclonic air stream to bounce off the inner surfaces which act as impact surfaces. For additional discussion of suitable turbulence promoter configurations, see PCT/US2005/032492, entitled, Dry Powder Inhalers That Inhibit Agglomeration, Related Devices and Methods.

[0117] The inhaler **10** can have a body that is a portable, relatively compact "pocket-sized" configuration. In some embodiments, the inhaler body can have a width/length that is less than about 115 mm (about 4.5 inches), typically less than about 89 mm (about 3.5 inches), and a thickness/depth of less than about 51 mm (about 2 inches), typically less than about 38 mm (about 1.5 inches). The inhaler body can also be configured to be generally planar on opposing primary surfaces to facilitate pocket storage.

[0118] The inhaler can include a circuit that can control certain operations of the inhaler **10**. The inhaler **10** can include a computer port (not shown). The port may be, for example, an RS 232 port, an infrared data association (IrDA) or universal serial bus (USB), which may be used to download or upload selected data from/to the inhaler to a computer application or remote computer, such as a clinician or other site. The inhaler **10** can be configured to via a wired or wireless communication link (one-way or two-way) to be able to communicate with a clinician or pharmacy for reorders of medicines and/or patient compliance. The inhaler **10** may also include a second-peripheral device communication port (not shown). The inhaler **10** may be able to communicate via the Internet, telephone, cell phone or other electronic communication protocol.

[0119] In some embodiments, the circuit can include computer program code and/or computer applications that communicate additional data to a user (optionally to the display) as noted above and/or communicate with another remote device (the term "remote" including communicating with devices that are local but typically not connected during normal inhalant use).

[0120] In some embodiments, the circuit can be in communication with a vibrator device (not shown). The vibrator device can be any suitable vibrator mechanism. The vibrator device can be configured to vibrate the dry powder in the airflow path. In some embodiments, the vibrator device can comprise a transducer that is configured to vibrate the opened cartridge(s) holding the dry powder. Examples of vibrator devices include, but are not limited to, one or more of: (a) ultrasound or other acoustic or sound-based sources (above, below or at audible wavelength) that can be used to instantaneously apply nonlinear pressure signals onto the dry powder; (b) electrical or mechanical vibration of the walls (sidewalls, ceiling and/or floor) of the inhalation flow channel, which can include magnetically induced vibrations and/or deflections (which can use electromagnets or permanent field magnets); (c) solenoids, piezoelectrically active portions and the like; and (d) oscillating or pulsed gas (airstreams), which can introduce changes in one or more of volume flow, linear velocity, and/or pressure. Examples of mechanical and/or electro-mechanical vibratory devices are described in U.S. Patent Nos. 5,727,607, 5,909,829 and 5,947,169. Combinations of different vibrating mechanisms can also be used.

[0121] In some embodiments, the vibrator device can include a commercially available miniature transducer from Star Micronics (Shizuoka, Japan), having part number QMB-105PX. The transducer can have resonant frequencies in the range of between about 400-600 Hz.

[0122] In certain embodiments, the inhaler **10** can include visible indicia (flashing light or display "error" or alert) and/or can be configured to provide audible alerts to warn a user that a dose was properly (and/or improperly) inhaled or released from the inhaler. For example, certain dry powder dose sizes are formulated so that it can be difficult for a user to know whether they have inhaled the medicament (typically the dose is aerosolized and enters the body with little or no taste and/or tactile feel for conformation). Thus, a sensor (not shown) can be positioned in communication with the flow path in an inhaler and configured to be in communication with a digital signal processor or microcontroller, each held in or on the inhaler. In operation, the sensor can be configured to detect a selected parameter, such as a difference in weight, a density in the exiting aerosol formulation, and the like, to confirm that the dose was released.

[0123] The sealed dose containers **30c** can be configured so that the water vapor transmission rate can be less than about 1.0g/100in^2/24hours, typically less than about 0.6 g/100in^2/24hours and an oxygen transmission rate that is suitable for the dry powder held therein. The dose container assemblies **20, 20'** can be configured with a stable shelf life of between about 1-5 years, typically about 4 years.

[0124] The dose containers **30c** can have a volume (prior to filling and sealing) that is less than about 24 mm^3, typically between 5-15 mm^3. The powder bulk density can be about 1 g/cm^3 while the power nominal density when filled (for reference) can be about 0.5 g/cm^3. The maximum compression of a drug by filling and sealing in the dose container **30c** can be less than about 5 %, typically less than about 2 %. The maximum heating of drug during the filling and sealing can be maintained to a desirable level so as not to affect the efficacy of the drug or the formulation.

[0125] **Figure 21** illustrates exemplary operations that can be used to operate an inhaler according to embodiments of the present invention. The device can be configured to have an automated three-stage operation at actuation to inhibit overdose delivery, e.g., it can serially: (a) pierce the sealant layers, (b) release the drug (typically followed close in time by delivery to a user), and (c) index to the next (unopened) dose container (thus isolating or closing any exit route for the released dry powder if not inhaled); or (a) index to a target dose container (thus isolating an earlier opened airway channel), (b) pierce the sealant layers and (c) release drug or dry powder from the opened dose container. A dose container ring having a staggered concentric arrangement of dose container apertures sealed by upper and lower sealant layers defining dose containers and attached to an underlying disk with a plurality of circumferentially spaced apart airway channels, one for each dose container, is provided (block **300**). The dose container with the underlying disk is rotated to a dispensing position in the inhaler (block **310**). The indexing can rotate the dose disk assembly about 6 degrees, repeated about 60 times to access 30 dose containers on the inner row and 30 dose containers on the outer row while rotating only about 360 degrees. The airway channel associated with the released dry powder is isolated from the inhalation path so that the used airflow channel is not used for any subsequent inhalation delivery or is used only one more time (block **325**).

[0126] In some embodiments, a piercing mechanism is advanced to open both sealant layers and release dry powder from the dose container in the dispensing position to the underlying airway channel (block **320**). The piercing mechanism can either remain extended or can be partially or fully retracted with the piercing mechanism or cooperating member thereof occluding the opening to the upper airway channel. In some embodiments, the piercing mechanism can be partially retracted, leaving at least a forward portion in the respective dose container aperture to occlude and/or plug the aperture. The isolating step can be in response to and/or after either the step of fully retracting the piercing mechanism from the dose container aperture (block **350**) or the rotating step (block **310**) or both.

[0127] The method can also optionally include flowably directing the released dry powder to a user via the airway channel.

[0128] **Figure 22** illustrates exemplary fabrication operations that can be used to assemble a dose container assembly according to embodiments of the present invention. As shown, a dose container disk (block **400**) with circumferentially spaced apart through apertures is provided. At least one sealant layer is attached to the upper or lower primary surface of the disk over or under the dose container apertures (block **410**) (e.g., a continuous layer or strips or small pieces of sealant layers can be positioned over the apertures). The dose container apertures are filled with dry powder (noting "filled" does not require volumetrically full) (block **420**). Typically, the powder is filled to between about 30-75% volume. The sealant layer can be attached to the other primary surface of the dose disk to provide sealed dose containers (block **430**). The dose container disk can be placed between upper and lower airway disks (block **440**). The dose containers can be aligned with circumferentially spaced apart airway channels on the airway disks so that each dose container is in communication with a different one of the airway channels in both the upper and lower disks (block **450**). The upper and lower disks can be attached to hold the dose container disk therebetween to provide a dose container assembly (block **460**).

[0129] The following exemplary claims are presented in the specification to support one or more devices, features, and methods of embodiments, of the present invention. While not particularly listed below, Applicant pre-

serves the right to claim other features shown or described in the application including, by way of example, one or more of the following in any combination with any features or depending from or in lieu of any of the original claims.

[0130] The dose container assembly can include two or more stacked disks. The stacked disks can reside under or over one airway disk or between a pair of airway disks.

[0131] A dry powder dose container assembly, wherein there are 30 dose container apertures in the first row and 30 dose container apertures in the second row, and wherein the first airway disk airway channels include alternating channels of different radial lengths, one length corresponding to channels extending from an inner or outer perimeter of the airway disk to dose containers in the first row and the other length corresponding to channels extending from an inner or outer perimeter of the airway disk to dose container apertures on the second row.

[0132] A dry powder dose container assembly, wherein the first airway disk is attached to the dose container disk to be able to rotate therewith, and wherein the airway channels extend radially across the first airway disk and are positioned relative to the dose container disk so that at least one airway channel is aligned with at least one dose container.

[0133] A dry powder dose container assembly in combination with an inhaler, wherein the inhaler comprises an inhaler body with an inhalation port and a piercing mechanism, wherein in operation, the piercing mechanism is configured to travel through the airway disk aperture in the first airway disk, pierce the first and second sealant layers, enter, then remain in or retract from at least the second disk airway channel, while occluding the first airway disk aperture.

[0134] The inhaler is configured to index/pierce/deliver or pierce/deliver/index to isolate the upper and lower airway channels corresponding to an opened dose container from an inhalation path.

[0135] The dose container disk includes a first row of circumferentially spaced apart apertures at a first radius and a second row of circumferentially spaced apart apertures at a second radius so that the first and second rows are concentric with respect to a center of the disk, and wherein the piercing mechanism includes first and second piercers, the first piercer configured to pierce the sealant over and under the respective dose container apertures in the first row, and the second piercer configured to pierce the sealant over and under the respective dose container apertures in the second row.

[0136] The piercer mechanism is configured to serially alternate between rows to pierce the sealants over and under a dose container in a first row of dose container apertures, then pierce the sealants over and under a dose container in a second row of dose container apertures.

[0137] The piercing mechanism comprises a fluted piercer configured to pierce the sealants.

[0138] The fluted piercer comprises three or four lobes, and wherein the first airway disk apertures have a corresponding three or four lobe perimeter shape.

[0139] An inhaler with a piercing mechanism that comprises a solid piercer.

[0140] An inhaler having a circular dose container disk having a plurality of circumferentially spaced apart dry powder chambers; and a first airway disk residing above or below the dose container disk, the airway disk comprising a plurality of circumferentially spaced apart radially oriented airway channels, wherein one airway channel is aligned with one of the dose containers and defines an airflow path in which airflow passes through one or more 90 degree turns with dry powder entrained therein after exiting a respective dose container to thereby inhibit agglomeration.

[0141] A dry powder inhaler, comprising:

an inhaler body with an inhalation port;
a dose container assembly held in the inhaler body, the dose container assembly comprising a dose container disk having a plurality of circumferentially spaced apart apertures, and a lower airway disk having a plurality of airway channels with upwardly extending sidewalls residing under the dose container disk, each of the lower airway channels being in communication with at least one dose container aperture, whereby the lower airway disk channels define a plurality of spaced apart inhalation delivery paths that individually communicate with the inhalation port;
a dose container opening mechanism in the inhaler body configured to open a dose container in a dispensing position in the inhaler; and
an indexing mechanism in the inhaler body configured to rotate the dose container assembly into the dispensing position.

[0142] A dry powder inhaler, comprising:

an inhaler body with an inhalation port;
a dose container assembly held in the inhaler body, the dose container assembly comprising:

a dose container disk having opposing upper and lower primary surfaces and a plurality of circumferentially spaced apart apertures with first and second sealant layers attached to the upper and lower primary surfaces of the dose container disk to define a respective floor and ceiling of the dose container apertures to form sealed dose containers holding dry powder therein;
an upper airway disk residing over the dose container disk, the upper airway disk comprising a plurality of circumferentially spaced apart airway channels with downwardly extending sidewalls; and
a lower airway disk residing under the dose container disk, the lower airway disk comprising a

plurality of circumferentially spaced apart airway channels with upwardly extending sidewalls, wherein pairs of the lower airway disk channels and the upper airway disk channels are aligned with at least one corresponding dose container therebetween;

a dose container opening mechanism configured to open a dose container in a dispensing position in the inhaler; and

an indexing mechanism configured to rotate the dose container assembly into the dispensing position.

[0143] The upper airway disk optionally includes circumferentially spaced apart apertures, one residing over a corresponding dose container, wherein the opening mechanism comprises a piercing head that is configured to pierce the first and second sealant layers. The dose container apertures are optionally arranged in a staggered concentric configuration of inner and outer rows.

[0144] The piercing head is configured to occlude or seal a respective upper airway disk aperture during inhalation.

[0145] The opening mechanism comprises a member that is configured to substantially seal the upper airway disk aperture during an inhalation.

[0146] A method of operating an inhaler, comprising:

providing a dose container ring having staggered concentric dose container apertures sealed by upper and lower sealant layers over and under the apertures to define sealed dose containers attached to at least one of an underlying or overlying airway disk having a plurality of circumferentially spaced apart airway channels, at least one dose container for each airway channel;

rotating the dose container ring and at least one airway disk together to present a respective dose container and a corresponding airway channel to a dispensing position in the inhaler;

advancing a piercing mechanism to open both sealant layers and release dry powder from the dose container to the corresponding airway channel;

delivering the released dose of the dry powder to a user via inhalation; and

isolating the airway channel associated with the released dry powder from an inhalation flow path so that the channel is reused only once or is not used for any subsequent inhalation delivery.

[0147] The method can optionally also include partially or fully retracting the piercing mechanism, while leaving at least a forward portion of the piercing mechanism in an airway disk aperture associated with the airway disk during the delivering step.

[0148] The method can include fully retracting the piercing mechanism from the airway disk aperture after the delivering step.

[0149] The isolating step can be carried out in response to the fully retracting step by automatically indexing the dose container ring when the piercing mechanism is fully retracted.

[0150] The isolating step can be carried out in response to opening or closing a cover associated with the inhaler by automatically indexing the dose container ring upon opening or closing the cover.

[0151] The method can include flowably directing the released dry powder to a user via inhalation out of a mouthpiece from the airway channel associated with the released dry powder before the fully retracting step.

[0152] The sealed dose containers can be arranged in staggered concentric front and back rows, and wherein the indexing and advancing steps are carried out to serially open one dose container on the front row then one dose container on the back row.

[0153] A dry powder inhaler, comprising:

a circular dose container disk assembly having a plurality of circumferentially spaced apart radially oriented airway channels aligned with a plurality of circumferentially spaced apart sealed drug chambers with dry powder therein held in first and second concentric rows of different radius, wherein prior to active dispensing, the airway channels are drug free, and wherein one end of the airway channels define exit flow paths that are in communication with a mouthpiece;

a mouthpiece configured to rotatably engage an outer perimeter of the dose container disk to serially communicate with the airway channels to entrain dry powder from an opened drug chamber to deliver dry powder to a user;

a piercing mechanism configured to open the dose container chambers to release the dry powder therein; and

an indexing mechanism in communication with the circular dose disk.

[0154] A dry powder inhaler comprising a circular dose container disk with a plurality of circumferentially spaced apart dosing chambers and a plurality of circumferentially spaced apart radially oriented airway channels, one aligned with one or more dosing chambers, wherein during inhalation air exits the inhaler with the dry powder entrained therein along a radius associated with a respective airway channel.

[0155] The foregoing is illustrative of the present invention and is not to be construed as limiting thereof. Although a few exemplary embodiments of this invention have been described, those skilled in the art will readily appreciate that many modifications are possible in the exemplary embodiments without materially departing from the novel teachings and advantages of this invention. In the claims, means-plus-function clauses, where used, are intended to cover the structures described herein as performing the recited function. Therefore, it is

to be understood that the foregoing is illustrative of the present invention and is not to be construed as limited to the specific embodiments disclosed. The invention is defined by the following claims.

Claims

1. A dry powder dose container assembly (20), comprising:

a dose container disk (30) having opposing upper and lower primary surfaces and a plurality of circumferentially spaced apart dose containers sized and shaped to accommodate a dry powder therein, wherein dose container apertures extend through the dose container disk, **characterized in that** the dose containers are sealed with respective upper and lower sealants (36, 37); and

a first airway disk (40) residing above or below the dose container disk (30), the first airway disk comprising a plurality of circumferentially spaced apart airway channels (41);

wherein the airway channels are elongate and extend in a radial direction across the respective airway disk, wherein the elongate channels have opposing first and second end portions (41a, 41b), with the first end portion (41b) being substantially open and the second end portion (41a) being substantially closed, and wherein the first end portion resides proximate an inner or outer perimeter of the dose container disk and the second end portion resides above or below a respective dose container.

2. A dry powder dose container assembly according to Claim 1, further comprising dry powder in the dose containers, wherein the dry powder dose container assembly further comprises a second airway disk that resides aligned with the first airway disk with the dose container disk therebetween, the second airway disk comprising a plurality of circumferentially spaced apart radially extending airway channels, and wherein at least one of the channels of the first airway disk is aligned with a corresponding at least one of the channels of the second airway disk with at least one dose container therebetween to define cooperating channels.

3. A dry powder dose container according to Claim 2, wherein the first airway disk abuts the upper or lower primary surface of the dose container disk and/or the sealant thereon, and the second airway disk abuts the other one of the upper or lower primary surface or the sealant thereon.

4. A dry powder dose container assembly according to Claim 1, wherein the upper sealant resides over the dose container apertures and the lower sealant resides under the dose container apertures, wherein the first airway disk comprises a plurality of circumferentially spaced apart apertures, at least one associated with each airflow channel, a respective one first airway disk aperture residing over or under a respective dose container with the upper or lower sealant therebetween.

5. A dry powder dose container according to any of Claims 2-3, wherein the cooperating airway disk channels define a single-use or dual-use airway path in an inhaler for delivering dry powder from the at least one dose container held therebetween.

6. A dry powder dose container assembly according to any of Claims 2-3 and 5, wherein the first airway disk has a floor with a closed surface under the first airway disk channels, wherein the first airway disk channels each include a pair of upwardly extending sidewalls, and wherein the second airway disk has a ceiling with circumferentially spaced apart apertures, with at least one aperture residing over each dose container aperture with the upper sealant therebetween, wherein the second airway disk channels each include a pair of downwardly extending sidewalls that face the sidewalls of the first airway disk channels.

7. A dry powder dose container assembly according to any of Claims 1-6, wherein the dose container disk includes a first row of circumferentially spaced apart apertures at a first radius and a second row of circumferentially spaced apart apertures at a second radius wherein the first row of dose container apertures have radially extending centerlines that are circumferentially spaced apart from radially extending centerlines of the second row of dose container apertures, so that the first and second rows are concentric with respect to a center of the disk, wherein the first airway disk airway channels include alternating channels of different radial lengths, one length corresponding to channels extending from an inner or outer perimeter of the airway disk to dose containers in the first row and the other length corresponding to channels extending from an inner or outer perimeter of the airway disk to dose container apertures on the second row.

8. A dry powder dose container assembly according to any of Claims 1-7, wherein the first airway disk includes a plurality of short airway channels and a plurality of long airway channels, the short airway channels associated with the first row of dose container apertures and the long airway channels associated with the second row of dose container apertures, and wherein short and long airway channels are arranged to reside adjacent to each other and alternate

circumferentially about the first airway disk.

9. A dry powder dose container assembly according to any of Claims 1-8, wherein the first airway disk channels are configured with a portion that rises a first distance above a respective dose container, then turns toward an inner or outer perimeter of the dose disk for a second distance, then travels down a third distance, wherein the third distance is at least the same as the first distance, to form a curvilinear airflow path portion to inhibit undesired spillage of the dry powder from the inhaler.

10. A dry powder dose container assembly according to any of Claims 2-3, and 5-6, wherein the dose container disk, and the first and second airway disks have a circular inner perimeter and each disk has substantially the same diameter, wherein the dose container disk includes a recess on the inner perimeter thereof, wherein the first airway disk includes downwardly extending circumferentially spaced apart tabs on the inner perimeter thereof and the second airway disk includes upwardly extending circumferentially spaced apart tabs on the inner perimeter thereof, wherein one of the tabs has a radially extending portion that engages the recess of the dose container disk to orient the dose container disk with respect to the first and second airway disks, wherein the tabs of at least one of the lower or upper airway disks include crush ribs, and wherein the upper and lower airway disks are press-fit together with the dose container disk sandwiched tightly therebetween to form an integral securely attached assembly.

11. A dry powder dose container assembly according to any of Claims 2-3, 5-6 and 10, wherein the cooperating channels are cooperating pairs of airway disk channels that are in fluid communication during dispensing of a respective dose container held therebetween, and together with the respective dose container define a generally U shape airflow path with long sides of the U corresponding to each channel oriented to extend in a radial direction across at least a portion of the disk.

12. A dry powder dose container assembly according to any of the preceding claims, wherein each airway channel of the first airway disk defines a corresponding dry powder exit aperture, and wherein the dry powder exit apertures are circumferentially spaced apart and reside on an outer perimeter of the first airway disk.

13. A dry powder dose container assembly according to any of Claims 1-12 in combination with an inhaler, wherein the inhaler comprises an inhaler body with an inhalation port, wherein the dose container disk and/or first airway disk is configured with a bias to travel in a predefined direction to sealably engage an interface or wall associated with an exit airflow path in the inhaler body, wherein the inhaler comprises a lever in communication with a loading post residing proximate an outer or inner perimeter of the dose container disk, whereby movement of the lever causes the loading post to push the dose container disk assembly against either a mouthpiece or an exit airflow path member in fluid communication with the mouthpiece.

14. A dry powder dose container assembly according to any of Claims 1-12 in combination with an inhaler, wherein the inhaler comprises an inhaler body with an inhalation port, wherein the inhaler comprises at least one seal residing between an outer or inner perimeter of the first airway disk and a wall associated with an exit airflow path in the inhaler.

15. A dry powder dose container assembly according to any of Claims 1-12 in combination with an inhaler that has a piercer mechanism, wherein the piercer mechanism comprises at least one of the following:

(a) a corkscrew piercer configured to pierce the upper and lower sealants with a straight vertical non-rotational movement;
(b) a fluted piercer configured to pierce the upper and lower sealants, wherein the fluted piercer comprises three or four lobes, and wherein the first airway disk has a flat surface with circumferentially spaced apart apertures having a perimeter shape with three or four lobes corresponding to the three or four lobes of the fluted piercer; or
(c) a solid piercer.

16. A dry powder inhaler configured to hold the dose container assembly of either of Claims 2 or 3, wherein the cooperating channels are cooperating pairs of airway channels that extend radially with the dose container held therebetween to define an airflow path in which airflow passes through one or more 90 degree turns with dry powder entrained therein after exiting a respective dose container to thereby inhibit agglomeration.

17. A dry powder dose assembly according to any of the preceding claims, wherein the dose container disk is provided as two or more stacked dose container disks that hold different dry powders to allow for combination drug delivery.

18. The combination of Claim 15, wherein the piercer mechanism is configured to serially alternate between rows to pierce the upper and lower sealants over and under a dose container in a first row of dose

container apertures, then pierce the upper and lower sealants over and under a dose container in a second row of dose container apertures.

19. A method of fabricating a dose container assembly, comprising:

providing a dose container disk having upper and lower primary surfaces with a plurality of circumferentially spaced apart dose container apertures;
attaching a sealant layer to one of the upper or lower primary surfaces of the dose container disk;
filling the dose container disk apertures with dry powder;
attaching a sealant layer to the other primary surface of the dose container to provide sealed dose containers;
providing at least one airway disk;
aligning the dose container disk with circumferentially spaced apart airway channels on the at least one airway disk so that each dose container aperture is in communication with one of the airway channels in the at least one airway disk; and
assembling the at least one airway disk to the dose container disk.

20. A method according to Claim 19, wherein the step of providing at least one airway disk is carried by providing two airway disks, an upper and lower airway disk, and wherein the aligning step is carried out so that the dose container apertures are aligned with circumferentially spaced apart airway channels on both the upper and lower airway disks so that each dose container aperture is in communication with one of the airway channels in both the upper and lower disks; and
wherein the step of assembly is carried out by press-fitting the upper and lower airway disks together and sandwiching the dose container disk snugly therebetween.

Patentansprüche

1. Trockenpulverdosisbehältnisanordnung (20), Folgendes umfassend:

eine Dosisbehältnisscheibe (30), versehen mit gegenüberliegenden oberen und unteren primären Oberflächen und einer Vielzahl von umlaufend beabstandeten Dosisbehältnissen, welche zum Aufbewahren von Trockenpulver darin abgemessen und geformt sind, wobei sich Dosisbehältnisöffnungen durch die Dosisbehältnisscheibe erstrecken, **dadurch gekennzeichnet, dass** die Dosisbehältnisse mit jeweiligen unteren und oberen Versiegelungen (36, 37) versiegelt sind; und
eine über oder unter der Dosisbehältnisscheibe (30) angeordnete erste Luftwegscheibe (40), wobei die erste Luftwegscheibe eine Vielzahl von umlaufend beabstandeten Luftwegkanälen (41) umfasst;
wobei die Luftwegkanäle länglich sind und sich in einer radialen Richtung über die jeweilige Luftwegscheibe erstrecken, wobei die länglichen Kanäle entgegengesetzte erste und zweite Endabschnitte (41a, 41b) umfassen, wobei der erste Endabschnitt (41b) im Wesentlichen offen ist und der zweite Endabschnitt (41a) im Wesentlichen geschlossen ist, und wobei der erste Endabschnitt nahe einem Innen- oder Außenrand der Dosisbehältnisscheibe angeordnet ist, und der zweite Endabschnitt über oder unter einem jeweiligen Dosisbehältnis angeordnet ist.

2. Trockenpulverdosisbehältnisanordnung nach Anspruch 1, ferner Trockenpulver in den Dosisbehältnissen umfassend, wobei die Trockenpulverdosisbehältnisanordnung ferner eine zweite Luftwegscheibe umfasst, welche mit der ersten Luftwegscheibe ausgerichtet mit der Dosisbehältnisscheibe dazwischen angeordnet ist, wobei die zweite Luftwegscheibe eine Vielzahl von umlaufend beabstandeten, sich radial erstreckenden Luftwegkanälen umfasst, und wobei zumindest einer der Kanäle der ersten Luftwegscheibe auf einen entsprechenden zumindest einen der Kanäle der zweiten Luftwegscheibe mit zumindest einem Dosisbehältnis dazwischen ausgerichtet ist, um zusammenwirkende Kanäle zu definieren.

3. Trockenpulverdosisbehältnis nach Anspruch 2, wobei die erste Luftwegscheibe auf der oberen oder unteren primären Oberfläche der Dosisbehältnisscheibe und/oder der Versiegelung darauf aufliegt, und die zweite Luftwegscheibe auf der anderen der oberen oder unteren primären Oberfläche oder der Versiegelung darauf aufliegt.

4. Trockenpulverdosisbehältnisanordnung nach Anspruch 1, wobei die obere Versiegelung über den Dosisbehältnisöffnungen angeordnet ist, und die untere Versiegelung unter den Dosisbehältnisöffnungen angeordnet ist, wobei die erste Luftwegscheibe eine Vielzahl von umlaufend beabstandeten Öffnungen umfasst, zumindest eine mit jedem Luftstromkanal verbunden, wobei eine entsprechende erste Luftwegscheibenöffnung über oder unter einem entsprechenden Dosisbehältnis mit der oberen oder unteren Versiegelung dazwischen angeordnet ist.

5. Trockenpulverdosisbehältnis nach einem der An-

sprüche 2-3, wobei die zusammenwirkenden Luftwegscheibenkanäle einen Luftwegpfad zur Einmalverwendung oder Zweimalverwendung in einem Inhalator zur Abgabe von Trockenpulver aus dem zumindest einen, darin eingefassten Dosisbehältnis umfassen.

6. Trockenpulverdosisbehältnisanordnung nach einem der Ansprüche 2-3 und 5, wobei die erste Luftwegscheibe mit einem Boden mit einer geschlossenen Oberfläche unter den ersten Luftwegscheibenkanälen versehen ist, wobei die ersten Luftwegscheibenkanäle jeweils ein Paar sich aufwärts erstreckender Seitenwände umfassen, und wobei die zweite Luftwegscheibe mit einer Decke mit umlaufend beabstandeten Öffnungen versehen ist, wobei zumindest eine Öffnung über jeder Dosisbehältnisöffnung mit der oberen Versiegelung dazwischen angeordnet ist, wobei die zweiten Luftwegscheibenkanäle jeweils ein Paar sich abwärts erstreckender Seitenwände umfassen, welche den Seitenwänden der ersten Luftwegscheibenkanäle gegenüber liegen.

7. Trockenpulverdosisbehältnisanordnung nach einem der Ansprüche 1-6, wobei die Dosisbehältnisscheibe eine erste Reihe umlaufend beabstandeter Öffnungen an einem ersten Radius und eine zweite Reihe umlaufend beabstandeter Öffnungen an einem zweiten Radius umfasst, wobei die erste Reihe Dosisbehältnisöffnungen sich radial erstreckende Mittellinien umfasst, welche umlaufend von sich radial erstreckenden Mittellinien der zweiten Reihe Dosisbehältnisöffnungen beabstandet sind, sodass die erste und zweite Reihe in Bezug auf eine Mitte der Scheibe konzentrisch sind, wobei die ersten Luftwegscheibenluftwegkanäle alternierende Kanäle verschiedener radialer Längen umfassen, wobei eine Länge Kanälen entspricht, welche sich von einem Innen- oder Außenrand der Luftwegscheibe zu Dosisbehältnissen in der ersten Reihe erstrecken, und die andere Länge Kanälen entspricht, die sich von einem Innen- oder Außenrand der Luftwegscheibe zu Dosisbehältnisöffnungen in der zweiten Reihe erstrecken.

8. Trockenpulverdosisbehältnisanordnung nach einem der Ansprüche 1-7, wobei die erste Luftwegscheibe eine Vielzahl von kurzen Luftwegkanälen und eine Vielzahl von langen Luftwegkanälen umfasst, wobei die kurzen Luftwegkanäle mit der ersten Reihe Dosisbehältnisöffnungen verbunden sind, und die langen Luftwegkanäle mit der zweiten Reihe Dosisbehältnisöffnungen verbunden sind, und wobei kurze und lange Luftwegkanäle derart positioniert sind, dass sie nebeneinander angeordnet sind und umlaufend um die erste Luftwegscheibe alternieren.

9. Trockenpulverdosisbehältnisanordnung nach einem der Ansprüche 1-8, wobei die ersten Luftwegscheibenkanäle mit einem Abschnitt ausgelegt sind, welcher um einen ersten Abstand über ein jeweiliges Dosisbehältnis gehoben wird, sich danach um einen zweiten Abstand zu einem Innen- oder Außenrand der Dosisscheibe dreht, sich anschließend um einen dritten Abstand nach unten bewegt, wobei der dritte Abstand zumindest gleich dem ersten Abstand ist, um einen kurvenförmigen Luftstrompfadabschnitt auszubilden, um ein ungewünschtes Ausrieseln des Trockenpulvers aus dem Inhalator zu verhindern.

10. Trockenpulverdosisbehältnisanordnung nach einem der Ansprüche 2-3 und 5-6, wobei die Dosisbehältnisscheibe und die erste und zweite Luftwegscheibe einen kreisförmigen Innenrand umfassen, und jede Scheibe im Wesentlichen den gleichen Durchmesser aufweist, wobei die Dosisbehältnisscheibe eine Vertiefung an dem Innenrand davon umfasst, wobei die erste Luftwegscheibe sich abwärts erstreckende, umlaufend beabstandete Nasen an dem Innenrand davon umfasst, und die zweite Luftwegscheibe sich aufwärts erstreckende, umlaufend beabstandete Nasen an dem Innenrand davon umfasst, wobei eine der Nasen einen sich radial erstreckenden Abschnitt umfasst, welcher die Vertiefung der Dosisbehältnisscheibe in Eingriff nimmt, um die Dosisbehältnisscheibe in Bezug auf die erste und zweite Luftwegscheibe auszurichten, wobei die Nasen von zumindest einer der unteren oder oberen Luftwegscheibe Stauchsteifen umfassen, und wobei die obere und untere Luftwegscheibe mit der fest dazwischen angeordneten Dosisbehältnisscheibe per Pressanschluss verbunden sind, um eine integrale, sicher befestigte Anordnung auszubilden.

11. Trockenpulverdosisbehältnisanordnung nach einem der Ansprüche 2-3, 5-6 und 10, wobei die zusammenwirkenden Kanäle zusammenwirkende Paare Luftwegscheibenkanäle sind, welche während der Abgabe eines jeweiligen, dazwischen eingefassten Dosisbehältnisses in Fluidkommunikation sind, und mit dem jeweiligen Dosisbehältnis zusammen einen im Allgemeinen hufeisenförmigen Luftstrompfad definieren, wobei die langen Seiten des Hufeisens jedem Kanal entsprechen, welcher derart ausgerichtet ist, dass er sich in einer radialen Richtung über zumindest einen Abschnitt der Scheibe erstreckt.

12. Trockenpulverdosisbehältnisanordnung nach einem der vorhergehenden Ansprüche, wobei jeder Luftwegkanal der ersten Luftwegscheibe eine entsprechende Trockenpulveraustrittsöffnung definiert, und wobei die Trockenpulveraustrittsöffnungen umlaufend beabstandet und an einem Außenrand der ersten Luftwegscheibe angeordnet sind.

13. Trockenpulverdosisbehältnisanordnung nach einem der Ansprüche 1-12 in Kombination mit einem Inhalator, wobei der Inhalator ein Inhalatorgehäuse mit einer Inhalatoröffnung umfasst, wobei die Dosisbehältnisscheibe und/oder erste Luftwegscheibe mit einer Neigung ausgelegt ist, damit sie sich in eine zuvor definierte Richtung bewegt, um eine Trennfläche oder Wand, welche mit einem Austrittsluftstrompfad in dem Inhalatorgehäuse verbunden ist, versiegelnd in Eingriff nimmt, wobei der Inhalator mit einem Hebel versehen ist, welcher mit einem Ladeelement kommuniziert, das nahe einem Außen- oder Innenrand der Dosisbehältnisscheibe angeordnet ist, wobei eine Bewegung des Hebels dazu führt, dass das Ladeelement die Dosisbehältnisscheibenanordnung entweder gegen ein Mundstück oder ein Austrittsluftstrompfadteil in Fluidkommunikation mit dem Mundstück drängt.

14. Trockenpulverdosisbehältnisanordnung nach einem der Ansprüche 1-12 in Kombination mit einem Inhalator, wobei der Inhalator ein Inhalatorgehäuse mit einer Inhalatoröffnung umfasst, wobei der Inhalator zumindest eine Abdichtung umfasst, welche zwischen einem Außen- oder Innenrand der ersten Luftwegscheibe und einer Wand angeordnet ist, welche mit einem Austrittsluftstrompfad des Inhalators verbunden ist.

15. Trockenpulverdosisbehältnisanordnung nach einem der Ansprüche 1-12 in Kombination mit einem Inhalator, welcher mit einem Dornmechanismus versehen ist, wobei der Dornmechanismus zumindest eines der Folgenden umfasst:

    (a) einen Korkenzieherdorn, dazu ausgelegt, dass er die obere und untere Versiegelung mit einer geraden vertikalen drehfreien Bewegung durchsticht;
    (b) einen gerillten Dorn, zum Durchstechen der oberen und unteren Versiegelung ausgelegt, wobei der gerillte Dorn drei oder vier Formkanten umfasst, und wobei die erste Luftwegscheibe eine flache Oberfläche mit umlaufend beabstandeten Öffnungen umfasst, welche eine Randform mit drei oder vier Formkanten aufweisen, die den drei oder vier Formkanten des gerillten Doms entsprechen; oder
    (c) einen festen Dorn.

16. Trockenpulverinhalator, zum Einfassen der Dosisbehältnisanordnung nach Anspruch 2 oder 3 ausgelegt, wobei die zusammenwirkenden Kanäle zusammenwirkende Paare Luftkanäle sind, welche sich radial mit dem dazwischen eingefassten Dosisbehältnis erstrecken, um einen Luftstrompfad zu definieren, in welchem ein Luftstrom mit darin mitgeführtem Trockenpulver nach dem Austritt aus einem jeweiligen Dosisbehältnis eine oder mehrere 90-Grad-Drehungen passiert, um somit eine Ansammlung zu verhindern.

17. Trockenpulverdosisanordnung nach einem der vorhergehenden Ansprüche, wobei die Dosisbehältnisscheibe als zwei oder mehr übereinandergestapelte Dosisbehältnisscheiben bereitgestellt ist, welche verschiedene Trockenpulver fassen, um eine kombinierte Arzneimittelabgabe zu ermöglichen.

18. Kombination nach Anspruch 15, wobei der Dornmechanismus zum seriellen Alternieren zwischen Reihen ausgelegt ist, um die oberen und unteren Versiegelungen über und unter einem Dosisbehältnis in einer ersten Reihe von Dosisbehältnisöffnungen zu durchstechen und danach die oberen und unteren Versiegelungen über und unter einem Dosisbehältnis in einer zweiten Reihe von Dosisbehältnisöffnungen zu durchstechen.

19. Herstellungsverfahren für eine Dosisbehältnisanordnung, Folgendes umfassend:

    Bereitstellen einer Dosisbehältnisscheibe, welche obere und untere primäre Oberflächen mit einer Vielzahl von umlaufend beabstandeten Dosisbehältnisöffnungen umfasst;
    Anbringen einer Versiegelungsschicht auf eine der oberen oder unteren primären Oberflächen der Dosisbehältnisscheibe;
    Füllen der Dosisbehältnisscheibenöffnungen mit Trockenpulver;
    Anbringen einer Versiegelungsschicht auf die andere primäre Oberfläche des Dosisbehältnisses, um versiegelte Dosisbehältnisse bereitzustellen;
    Bereitstellen zumindest einer Luftwegscheibe;
    Ausrichten der Dosisbehältnisscheibe auf umlaufend beabstandete Luftwegkanäle an der zumindest einen Luftwegscheibe, sodass jede Dosisbehältnisöffnung in Kommunikation mit einem der Luftwegkanäle in der zumindest einen Luftwegscheibe steht; und
    Montieren der zumindest einen Luftwegscheibe an die Dosisbehältnisscheibe.

20. Verfahren nach Anspruch 19, wobei der Schritt des Bereitstellens zumindest einer Luftwegscheibe durch Bereitstellen von zwei Luftwegscheiben, einer oberen und unteren Luftwegscheibe, ausgeführt wird, und wobei der Ausrichtungsschritt derart ausgeführt wird, dass die Dosisbehältnisöffnungen auf die umlaufend beabstandeten Luftwegkanäle sowohl an der oberen als auch der unteren Luftwegscheibe ausgerichtet sind, sodass jede Dosisbehältnisöffnung in Kommunikation mit einem der Luftwegkanäle sowohl in der oberen als auch der unteren

Scheibe steht; und
wobei der Schritt des Montierens per Pressanschluss der unteren und oberen Luftwegscheibe und Dazwischenanordnen der Dosisbehältnisscheibe in satt anliegender Weise ausgeführt wird.

Revendications

1. Ensemble de contenants de doses de poudre sèche (20), comprenant:

un disque de contenants de doses (30) ayant des surfaces primaires supérieures et inférieures opposées et une pluralité de contenants de dose espacés de manière circonférentielle, dimensionnés et façonnés pour y recevoir une poudre sèche, où les ouvertures de contenant une dose s'étendent à travers le disque de contenants de doses, **caractérisé en ce que** les contenants de dose sont scellés avec des produits d'étanchéité supérieur et inférieur respectifs (36, 37); et
un premier disque de polissage (40) des voies respiratoires situé au-dessus ou au-dessous du disque de contenants de doses (30), le premier disque de polissage des voies respiratoires comprenant une pluralité de canaux de polissage des voies respiratoires espacés de manière circonférentielle (41);
où les canaux de polissage des voies respiratoires sont allongés et s'étendent dans une direction radiale à travers le disque de polissage des voies respiratoires respectif, où les canaux allongés ont des première et seconde parties d'extrémité opposées (41a, 41b), avec la première partie d'extrémité (41b) étant sensiblement ouverte et la seconde partie d'extrémité (41a) étant sensiblement fermée, et dans lequel la première partie d'extrémité réside près d'un périmètre intérieur ou extérieur du disque de contenants de doses et l'autre partie d'extrémité se trouve au-dessus ou au-dessous d'un contenant une dose respectif.

2. Ensemble de contenants de doses de poudre sèche selon revendication 1, comprenant en outre de la poudre sèche dans les contenants de dose, où l'ensemble de contenants de doses de poudre sèche comprend en outre un second disque de polissage des voies respiratoires, est aligné avec le premier disque de polissage des voies respiratoires, tous deux séparés par le disque de contenants de doses, le second disque de polissage des voies respiratoires comprenant une pluralité de canaux de polissage des voies respiratoires espacés de manière circonférentielle, et où au moins l'un des canaux du premier disque de polissage des voies respiratoires est aligné avec l'un au moins l'un des canaux correspondants du second disque de polissage des voies respiratoires, tous deux séparés par au moins un contenant le disque de dose pour définir des canaux coopérants.

3. Ensemble de contenants de doses de poudre sèche selon revendication 2, où le premier disque de polissage des voies respiratoires est contiguë à la surface primaire supérieure ou inférieure du disque de contenants de doses et/ou au produit d'étanchéité présent sur celle-ci, et le second disque de polissage des voies respiratoires est contiguë à l'autre de la surface primaire supérieure ou inférieure ou au produit d'étanchéité présent sur celle-ci.

4. Ensemble de contenants de doses de poudre sèche selon revendication 1, où le produit d'étanchéité supérieur repose sur les ouvertures de contenant une dose et le produit d'étanchéité inférieur réside sous les ouvertures de contenant une dose, où le premier disque de polissage des voies respiratoires comprend une pluralité d'ouvertures espacées de manière circonférentielle, au moins une associée à chaque canal d'écoulement d'air, une première ouverture du disque de polissage des voies respiratoires respective résidant sur ou sous un conteneur de dose respectif, tous deux séparés par un produit d'étanchéité supérieur ou inférieur.

5. Ensemble de contenants de doses de poudre sèche selon l'une quelconque des revendications 2 à 3, où les canaux de disque de voies aérienne coopérant définissent un canal de polissage des voies respiratoires à usage unique ou double dans un inhalateur permettant d'administrer de la poudre sèche à partir dudit au moins un contenant une dose maintenu entre ceux-ci.

6. Ensemble de contenants de doses de poudre sèche selon l'une quelconque des revendications 2 à 3 et 5, où le premier disque de polissage des voies respiratoires comporte un fond avec une surface fermée sous les canaux du premier du disque de polissage des voies respiratoires, où les canaux du premier disque de polissage des voies respiratoires comprennent chacun une paire de parois s'étendant vers le haut, et où le second disque de polissage des voies respiratoires comprend un plafond avec des ouvertures espacées de manière circonférentielle, avec au moins une ouverture située sur chaque ouverture contenant une dose, toutes deux séparées par le produit d'étanchéité, où les canaux du second disque de polissage des voies respiratoires comprennent chacune une paire de parois s'étendant vers le bas faisant face aux parois latérales des canaux du premier disque de polissage des voies respiratoires.

7. Ensemble de contenants de doses de poudre sèche selon l'une quelconque des revendications 1 à 6, où le disque de contenants de doses comprend une première rangée d'ouvertures espacées de manière circonférentielle avec un premier rayon et une seconde rangée d'ouvertures espacées de manière circonférentielle avec un second rayon où la première rangée d'ouvertures de contenant une dose présente des lignes médianes s'étendant radialement, qui sont espacés de manière circonférentielle à partir de lignes médianes s'étendant radialement de la seconde rangée d'ouvertures de contenant une dose, de sorte que les première et seconde rangées sont concentriques par rapport à un centre du disque, où les canaux du premier disque de polissage des voies respiratoires comprennent des canaux alternatifs de différentes longueurs radiales, une longueur correspondant aux canaux s'étendant à partir d'un périmètre intérieur ou extérieur du disque de polissage des voies respiratoires vers les contenants de dose dans la première rangée et l'autre longueur correspondant aux canaux s'étendant à partir d'un périmètre intérieur ou extérieur du disque de polissage des voies respiratoires vers les ouvertures de contenant une dose sur la seconde rangée.

8. Ensemble de contenants de doses de poudre sèche selon l'une quelconque des revendications 1 à 7, où le premier disque de polissage des voies respiratoires inclut une pluralité de courts canaux de polissage des voies respiratoires et une pluralité de longs canaux de polissage des voies respiratoires, les courts canaux de polissage des voies respiratoires associés à la première rangée d'ouvertures de contenant une dose et les longs canaux de polissage des voies respiratoires associés à la seconde rangée d'ouvertures de contenant une dose, et où les courts et longs canaux de polissage des voies respiratoires sont disposés adjacents les uns aux autres et alternent de manière circonférentielle autour du premier disque de polissage des voies respiratoires.

9. Ensemble de contenants de doses de poudre sèche selon l'une quelconque des revendications 1 à 8, où les canaux du premier disque de polissage des voies respiratoires sont configurés avec une partie qui s'élève d'une première distance au-dessus d'un contenant une dose respectif, puis tourne vers un périmètre intérieur ou extérieur du disque de dose sur une deuxième distance, avant de parcourir une troisième distance, où la troisième distance est au moins la même que la première distance, pour former une partie de trajet d'écoulement d'air curviligne et ainsi inhiber tout déversement indésirable de poudre sèche à partir de l'inhalateur.

10. Ensemble de contenants de doses de poudre sèche selon l'une quelconque des revendications 2 à 3, et 5 à 6, dans lequel le disque de contenants de doses, et les premier et second disques de polissage des voies respiratoires ont un périmètre intérieur circulaire et chaque disque a sensiblement le même diamètre, où la disque de contenants de doses comporte un évidement sur son périmètre intérieur, où le premier disque de polissage des voies respiratoires comprend des languettes s'étendant vers le bas et espacées de manière circonférentielle sur son périmètre intérieur et le second disque de polissage des voies respiratoires comprend des languettes s'étendant vers le haut et espacées de manière circonférentielle sur son périmètre intérieur où l'une des languettes possède une partie s'étendant radialement et s'enclenchant dans l'évidement du disque de contenants de doses pour orienter le disque de contenants de doses par rapport aux premier et second disques de polissage des voies respiratoires, où les languettes d'au moins l'un des disques inférieur ou supérieur de polissage des voies respiratoires comprend des nervures d'absorption des chocs, et où les disques supérieur et inférieur de polissage des voies respiratoires sont ajustés de manière forcée avec le contenant une dose, serrés en sandwich pour constituer un ensemble fixé de manière solidaire.

11. Ensemble de contenants de doses de poudre sèche selon l'une quelconque des revendications 2 à 3, 5 à 6 et 10, dans lequel les canaux coopérants sont des paires coopérantes canaux de disques de polissage des voies respiratoires qui sont en communication fluide pendant l'administration d'un contenant une dose respectif maintenu entre ceux-ci, et ensemble avec le conteneur de dose respectif définissent un trajet d'écoulement d'air en forme globale de U, avec les longs côtés du U correspondant à chaque canal orienté pour s'étendre dans une direction radiale de part et d'autre d'au moins une partie du disque.

12. Ensemble de contenants de doses de poudre sèche selon l'une quelconque des revendications précédentes, où chaque canal de polissage des voies respiratoires du premier disque de polissage des voies respiratoires définit une ouverture de sortie de poudre sèche correspondante, et où les ouvertures de sortie de poudre sèche sont espacées de manière circonférentielle et se trouvent sur un périmètre extérieur du premier disque de polissage des voies respiratoires.

13. Ensemble de contenants de doses de poudre sèche selon l'une quelconque des revendications 1 à 12 en combinaison avec un inhalateur, où l'inhalateur est composé d'un corps d'inhalateur avec un port d'inhalation, où la disque de contenants de doses et/ou le premier disque de polissage des voies res-

piratoires est configuré avec un biais pour circuler dans une direction prédéfinie et s'enclencher de manière hermétique dans une interface ou une paroi associée à un trajet d'écoulement d'air de sortie dans le corps d'inhalateur, où l'inhalateur comprend un levier en communication avec un poste de chargement situé à proximité d'un périmètre extérieur ou intérieur du disque de contenants de doses, où le mouvement du levier conduit le poste de chargement à repousser l'ensemble de contenants de doses contre un embout buccal ou une partie du trajet d'écoulement d'air de sortie en communication fluide avec l'embout buccal.

14. Ensemble de contenants de doses de poudre sèche selon l'une quelconque des revendications 1 à 12 en combinaison avec un inhalateur, où l'inhalateur est composé d'un corps d'inhalateur avec un port d'inhalation, où l'inhalateur est composé d'au moins un joint situé entre un périmètre extérieur ou intérieur du premier disque de polissage des voies respiratoire et une paroi associée à un trajet d'écoulement d'air de sortie dans l'inhalateur.

15. Ensemble de contenants de doses de poudre sèche selon l'une quelconque des revendications 1 à 12 en combinaison avec un inhalateur présentant un mécanisme de percement, où le mécanisme de percement comprend au moins l'un des éléments suivants:

(a) un perceur de type tire-bouchon configuré pour percer les joints supérieur et inférieur dans un mouvement droit vertical sans rotation;
(b) un perceur cannelé configuré pour percer les joints supérieur et inférieur, où le perceur cannelé comporte trois ou quatre lobes, et où le premier disque de polissage des voies respiratoire a une surface plane avec des ouvertures espacées de manière circonférentielle et présentant une forme de périmètre avec trois ou quatre lobes correspondant aux trois ou quatre lobes du perceur cannelé; ou
(c) un perceur solide.

16. Inhalateur de poudre sèche configuré pour contenir l'ensemble de contenants de doses selon l'une ou l'autre des revendications 2 ou 3, où les canaux coopérants sont des paires coopérantes de canaux de polissage des voies respiratoires s'étendant radialement avec le contenant de dose maintenu entre ces derniers pour définir un trajet d'écoulement d'air dans lequel l'air passe par un ou plusieurs virages à 90 degrés en entraînant de la poudre sèche après être sorti d'un contenant de dose respectif pour ainsi empêcher toute agglomération.

17. Ensemble de contenants de doses de poudre sèche selon l'une quelconque des revendications précédentes, dans lequel le disque de contenants de doses est sous forme de deux ou plusieurs disques contenant une dose, renfermant différentes poudres sèches pour une administration combinée de médicaments.

18. Combinaison selon la revendication 15, dans laquelle le mécanisme de percement est configuré pour alterner en série entre des rangées pour percer les joints supérieurs et inférieurs au-dessus et au-dessous d'un contenant de dose dans une première rangée d'ouvertures de contenant de dose, puis percer les joints supérieurs et inférieurs au-dessus et au-dessous d'un contenant de dose dans une seconde rangée d'ouvertures de contenant de dose.

19. Procédé de fabrication d'un ensemble de contenants de doses, comprenant:

la fourniture d'un disque de contenants de doses présentant des surfaces primaires supérieure et inférieure avec une pluralité d'ouvertures de contenants de doses espacées de manière circonférentielle;
la fixation d'une couche de produit d'étanchéité à l'une des surfaces primaires supérieure ou inférieure de disque de contenants de doses ;
le remplissage des ouvertures de disques de contenants de doses avec de la poudre sèche;
la fixation d'une couche de produit d'étanchéité à l'autre surface primaire du contenant de dose pour produire des contenants de doses scellés;
la fourniture d'au moins un disque de polissage des voies respiratoires;
l'alignement du disque de contenants de doses avec des canaux de polissage des voies respiratoires espacées de manière circonférentielle sur ledit au moins un disque de polissage des voies respiratoires pour que chaque ouvertures de contenants de doses soit en communication avec l'un des canaux de polissage des voies respiratoires dans au moins l'un des disques de polissage des voies respiratoires; et l'assemblage dudit au moins un disque de polissage des voies respiratoires avec le disque de contenants de doses.

20. Procédé selon la revendication 19, où l'étape consistant à fournir au moins un disque de polissage des voies respiratoires revient à fournir deux disques de polissage des voies respiratoires, un disque supérieur de polissage des voies respiratoires et un disque inférieur de polissage des voies respiratoires, et dans lequel la phase d'alignement est réalisée de sorte que les ouvertures de contenants de dose soient alignées avec les canaux de polissage des voies respiratoires espacés de manière circonféren-

tielle à la fois sur les disques supérieurs de polissage des voies respiratoires et les disques inférieurs de polissage des voies respiratoires pour que chaque ouverture de contenants de doses soit en communication avec l'un des canaux de polissage des voies respiratoires dans au moins l'un des disques supérieurs et inférieurs de polissage des voies respiratoires; et

où l'étape d'assemblage réalisé par ajustement forcé des disques supérieurs et inférieurs de polissage des voies respiratoires et prise en sandwich du disque de contenants de doses de manière serrée.

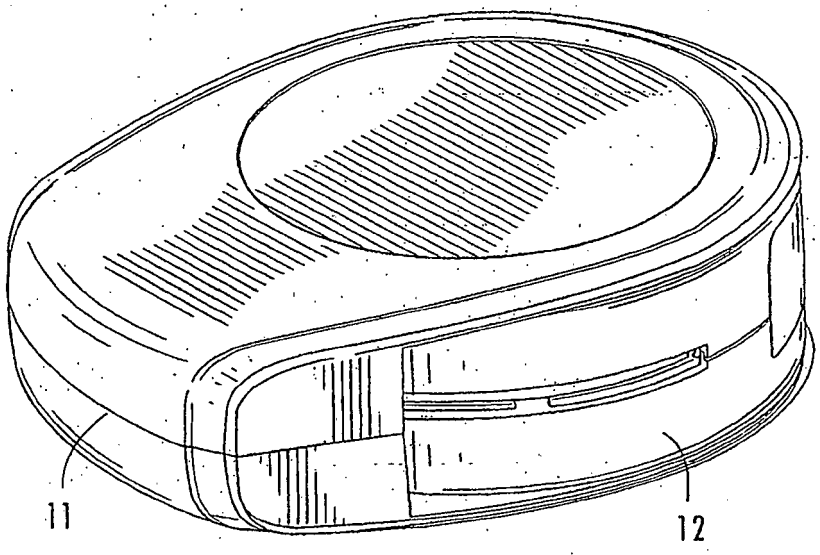


FIG. 1A

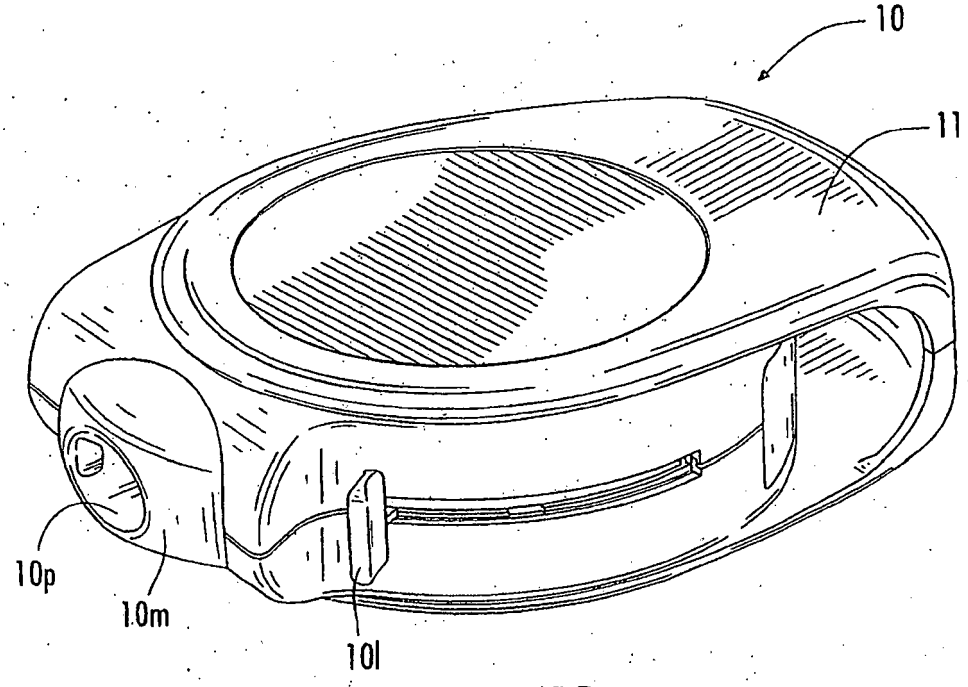


FIG. 1B

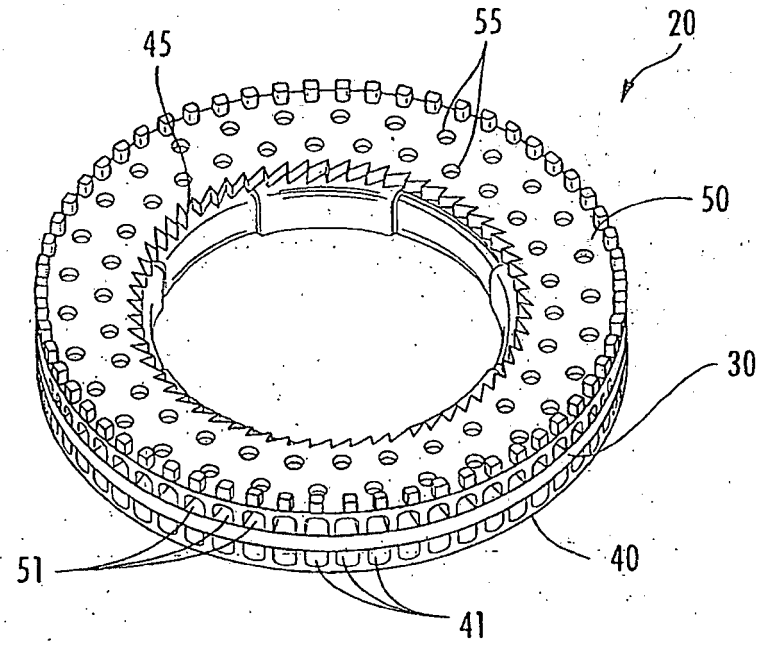


FIG. 2A

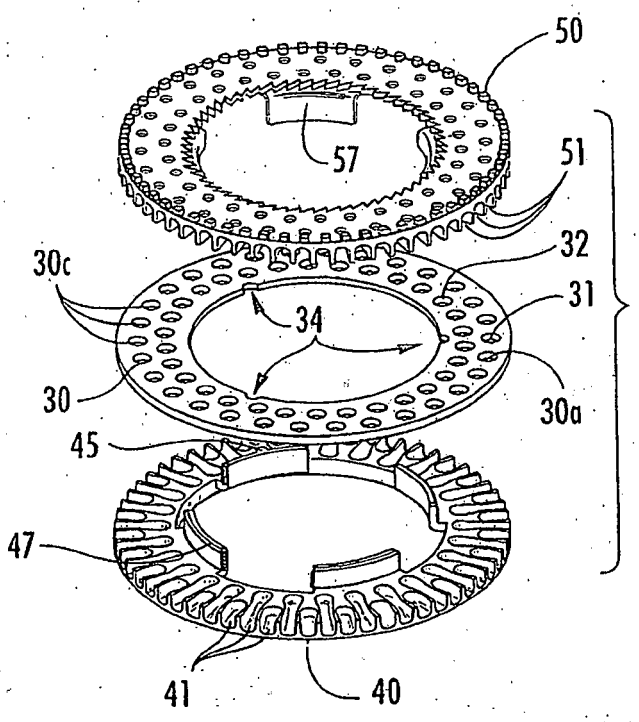


FIG. 2B

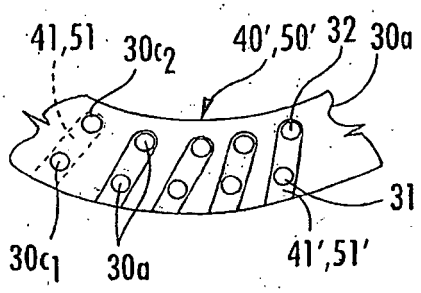


FIG. 2C

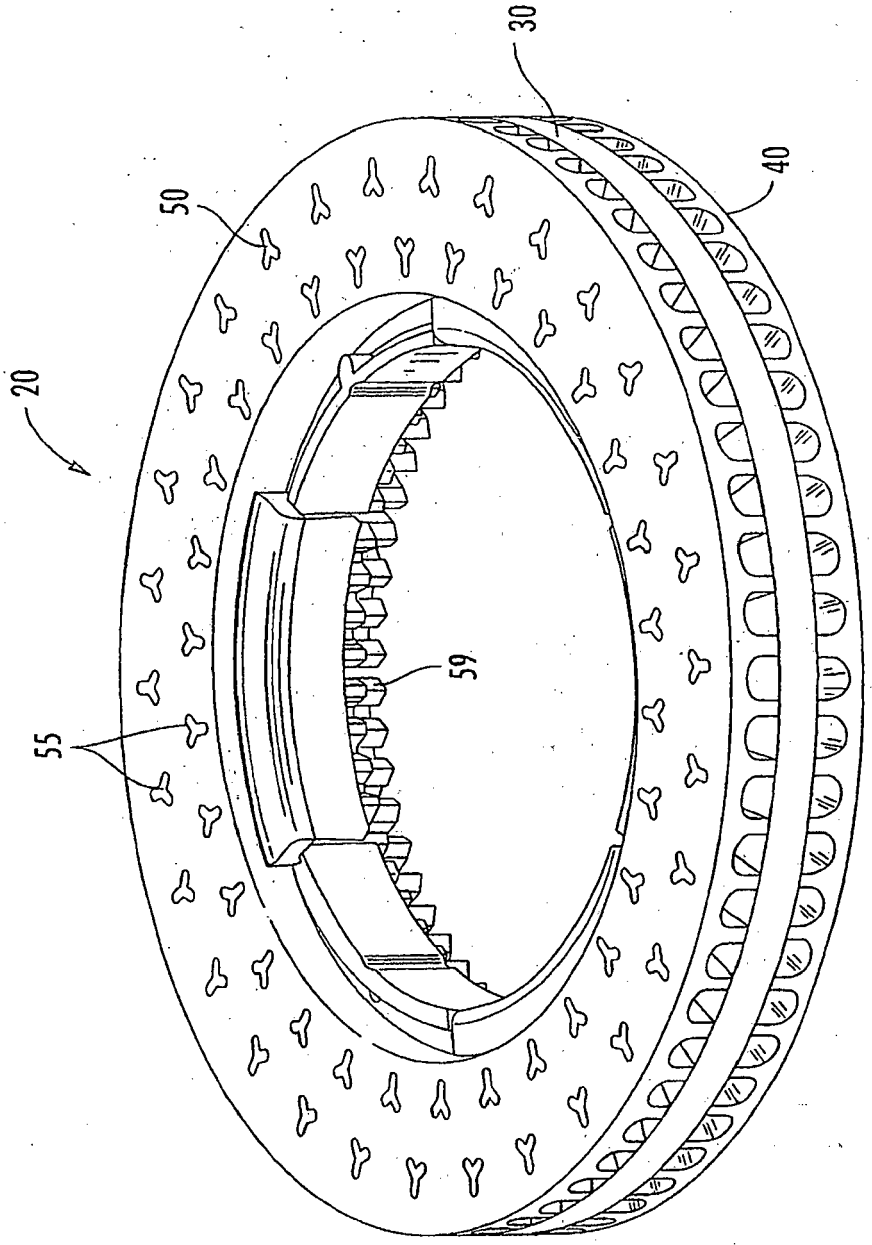


FIG. 2D

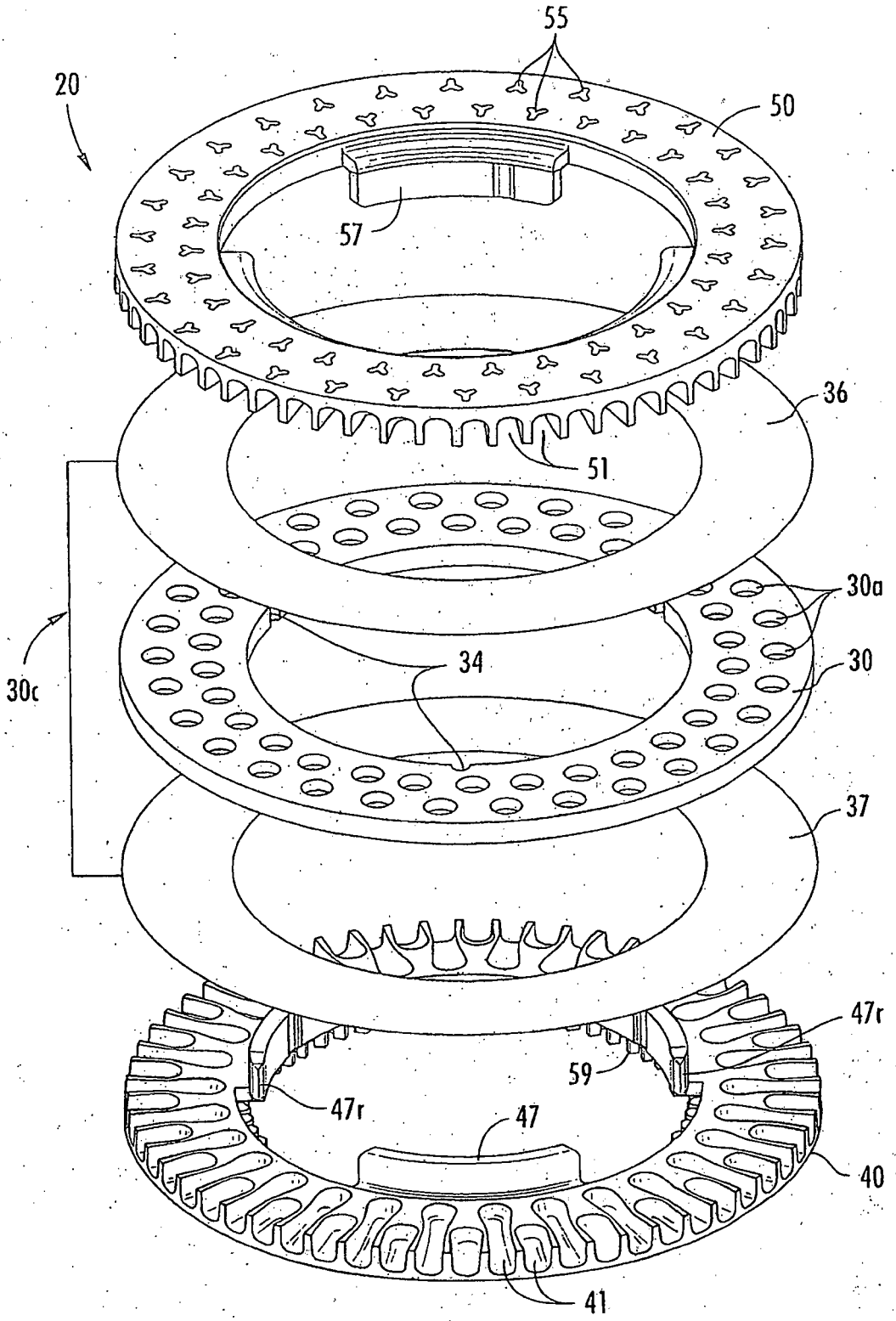
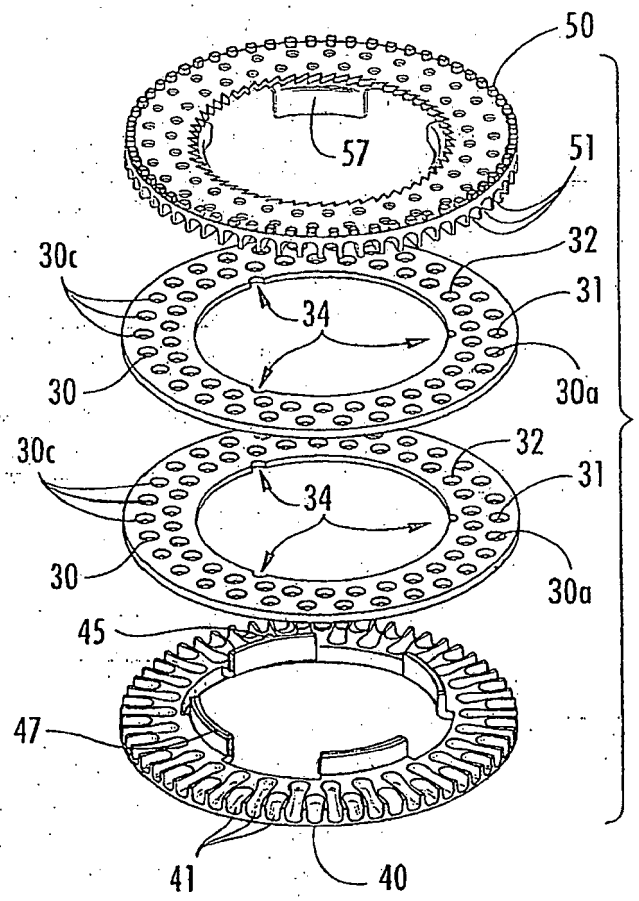


FIG. 2E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57
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30a
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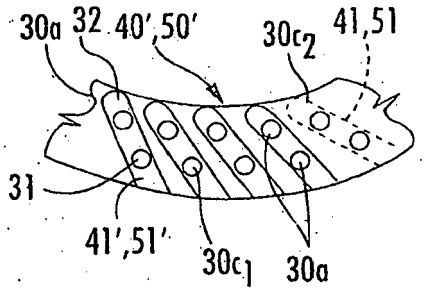
FIG. 2F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30c2
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31
41',51'
30c1
30a

FIG. 2G

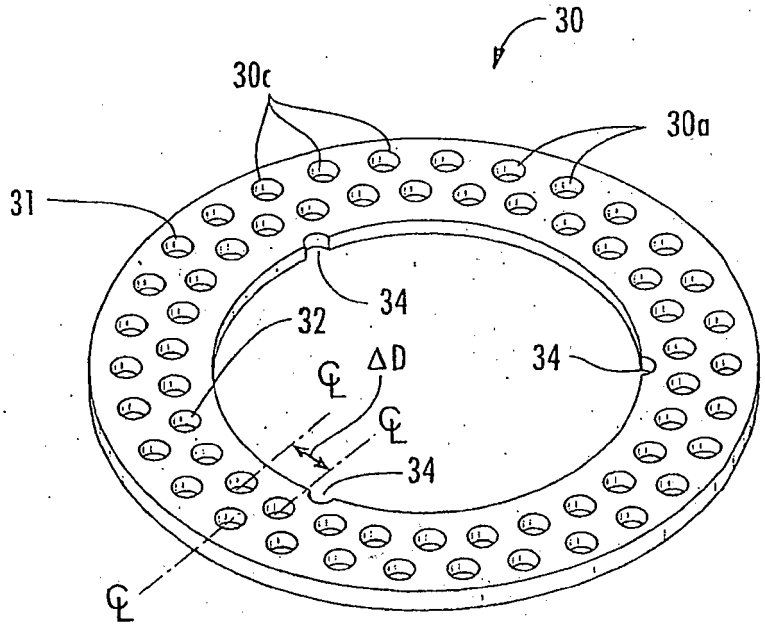


FIG. 3A

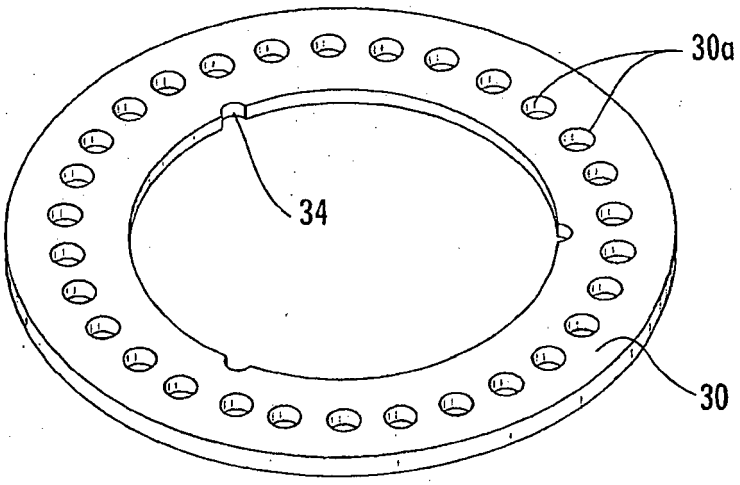


FIG. 3B

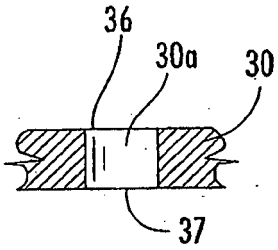


FIG. 3C

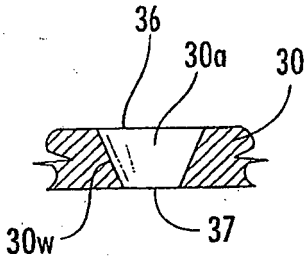
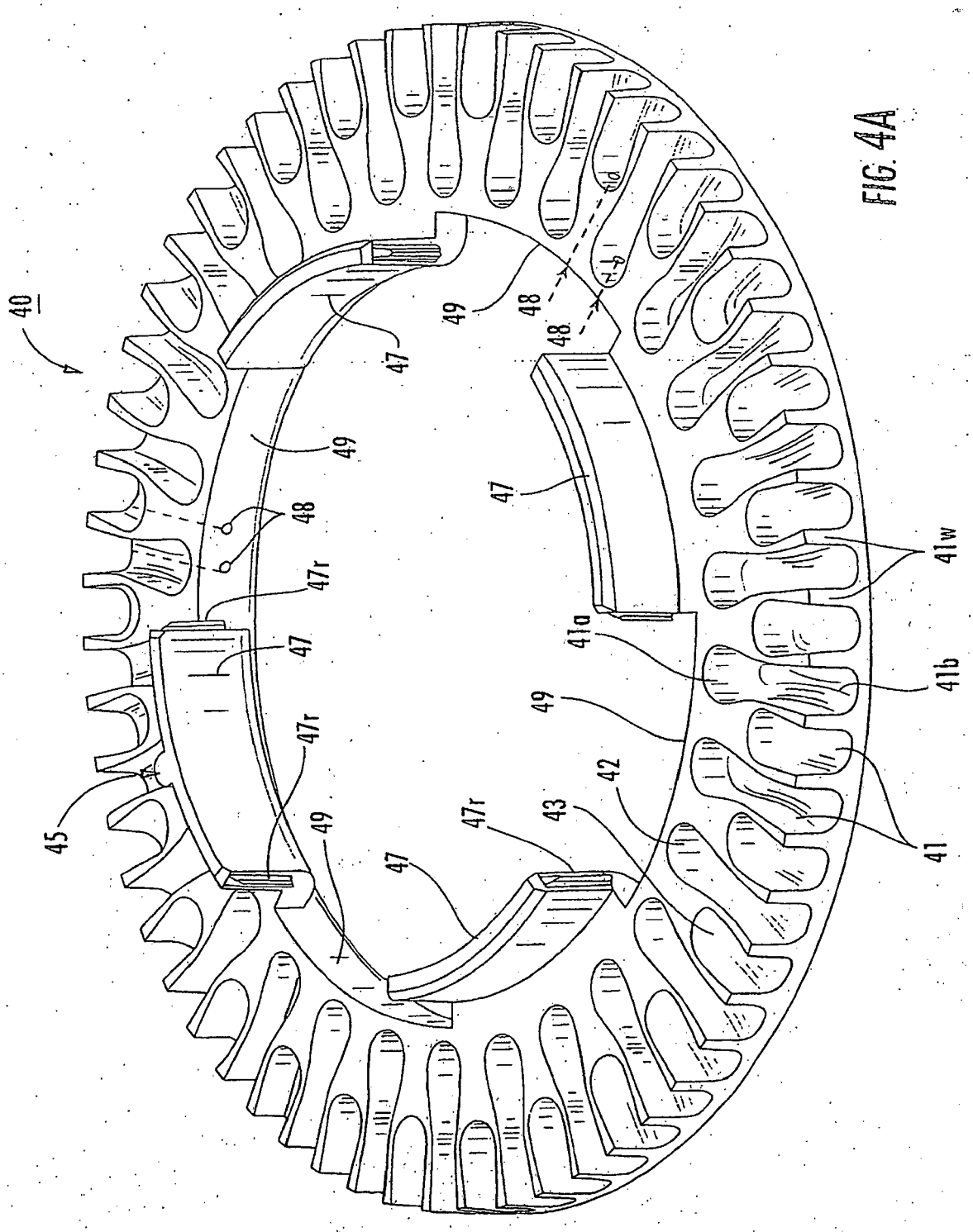


FIG. 3D



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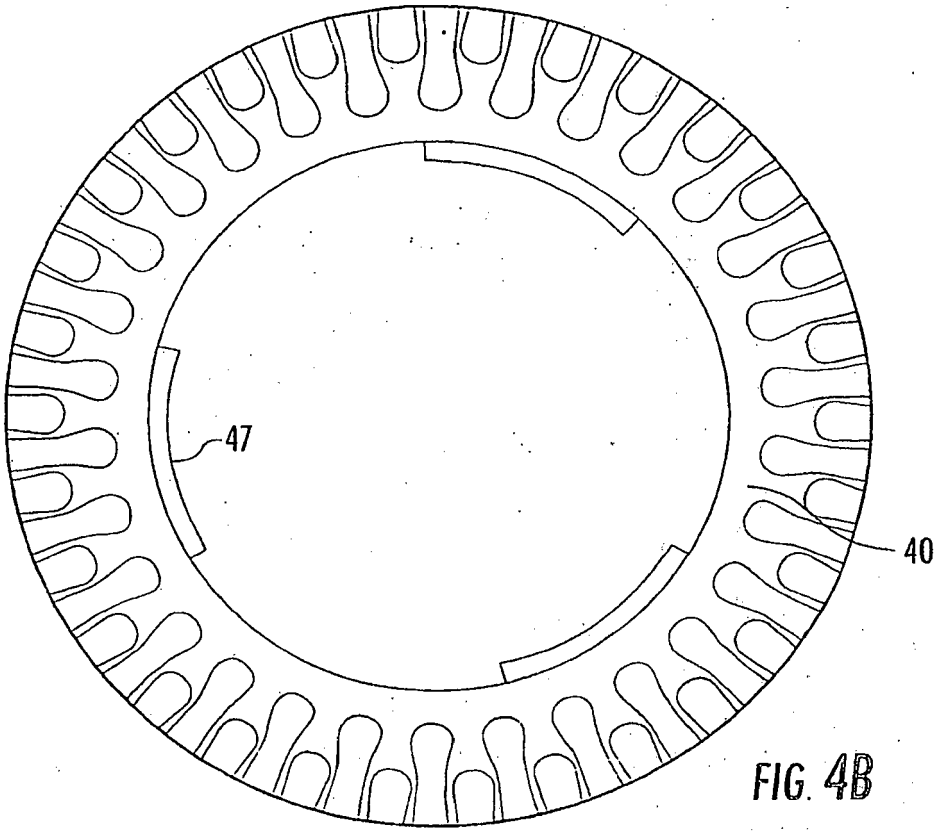


FIG. 4B

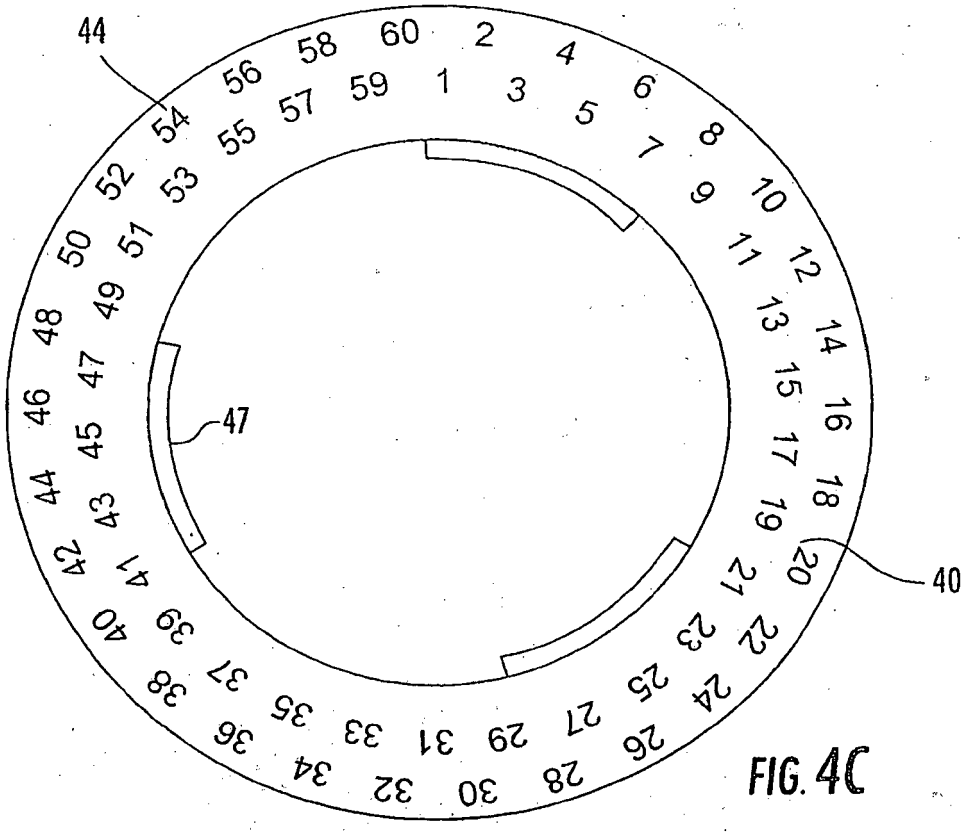


FIG. 4C

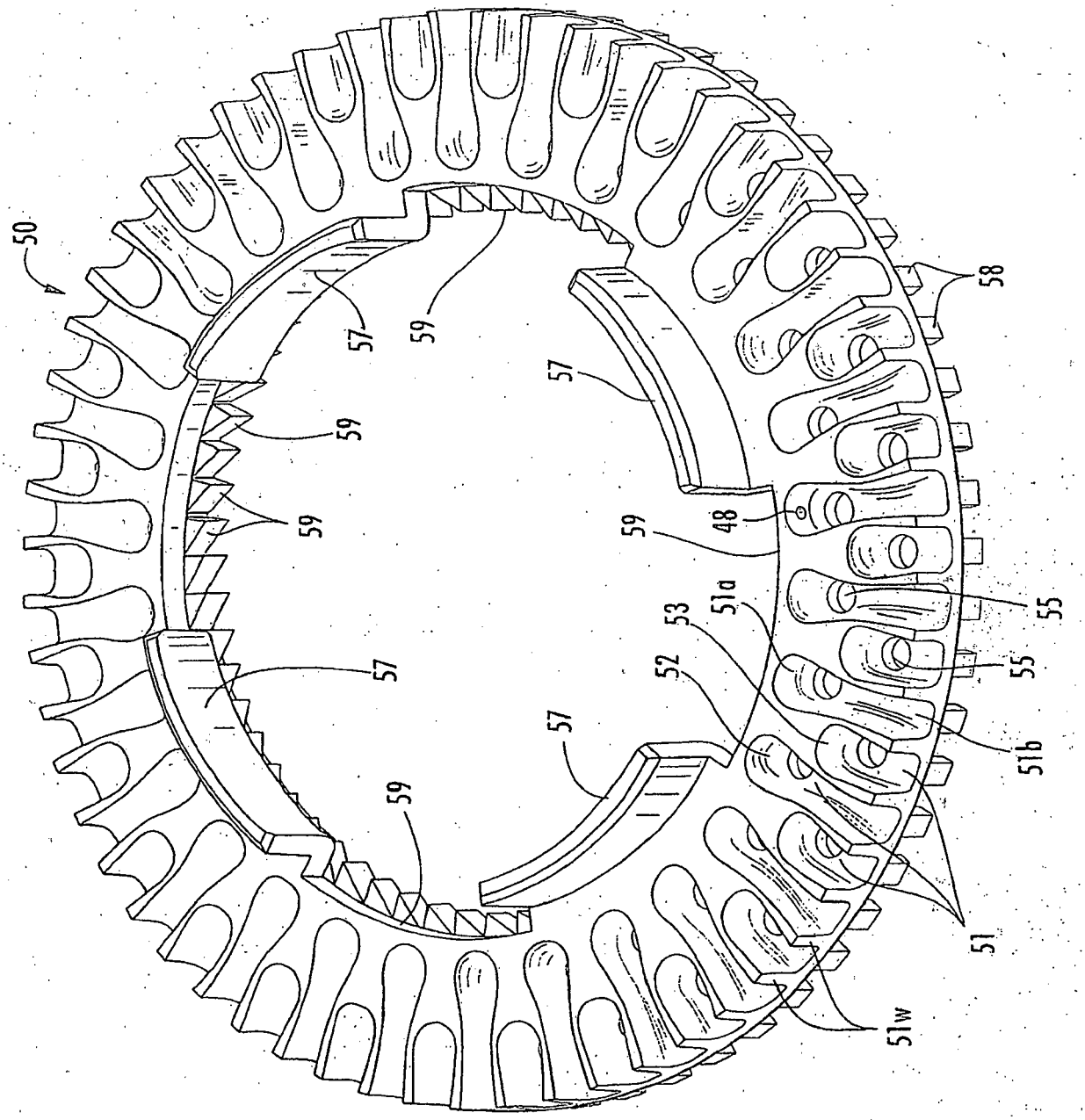


FIG. 5A

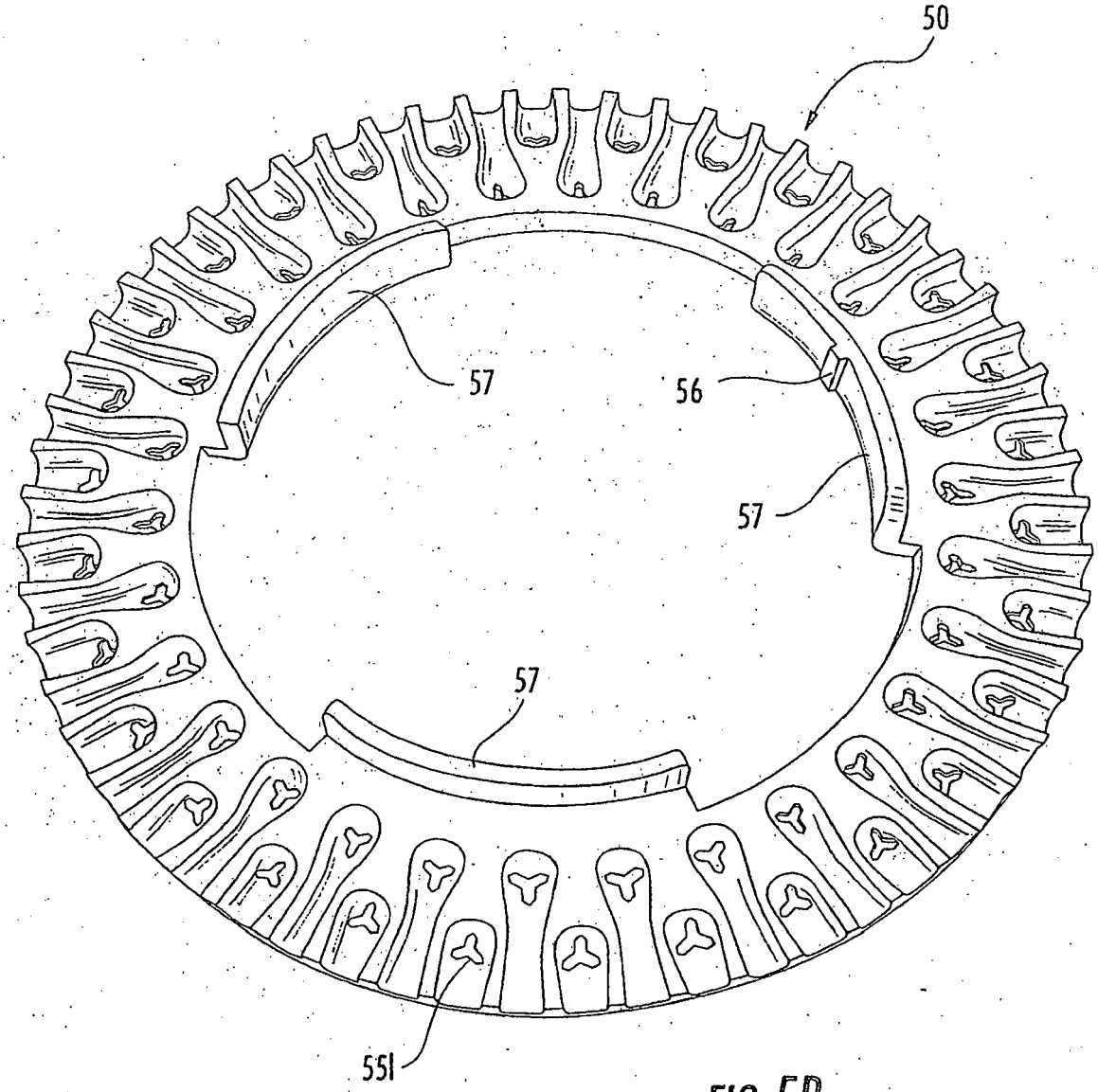


FIG. 5B

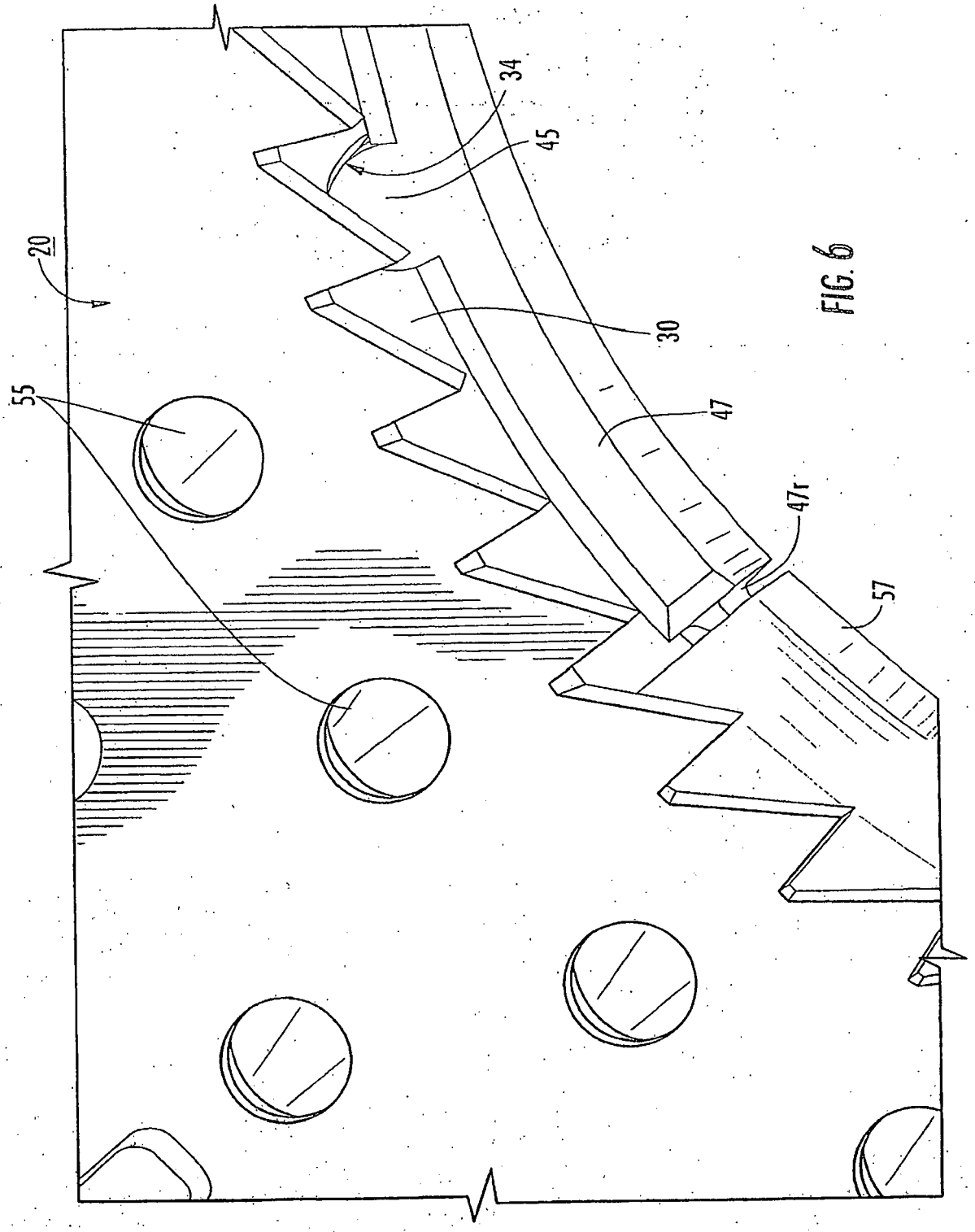


FIG. 6

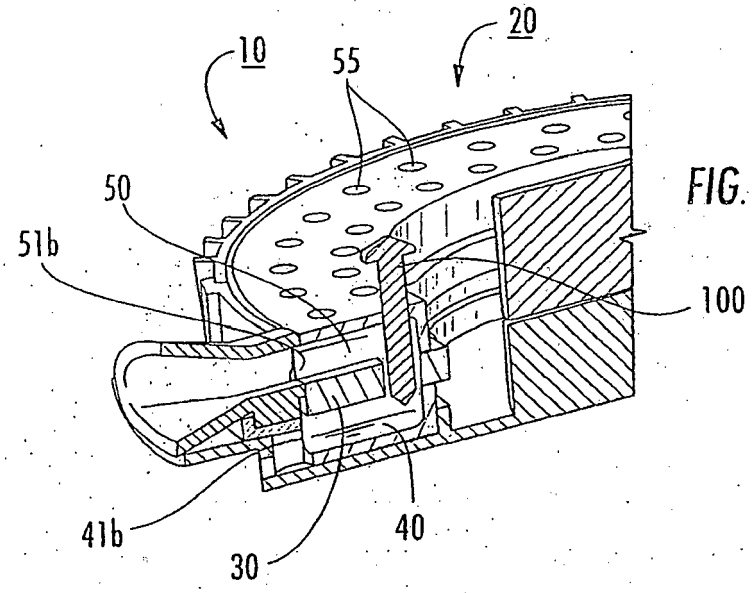


FIG. 7A

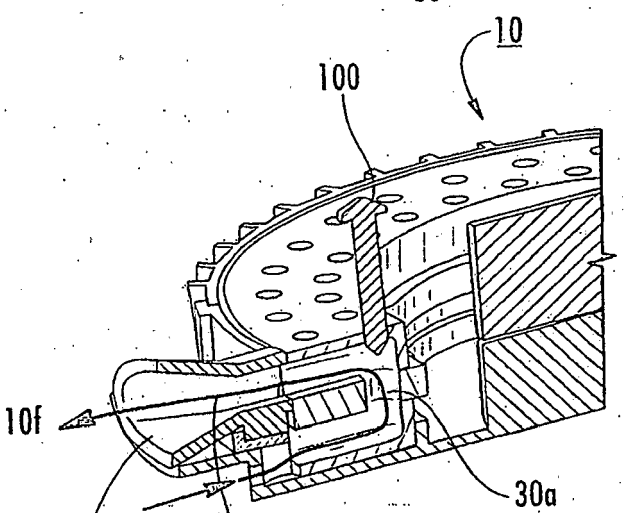


FIG. 7B

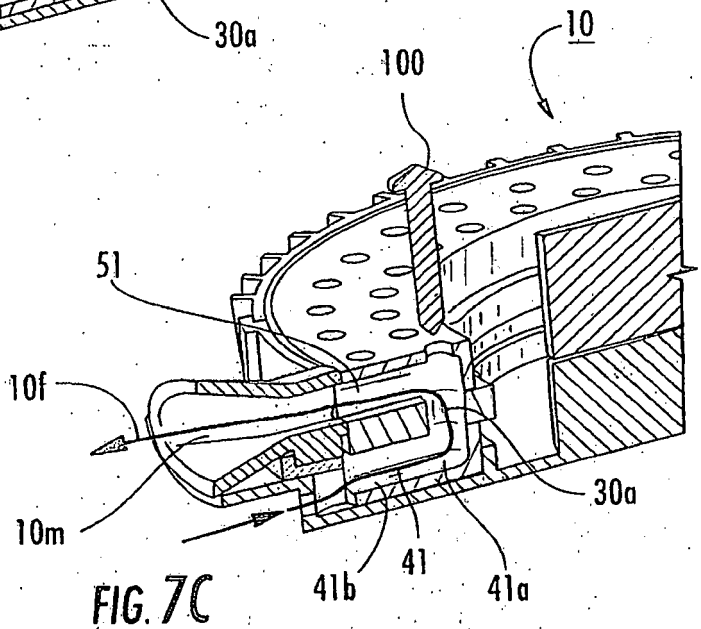
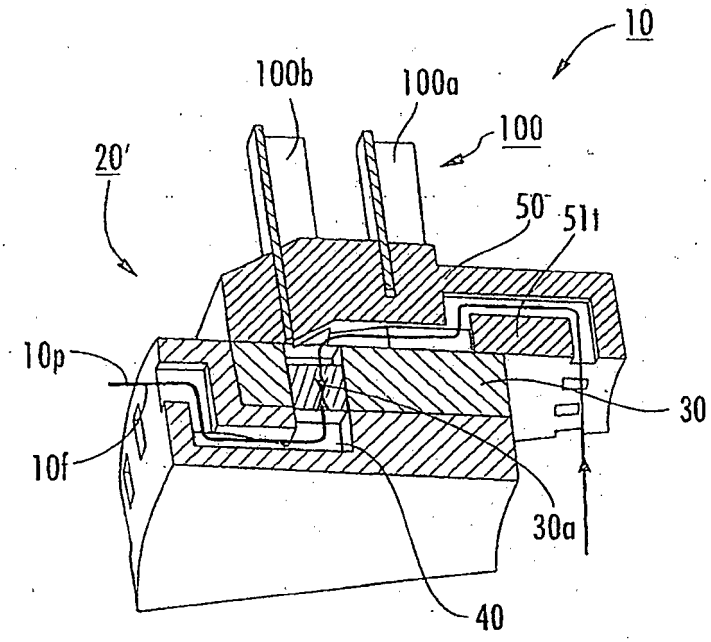


FIG. 7C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100b
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20'
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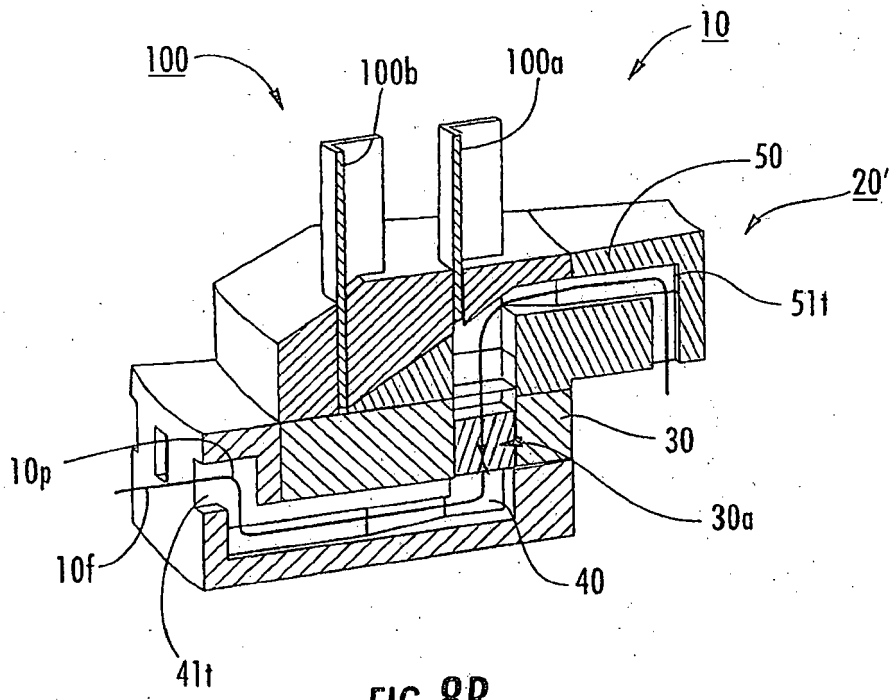
51t
10p
30
10f
30a
40

FIG. 8A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10f
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41t

FIG. 8B

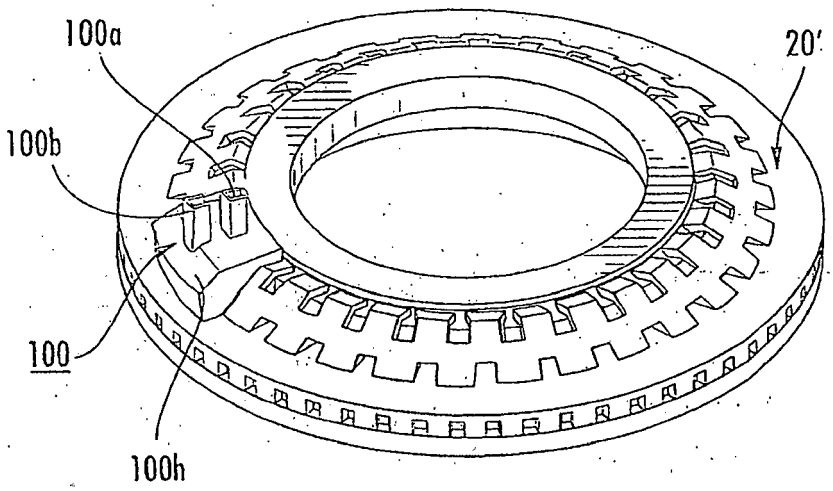


FIG. 9A

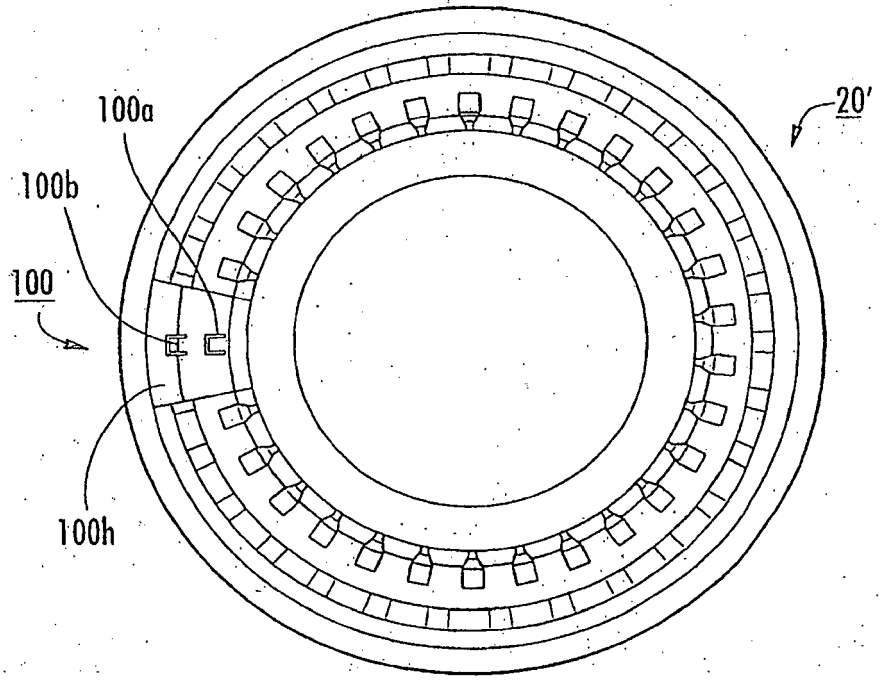


FIG. 9B

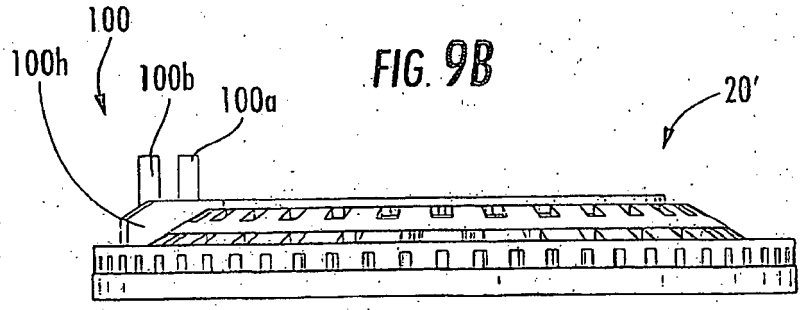


FIG. 9C

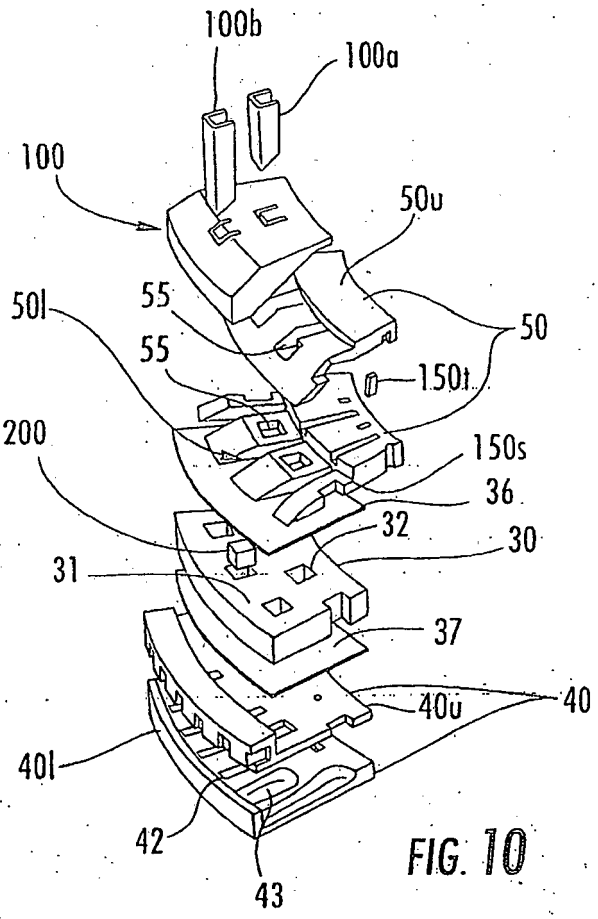


FIG. 10

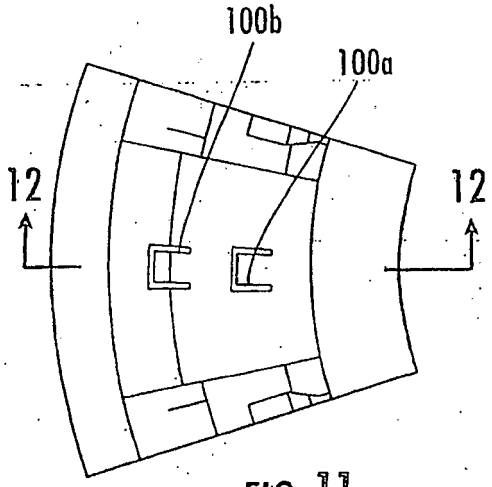


FIG. 11

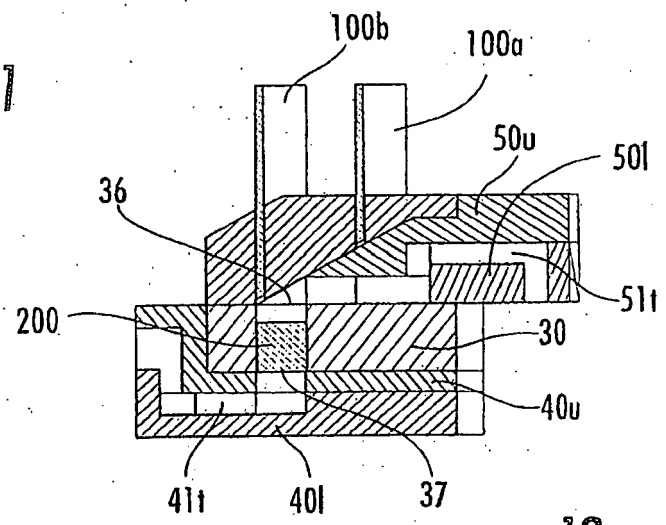


FIG. 12

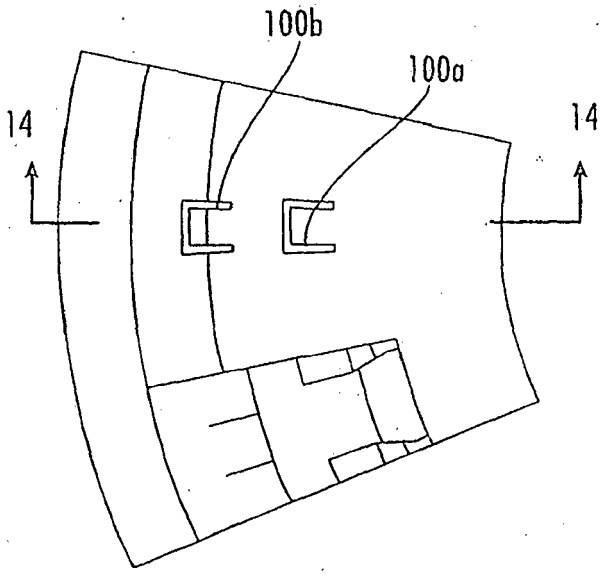


FIG. 13

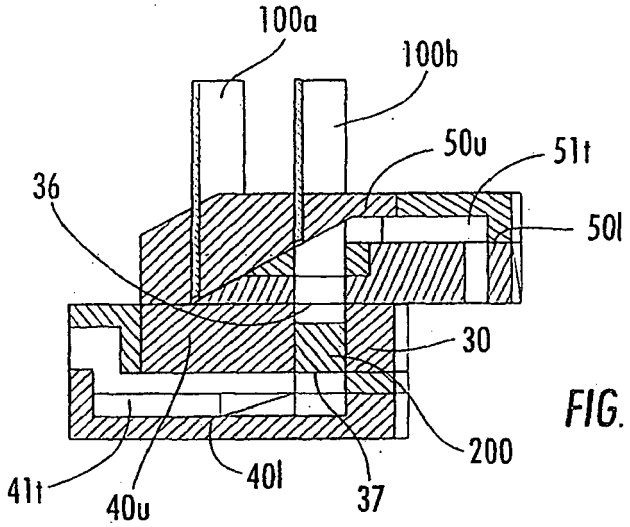


FIG. 14

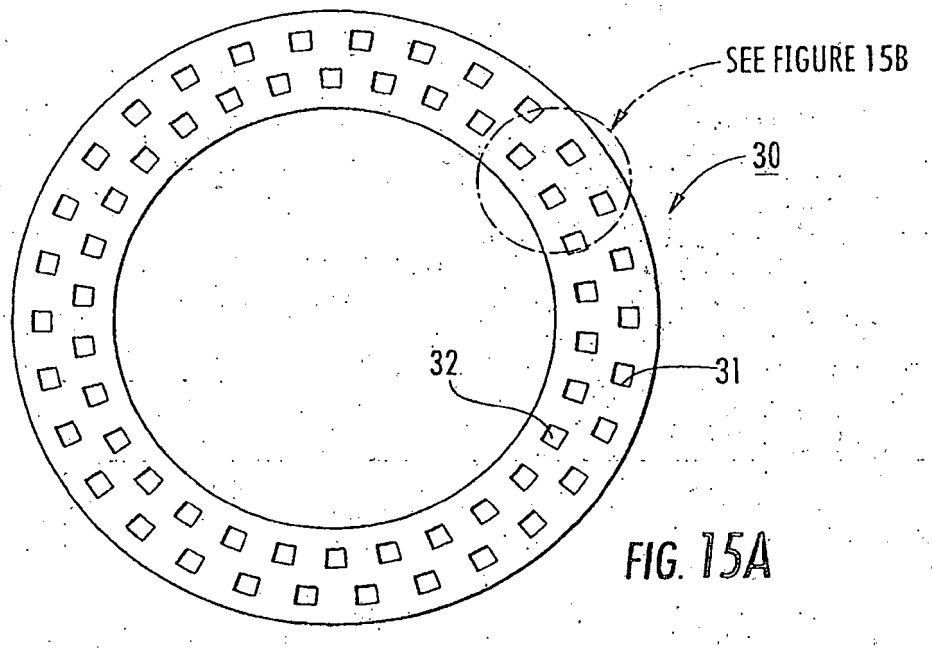


FIG. 15A

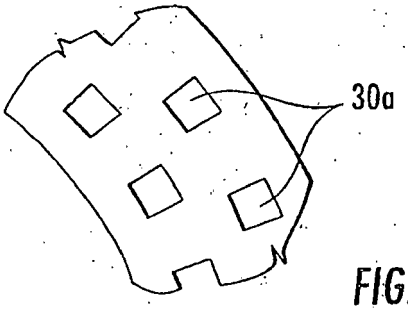


FIG. 15B

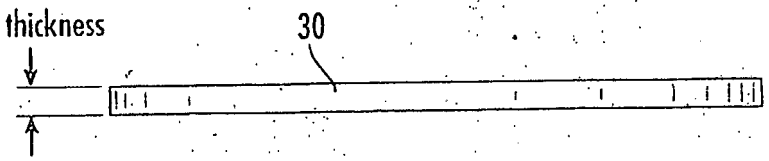


FIG. 16

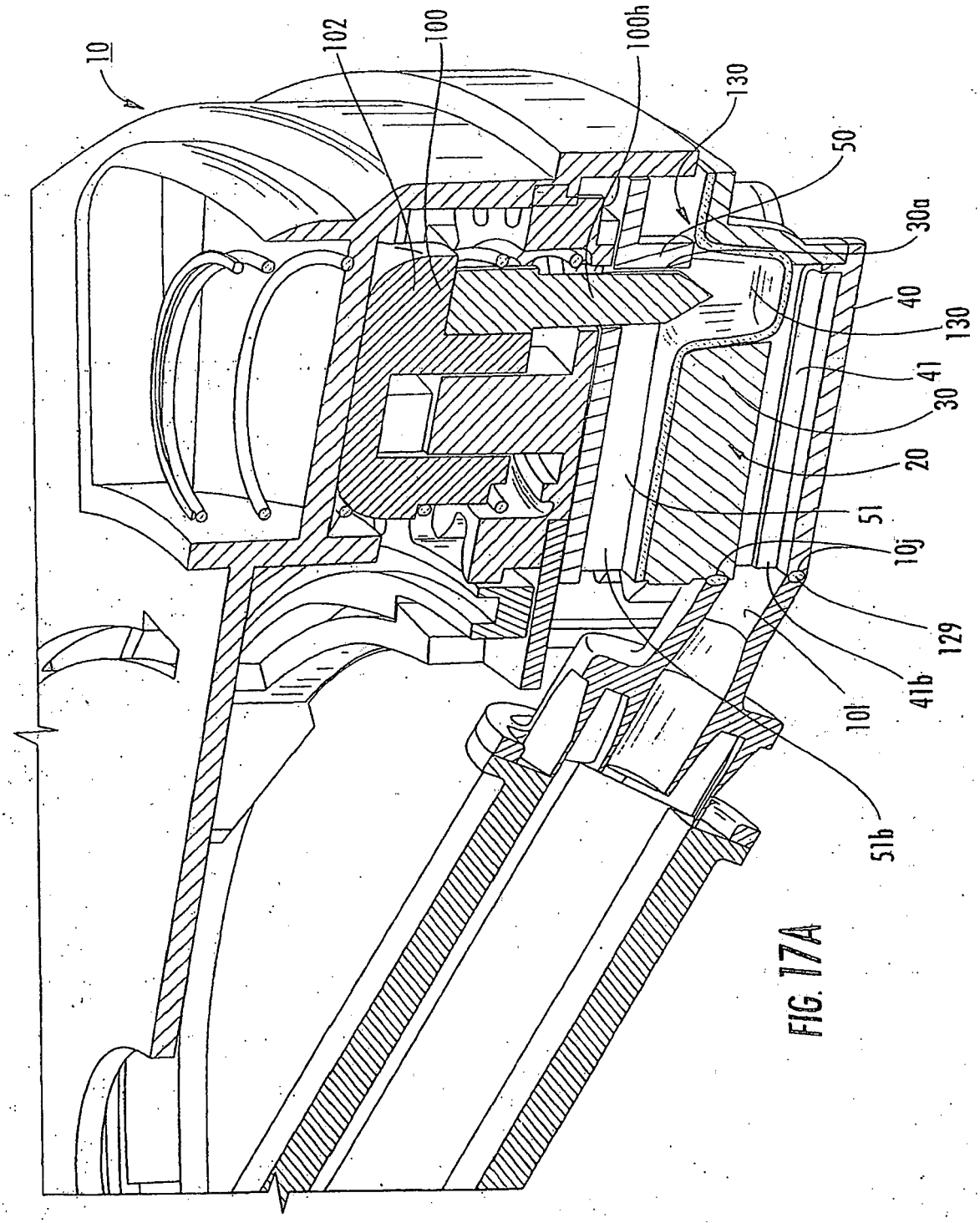


FIG. 17A

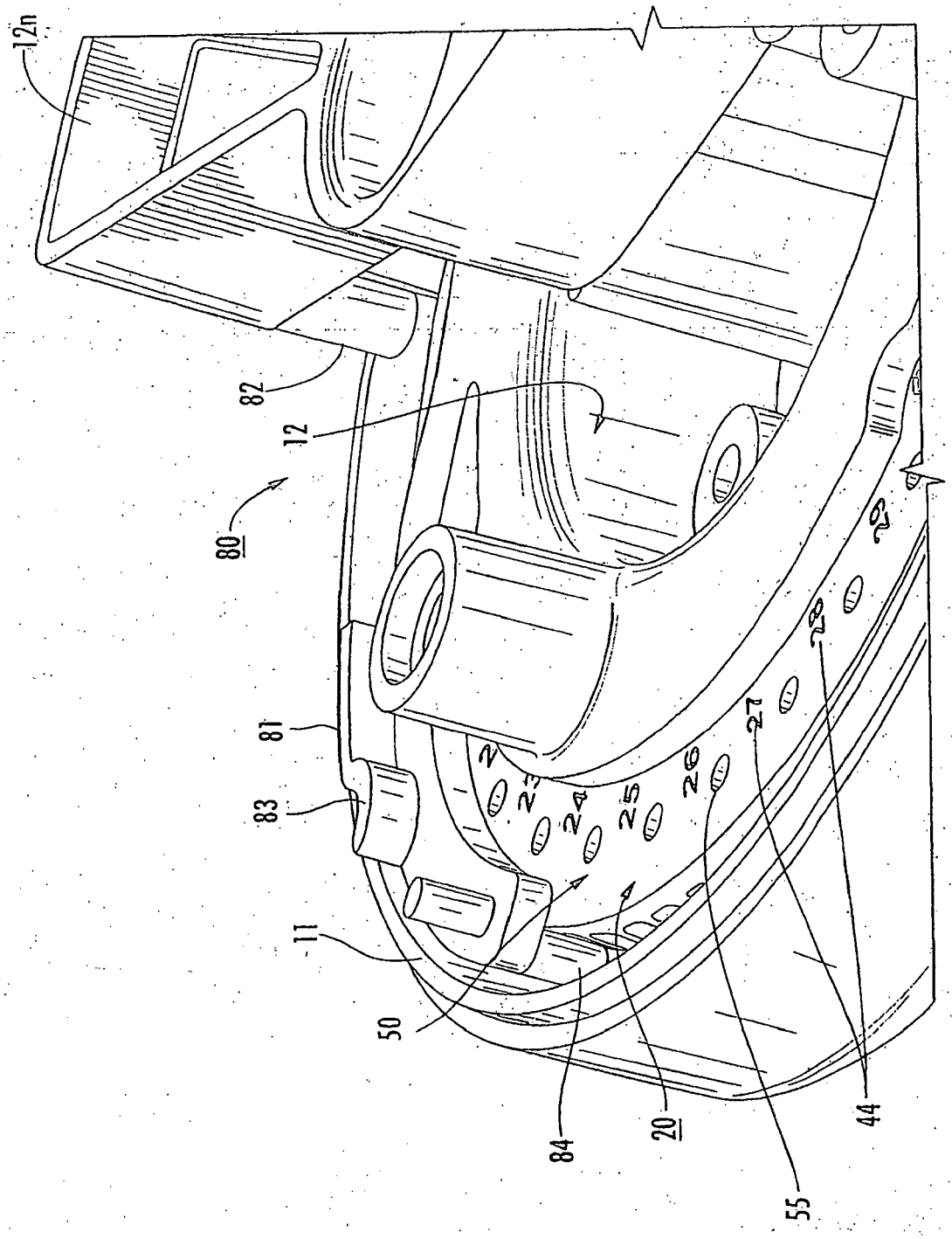


FIG. 17B

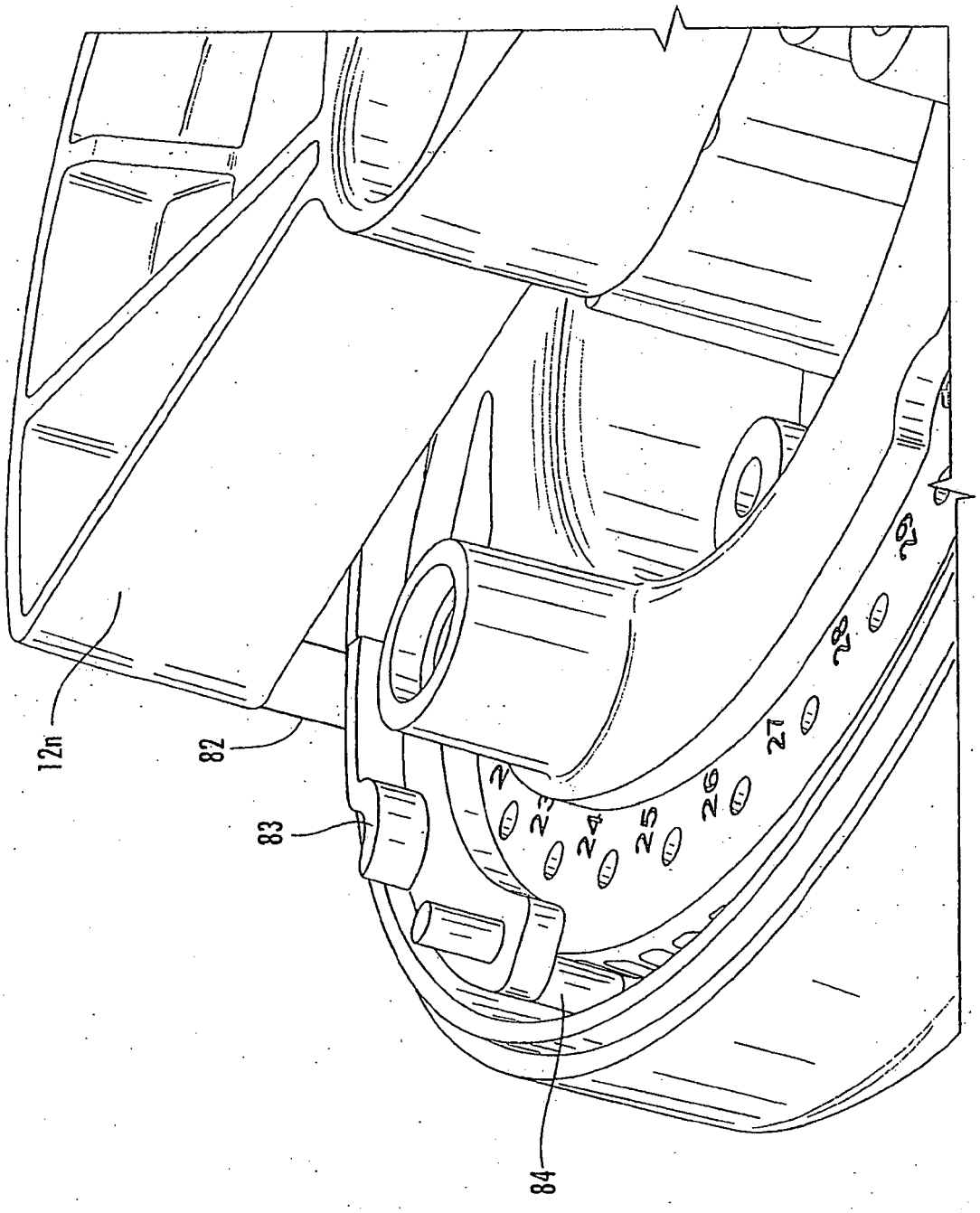


FIG. 17C

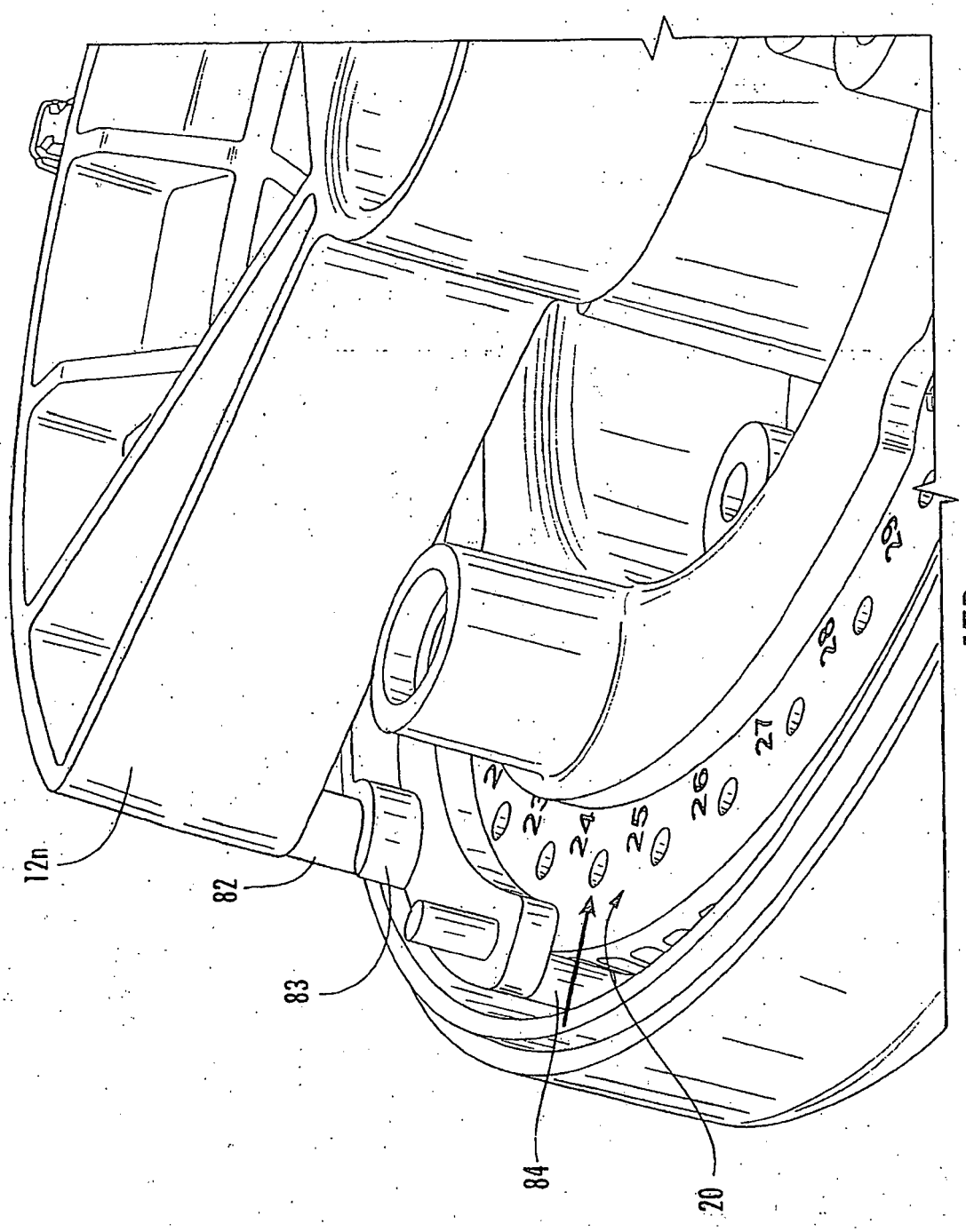


FIG. 17D

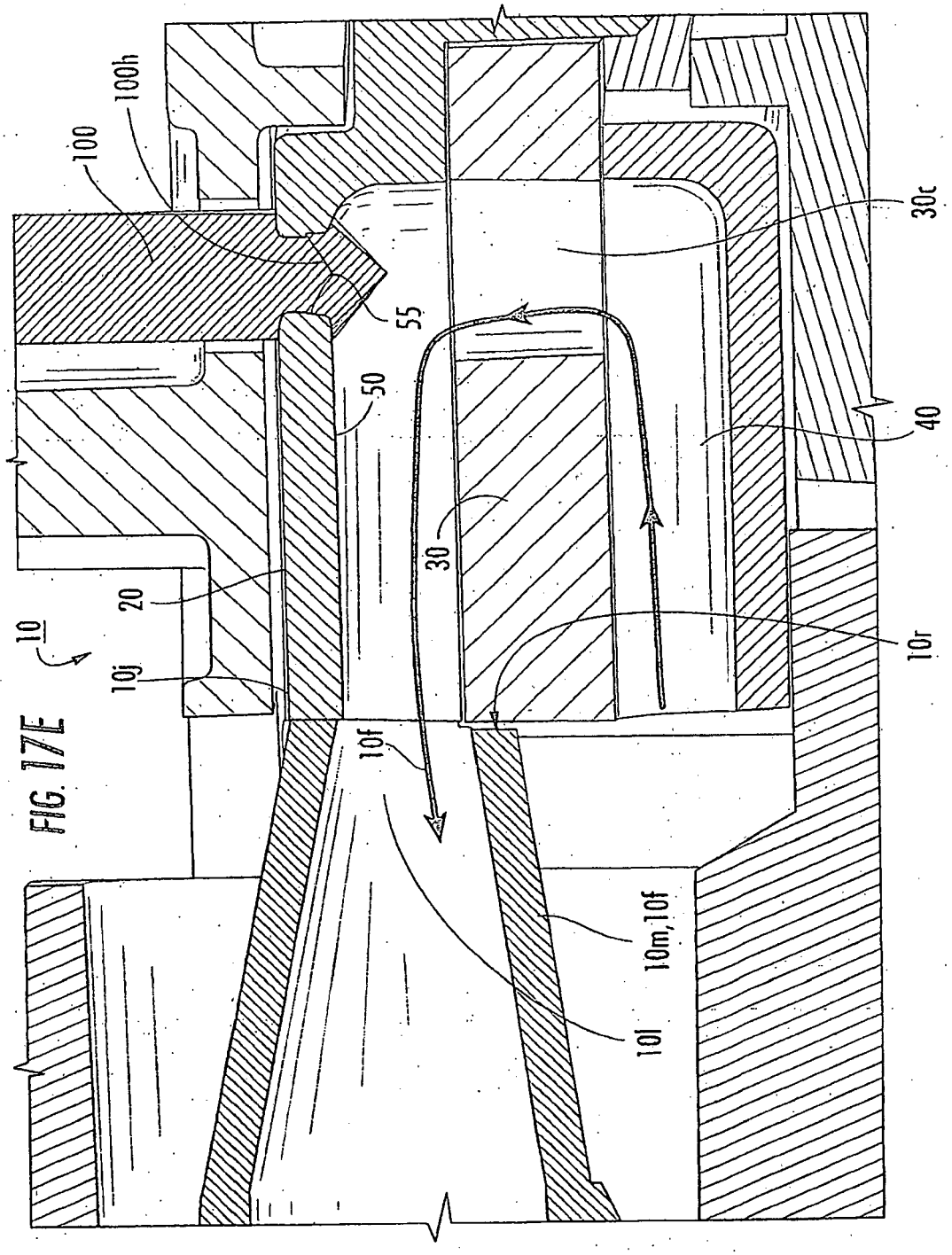


FIG. 17E

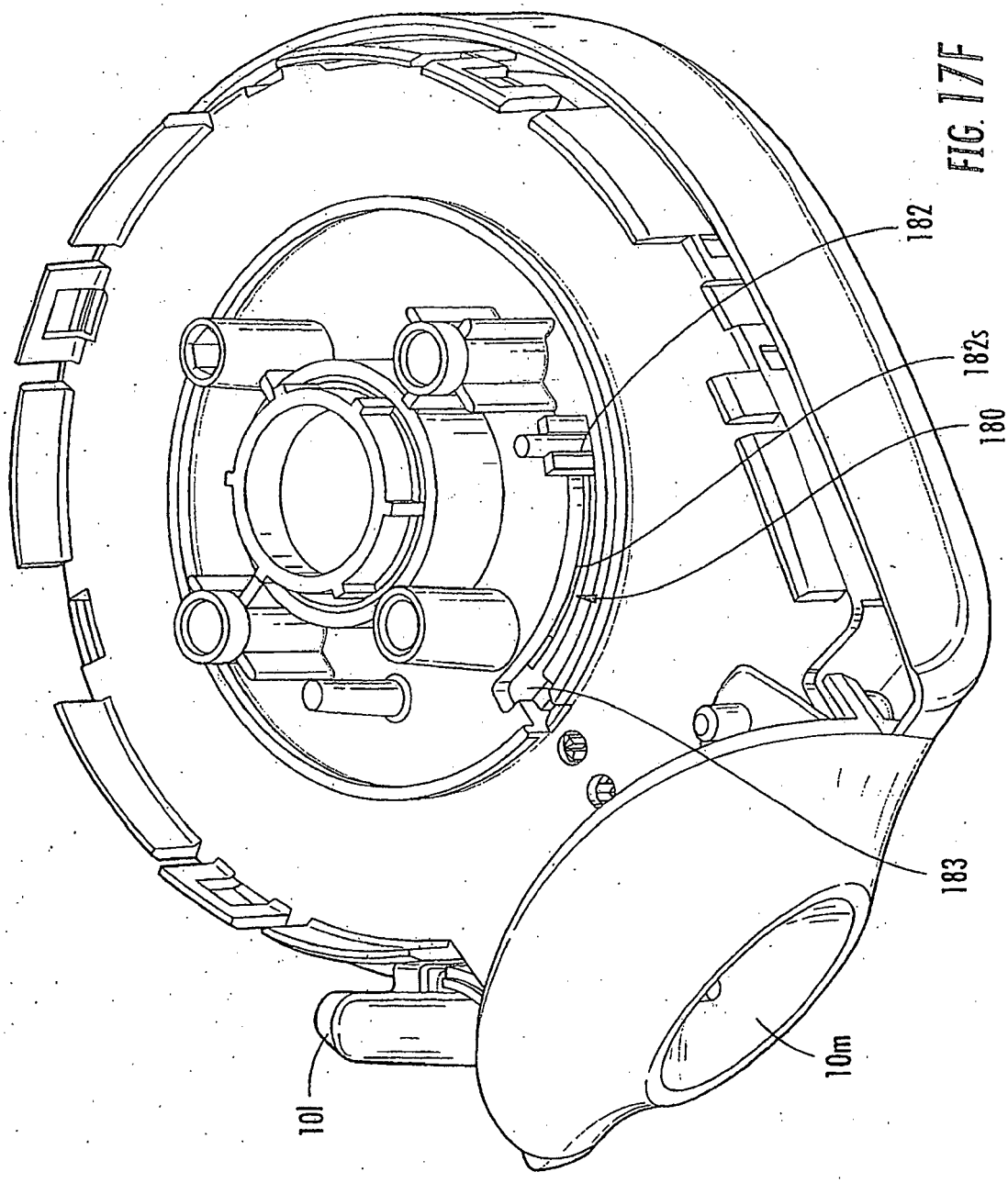


FIG. 17F

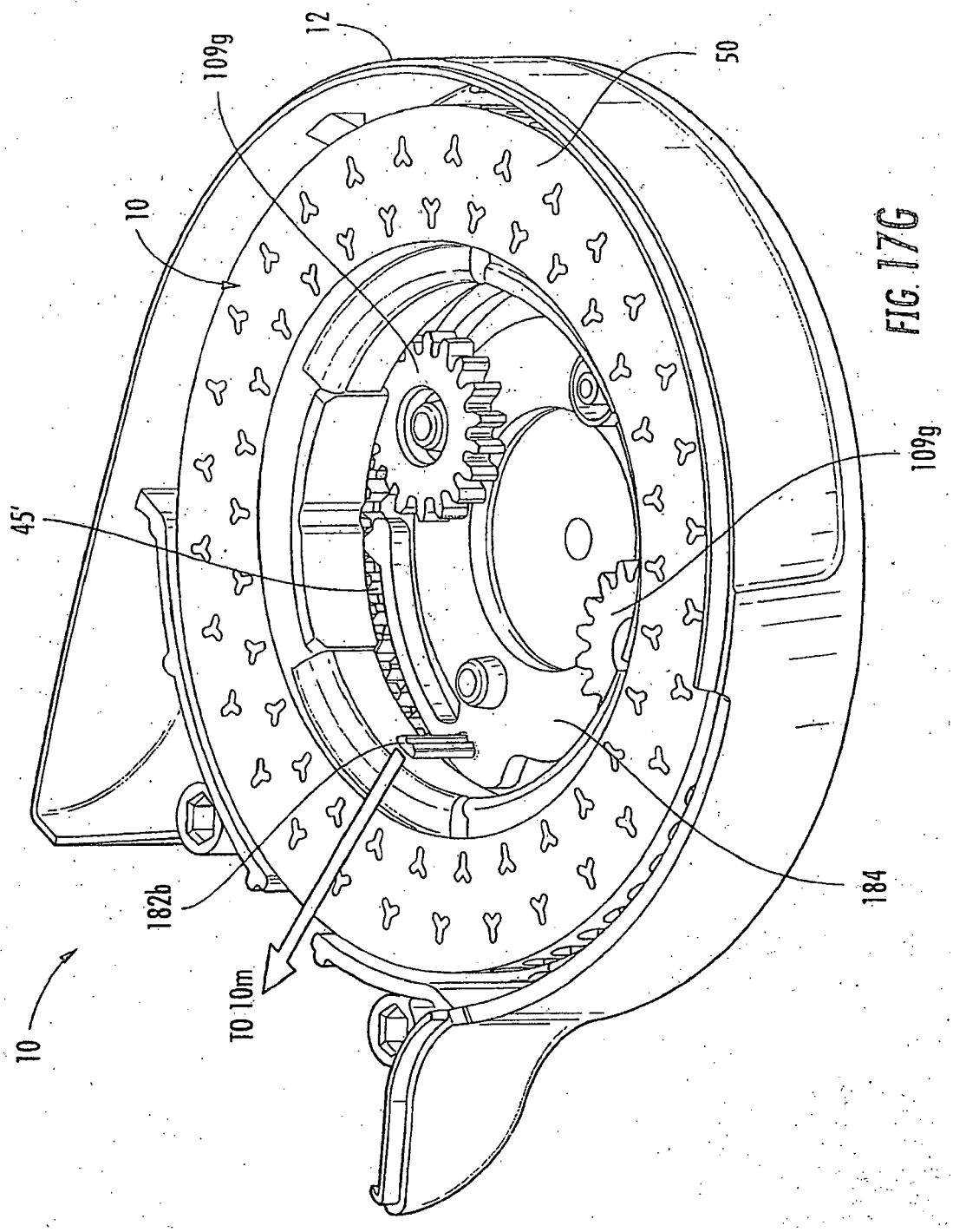


FIG. 17G

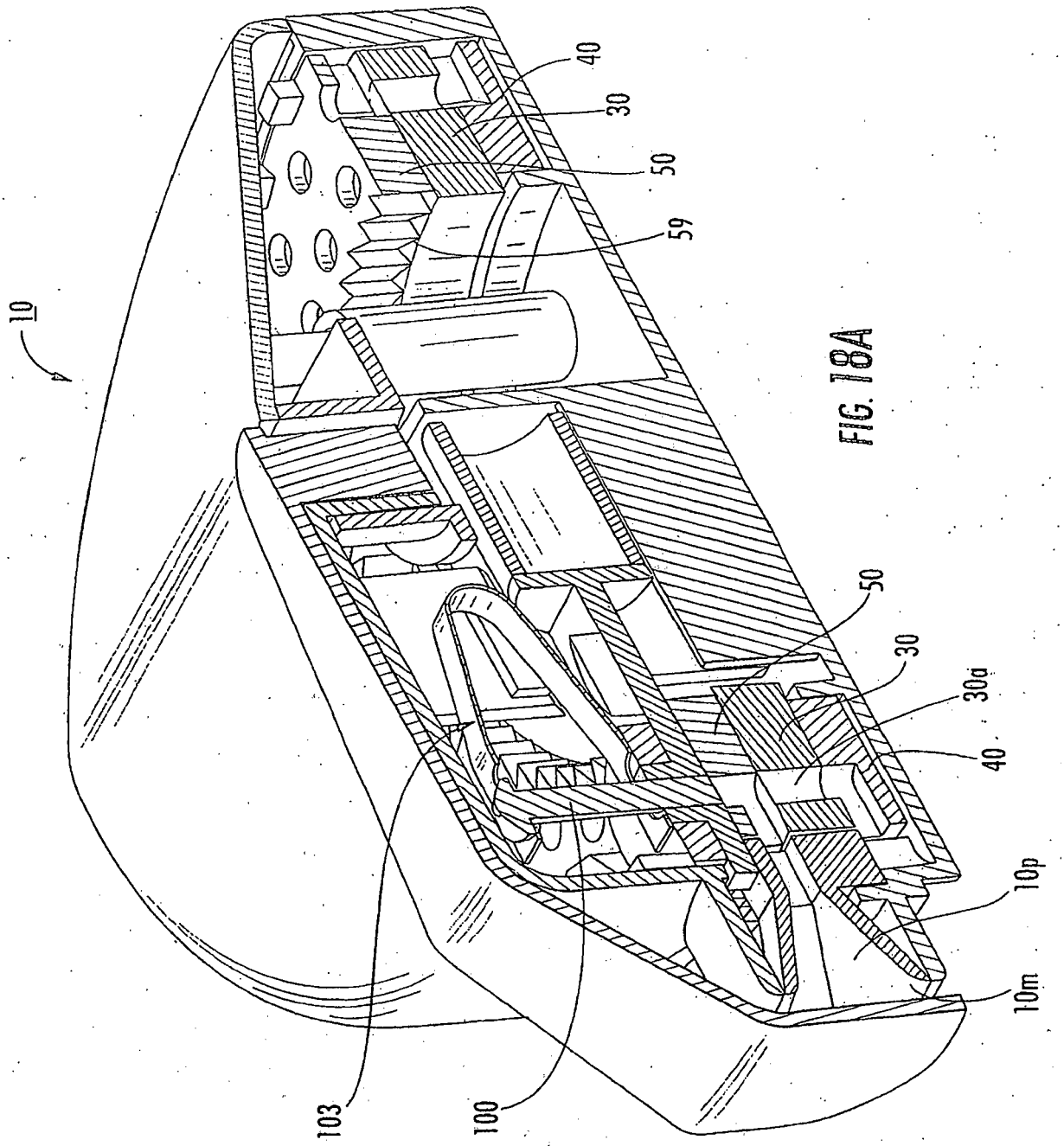


FIG. 18A

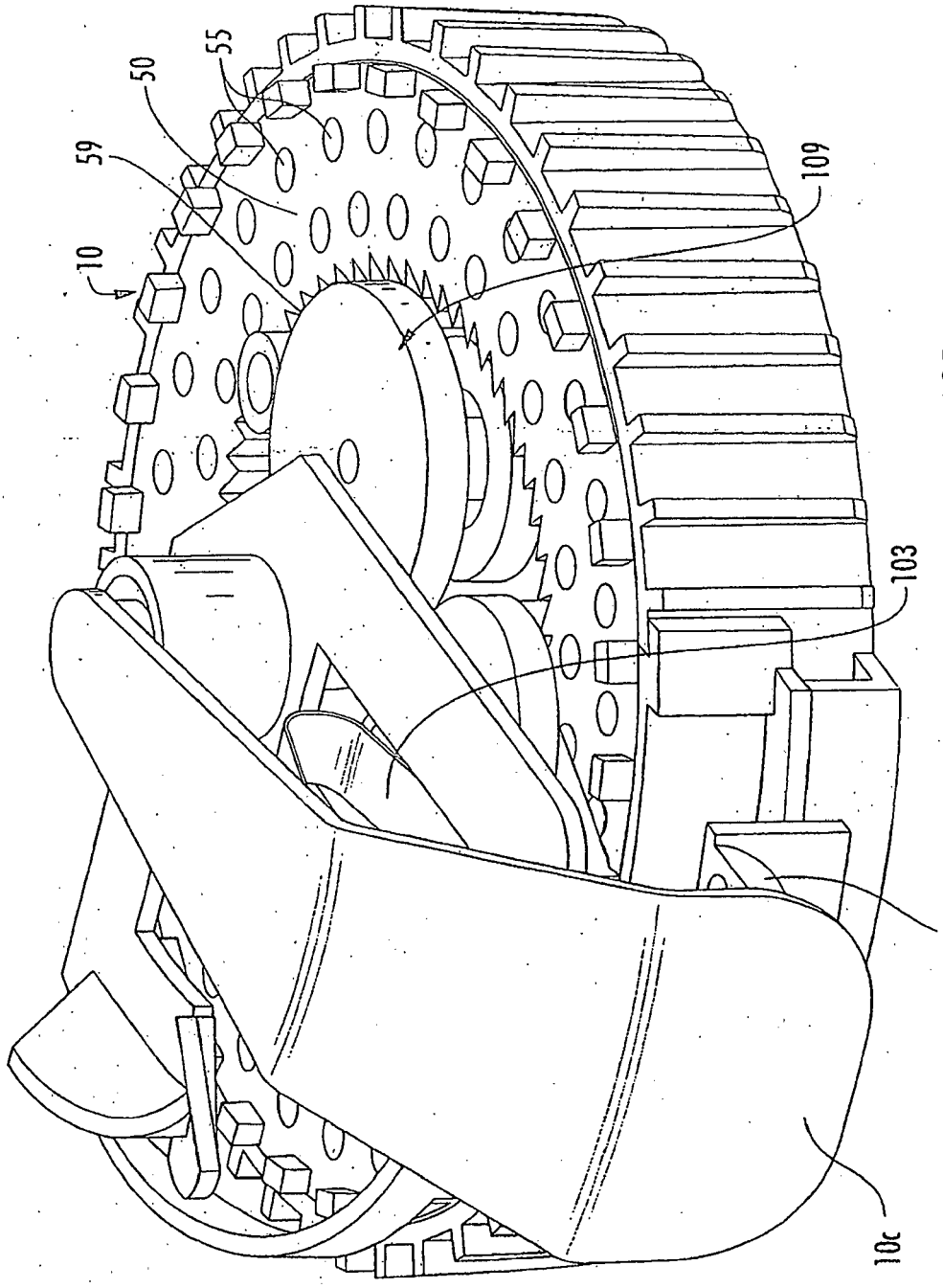
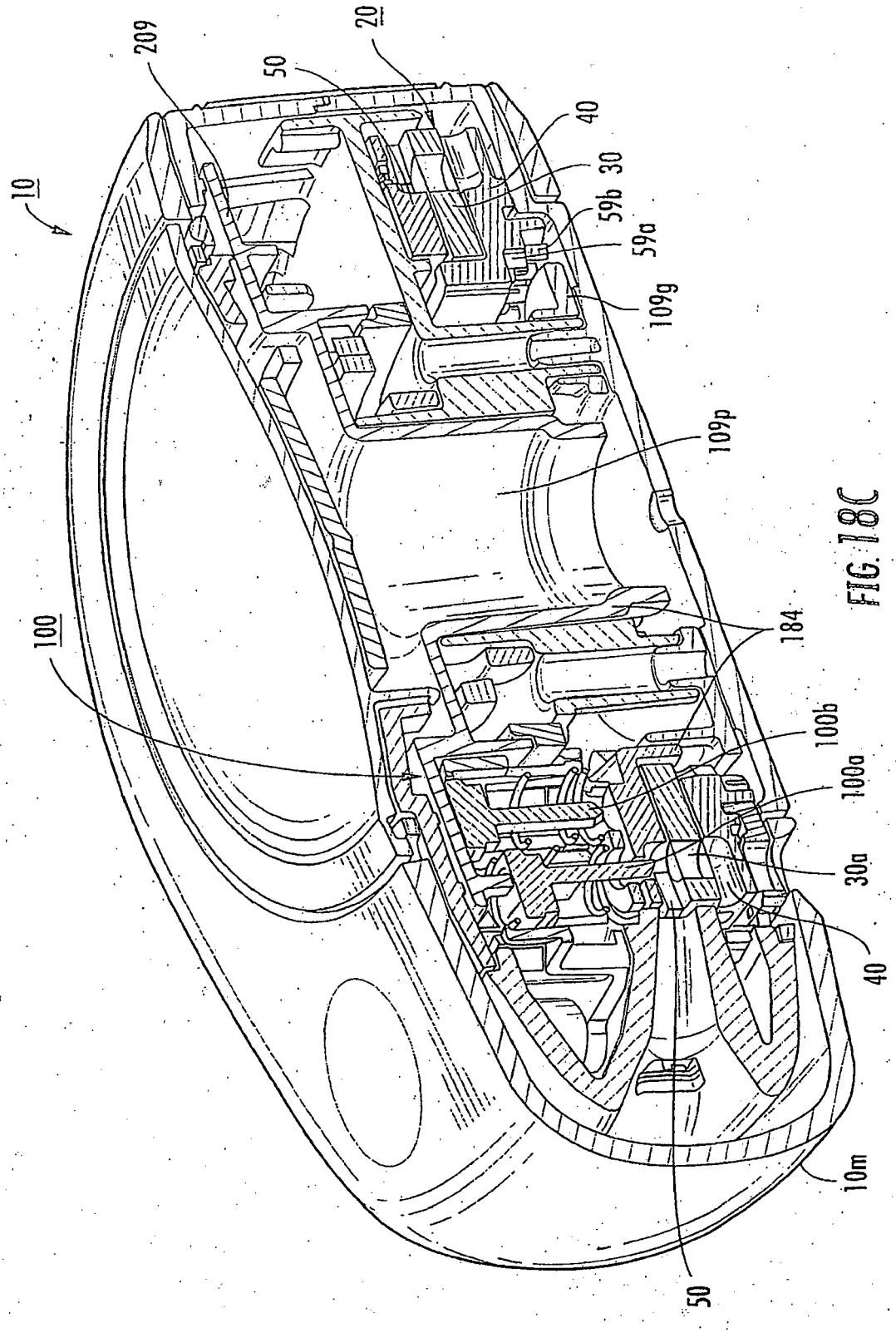


FIG. 18B


209
50
20
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30
59b
59a
109g
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109p
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184
100b
100a
30a
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10m
50

FIG. 18C

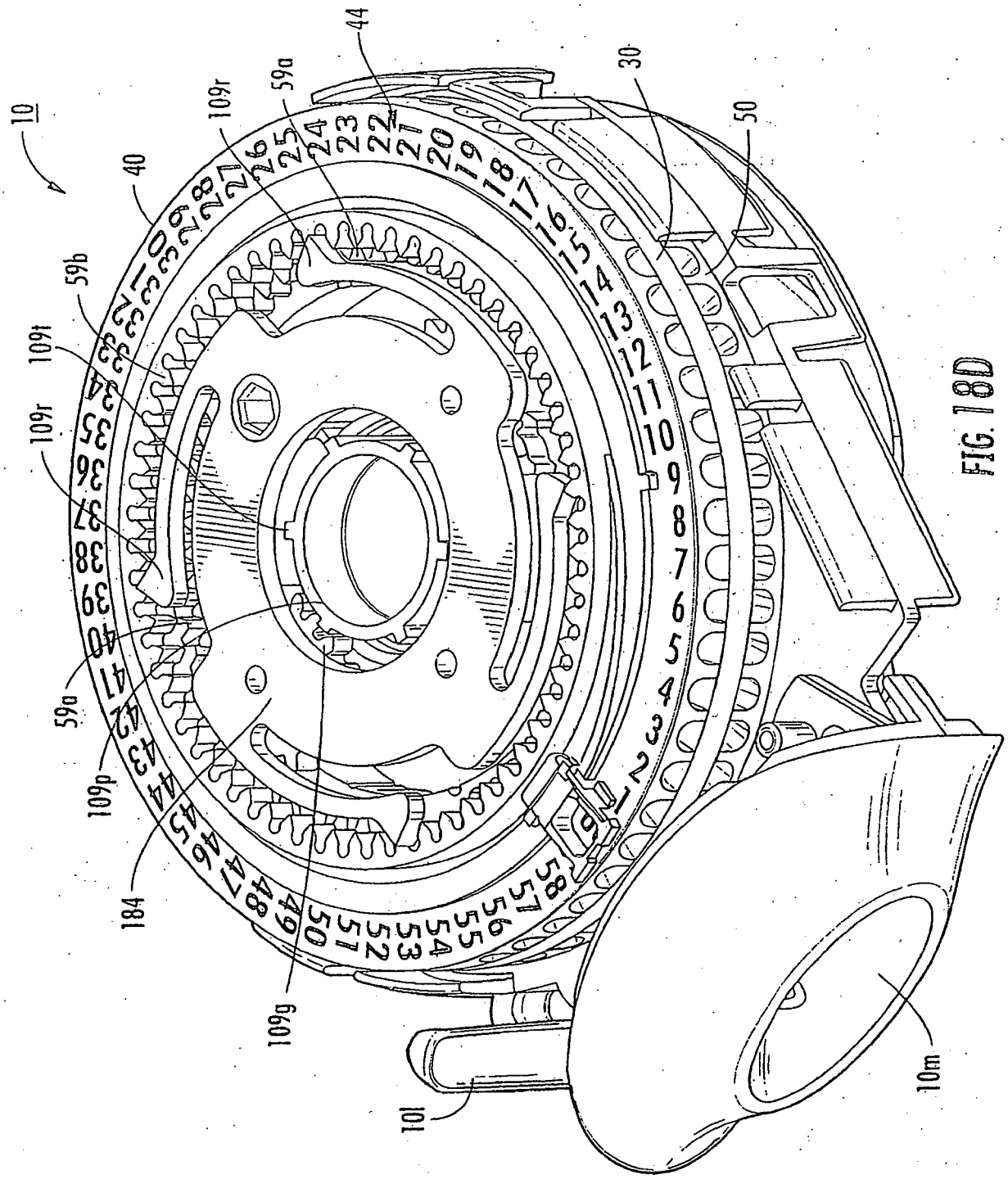
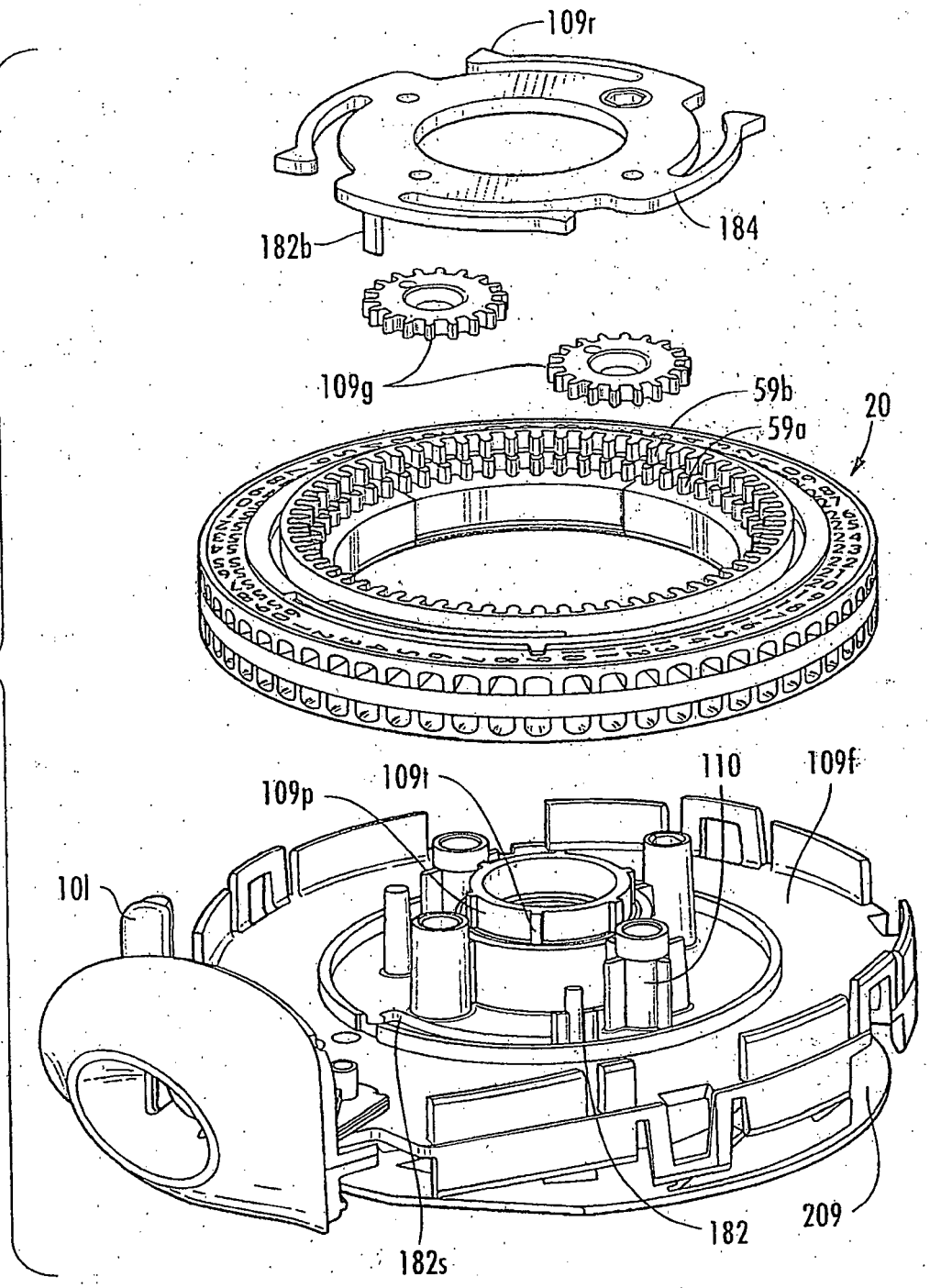


FIG. 18D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109f
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209
182s

FIG. 18E

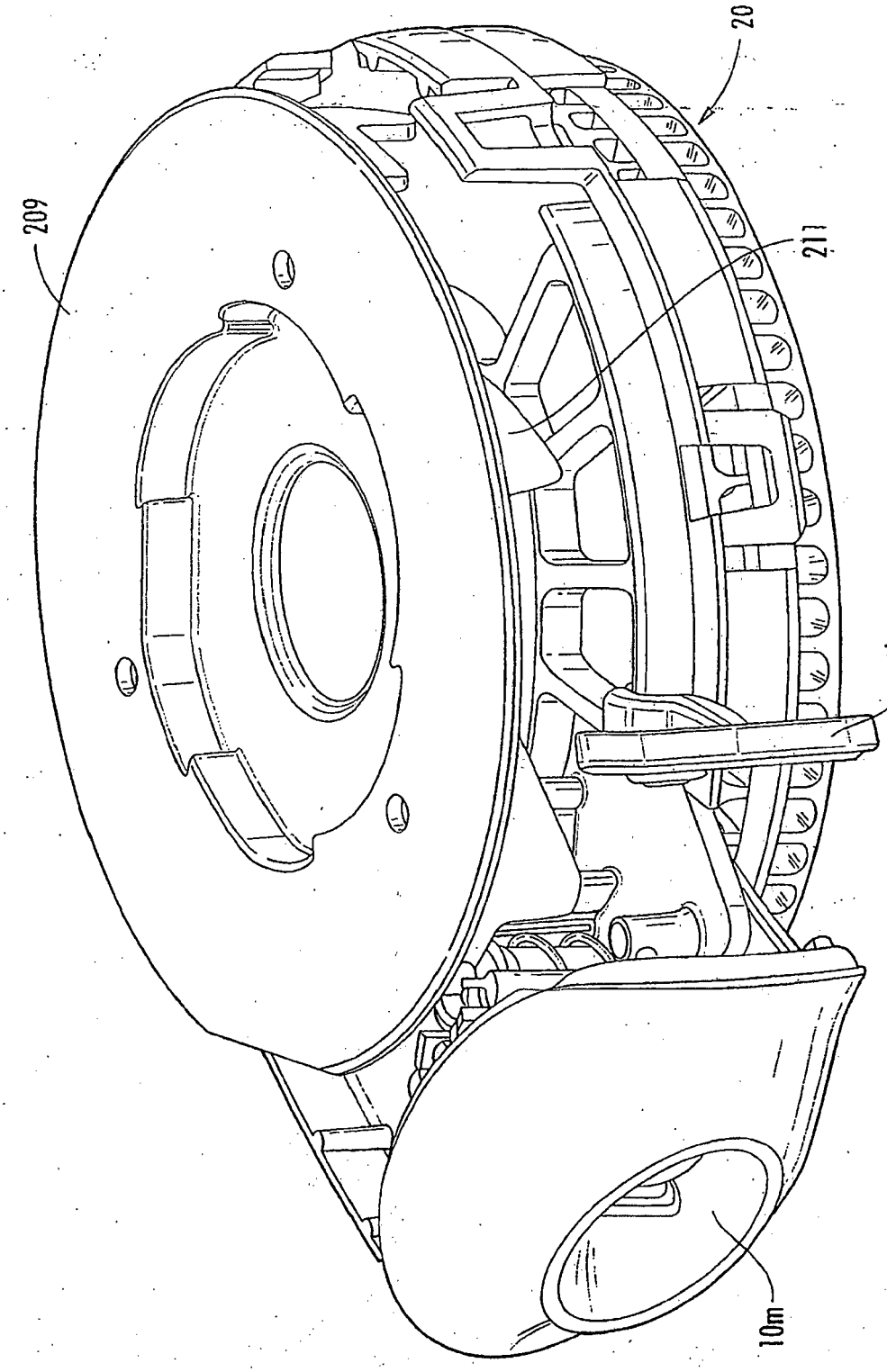

FIG. 18F

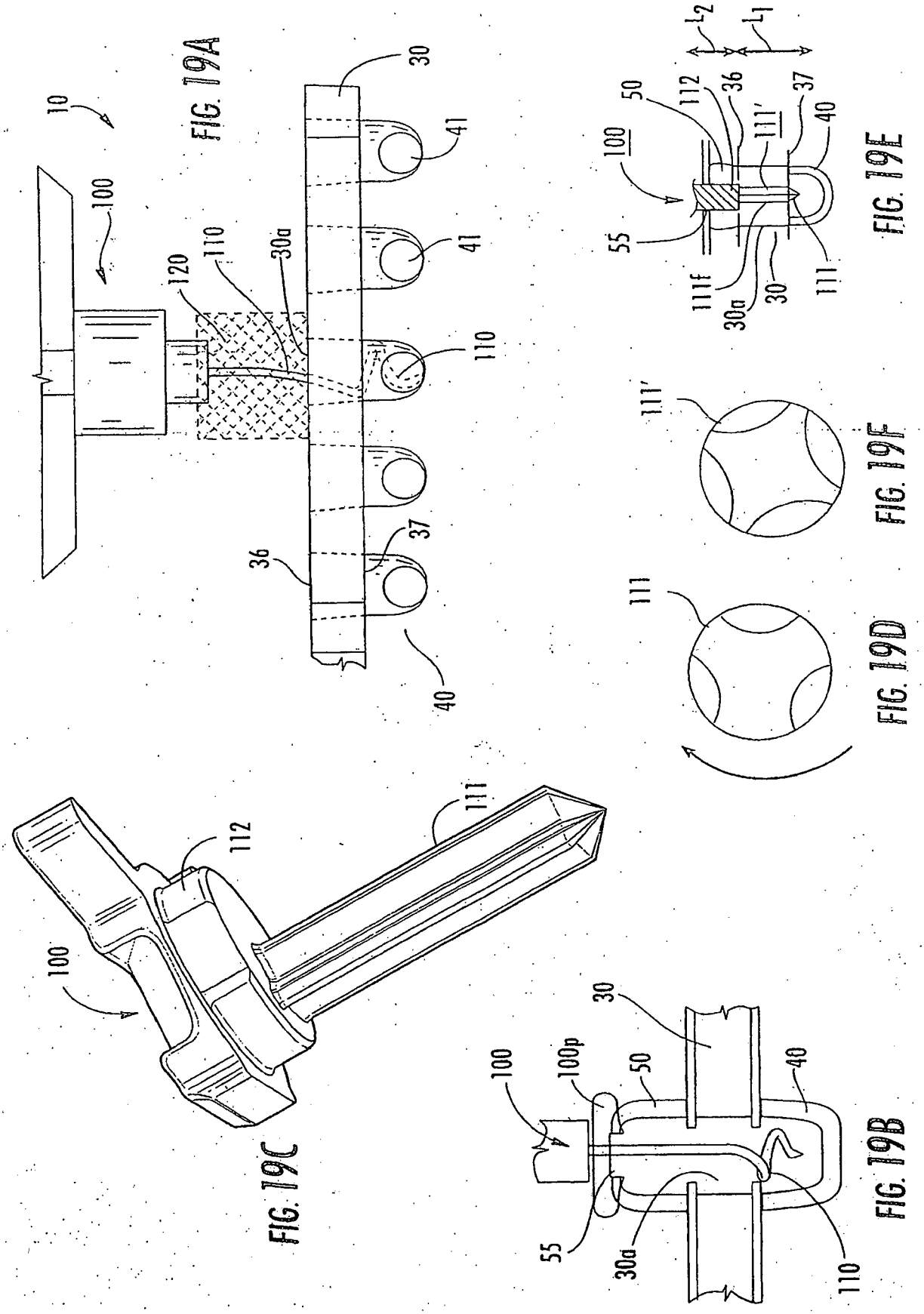
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FIG. 19A
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111
FIG. 19C
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100p
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30
40
55
30a
110
FIG. 19B
111
111'
FIG. 19D
111'
FIG. 19F
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L1
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111'
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100
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111f
30a
30
111
FIG. 19E

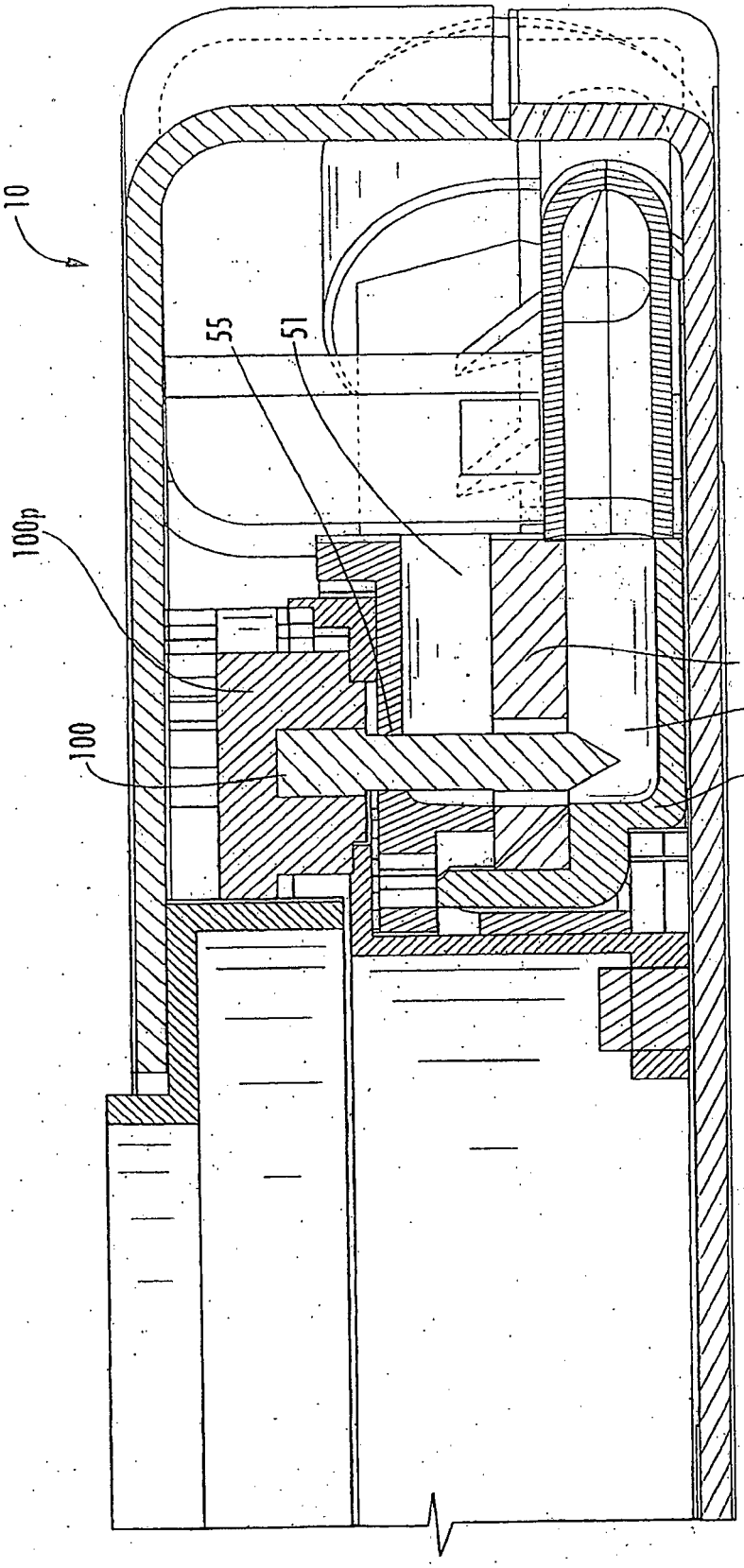
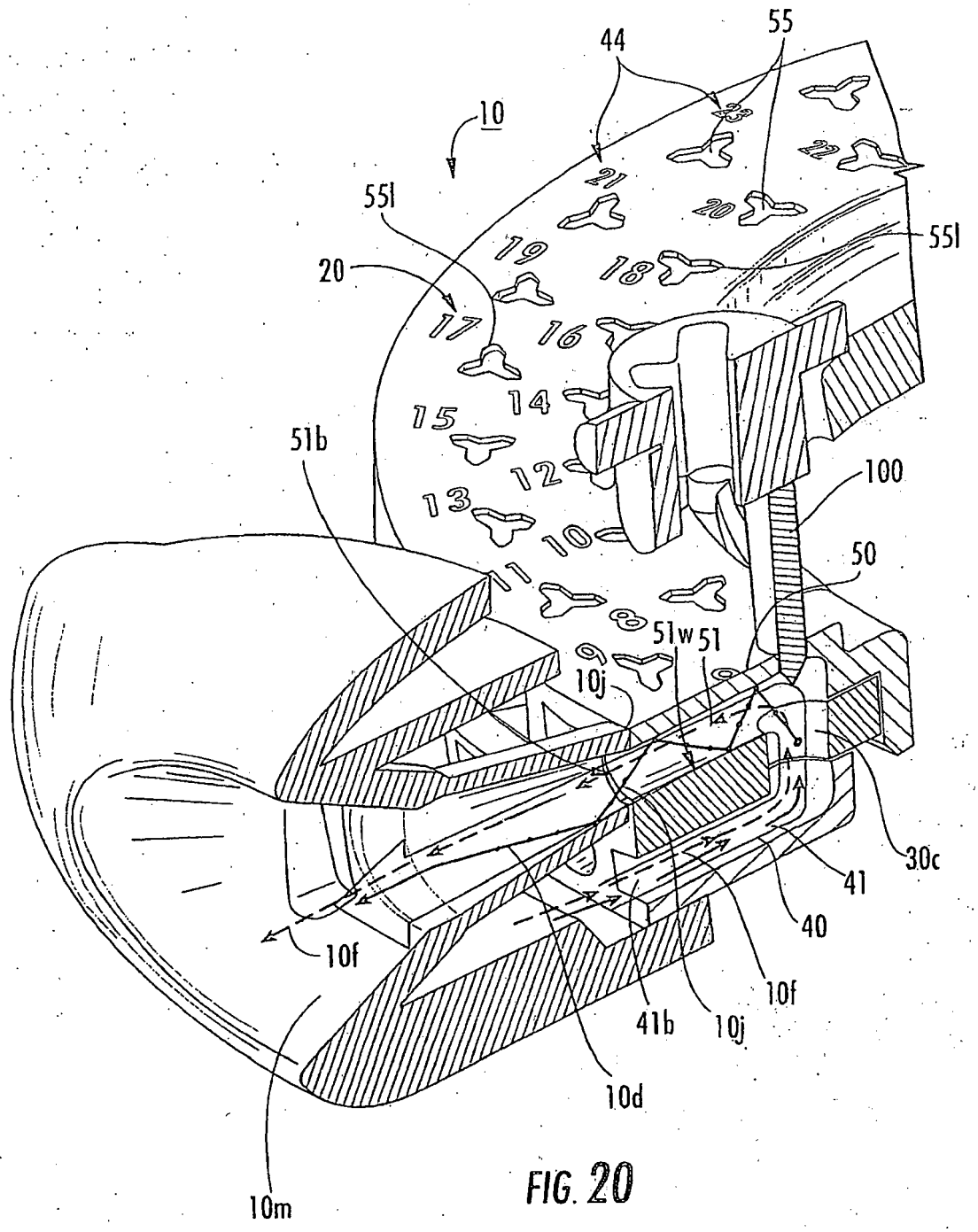


FIG. 19G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41b
10j
10d
10f
10m

FIG. 20

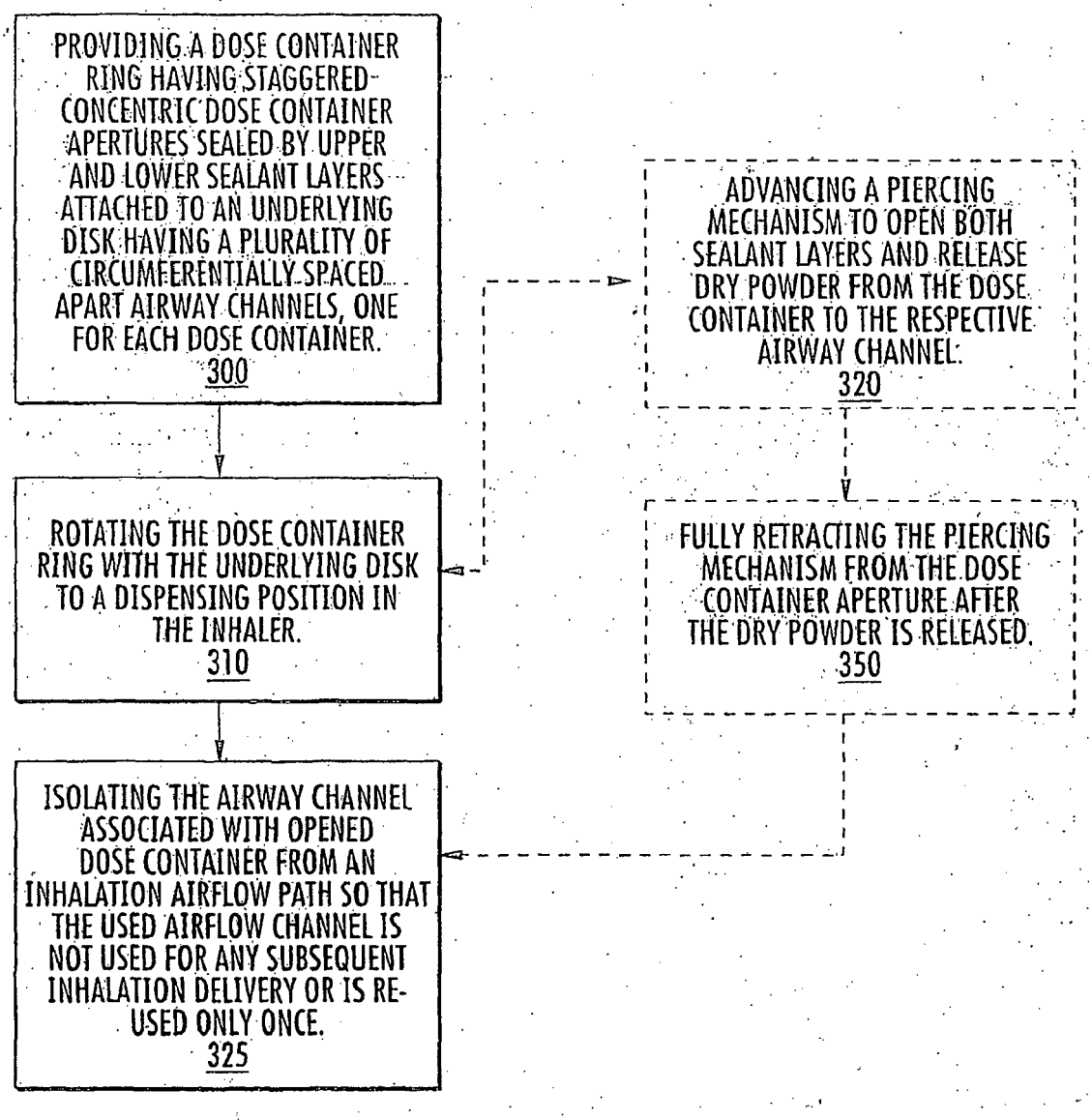
PROVIDING A DOSE CONTAINER RING HAVING STAGGERED CONCENTRIC DOSE CONTAINER APERTURES SEALED BY UPPER AND LOWER SEALANT LAYERS ATTACHED TO AN UNDERLYING DISK HAVING A PLURALITY OF CIRCUMFERENTIALLY SPACED APART AIRWAY CHANNELS, ONE FOR EACH DOSE CONTAINER.
300
ROTATING THE DOSE CONTAINER RING WITH THE UNDERLYING DISK TO A DISPENSING POSITION IN THE INHALER.
310
ISOLATING THE AIRWAY CHANNEL ASSOCIATED WITH OPENED DOSE CONTAINER FROM AN INHALATION AIRFLOW PATH SO THAT THE USED AIRFLOW CHANNEL IS NOT USED FOR ANY SUBSEQUENT INHALATION DELIVERY OR IS RE-USED ONLY ONCE.
325
ADVANCING A PIERCING MECHANISM TO OPEN BOTH SEALANT LAYERS AND RELEASE DRY POWDER FROM THE DOSE CONTAINER TO THE RESPECTIVE AIRWAY CHANNEL.
320
FULLY RETRACTING THE PIERCING MECHANISM FROM THE DOSE CONTAINER APERTURE AFTER THE DRY POWDER IS RELEASED.
350

FIG. 21

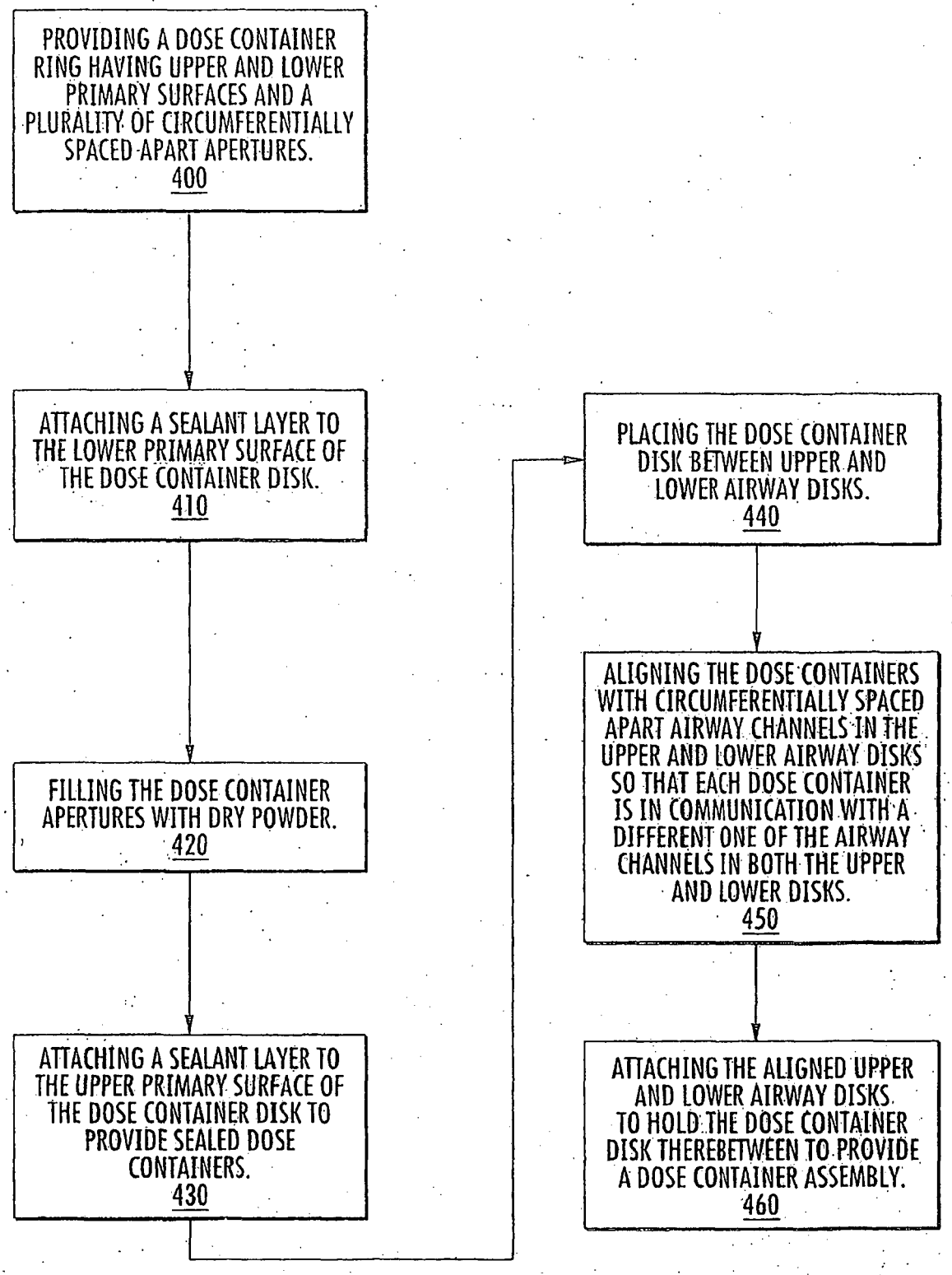
PROVIDING A DOSE CONTAINER RING HAVING UPPER AND LOWER PRIMARY SURFACES AND A PLURALITY OF CIRCUMFERENTIALLY SPACED APART APERTURES. 400
ATTACHING A SEALANT LAYER TO THE LOWER PRIMARY SURFACE OF THE DOSE CONTAINER DISK. 410
FILLING THE DOSE CONTAINER APERTURES WITH DRY POWDER. 420
ATTACHING A SEALANT LAYER TO THE UPPER PRIMARY SURFACE OF THE DOSE CONTAINER DISK TO PROVIDE SEALED DOSE CONTAINERS. 430
PLACING THE DOSE CONTAINER DISK BETWEEN UPPER AND LOWER AIRWAY DISKS. 440
ALIGNING THE DOSE CONTAINERS WITH CIRCUMFERENTIALLY SPACED APART AIRWAY CHANNELS IN THE UPPER AND LOWER AIRWAY DISKS SO THAT EACH DOSE CONTAINER IS IN COMMUNICATION WITH A DIFFERENT ONE OF THE AIRWAY CHANNELS IN BOTH THE UPPER AND LOWER DISKS. 450
ATTACHING THE ALIGNED UPPER AND LOWER AIRWAY DISKS TO HOLD THE DOSE CONTAINER DISK THEREBETWEEN TO PROVIDE A DOSE CONTAINER ASSEMBLY. 460

FIG. 22

REFERENCES CITED IN THE DESCRIPTION

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- WO 02053215 A **[0003]**
- US 2007235029 A **[0003]**
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- **HICKEY et al.** A new millennium for inhaler technology. *Pharm. Tech.,* 1997, vol. 21 (6), 116-125 **[0003]**
- **WOLFF et al.** Generation of Aerosolized Drugs. *J. Aerosol. Med.,* 1994, 89-106 **[0040]**