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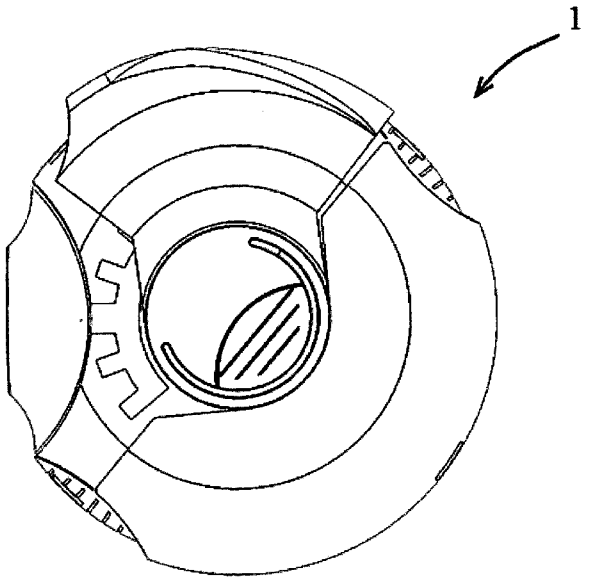
(54) **Title**: DRY POWDER INHALER MOUTHPIECE BUTTON

FIG.1



(57) **Abstract**: The present invention relates to an inhaler which is appropriate for delivering the medicament in dry powder form used in the treatment of respiratory diseases, particularly in asthma, chronic obstructive pulmonary disease (COPD) and allergic rhinitis. Furthermore, the inhaler pertaining to the present invention is an inhaler contributing to realize a hygienic and an effective inhalation.

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INHALER DEVELOPED FOR DELIVERING MEDICAMENT IN DRY POWDER FORM

Field of Invention

The present invention relates to an inhaler which is appropriate for delivering the medicament in dry powder form used in the treatment of respiratory diseases, particularly in asthma and chronic obstructive pulmonary disease (COPD). In addition, the present invention relates to an inhaler developed for delivering the medicament in dry powder form.

Description of the Prior Art

It is well known to use inhalers for delivering medicaments utilized in the treatment and prophylaxis of respiratory diseases by the oral route. Inhalation treatment is the most commonly preferred treatment method in these diseases as the inhalers provide ease of use; the medicaments have more rapid onset of time resulting from local administration and they have fewer side effects. Various inhalers have been designed in order to provide effective and sufficient delivery of the medicaments used in the treatment of respiratory diseases, particularly in asthma and chronic obstructive pulmonary disease. These inhalers vary according to their operating mechanisms, some properties they hold and the physical form of the medicament to be delivered.

It is possible to obtain more effective results by delivering the medicaments in dry powder form compared to delivery in other forms in terms of enabling controlled dosing. However, some problems may be encountered in the delivery of the medicament in dry powder form. One of the most significant problems encountered in the delivery of the medicament in dry powder form is bacterial ingress into the device and failure in realizing hygienic inhalation resulting from bacterial accumulation in the mouthpiece of the device that is in contact with the patient's mouth during the inhalation as the inhaler carrying medicament in dry powder form cannot be protected properly and taken everywhere. To bring various conventional solutions aiming this problem such as developing covers which protect the mouthpiece and the inner mechanism of the device better can enable hygienic inhalation to a certain extent, yet fail to prevent some amount of the dry powder medicament to remain in the device.

The inhaler marketed under the trade mark Diskus® by GlaxoSmithKlein and the inhaler marketed under the trademark SPIRIVA® Handihaler® by Boehringer Ing. and Pfizer are among the most well-known inhalers on the market. These devices are commonly used inhalers in delivery of medicament in dry powder form; however, they do not have the characteristics that guarantee the realization of effective and hygienic inhalation in each actuation of the device.

The inventor has surprisingly found that the amount of residual dry powder medicament in the device significantly decreases in addition to attaining to hygienic inhalation in the case that each component of the device, particularly the components that the medicament in dry powder form passes through in course of the inhalation, is coated with antistatic materials and antibacterial substances or these components are manufactured from substances comprising antistatic and antibacterial substances in the inhalers appropriate for delivery of dry powder medicament.

To this respect, the present invention relates to inhalers which enable hygienic and effective inhalation used for delivery of medicaments in dry powder form.

Summary of the Invention

An inhaler suitable for delivery of the medicament in dry powder form according to the present invention is characterized in that each component of the device,

- is coated with antistatic substance and/or antibacterial substance, or
- is made of substances comprising antistatic and/or antibacterial substance.

The components possessing the characteristics specified above are preferably the components that the medicament in dry powder form passes through in course of inhalation.

The components defined as the components that the medicament in dry powder form passes through during inhalation are mouthpiece; the component which is generally called as the manifold that resides between the mouthpiece and the place that the dry powder medicament is situated; the channel or the channels interconnecting the manifold and the mouthpiece; the apertures that the medicament in dry powder form passes through and the components that the medicament in dry powder form is in contact with

such as sieves. In addition to this, the surfaces that the medicament in dry powder form is in contact with are the inner faces of the device.

In course of the inhalation, bacteria in the mouth or external bacteria that adhere on the mouthpiece accumulate in the mouthpiece part of the device which is in contact with the mouth. In addition, external bacteria may accumulate in the device since the device can be taken everywhere. The fact that the bacteria accumulated in certain parts of the device are inhaled with the medicament in dry powder form as all parts of the device cannot be cleaned or the mouthpiece of the device cannot be cleaned frequently and adequately causes an unhealthy inhalation to be realized. To this end, the surface of each component of the device particularly the mouthpiece part and the components that the medicament in dry powder form passes through are coated with antibacterial substance or these components are made of materials comprising antibacterial substance.

The expression "an effective inhalation" refers to an inhalation enabling the delivery of the required amount of the active agent for the treatment to the lungs of the patient.

So as to realize an hygienic and effective inhalation, surface of each component of the inhaler, preferably the components that the medicament in dry powder form passes through, is coated with antibacterial and/or antistatic substance. The coating on the surfaces of said components of the device pertaining to the present invention is made preferably using fluids comprising antibacterial substance and/or antistatic substance. Furthermore, antibacterial and/or antistatic substance-coated zones can be created on the surface of each component of the device pertaining to the present invention. Each of these zones can comprise solely antibacterial substance or solely antistatic substance or both antibacterial and antistatic substance. Nevertheless, each of these zones can comprise antibacterial and/or antistatic substances at different density. In addition, the coating comprising antibacterial and/or antistatic substance can be coated on the specified components of the device preferably by surface spraying procedure.

The coating containing antibacterial and/or antistatic substances which is used to coat the specified components of the device pertaining to the present invention with the purpose of realizing a hygienic and effective inhalation comprises;

- antibacterial substance in the range of 0,002% to 7%, preferably in the range of 0,01% to 4% of the total weight of the coating, and/or

- antistatic substance in the range of 0,001% to 6%, preferably in the range of 0,01% to 5% of the total weight of the coating.
- The specified components of the device pertaining to the present invention can be made of materials comprising antibacterial and/or antistatic substances in order to realize a hygienic and effective inhalation. Each component of the inhaler comprising antibacterial substance and/or antistatic substance comprises;
- antibacterial substance in the range of 0,001% to 8%, preferably in the range of 0,01% to 5% of the total weight of the device component, and/or
- antistatic substance in the range of 0,002% to 8%, preferably in the range of 0,01% to 6% of the total weight of the device component.

In addition, said components of the inhaler pertaining to the present invention can be made of materials comprising either antibacterial substance or antistatic substance, or they can be coated with coatings comprising either one of these. Furthermore, said components of the inhaler pertaining to the present invention can be made of materials comprising both an antibacterial substance and an antistatic substance, or they can be coated with coatings comprising both substances.

The inhaler pertaining to the present invention is an inhalation device enabling delivery of medicament in dry powder form to the patient such as Foradil (NOVARTIS), Diskus /Glaxo Smithkline), SPIRIVA® Handihaler® (Boehringer Ing. and Pfizer). This device enables delivery of the medicament in dry powder form from blister package, capsule or reservoir.

The blister package providing to carry the medicament in dry powder form in the inhaler pertaining to the present invention is composed of blister pockets each of which generally contain one dose of medicament in dry powder form. The capsule used to carry the medicament in dry powder form generally contains one dose of medicament in dry powder form. In both inhaler types, the dry powder medicament in the capsule or the blister pocket that is opened upon the actuation of the device is generally entrained to the mouthpiece through the manifold. As the air flow which enters the device upon the inhalation of the patient and entrains the medicament in dry powder form passes through the manifold faster than it passes through the other components, the rate of electrostatic charge generation in the manifold is far more than the other components in course of the inhalation. To this respect, the surface of the manifold through which the airflow

entraining the medicament in dry powder form passes, particularly the inner surface of the manifold that is in contact with the air, can preferably be coated with a coating comprising only antistatic substance or the manifold component can preferably be made of a material comprising only antistatic substance in order to lower the manufacturing costs. In addition, some other components through which the airflow containing the medicament in dry powder form passes rapidly such as the channel which interconnects the manifold and the mouthpiece and through which the medicament in dry powder form passes in some devices. These components can preferably be made of materials comprising only antistatic substance and the inner surface through which the airflow containing the medicament in dry powder form passes can be coated with a coating comprising only antistatic substance. Thus, the amount of the dry powder medicament which remains in the device during the inhalation is substantially reduced.

The mouthpiece which is in contact with the patient's mouth in course of inhalation is the device component wherein the most bacteria are accumulated. To this respect, the mouthpiece of the device can preferably be coated with a coating comprising only antibacterial substance or it can preferably be made of a material comprising only antibacterial substance in order to decrease the manufacturing costs. Hygienic inhalation of the medicament in dry powder is substantially enabled in this way.

The antistatic substances mentioned in the present invention are preferably selected from a group comprising nitrogenous compounds such as long chain amines, amides, quaternary bases and salts thereof; glycerin esters; sulphonic acids or sulphonates; phosphoric acids or salts thereof; polyglycol or polyalcohol derivatives; monoglycerides of saturated natural fats; cholinesterase chlorides of straight-chain natural fatty acids; dietanolamid of natural saturated fatty acids with lauric acid dietanolamid; sodium pyrophosphate; potassium acetate or combinations thereof.

The antibacterial substances mentioned in the present invention are preferably selected from a group comprising organic compounds such as halogenated diphenyl ethers (e.g. Triclosan), phenyl compounds, halophenoics and bisphenolic compounds, resorcinol and derivatives thereof, benzoic esters, quaternary ammonium compounds; metals such as silver, zinc and copper; other inorganic compounds such as zeolites and Na-Al silicates; natural products comprising chitosan and vegetable oils or combinations thereof.

The blister package used in the inhaler comprising blister package pertaining to the present invention carries the medicament in dry powder form in one-dose portions and it is preferably a blister strip and it is preferably peelable. The blister pockets of the blister package each of which contains one dose dry powder medicament are spaced in equal intervals.

According to the present invention, the lid and the base sheets constituting the blister package preferably consist of a plurality of layers. Each of these layers are preferably chosen from a group comprising polymeric layers that are made of various polymeric substances; aluminum foil and fluoropolymer film.

According to the present invention, the lid and base sheets composing the blister package, are sealed very tightly by at least one of the methods comprising cold formed bonding, hot metal bonding, hot metal welding, radio frequency welding, laser welding or ultrasonic welding in order to provide impermeability, more preferably by cold formed bonding method. Since these cold formed bonding methods can be carried out at lower temperatures than hot sealing methods, they are the most appropriate methods to use in the case that the medicament carried in the blister is heat sensitive.

Fluoropolymer film is a polymeric film which is used in blister packs and provides excellent moisture barrier. This chemically inert polymeric film does not cause any change in the taste of the formulation when it is in contact with the dry powder formulation. In addition, it easily constitutes a layered structure with the other polymeric layers which are composed of various polymers. It is appropriate to be transacted with heat.

For preserving the stability of the dry powder formulation stored in the blister package, preferably at least one of the polymeric layers comprises at least one desiccant agent including silica gel, zeolite, alumina, bauxite, anhydrous calcium sulfate, activated carbon and clay which has the property of water absorption in order to decrease gas and moisture permeability of the layer.

According to the invention, the thickness of the aluminum foil in the lid and the base sheets of the blister package are preferably chosen to be in the range of 5 to 80 μm, more preferably in the range of 15 to 65 μm.

According to the invention, the polymeric layers in the lid and the base sheets of the blister pack are made of the same or different polymers. The thickness of these polymeric layers varies according to the type of the polymeric substance used and its properties while they are preferably in the range of 5 to 100 μm, more preferably in the range of 15-60 μm.

The polymers composing the polymeric layer are preferably selected from thermoplastics such as polyethylene, polypropylene, polystyrene, polyolefin, polyamide, polyvinyl chloride, polyurethane or synthetic polymers.

The blister pockets in the blister package can be in any appropriate shape. The plurality of blister pockets spaced at equal intervals on the base sheet of the blister package can be in the same or different shape, structure or volume.

The capsule used in the inhaler comprising capsules pertaining to the present invention can be made of a substance chosen from the group comprising gelatin, chitosan, starch and/or starch derivatives, cellulose ad/or cellulose derivatives or synthetic polymers and it is comprised of intertwining upper and lower compartments. The upper and the lower compartments of said capsule can be made of the same or different materials.

According to this, the capsule material can be selected from, but not limited to, a group comprising hydroxypropyl cellulose, hydroxypropylmethyl cellulose, methyl cellulose, hydroxymethyl cellulose, hydroxyethyl cellulose in the case that the capsule used in the present invention is made of cellulose or its derivatives.

In the case that the capsule used in the present invention is synthetic polymer, the capsule material can be selected from, but not limited to, a group including polyethylene, polyester, polyetheleneteraphtalate, polycarbonate or polypropylene.

In the case that the capsule material used in the present invention is gelatine, additional agents such as polyethylene glycol, sorbitol, glycerol, propylene glycol, polyethylene oxide - polypropylene oxide block copolymers and/or other polyalcohols or polyethers at different molecular weights can be added into it.

Each component of the device pertaining to the present invention can be made of any appropriate substance while it is preferably selected from a group comprising styrene-

acrylonitrile, polyoxymethylene (it is generally named as POM and it is also known as polyacetal or polyformaldehyde), acrylic-polymethylmetacrylate, cellulose acetate, polyetheretherketone, polyvinyl choloride, polyethylene, polypropylene, acrylonitrile butadiene styrene, silicon, polycarbonate, polyamide, polystyrene, polyurathane or fluoropolymer types. The mouthpiece of the device pertaining to the present invention is preferably made of silicon, acrylonitrile butadiene styrene or polyoxymethylene plastics. In addition, the manifold of the inhaler pertaining to the present invention is preferably made of acrylonitrile butadiene styrene or polyoxymethylene plastics. The components made of plastics can be produced by methods such as injection molding. Furthermore, each component of the device can be in any appropriate color.

The reference numbers of the drawings added to exemplify the inhaler pertaining to the present invention which is used to deliver medicament in dry powder form and the detailed description of the invention according to these drawings are given below but the scope of the invention should not be limited to these drawings.

Brief Description of the Drawings

Figure 1 is a perspective view of an inhaler according to the inhaler described in the present invention;

Figure 2 is an exploded view of the inhaler pertaining to the invention;

Figure 3 is a perspective view of the blister pack for use with the inhaler pertaining to the invention;

Figure 4a is a perspective view of the mouthpiece cover of the inhaler pertaining to the invention;

Figure 4b is an exploded view of the communication between the mouthpiece cover, the drive gear and the stabilizing resilient covers in the inhaler pertaining to the invention;

Figure 4c is a cross-sectional view of the communication between the mouthpiece cover, the drive gear and the stabilizing resilient covers in the inhaler pertaining to the invention;

Figure 4d is a cross-sectional view of the communication between the mouthpiece cover, the drive gear and the stabilizing resilient covers in the inhaler pertaining to the invention;

Figure 5 is a lateral view of the inhaler pertaining to the present invention;

Figure 6 is a cross-sectional view of the engagement of the gears composing the gear mechanism with each other in the inhaler pertaining to the present invention;

Figure 7 is a cross-sectional view of the engagement of the gears composing the gear mechanism with each other in the inhaler pertaining to the present invention;

Figure 8 is a cross-sectional view of the blister package delaminating in course of operation of the inhaler pertaining to the present invention.

Detailed Description of the Drawings

The inhaler (1) pertaining to the present invention comprises a gear mechanism situated in the housing (10) between the upper housing member (4a) and the lower housing member (4b) in order to enable the inhalation of the dry powder medicament carried in a blister package (15) as displayed in figures 1 and 2. Each component of the inhaler (1) is positioned at suitable spots on the housing (10) to guarantee their working properly and accurately.

The inhaler (1) pertaining to the present invention shown in Figure 1 is ready for inhalation. In this case, the mouthpiece cover (2) is in the second position and the mouthpiece (14) is entirely exposed. The mouthpiece cover (2) has to be rotated by holding on the carved part (2a) on one end of the mouthpiece cover (2) in order to switch to the second position from the first position wherein the mouthpiece is completely covered. In this way, the mouthpiece (14) is completely exposed when the mouthpiece cover (2) is switched to the second position from the first position and the gear mechanism is triggered by the drive gear (12). The drive gear (12) precisely transmits the movement of the mouthpiece cover (2) to the indexing ratchet wheel (3).

The indexing wheel (8) which engages with the indexing ratchet wheel (3) enables the blister package (15) shown in figure 3 to be indexed. The blister pockets (15a) composing the blister package are received in the recesses (8a) on the indexing wheel and the blister package (15) is indexed when the indexing wheel (8) rotates. In the inhaler

pertaining to the present invention, shapes of the recesses (8a) on the indexing wheel (8) have been designed to match the shapes of the blister pockets (15) composing the blister package (15) for the blister package to be indexed properly.

The blister package (15) shown in figure 3 is composed of the lid sheet (15b) which provides impermeability and the base sheet (15c) on which the blister pockets (15a) are spaced at equal intervals. Each blister pocket contains one dose of medicament in dry powder form comprising one or more active agents.

The rotational movement that the mouthpiece cover (2) of the device executes while switching from the first position to the second is transmitted to the indexing ratchet wheel (3) via the drive gear (12) that the mouthpiece cover (2) engages with. As displayed in figure 2, arms (3a) of the indexing ratchet wheel interlock with the protrusions inside the indexing wheel (8) and rotate the indexing wheel (8) unidirectionally. Therefore, the blister package (15) is indexed forward while the indexing wheel (8a) rotates as the blister pockets (15a) composing the blister package (15) are received in the recesses (8a) of the indexing wheel. The beak (16) in the housing (10) provides the blister package (15) to be peeled while the blister package (15) is indexed and provides one blister pocket (15a) to be opened in response to each actuation of the device (1).

The winding wheel gear (6), which is another component of the gear mechanism, engages with the indexing wheel (8) as displayed in figure 2. The mechanism gear (5) that interlocks the winding wheel (13) from inside has arms (5a) to interlock with the interior teeth of the winding wheel gear (6). When the indexing wheel (12) rotates the winding wheel gear (6), the winding wheel rotates unidirectionally owing to the arms of the mechanism gear (5a) which interlocks with the interior teeth of the winding wheel gear (6) and the lid sheet (15b) which is peeled away while the blister package is indexed is tightly coiled on the resilient wings (13a) of the winding wheel. The base sheet (15c) of the blister package (15) where the blister pockets are spaced is accumulated in a separate part (18a) of the device.

The mouthpiece cover (2) which engages with the gear mechanism and enables to actuate the device is displayed in figure 4a. One end (2a) of the mouthpiece cover is carved such that the mouthpiece cover can be rotated easily. The mouthpiece cover (2) is joined with the gear mechanism via the connection points (29, 30) on both sides of the device (1).

The drive gear (12) is joined with the connection points (30; 29) via the side covers (31a, 31c) as it can clearly be seen in figures 4b, 4c and 4d displaying the communication between the mouthpiece (2), the drive gear (12), the side covers (31a, 31c) and the stabilizing resilient covers (32, 33). Both ends (12a; 12b) of the drive gear are carved such that the ends (31b; 31d) of the side covers can engage.

One end (2a) of the mouthpiece cover (2) is carved such that the thumb can fix on it in order to move the mouthpiece cover easily and rapidly. In the lateral view of the device illustrated in figure 5, the carved part of the mouthpiece cover can also be seen.

There is one stabilizing resilient cover (33; 32) on each connection point (29; 30) of the mouthpiece and on each side cover (31c; 31a), as displayed in figures 4b-4d. These pawls (32a, 33a) under the stabilizing resilient covers interlock with the mouthpiece cover (2) on both sides and hinder the mouthpiece cover's rotation.

Before the inhalation, the resilient parts (32d, 33d) of stabilizing resilient covers illustrated in figures 4b-4d are pressed on for raising the pawls (32a, 33a) and releasing the mouthpiece cover (2) in order to actuate the gear mechanism of the device to prepare one dose of dry powder medicament. Therefore, the gear mechanism of the device is actuated and one blister pocket (15a) is opened for one dose of the dry powder medicament to be ready for inhalation when the resilient parts (32d, 33d) of the stabilizing resilient covers are pressed on and the mouthpiece cover (2) is switched from the first position to the second position simultaneously.

The air which enters the device upon the patient's inhalation passes through the manifold (20), reaches the opened blister, entrains the dry powder medicament in the opened blister and takes it back to the manifold (20). There is a tapered channel between the manifold (20) and the mouthpiece (14) which interconnects these two (figure 2). One half (25a) of this channel is comprised in the upper housing member (4a) while the other half of it (25b) is comprised in the lower housing member. The channel is constituted as a whole when the upper (4a) and the lower (4b) housing members are joined together. Therefore, the medicament in dry powder form entrained by the airflow which enters the device upon the inhalation of the patient is provided to be delivered to the patient by passing through the manifold (20), the channel (25a and 25b) interconnecting the manifold (20) and the mouthpiece, and the mouthpiece (14) respectively.

As can clearly be seen in figures 6 and 7, the indexing wheel (8) which synchronizes with the indexing ratchet wheel (3) is engaged with the winding wheel gear (6) and the pinion gear (11) and the rotation of the indexing wheel (8) causes the pinion gear (11) and the winding wheel gear (6) to rotate. Thus, both the peeled lid sheet (15b) of the indexed blister package (15) is tightly coiled on the resilient wings (13a) of the winding wheel (13) engaging with the mechanism gear (5) which interlocks with the winding wheel gear (6) from inside and also the counter wheel (9) is provided to be moved by the pinion gear (11) and the base gear (7) as a result of the rotation of the indexing wheel (8). It is the small gear (7a) which is under the base gear (7) as attached and directly engages with the counter gear (9). Therefore, the rotation transmitted to the base gear (7) by the pinion gear (11) is transmitted to the counter gear (9) via the small gear (7a) to enable the counter gear (9) to rotate.

As is seen in figure 8, the lid sheet (15b) of the blister package (15) which is peeled away by the beak (16) and the base sheet (15c) are enclosed in separate compartments. The lid sheet (15b) that provides impermeability is indexed over the beak (16) and tightly coiled on the wings (13a) of the winding wheel. The base sheet (15c) of the blister package (15) where the blister pockets (15a) each of which carries one dose of the dry powder medicament are spaced is accumulated in the separated compartment (18a) of the housing (10). In response to each actuation of the device (1), one dose of the dry powder medicament which is prepared for inhalation after one blister pocket (15a) is opened and the air entering the device through the air inlet (22) upon the inhalation of the patient provides to deliver one dose of the dry powder medicament to the patient by entraining it from the blister pocket (15a) to the mouthpiece (14).

The medicament in dry powder form which is stored in blister cavities is manufactured according to the prior art. According to the present invention, the particle sizes of the active agents comprised in the dry powder medicament are smaller than 20 μm, preferably smaller than 10 μm.

The inhaler pertaining to the present invention has been designed so as to deliver the dry powder medicament used in monotherapy or combined therapy. The term "monotherapy" refers to inhalation treatments in which dry powder medicaments comprising a single active agent are used whereas the term "combined therapy" refers to

inhalation treatments in which dry powder medicaments comprising more than one active agents are use used.

The dry powder medicament delivered via the device pertaining to the present invention comprises at least one excipient in addition to the active agent or agents. These excipients are generally chosen from a group comprising monosaccharides (glucose, arabinose, etc.), disaccharides (lactose, saccharose, maltose, etc.), oligo- and polysaccharides (dextran, etc.), polyalcohols (sorbite, mannite, xylite), salts (sodium chloride, calcium carbonate, etc.) or combinations thereof. According to the present invention, the medicament in dry powder form comprises lactose as the excipient. The medicament in dry powder form comprises fine or coarse excipients particles preferably having various particle size ranges in order to deliver the required amount to the lungs.

The active agent or the active agents comprised in the dry powder medicament which is stored in blister packages used in the device pertaining to the present invention can be selected from a group comprising cromolyns, anti-infectives, antihistamines, anti-inflammatories, bronchodilators, steroids, leukotirene inhibitors, PDE IV inhibitors, antitussives, diuretics, anticholinergics, hormones, xanthines and pharmaceutically acceptable combinations thereof.

The active agent comprised in the medicament in dry powder form delivered via the inhaler pertaining to the present invention is preferably selected from a group comprising tiotropium, oxitropium, flutropium, ipratropium, glicopironium, flunisolid, beclomethasone, budesonide, fluticasone, mometasone, ciclesonide, rofleponide, dexamethasone, montelukast, methylcyclopropane acetic acid, sodium cromoglicat, nedocromil sodium, Npropylene, teophylline, roflumilast, ariflo (cilomilast), salmeterol, salbutamol, formoterol, terbutaline, carmoterol, indacaterol, cetirizine, levocetirizine, efletirizine, fexofenadine and their racemates, free base, enantiomers or diastereomers and their pharmaceutically acceptable salts, solvates and/or hydrates or a combination of said active agents.

The device pertaining to the present invention is used in the administration of the medicament in dry powder form which is utilized in the treatment of many respiratory diseases, particularly in asthma, chronic obstructive pulmonary disorder (COPD) and allergic rhinitis. Accordingly, the respiratory diseases include, but not restricted to, allergic or non-allergic asthma at any phases, acute lung injury (ALI), acute respiratory

distress syndrome (ARDS), exacerbation of airways hyperactivity, bronchiectasis, chronic obstructive pulmonary including emphysema and chronic bronchitis, airways or lung diseases (COPD, COAD or COLD), pneumoconiosis, aluminosis, anthracosis, asbestosis, chalicosis, ptilosis, siderosis, silicosis, tabacosis and byssinosis. The device pertaining to the invention can be used in prophylactic or symptomatic treatment. In addition, the medicament in dry powder form which is preferably used in the symptomatic treatment of allergic asthma and COPD is administered to the patient via the device pertaining to the present invention.

Claims

1. An inhaler (1) suitable for delivery of the medicament in dry powder form characterized in that each component of said device,

- is coated with antistatic substance and/or antibacterial substance, or
- is made of a material comprising antistatic and/or antibacterial substance.

2. The inhaler according to claim 1, wherein said device components are preferably the components through which the medicament in dry powder form passes in course of inhalation.

3. The inhaler according to claim 2, wherein the components that the medicament in dry powder form passes through are preferably the mouthpiece (14); the component which is generally called as the manifold (20) that resides between the mouthpiece (14) and the place that the dry powder medicament is situated; the channel (25a; 25b) or the channels interconnecting the manifold (20) and the mouthpiece (14); the apertures (22) that the medicament in dry powder form passes through and the sieve.

4. The inhaler according to claim 1, wherein the coating on said components of the device is made preferably using fluids comprising antibacterial substance and/or antistatic substance.

5. The inhaler according to claim 1, wherein the coating comprising antibacterial and/or antistatic substance which is used to coat each of said device components comprises;

- antibacterial substance in the range of 0,002% to7%, preferably in the range of 0,01% to 4% of the total weight of the coating, and/or
- antistatic substance in the range of 0,001% to 6%, preferably in the range of 0,01% to 5% of the total weight of the coating.

6. The inhaler according to claim 1, wherein each of said device components containing antibacterial substance and/or antistatic substance comprises;

- antibacterial substance in the range of 0,001% to 8%, preferably in the range of 0,01% to 5% of the total weight of the device component, and/or
- antistatic substance in the range of 0,002% to 8%, preferably in the range of 0,01% to 6% of the total weight of the device component.

7. The inhaler according to claim 1, wherein antibacterial and/or antistatic substance-coated zones can be created on the surface of each of said components.

8. The inhaler according to claim 7, wherein each of said zones can comprise solely antibacterial substance or solely antistatic substance or both antibacterial and antistatic substance.

9. The inhaler according to any one of the preceding claims, wherein said antistatic substances are selected from a group comprising nitrogenous compounds such as long chain amines, amides, quaternary bases and salts thereof; glycerin esters; sulphonic acids or sulphonates; phosphoric acids or salts thereof; polyglycol or polyalcohol derivatives; monoglycerides of saturated natural fats; cholinesterase chlorides of straight-chain natural fatty acids; dietanolamid of natural saturated fatty acids with lauric acid dietanolamid; sodium pyrophosphate; potassium acetate or combinations thereof.

10. The inhaler according to any one of the preceding claims, wherein said antibacterial substances are selected from a group comprising organic compounds such as halogenated diphenyl ethers (e.g. Triclosan), phenyl compounds, halophenoics and bisphenolic compounds, resorcinol and derivatives thereof, benzoic esters, quaternary ammonium compounds; metals such as silver, zinc and copper; other inorganic compounds such as zeolites and Na-Al silicates; natural products comprising chitosan and vegetable oils or combinations thereof.

11. The inhaler according to any one of the preceding claims, wherein said inhaler is suitable for delivery of medicament in dry powder form.

12. The inhaler according to any one of the preceding claims, wherein said inhaler comprises capsules or blister package (15) enabling to carry the medicament in dry powder form.

13. The inhaler appropriate for delivery of the medicament in dry powder form according to any one of the preceding claims, wherein said medicament in dry powder form comprises at least one active agent selected from the group comprising cromolyns, steroids, anti-infectives, antihistamines, anti-inflammatories, bronchodilators, leukotirene inhibitors, PDE IV inhibitors, antitussives, diuretics, anticholinergics, hormones, xanthines or pharmaceutically acceptable combinations thereof.

14. The inhaler appropriate for delivery of the medicament in dry powder form according to any one of the preceding claims, wherein said medicament in dry powder form is used in monotherapy or combined therapy.

15. The inhaler appropriate for delivery of the medicament in dry powder form according to any one of the preceding claims, wherein said medicament comprises at least one excipient along with the active agent or agents it comprises.

16. The inhaler according to claim 15, wherein the excipient comprised by said dry powder medicament can be selected from a group comprising monosaccharides (glucose, arabinose, etc.), disaccharides (lactose, saccharose, maltose, etc.), oligo- and polysaccharides (dextran, etc.), polyalcohols (sorbite, mannite, xylite), salts (sodium chloride, calcium carbonate, etc.) or combinations thereof.

17. The inhaler according to claim 15 or 16, wherein the excipient comprised in said dry powder medicament is preferably lactose.

18. The inhaler according to any one of the preceding claims, wherein said device components can be made of a material selected from a group comprising styrene-acrylonitrile, polyoxymethylene, acrylic-polymethylmetacrylate, cellulose acetate, polyetheretherketone, polyvinyl choloride, polyethylene, polypropylene, acrylonitrile butadiene styrene, cellulose, polycarbonate, polyamide, polystyrene, polyurathane or fluoropolymer types.

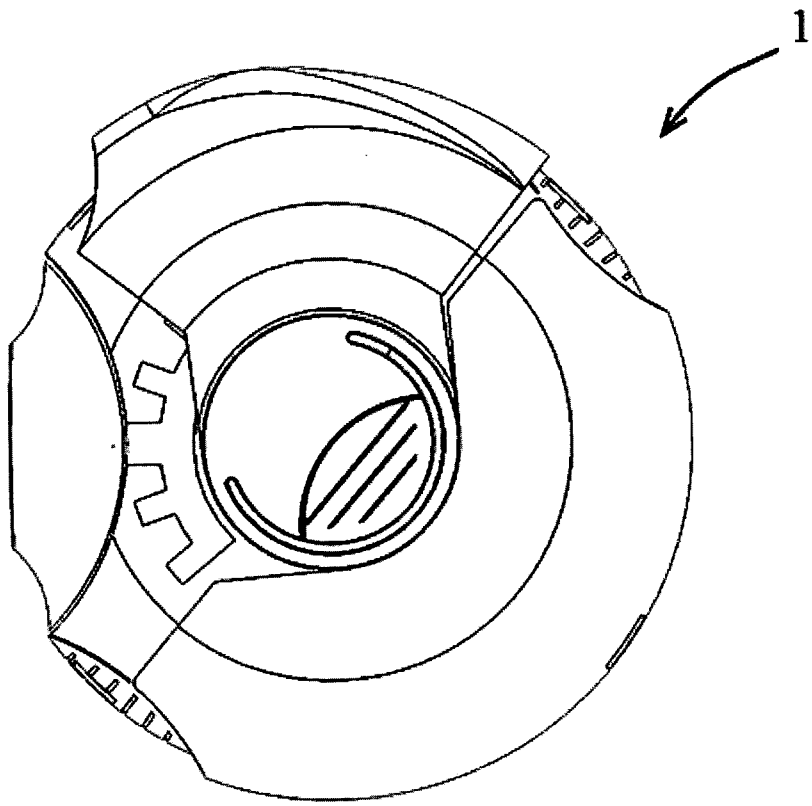
19. The inhaler according to any one of the preceding claims, wherein the surface of said manifold can preferably be coated with a coating comprising only antistatic substance or the manifold component can preferably be made of a material comprising only antistatic substance.

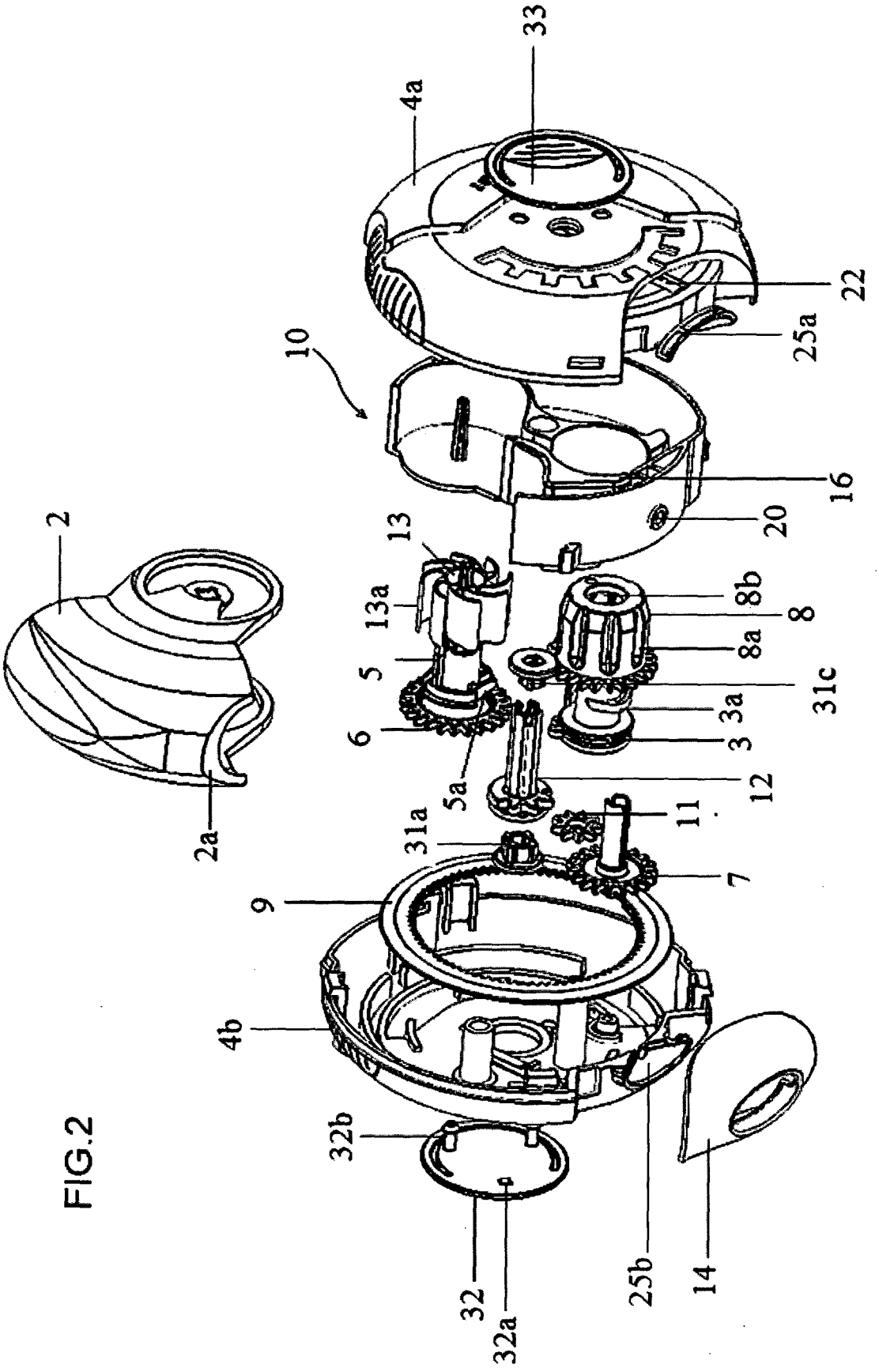
20. The inhaler according to any one of the preceding claims, wherein the mouthpiece of said device can preferably be coated with a coating comprising only antibacterial substance or it can preferably be made of a material comprising only antibacterial substance.

21. The inhaler according to claim 18, wherein said manifold component (20) is preferably made of acrylonitrile butadiene styrene or polyoxymethylene.

22. The inhaler according to claim 18, wherein said mouthpiece component (14) is preferably made of silicone, acrylonitrile butadiene styrene or polyoxymethylene.

FIG.1

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4a
22
25a
10
16
20
2
13
13a
8b
8
8a
5
31c
3a
6
3
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12
11
31a
7
9
4b
32b
32
32a
25b
14
2a

FIG.2

FIG.3

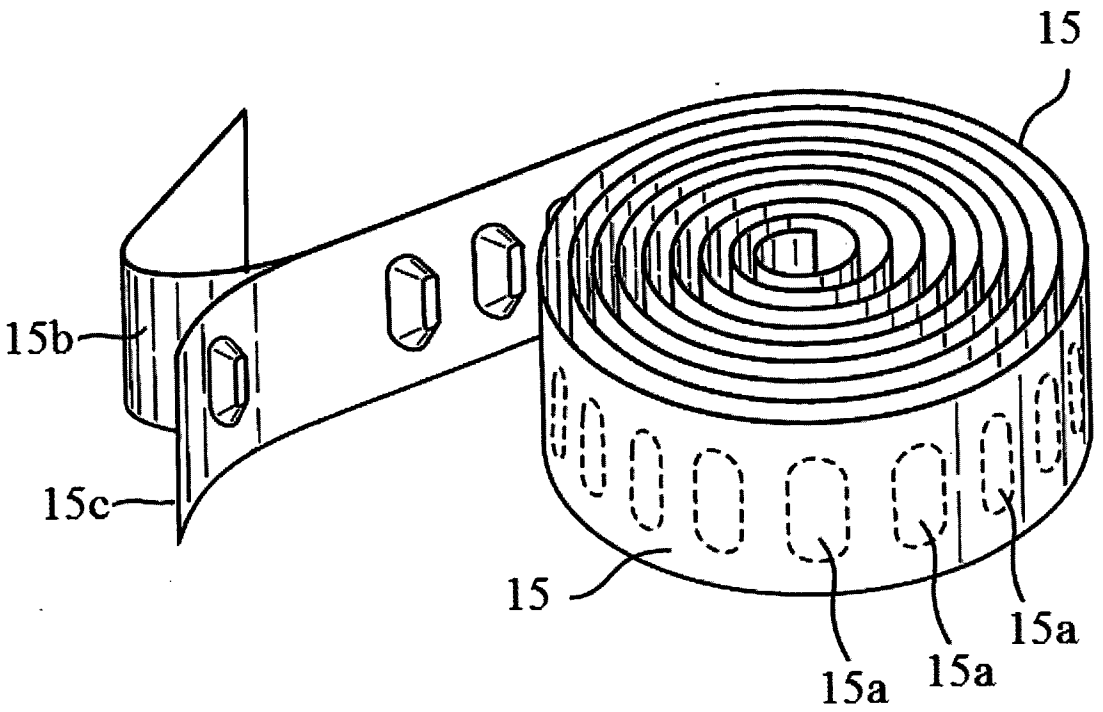


FIG. 4a

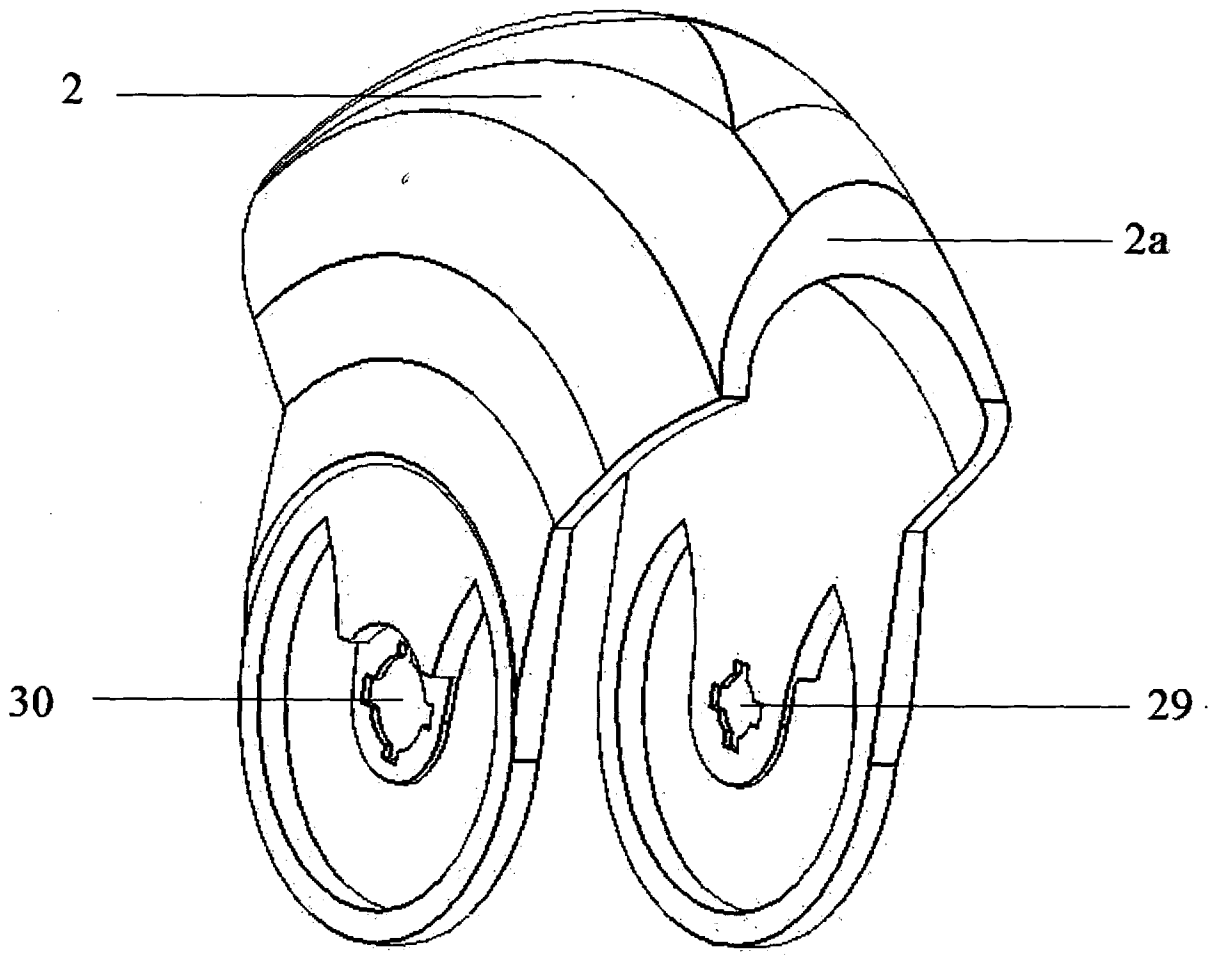


FIG. 4b

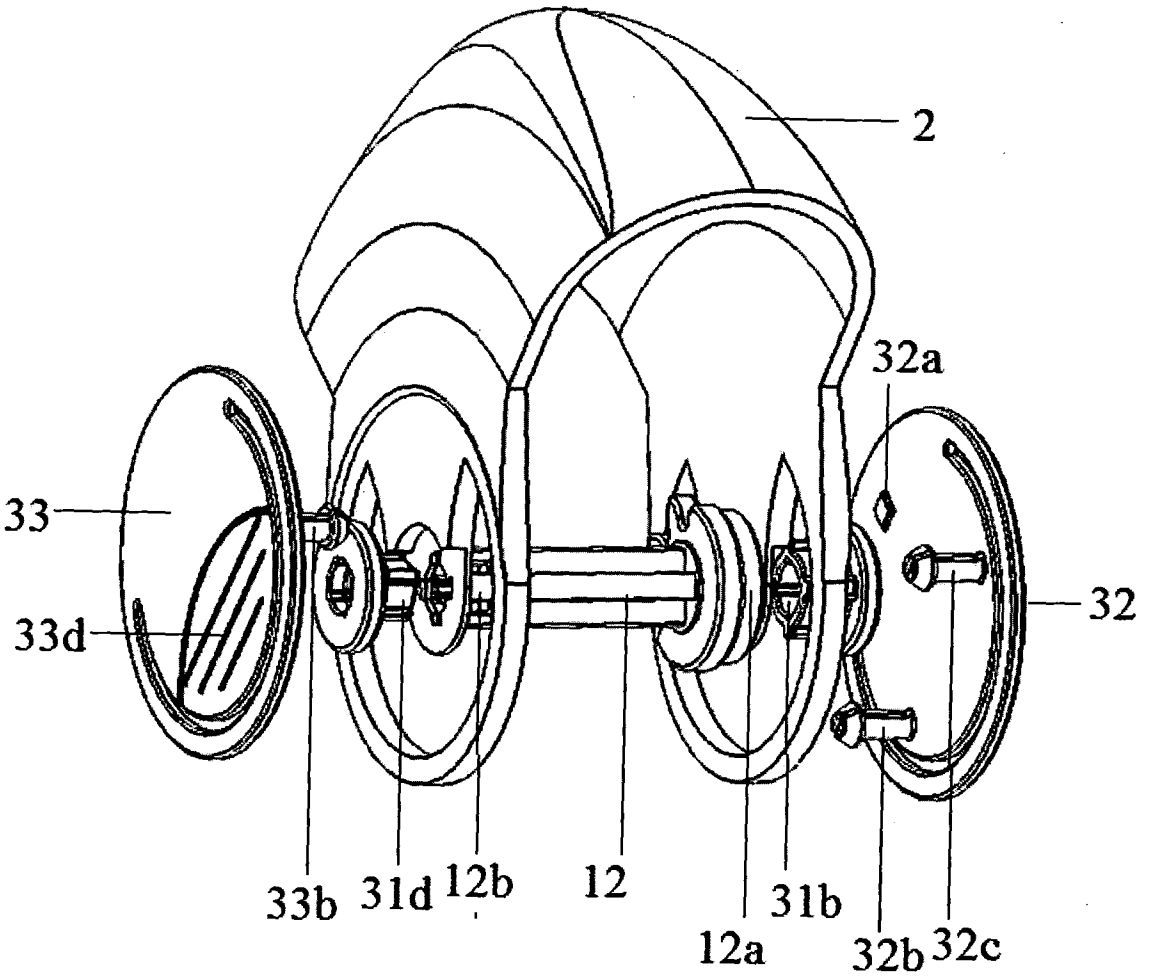


FIG. 4c

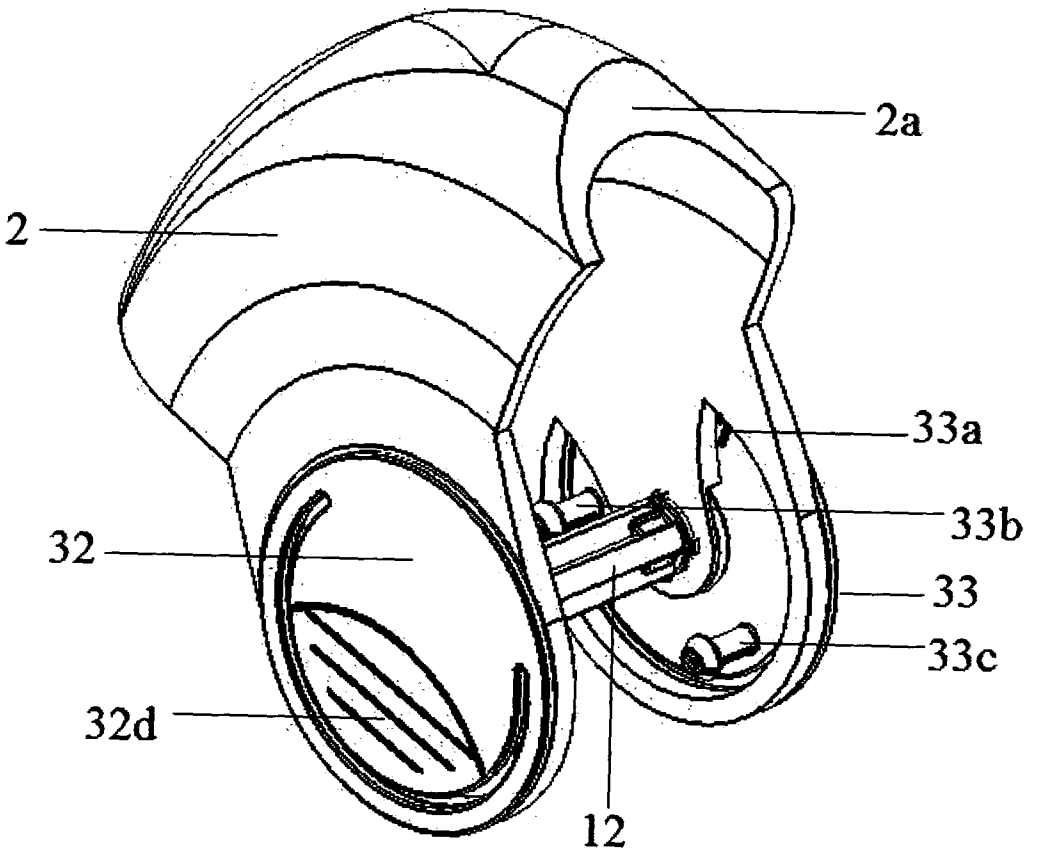


FIG. 4d

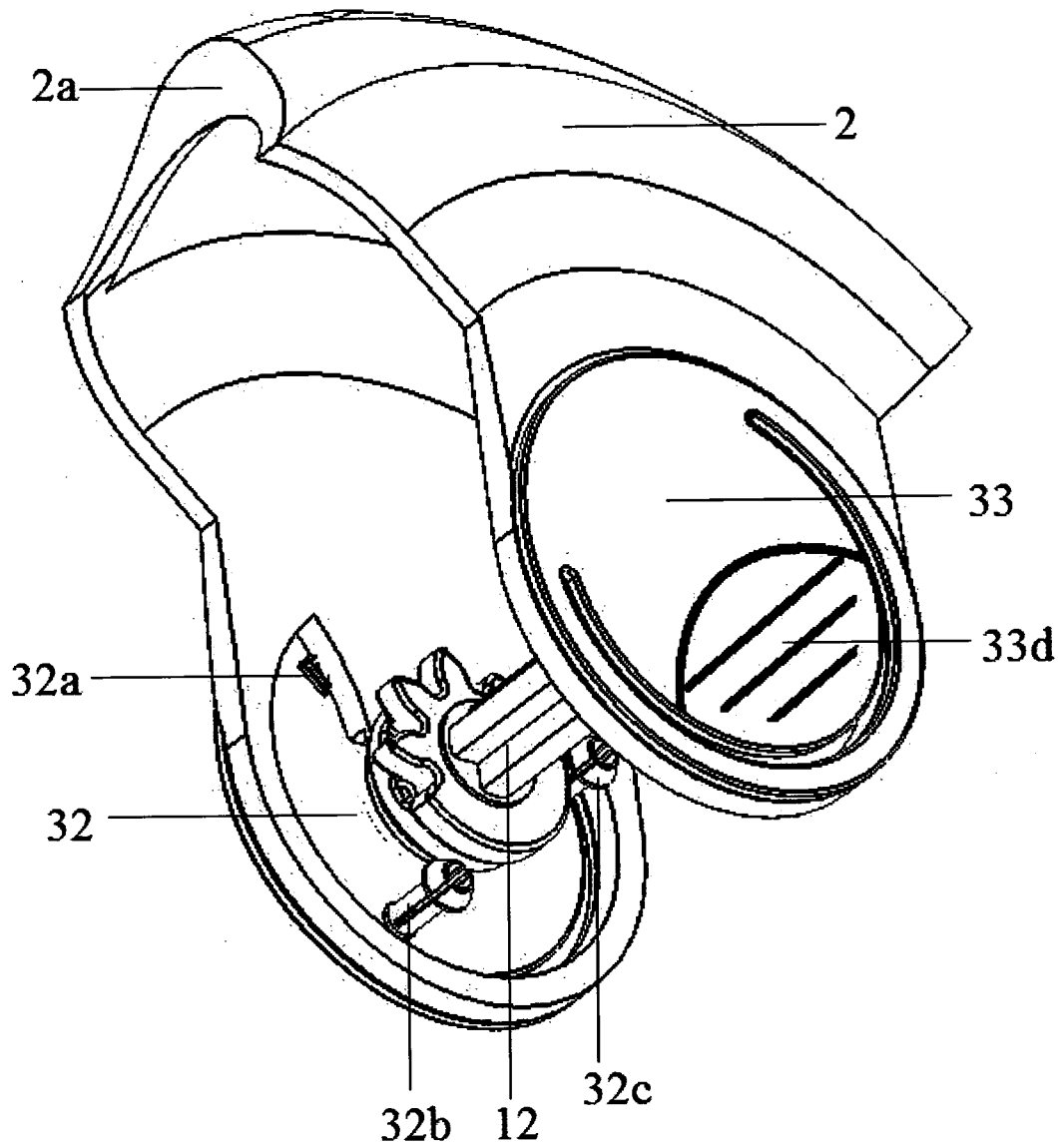


FIG. 5

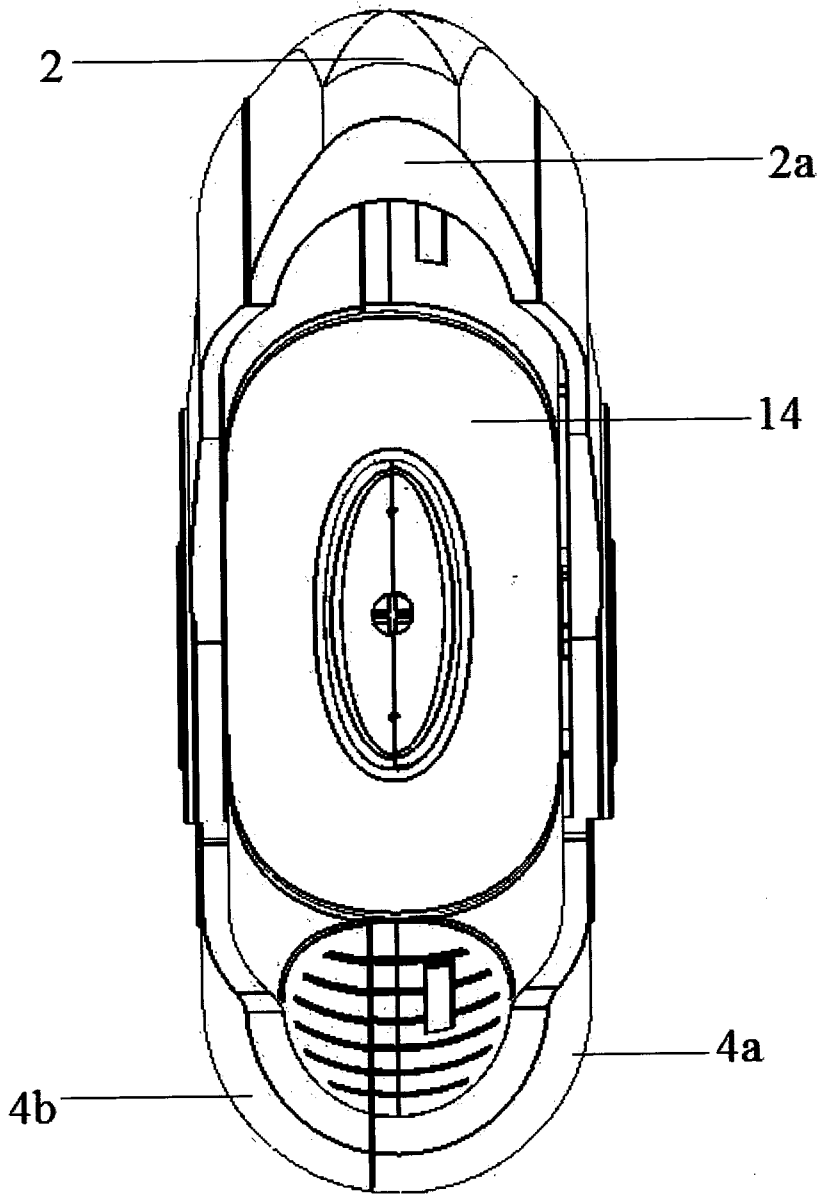


FIG. 6

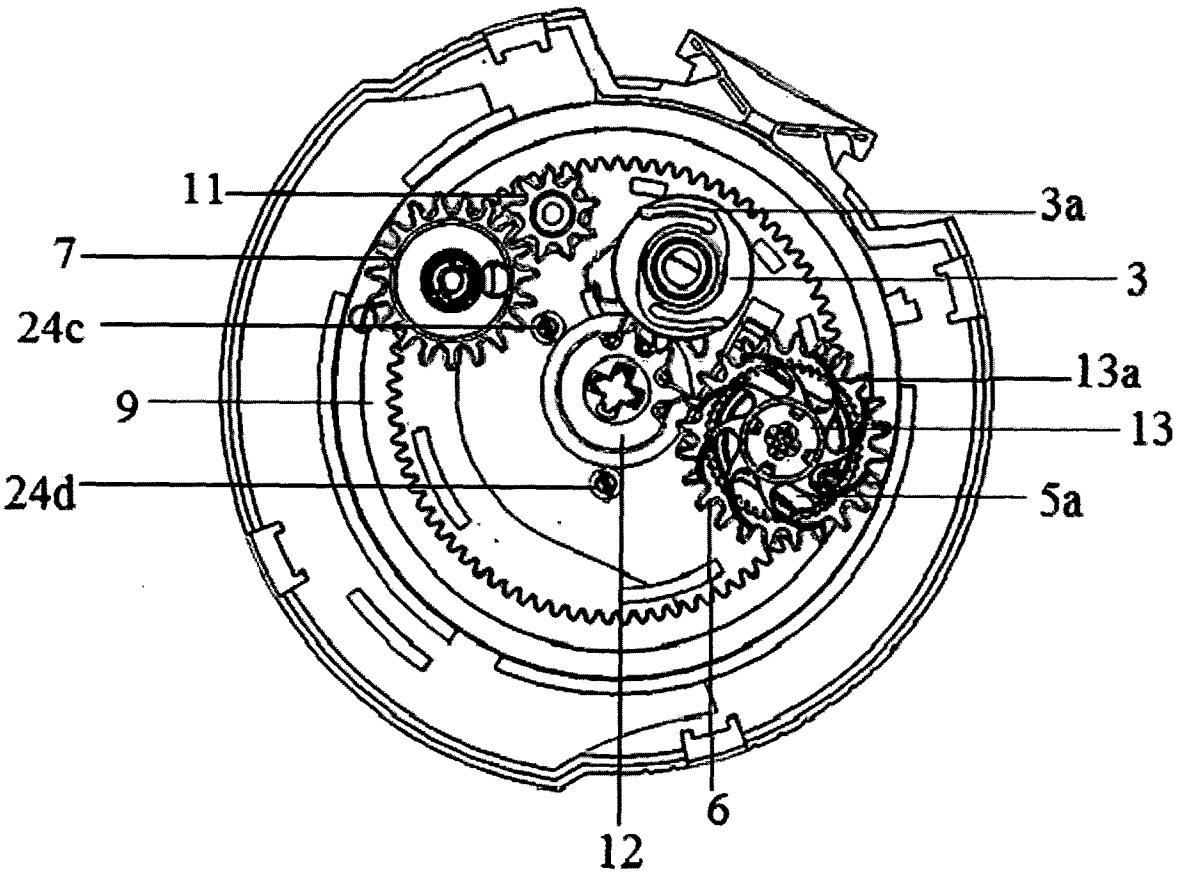


FIG. 7

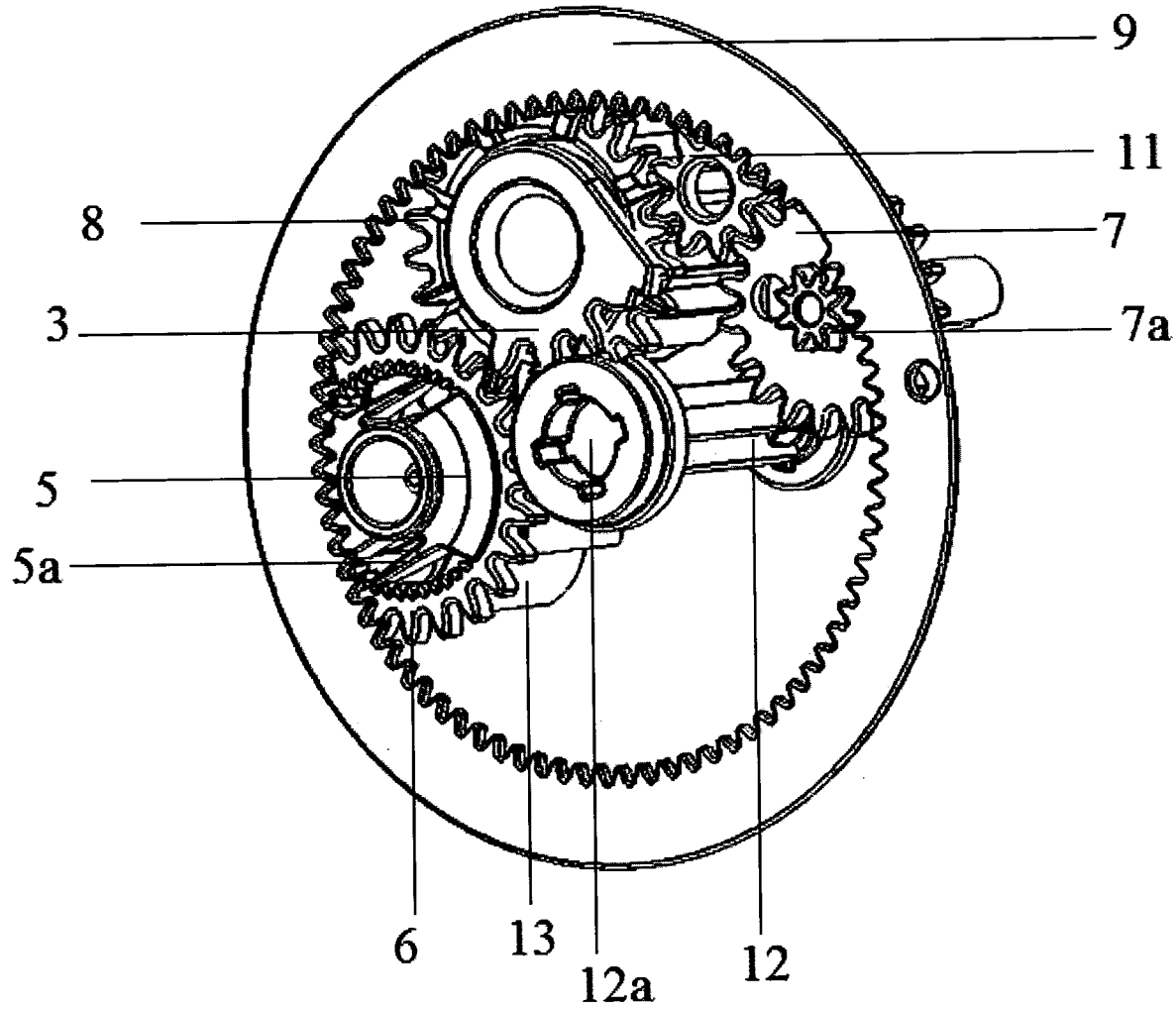
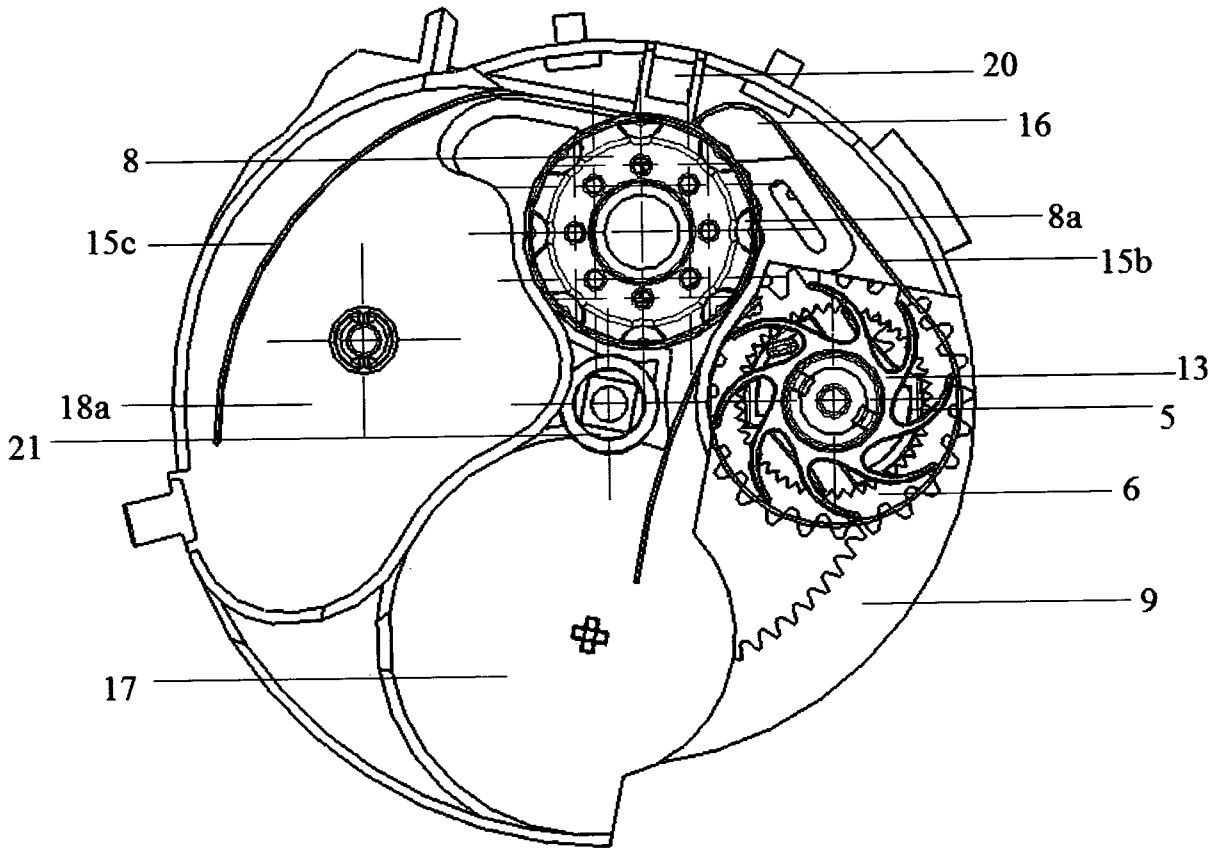


FIG. 8



INTERNATIONAL SEARCH REPORT

International application No
PCT/TR2011/000087

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61M15/00
ADD.

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

B. FIELDS SEARCHED

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

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 6 092 522 A (CALVERT JOHN RICHARD [GB] ET AL) 25 July 2000 (2000-07-25) columns 1-12; figures 1-20	1-22
X	GB 1 459 426 A (ALLEN & HANBURYS LTD) 22 December 1976 (1976-12-22) the whole document	1-22
A	US 6 234 365 B1 (BOUGAMONT JEAN-LOUIS [FR] ET AL) 22 May 2001 (2001-05-22) columns 1-4; figures 1,2	1-22

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

☒ See patent family annex.

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"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
11 August 2011	18/08/2011

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Loughman, John

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/TR2011/000087

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 6092522 A	25-07-2000	AT 162727 T	15-02-1998
		AT 223242 T	15-09-2002
		AU 662686 B2	07-09-1995
		AU 652163 B2	18-08-1994
		CA 2084400 A1	15-12-1991
		CA 2363047 A1	26-12-1991
		CS 9101802 A3	15-01-1992
		DE 69128831 D1	05-03-1998
		DE 69128831 T2	23-07-1998
		DE 69133101 D1	10-10-2002
		DE 69133101 T2	22-05-2003
		DK 0533747 T3	21-09-1998
		EP 0533747 A1	31-03-1993
		EP 0804935 A2	05-11-1997
		ES 2113377 T3	01-05-1998
		ES 2179246 T3	16-01-2003
		FI 925651 A	11-12-1992
		FI 20000886 A	13-04-2000
		WO 9119524 A2	26-12-1991
		GR 3026371 T3	30-06-1998
		HU 64241 A2	28-12-1993
		IE 912015 A1	18-12-1991
		IL 98441 A	31-12-1995
		IL 111254 A	30-10-1998
		JP 3220453 B2	22-10-2001
		JP 5507637 T	04-11-1993
		JP 3381221 B2	24-02-2003
		JP 2001309978 A	06-11-2001
		NO 924810 A	11-12-1992
		NZ 238489 A	26-09-1995
		NZ 250988 A	26-09-1995
		PL 167429 B1	30-09-1995
		PT 97949 A	31-08-1993
		RU 2106881 C1	20-03-1998
		US 5522383 A	04-06-1996
GB 1459426 A	22-12-1976	AU 6539674 A	14-08-1975
		BE 811566 A1	26-08-1974
		CA 1048884 A1	20-02-1979
		CH 563168 A5	30-06-1975
		DE 2408791 A1	05-09-1974
		FR 2218905 A1	20-09-1974
		IT 1008929 B	30-11-1976
		JP 1154491 C	15-07-1983
		JP 50025092 A	17-03-1975
		JP 57050505 B	27-10-1982
GB 1459426 A		NL 7402230 A	28-08-1974
		US 3858583 A	07-01-1975
		ZA 7400553 A	27-11-1974
US 6234365 B1	22-05-2001	AT 275997 T	15-10-2004
		AU 1247099 A	15-06-1999
		BR 9815111 A	10-10-2000
		CA 2311655 A1	03-06-1999
		CN 1280512 A	17-01-2001
		DE 69826311 D1	21-10-2004
		DE 69826311 T2	20-10-2005

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/TR2011/000087

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
		DK 1032447 T3	24-01-2005
		EP 1032447 A1	06-09-2000
		ES 2232971 T3	01-06-2005
		FR 2771296 A1	28-05-1999
		WO 9926688 A1	03-06-1999
		HK 1033100 A1	30-09-2004
		JP 2001523533 A	27-11-2001
		PT 1032447 E	31-01-2005