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(54) INHALER

(75) Inventors: **Stephen William Eason**, Diss (GB); **Matthew Sarkar**, Cambridge (GB); **Graham Gibbins**, Fakenham (GB); **Nicholas John Campling**, Bretton (GB); **Howard William Biddle**, Histon (GB); **Tristian Roger Thornhill**, Peterborough (GB); **Duncan James Bradley**, Ewhurst (GB)

Correspondence Address:
Davidson, Davidson & Kappel, LLC
485 7th Avenue, 14th Floor
New York, NY 10018 (US)

(73) Assignee: **Ventura Delivery Devices Limited**, Chippenham (GB)

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Related U.S. Application Data

(63) Continuation of application No. 12/217,609, filed on Jul. 7, 2008, now abandoned, which is a continuation-in-part of application No. 11/881,582, filed on Jul. 27, 2007.

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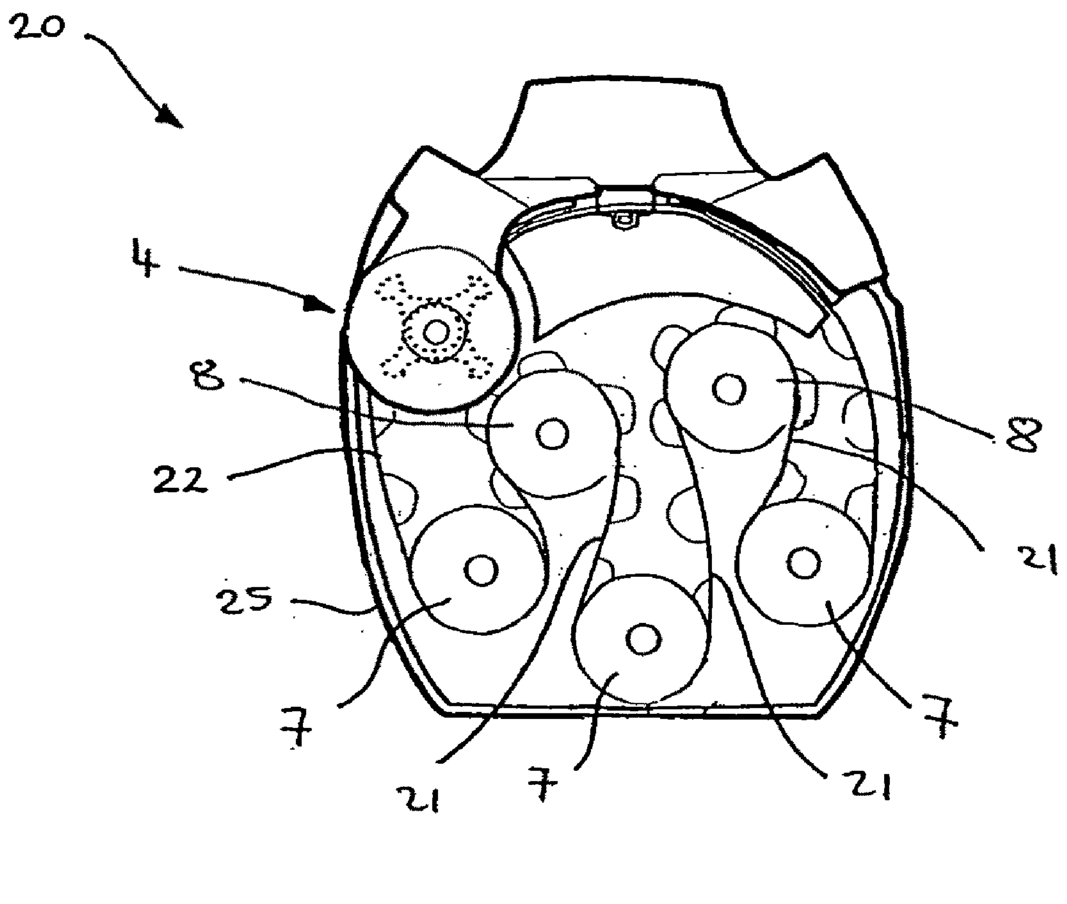
(57) **ABSTRACT**

An inhaler is disclosed. It comprises a housing to receive an elongate strip of blisters each containing a dose of medicament and being sequentially movable into alignment with means for breaching a blister to enable a user to inhale said dose contained therein. The device comprises a spiral wound element within the housing that receives and coils said strip of blisters that have been breached.



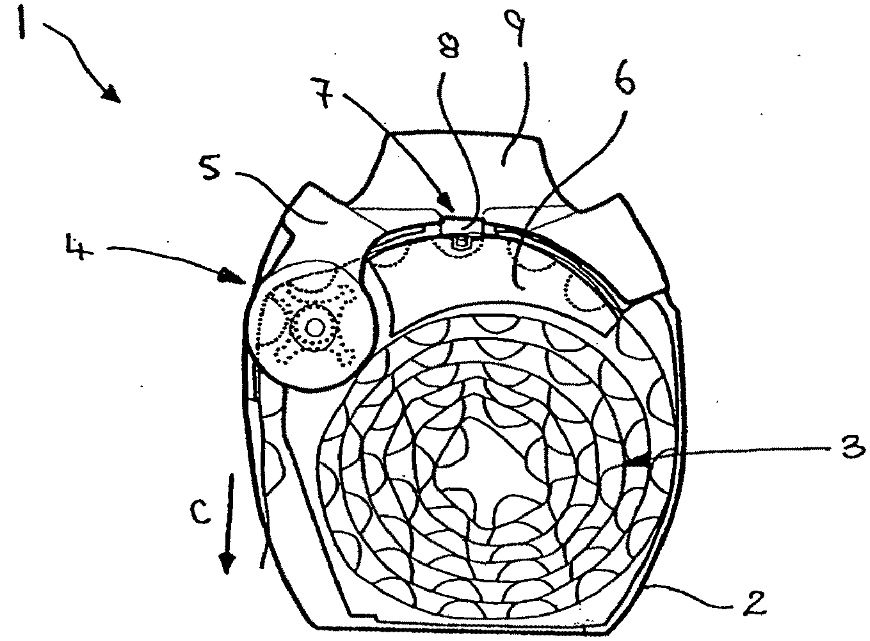


FIGURE 1(a)
(PRIOR ART)

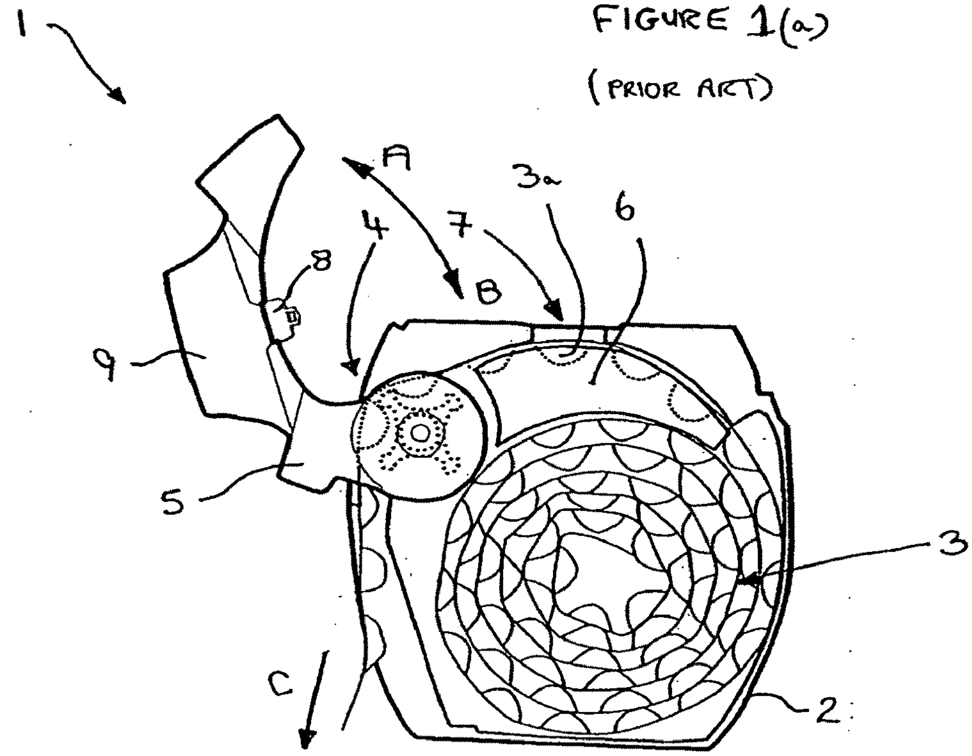


FIGURE 1(b)
(PRIOR ART)

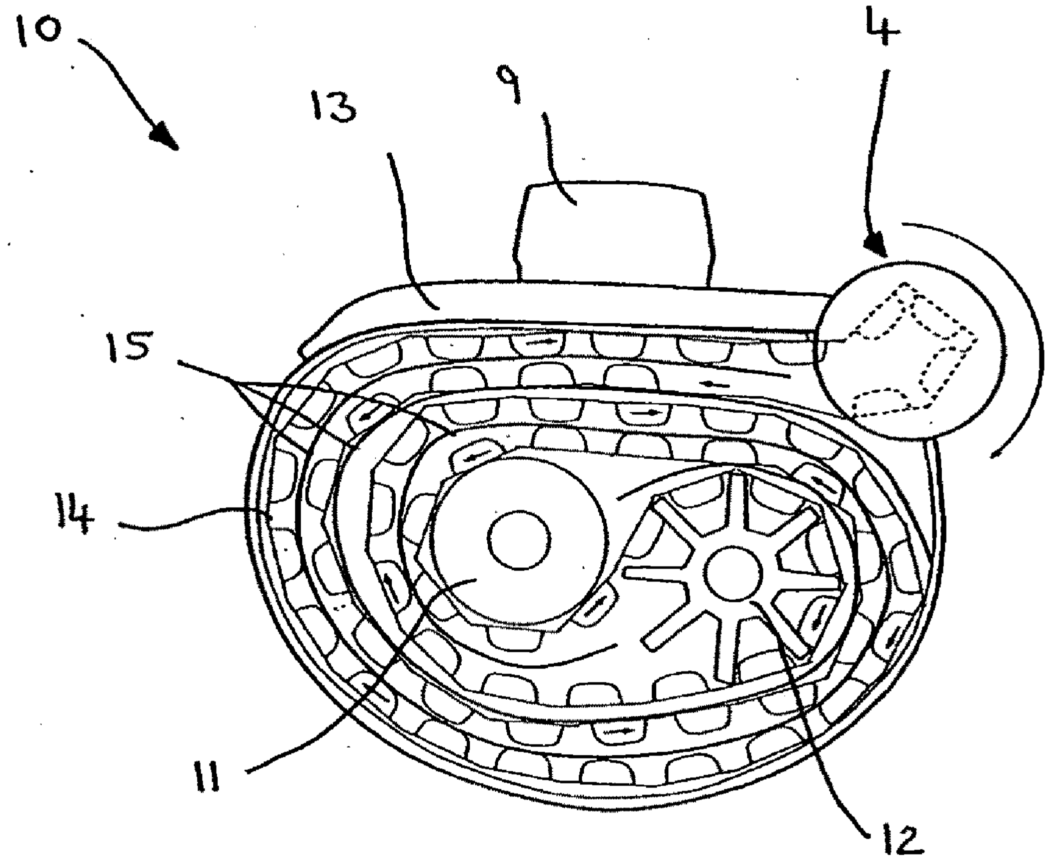


FIGURE 2
(PRIOR ART)

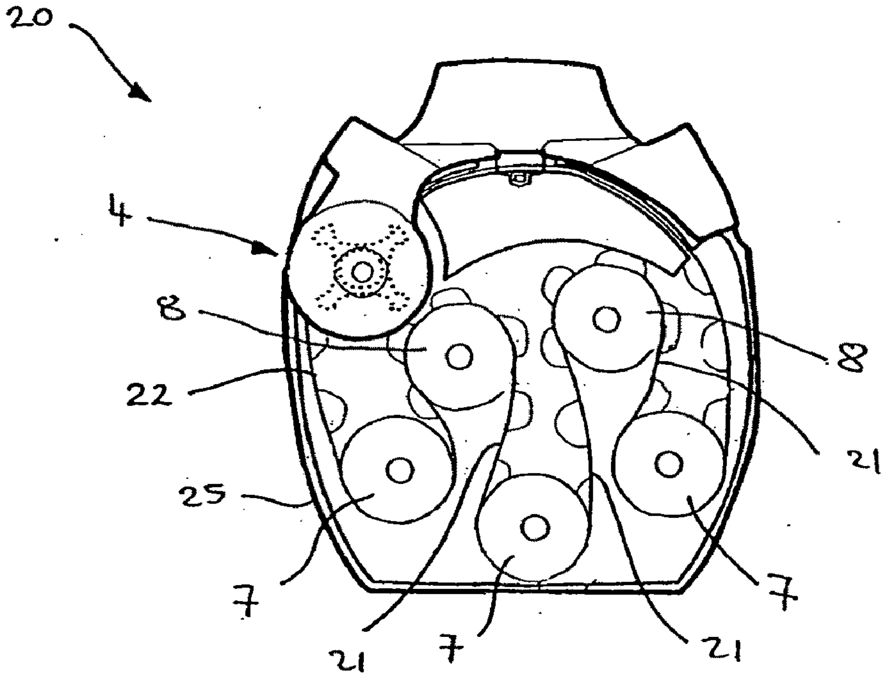


FIGURE 3 (a)

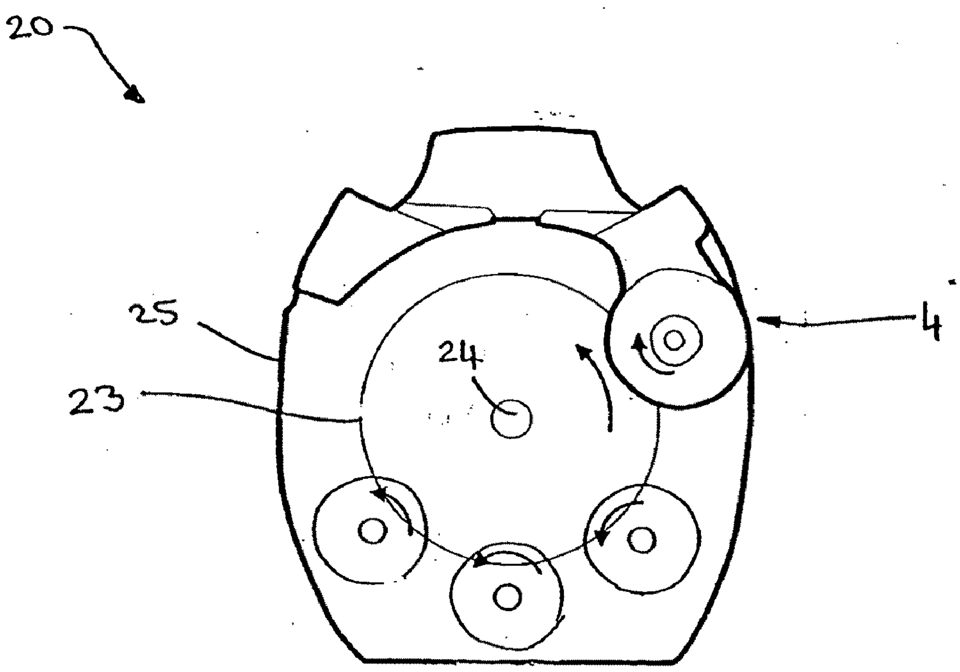


FIGURE 3(b)

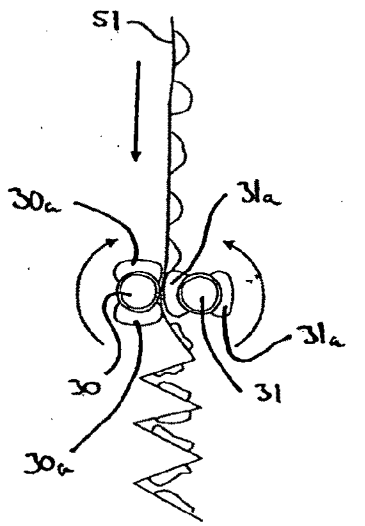


FIGURE 4 (a)

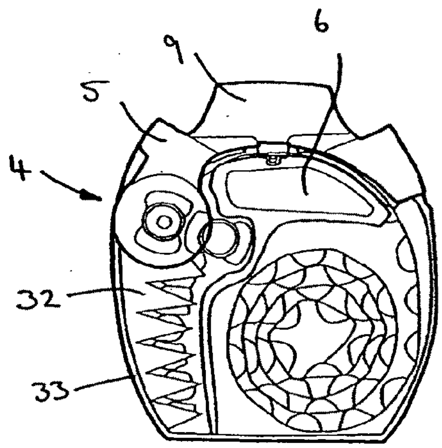


FIGURE 4 (b)

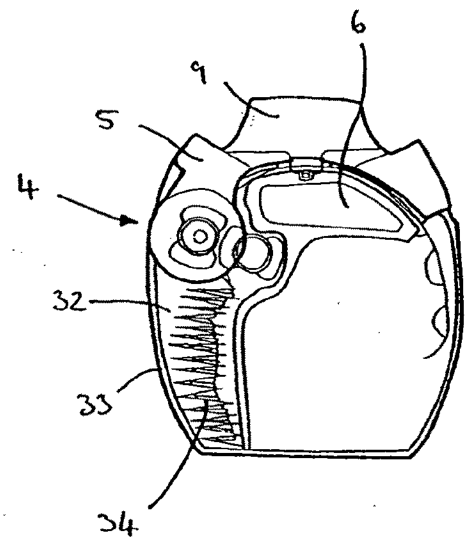


FIGURE 4 (c)

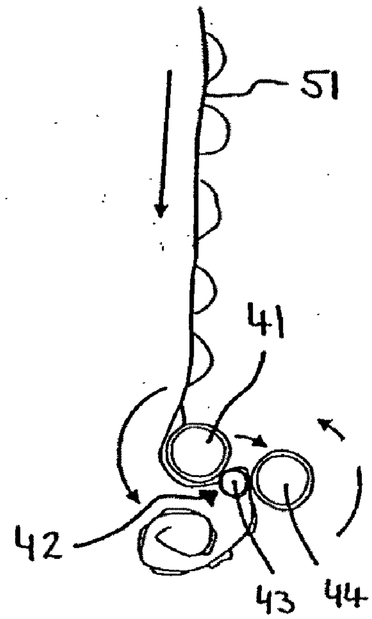


FIGURE 5(a)

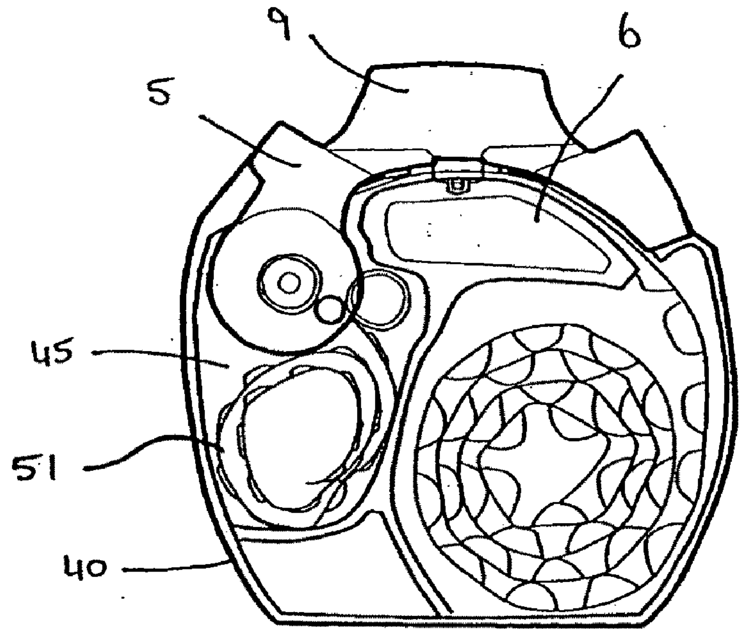


FIGURE 5(b)

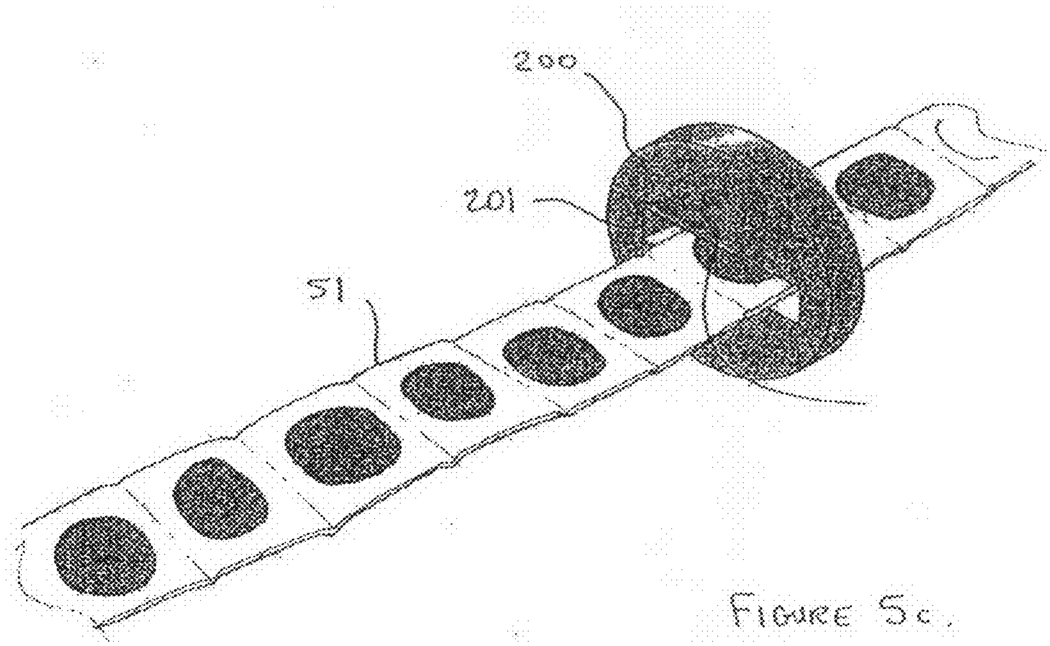


FIGURE 5c.

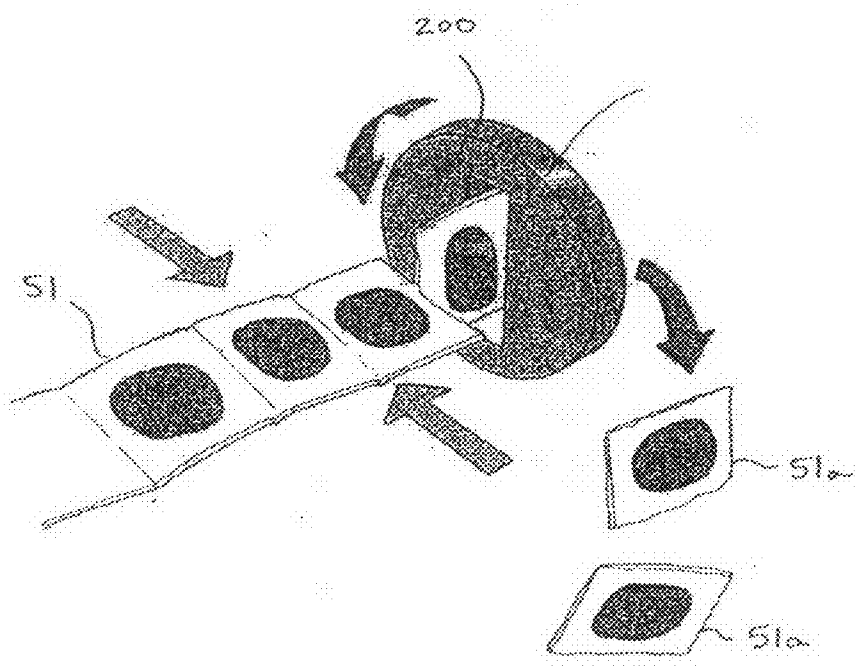


FIGURE 5d.

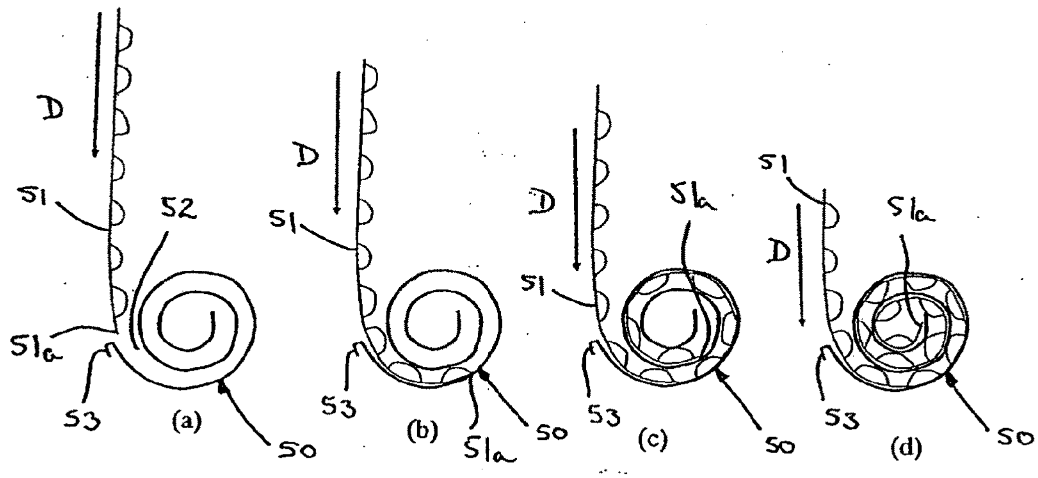


FIGURE 6

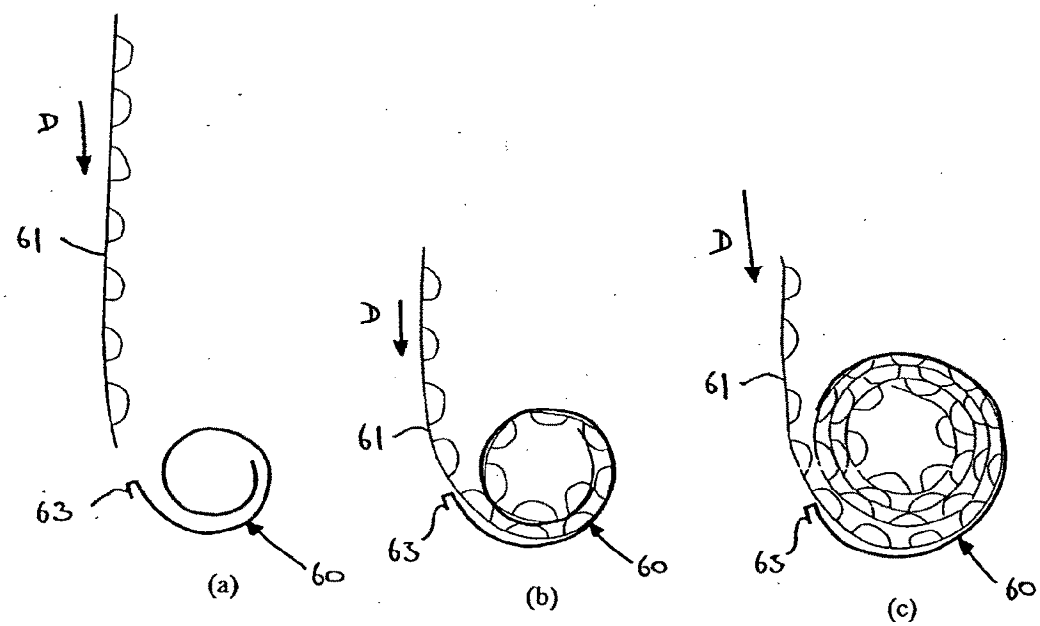


FIGURE 7

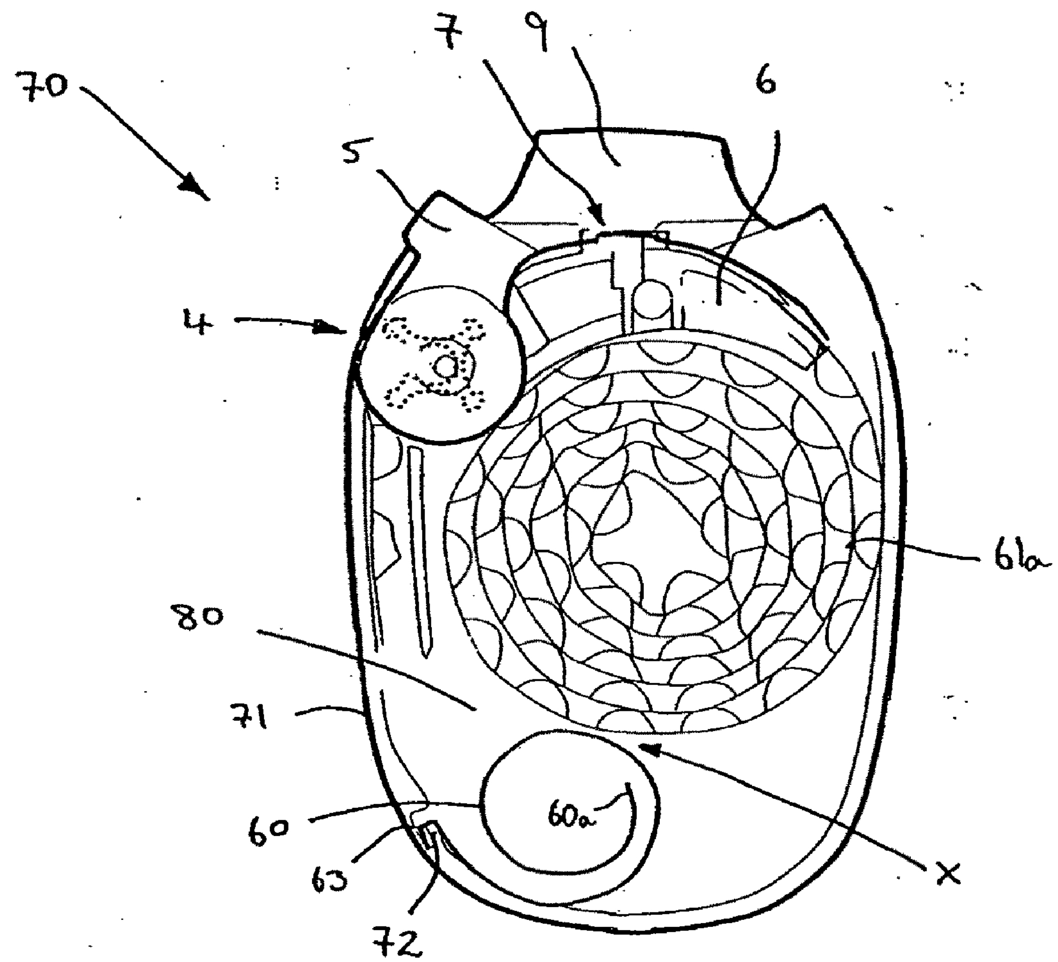


FIGURE 8

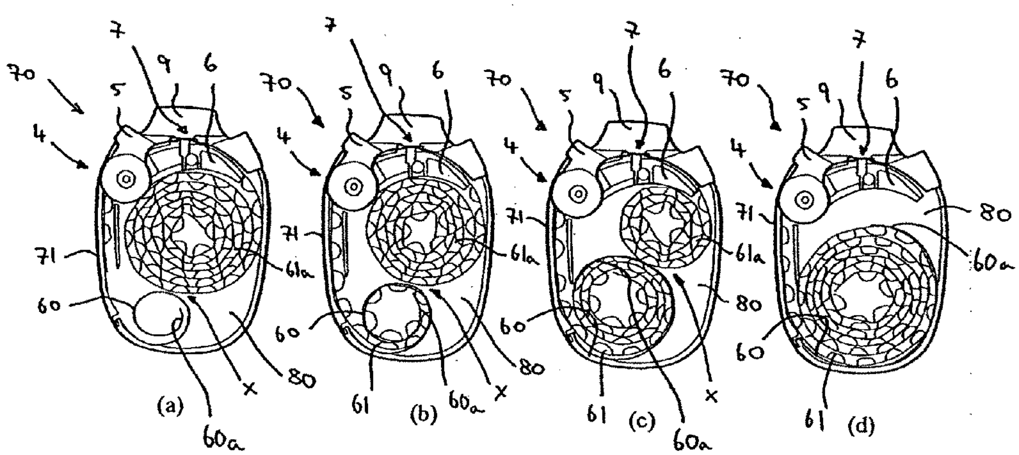


FIGURE 9

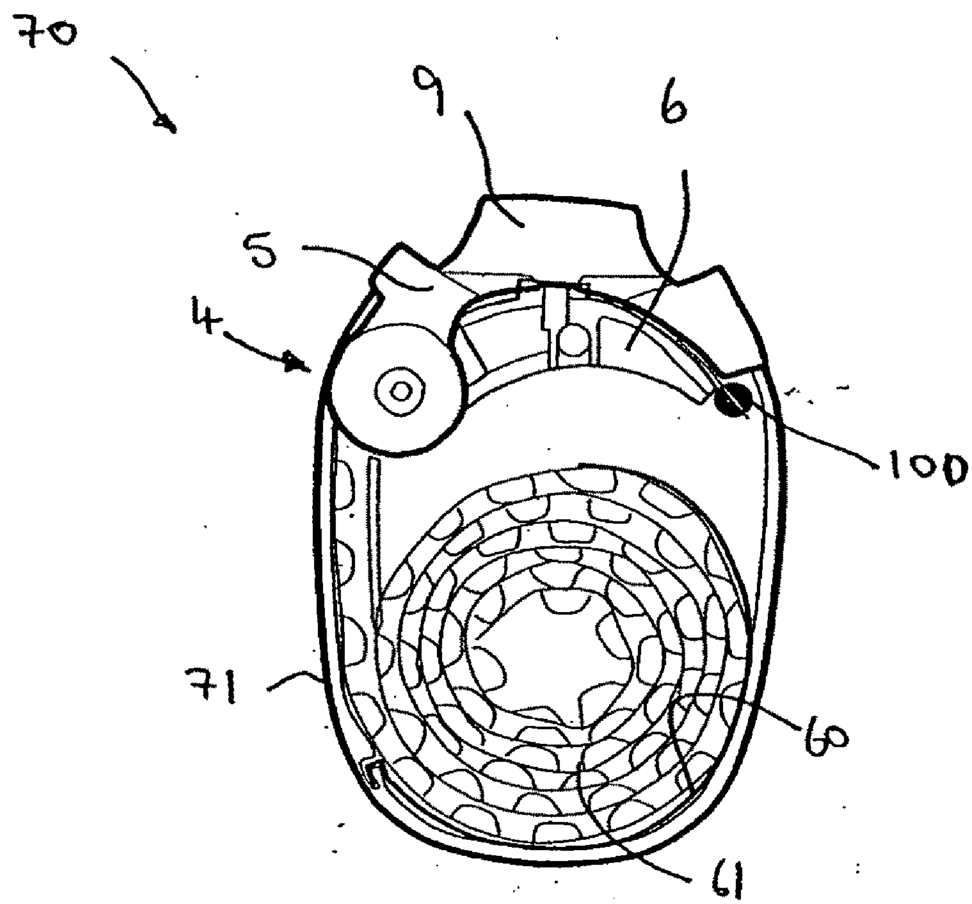


FIGURE 9(c)

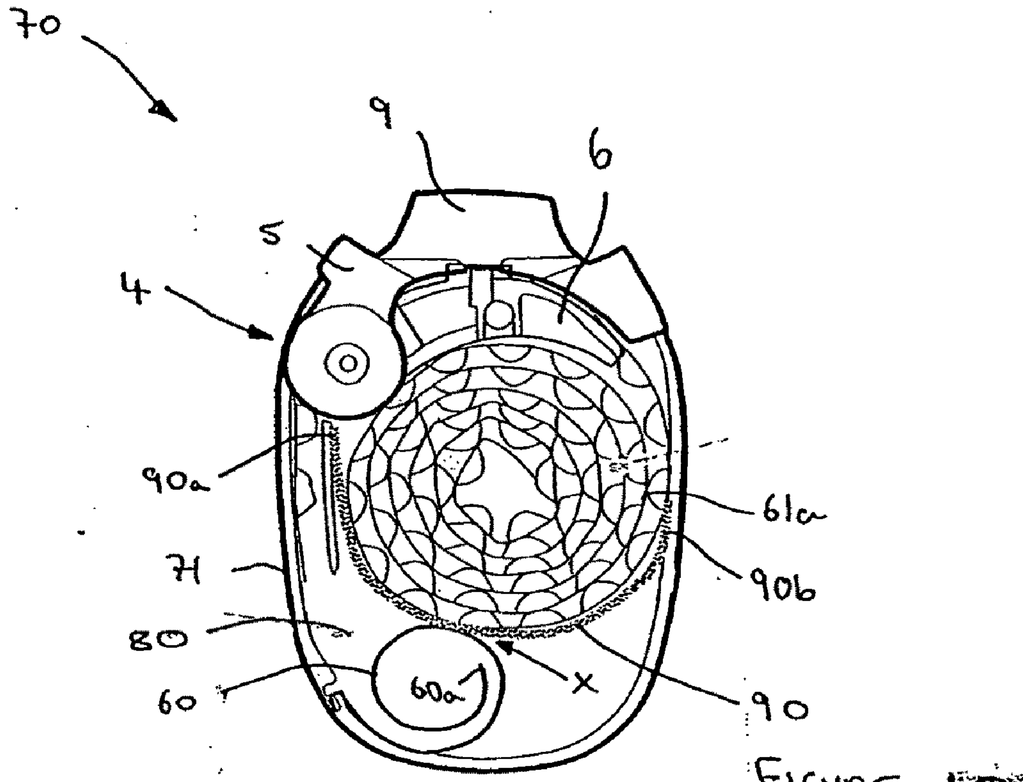


FIGURE 10

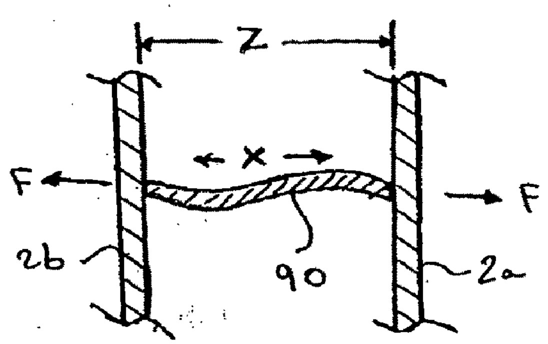


FIGURE 11

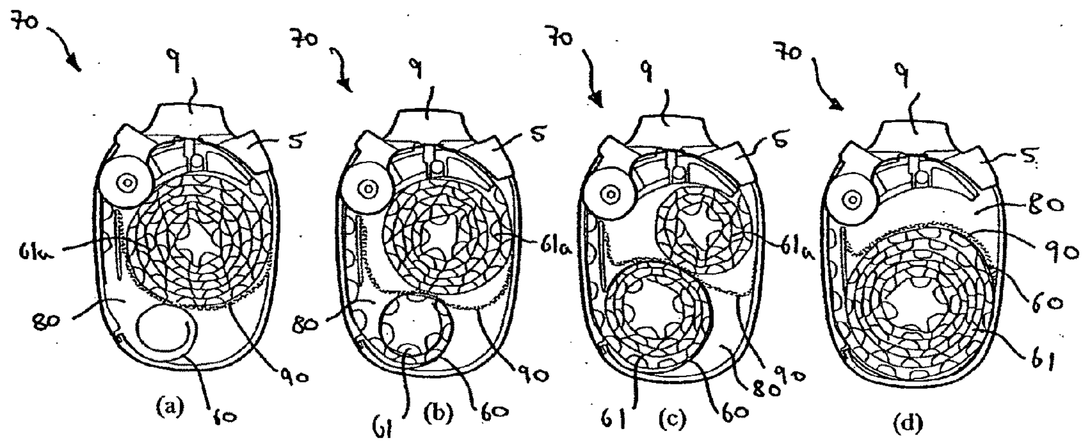


FIGURE 12

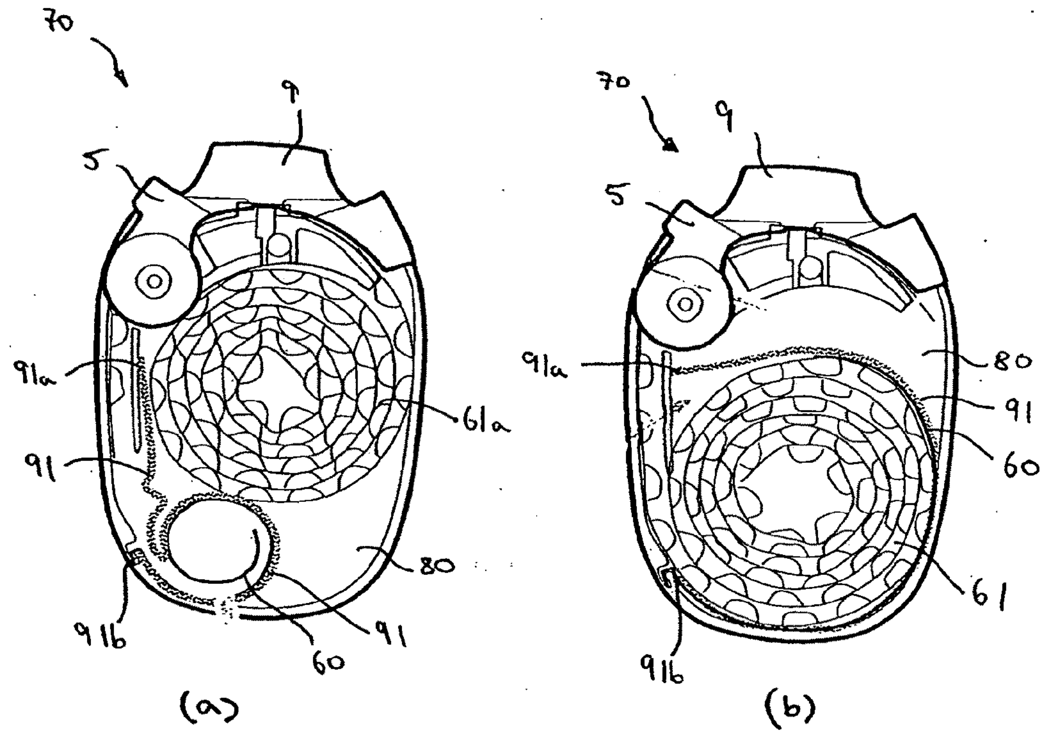


FIGURE 13

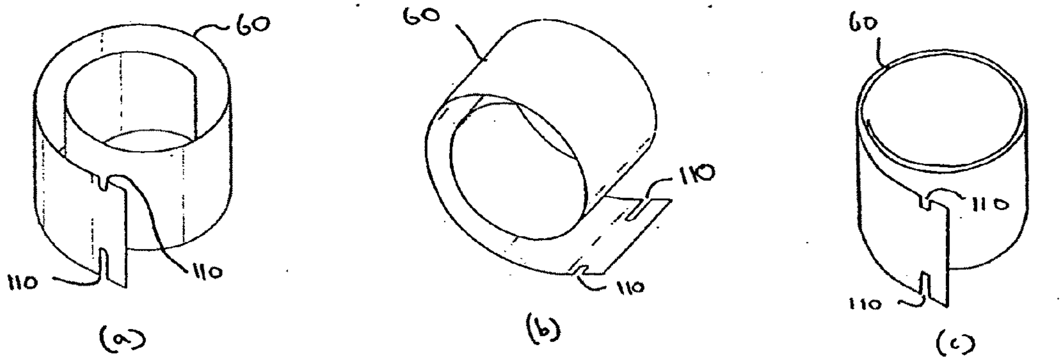


FIGURE 14

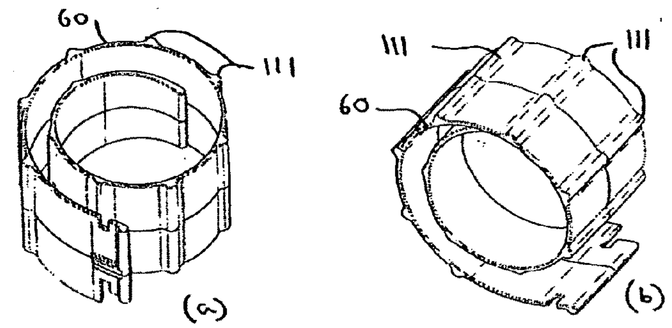


FIGURE 15

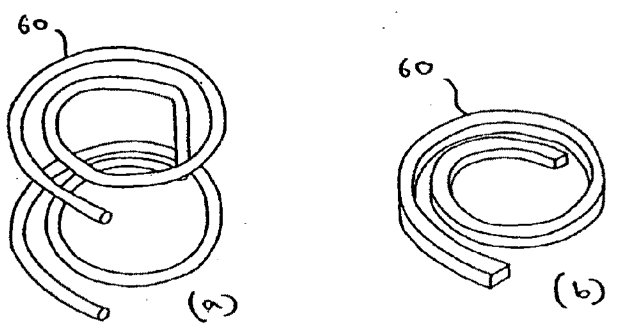
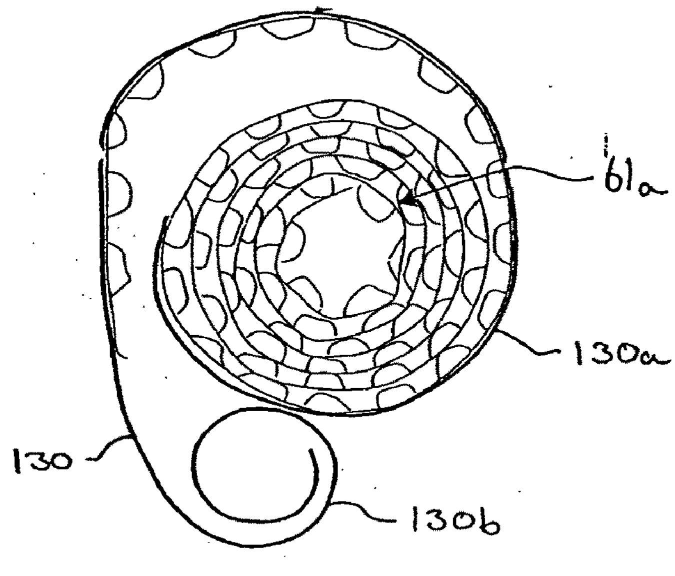
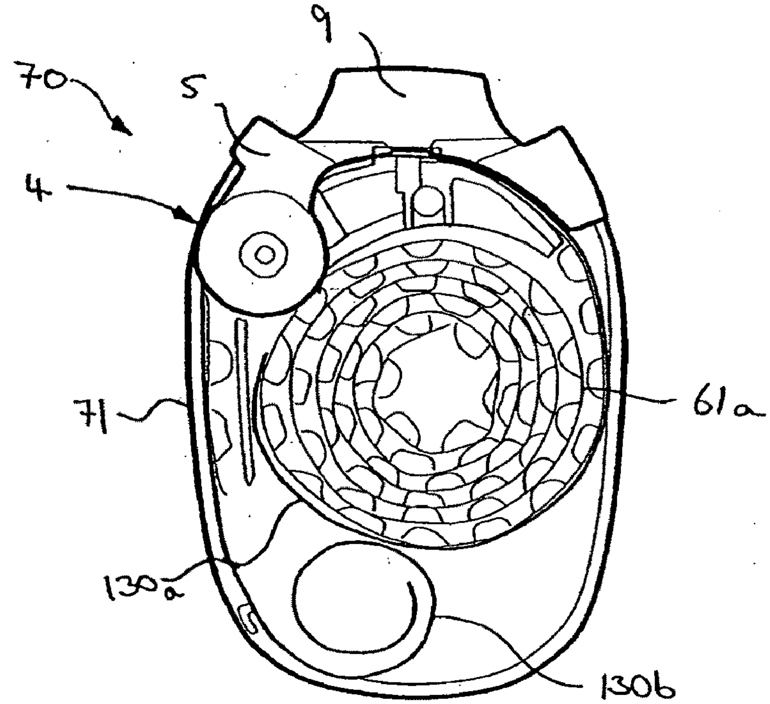


FIGURE 16



(a)



(b)

FIGURE 17

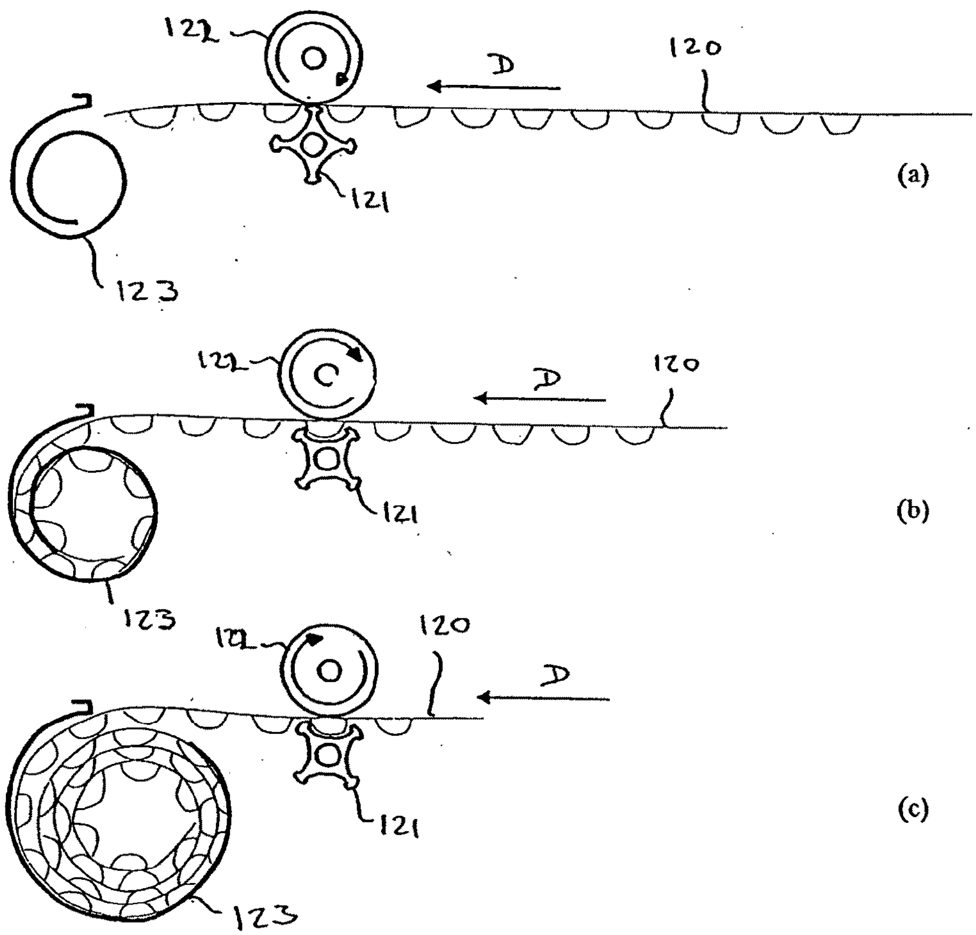


FIGURE 18

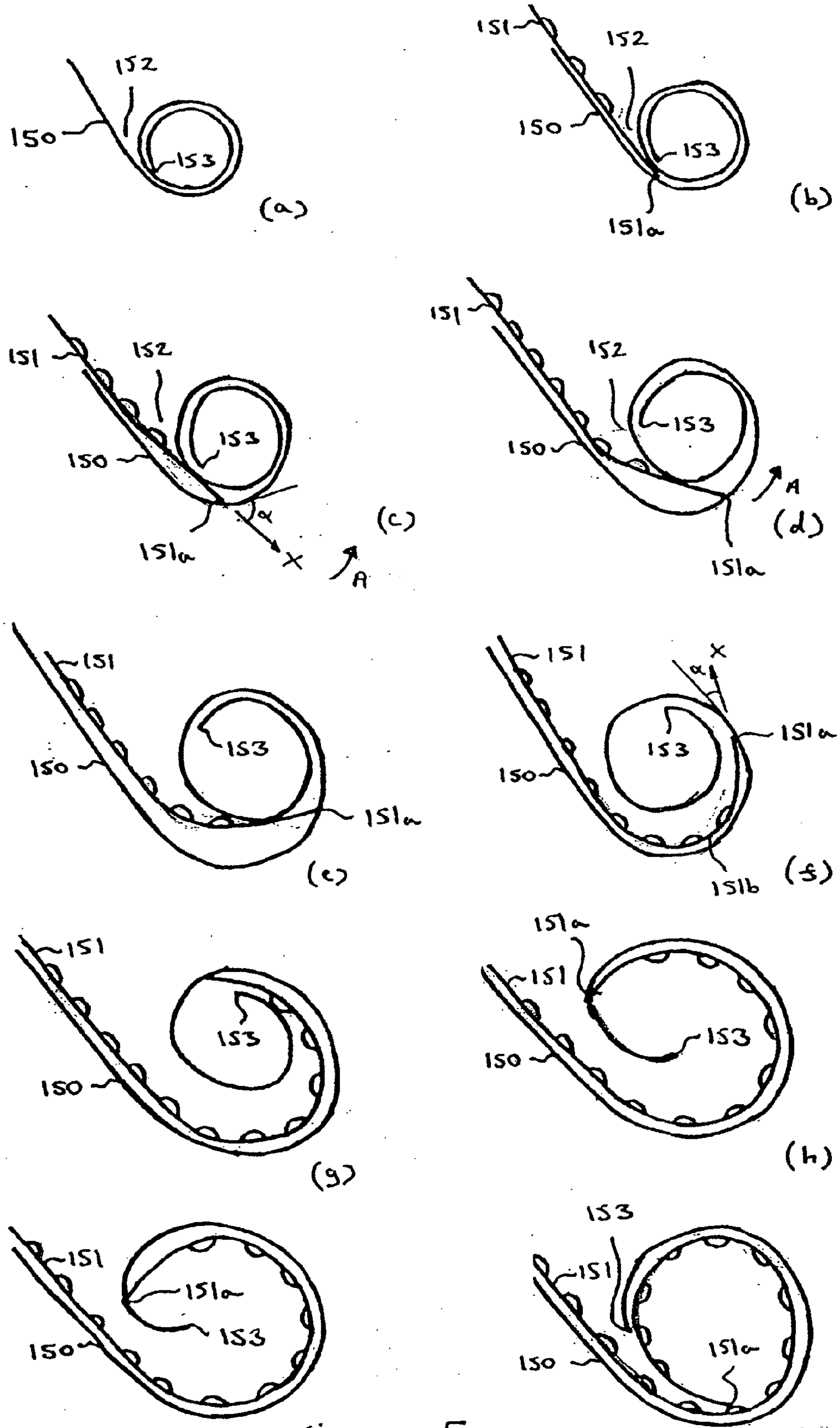
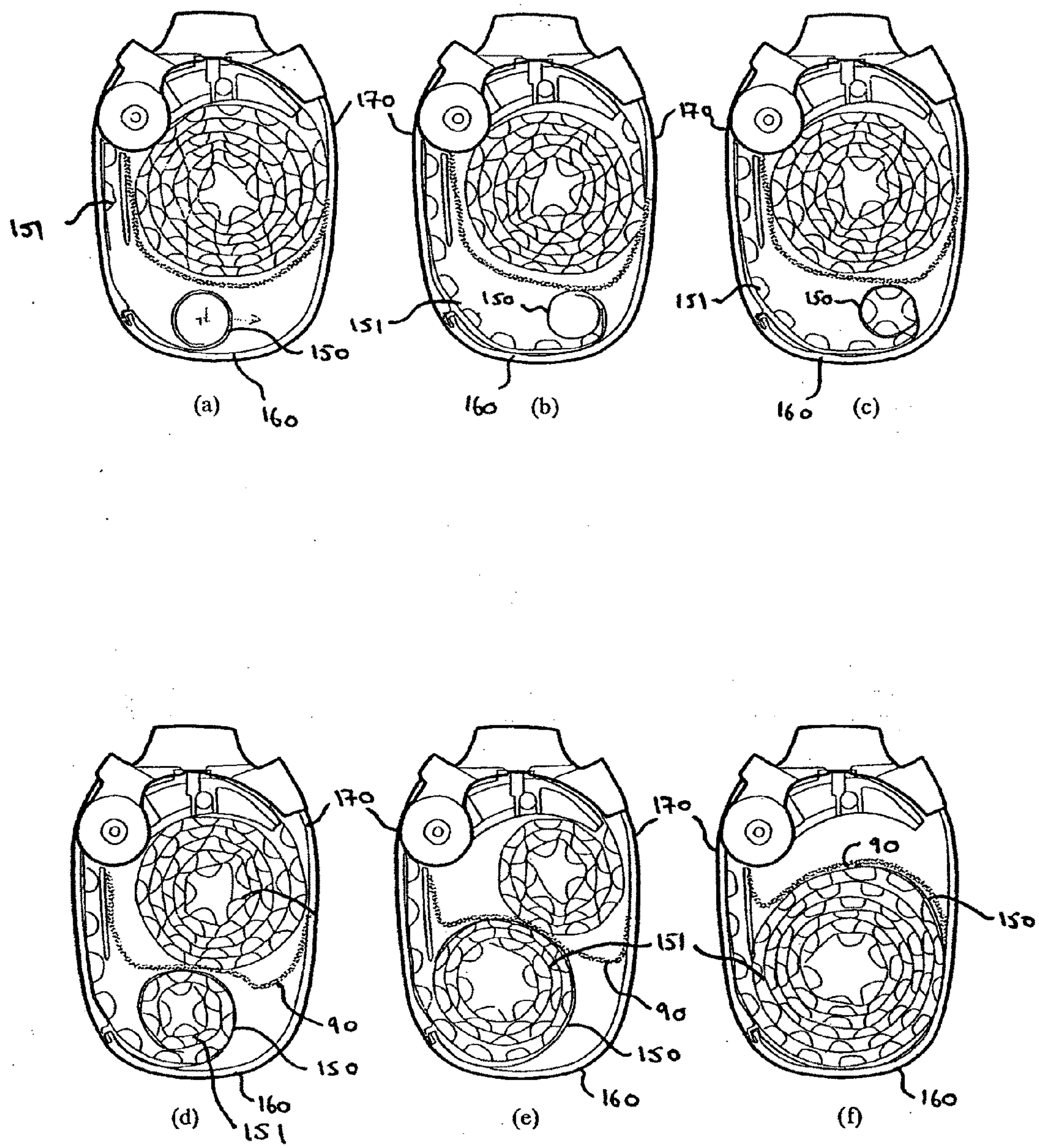


FIGURE 19


170
151
150
160
(a)
170
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150
160
(b)
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151
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160
(c)
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90
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(d)
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(e)
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90
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151
160
(f)

FIGURE 20

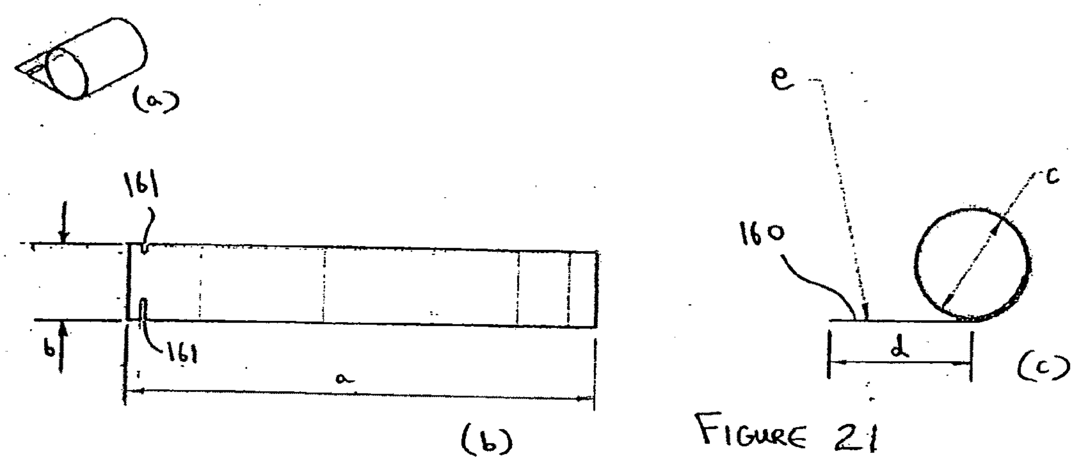


FIGURE 21

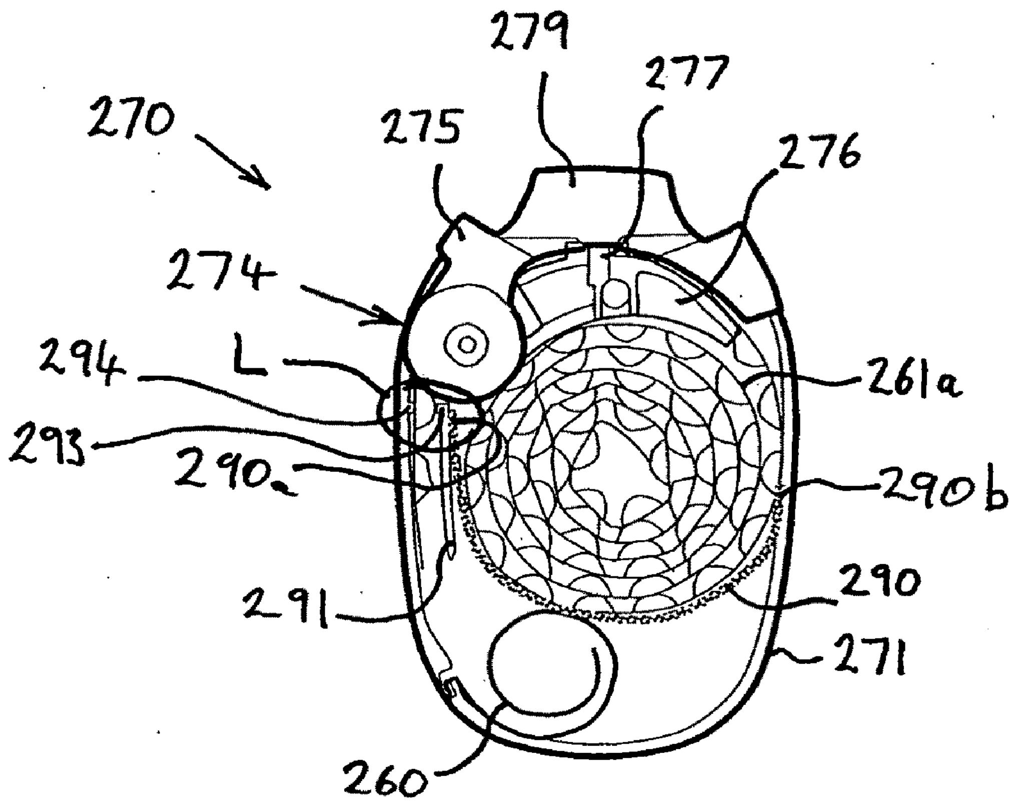


FIGURE 22

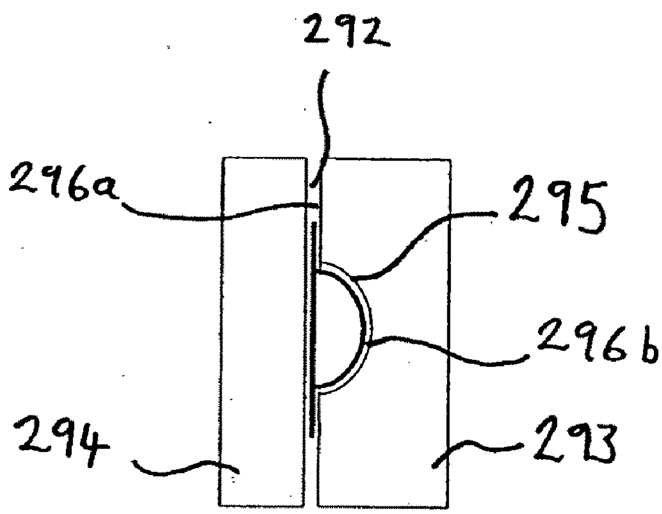


FIGURE 23

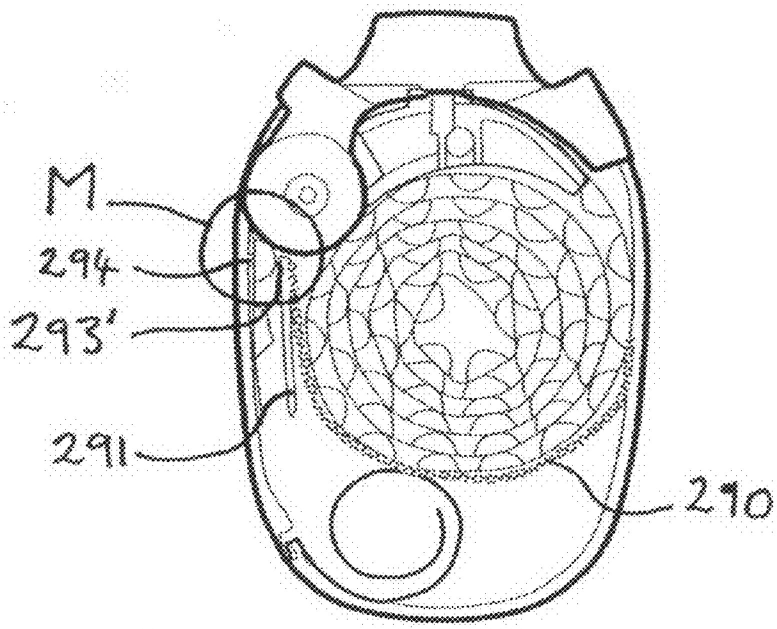


FIGURE 24

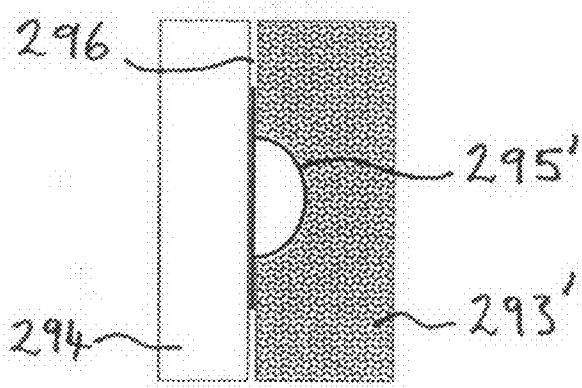


FIGURE 25

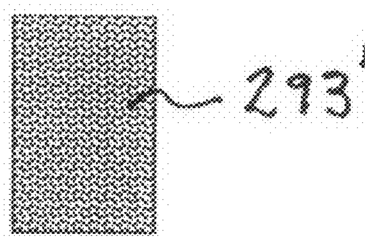


FIGURE 26A

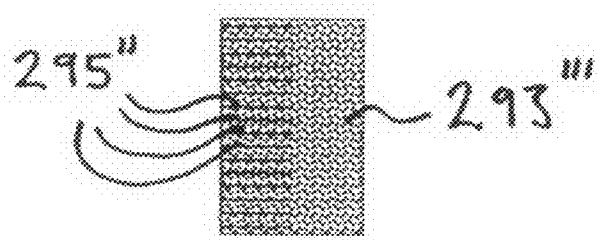


FIGURE 26B

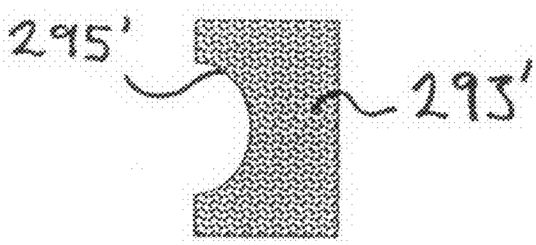


FIGURE 26C

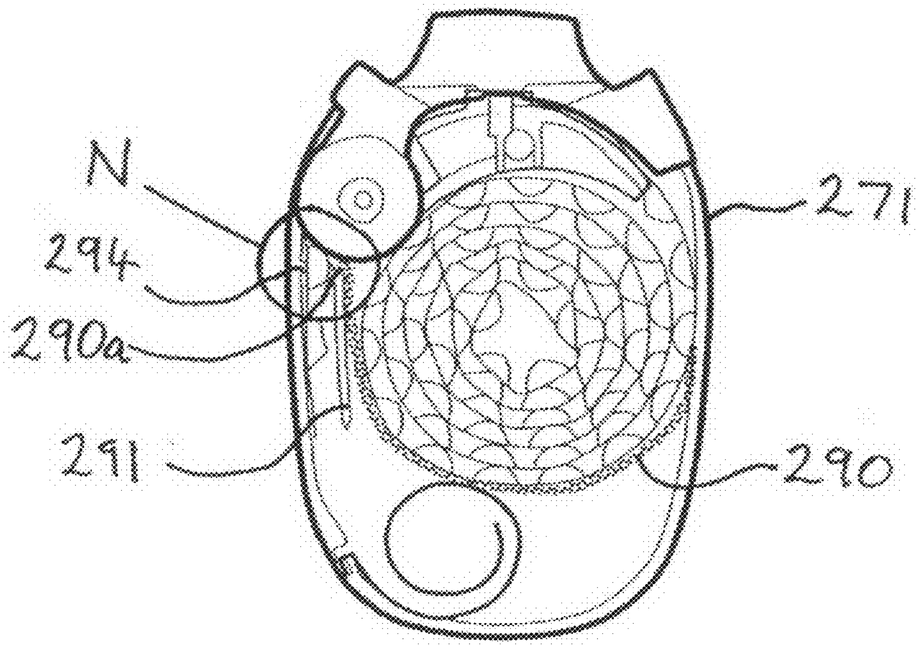


FIGURE 27

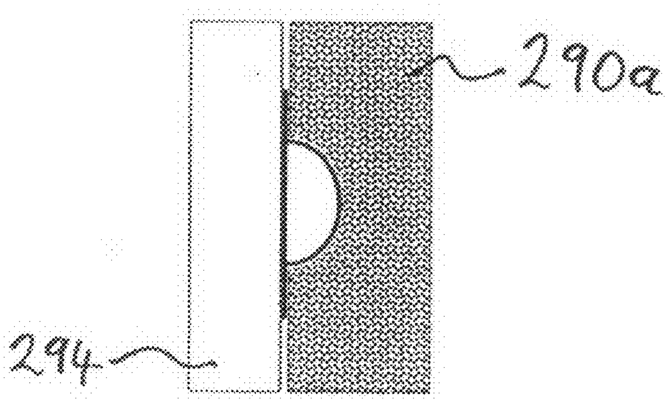


FIGURE 28

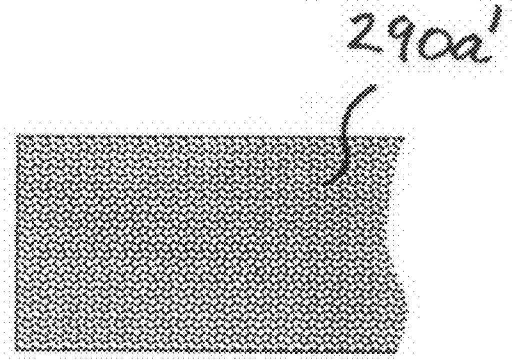


FIGURE 29A

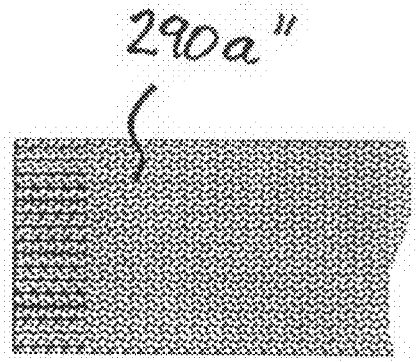


FIGURE 29B

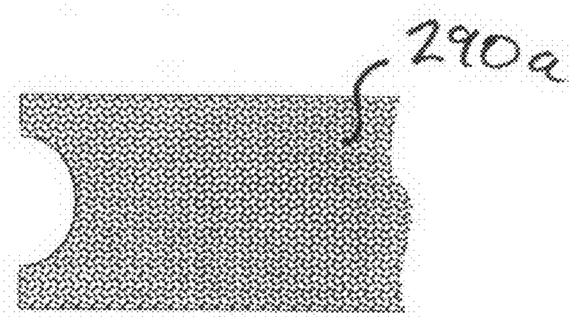


FIGURE 29C

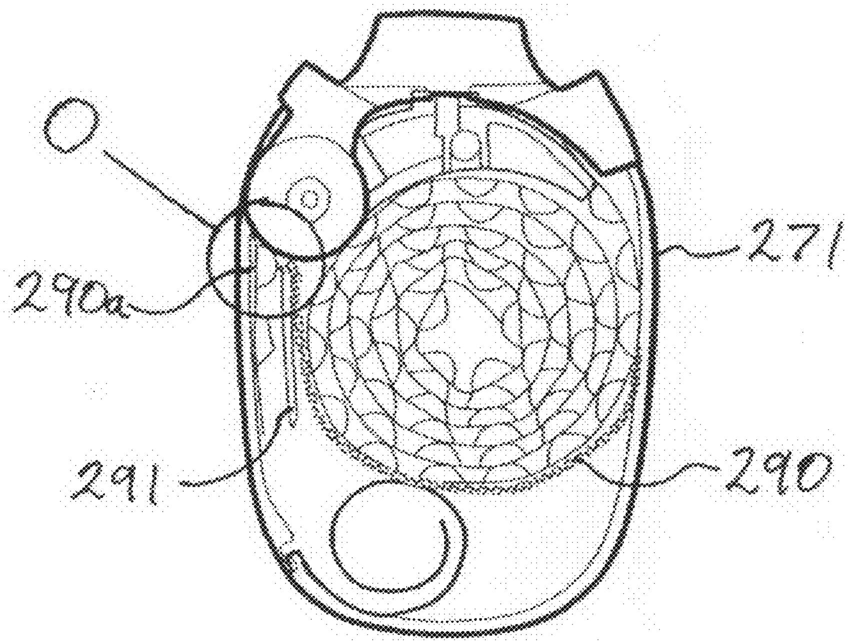


FIGURE 30

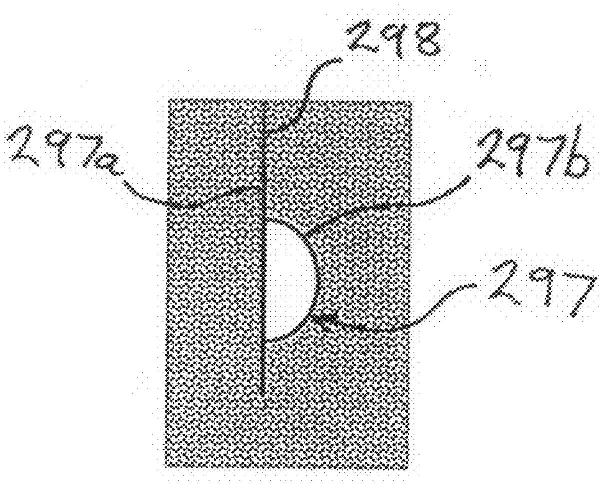


FIGURE 31

INHALER

[0001] The present invention relates to an inhalation device for oral or nasal delivery of medicament in powdered form and to an inhaler containing a strip of blisters each having a breachable lid and/or base that contains a dose of medicament for inhalation by a user of the device.

[0002] Oral or nasal delivery of a medicament using an inhalation device is a particularly attractive method of drug administration as these devices are relatively easy for a patient to use discreetly and in public. As well as delivering medicament to treat local diseases of the airway and other respiratory problems, they have more recently also been used to deliver drugs to the bloodstream via the lungs thereby avoiding the need for hypodermic injections.

[0003] It is common for dry powder formulations to be pre-packaged in individual doses, usually in the form of capsules or blisters which each contain a single dose of the powder which has been accurately and consistently measured. A blister is generally cold formed from a ductile foil laminate or a plastics material and includes a puncturable or peelable lid which is heat-sealed around the periphery of the blister during manufacture and after introduction of the dose into the blister. A foil blister is preferred over a polymer blister or gelatine capsule as each dose is protected from the ingress of water and penetration of gases such as oxygen in addition to being shielded from light and UV radiation all of which can have a detrimental effect on the delivery characteristics of the inhaler if a dose becomes exposed to them. Therefore, a blister offers excellent environmental protection to each individual drug dose.

[0004] Inhalation devices that receive a blister pack comprising a number of blisters each of which contain a pre-metered and individually packaged dose of the drug to be delivered are known. Actuation of the device causes a mechanism to breach or rupture a blister, such as by puncturing it or peeling the lid off, so that when the patient inhales, air is drawn through the blister entraining the dose therein that is then carried out of the blister through the device and via the patient's airway down into the lungs. Pressurized air or gas or other propellants may also be used to carry the dose out of the blister. Alternatively, the mechanism that punctures or opens the blister may also push or eject the dose out of the blister into a receptacle from which the dose may subsequently be inhaled.

[0005] It is advantageous for the inhaler to be capable of holding a number of doses to enable it to be used repeatedly over a period of time without the requirement to open and/or insert a blister into the device each time it is used. Therefore, many conventional devices include means for storing a number or strip of blisters each containing an individual dose of medicament. When a dose is to be inhaled, an indexing mechanism moves a previously emptied blister away from the opening mechanism so that a fresh one is moved into a position ready to be opened for inhalation of its contents.

[0006] An inhaler of the type described above is known from the Applicant's own co-pending international application no. PCT/GB2004/004416 filed on 18^{th} Oct. 2004 and claiming priority from GB application no. 0324358.1 filed 17^{th} Oct. 2003. This international application has been published as WO 2005/037353 A1.

[0007] According to one embodiment described and claimed in WO 2005/037353 A1, and illustrated in FIGS. **1***a* and **1***b* of the accompanying drawings, an inhaler **1** has a housing **2** containing a coiled strip of blisters **3**. An indexing mechanism **4** comprising a single actuating lever **5** unwinds the coil **3** one blister at a time so that they pass over a blister locator chassis **6** and successively through a blister piercing station **7**, when the actuator **5** is pivoted in a direction indicated by arrow "A" in FIG. **1***b*. The blister **3***a* located at the blister piercing station **7** on each movement of the actuator **5** is pierced on the return stroke of the actuator **5** (in the direction indicated by arrow "B" in FIG. **1***b*) by piercing elements **8** on the actuator **5** itself so that, when a user inhales through a mouthpiece **9**, an airflow is generated within the blister **3***a* to entrain the dose contained therein and carry it out of the blister **3***a* via the mouthpiece **9** and into the user's airway.

[0008] Although the inhalation device referred to above and described in the aforementioned publication has addressed many of the known problems associated with these types of devices, it is designed so as to store only a small number of used blisters within the device so that, when that number of blisters is exceeded, they extend out of the housing of the device so that the user must separate those used blisters from those unused blisters that remain within the device and discard the detached portion of the strip. The direction of movement of the used blisters is indicated by arrow "C" in FIGS. **1***a* and **1***b*. The blister strip **3** may be perforated or weakened between each or a number of blisters to facilitate the tearing of used blisters from the strip **3**.

[0009] Although devices that eject used blisters have the advantage of being particularly small and lightweight, it is desirable to provide a fully integrated device in which all the used blisters are retained within the device so that separation of used blisters from those that remain in the device is no longer necessary. Not only would this make the device simpler to use because the user no longer has to concern themselves with periodic detachment and disposal of a used portion of the blister strip but any potential contamination of the fingers by residual drug remaining on the used blisters can be avoided because there is no need for the user to come into contact with any of the used blisters. Therefore, the entire strip can be effectively sealed within the housing of the device.

[0010] Used blisters can be simply wound around a take-up spool within the device. However, such devices are large and require means to rotate the spool to wind up the used blisters. The leading end of the strip must also be pre-attached to the spool so that the strip starts to wind around the spool as the spool is rotated.

[0011] WO 2005/037353 also discloses an embodiment in which all the blisters are retained within the device and in which the blister strip takes the form of an endless loop that is wrapped around itself. Such a device **10** is shown in FIG. **2**. If suitable low friction materials are used, the two centre spools **11**,**12** need not be driven, the drive being solely provided by the indexing mechanism **4** that is concentric with the actuator pivot and which rotates in response to pivotal movement of the actuator **13** by the user, as described with reference to the device shown in FIGS. **1***a* and **1***b*. Although this device provides a compact arrangement, if the strip **14** is too long it tends to jam on the walls **15** separating the elements of the strip **14** in the manner of a wrap-spring clutch or a rope passed around a cylinder preventing proper indexing of the strip **14**.

[0012] A previously undisclosed version of a loop type device **20** is shown in FIGS. **3***a* and **3***b* in which the inherent potential for jamming is minimised by providing drive to successive parts **21** of the strip **22** at several points along its length. As shown in the rear view of FIG. **3***a*, the loop **22** follows a serpentine path around a number of wheels **7**, at least some of which are driven from the main indexing wheel **4**, the remaining wheels being idler wheels **8** which guide the successive parts of the strip **21** of the loop **22**. In the front view of FIG. **3***b*, it can be seen that the indexing mechanism **4** and the three secondary driving wheels **7** are toothed and are geared to a single larger toothed gear wheel **23** mounted for rotation on a central spindle **24** on the rear of the housing **25**.

[0013] The present invention seeks to provide an inhalation device that retains a used strip of blisters within the housing of the device whilst maintaining simplicity and compactness of the device, as well as ease of use.

[0014] Although the device may be disposable after all the blisters contained within it have been exhausted, it is envisaged that it may be possible to open the housing to enable the old strip to be removed and a fresh one inserted. It is also envisaged that blisters may be retained within a portion of the housing of the device which is detachable from the remainder of the housing in which the indexing and piercing mechanism is located, thereby forming a replaceable cartridge. This would enable an exhausted blister strip to be removed without direct contact by the patient.

[0015] A potential complication with inhalation devices that retains used blisters is that a small amount of the powdered dose, typically between 1%-5%, may remain in each blister after inhalation. Furthermore, if a patient indexes the strip without having previously inhaled the dose in a blister that has been pierced or breached, the amount of residual powder will be substantial. It is therefore important to prevent the unused blisters from becoming contaminated with loose powder that could have a detrimental effect on the operation of the device and also result in the patient exceeding an intended dose as they may inhale some of the residual powder as well as the contents of a pierced blister. Furthermore, if the residual powder has been exposed to the atmosphere, it may have also degraded making it unsuitable for inhalation.

[0016] In view of the foregoing, the present invention also seeks to address the problem of residual powder containment to prevent residual powder from contaminating unused blisters remaining in the device and from being inhaled by a user of the device.

[0017] According to one aspect of the invention, there is provided an inhaler comprising a housing to receive a strip of blisters each containing a dose of medicament and means to sequentially move each blister into alignment with means for opening a blister to enable a user to inhale said dose and, a spiral wound element or former to coil said strip.

[0018] Preferably, the spiral wound element is configured so that a used portion of the strip, which is made up of blisters which have been aligned with the means for opening a blister, is gradually coiled within the spiral wound element as the device is used.

[0019] In one embodiment, the spiral wound element is rigid. However, in a more preferable embodiment, the spiral wound element is formed from a flexible material.

[0020] The spiral wound element may be formed from a deformable non-resilient material.

[0021] However, in a preferred embodiment it is formed from a resilient deformable material.

[0022] The resiliency of the spiral wound element is preferably selected in dependence on the stiffness of a used portion of a blister strip so that a first closed coil of a used portion of a blister strip is formed in the spiral wound element prior to any substantial deformation or expansion of the spiral wound element. Alternatively the configuration of a more resilient spiral wound element can be arranged such that a first closed coil is formed during initial deflection of the element. In one preferred embodiment, the spiral wound element is configured so that it expands radially as the length of the used blister strip coiled within it increases as more blisters are breached.

[0023] Conveniently, the spiral wound element has at least one winding that extends over 360 degrees.

[0024] The stiffness of the spiral wound element may advantageously vary along at least a portion of its length. In particular, the stiffness of the spiral wound element may decrease towards its inner end.

[0025] One approach to achieving the reduction in stiffness is for the thickness of the spiral wound element to gradually reduce towards its inner end and/or its width to gradually reduce towards its inner end.

[0026] In one embodiment, holes, slots or other apertures are formed in the spiral wound element close to or at its inner end.

[0027] The spiral wound element may be formed for example from phosphor bronze, stainless steel, titanium, spring steel, shape memory alloy, nylon, acetal, PTFE or polypropylene.

[0028] The spiral wound element may also be coated with a low friction material to aid smooth winding of the breached blister strip, for example, a PTFE coating. Alternatively the surface finish or texture of the spiral wound element can be selected to provide a low friction surface.

[0029] The spiral wound element can be formed from flat strip material, or from square, circular or rectangular section material. Alternatively, the spiral may be formed from one or more wire elements wound into a spiral. This reduces the contact area with the strip and therefore reduces friction.

[0030] The materials and components may be used separately or in combination to give the desired characteristics.

[0031] In a preferred embodiment, the spiral wound element is a coil spring formed from a thin sheet of material.

[0032] One embodiment may comprise a passage between the first and second compartments, and blocking means in said passage to prevent the egress of powdered medicament from the first blister compartment into the second blister compartment through the passage.

[0033] The blocking means may be shaped to conform to the shape of the blister strip, and may include a resilient member to effect a seal against the blister strip. The blocking means may be disposed such that it is aligned with a blister of the blister strip when another blister is aligned with said means for opening a blister.

[0034] According to one aspect of the invention, there is provided a housing to receive a strip of blisters each containing a dose of medicament and means to sequentially move each blister into alignment with means for opening a blister to enable a user to inhale said dose, the inhaler having a first compartment to contain unused blisters and a second compartment to receive used blisters, the first and second compartments being separated by a flexible and/or movable dividing wall.

[0035] Preferably, an aperture is provided in the flexible and/or movable dividing wall for the passage of the blister strip from the first compartment into the second compartment, said aperture including means to prevent the egress of powdered medicament from the used blister compartment in to the unused blister compartment through the aperture. The means may be a brush or elastomeric element.

[0036] Preferably, said means to prevent egress of powdered medicament includes a portion of the housing which is shaped to conform to the shape of the blister strip. Alternatively, said means to prevent egress of powdered medicament may include a resilient member to effect a seal against the blister strip.

[0037] Said resilient member may be shaped to conform to the shape of the blister strip, and the resilient member may be formed integrally with the dividing wall.

[0038] The means to prevent egress of powdered medicament may be disposed such that it is aligned with a blister of the blister strip when another blister is aligned with said means for opening a blister.

[0039] Although the unused blister strip and the breached blisters may be housed in separate compartments, in one embodiment the housing comprises a common chamber to receive both an unused and a used portion of the blister strip.

[0040] Advantageously, the chamber is configured so that the used portion of the strip occupies a region of the chamber-initially occupied by an unused portion of the blister strip as the size of the used portion of the strip increases.

[0041] In one embodiment, the dividing wall may be rigid but configured so as to be slideable within the housing so that the relative sizes of the unused and used blister compartments can be altered.

[0042] The flexible dividing wall may be fixed to the housing at one or both ends and may comprise a foam strip which can include a stiffening element. In one embodiment, the flexible dividing wall is movable and fixed to the housing at one end so as to pivot about said end within the housing.

[0043] In one embodiment, the flexible and/or movable dividing wall is flexible and configured so that it extends across said space between said sidewalls of the inhaler to prevent passage of powdered dose between the unused and used blister compartments. In one embodiment, the flexible dividing wall is at least partially attached to the spiral wound element.

[0044] The flexible dividing wall can also be designed to exert a constraining or steadying force on one or both of the blister coils. This constraining force can be achieved by, for example, the stiffness of the dividing wall or by the friction created as the dividing wall slides relative to the walls of the housing. This can be particularly beneficial if the spiral wound element containing the used portion of the blister coil is selected to be very resilient, and can help to ensure that the coil of used blisters is kept as small as possible.

[0045] In one embodiment, the inhaler may comprise a second spiral wound element within which an unused blister strip may be coiled up within said housing such that the second spiral wound element retracts as the first spiral wound element expands, as the size of the coil formed from a used portion of the strip increases and the size of the coil forming the unused portion of the strip decreases.

[0046] According to another aspect of the invention, there is provided an inhaler comprising a housing to receive a strip of blisters each containing a dose of medicament and means to sequentially move each blister into alignment with means for opening a blister to enable a user to inhale said dose, wherein the housing comprises a common chamber to receive an unused blister strip and, a used portion of that strip, a flexible and/or movable dividing wall separating the chamber into an unused and a used blister compartment

[0047] The flexible dividing wall may be fixed to the housing at each end.

[0048] In one embodiment, the dividing wall is flexible and configured so that it extends across said space between the sidewalls of the inhaler to prevent passage of powdered dose between the unused and used blister compartments.

[0049] Preferably, the width of the dividing wall is greater than the distance between the sidewalls so that the flexible dividing wall is held in compression between the sidewalls so as to prevent passage of powder between the two regions of the chamber around the edges of the dividing wall and the walls of the chamber.

[0050] The flexible dividing wall preferably comprises a foam strip.

[0051] In one embodiment, the inhalation device comprises a second spiral wound element to receive an unused blister strip prior to insertion of the strip into the housing such that the second spiral wound element retracts as the first spiral wound element expands as the size of the coil formed from a used portion of the strip increases and the size of the coil formed from an unused portion of the strip decreases.

[0052] Preferably, the spiral wound element is configured so that it is partially unrolled or unwound by the leading edge of a used portion of a blister strip on initial contact of the leading edge of the strip against the spiral wound element, prior to any substantial deformation of the strip caused by the spiral wound element.

[0053] According to the invention, there is also provided a method of controlling a strip of blisters within an inhalation device in which unused blisters are sequentially movable into alignment with means for opening a blister to enable a user to inhale a dose, the method including the step of feeding a used portion of the strip into a spiral wound element to coil said used portion of the strip.

[0054] According to the invention, there is also provided a method of forming a coiled strip of blisters for insertion into an inhalation device, the method including the steps of feeding an end of the strip of blisters into a spiral wound element such that the strip is coiled within said spiral wound element.

[0055] According to another aspect of the invention, there is provided an inhaler comprising a housing to receive a strip of blisters each containing a dose of medicament and means to sequentially move each blister into alignment with means for opening a blister to enable a user to inhale said dose, the housing including a chamber to receive used blisters and means to compress, crush, tear, cut-up and/or fold said used blisters.

[0056] It will be appreciated that different aspects of the invention may be used independently or in any combination with other aspects of the invention. For example, the spiral wound element can be used in conjunction with the flexible wall and/or a device to crush used blisters.

[0057] It will be appreciated that the inhaler of the invention may be either a passive or active device. In a passive device, the dose is entrained in a flow of air caused when the user inhales through the mouthpiece. However, in an active device, the inhaler would include means for generating a pressurised flow of gas or air through the blister to entrain the dose and carry it out of the blister through the mouthpiece and into the user's airway. In one embodiment, the inhaler may be provided with a source of pressurised gas or air within the housing.

[0058] Embodiments of the invention will now be described, by way of example only, with reference to FIGS. **4** to **20** of the accompanying drawings, in which:—

[0059] FIGS. **1***a* and **1***b* are side sectional views of a conventional inhalation device to show how the blisters of a strip are sequentially moved into alignment with a blister piercing station by movement of an actuator from the position shown in FIG. **1***a* to the position shown in FIG. **1***b* which drives an indexing wheel. A piercing head on the actuator pierces the lid of an aligned blister when the actuator is returned to its normal position as shown in FIG. **1***a*.

[0060] FIG. **2** is a sectional view of an inhalation device in which all the blisters are retained within the device and in which the blister strip takes the form of an endless loop which is wrapped around itself;

[0061] FIGS. **3***a* and **3***b* show front and rear sectional views of another version of a previously undisclosed endless loop device in which the strip is driven at several locations along its length;

[0062] FIGS. **4***a* to **4***c* shows an embodiment according to one aspect of the invention in which the used portion of a strip of blisters are folded in a zig-zag or concertina fashion and the blister cavities are crushed so that the used blisters form a neat stack within an enclosed chamber in the housing of the device;

[0063] FIGS. **5***a* and **5***b* show another embodiment according to one aspect of the invention in which the used portion of the blister strip is driven through a nip between at least one pair of rollers to crush the blister cavities and impart a curvature to the strip so that it coils up within an enclosed chamber in the housing of the device;

[0064] FIGS. **5***c* and **5***d* shows a simplified embodiment of a mechanism for tearing or otherwise detaching used blisters, which may have been crushed, from remaining blisters;

[0065] FIG. **6***a* to **6***d* shows a sequence of drawings to show how the used portion of the blister strip may be fed into a rigid spiral wound element so as to cause the used portion of the strip to coil up as it is guided by the surface of the spiral wound element, according to an embodiment of the invention;

[0066] FIG. **7***a* to **7***c* shows a sequence of drawings to show how the used portion of the blister strip may be fed into a flexible spiral wound element that expands as the used portion of the coiled blister strip grows within it, according to an embodiment of the invention;

[0067] FIG. **8** shows an embodiment of an inhalation device incorporating a coil such as that shown in FIG. **7**;

[0068] FIG. **9***a* to **9***d* shows a sequence of drawings to show how the unused portion of a coiled strip of blisters gradually unwinds as the blisters pass the blister piercing station and the used portion of the blister strip is coiled up within the spiral wound element;

[0069] FIG. **9***e* shows an embodiment similar to that shown in FIG. **8** but in which a blocking element is secured to the end of the blister strip;

[0070] FIG. **10** shows an embodiment of an inhalation device having a housing defining an interior chamber containing a coiled, unused strip of blisters and a spiral wound element to receive a used portion of that blister strip, the chamber is divided into two between the unused blisters and the spiral wound element by a flexible dividing wall to form an unused and a used blister compartment;

[0071] FIG. **11** shows a partial side sectional view across the housing to illustrate how the flexible dividing wall is held in compression between the sidewalls of the housing;

[0072] FIG. **12***a* to **12***d* shows a sequence of drawings to shown how the flexible dividing wall moves as the spiral wound element expands as it fills up with used portion of the blister strip;

[0073] FIGS. **13***a* and **13***b* show a modified version of the inhalation device illustrated in FIG. **11***a* and in which the flexible dividing wall surrounds, and is at least partially attached to, the outer surface of the spiral wound element. In FIG. **13***a*, none of the blisters have been used and so the spiral wound element is empty. However, in FIG. **13***b*, all the blisters have been used and the spiral wound element has expanded to its maximum extent together with the flexible dividing wall;

[0074] FIGS. **14***a*, **14***b* and **14***c* show three perspective views of a spiral wound element which have notches close to its outer end for attachment to the internal wall of the housing of an inhaler;

[0075] FIGS. **15***a* and **15***b* show two perspective views of a moulded spiral wound element;

[0076] FIGS. **16***a* and **16***b* shows a spiral wound element formed from a wire or from a material having a rectangular section, respectively;

[0077] FIGS. **17***a* and **17***b* show a twin spiral wound element prior to and after insertion into an inhalation device, respectively;

[0078] FIG. **18***a* to **18***c* show a sequence of drawings to illustrate how a fresh strip of unused blisters may be coiled within a spiral wound element prior to insertion into the housing of an inhalation device;

[0079] FIG. **19**(*a*) to **19**(*j*) are a sequence of drawings to show how a coil of used portion of a blister strip is formed in a spiral wound element according to another embodiment;

[0080] FIG. **20**(*a*) to **20**(*f*) show how a coil of a used portion of a blister strip is formed with the spiral wound element of FIG. **18** when located in an inhalation device;

[0081] FIG. **21**(*a*) to **21**(*c*) shows a perspective view, an unrolled plan view and, a side view of the more flexible spiral wound element shown in FIGS. **19** and **20**;

[0082] FIG. **22** shows another embodiment of an inhalation device similar to that of FIG. **10**, but including means to prevent residual powdered medicament passing from a used blister compartment to the unused blister compartment through the passage between the two through which the blister strip passes;

[0083] FIG. **23** shows a partial sectional plan view from above of the area within circle L in FIG. **22**;

[0084] FIG. **24** shows an alternative embodiment of an inhalation device similar to that of FIG. **22**;

[0085] FIG. **25** shows a partial sectional plan view from above of the area within circle M in FIG. **24**;

[0086] FIGS. **26**A-**26**C show alternative configurations of resilient members of the embodiment of FIGS. **24** and **25**;

[0087] FIG. **27** shows an alternative embodiment of an inhalation device similar to that of FIGS. **22** and **24**;

[0088] FIG. **28** shows a partial sectional plan view from above of the area within circle N in FIG. **26**;

[0089] FIGS. **29**A-**29**C show alternative configurations of resilient members of the embodiment of FIGS. **28** and **28**;

[0090] FIG. **30** shows an alternative embodiment of an inhalation device similar to that of FIGS. **22**, **24** and **27**; and

[0091] FIG. **31** shows a partial sectional plan view from above of the area within circle O in FIG. **30**

[0092] Reference is made throughout this specification to both "unused" and "used" blisters. It will be appreciated that "unused" blisters refer to those blisters that have not passed the blister piercing station and which remain intact with the dose contained therein. "Used" blisters refer to those blisters which have passed the blister piercing station in response to movement of the actuator by a user and which have been pierced to enable access to the dose contained therein to be obtained. Although in general, a "used" blister refers to a blister from which a dose has been inhaled, it should also be taken to include blisters which have passed the blister piercing station and have been pierced but which still contain either some or all of the dose contained therein. This may happen, for example, when a user moves the actuator to move the blister strip without inhaling the dose from a previously pierced blister.

[0093] An alternative to both the conventional approach of spooling used blisters, and the loop drive described above, is to employ a mechanism to impart folds to a used strip so that it is encouraged to form a concertina. The device can, alternatively or in addition to a folding mechanism, also include means for crushing the used blister cavities so as to reduce their volume and so that a compacted stack of used blisters is formed, thereby minimising the volume of space occupied by the used blisters.

[0094] One way in which the concertina folds and crushing of the used blister cavities can be carried out is shown in FIGS. **4***a* to **4***c*, from which it can be seen that two lobed rollers **30**,**31** are configured so as to intermesh with a small gap between them which is less than the depth of a blister cavity. The lobed rollers **30**,**31** may be connected by integral toothed gear wheels (not shown) so that both are driven, possibly in response to movement of the actuator **5**. As a used blister strip **51** passes between the lobed rollers **30**,**31**, the lobes **30***a*, **31***a* produce a zig-zag or fold in alternate directions into the flattened strip so as to form a concertina. Each roller has the same construction but they are mounted so the lobes **30***a* on one roller are 90 degrees out of phase with the lobes **31***a* on the other roller so that, as the rollers **30**,**31** rotate, the lobes **30***a*,**31***a* on one roller **30**,**31** engage the strip and press it against the other roller between the lobes **30**,**31***a* of that roller **30**,**31**. As shown in FIGS. **4***b* and **4***c*, if the concertina is forced into an enclosed space **32** within the housing **33** of the inhaler, a compacted stack **34** (see FIG. **4**(*c*)) of used blisters is created. The enclosed space **32** may be provided with a wall or piston (not shown) slidable against a bias provided by a spring (not shown) in response to pressure applied thereto by the used blisters **51** entering the enclosed space **32**, so as to minimise the volume occupied by the blisters **51** and maintain the concertina form.

[0095] It will also be appreciated that, in place of the lobes **30***a*, **31***a*, one or both of the rollers **30**,**31** may be provided with an arm having a cutting blade (not shown) affixed to its tip so that rather than fold the strip, the cutting blade engages the strip **51** to cut it or chop it up into sections or individual blisters.

[0096] In another modification, illustrated in FIGS. **5***a* and **5***b*, the blister cavities of the used blister strip **51** can simply be crushed without imparting any fold to the strip **51**. If the strip **51** is passed around a roller **41** and through a nip **42** between that roller **41** and at least one other roller **43**, **44**, the rollers **41**,**43**,**44** will crush the cavities and will also tend to form a curvature in the strip **51** such that a coil is formed which can be directed into an enclosed space **45** within the housing **40**, as shown in FIG. **5***b*.

[0097] It will be appreciated that techniques other than rollers can be used to crush or flatten the blisters in order to reduce their size. They may be compressed between moving parts, or between a moving part and an anvil. The moving part may be driven by the actuator or by separate means. The blister form may be weakened in manufacture to reduce the force needed to crush the blister, for example by scoring the blister form.

[0098] In one unillustrated embodiment, the indexing wheel forming part of the indexing mechanism and which rotates to draw the blister strip through the device past the piercing station may be itself be used to squeeze the used blister cavities as they pass around it, thereby at least partially crushing them. This is achieved by enlarging the axle or hub of the indexing wheel so that the distance between the hub and the casing of the device, or a component fixed to the casing, is less than the maximum height of a blister cavity. As the blister cavities are entrained between the spokes of the indexing wheel, onward rotation of the wheel causes the cavities to be at least partially squashed or sandwiched between the enlarged hub of the indexing wheel and the casing of the device.

[0099] In FIGS. **5***c* and **5***d*, a mechanism for tearing or separating a used blister **51***a* from the strip **51** is shown. The used blisters may or may not have been crushed prior to being separated. As can be seen from FIG. **5***a*, the strip **51** passes through a "letterbox" shaped opening **201** in a rotatably mounted tearing wheel **200**. Means (not shown) are provided to keep the strip in a fixed position upstream from the point at which it passes through the tearing wheel **200** so that, when the tearing wheel **200** rotates a section of the strip **51** is torn off. The tearing wheel **200** may be driven by gear wheels that rotate in response to movement of the actuator **5**. The detached blisters **51***a* are allowed to fall into a containment section or enclosed space within the housing **2**.

[0100] Referring now to FIG. **6**, there is shown a rigid spiral wound element **50** and a used portion of a strip of blisters **51**. As the used portion of the strip of blisters **51** sequentially move through the device in response to successive actuation of an indexing mechanism by the user, the used portion of the strip **51** moves in the direction of arrow "D" as the size of the used portion of the blister strip gradually increases. As shown in FIG. **6**(*a*), the leading end **51***a* of the used portion of the strip is about to enter the mouth **52** of the spiral wound element **50**. In FIG. **6**(*b*), the used portion of the strip **51** has entered the mouth **52** and has been deflected by the surface of the spiral wound element **50** so that it begins to follow a curved path guided by the surface of the spiral wound element **50**. In FIG. **6**(*c*), the used portion of the strip **51** has passed further into the spiral wound element **50** so as to form a complete coil. Further movement of the used portion of the strip **51** into the spiral wound element **50** results in the formation of multiple coils from the used portion of the blister strip, as shown in FIG. **6**(*d*). As the spiral wound element **50** is rigid, no more blisters can be received within the spiral wound element when the leading end **51***a* of the used portion of the blister strip **51** reaches the centre of the spiral, as shown in FIG. **6**(*d*).

[0101] It will be appreciated that when the leading end **51***a* of the used portion of the strip **51** reaches the centre of the spiral, no more can be inserted as the spiral wound element **50**

shown in FIG. **6** is rigid. Therefore, in a more preferable configuration, the spiral wound element **60** is formed from a flexible, preferably resilient, material so that it expands as the number of coils of used blisters **61** increase, as shown in the sequence of drawings of FIG. **7**. Once a coil of blisters **61** has been formed within the spiral wound element **60**, further movement of the used portion of the strip **61** into the spiral wound element **60** causes it to expand as the coiled used portion of the blister strip **61** grows, as shown in FIG. **7***c*. The initial size and rigidity of the spiral wound element **60** may be selected in dependence on the stiffness of the used portion of the blister strip **61** such that, as the used portion of the strip **61** is received in the spiral wound element **60**, it is guided by the spiral wound element **60** until it forms a first closed coil, as shown in FIG. **7***b*. Only once this first closed coil has been formed does any expansion of the spiral wound element **60** take place. In practice, a blister strip **61** consisting of 16, 30 or 60 or more blisters can be successfully formed into a coil in this way. It will of course be appreciated that there may be some initial expansion of the spiral wound element **60** during formation of the first closed coil.

[0102] In both versions of the spiral wound element shown in FIGS. **6** and **7**, the outer end of the spiral has a hook **53**, **63** to facilitate the attachment of the spiral wound element **50**,**60** to a suitable formation on the inner wall of a housing of a device. Other means of providing corresponding locating features to secure the element may be used. FIG. **14**(*a*), (*b*) and (*c*) show a spiral wound element **60** with notches **110** formed in it close to its outer end for location on corresponding formations on the housing.

[0103] Although the blister strip **51**, **61**, in the embodiments of FIGS. **6** and **7**, is shown coiling up within the spiral wound element **50**,**60** with the pierced upper surface of the blister strip facing outward, i.e. facing the surface of the spiral wound element **51**, **61**, it will also be appreciated that the blister strip can be encouraged to coil with the pierced upper surface facing the centre of the spiral wound element. In this way, the strip itself serves as a flexible wall to prevent the passage of residual powder around the strip. To assist in this, the blister strip can be made slightly wider than the distance between the walls of the device and more flexible so that it constantly engages with the walls of the device with sufficient force to prevent the passage of residual powder around the strip but still enabling coiling and indexing of the strip. The coil thereby effectively becomes a self-sealing enclosure preventing escape of residual powder out of the coil.

[0104] An embodiment of an inhalation device **70** incorporating a spiral wound element **60** to form a coil from a used portion of a blister strip **61** in the way described with reference to FIG. **7** is illustrated in FIGS. **8** and **9**. It will be appreciated that the general construction and operation of the device shown in FIG. **8** is similar to that of the device shown in FIGS. **1***a* and **1***b*, except that the used part of the blister strip **61** is retained within the device **70** and formed into a coil by a spiral wound element **60** located within the housing **71** of the device, rather than being ejected from it. Accordingly, the indexing mechanism **4** pushes the used portion of the strip **61** into the spiral wound element **60** as well as drawing the unused portion of the strip **61***a* from the starting coil over the blister location chassis **6** and past the blister piercing station **7**. The indexing mechanism **4** moves the strip **61** incrementally one blister at a time, i.e. activation of the indexing mechanism sequentially moves a blister into alignment with the blister piercing station so that access to the contents of each blister may be obtained one by one.

[0105] As can be seen most clearly from FIG. **8**, the hook **63** on the spiral wound element **60** hooks over a protrusion **72** formed within the wall of the housing to attach the spiral wound element **60** thereto.

[0106] It will be appreciated that the dimensions of the device shown in FIG. **8** are generally the same as that of the device shown in FIG. **1**, except that the housing **71** is elongated by the starting diameter of the spiral wound element **60**, which is typically 20 mm or less.

[0107] For obvious reasons, it is desirable to ensure that the dimensions of the device are kept within reasonable limits. This enhances patient acceptability and portability of the device. Therefore, the housing has a common chamber **80** within it that receives both unused and used portions of the blister strip. Prior to use of the inhaler **70**, a large proportion of the chamber **80** is occupied by the coil of unused blisters **61***a*, the remaining, much smaller portion, being occupied by the spiral wound element **60**. As the diameter or size of the unused portion of the strip **61***a* reduces during use, the coil formed from the used portion of the strip **61** increases in diameter causing the spiral wound element **60** to expand and increase in diameter as more and more of the blisters are used and coil up within it. As the size of the coil formed from the used portion of the strip **61** increases, and the spiral wound element **60** expands and grows, it occupies the space previously occupied by the unused portion of the strip of blisters **61***a*. Therefore, the chamber **80** is common to both used 61 and unused **61***a* portions of the strip, as opposed to having a separate chamber for each. Consequently, the overall size of the device **70** can be kept to a minimum.

[0108] It is desirable for the coil formed from the used portion **61** of the blister strip in its initial state to occupy as little space as possible and in its final state to occupy as much of the space previously occupied by the unused portion **61***a* of the blister strip as possible. Preferably the unfilled spiral wound element **60** has a diameter less than 50% of the diameter of the coil of the unused portion **61***a* of the blister strip and more preferably less than 40%. In yet further preferred embodiments, the unfilled spiral wound element **60** has a diameter less than 20-40% of the diameter of the coil of the unused portion **61***a* of the blister strip and more preferably still less than 25%. In the embodiment of FIG. **8** it has a diameter of 38% of the diameter of the coil of the unused blisters **61***a*. Preferably the coil of used blisters **61** in its final state occupies greater than 50% of the space previously occupied by the unused portion **61***a* of the blister strip.

[0109] It can be advantageous for the outer surface of the spiral wound element **60** to press against or contact the coil formed from the unused portion **61***a* of the blister strip, as generally indicated by arrow "X" in FIGS. **8** and **9**, as the unused portion **61***a* of the blister strip reduces in diameter and the used portion **61** of the blister strip increases in diameter. This can assist in steadying the spiral wound element **60** as it expands and also helps maintain a tighter coil formed from the unused portion **61***a* of the blister strip.

[0110] The spiral wound element **60** for coiling up the used portion **61** of the blister strip has been found to work with blister strips of varying degrees of thickness. The strip is required to have at least a certain degree of rigidity and stiffness otherwise it cannot withstand the compressive force exerted on it by the indexing mechanism **4** and buckles. Devices with spiral wound elements **60** have been proven to work with blister strips formed from a base layer of either 25 μm nylon/45 μm aluminium/30 μm PVC or 25 μm nylon/45 μm aluminium/60 μm PVC, containing over 60 blisters and over 660 mm in length. Spiral wound springs, such as a coil spring, have been formed from phosphor bronze, stainless steel, nylon, acetal and polypropylene. It will be appreciated that the device **70** will function adequately with a wide range of materials and dimensions for both the blister strip and the spiral wound element **60**.

[0111] The spiral wound element **60** is generally formed from a thin sheet of material (as shown, for example, in FIGS. **14***a* and **14***b*) or, it can be moulded in the form of a spiral (see FIGS. **15**(*a*) and **15**(*b*). When moulded, the surface of the element **60** may be provided with raised regions **111** to facilitate ejection of the element from the mould. It can be also be formed from wire or a thicker rectangular section material, as shown in FIGS. **16**(*a*) and **16**(*b*), so that friction between the blister strip and the surface of the spiral wound element **60** is reduced due to a smaller region of contact between the strip and the element **60**. As described earlier a range of materials can be used in the construction of the spiral **60**.

[0112] Although the spiral wound element **60** preferably has a degree of resilience, it is also envisaged that the spiral wound element **60** could be constructed from a material, such as a polymer, which creeps and relaxes as it expands thereby relieving the load on the wound blister coil. Creep may occur to at least some extent even in a resilient spiral wound element **60** as all polymers are subject to at least some degree of creep.

[0113] The spiral wound element **60** preferably has at least one complete spiral or coil extending over an angle that exceeds 360 degrees. However, it will be appreciated that it may also have a plurality of coils or portion of a coil. FIGS. **14***a* and **14***b* show a spiral wound element with one and a half turns, or 540 degrees. The coil in FIG. **14***a* can be formed from stainless steel between 0.8 and 0.15 mm thick, preferably 0.12 mm thick. Such a coil can also be formed from phosphor bronze between 0.1 mm and 0.18 mm thick, preferably 0.15 mm thick. The coil in FIG. **13***c* can be moulded from acetal with a nominal thickness of between 0.3 mm and 1.0 mm, preferably 0.5 mm.

[0114] These thicknesses are selected to give a similar stiffness irrespective of the material. Stiffness of a flat spring is proportional to Young's Modulus and the cube of the material thickness. The Young's Moduli of stainless steel, phosphor bronze and acetal are 192, 103 and 3.1 GPa respectively. Hence nominal thicknesses of 0.12, 0.15 and 0.5 mm will give similar stiffness.

[0115] Coils with two or more turns can also be used. These perform well with thinner material, for example stainless steel 0.05 mm thick. This will have a stiffness approximately 7% of that of a coil formed from material 0.12 mm thick, and it behaves in a different way, as shown in FIGS. **19** and **20** and as will be explained later. The increased flexibility of the thinner material also allows a smaller coil to be used. In one example used to accommodate a 60 blister coil, a coil of the type shown in FIG. **14***a* with a nominal starting diameter of 20 mm could be replaced by a longer thinner coil with a starting diameter of 12 mm. The more flexible coil has the further advantage that it is more tolerant of friction caused, for example, by waste powder rubbing between the coil and the strip.

[0116] In any embodiment that employs a spiral wound element of the type described, the stiffness of the spiral wound element may be constant along its length. However, it can be advantageous to provide the spiral wound element with a region of reduced stiffness towards its inner end **60***a* as this helps the spiral wound element to assume a rounder form as it expands and helps to prevent the end of the spiral wound element from "clawing" against the surface of the blister strip. The stiffness can easily be varied by changing the thickness or width of the spiral wound element or forming it so that it tapers towards its inner end **60***a*. In a preferred arrangement, the spiral wound element tapers for a portion of its length towards the inner end. A 50% reduction in section area over the last 20 mm of the length of the spiral has been found to work well. The spiral wound element can also be provided with a series of holes or slots in it to reduce its stiffness.

[0117] It will be appreciated that any embodiment that employs a spiral wound element for coiling up a used portion of a blister strip can also employ means for crushing the blister cavities prior to the used portion of the blister strip being received within the spiral wound element, such as those means described previously.

[0118] When the end of the strip is reached, it passes through the blister location chassis **6** and indexing mechanism **4**. However, it may be desirable to implement a blocking feature so that repeated actuation of the device when the blister strip has been exhausted is prevented. This would clearly indicate to the patient that all doses have been taken. The blocking feature may take the form of an enlargement attached to or formed from the end of the strip that is physically too large to pass through the blister location chassis **6**. For example, as illustrated in FIG. **9***e*, a cylindrical or spherical plastic moulding **100** is securely clipped to the end of the blister strip during assembly. The moulding **100** has no effect on the operation of the device until the end of the strip reaches the blister location chassis **6**, where further movement of the strip and actuator **5** is prevented. It will be appreciated that many other methods of creating a blocking element on the end of the strip could be used, including various shapes of plastic moulding or by forming and/or folding the end of the strip itself. However, it will be appreciated that a blocking element is not essential and, once all the blisters of a strip have been used, continued operation of the indexing mechanism will result in almost the entire length of the strip being coiled within the spiral wound element, the used portion of the strip will then comprise all the blisters of that strip.

[0119] Although the housing of an inhalation device may be provided with a common chamber **80** that stores the unused portion of the blister strip **61***a*, powder contamination of the unused portion **61** of the blister strip needs to be addressed for reasons that have already been described.

[0120] The aforementioned problem is at least partially addressed by the provision of the spiral wound element **60** because the opening in at least some of the used blister cavities lies against the inner surface of the element **60**, thereby preventing escape of residual powder from the blister cavities. It is also envisaged that the edges of the spiral wound element **60** may be provided with sealing elements, such as plastic strips formed in a U-shape to create lip seals, brushes or wipers, where they contact adjacent walls of the chamber to assist in retaining residual powder that does escape from the blister cavities within the coils of the spiral wound element **60**. As long as the sealing elements are thin and flexible, the strip can seal between the inner surfaces of the housing without impeding expansion of the spiral wound element **60**.

[0121] In another alternative arrangement, a spiral wound element **60** may be lined with a flexible tape that overlaps the edges of the element so as to create a wiper seal against the surfaces of the device walls. However, the sealing effect provided by the spiral wound element **60** itself may not alone be sufficient to prevent powder contamination of the unused portion of the blister strip **61***a*. Furthermore, to provide a complete barrier around the used portion of the blister strip **61** requires a longer spiral wound element **60** because, as the spiral wound element expands, a section of the spent coil and its associated cavities becomes exposed.

[0122] To at least partially overcome the problem of contamination of unused blisters with residual powdered dose, the Applicant's have proposed the provision of a flexible, or inflexible but movable, dividing wall so as to separate the interior of the housing into a unused blister chamber and, a used blister chamber. This wall constrains any residual powder within the used blister portion of the housing.

[0123] To reduce the size of an inhalation device, the Applicants have proposed allowing the space initially occupied by the unused portion **61***a* of the blister strip to be being slowly taken up by the used portion **61** of the blister strip as the size of the used portion **61** of the blister strip increases and the size of the unused portion **61***a* of the blister strip decreases. To address the problem of powder contamination, a flexible and/or movable dividing wall **90** is interposed between the unused portion **61***a* of the blister strip and the part of the housing **71** that receives the used portion **61** of the blister strip so as to divide the chamber **80** into "clean" and "contaminated" regions containing the unused blisters **61***a* and the used blisters **61**, respectively.

[0124] It will be appreciated that a flexible and/or movable dividing wall **90** can be used in an inhaler **70** with, or without, the spiral wound element **60** described previously, although particular benefits have been obtained as a result of using both a flexible dividing wall **90** and a spiral wound element **60** in combination as the interaction between these components has some advantages, as will become apparent from the following description.

[0125] In one unillustrated embodiment, the dividing wall may simply be a rigid element which is fixed at one end so that it can pivot about this point. Alternatively, it can be slideably fixed to the housing so that it slides depending on the relative size of the unused and used blister strips. However, in a preferred embodiment, and as shown in FIGS. **10** to **13**, the dividing wall **90** is flexible and resilient in nature and has one or both ends immovably fixed in place within the housing **71** of the device. It is also envisaged that a flexible dividing wall **90** may be elastomeric in nature so that it can expand and lengthen as pressure is applied to it by an expanding spiral wound element **60** or used blister coil **61**.

[0126] Although the flexibility of the dividing wall **90** may be such as to allow the relative sizes of the unused and used blister strip compartments to change as the device is used, the flexibility also improves or assists in the sealing of the edges of the dividing wall **90** against the walls **2***a*,**2***b* of the device housing **71** against which they rub. The width of the dividing wall **90** may be greater than the width of the space, defining the unused and used blister chamber, between the side walls **2***a*,**2***b* so that the dividing wall **90** is always held in compression between the sidewalls **2***a*,**2***b* in a direction extending across its width so as to maintain the edges of the dividing wall **90** in close contact with the sidewalls **2***a*,**2***b* of the housing, thereby minimising egress of powder from the used blister strip compartment into the unused blister compartment between the edges of the dividing wall **90** and the sidewalls **2***a*,**2***b* of the housing **71** against which they are held in contact. It is also possible to provide the edges of the dividing wall **90** with sealing elements (not shown), such as plastic strips formed in a U-shape to create lip seals, brushes or wipers, where they contact adjacent walls **2***a*,**2***b* of the housing **71** to assist in retaining residual powder that does escape from the blister cavities within the contaminated compartment of the housing **71**.

[0127] FIG. **10** illustrates an embodiment of the invention in which a flexible movable dividing wall **90** extends over the spiral wound element **60** and separates the used portion **61** of the blister strip from the unused portion **61***a* from each other. The dividing wall **90** is fixed at each end **90***a*,**90***b* to the walls of the device. FIG. **11** illustrates a partial sectional view to illustrate how the dividing wall **90** is resiliently flexible in a direction across its width "X" and is wider than the distance "Z" between the two facing sidewalls **2***a*,**2***b* of the housing **2**, so that the dividing wall **90** is slightly deformed and held in compression between the two sidewalls **2***a*,**2***b* in a direction across its width so that the edges of the dividing wall **90** apply pressure to the sidewalls **2***a*,**2***b* in the direction indicated by "F" in FIG. **11**. Although the pressure applied to the sidewalls **2***a*,**2***b* by the dividing wall **90** needs to be sufficient to prevent escape of powder from the used blister compartment to the unused blister compartment, it is important to ensure that the pressure is not so great that the friction between the dividing wall **90** and the side walls **2***a*,**2***b* is too great so as to disrupt or prevent fluid movement of the dividing wall **90** as the used blister strip **61** or spiral wound element **60** expands and pushes against it.

[0128] FIGS. **12***a* to **12***d* show how the flexible dividing wall **90** is moved or resiliently deformed by a strip of used blisters or, the expanding spiral wound element **60**, during the life of the device **70** and as the unused portion **61***a* of the blister strip unwinds and the used portion **61** of the blister strip winds up within the spiral wound element **60** or is otherwise contained within the used blister compartment.

[0129] In one embodiment, the flexible dividing wall **90** can be formed from a flexible foam strip which is dimensioned so that it is lightly compressed between the front and rear housing walls so that an effective powder seal is maintained even as the foam strip is moved by pressure applied to it by the expanding spiral wound element **60**. Foam provides a good balance between flexibility and low frictional resistance. Foams can be produced from EVA, PVA, PU and silicone, although it will be appreciated that many other materials could be used instead.

[0130] Depending on the stiffness of the foam strip, a stiffening strip (not shown), narrower than the foam strip, may be fixed to the foam strip to increase stiffness. Alternatively, a strip formed of linked rigid sections can be fixed to the flexible sealing strip to control its movement. In another unillustrated embodiment, the dividing wall **90** may itself be formed from a chain of individually rigid segments pivotally linked to each other.

[0131] In another modified arrangement, a flexible dividing wall **91** or a portion of it can be at least partially fixed to the outer surface of the spiral wound element **60**, as shown in FIG. **13**. As with the embodiment of FIG. **12**, at least one end of the dividing wall **91***a,b* can be fixed to the walls of the device.

[0132] The provision of a spiral wound element **60** having a stiffness which is sufficient to ensure that there is little or no expansion until a first closed coil of a used portion of the blister strip is formed has proved to successfully control the coiling and storage of the used portion of the blister strip within the device. However, it has been found that in circumstances where a relatively large amount of residual drug remains within the device, such as may occur when a blister is pierced but the dose is not inhaled prior to indexing to the next blister, it can find its way between the used portion **61** of the blister strip and the surface of the spiral wound element **60** which can result in an increase in friction between these components and ultimately cause the used portion **61** of the blister strip to jam within the coil **60**. The extent to which this may occur depends not only on the amount of residual drug but also on the type of drug itself and the particle size.

[0133] With the aim of minimising the occurrence of jamming, the use of a much thinner, more flexible and so less stiff spiral wound element is envisaged. In fact, the use of a foil sheet-like spiral wound element has been found sufficient to adequately coil used blisters. The coils of this element are closely wound, preferably such that adjacent coils lie in contact with each other and there is no space between them in the absence of a used portion of a blister strip. As the spiral wound element is considerably more flexible than the spiral wound elements of previous embodiments, the frictional forces between the used portion of the blister strip and the spiral wound element are considerably reduced.

[0134] The coil of a used portion of the blister strip is formed in a different way with a more flexible spiral wound element as the spiral wound element begins to move as soon as it is contacted by the leading edge of the used portion of the blister strip. The steps in the formation of a coil of blisters are shown in the sequence of drawings of FIG. **19**(*a*) to **19**(*j*).

[0135] FIG. **19**(*a*) shows a spiral wound element **150** in a stable unstressed state according to this embodiment of the invention which is formed from a flat elongate sheet of thin, flexible foil-like material. The walls of the spiral wound element **150** may all lie in contact although there may also be a space between the walls, as shown in FIG. **1**(*a*).

[0136] FIG. **19**(*b*) shows the same spiral wound element **150** as the leading edge **151***a* of a used portion of a blister strip **151** is received within the mouth **152** of the spiral wound element **150**. At this point, the leading edge **151***a* has come into contact with the curved surface of the spiral wound element **150** but there is generally no flexing or deformation of the used portion of the blister strip **151** or the spiral wound element **150**.

[0137] FIG. **19**(*c*) shows the spiral wound element **150** after the used portion of the blister strip **151** has moved further towards the spiral wound element **150** and from which it can be seen that the strip **151** begins to flex as the leading edge **151***a* starts to travel up the curved inner wall surface of the outer coil of the spiral wound element **150**, in the direction shown by arrow "A" in the Figure, and the outer coil of the spiral wound element **150** begins to move away from its adjacent inner coil and begin to straighten out due to the force of the leading end **151***a* of the relatively stiff used portion of the blister strip **151** against the flexible spiral wound element **150**.

[0138] FIG. **19**(*d*) shows the spiral wound element **150** after the used portion of the blister strip **151** has been moved further into or towards the spiral wound element **150** and from which it can be seen that the leading edge **151***a* of the blister strip **151** has traveled further up the curved inner surface of the outer coil and the blister strip **151** has deformed further pushing out and further straightening the outer coil and effectively unwinding or unrolling the spiral wound element **150**, as can be seen from the position of the trailing end **153** of the spiral wound element **150**.

[0139] FIG. **19**(*e*) shows the spiral wound element **150** after the used portion of the blister strip **151** has been moved further towards the spiral wound element **150** and from which it can be seen that the leading edge **151***a* of the blister strip **151** has traveled yet further up the curved inner surface of the outer coil, the blister strip **151** further deforming and assuming a curved shape close to its leading edge **151***a*. Further unwinding or unrolling of the spiral wound element **150** is apparent due to the load applied to the spiral wound element **150** by the leading end **151***a* of the stiffer blister strip **151**.

[0140] FIG. **19**(*f*) shows the spiral wound element **150** after the used portion of the blister strip **151** has been moved even further forward toward and into the spiral wound element **150** and from which it can be seen that the leading edge **151***a* of the blister strip **151** is now almost parallel to the inner wall surface of the outer coil of the spiral wound element **150** with the lower surface **151***b* of the blister strip **151** generally in contact with the inner wall surface.

[0141] It will be appreciated that in the transition from the position shown in FIGS. **19**(*c*) to **19**(*f*), the direction of the force applied to the spiral wound element **150** by the leading end **151***a* of the used portion of the blister strip **151** changes. In FIG. **19**(*c*), the direction in which the primary component "X" of the load acts against the spiral wound element **150** is at an angle "α" to a tangent extending along the wall surface of the spiral wound element **150** from the point of contact of the leading edge **151***a* of the strip **151** with the spiral wound element **150**, which tends to cause the spiral wound element **150** to unroll or unwind. However, in FIG. **19**(*f*) the primary component of the load acts at a much smaller angle to a tangent extending along the wall surface of the spiral wound element **150** from the point of contact of the leading edge **151***a* of the strip **151** with the spiral wound element **150** so that the strip **151** tends to more closely follow the wall surface of the spiral wound element **150** and slide along the wall surface so as to coil up within the spiral wound element **150** rather than continue to unroll or unwind it.

[0142] FIG. **19**(*g*) to **19**(*i*) shows the spiral wound element **150** after the used portion of the blister strip **151** has advanced further forward into the spiral wound element **150** and from which it can be seen that the strip **151** generally assumes a curvature which is similar to the curvature of the spiral wound element **150** and that the spiral wound element **150** begins to expand as more of the strip **151** is fed into it.

[0143] In FIG. **19**(*j*), a complete closed coil of a used portion of the blister strip has been formed. As further blisters are used up, the spiral wound element **150** expands to accommodate more blisters and to form further coils.

[0144] The sequence of FIG. **19**(*a*) to **19**(*j*) demonstrates how deformation occurs with the spiral wound element **150** in isolation, i.e. without being acted on by any external forces resulting from, for example, contact of the spiral wound element against the walls of the housing of the device and/or against a flexible dividing wall separating the chamber into two regions containing used and unused portions of the blister strip, respectively.

[0145] FIGS. **20**(*a*) to **20**(*f*) show how deformation occurs in practice and when the spiral wound element **150** is constrained between the housing wall **160** below the spiral wound element **150** and a flexible dividing wall **90** above the spiral wound element **150** or, if no dividing wall **90** is present, the unused portion of the blister strip. Generally, the spiral wound element **150** deforms in the same way although, as can be seen from FIGS. **20**(*a*) to **20**(*c*), the spiral wound element **150** unrolls or unwinds along the end wall surface **160** of the housing **170** prior to expansion. The resulting coil formed from the used portion of the blister strip is also noticeably and usefully smaller than the coil created by an unconstrained spiral wound element.

[0146] In practice, it has been found that, when the spiral wound element **150** has expanded to the extent shown in FIGS. **20**(*d*) and **20**(*e*), the coil formed from the used portion of the blister strip becomes very loose due to the flexibility of the spiral wound element **150** which places a load on the coil which is insufficient to keep it close wound or tight. This problem can be mitigated by using the flexible dividing wall **90**, the unused portion of the blister strip if no dividing wall is present, or some other dedicated element, to steady the spiral wound element **150** and used portion of the blister strip **151** as it expands, thereby preventing over expansion and maintaining relative tightness between the windings. As shown in FIGS. **20**(*a*) to **20**(*f*), expansion of the spiral wound element **150** is controlled, supported or at least steadied by its contact with the flexible dividing wall **90**. As mentioned previously, the spiral wound element and flexible dividing wall may be at least partially attached to each other so that the dividing wall expands together with the spiral wound element, thereby providing additional control of expansion of the spiral wound element.

[0147] FIGS. **21**(*a*) to **21**(*c*) show the spiral wound element according to this embodiment of the invention. FIGS. **21**(*a*) and **21**(*c*) show the spiral wound element in its normal relaxed coiled state from which it can be seen that it has a generally planar or uncoiled leading edge portion **160** with slots **161** to facilitate its connection to corresponding lugs in the device housing. FIG. **21**(*b*) shows a plan view of the spiral wound element after it has been flattened out. Table 1 shows preferred dimensions of the spiral wound element according to one preferred embodiment of the invention. As the diameter of a coiled strip of a used portion of a blister strip may exceed 50 mm, the diameter of the spiral wound element prior to receiving the strip may be less than 25% of its maximum diameter, i.e. when filled with a used portion of a strip of blisters having a diameter in the region of 50 mm.

TABLE 1

Length (a)	~104 mm
Width (b)	~17.5 mm
Diameter (c) unstressed	~12.4 mm
Length (d) of initial portion	~16 mm
Thickness (e) of material	~0.0508 mm

[0148] Although embodiments of the invention have been described in which a spiral wound element is provided only for coiling up a used portion of a blister strip, it is also envisaged that a second spiral wound element could be provided to contain the unused blister strip. In this situation, the unused blister strip may be wound into a coil within a spiral wound element that is then located in the housing of the device during assembly. As the device is used, the spiral wound element containing the coiled up strip of unused blisters gradually retracts as the coil unwinds whereas the spiral wound element that receives the used portion of the strip expands as the used portion of the strip is coiled up within it. The spiral wound elements **130***a*,**130***b* may be formed integrally as a single unit and be fixed to the housing **71** together, as shown in FIG. **17***a* which illustrates a "twin coil" spiral wound element **130** together with a strip **61***a* of unused blisters received therein and, FIG. **17***b* which illustrates the coil once loaded into an inhalation device **70** so as to form an integral part of the device. Since identical materials can be used for each spiral wound element **130***a*,**130***b*, this reduces the overall component count and simplifies the assembly process. It will be appreciated that an aperture (not shown) may need to be made in the twin spiral wound element **130** at the blister piercing station **7** to allow the piercing elements **8** to extend through the aperture into a blister located beneath it.

[0149] In an alternative arrangement, it is envisaged that two separate spiral wound elements may be used. Means to fix the twin coil element to the device housing may take the same form as the slots **161** illustrated in FIG. **21**. These slots may be formed, for example, in the spiral wound element between the two coils.

[0150] If a spiral wound element is used for the unused blister strip, the assembly of the device is greatly simplified because the coil of unused blisters is essentially preformed and held together in its coiled formation by the spiral wound element ready for insertion into the device during assembly. Preferably, the spiral wound element containing the unused blister strip is loaded into the housing of an inhaler together with the strip. However, it is envisaged that the coiled strip could be pressed out of the spiral wound element containing it immediately prior to or during insertion into the housing so that the unused strip is maintained in in its coiled state only by being constrained by the housing walls.

[0151] Blister strips are typically produced by a form/fill/seal machine which produces flat strips that must be wound into a coil prior to insertion into the device housing. Conventionally, this is achieved by gripping the end of a strip on a winding spindle and rotating the spindle until the coil is formed. Although this procedure works satisfactorily, the step of gripping the end of the strip is intricate and complex to automate. Therefore, it is advantageous to avoid having to locate and grip the strip. This is achieved with the spiral wound element of the present invention because the end of the strip can simply be fed into the mouth of the spiral wound element. As more of the strip is fed into the coil, it is wound up within it in the same way that the used blister strip is wound up within the inhalation device during use.

[0152] A sequence of drawings to show how a flat strip of unused blisters **120** which have been produced using a form/fill/seal blister strip forming machine (not shown) can be fed into and wound up within a spiral wound element **123** ready for insertion into the chamber of a device, is shown in FIGS. **18***a* to **18***c*. It will be appreciated that the strip can either be pre-cut or be cut as part of the winding process. The drive to the strip can be achieved with a driving wheel **121** and a pinch wheel **122** to give positive grip to the strip to drive it in the direction of the arrow "D" in the drawings.

[0153] As mentioned above, when the strip is fully wound it can be transferred into the device by sliding it axially out of the spiral wound element and into the device housing. Alternatively, the spiral wound element **123** ("former") can be loaded into the device housing together with the strip **120** to become a component of the device. The loaded spiral formers **123** can also be used to contain and protect the strip **120** during assembly or storage operations, as in this form it is more compact and more robust than a flat length of strip.

[0154] FIG. **22** illustrates a further embodiment of the invention which is similar to that shown and described in FIGS. **10**-**12***d*, and comprises an inhalation device **270** having a housing **271** and a flexible movable dividing wall **290** which extends over a spiral wound element **260** and separates a used portion **261** of the blister strip and an unused portion **261***a* from each other. The device **270** includes an indexing mechanism **274** comprising an actuating lever **275** which unwinds the coil one blister at a time so that they pass over a blister locator chassis **276** and successively through a blister piercing station **277**, when the actuator **275** is pivoted as described previously. When a user inhales through a mouthpiece **279**, an airflow is generated within the blister to entrain the dose contained therein and carry it out of the blister via the mouthpiece **279** and into the user's airway

[0155] The dividing wall **290** is fixed at each end **290***a*,**290***b* to the walls of the device. As with the embodiment shown in FIG. **10**, the dividing wall **290** may be resiliently flexible in a direction across its width and wider than the distance between the two facing sidewalls of the housing so that the dividing wall **290** is slightly deformed and held in compression between the two sidewalls, as described previously.

[0156] The first end **290***a* of the flexible dividing wall **290** is mounted to a support rib **291** formed in the housing **271** and extends between the side walls of the housing **271**. Thereby, the side walls and edge wall (on the left of FIG. **22**) of the housing **271**, together with the support rib **291**, define a passage **292** though which the used portion **261** of the blister strip initially passes into the used compartment from the unused compartment. Accordingly, it will be appreciated that the passage **292** is the only path through which it may be possible for residual powder to pass from the used blister compartment to the unused blister compartment of the housing. Therefore, the embodiment of the invention shown in FIG. **22** differs from that of FIG. **10** in that it includes means across the passage to substantially close the passage around the blister strip to minimise or substantially eliminate the possibility of residual powder passing from the used blister compartment to the unused blister compartment of the housing. Various configurations of such means are envisaged within the scope of the invention, some of which will be described hereafter.

[0157] FIGS. **22** and **23** show the passage **292** of the housing **271** is provided with a first element **293** projecting from the support rib **291** towards the outer wall of the housing **271**, and a second element **294** on the outer wall of the housing **271** opposite to and projecting towards the first element **293**. The first element **293** includes an arcuate cut-out **295** and it may be formed integrally with the support rib or a separate component mounted to the support rib **291**. The first and second elements **293**,**294** are spaced from each other, such that an aperture **296** is formed therebetween in the shape of a rectangular slot **296***a* with a segment or semi-circular portion **296***b* with its flat edge against one long side of the slot **296***a*. The resulting aperture **296** is thereby shaped such that the blister strip can pass through the aperture **296** with the flat portion of the blister strip located within the slot **296***a* and the blister within the segment portion **296***b*. This is shown more clearly by the enlarged partial cross-sectional view of FIG. **23**. The aperture **296** is dimensioned such it is only very slightly larger than the corresponding dimensions of the blister strip, so that the blister strip and blister thereof form a close clearance through the aperture **296**. Thereby, the passage of powder from the used blister compartment into the unused blister compartment is minimised or substantially prevented.

[0158] It should be appreciated that the indexing mechanism **274** of the inhaler **270** only causes the blister strip to be moved when the user operated the actuating lever **275**, and thus the blister strip remains in the same position during piercing and inhalation, and thereafter the same storage position until the actuating lever **275** is operated again. Furthermore, the regular spacing of the blisters in the blister strip means that each operation of the actuating lever **275** results in the blister strip being incrementally moved such that next blister along in the blister strip is positioned in the same location as the previous blister. Accordingly, the first and second elements **293**, **294** are located in the housing **271** such that a blister of the blister strip is centrally located in the aperture **296** in the piercing/inhalation/storage position of the blister strip so that the close fit of the aperture **296** around the blister and blister strip is maintained at all times except for the very brief moment of operating the actuating lever **275** to index the blister strip along.

[0159] A further variation of the embodiment shown in FIGS. **22** and **23**, is shown in FIGS. **24** and **25**. Like components retain the same reference numerals and description thereof will not be repeated. The embodiment of FIGS. **24** and **25** differs from that of FIGS. **22** and **23** in that the first element **293'** is made of a resilient material, such as foam or rubber for example, and is secured to the support rib **291**. The arcuate cut out **295'** and first element **293'** is dimensioned so that the aperture **296** is the same size as or slightly smaller than, the cross-sectional dimensions of the blister strip and blister, such that the resilient material forms a contact fit thereagainst and may deform slightly, to achieve an effective seal between the used and unused blister compartments.

[0160] With the embodiment shown in FIGS. **24** and **25**, it is intended that alternative configurations of resilient first elements **293"**, **293'"** may also be included within the scope of the invention, and are shown in FIGS. **26**A-**26**C. FIG. **26**A shows a first alternative where there is no concave cut-out portion **295'** and instead, the end is just flat. In this embodiment, the resilient member **293"** would simply be deflected around the shape of the blisters as the blister strip was indexed along. FIG. **26**B shows a second alternative **293'"** in which there is no cut-out portion **295'**, but instead of having a solid flat end as with the resilient element **293"** of FIG. **26**A, the flat end has a plurality of cuts **295"** extending into the resilient element **293'"** to form a comb or brush structure. This would enable the blisters to deform each 'finger' of the comb/brush structure as necessary as the blister strip is advanced, thereby creating less resistance to movement of the blister strip than the solid flat-ended embodiment of FIG. **26**A, whilst also maintaining a seal against the blister. FIG. **26**C shows the first resilient element **293'** of the embodiment of FIGS. **24** and **25** having the arcuate cut-out **295'**.

[0161] In all of the embodiments shown in FIGS. **22**-**26**C, the first element **293**,**293'**,**293"**,**293'"** is either formed as part of the support rib **291**, or is a separate element mounted to the support rib **291**. However, it is envisaged that the first element may instead be formed as part of the dividing wall **290**. Such an embodiment is shown in FIGS. **27** and **28**. Again, like components retain the same reference numerals and description thereof will not be repeated. The flexible dividing wall **290** extends over the top of the support rib **291** and the end portion **290***a* extends towards the second element **294**. The end **290***a* of the dividing wall **290** is spaced from the second element **294** and shaped with an arcuate cut-out as with the embodiment shown in FIGS. **24** and **25**, and so performs the same function as described above for that embodiment. In addition, the end **290***a* of the dividing wall **290** may alternatively be shaped with a flat end **290***a*' or a comb/brush structure end **290***a*", as described above with reference to FIGS. **26**A and **26**B. These alternatives are shown in FIGS. **29**A and **29**B and have the same function and advantages as described previously FIG. **29**C shows the end **290***a* of the dividing wall of FIGS. **27** and **28**.

[0162] All of the embodiments shown and described in FIGS. **27-29**C include the second element **294** as a separate element to the dividing wall **290**, formed integrally with or mounted to the wall of the housing **271**. However, an alternative embodiment is shown in FIGS. **30** and **31**, in which no separate second element is provided. Instead, the dividing wall **290** extends over the top of the support rib **291** and the end portion **290***a* all the way to the wall of the housing **271** where it is secured, for example, by being bonded thereto. To allow the blister strip to pass through the passage **292** from the unused compartment to the used compartment, an aperture **297** is formed in the dividing wall **290** between the support rib **291** and the wall of the housing **271**, and is shaped as a slit **297***a* with a segment-shaped portion **297***b*, to accommodate the blister strip and blister as shown in FIG. **31**. As above, the aperture **297** may be dimensioned to be the same size or slightly smaller than the cross-sectional dimensions of the blister strip and blister, such that the resilient material forms a contact fit thereagainst and may deform slightly, to achieve an effective seal between the used and unused blister compartments. The dividing wall also includes a slit **298** extending from the aperture **297** to the edge of the dividing wall **290**. This enables a blister strip to be loaded in the inhaler **270** and positioned in the aperture **297** in the dividing wall **290** by sliding it though the slit **298**, without having to feed one remote end of the blister strip though the aperture **297**.

[0163] In a further un-illustrated embodiment of the invention, the inhaler could be provided as shown in FIGS. **30** and **31**, except that the end **290***a* of the dividing wall may not be secured to the wall of the housing **271**, and would not have an aperture **297** formed therein. Instead, a remote end of the dividing wall **290** would include an arcuate cut out and be configured to bias towards the wall of the housing **271** away from the support rib **291**. In use, the end of the dividing wall would bias the blister strip against the wall of the housing **271**, with the arcuate cut-out conforming around the blister, to effect the seal in the passage **292** between the used and unused blister compartments. Also, the end of the dividing wall may be flat ended or have a comb/brush configuration as described above with reference to other embodiments, instead of having an arcuate cut-out portion.

[0164] It should be appreciated that in the above-described embodiments that include a second element **294**, this may be made from a resilient material secured to the wall of the housing **271**, to effect a snug fit against the blister strip, as well as being a solid element formed integrally with or secured to the housing **271**.

[0165] A variety of medicaments may be administered alone by using inhalers of the invention. Such medicaments include those that are suitable for the treatment of asthma, chronic obstructive pulmonary diseases (COPD), respiratory infections, rhinitis, allergic rhinitis, nasal diseases and disorders; general and specific conditions, and systemic diseases with the lung or nasal cavity as the site of delivery. Such medicaments include, but are not limited to, β_2-agonists, eg carmoterol, fenoterol, formoterol, levalbuterol, pirbuterol, reproterol, metaproterenol, rimiterol, salbutamol, salmeterol, indacaterol, terbutaline, orciprenaline, clenbuterol, bambuterol, procaterol, broxaterol, picumeterol, and bitolterol; non-selective β-stimulants such as ephedrine and isoprenaline; phosphodiesterase (PDE) inhibitors, eg methylxanthines, theophylline, aminophylline, choline theophyllinate, and selective PDE isoenzyme inhibitors, PDE 3 inhibitors, eg milrinone and motapizone; PDE 4 inhibitors, eg rolipram, cilomilast, roflumilast, oglemilast, and ONO **6126**; PDE 3/4 inhibitors, eg zardaverine and tolafentrine; inducers of HDAC2 eg theophylline; anticholinergics including muscarinic receptor (M1, M2, and M3) antagonists eg atropine, hyoscine, glycopyrrolate, ipratropium, tiotropium, oxitropium, NVA237, pirenzepine, and telenzepine; mast cell stabilisers, eg cromoglycate and ketotifen; bronchial anti-inflammatory agents, eg nedocromil; steroids, eg beclometasone, dexamethasone, fluticasone, budesonide, flunisolide, rofleponide, triamcinolone, butixocort, mometasone, and ciclesonide; disease modifying agents such as methotrexate, leflunomide, teriflunomide, and hydroxychloroquine; histamine type 1 receptor antagonists, eg cetirizine, loratadine, desloratadine, fexofenadine, acrivastine, terfenadine, astemizole, azelastine, levocabastine, chlorpheniramine, promethazine, cyclizine, and mizolastine; antibacterial agents and agents for cystic fibrosis and/or tuberculosis treatment, eg *Pseudomonas aeruginosa* infection vaccines (eg Aerugen®), mannitol, denufosol, glutathione, N-acetylcysteine, amikacin duramycin, gentamycin, tobramycin, dornase alfa, alpha 1-antitrypsin, heparin, dextran, capreomycin, vancomycin, meropenem, ciprofloxacin, piperacillin, and rifampicin; mucolytic agents for the treatment of COPD and cystic fibrosis, eg N-acetylcysteine, and ambroxol; histamine type 2 receptor antagonists; tachykinin neurokinin antagonists; triptans, eg almotriptan, rizatriptan, naratriptan, zolmitriptan, sumatritpan, eletriptan, and frovatriptan; neurological agents eg apomorphine, dronabinol, dihydroergotamine, and loxapine; antiviral agents eg foscarnet, acyclovir, famciclovir, valacyclovir, ganciclovir, cidofovir; amantadine, rimantadine; ribavirin; zanamivir and oseltamavir and pleconaril, protease inhibitors (eg ruprintrivir, indinavir, nelfinavir, ritonavir, and saquinavir), nucleoside reverse transcriptase inhibitors (eg didanosine, lamivudine, stavudine, zalcitabine, and zidovudine), and non-nucleoside reverse transcriptase inhibitors (eg nevirapine and efavirenz); α-1/α-2 adrenoceptor agonists, eg propylhexedrine, phenylephrine, phenylpropanolamine, ephedrine, pseudoephedrine, naphazoline, oxymetazoline, tetrahydrozoline, xylometazoline, tramazoline, and ethylnorepinephrine; platelet aggregation inhibitors/anti-inflammatory agents, eg bemiparin, enoxaparin, heparin; anti-infectives, eg cephalosporins, penicillins, tetracyclines, macrolides, beta-lactams, fluoroquinolones, streptomycin, sulphonamides, aminoglycosides (eg tobramycin), doripenem, pentamidine, colistimethate, and aztreonam; agents for sexual health, sexual dysfunction including premature ejaculation; eg. apomorphine, VR776, agents that acts via 5HT- and noradrenergic-mediated pathways in the brain, leuprolide, and PDE 5 inhibitors eg, sildenafil, tadalafil, and vardenafil; leukotriene modifiers, eg zileuton, fenleuton, tepoxalin, montelukast, zafirlukast, ontazolast, ablukast, pranlikast, verlukast, and iralukast; inducible nitric oxide synthase (iNOS) inhibitors; antifungals, eg amphotericin B, natamycin, and nystatin; analgesics, eg codeine, dihydromorphine, ergotamine, fentanyl, cannabinoids, and morphine; anxiolytic/antidepressive agents, eg benzodiazepines and benzodiazepine derivatives, diazepam, midazolam, chlordiazepoxide, lorazepam, oxazepam, clobazam, alprazolam, clonazepam, flurazepam, zolazepam; tryptase and elastase inhibitors; beta-2 integrin antagonists; adenosine receptor agonists or antagonists, eg adenosine **2***a* agonists; calcium channel blockers, eg gallopamil, and diltiazem; prostacyclin analogues, eg iloprost; endothelin-receptor antagonists, eg LU-135252; cytokine antagonists, eg chemokine antagonists and inhibitors and modifiers of cytokine synthesis including modifiers and inhibitors of the pro-inflammatory transcription factor, NFkB; interleukins and inhibitors of interleukins, eg aldesleukin; therapeutic proteins and peptides, eg insulin, insulin aspart, insulin glulisine; insulin lispro, neutral, regular and soluble insulins, isophane insulins, insulin zinc, protamine zinc insulin, insulin analogues, acylated insulin, insulin glargine, insulin detemir, glucagon, glucagon-like peptides, and exendins; enzymes, eg dornase alfa; systemically active macromolecules, eg human growth hormone, leuprolide, alpha-interferon, growth factors (eg insulin-like growth factor type 1), hormones, eg epinephrine, testosterone, and parathyroid hormone and analogues (eg Ostabolin-C); osteoporosis agents, eg bisphosphonates; anticancer agents, eg anthracyclines, doxorubicin, idarubicin, epirubicin, methotrexate, taxanes, paclitaxel, docetaxel, ciplatin, vinca alkaloids, vincristine, and 5-fluorouracil; anticoagulants, eg blood factors and blood factor constructs, eg FVIII-Fc and FIX-Fc; eg FV111-Fc; immunomodulators, eg cyclosporine, sirolimus, and tacrolimus; antiproliferative immunosuppressants, eg azathioprine, and mycophenolate mofetil; cytokines (eg interferons, interferon β, interleukins, and interleukin antagonists and inhibitors); nucleic acids; vaccines, eg flumist; anti-obesity agents; diagnostics and gene therapies. It will be clear to a person skilled in the art that, where appropriate, the medicaments may be linked to a carrier molecule or molecules and/or used in the form of prodrugs, salts, as esters, or as solvates to optimise the activity and/or stability of the medicament.

[0166] Inhalers according to the invention may also be used to deliver combinations of two or more different medicaments. Specific combinations of two medicaments which may be mentioned include combinations of steroids and β_2-agonists. Examples of such combinations are beclomethasone and formoterol; beclomethasone and salmeterol; fluticasone and formoterol; fluticasone and salmeterol; budesonide and formoterol; budesonide and salmeterol; flunisolide and formoterol; flunisolide and salmeterol; ciclesonide and salmeterol; ciclesonide and formoterol; mometasone and salmeterol; and mometasone and formoterol. Specifically inhalers according to the invention may also be used to deliver combinations of three different medicaments.

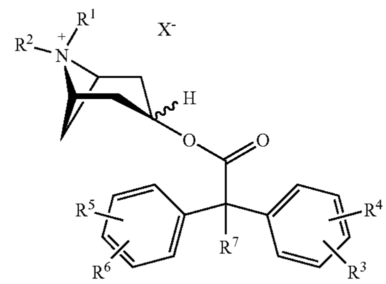
[0167] It will be clear to a person skilled in the art that, where appropriate, the medicaments may be linked to a carrier molecule or molecules and/or used in the form of prodrugs, salts, as esters, or as solvates to optimise the activity and/or stability of the medicament.

[0168] It is also envisaged that the pharmaceutical composition may comprise one or more, preferably one, anticholinergic **1**, optionally in combination with a pharmaceutically acceptable excipient.

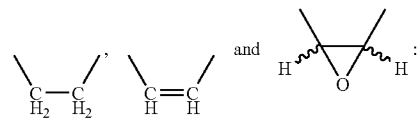
[0169] The anticholinergic **1** can be selected from the group consisting of

a) tiotropium salts **1***a,*
b) compounds of formula 1c

1c



wherein
A denotes a double-bonded group selected from among



[0170] X^- denotes an anion with a single negative charge, preferably an anion selected from the group consisting of fluoride, chloride, bromide, iodide, sulphate, phosphate, methanesulphonate, nitrate, maleate, acetate, citrate, fumarate, tartrate, oxalate, succinate, benzoate and p-toluenesulphonate,

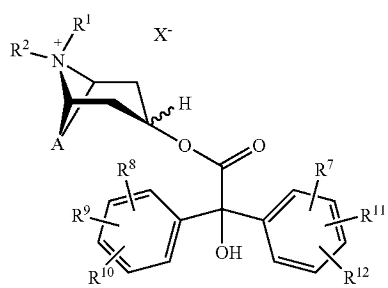
[0171] R^1 and R^2 which may be identical or different denote a group selected from among methyl, ethyl, n-propyl and iso-propyl, which may optionally be substituted by hydroxy or fluorine, preferably unsubstituted methyl;

[0172] R^3, R^4, R^5 and R^6, which may be identical or different, denote hydrogen, methyl, ethyl, methyloxy, ethyloxy, hydroxy, fluorine, chlorine, bromine, CN, CF_3 or NO_2;

[0173] R^7 denotes hydrogen, methyl, ethyl, methyloxy, ethyloxy, —CH_2—F, —CH_2—CH_2—F, -0-CH_2—F, -0-CH_2—CH_2—F, —CH_2—OH, —CH_2—CH_2—OH, CF_3, —CH_2—OMe, —CH_2—CH_2-OMe, —CH_2—OEt, —CH_2—CH_2-OEt, —O—COMe, —O—COEt, -Q-$COCF_3$, -Q-$COCF_3$, fluorine, chlorine or bromine;

c) compounds of formula 1d

1d

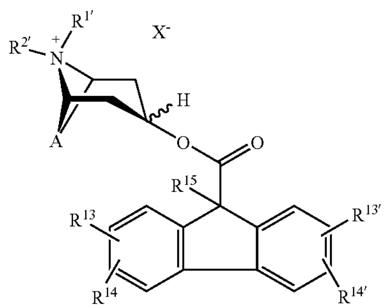


[0174] wherein

[0175] A, X^{-1}, R^1 and R^2 may have the meanings as mentioned hereinbefore and wherein R^7, R^8, R^9, R^{10},

R^{11} and R^{12}, which may be identical or different, denote hydrogen, methyl, ethyl, methyloxy, ethyloxy, hydroxy, fluorine, chlorine, bromine, CN, CF_3 or NO_2, with the proviso that at least one of the groups R^7, R^8, R^9, R^{10}, R^{11} and R^{12} is not hydrogen,

d) compounds of formula 1e



1e

[0176] wherein A and X^- may have the meanings as mentioned hereinbefore, and wherein

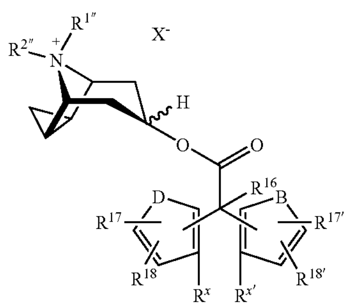
[0177] R^{15} denotes hydrogen, hydroxy, methyl, ethyl, —CF_3, CHF_2 or fluorine;

[0178] $R^{1'}$ and $R^{2'}$ which may be identical or different denote C_1-C_5-alkyl which may optionally be substituted by C_3-C_6-cycloalkyl, hydroxy or halogen, or

[0179] $R^{1'}$ and $R^{2'}$ together denote a —C_3-C_5-alkylene-bridge;

[0180] R^{13}, R^{14}, $R^{13'}$ and $R^{14'}$ which may be identical or different denote hydrogen, —C_1-C_4-alkyl, —C_1-C_4-alkyloxy, hydroxy, —CF_3, —CHF_2, CN, NO_2 or halogen,

e) compounds of formula 1f



1f

[0181] wherein X^- may have the meanings as mentioned hereinbefore, and wherein

[0182] D and B which may be identical or different, preferably identical, denote —O, —S, —NH, —CH_2, —CH═CH, or —N(C_1-C_4-alkyl)-;

[0183] R^{16} denotes hydrogen, hydroxy, —C_1-C_4-alkyl, —C_1-C_4-alkyloxy, —C_1-C_4-alkylene-Halogen, —O—C_1-C_4 alkylene-halogen, —C_1-C_4-alkylene-OH, —CF_3, CHF_2, —C_1-C_4-alkylene-C_1-C_4 alkyloxy, —O—COC_1-C_4-alkyl, —O—COC_1-C_4-alkylene-halogen, —C_1-C_4-alkylene-C_3-C_6-cycloalkyl, —O—$COCF_3$ or halogen;

[0184] $R^{1''}$ and $R^{2''}$ which may be identical or different, denote —C_1-C_5-alkyl, which may optionally be substituted by —C_3-C_6-cycloalkyl, hydroxy or halogen, or

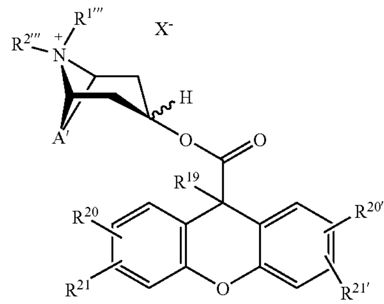
[0185] $R^{1''}$ and $R^{2''}$ together denote a —C3-C5-alkylene bridge;

[0186] R^{17}, R^{18}, $R^{17'}$ and $R^{18'}$, which may be identical or different, denote hydrogen, C_1-C_4-alkyl, C_1-C_4-alkyloxy, hydroxy, —CF_3, —CHF_2, CN, NO_2 or halogen;

[0187] R^x and $R^{x'}$ which may be identical or different, denote hydrogen, C_1-C_4-alkyl, C_1-C_4-alkyloxy, hydroxy, —CF_3, —CHF_2, CN, NO_2 or halogen or

[0188] R^x and $R^{x'}$ together denote a single bond or a bridging group selected from among the bridges —O, —S, —NH, —CH_2, —CH_2—CH_2—, —N(C_1-C_4-alkyl), —CH(C_1-C_4-alkyl)- and —C(C_1-C_4-alkyl)$_2$, and

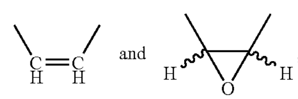
f) compounds of formula 1g



1g

[0189] wherein X^- may have the meanings as mentioned hereinbefore, and wherein

[0190] A' denotes a double-bonded group selected from among



[0191] R^{19} denotes hydroxy, methyl, hydroxymethyl, ethyl, —CF_3, CHF_2 or fluorine;

[0192] $R^{1'''}$ and $R^{2'''}$ which may be identical or different denote C_1-C_5-alkyl which may optionally be substituted by C_3-C_6-cycloalkyl, hydroxy or halogen, or

[0193] $R^{1'''}$ and $R^{2'''}$ together denote a —C_3-C_5-alkylene-bridge;

[0194] R^{20}, R^{21}, $R^{20'}$ and $R^{21'}$ which may be identical or different denote hydrogen, —C_1-C_4-alkyl, —C_1-C_4-alkyloxy, hydroxy, —CF_3, —CHF_2, CN, NO_2 or halogen.

[0195] The compounds of formula 1c are known in the art (WO 02/32899).

[0196] In a preferred embodiment of the invention the method comprises administration of compounds of formula 1c, wherein

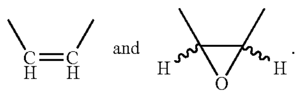
[0197] X^- denotes bromide;

[0198] R^1 and R^2 which may be identical or different denote a group selected from methyl and ethyl, preferably methyl;

[0199] R^3, R^4, R^5 and R^6, which may be identical or different, denote hydrogen, methyl, methyloxy, chlorine or fluorine;

[0200] R^7 denotes hydrogen, methyl or fluorine, optionally together with a pharmaceutically acceptable excipient.

[0201] Of particular importance are compounds of general formula 1c, wherein A denotes a double-bonded group selected from among



[0202] The compounds of formula 1c, may optionally be administered in the form of the individual optical isomers, mixtures of the individual enantiomers or racemates thereof.

[0203] Of particular importance within a method according to the invention are the following compounds of formula 1c:

[0204] tropenol 2,2-diphenylpropionic acid ester methobromide,

[0205] scopine 2,2-diphenylpropionic acid ester methobromide,

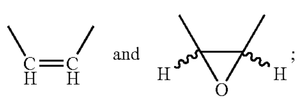
[0206] scopine 2-fluoro-2,2-diphenylacetic acid ester methobromide and

[0207] tropenol 2-fluoro-2,2-diphenylacetic acid ester methobromide.

[0208] The compounds of formula 1d are known in the art (WO 02/32898).

[0209] In a preferred embodiment of the invention the method comprises administration of compounds of formula 1d, wherein

[0210] A denotes a double-bonded group selected from among



[0211] X^- denotes bromide;

[0212] R^1 and R^2 which may be identical or different denote methyl or ethyl, preferably methyl;

[0213] R^7, R^8, R^9, R^{10}, R^{11} and R^{12}, which may be identical or different, denote hydrogen, fluorine, chlorine or bromine, preferably fluorine with the proviso that at least one of the groups R^7, R^8, R^9, R^{10}, R^{11} and R^{12} not hydrogen, optionally together with a pharmaceutically acceptable excipient.

[0214] Of particular importance within the method according to the invention are the following compounds of formula 1d:

[0215] tropenol 3,3',4,4'-tetrafluorobenzilic acid ester methobromide,

[0216] scopine 3,3',4,4'-tetrafluorobenzilic acid ester methobromide,

[0217] scopine 4,4'-difluorobenzilic acid ester methobromide,

[0218] tropenol 4,4'-difluorobenzilic acid ester methobromide,

[0219] scopine 3,3'-difluorobenzilic acid ester methobromide, and

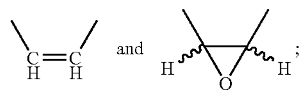
[0220] tropenol 3,3'-difluorobenzilic acid ester methobromide.

[0221] The pharmaceutical compositions according to the invention may contain the compounds of formula 1d optionally in the form of the individual optical isomers, mixtures of the individual enantiomers or racemates thereof.

[0222] The compounds of formula 1e are known in the art (WO 03/064419).

[0223] In a preferred embodiment of the invention the method comprises administration of compounds of formula 1e, wherein

[0224] A denotes a double-bonded group selected from among



[0225] X^- denotes an anion selected from among chloride, bromide and methanesulphonate, preferably bromide;

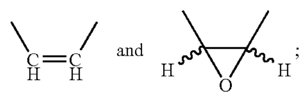
[0226] R^{15} denotes hydroxy, methyl or fluorine, preferably methyl or hydroxy;

[0227] $R^{1'}$ and $R^{2'}$ which may be identical or different represent methyl or ethyl, preferably methyl;

[0228] R^{13}, R^{14}, $R^{13'}$ and $R^{14'}$ which may be identical or different represent hydrogen, $—CF_3$, $—CHF_2$ or fluorine, preferably hydrogen or fluorine, optionally together with a pharmaceutically acceptable excipient.

[0229] In another preferred embodiment of the invention the method comprises administration of compounds of formula 1e, wherein

[0230] A denotes a double-bonded group selected from among



[0231] X^- denotes bromide;

[0232] R^{15} denotes hydroxy or methyl, preferably methyl;

[0233] $R^{1'}$ and $R^{2'}$ which may be identical or different represent methyl or ethyl, preferably methyl;

[0234] R^{13}, R^{14}, $R^{13'}$ and $R^{14'}$ which may be identical or different represent hydrogen or fluorine, optionally together with a pharmaceutically acceptable excipient.

[0235] Of particular importance within the method according to the invention are the following compounds of formula 1e:

[0236] tropenol 9-hydroxy-fluorene-9-carboxylate methobromide;

[0237] tropenol 9-fluoro-fluorene-9-carboxylate methobromide;

[0238] scopine 9-hydroxy-fluorene-9-carboxylate methobromide;

[0239] scopine 9-fluoro-fluorene-9-carboxylate methobromide;

[0240] tropenol 9-methyl-fluorene-9-carboxylate methobromide;

[0241] scopine 9-methyl-fluorene-9-carboxylate methobromide.

[0242] The pharmaceutical compositions according to the invention may contain the compounds of formula 1e optionally in the form of the individual optical isomers, mixtures of the individual enantiomers or racemates thereof.

[0243] The compounds of formula 1f are known in the art (WO 03/064418)

[0244] In another preferred embodiment of the invention the method comprises administration of compounds of formula if wherein

[0245] X^- denotes chloride, bromide, or methanesulphonate, preferably bromide; D and B which may be identical or different, preferably identical, denote —O, —S, —NH or —CH═CH—;

[0246] R^{16} denotes hydrogen, hydroxy, —C_1-C_4-alkyl, —C_1-C_4 alkyloxy, —CF_3, —CHF_2, fluorine, chlorine or bromine;

[0247] $R^{1''}$ and $R^{2''}$ which may be identical or different, denote C_1-C_4-alky, which may optionally be substituted by hydroxy, fluorine, chlorine or bromine, or

[0248] $R^{1''}$ and $R^{2''}$ together denote a —C_3-C_4-alkylene-bridge;

[0249] R^{17}, R^{18}, $R^{17'}$ and $R^{18'}$, which may be identical or different, denote hydrogen, C_1-C_4-alkyl, C_1-C_4-alkyloxy, hydroxy, —CF_3, —CHF_2, CN, NO_2, fluorine, chlorine or bromine;

[0250] R^x and $R^{x'}$ which may be identical or different, denote hydrogen, C_1-C_4-alkyl, C_1-C_4-alkyloxy, hydroxy, —CF_3, —CHF_2, CN, NO_2, fluorine, chlorine or bromine or

[0251] R^x and $R^{x'}$ together denote a single bond or a bridging group selected from among the bridges —O, —S, —NH— and —CH_2—, optionally together with a pharmaceutically acceptable excipient.

[0252] In another preferred embodiment of the invention the method comprises administration of compounds of formula 1f, wherein

[0253] X^- denotes chloride, bromide, or methanesulphonate, preferably bromide; D and B which may be identical or different, preferably identical, denote —S or —CH═CH—;

[0254] R^{16} denotes hydrogen, hydroxy or methyl;

[0255] $R^{1''}$ and $R^{2''}$ which may be identical or different, denote methyl or ethyl;

[0256] R^{17}, R^{18}, $R^{17'}$ and $R^{18'}$, which may be identical or different, denote hydrogen, —CF_3 or fluorine, preferably hydrogen;

[0257] R^x and $R^{x'}$ which may be identical or different, denote hydrogen, —CF_3 or fluorine, preferably hydrogen or

[0258] R^x and $R^{x'}$ together denote a single bond or the bridging group —O—, optionally together with a pharmaceutically acceptable excipient.

[0259] In another preferred embodiment of the invention the method comprises administration of compounds of formula 1f wherein

[0260] X^- denotes bromide;

[0261] D and B denote —CH═CH—;

[0262] R^{16} denotes hydrogen, hydroxy or methyl;

[0263] $R^{1''}$ and $R^{2''}$ denote methyl;

[0264] R^{17}, R^{18}, $R^{17'}$ and $R^{18'}$, which may be identical or different, denote hydrogen or fluorine, preferably hydrogen;

[0265] R^x and $R^{x'}$ which may be identical or different, denote hydrogen or fluorine, preferably hydrogen or

[0266] R^x and $R^{x'}$ together denote a single bond or the bridging group —O—, optionally together with a pharmaceutically acceptable excipient.

[0267] Of particular importance within the method according to the invention are the following compounds of formula 1f:

[0268] cyclopropyltropine benzilate methobromide;

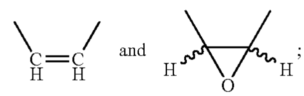
[0269] cyclopropyltropine 2,2-diphenylpropionate methobromide; cyclopropyltropine 9-hydroxy-xanthene-9-carboxylate methobromide; cyclopropyltropine 9-methyl-fluorene-9-carboxylate methobromide; cyclopropyltropine 9-methyl-xanthene-9-carboxylate methobromide; cyclopropyltropine 9-hydroxy-fluorene-9-carboxylate methobromide; cyclopropyltropine methyl 4,4'-difluorobenzilate methobromide.

[0270] The pharmaceutical compositions according to the invention may contain the compounds of formula 1f optionally in the form of the individual optical isomers, mixtures of the individual enantiomers or racemates thereof.

[0271] The compounds of formula 1g are known in the art (WO 03/064417).

[0272] In another preferred embodiment of the invention the method comprises administration of compounds of formula 1g wherein

[0273] A' denotes a double-bonded group selected from among



[0274] X^- denotes chloride, bromide or methanesulphonate, preferably bromide;

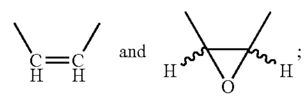
[0275] R^{19} denotes hydroxy or methyl;

[0276] $R^{1'''}$ and $R^{2'''}$ which may be identical or different represent methyl or ethyl, preferably methyl;

[0277] R^{20}, R^{21}, $R^{20'}$ and $R^{21'}$ which may be identical or different represent hydrogen, —CF_3, —CHF_2 or fluorine, preferably hydrogen or fluorine, optionally together with a pharmaceutically acceptable excipient.

[0278] In another preferred embodiment of the invention the method comprises administration of compounds of formula 1g wherein

[0279] A' denotes a double-bonded group selected from among



[0280] X^- denotes bromide;

[0281] R^{19} denotes hydroxy or methyl, preferably methyl;

[0282] $R^{1'''}$ and $R^{2'''}$ which may be identical or different represent methyl or ethyl, preferably methyl;

[0283] R^3, R^4, $R^{3'}$ and $R^{4'}$ which may be identical or different represent hydrogen or fluorine, optionally together with a pharmaceutically acceptable excipient.

[0284] Of particular importance within the method according to the invention are the following compounds of formula 1g:

[0285] tropenol 9-hydroxy-xanthene-9-carboxylate methobromide;

[0286] scopine 9-hydroxy-xanthene-9-carboxylate methobromide;

[0287] tropenol 9-methyl-xanthene-9-carboxylate methobromide;

[0288] scopine 9-methyl-xanthene-9-carboxylate methobromide;

[0289] tropenol 9-ethyl-xanthene-9-carboxylate methobromide;

[0290] tropenol 9-difluoromethyl-xanthene-9-carboxylate methobromide;

[0291] scopine 9-hydroxymethyl-xanthene-9-carboxylate methobromide.

[0292] The pharmaceutical compositions according to the invention may contain the compounds of formula 1g optionally in the form of the individual optical isomers, mixtures of the individual enantiomers or racemates thereof.

[0293] The alkyl groups used, unless otherwise stated, are branched and unbranched alkyl groups having 1 to 5 carbon atoms. Examples include: methyl, ethyl, propyl or butyl. The groups methyl, ethyl, propyl or butyl may optionally also be referred to by the abbreviations Me, Et, Prop or Bu. Unless otherwise stated, the definitions propyl and butyl also include all possible isomeric forms of the groups in question. Thus, for example, propyl includes n-propyl and iso-propyl, butyl includes iso-butyl, sec. butyl and tert.-butyl, etc.

[0294] The cycloalkyl groups used, unless otherwise stated, are alicyclic groups with 3 to 6 carbon atoms. These are the cyclopropyl, cyclobutyl, cyclopentyl and cyclohexyl groups. According to the invention cyclopropyl is of particular importance within the scope of the present invention.

[0295] The alkylene groups used, unless otherwise stated, are branched and unbranched double-bonded alkyl bridges with 1 to 5 carbon atoms. Examples include: methylene, ethylene, propylene or butylene.

[0296] The alkylene-halogen groups used, unless otherwise stated, are branched and unbranched double-bonded alkyl bridges with 1 to 4 carbon atoms which may be mono-, di- or trisubstituted, preferably disubstituted, by a halogen. Accordingly, unless otherwise stated, the term alkylene-OH groups denotes branched and unbranched double-bonded alkyl bridges with 1 to 4 carbon atoms which may be mono-, di- or trisubstituted, preferably monosubstituted, by a hydroxy.

[0297] The alkyloxy groups used, unless otherwise stated, are branched and unbranched alkyl groups with 1 to 5 carbon atoms which are linked via an oxygen atom. The following may be mentioned, for example: methyloxy, ethyloxy, propyloxy or butyloxy. The groups methyloxy, ethyloxy, propyloxy or butyloxy may optionally also be referred to by the abbreviations MeO, EtO, PropO or BuO. Unless otherwise stated, the definitions propyloxy and butyloxy also include all possible isomeric forms of the groups in question. Thus, for example, propyloxy includes n-propyloxy and iso-propyloxy, butyloxy includes iso-butyloxy, sec. butyloxy and tert.-butyloxy, etc. The word alkoxy may also possibly be used within the scope of the present invention instead of the word alkyloxy. The groups methyloxy, ethyloxy, propyloxy or butyloxy may optionally also be referred to as methoxy, ethoxy, propoxy or butoxy.

[0298] The alkylene-alkyloxy groups used, unless otherwise stated, are branched and unbranched double-bonded alkyl bridges with 1 to 5 carbon atoms which may be mono-, di- or trisubstituted, preferably monosubstituted, by an alkyloxy group.

[0299] The —O—CO-alkyl groups used, unless otherwise stated, are branched and unbranched alkyl groups with 1 to 4 carbon atoms which are bonded via an ester group. The alkyl groups are bonded directly to the carbonylcarbon of the ester group. The term —O—CO-alkyl-halogen group should be understood analogously. The group —O—CO—CF_3 denotes trifluoroacetate.

[0300] Within the scope of the present invention halogen denotes fluorine, chlorine, bromine or iodine. Unless otherwise stated, fluorine and bromine are the preferred halogens. The group CO denotes a carbonyl group.

[0301] One aspect of the invention is directed to an inhalation device, in which the plural of doses are contained in one reservoir. In another aspect of the invention, the inhalation device comprises the plural of doses in a multi-dose blister pack. In another aspect of the invention the inhalation device comprises the multi-dose blister pack in form of blister strip.

[0302] The inhalation device according to the invention comprises the compounds of formula 1 preferably in admixture with a pharmaceutically acceptable excipient to form a powder mixture. The following pharmaceutically acceptable excipients may be used to prepare these inhalable powder mixtures according to the invention: monosaccharides (e.g. glucose or arabinose), disaccharides (e.g. lactose, saccharose, maltose, trehalose), oligo- and polysaccharides (e.g. dextrane), polyalcohols (e.g. sorbitol, mannitol, xylitol), salts (e.g. sodium chloride, calcium carbonate) or mixtures of these excipients with one another. Preferably, mono- or disaccharides are used, while the use of lactose or glucose is preferred, particularly, but not exclusively, in the form of their hydrates. For the purposes of the invention, lactose and trehalose are the particularly preferred excipients, while lactose, preferably in form of its monohydrate is most particularly preferred.

[0303] The compounds of formula 1 may be used in the form of their racemates, enantiomers or mixtures thereof. The separation of enantiomers from the racemates may be carried out using methods known in the art (e.g. by chromatography on chiral phases, etc.).

[0304] Optionally, the inhalation device according to the invention contains plural of doses of a medicament in powder form that contains, beside one compound of formula 1, another active ingredient.

[0305] Preferably the additional active ingredient is a $beta_2$ agonists 2 which is selected from the group consisting of albuterol, bambuterol, bitolterol, broxaterol, carbuterol, clenbuterol, fenoterol, formoterol, hexoprenaline, ibuterol, isoetharine, isoprenaline, levosalbutamol, mabuterol, meluadrine, metaproterenol, orciprenaline, pirbuterol, procaterol, reproterol, rimiterol, ritodrine, salmeterol, salmefamol, soterenot, sulphonterol, tiaramide, terbutaline, tolubuterol, CHF-1035, HOKU-81, KUL-1248, 3-(4-{6-[2-Hydroxy-2-(4-hydroxy-3-hydroxymethyl-phenyl)-ethylamino]-hexyloxy}-butyl)-benzenesulfoneamide, 5-[2-(5,6-Diethyl-indan-2-ylamino)-1-hydroxy-ethyl]-8-hydroxy-1H-quinolin-2-one, 4-hydroxy-7-[2-{[2-{[3-(2-phenylethoxy)propyl] sulphonyl}ethyl]-amino}ethyl]-2(3H)-benzothiazolone, 1-(2-fluoro-4-hydroxyphenyl)-2-[4-(1-benzimidazolyl)-2-methyl-2-butylamino]ethanol, 1-[3-(4-methoxybenzyl-amino)-4-hydroxyphenyl]-2-[4-(1-benzimidazolyl)-2-methyl-2-butylamino]ethanol, 1-[2H-5-hydroxy-3-oxo-4H-1,4-benzoxazin-8-yl]-2-[3-(4-N,N-dimethylaminophenyl)-2-methyl-2-propylamino]ethanol, 1-[2H-5-hydroxy-3-oxo-4H-1,4-benzoxazin-8-yl]-2-[3-(4-methoxyphenyl)-2-methyl-2-propylamino]ethanol, 1-[2H-5-hydroxy-3-OXO-4H-1,4-benzoxazin-8-yl]-2-[3-(4-n-butyloxyphenyl)-2-methyl-2-propylamino]ethanol, 1-[2H-5-hydroxy-3-oxo-4H-1,4-benzoxazin-8-yl]-2-{4-[3-(4-methoxyphenyl)-1,2,4-

triazol-3-yl]-2-methyl-2-butylamino}ethanol, 5-hydroxy-8-(1-hydroxy-2-isopropylaminobutyl)-2H-1,4-benzoxazin-3-(4H)-one, 1-(4-amino-3-chloro-5-trifluormethylphenyl)-2-tert.-butylamino) ethanol and 1-(4-ethoxycarbonylamino-3-cyano-5-fluorophenyl)-2-(tert.-butylamino)ethanol, optionally in the form of the racemates, the enantiomers, the diastereomers and optionally the pharmacologically acceptable acid addition salts and the hydrates thereof.

[0306] According to the instant invention more preferred $beta_2$ agonists 2 are selected from the group consisting of bambuterol, bitolterol, carbuterol, clenbuterol, fenoterol, formoterol, hexoprenaline, ibuterol, pirbuterol, procaterol, reproterol, salmeterol, sulphonterol, terbutaline, tolubuterol, 3-(4-{6-[2-Hydroxy-2-(4-hydroxy-3-hydroxymethyl-phenyl)-ethylamino]-hexyloxy}-butyl)-benzenesulfoneamide, 5-[2-(5,6-Diethyl-indan-2-ylamino)-1-hydroxy-ethyl]-8-hydroxy-1H-quinolin-2-one, 4-hydroxy-7-[2-{[2-{[3-(2-phenylethoxy)propyl]sulphonyl}ethyl]-amino}ethyl]-2(3H)-benzothiazolone, 1-(2-fluoro-4-hydroxyphenyl)-2-[4-(1-benzimidazolyl)-2-methyl-2-butylamino]ethanol, 1-[3-(4-methoxybenzyl-amino)-4-hydroxyphenyl]-2-[4-(1-benzimidazolyl)-2-methyl-2-butylamino]ethanol, 1-[2H-5-hydroxy-3-oxo-4H-1,4-benzoxazin-8-yl]-2-[3-(4-N,N-dimethylaminophenyl)-2-methyl-2-propylamino]ethanol, 1-[2H-5-hydroxy-3-oxo-4H-1,4-benzoxazin-8-yl]-2-[3-(4-methoxyphenyl)-2-methyl-2-propylamino]ethanol, 1-[2H-5-hydroxy-3-OXO-4H-1,4-benzoxazin-8-yl]-2-[3-(4-n-butyloxyphenyl)-2-methyl-2-propylamino]ethanol, 1-[2H-5-hydroxy-3-oxo-4H-1,4-benzoxazin-8-yl]-**2**-{4-[3-(4-methoxyphenyl)-1,2,4-triazol-3-yl]-2-methyl-2-butylamino}ethanol, 5-hydroxy-8-(1-hydroxy-2-isopropylaminobutyl)-2H-1,4-benzoxazin-3-(4H)-one, 1-(4-amino-3-chloro-5-trifluormethylphenyl)-2-tert.-butylamino) ethanol and 1-(4-ethoxycarbonylamino-3-cyano-5-fluorophenyl)-2-(tert.-butylamino) ethanol, optionally in the form of the racemates, the enantiomers, the diastereomers and optionally the pharmacologically acceptable acid addition salts and the hydrates thereof.

[0307] More preferably, the betamimetics 2 used as within the compositions according to the invention are selected from among fenoterol, formoterol, salmeterol, 3-(4-{6-[2-Hydroxy-2-(4-hydroxy-3-hydroxymethyl-phenyl)-ethylamino]-hexyloxy}-butyl)-benzenesulfoneamide, 5-[2-(5,6-Diethyl-indan-2-ylamino)-1-hydroxy-ethyl]-8-hydroxy-1H-quinolin-2-one, 1-[3-(4-methoxybenzyl-amino)-4-hydroxyphenyl]-2-[4-(1-benzimidazolyl)-2-methyl-2-butylamino]ethanol, 1-[2H-5-hydroxy-3-oxo-4H-1,4-benzoxazin-8-yl]-2-[3-(4-N,N-dimethylaminophenyl)-2-methyl-2-propylamino]ethanol, 1-[2H-5-hydroxy-3-oxo-4H-1,4-benzoxazin-8-yl]-2-[3-(4-methoxyphenyl)-2-methyl-2-propylamino]ethanol, 1-[2H-5-hydroxy-3-oxo-4H-1,4-benzoxazin-8-yl]-2-[3-(4-n-butyloxyphenyl)-2-methyl-2-propylamino]ethanol, 1-[2H-5-hydroxy-3-oxo-4H-1,4-benzoxazin-8-yl]-**2**-{4-[3-(4-methoxyphenyl)-1,2,4-triazol-3-yl]-2-methyl-2-butylamino}ethanol, optionally in the form of the racemates, the enantiomers, the diastereomers and optionally the pharmacologically acceptable acid addition salts thereof, and the hydrates thereof. Of the betamimetics mentioned above the compounds formoterol, salmeterol, 3-(4-{6-[2-Hydroxy-2-(4-hydroxy-3-hydroxymethyl-phenyl)-ethylamino]-hexyloxy}-butyl)-benzenesulfoneamide, and 5-[2-(5,6-Diethyl-indan-2-ylamino)-1-hydroxy-ethyl]-8-hydroxy-1H-quinolin-2-one are particularly preferred, optionally in the form of the racemates, the enantiomers, the diastereomers and optionally the pharmacologically acceptable acid addition salts thereof, and the hydrates thereof. Of the betamimetics mentioned above the compounds formoterol and salmeterol are particularly preferred, optionally in the form of the racemates, the enantiomers, the diastereomers and optionally the pharmacologically acceptable acid addition salts thereof, and the hydrates thereof.

[0308] Examples of pharmacologically acceptable acid addition salts of the betamimetics 2 according to the invention are the pharmaceutically acceptable salts which are selected from among the salts of hydrochloric acid, hydrobromic acid, sulphuric acid, phosphoric acid, methanesulphonic acid, acetic acid, fumaric acid, succinic acid, lactic acid, citric acid, tartaric acid, 1-hydroxy-2-naphthalenecarboxylic acid, 4-phenylcinnamic acid, 5-(2,4-difluorophenyl)salicylic acid or maleic acid. If desired, mixtures of the abovementioned acids may also be used to prepare the salts **2**.

[0309] According to the invention, the salts of the betamimetics 2 selected from among the hydrochloride, hydrobromide, sulphate, phosphate, fumarate, methanesulphonate, 4-phenylcinnamate, 5-(2,4-difluorophenyl)salicylate, maleate and xinafoate are preferred. Particularly preferred are the salts of 2 in the case of salmeterol selected from among the hydrochloride, sulphate, 4-phenylcinnamate, 5-(2,4-difluorophenyl)salicylate and xinafoate, of which the 4-phenylcinnamate, 5-(2,4-difluorophenyl)salicylate and especially xinafoate are particularly important. Particularly preferred are the salts of 2 in the case of formoterol selected from the hydrochloride, sulphate and fumarate, of which the hydrochloride and fumarate are particularly preferred. Of exceptional importance according to the invention is formoterol fumarate.

[0310] Salts of salmeterol, formoterol, 3-(4-{6-[2-Hydroxy-2-(4-hydroxy-3-hydroxymethyl-phenyl)-ethylamino]-hexyloxy}-butyl)-benzenesulfoneamide, and 5-[2-(5,6-Diethyl-indan-2-ylamino)-1-hydroxy-ethyl]-8-hydroxy-1H-quinolin-2-one, are preferably used as the betamimetics 2 according to the invention. Of particular importance according to the invention are salmeterol and formoterol salts. Any reference to the term betamimetics 2 also includes a reference to the relevant enantiomers or mixtures thereof. In the pharmaceutical compositions according to the invention, the compounds 2 may be present in the form of their racemates, enantiomers or mixtures thereof. The separation of the enantiomers from the racemates may be carried out using methods known in the art (e.g. by chromatography on chiral phases, etc.) If the compounds 2 are used in the form of their enantiomers, it is particularly preferable to use the enantiomers in the R configuration at the C—OH group.

[0311] Optionally, the inhalation device according to the invention contains plural of doses of a medicament in powder form, that contains beside one compound of formula 1 a steroid 3 as another active ingredient.

[0312] In such medicament combinations the steroid 3 is preferably selected from among prednisolone, prednisone, butixocortpropionate, RPR-166541, flunisolide, beclomethasone, triamcinolone, budesonide, fluticasone, mometasone, ciclesonide, rofleponide, ST-126, dexamethasone, (S)-fluoromethyl 6α,9α-difluoro-17α-[(2-furanylcarbonyl)oxy]-11[beta]-hydroxy-16α-methyl-3-oxo-androsta-1,4-diene-17β-carbothioate, (S)-(2-oxo-tetrahydro-furan-3S-yl)6α,9α-difluoro-1 1 β-hydroxy-16α-methyl-3-oxo-17α-propionyloxy-androsta-1,4-diene-17β-carbothionate, and etiprednol-dichloroacetate (BNP-166), optionally in the form of the racemates, enantiomers or diastereomers thereof and optionally in the form of the salts and derivatives thereof, the solvates and/or hydrates thereof.

[0313] In particularly preferred medicament combinations the steroid 3 is selected from the group comprising flunisolide, beclomethasone, triamcinolone, budesonide, fluticasone, mometasone, ciclesonide, rofleponide, ST-126, dexamethasone, (S)-fluoromethyl 6α,9α-difluoro-1 Ia-[(2-furanylcarbonyl)oxy]-11 β-hydroxy-16α-methyl-3-oxo-androsta-1,4-diene-17β-carbothionate, (S)— (2-oxo-tetrahydro-furan-3S-yl)6α,9α-difluoro-11β-hydroxy-16α-methyl-3-oxo-17α-propionyloxy-androsta-1,4-diene-17β-carbothionate, and etiprednol-dichloroacetate, optionally in the form of the racemates, enantiomers or diastereomers thereof and optionally in the form of the salts and derivatives thereof, the solvates and/or hydrates thereof.

[0314] In particularly preferred medicament combinations the steroid 3 is selected from the group comprising budesonide, fluticasone, mometasone, ciclesonide, (S)-fluoromethyl 6α,9α-difluoro-1 Ia-[(2-furanylcarbonyl)oxy]-11 β-hydroxy-16α-methyl-3-oxo-androsta-1, A-diene-17β-carbothionate, and etiprednol-dichloroacetate, optionally in the form of the racemates, enantiomers or diastereomers thereof and optionally in the form of the salts and derivatives thereof, the solvates and/or hydrates thereof.

[0315] Any reference to steroids 3 includes a reference to any salts or derivatives, hydrates or solvates thereof which may exist. Examples of possible salts and derivatives of the steroids 3 may be: alkali metal salts, such as for example sodium or potassium salts, sulphobenzoates, phosphates, isonicotinates, acetates, propionates, dihydrogen phosphates, palmitates, pivalates or furcates.

[0316] Optionally, the inhalation device according to the invention contains plural of doses of a medicament on powder form, that contains beside one compound of formula 1 additionally both, one of the betamimetics 2 mentioned hereinbefore and one of the steroids 3 mentioned hereinbefore.

[0317] Accordingly, in a preferred embodiment the invention relates to an inhalation device comprising a housing and a blister strip, the strip being movable to sequentially align each blister with means for opening a blister to enable a user to inhale said dose and, a spiral wound element to receive and coil the strip, wherein each blister contains a pharmaceutical composition in powder form wherein the pharmaceutical composition comprises one or more, preferably one, compound of formula 1.

[0318] In another embodiment, the invention relates to an inhalation device comprising a housing and a blister strip, the strip being movable to sequentially align each blister with means for opening a blister to enable a user to inhale said dose, the housing comprising a common chamber to receive the blister strip and a coil of breached blisters of that strip, the chamber being configured so that the coil of breached blisters occupies more of the space in the chamber initially occupied by the blister strip as more of the blisters of the strip are breached, wherein each blister contains a pharmaceutical composition in powder form wherein the pharmaceutical composition comprises one or more, preferably one, compound of formula 1.

[0319] Within the scope of the inhalable powders according to the invention the excipients have a maximum average particle size of up to 250 μm, preferably between 10 and 150 μm, most preferably between 15 and 80 μm. It may sometimes seem appropriate to add finer excipient fractions with an average particle size of 1 to 9 μm to the excipients mentioned above. These finer excipients are also selected from the group of possible excipients listed hereinbefore. Finally, in order to prepare the inhalable powders according to the invention, micronised active substance I—, and optionally 2 and/or 3, preferably with an average particle size of 0.5 to 10 μm, more preferably from 1 to 6 μm, is added to the excipient mixture. Processes for producing the inhalable powders according to the invention by grinding and micronising and finally mixing the ingredients together are known from the prior art.

[0320] For the methods of preparing the pharmaceutical compositions in powder form reference may be made to the disclosure of WO 02/30390, WO 03/017970, or WO 03/017979 for example. The disclosure of WO 02/30390, WO 03/017970, and WO 03/017979 is hereby incorporated by reference into the instant patent application in its entirety.

[0321] As an example, the pharmaceutical compositions according to the invention may be obtained by the method described below.

[0322] First, the excipient and the active substance are placed in a suitable mixing container. The active substance used has an average particle size of 0.5 to 10 μm, preferably 1 to 6 μm, most preferably 2 to 5 μm. The excipient and the active substance are preferably added using a sieve or a granulating sieve with a mesh size of 0.1 to 2 mm, preferably 0.3 to 1 mm, most preferably 0.3 to 0.6 mm. Preferably, the excipient is put in first and then the active substance is added to the mixing container. During this mixing process the two components are preferably added in batches. It is particularly preferred to sieve in the two components in alternate layers. The mixing of the excipient with the active substance may take place while the two components are still being added. Preferably, however, mixing is only done once the two components have been sieved in layer by layer.

[0323] If after being chemically prepared the active substance used in the process described above is not already obtainable in a crystalline form with the particle sizes mentioned earlier, it can be ground up into the particle sizes which conform to the above-mentioned parameters (so-called micronising).

[0324] Many modifications and variations of the invention falling within the terms of the following claims will be apparent to those skilled in the art and the foregoing description should be regarded as a description of the preferred embodiments of the invention only. Furthermore, reference to an aperture formed in the wall to allow passage of a blister strip from the unused side of the device to the used side in the description above, may comprise an aperture formed between the end of the wall and the housing of the inhaler, as well as an aperture within the wall spaced from a remote end thereof, and such variations are intended to fall within the scope of the invention and claims hereafter.

1. An inhaler comprising a housing to receive a strip of blisters each containing a dose of medicament and means to sequentially move each blister into alignment with means for opening a blister to enable a user to inhale said dose and, a spiral wound element to coil the strip.

2. An inhaler according to claim **1**, wherein the spiral wound element is configured so that a used portion of the strip formed from blisters which have been aligned with said means for opening a blister, is gradually coiled within the spiral wound element.

3. An inhaler according to claim **1**, wherein the spiral wound element is rigid.

4. An inhaler according to claim **1**, wherein the spiral wound element is formed from a flexible material.

5. An inhaler according to claim **4**, wherein the spiral wound element is formed from a deformable non-resilient material.

6. An inhaler according to claim **5**, wherein the spiral wound element is formed from a resiliently deformable material.

7. An inhaler according to claim **6**, wherein the resiliency of the spiral wound element is selected in dependence on the stiffness of a blister strip so that a first closed coil of a used portion of a blister strip is formed in the spiral wound element prior to any substantial deformation or expansion of the spiral wound element.

8. An inhaler according to claim **4**, wherein the spiral wound element is configured so that it expands as the length of the used portion of the blister strip coiled within it increases.

9. An inhaler according to claim **1**, wherein the spiral wound element has at least one winding that extends over 360 degrees.

10. An inhaler according to claim **1**, wherein the stiffness of the spiral wound element varies along at least a portion of its length.

11. An inhaler according to claim **10**, wherein the spiral wound element has an outer end that is connected to the housing and an inner end remote from the outer end, the stiffness of the spiral wound element decreasing towards at least a portion of the inner end.

12. An inhaler according to claim **11**, wherein the thickness of the spiral wound element gradually reduces towards the inner end.

13. An inhaler according to claim **11** wherein the section of the spiral wound element gradually reduces towards the inner end.

14. An inhaler according to claim **11**, wherein holes are formed in the spiral wound element close to its inner end.

15. An inhaler according to claim **1**, wherein the spiral wound element is formed from phosphor bronze, stainless steel, nylon, acetal or polypropylene.

16. An inhaler according to claim **1**, wherein the spiral wound element is a coil spring.

17. An inhaler according to claim **1**, wherein the housing comprises a first compartment to contain unused blisters and a second compartment to receive used blisters, the first and second compartments being separated by a flexible or movable dividing wall.

18. An inhaler according to claim **17** comprising a passage between the first and second compartments, and blocking means in said passage to prevent the egress of powdered medicament from the first blister compartment into the second blister compartment through the passage.

19. An inhaler according to claim **18** wherein the blocking means is shaped to conform to the shape of the blister strip.

20. An inhaler according to claim **19** wherein said blocking means includes a resilient member to effect a seal against the blister strip.

21. An inhaler according to claim **20** wherein the blocking means is disposed such that it is aligned with a blister of the blister strip when another blister is aligned with said means for opening a blister.

22. An inhaler according to claim **1** any preceding claim, including means to crush and/or tear opened blisters prior to entry into the spiral wound element.

23. An inhaler comprising a housing to receive a strip of blisters each containing a dose of medicament and means to sequentially move each blister into alignment with means for opening a blister to enable a user to inhale said dose, the inhaler having first compartment to contain unused blisters and a second compartment to receive used blisters, the first and second compartments being separated by a flexible or movable dividing wall.

24. An inhaler according to claim **23**, comprising an aperture in the dividing wall for the passage of the blister strip from the first compartment into the second compartment, said aperture including means to prevent the egress of powdered medicament from the used blister compartment into the unused blister compartment through the aperture.

25. An inhaler according to claim **24** wherein said means to prevent egress of powdered medicament includes a portion of the housing which is shaped to conform to the shape of the blister strip.

26. An inhaler according to claim **24** wherein said means to prevent egress of powdered medicament includes a resilient member to effect a seal against the blister strip.

27. An inhaler according to claim **26** wherein said resilient member is shaped to conform to the shape of the blister strip.

28. An inhaler according to claim **27** wherein the resilient member is formed integrally with the dividing wall.

29. An inhaler according to claim **24**, wherein said means to prevent egress of powdered medicament is disposed such that it is aligned with a blister of the blister strip when another blister is aligned with said means for opening a blister.

30. An inhaler according to claim **24**, wherein said means includes a brush or elastomeric element extending at least partially across the aperture in the dividing wall.

31. An inhaler according to claim **1**, wherein the housing comprises a common chamber to receive both unused and used portions of the blister strip.

32. An inhaler according to claim **26**, wherein the chamber is configured so that the used portion of the blister strip occupies a region of the chamber initially occupied by an unused portion of the blister strip as the size of the used portion of the strip increases.

33. An inhaler according to claim **32**, wherein the common chamber is separated into a unused blister compartment and a used blister compartment by a flexible and/or movable dividing wall.

34. An inhaler according to claim **33**, wherein the dividing wall is rigid but configured so as to be slidable within the housing so that the relative sizes of the unused and used blister compartments can be altered.

35. An inhaler according to claim **33**, wherein the flexible and/or movable dividing wall is fixed to the housing at one or both ends.

36. An inhaler according to claim **33**, wherein the dividing wall is movable and fixed to the housing at one end so as to pivot about said end within the housing.

37. An inhaler according to claim **33**, wherein the dividing wall is flexible and configured so that it extends across said space between facing sidewalls of the inhaler to prevent passage of powdered dose between the unused and used blister compartments.

38. An inhaler according to claim **37**, wherein the width of the flexible dividing wall in a direction extending between the sidewalls is greater than the distance between the sidewalls so that the flexible dividing wall is held in compression between the sidewalls.

39. An inhaler according to claim **33**, wherein the dividing wall is movable and fixed to the housing at one end so as to pivot about said end within the housing, wherein the dividing wall is flexible and configured so that it extends across said space between facing sidewalls of the inhaler to prevent passage of powdered dose between the unused and used blister compartments, wherein the flexible dividing wall comprises a foam strip.

40. An inhaler according to claim **39**, wherein the foam strip includes a stiffening element.

41. An inhaler according to claim **33**, wherein said flexible dividing wall is at least partially attached to the spiral wound element.

42. An inhaler according to claim **22**, including means to crush, cut-up and/or tear a used portion of the blister strip.

43. An inhaler according to claim **1**, comprising a second spiral wound element, the unused blister strip being coiled up within said second spiral wound element and located within the housing during assembly, the arrangement being such that, during use of the inhaler, the second spiral wound element retracts as the first spiral wound element expands, as the size of the coil formed from a used portion of the strip increases and the size of the coil formed from an unused portion of the strip decreases.

44. An inhaler comprising a housing to receive a strip of blisters each containing a dose of medicament and means to sequentially move each blister into alignment with means for opening a blister to enable a user to inhale said dose, wherein the housing comprises a common chamber to receive an unused blister strip and a used portion of that strip, wherein a flexible and/or movable dividing wall separates the chamber into an unused and a used blister compartment.

45. An inhaler according to claim **1**, wherein the housing includes a common chamber to receive an unused blister strip and an a used portion of that strip, wherein a flexible and/or movable dividing wall separates the chamber into a used and unused blister compartment.

46. An inhaler according to claim **44**, wherein the flexible dividing wall is fixed to the housing at both ends.

47. An inhaler according to claim **44**, wherein the dividing wall is flexible and configured so that it extends across said space between sidewalls of the inhaler to prevent passage of powdered dose between the unused and used blister compartments.

48. An inhaler according to claim **47**, wherein the width of the flexible dividing wall is greater than the distance between the sidewalls so that the flexible dividing wall is held in compression between the sidewalls.

49. An inhaler according to claim **44**, wherein the flexible dividing wall comprises a foam strip.

50. An inhaler according to claim **49**, wherein the foam strip includes a stiffening element.

51. An inhaler according to claim **45**, comprising a second spiral wound element to receive an unused blister strip for insertion into the housing during assembly, the arrangement being such that the second spiral wound element retracts as the first spiral wound element expands as the size of the coil formed from a used portion of the strip increases and the size of the coil formed from an unused portion of the strip decreases.

52. An inhaler according to claim **1**, wherein the spiral wound element is configured so that it is partially unrolled or unwound by a used portion of a blister strip on initial contact of the leading edge of the used portion of the strip against the spiral wound element, prior to any substantial deformation of the used portion of the strip caused by the spiral wound element.

53. An inhaler according to claim **52**, wherein the spiral wound element is configured so that it partially unrolls or unwinds across an inner wall forming part of the housing.

54. An inhaler according to claim **52**, including means to steady the spiral wound element to prevent over-expansion as the length of the used portion of the strip received within the spiral wound element increases.

55. An inhaler according to claim **54**, wherein said means is the flexible dividing wall separating the common chamber into unused and used blister compartments.

56. An inhaler according to claim **55**, wherein the flexible dividing wall is at least partially attached to the spiral wound element.

57. An inhaler according to claim **1**, wherein the spiral wound element is configured so that its diameter increases by a factor of at least 3 when filled with a used portion of a strip of blisters relative to when the spiral wound element is empty.

58. An inhaler according to claim **1**, wherein the housing contains a coiled strip of blisters.

59. An inhaler according to claim **58**, wherein at least some of the coiled strip of blisters have past the means for opening a blister to form a used portion, said used portion of the strip being coiled within said spiral wound element.

60. A method of controlling a strip of blisters within an inhalation device in which unused blisters are sequentially movable into alignment with means for opening a blister to enable a user to inhale said dose, the method including the step of feeding a used portion of the strip into a spiral wound element to coil said used portion of the strip.

61. A method according to claim **60**, wherein the method includes the step of forming the spiral wound element such that it is partially unrolled or unwound by the used portion of the blister strip on initial contact of the leading edge of the used portion of the blister strip against the spiral wound element prior to any substantial deformation of the used portion of the strip caused by the spiral wound element.

62. A method of forming a coiled strip of blisters for insertion into an inhalation device, the method including the steps of feeding an end of a strip of blisters into a spiral wound element such that the strip is coiled up within said spiral wound element.

63. A method according to claim **62**, including the step of separating the coiled strip of blisters from the spiral wound element prior to insertion of the strip into the device.

64. An inhaler comprising a housing to receive a strip of blisters each containing a dose of medicament and means to sequentially move each blister into alignment with means for opening a blister to enable a user to inhale said dose, the housing including a chamber to receive used blisters and means to compress, crush, tear, cut-up and/or fold said used blisters.

65. An inhaler according to claim **64**, including an indexing mechanism for advancing the blisters, the indexing mechanism including a wheel around which empty blisters are fed and which rotates in response to movement of an actuator to draw the blister strip through the device, wherein the wheel is positioned relative to a wall of the housing such that blister cavities are partially squashed between the indexing wheel and the wall as they pass around the indexing wheel.

66. An inhaler according to claim **65**, wherein the indexing wheel comprises a plurality of pockets to receive blister cavities, the maximum depth of each pocket being less than the maximum depth of a blister cavity such that the cavities protrude from the pockets by a distance which is greater than a gap between a top of the pockets and said wall, such that the cavities are squashed as they pass through said gap.

67. An inhaler according to claim **23**, including means to crush, cut-up and/or tear a used portion of the blister strip.

68. An inhaler according to claim **45**, wherein the flexible dividing wall is fixed to the housing at both ends.

69. An inhaler according to claim **45**, wherein the dividing wall is flexible and configured so that it extends across said space between sidewalls of the inhaler to prevent passage of powdered dose between the unused and used blister compartments.

70. An inhaler according to claim **45**, wherein the flexible dividing wall comprises a foam strip.

71. An inhaler according to claim **70**, wherein the foam strip includes a stiffening element.

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