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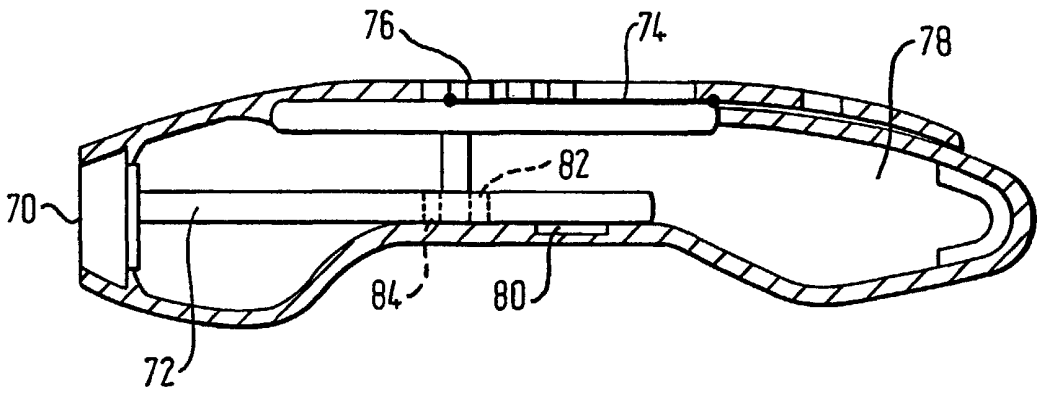

(57) Abstract: There is provided a medicament dispenser comprising a body (4), a medicament carrier (80), an exit channel (70) for passage of the medicament to a patient, and access means for directly or indirectly exposing the exit channel (70) for use by the patient, wherein the access means (70) comprises an access coupling (74). The coupling (74) is reversibly deformable in response to the application of non-mechanical energy thereto. The non-mechanical energy may comprise heat energy, electrical current energy, electrical field energy or magnetic field energy.

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Medicament Dispenser

This invention relates to a medicament dispenser having an exit channel for passage of the medicament to a patient. The dispenser is particularly suitable for use as an inhalation device.

It is well known to treat patients with medicaments contained in an aerosol, for example, in the treatment of respiratory disorders. It is also known to use for such treatment, medicaments which are contained in an aerosol and are administered to a patient by means of an inhalation device comprising a tubular housing or sleeve in which the aerosol container is located and an outlet tube leading out of the tubular housing. Such inhalation devices are generally referred to as metered dose inhalers (MDIs). The aerosol containers used in such inhalation devices are designed to deliver a predetermined dose of medicament upon each actuation by means of an outlet valve member at one end which can be opened either by depressing the valve member while the container is held stationary or by depressing the container while the valve member is held stationary. In the use of such devices, the aerosol container is placed in the tubular housing with the outlet valve member of the container communicating via a support with the outlet tube, for example a nozzle or mouthpiece. When used for dispensing medicaments, for example in bronchodilation therapy, the patient then holds the housing in a more or less upright condition and the mouthpiece or nozzle of the inhalation device is placed in the mouth or nose of the patient. The aerosol container is pressed towards the support to dispense a dose of medicament from the container which is then inhaled by the patient.

It is also known to use dry powder inhalation devices for the delivery of inhalable medicament. In one aspect, such dispensers comprise pre-metered doses of powdered medicament, for example in capsules or blisters. In another aspect, such dispensers comprise a reservoir of powdered medicament from which doses are metered prior to or concurrent with the delivery process. In either

case, the device may be designed for passive release of medicament, where the medicament is simply made available at a delivery position for aerosolisation in response to the inhalation of the patient. Alternatively, an active release mechanism may be used whereby a 'puff' of compressed gas or air is provided to the delivery position to assist in aerosolisation of the powder prior to or concurrent with the inhalation of the patient. Such devices are generally called active release dry powder inhalers (active DPIs). The source of the compressed gas or air is generally an aerosol container.

It is also well known to use syringes for the delivery of injectable medicament to a patient. Traditional syringes rely on puncturing of the patient's skin by a hollow needle through which the injectable medicament (in solution or suspension form) is delivered to the muscle or tissue of the patient. Recently developed needleless systems for the delivery of injectables employ high velocity injection of particle formulated drugs or vaccine through the skin and into any physically accessible tissue. Other needleless systems employ similar high velocity injection of drug or vaccine coated on to a suitable carrier particle. Such needleless systems may be configured to include a source of compressed air or gas, which on release provides energy to propel the medicament particles for injection into the skin.

In a typical dispensing operation the body of the device is held by the patient and the exit channel (or nozzle) of the device is placed in the mouth, or the nose or on the skin of the patient.

When not in use it is desirable, from a hygiene standpoint, that the exit channel is provided with some kind of protective cover. The cover desirably acts both to prevent build-up of dirt on the exit channel and to prevent ingress of dirt into the body of the device through the channel, which might then be subject to administration by a patient.

It is known to provide the exit channel with a protective cap which acts as a protective cover. The cap may either be an entirely separate element or it may be joined to the body of the device in some way. DE-A-3,639,836, for example, describes a device in which the protective cap is mounted on an arm, which is pivotally mounted to the body of the device.

As an alternative to the use of a protective cap, one might envisage a device having an exit channel which is reversibly retractable from a storage position in which the channel is contained within the body of the device to a dispensing position in which the channel protrudes from the body of the device. In a device of this type the body of the device itself acts as the protective cover when the exit channel is in the storage position. The exit channel cover is thus an integral part of the device, avoiding contamination problems of prior art devices caused by the loss of removable covers.

For the convenience of the user, it is desirable that the dispenser is arranged to allow movement of the exit channel from the storage to dispensing position (and vice-versa) by a one-handed operation.

The Applicants have now developed a medicament dispenser where access means control the state of access of the exit channel to the patient. Actuation of the access means is responsive to the application of non-mechanical energy to a coupling element of the access means. The non-mechanical energy can be in the form of heat provided by electrical current flow through the coupling element, which in turn can be provided in response to the sensing of the breath of a patient. Alternatively, the non-mechanical energy can be in the form of a magnetic field provided by a suitable magnetic field source such as a permanent magnet or an electromagnet.

US patent no. 5,061,914 describes a shape memory alloy micro-actuator. The actuator comprises a nickel-titanium alloy material which undergoes a

temperature induced phase transition when heated. The phase transition results in contraction of the actuator. The actuator can be mechanically coupled to a micro-mechanical element for motion thereof.

US patent no. 5,958,154 describes alloy materials which undergo a phase transition in response to the application of a magnetic field.

Accordingly, in one aspect the invention provides medicament dispenser comprising a body, a medicament carrier, an exit channel for passage of the medicament to a patient, and access means for directly or indirectly exposing the exit channel for use by the patient, wherein the access means comprises an access coupling which is reversibly deformable in response to the application of non-mechanical energy thereto.

As used herein the term exit channel refers to any exitway for transport of the medicament to a patient and may include a mouthpiece or nosepiece or skin contacting or skin penetrating channel.

The exit channel may be movable relative to the body from a non-dispensing position to a dispensing position wherein a portion of the exit channel protrudes from the body and wherein it is in communication with the medicament carrier to allow passage of medicament therebetween.

Preferably, the access means is coupled to the exit channel such that actuation of the access means moves the exit channel towards the non-dispensing position and deactuation of the access means moves the exit channel towards the dispensing position.

Movement of the access means in a first direction may move the exit channel towards the non-dispensing position and movement of the access means in a second direction may move the exit channel towards the dispensing position.

Typically, the medicament dispenser further comprises a protective cap or lid or cover or plug which covers the exit channel.

The protective cap/lid/cover/plug may take the form of a slide-cover and/or flip-top cover, and/or a shutter arrangement (e.g. as in a camera lens), and/or a plunger.

In one embodiment, the access means may be coupled to the cap/lid/cover/plug such that actuation of the access means reversibly removes the cap/lid/cover/plug from the exit channel and de-actuation of the access means re-covers the exit channel therewith.

The access means may comprise a rack and pinion mechanism, and/or a hinged lever mechanism and/or an electronic driven cam mechanism.

In one embodiment, the medicament carrier may be housed within the body or else is attachable to exterior of the body.

Preferably, the access means and the exit channel may be directly coupled.

The exit channel may be comprised of an elastic material. In addition, the exit channel may be provided with a cover comprised of an elastic material.

The medicament dispenser may additionally comprise a curtain arrangement contractable by the exit channel on movement of the exit channel from the non-dispensing to the dispensing position. The curtain arrangement may comprise a plurality of curtains comprised of an elastomeric material.

Preferably, the access means are provided with a safety trigger mechanism to prevent accidental actuation thereof.

Preferably, at least a portion of the access means may be shaped for ease of grip by the user.

Typically, at least a portion of the access means has a friction-enhancing coating.

In one embodiment the medicament dispenser comprises no biasing means acting such as to bias the access means towards either the non-dispensing or the dispensing position.

Preferably, the access means is actuable by a sliding thumb motion or a depressing motion.

In one embodiment, the dispenser is characterised in that the translational path definable by the movement of the exit channel from the non-dispensing position to the dispensing position does not bisect the rotational path defined by the rotation of the access means.

Most preferably, the access means is actuable by one-handed operation. Preferably, the device is suitable for left- and right-handed patients. The device may be shaped specifically for left- or right-handed patients.

A reset mechanism may be provided for resetting the access means after actuation thereof. The reset mechanism may for example, comprise a spring, motor, mechanical arrangement or a reset coupling which is reversibly deformable in response to the application of non-mechanical energy thereto.

The term 'non-mechanical energy' herein is used to mean essentially any energy type which is not mechanical energy. The coupling and any reset coupling herein typically comprise a material which deforms, or undergoes a phase transition in

response to the application of non-mechanical energy, thereby resulting in a change in shape/dimension of the coupling which serves to actuate the access means. In embodiments the energy may be in the form of heat energy, electrical current energy, electrical field energy and magnetic field energy.

Preferably, the non-mechanical energy comprises electric current flow through the coupling or reset coupling.

Preferably, the coupling or reset coupling comprises a wire, strip, coil or tube.

Arrangements comprising multiple strips, wires, coils, or tubes are also envisaged. The multiple strips, wires, coils, or tubes may be arranged in any suitable fashion including parallel or series arrangements and bundle arrangements.

The coupling may be coated with any suitable coating, or encased within any suitable encasing including a shrink-wrap sheath.

In one particular aspect, the coupling or reset coupling comprises one or more wires which contract in response to application of non-mechanical energy thereto.

Preferably, the degree of contraction of the coupling is from 2% to 8%.

In embodiments, the coupling comprises an alloy which undergoes a phase transition on heating (shape memory alloys). Certain shape memory alloys also undergo a change in shape on recooling without externally applied energy. Such two way shape memory alloys are also envisaged for use herein.

In one embodiment, the shape memory alloy is preferably a nickel-titanium alloy such as a nickel-titanium alloy comprising from 5% to 95%, preferably from 20%

to 80%, nickel by weight and from 95% to 5%, preferably from 80% to 20%, titanium by weight. By nickel-titanium alloy it is meant an alloy comprised essentially of nickel and titanium, although other elements such as Cu and Nb may be present in small (e.g. trace) amounts.

In other embodiments, the shape memory alloy is preferably a copper-aluminium-nickel alloy or a copper-zinc-aluminium alloy. Trace amounts of other elements may also be present.

In further embodiments, the coupling comprises an alloy which undergoes a phase transition on application of a magnetic field thereto (magnetic shape memory alloys). These materials are generally intermetallic, ferromagnetic alloys that exhibit twin variants in the martensitic, or low-temperature, phase of the material. Suitable magnetic shape memory alloys are for example, described in US Patent No. 5,958,154.

In one embodiment, the magnetic shape memory alloy exhibits an austenitic crystal structure above a characteristic phase transformation temperature and also exhibits a martensitic twinned crystal structure below the phase transformation temperature. The alloy has a magnetocrystalline anisotropy energy that is sufficient to enable motion of twin boundaries of the martensitic twinned crystal structure in response to application of a magnetic field to the martensitic twinned crystal structure.

Where a magnetic shape memory alloy is employed the medicament dispenser preferably includes a magnetic field source disposed with respect to the coupling in an orientation that applies to the coupling a magnetic actuation field in a direction that is substantially parallel with a selected twin boundary direction of the martensitic twinned crystal structure of the coupling material.

Alternatively, the medicament dispenser preferably includes a magnetic bias

field source disposed with respect to the coupling in an orientation that applies a magnetic bias field to the coupling, and a magnetic actuation field source disposed with respect to the coupling in an orientation that applies a magnetic actuation field to the coupling material in a direction that is substantially perpendicular to the orientation of the applied magnetic bias field.

A preferred magnetic shape memory alloy is the actuator material comprising an alloy composition defined as $Ni_{65-x-y}Mn_{20}+xGa_{15}+y$, where x is between 3 atomic % and 15 atomic % and y is between 3 atomic % and 12 atomic %. Preferably, the actuator material comprises an alloy composition defined as $Ni_{65-x-y}Mn_{20}+xGa_{15}+y$, where x is between 6 atomic % and 10 atomic % and y is between 5 atomic % and 9 atomic %; or where x is between 12 atomic % and 15 atomic % and y is between 3 atomic % and 6 atomic %; or where x is between 10 atomic % and 14 atomic % and y is between 3 atomic % and 6 atomic %; or where x is between 7 atomic % and 11 atomic % and y is between 3 atomic % and 7 atomic %. In a particularly preferred aspect, the alloy is $Ni_{50}Mn_{25}Ga_{25}$.

Another preferred magnetic shape memory alloy is the alloy having the composition $(Ni_aFe_bCo_c)_{65-x-y}(Mn_dFe_eCo_f)_{20}+x(Ga_gSi_hAl_i)_{15}+y$, where x is between 3 atomic % and 15 atomic % and y is between 3 atomic % and 12 atomic %, and where a+b+c=1, where d+e+f=1, and g+h+i=1.

In preferred aspects, b is between zero and 0.6, c is between zero and 0.6, and e, f, h and i are each zero; or b and c are each zero, e is between zero and 0.6, f is between zero and 0.6, and h and i are each zero; or b, c, e and f are each zero, h is between zero and 0.5, and i is between zero and 0.5.

Other suitable shape memory alloys include those based on ion-exchange polymer composites such as are described in 'Ionic Polymer-Metal Composites (IPMC) As Biomimetic Sensors, Actuators & Artificial Muscles – A Review', M. Shahinpoor, Y. Bar-Cohen, J. O. Simpson and J. Smith as published at

http://www.unm.edu/~amri/paper.html.

Other potentially suitable shape memory alloys include those based on contractile polymers such as are described in 'Review of Artificial Muscle based on Contractile Polymers', Massachusetts Institute of Technology Artificial Intelligence Laboratory Memo No. 1330, November 1991, David L. Brock.

Preferably, the one or more wires have a diameter from 30 to 400 micrometers, preferably from 50 to 150 micrometers.

Preferably, the coupling comprises from two to twenty, preferably six to twelve wires which contract in response to the application of non-mechanical energy thereto. The wires may be arranged in any suitable fashion including parallel or series arrangements and bundle arrangements.

In another aspect, the coupling comprises a strip which comprises multiple layers of different metals. Suitable strips typically comprise a plurality of layers of material, each material having a different coefficient of thermal expansion.

Preferred examples of strips include those comprising multiple layers of different metals (e.g. bimetallic strips) and strips comprising at least one piezoelectric material. Suitable piezoelectric materials include piezoelectric ceramics, such as compounds of lead zirconate and lead titanate, and piezoelectric crystals which are generally polycrystalline ferroelectric materials with the perovskite structure. Such piezoelectric materials generally deform in response to the application of an electric field.

In one aspect, the coupling is deformable in response to heating arising from electrical current flow in the range from 0.01A to 100A, preferably from 0.1A to 5A.

In another aspect, the coupling is deformable in response to the application of an electrical field, particularly where the coupling comprises a piezoelectric material.

In a further aspect, the coupling is deformable in response to a magnetic field of from 0.01 to 100 Tesla. The magnetic field may for example, be produced by a permanent magnet or by an electromagnet.

Preferably, the medicament dispenser additionally comprises an electrical energy source for providing electric current, or for providing an electric field, or for powering an electromagnet to provide a magnetic field. In one aspect, the electrical energy source comprises a voltaic cell or battery of voltaic cells which may be rechargeable. In another aspect, the electrical energy source comprises a photovoltaic cell or battery of photovoltaic cells. In a further aspect, the electrical energy source comprises a converter for converting mechanical energy into electrical energy. In a further aspect, the electrical energy source comprises a capacitor for local storage of charge. Suitable capacitors comprise those known as 'super capacitors' with a high capacitance to size ratio, such as those consisting of solid electrodes and liquid electrolyte.

Actuation/deactuation of the access means may power up/shut down respectively, any energy sources or stores within or associated with the dispenser.

Any known systems for power management and conservation may be employed with the electrical energy source to manage and/or conserve the power output thereof.

Energy may be conserved by a variety of means to enable the device to operate for longer on a given source of energy, such as a battery. Energy conservation or saving methods have additional advantages in terms of reducing the size

requirements of the power source (e.g. battery) and thus the weight and portability of the inhalation device.

A variety of energy saving methods are available which generally involve reducing power consumption. One such method is to use a clock or timer circuit to switch the power on and off at regular or predetermined intervals. In another method the system can selectively switch on/off specific electronic devices, such as visual display units or sensors, in order to power these devices only when they are required to perform a particular sequence of events. Thus different electronic devices may be switched on and off at varying intervals and for varying periods under control of the system. The power sequencing system may also respond to a sensor, such as a motion or breath sensor, which is activated on use of the device.

Low power or "micropower" components should be used within the electronics where possible and if a high power device is required for a particular function this should be put into a low power standby mode or switched off when not required. Similar considerations apply in the selection of transducers.

Operation at low voltage is desirable since power dissipation generally increases with voltage.

For low power digital applications complementary metal oxide semi-conductor (CMOS) devices are generally preferred and these may be specially selected by screening for low quiescent currents. Clock speeds of processors and other logic circuits should be reduced to the minimum required for computational throughput as power consumption increases with frequency. Supply voltages should also be kept at minimal values consistent with reliable operation because power dissipation in charging internal capacitance's during switching is proportional to the square of the voltage. Where possible, supply voltages should be approximately the same throughout the circuit to prevent current flowing through input protection circuits. Logic inputs should not be left floating

and circuits should be arranged so that power consumption is minimised in the most usual logic output state. Slow logic transitions are undesirable because they can result in relatively large class-A currents flowing. Resistors may be incorporated in the power supply to individual devices in order to minimise current in the event of failure.

In some control applications, devices that switch between on and off states are preferred to those that allow analog (e.g. linear) control because less power is dissipated in low resistance on states and low current off states. Where linear components are used (e.g. certain types of voltage regulators) then types with low quiescent currents should be selected. In some circuit configurations it is preferable to use appropriate reactive components (i.e. inductors and capacitors) to reduce power dissipation in resistive components.

Any electrical circuit may incorporate voltage amplification means for generating a higher voltage than that supplied by the voltaic cell or battery of voltaic cells, for example a step-up or inverting switching circuit or a dc-dc converter incorporating an oscillator, transformer and rectifier.

The electrical circuit may incorporate one or more energy storage components such as capacitors or inductors in order to supply a high enough instantaneous current to raise the temperature of the strips or wires at the required rate to the required temperature.

The input to the electrical circuit may be connected to the electrical energy source by means of a mechanical, electro-mechanical or electronic switching component.

The output of the electrical circuit may be connected to the strips or wires or to an electromagnet by means of a mechanical, electro-mechanical or electronic switching component or by a component allowing the output current to be

controlled in a linear or digital (e.g. pulse width modulated) manner.

Suitable control profiles (e.g. via pulse width modulation) include those where the temperature of a shape memory alloy coupling is initially raised to a holding temperature (H) which is just below the transition temperature (T). Actuation of the coupling is then achievable by heating the coupling to a temperature (A) just above the transition temperature. This can be achieved rapidly because the holding temperature (H) is close to the transition temperature (T). When the source of heating is switched off, deactuation also occurs rapidly because the cooling from a temperature (A) only just above the transition temperature (T) to the transition temperature involves only a small temperature decrease.

The strip or wire components may be powered from the battery using a switching component without additional power supply circuitry.

Suitably, the medicament dispenser additionally comprises a controller for controlling the amount of electrical current flow through the coupling or to an electromagnet.

Suitably, the medicament dispenser additionally comprises a timer for controlling the duration of electrical current flow through the coupling or to an electromagnet.

Suitably, the medicament dispenser additionally comprises a local electrical source such as a capacitor or inductor.

The additional energy source may be mechanically generated, for example, the energy source may comprise a biasable resilient member e.g. a spring. Alternatively, the energy source may comprise a source of compressed fluid, preferably compressed gas. The energy source may comprise a chemical energy source or a physically explosive energy source.

Preferably, deformation of the coupling and hence, actuation of the access means is responsive to a patient-actuable mechanism.

In one aspect, said mechanism comprises a button, switch or lever arrangement.

In another aspect, the medicament dispenser is in the form of an inhaler for the delivery of inhalable medicament. Preferably, deformation of the coupling and hence, actuation of the access means is responsive to a patient-actuable mechanism comprising a sensor which senses the breath of a patient. The deformation of the coupling (e.g. by electrical current flow therethrough) may be responsive to the detection of the inward breath of a patient. Alternatively, deformation of the coupling (e.g. by electrical current flow therethrough) may be responsive to a mechanism coupled to any point in the breathing pattern of the patient, such as the end of the outward breath.

In one aspect, the sensor comprises a breath-movable element which is movable in response to the breath of a patient. Preferably, the breath-movable element is selected from the group consisting of a vane, a sail, a piston, a diaphragm and an impeller.

Movement of the breath-movable element may be detectable by any suitable technique for detecting movement. Suitable techniques include optical detectors, magnetic detectors or detectors using detection of capacitative effects.

Optical detectors may be used to detect movement of the breath-movable element by providing the element with a patterned outer surface, for example strips in a barcode type arrangement, and locating the optical detector so that it points towards the patterned surface. Movement of the breath-movable element alters the amount of the light source which reflects back onto the optical detector as the beam passes over the patterned surface. The strips may be arranged so

that the direction of movement of the element can be detected.

Magnetic detectors may be used to detect the movement of breath-movable element by the use of a magnetic switch device. A reader is located on the dispenser and magnetic material embedded within the breath-movable element (or vice-versa). Movement of the breath-movable element results in a change of the magnetic field experienced by the reader. Alternatively, a Hall effect device can be used whereby a semiconductor measures the strength of the magnetic field of the magnetic material on the breath-movable element.

Detection of capacitative effects may be used to detect movement of the breath-movable element by adding a conductive part to the element and also to a second fixed part of the dispenser. Movement of the breath-movable element results in a change in capacitance which can be measured.

In another aspect, the sensor comprises a pressure sensor for sensing the pressure profile associated with the breath of a patient. A pressure transducer is an example of a suitable pressure sensor.

In another aspect, the sensor comprises an airflow sensor for sensing the airflow profile associated with the breath of a patient.

In another aspect, the sensor comprises a temperature sensor for sensing the temperature profile associated with the breath of a patient.

In another aspect, the sensor comprises a moisture sensor for sensing the moisture profile associated with the breath of a patient.

In another aspect, the sensor comprises a gas sensor for sensing the oxygen or carbon dioxide profile associated with the breath of a patient. The chemical profile of the inhaled and exhaled part of the breath cycle varies and this further

may be used as a measurement tool.

Suitably, the breath data includes breath cycle data, FEV_1 and/or peak flow data.

In one aspect, the coupling is exposable to the airflow arising from the inhalation or expiration of the patient to assist in the cooling of the coupling post-actuation of the reset means. Other active cooling mechanisms may be employed, such as fan cooling.

Preferably the medicament dispenser comprises an actuation or dose counter for counting the number of actuations of the access means. The actuation or dose counter may be mechanical or electronic. More preferably the actuation or dose counter is independent of the coupling so that counting will occur even if the access means is manually actuated.

Suitably, the medicament dispenser additionally comprises an electronic data management system. The electronic data management system has input/output capability and comprises a memory for storage of data; a microprocessor for performing operations on said data; and a transmitter for transmitting a signal relating to the data or the outcome of an operation on the data.

Suitably, the electronic data management system comprises an electronic control system for controlling the supply of energy to the coupling. Thus, in aspects the control system may regulate flow of electrical current to the coupling or to any heater or electromagnet source associated therewith.

The control system may form part of a larger electronic data management system capable of receiving inputs from other electronic components. In particular, inputs may be received from any sensor to enable actuation of the coupling in response to sensor, particularly breath sensor input.

The control system may be arranged to accomplish any suitable control of actuation of the coupling including varying the amount of energy supplied thereto, the rate of energy supplied thereto, pulsing patterns of energy supply to the coupling, and more complex control patterns.

Suitably, the electronic data management system is arranged to be responsive to or activated by the voice of a user. Thus, for example the system may be switched on or off in response to a voice command.

The electronic data management system may be integral with the body. Alternatively, the electronic data management system forms part of a base unit which is reversibly associable with the body.

Suitably, the medicament dispenser additionally comprises a data input system for user input of data to the electronic data management system. Preferably, the data input system comprises a man machine interface (MMI) preferably selected from a keypad, voice or noise recognition interface, graphical user interface (GUI) or biometrics interface.

Suitably, the system additionally comprises a visual display unit for display of data from the electronic data management system to the user. The display may for example, comprise a screen such as an LED or LCD screen. More preferably the visual display unit is associable with the housing. More basic display units are envisaged also including those in which a light or pattern of lights is employed to act as a signal to the patient.

The electronic data management system may further comprise a voice synthesiser for verbal communication of data, instructions and feedback to a user.

Suitably, the medicament dispenser additionally comprises a datalink for linking

to a local data store to enable communication of data between the local data store and the electronic data management system. The datastore may also comprise data management, data analysis and data communication capability.

The datastore may itself form part of a portable device (e.g. a handheld device) or it may be sized and shaped to be accommodated within the patient's home. The datastore may also comprise a physical storage area for storage of replacement medicament containers. The datastore may further comprise a system for refilling medicament from a reservoir of medicament product stored therewithin. The datastore may further comprise an electrical recharging system for recharging any electrical energy store on the medicament dispenser, particularly a battery recharging system.

The datalink may for example enable linking with a docking station, a personal computer, a network computer system or a set-top box by any suitable method including a hard-wired link, an infra red link or any other suitable wireless communications link.

Suitably, the medicament dispenser additionally comprises an actuation detector for detecting actuation of the reset means wherein said actuation detector transmits actuation data to the electronic data management system.

The medicament dispenser may additionally comprise a safety mechanism to prevent unintended multiple actuations of the reset means. The patient is thereby protected from inadvertently receiving multiple doses of medicament in a situation where they take a number of short rapid breaths. More preferably, the safety mechanism imposes a time delay between successive actuations of the reset means. The time delay is typically of the order of from three to thirty seconds.

Suitably, the medicament dispenser additionally comprises a release detector for

detecting release of medicament from the medicament container, wherein said release detector transmits release data to the electronic data management system.

Suitably, the medicament dispenser additionally comprises a shake detector for detecting shaking of the medicament container (e.g. prior to actuation of the dispenser), wherein said shake detector transmits shake data to the electronic data management system.

Suitably, the electronic data management system includes a predictive algorithm or look-up table for calculating the optimum amount of medicament to dispense.

Suitably, the memory on the electronic data management system includes a dose memory for storing dosage data and reference is made to the dose memory in calculating the optimum amount of medicament to dispense.

Suitably, the medicament dispenser additionally comprises a selector for selecting the amount of medicament to dispense from the dispenser. In one aspect, the selector is manually operable. In another aspect, the selector is operable in response to a signal from the transmitter on the electronic data management system.

Suitably, the medicament dispenser comprises in association with a body or housing thereof, a first transceiver for transmitting and receiving data and in association with the medicament container, a second transceiver for transmitting and receiving data, wherein data is transferable in two-way fashion from the first transceiver to the second transceiver. The data is preferably in digital form and suitable for transfer by electronic or optical means. A medicament dispenser of this general type is described in pending UK Patent Application No. 0020538.5.

The body or housing of the medicament dispenser is typically shaped to define a

cavity within which the medicament container is receivable. The body and/or medicament container may be further shaped with any manner of grooves, indentations or other shaping or surface details to define a 'lock and key' relationship between the body and the container. Colour guides, arrows and any other surface markings may also be employed.

One advantage of embodiments of this type is the ability to store many types of information in different parts of the memory structure of the transceivers. The information is furthermore stored in a form which is readily and accurately transferable. The information could for example, include manufacturing and distribution compliance information written to the memory at various points in the manufacturing or distribution process, thereby providing a detailed and readily accessible product history of the dispenser. Such product history information may, for example, be referred to in the event of a product recall. The compliance information could, for example, include date and time stamps. The information could also include a unique serial number stored in encrypted form or in a password protectable part of the memory which uniquely identifies the product and therefore may assist in the detection and prevention of counterfeiting. The information could also include basic product information such as the nature of the medicament and dosing information, customer information such as the name of the intended customer, and distribution information such as the intended product destination.

On loading or reloading the dispenser with a medicament container (such as an aerosol canister or dry powder cassette) the second transceiver may, for example, read the unique serial number, batch code and expiry date of the medicament and any other information on the second transceiver. In this way the nature and concentration of the medicament, together with the number of doses used or remaining within the container, may be determined. This information can be displayed to the patient on a visual display unit. Other information, such as the number of times the dispenser has been reloaded with a medicament

container, may also be displayed.

Similarly, should the container be removed from the housing before the supply of medicament is exhausted, the same data can be read from the second transceiver and the number of doses remaining or used determined. Other information, such as the date and time of administration of the drug, or environmental exposure data such as the minimum / maximum temperatures or levels of humidity the medicament container has been exposed to, may also be read and displayed to the user.

In the event that the supply of medicament within the container becomes exhausted, or that the shelf life of the medicament has expired, or that the first transceiver does not recognise the batch code on the second transceiver, activation of the dispenser may be prevented to safeguard the user. Activation may also be prevented if the medicament has been exposed to extreme environmental conditions for periods outwith the manufacturer's guidelines.

Data may be transferred to and from any transceiver during the period of use of the medicament dispenser by the patient. For example, the medicament dispenser may include an electronic data management system having various sensors associated therewith. Any data collected by the sensors or from any data collection system associated with the electronic data management system including a clock or other date/time recorder is transferable.

Data may be transferred each time the patient uses the device. Or alternatively, data may be stored in a database memory of the electronic data management system and periodically downloaded to any transceiver. In either case, a history of the usage of the device may be built up in the memory of a transceiver.

In one embodiment herein, a history of the usage of the medicament dispenser is transferred to the second transceiver on the aerosol container. When the

medicament container is exhausted it is exchanged by the patient for a new refill container. At the point of exchange, which will typically occur at the pharmacy, data may be transferred from the exhausted container to the refill and vice-versa. Additionally, usage history data may be read from the refill and transferred to a healthcare data management system for example comprising a network computer system under the control of a healthcare data manager.

Methods are envisaged herein whereby the patient is given some sort of reward for returning the refill and making available the data comprised within the second transceiver. Methods are also envisaged herein whereby the healthcare data manager is charged for either receipt of the data from the second transceiver or for its use for commercial purposes. Any rewards or charging may be arranged electronically. The methods may be enabled by distributed or web-based computer network systems in which any collected data is accessible through a hub on the network. The hub may incorporate various security features to ensure patient confidentiality and to allow selective access to information collected dependent upon level of authorisation. The level of user authorisation may be allocated primarily to safeguard patient confidentiality. Beyond this the level of user authorisation may also be allocated on commercial terms with for example broader access to the database being authorised in return for larger commercial payments.

Suitably, the first and second transceiver each comprise an antenna or equivalent for transmitting or receiving data and connecting thereto a memory. The memory will typically comprise an integrated circuit chip. Either transceiver may be configured to have a memory structure which allows for large amounts of information to be stored thereon. The memory structure can be arranged such that parts of the memory are read-only, being programmed during/after manufacture, other parts are read/write and further parts are password protectable. Initial transfer of information (e.g. on manufacture or one dispensing) to or from any transceiver can be arranged to be readily achievable

by the use of a reader which is remote from the medical dispenser, thereby minimising the need for direct product handling. In further aspects, the reader can be arranged to simultaneously read or write to the memory of multiple transceivers on multiple medicament dispensers.

A suitable power source such as a battery, clockwork energy store, solar cell, fuel cell or kinetics-driven cell will be provided as required to any electronic component herein. The power source may be arranged to be rechargeable or reloadable.

Suitably, data is transferable in two-way fashion between the first and second transceiver without the need for direct physical contact therebetween.

Preferably, data is transferable wirelessly between the first and second transceiver.

Suitably, the first transceiver is an active transceiver and the second transceiver is a passive transceiver. The term active is used to mean directly powered and the term passive is used to mean indirectly powered.

Suitably, the second transceiver comprises a label or tag comprising an antenna for transmitting or receiving energy; and an integrated circuit chip connecting with said antenna, and the first transceiver comprises a reader for said label or tag. In this case the label or tag is a passive transceiver and the reader is an active transceiver. Preferably, the reader will not need to be in direct contact with the tag or label to enable the tag or label to be read.

The tag may be used in combination and/or integrated with other traditional product labelling methods including visual text, machine-readable text, bar codes and dot codes.

Suitably, the integrated circuit chip has a read only memory area, a write only memory area, a read/write memory area or combinations thereof.

Suitably, the integrated circuit chip has a one-time programmable memory area. More preferably, the one-time programmable memory area contains a unique serial number.

Suitably, the integrated circuit chip has a preset memory area containing a factory preset, non-changeable, unique data item. The preset memory item is most preferably in encrypted form.

Suitably, the integrated circuit chip has plural memory areas thereon. Suitably, any memory area is password protected.

Suitably, any memory area contains data in encrypted form. Electronic methods of checking identity, error detection and data transfer may also be employed.

In one aspect, the integrated circuit has plural memory areas thereon including a read only memory area containing a unique serial number, which may for example be embedded at the time of manufacture; a read/write memory area which can be made read only once information has been written thereto; and a password protected memory area containing data in encrypted form which data may be of anti-counterfeiting utility.

Suitably, the tag is on a carrier and the carrier is mountable on the body or housing of the medicament dispenser or the medicament container.

In one aspect, the carrier is a flexible label. In another aspect, the carrier is a rigid disc. In a further aspect, the carrier is a rectangular block. In a further aspect, the carrier is a collar ring suitable for mounting to the neck of an aerosol container. Other shapes of carrier are also envisaged.

Suitably, the carrier is mouldable or weldable to the medicament container or housing. Suitably, the carrier encases the tag. More preferably, the carrier forms a hermetic seal for the tag.

In one aspect, the carrier comprises an insulating material such as a glass material or, a paper material or an organic polymeric material such as polypropylene. Alternatively, the carrier comprises a ferrite material.

The energy may be in any suitable form including ultrasonic, infrared, radiofrequency, magnetic, optical and laser form. Any suitable channels may be used to channel the energy including fibre optic channels.

In one aspect, the second transceiver comprises a radiofrequency identifier comprising an antenna for transmitting or receiving radiofrequency energy; and an integrated circuit chip connecting with said antenna, and the first transceiver comprises a reader for said radiofrequency identifier. In this case the radiofrequency identifier is a passive transceiver and the reader is an active transceiver. An advantage of radiofrequency identifier technology is that the reader need not be in direct contact with the radiofrequency identifier tag or label to be read.

The radiofrequency identifier can be any known radiofrequency identifier. Such identifiers are sometimes known as radiofrequency transponders or radiofrequency identification (RFID) tags or labels. Suitable radiofrequency identifiers include those sold by Phillips Semiconductors of the Netherlands under the trade marks Hitag and Icode, those sold by Amtech Systems Corporation of the United States of America under the trade mark Intellitag, and those sold by Texas Instruments of the United States of America under the trade mark Tagit.

Suitably, the antenna of the RFID tag is capable of transmitting or receiving radiofrequency energy having a frequency of from 100 KHz to 2.5 GHz. Preferred operating frequencies are selected from 125 KHz, 13.56 MHz and 2.4 GHz.

In one aspect, the second transceiver comprises a magnetic label or tag comprising an antenna for transmitting or receiving magnetic field energy; and an integrated circuit chip connecting with said antenna, and the first transceiver comprises a reader for said magnetic label or tag. In this case the magnetic label or tag is a passive transceiver and the reader is an active transceiver.

A suitable magnetic label or tag comprises plural magnetic elements in mutual association whereby the magnetic elements move relative to each other in response to an interrogating magnetic field. A magnetic label or tag of this type is described in U.S. Patent No. 4,940,966. Another suitable magnetic label or tag comprises a magnetorestrictive element which is readable by application of an interrogating alternating magnetic field in the presence of a magnetic bias field which results in resonance of the magnetorestrictive elements at different predetermined frequencies. A magnetic label of this type is described in PCT Patent Application No. WO92/12402. Another suitable magnetic label or tag comprising plural discrete magnetically active regions in a linear array is described in PCT Patent Application No. WO96/31790. Suitable magnetic labels and tags include those making use of Programmable Magnetic Resonance (PMR) (trade name) technology.

In another aspect, the second transceiver comprises a microelectronic memory chip and the first transceiver comprises a reader for said microelectronic memory chip. The microelectronic memory chip may comprise an Electrically Erasable Programmable Read Only Memory (EEPROM) chip or a SIM card-type memory chip. In this case the microelectronic memory chip is a passive transceiver and the reader is an active transceiver.

Any transceiver herein, particularly a passive transceiver may be mounted on or encased within any suitable inert carrier. The carrier may comprise a flexible sheet which may in embodiments be capable of receiving printed text thereon.

In one aspect, the first transceiver is integral with the body such that a single unit is comprised. The first transceiver may for example be encased within or moulded to the body.

In another aspect, the first transceiver forms part of a base unit which is reversibly associable with the body. The base unit may for example, form a module receivable by the body such as a snap-in module.

Suitably, the medicament dispenser additionally comprises a communicator for wireless communication with a network computer system to enable transfer of data between the network computer system and the electronic data management system. Dispensers employing such communicators are described in pending PCT Applications No.s PCT/EP00/09291 (PG3786), PCT/EP00/09293 (PG4029) and PCT/EP00/09292 (PG4159). Preferably, the communicator enables two-way transfer of data between the network computer system and the electronic data management system.

Suitably, the data is communicable between the network computer system and the electronic data management system in encrypted form. All suitable methods of encryption or partial encryption are envisaged. Password protection may also be employed. Suitably, the communicator employs radiofrequency or optical signals.

In one aspect, the communicator communicates via a gateway to the network computer system. In another aspect, the communicator includes a network server (e.g. a web server) such that it may directly communicate with the

network.

In a further aspect, the communicator communicates with the gateway via a second communications device. Preferably, the second communications device is a telecommunications device, more preferably a cellular phone or pager. Preferably, the communicator communicates with the second communications device using spread spectrum radiofrequency signals. A suitable spread spectrum protocol is the Bluetooth (trade mark) standard which employs rapid (e.g. 1600 times a second) hopping between plural frequencies (e.g. 79 different frequencies). The protocol may further employ multiple sending of data bits (e.g. sending in triplicate) to reduce interference.

In one aspect, the network computer system comprises a public access network computer system. The Internet is one suitable example of a public access network computer system, wherein the point of access thereto can be any suitable entrypoint including an entrypoint managed by an Internet service provider. The public access network computer system may also form part of a telecommunications system, which may itself be either a traditional copper wire system, a cellular system or an optical network.

In another aspect, the network computer system comprises a private access network computer system. The private access network system may for example, comprise an Intranet or Extranet which may for example, be maintained by a health service provider or medicament manufacturer. The network may for example include password protection; a firewall; and suitable encryption means.

Preferably, the communicator enables communication with a user-specific network address in the network computer system.

The user-specific network address may be selected from the group consisting of a web-site address, an e-mail address and a file transfer protocol address.

Preferably, the user-specific network address is accessible to a remote information source such that information from said remote information source can be made available thereto. More preferably, information from the user-specific network address can be made available to the remote information source.

In one aspect, the remote information source is a medicament prescriber, for example a doctor's practice. Information transferred from the medicament prescriber may thus, comprise changes to prescription details, automatic prescription updates or training information. Information transferred to the medicament prescriber may comprise compliance information, that is to say information relating to the patient's compliance with a set prescribing programme. Patient performance information relating for example, to patient-collected diagnostic data may also be transferred to the medicament prescriber. Where the dispenser is an inhaler for dispensing medicament for the relief of respiratory disorders examples of such diagnostic data would include breath cycle data or peak flow data.

In another aspect, the remote information source is a pharmacy. Information transferred from the pharmacy may thus, comprise information relating to the medicament product. Information sent to the pharmacy may thus include prescription requests which have been remotely pre-authorised by the medicament prescriber.

In a further aspect, the remote information source is an emergency assistance provider, for example a hospital accident and emergency service or an emergency helpline or switchboard. The information may thus, comprise a distress or emergency assist signal which requests emergency assistance.

In a further aspect, the remote information source is a manufacturer of medicament or medicament delivery systems. Information transferred to the

system may thus, comprise product update information. The system may also be configured to feed information back to the manufacturer relating to system performance.

In a further aspect, the remote information source is a research establishment. In a clinical trial situation, information may thus be transferred relating to the trial protocol and information relating to patient compliance fed back to the research establishment.

In a further aspect, the remote information source is an environmental monitoring station. Information relating to weather, pollen counts and pollution levels may thus be made accessible to the system.

In a further aspect, the remote information source is a computer software download site from which software may be downloaded for use in the electronic data management system. Embodiments are envisaged in which such software downloads are employed to upgrade or modify any existing software employed by the electronic data management system.

Suitably, the medicament dispenser additionally comprises a geographic positioning system such as a global positioning system or a system which relies on the use of multiple communications signals and a triangulation algorithm.

The dispenser may further comprise dose-metering means and/or transport means and/or release means and/or climate control means.

At least one of the dose-metering means and/or transport means and/or release means and/or climate control means may be directly or indirectly actuable by the access means

The dose-metering means may comprise a weight and/or a volume and/or a time and/or a surface-area regulated mechanism.

In one embodiment the dose-metering means may comprise a valve (for example, a linear or rotary valve) and/or a piston and/or a load cell and/or a pump and/or a plunger.

The pump may comprise a pump mechanism such as might be found in a dispenser for dispensing liquid or solution (e.g. aqueous solution) form medicament. The pump may deliver the medicament directly to the patient (e.g. as a nasal spray) or the pump may deliver the medicament to an intermediate position at which further energy is supplied thereto to further propel, aerosolize or otherwise direct the medicament dose to the patient.

The dispenser may comprise multiple plungers and multiple syringe chambers. The syringe contents may for example, be liquid, solutions, suspensions, particulates or in freeze-dried form. A retract or reset mechanism is typically provided for the plunger.

Traditional syringes rely on puncturing of the patient's skin by a hollow needle through which the injectable medicament (in solution or suspension form) is delivered to the muscle or tissue of the patient. Recently developed neeedleless systems for the delivery of injectables employ high velocity injection of particle formulated drugs or vaccine through the skin and into any physically accessible tissue. Other needleless systems employ similar high velocity injection of drug or vaccine coated onto a suitable carrier.

Typically, the actuation of the access means primes the dispenser to release a dose of medicament, for example by actuation of the dose-metering means.

The transport means may transport an amount of medicament from a rest position to a delivery position. In one embodiment, the transport means may take the form of a perforated strip and claw advancement mechanism. In another embodiment, the transport means may take the form of a ratchet wheel and a driving pawl advancement mechanism.

As used herein, the term "release means" refers to the means for the making available of the dose for release to the patient, for example, the actual dispensing (whether passive or active) to the patient. The release may be active in the sense that medicament is actively dispensed from the container, or the release may be passive in the sense that medicament is merely made available for release when the release means is actuated.

The release means may comprise (i) a passive and/or (ii) an active dose-release mechanism.

Typically, the release means is linked to the transport means such that the release means is actuated immediately after metering and transport of a dose.

In one embodiment, the release means is passive and comprises making the metered dose available to the patient for inhalation thereby.

In another embodiment, the release means is active and comprises means to propel pressurised gas in the direction of patient inhalation. In this embodiment, the patient receives a positive signal that the dose has been dispensed which may add to patient confidence. An active release means may also increase the efficacy of delivery of the medicament, for example, the drug may be released in a more focussed plume or cloud towards the back of the inhaler's nose or throat. Preferably, the gas-propelling means provides at least one pulse of gas on actuation.

The gas-propelling means may provide one pulse of gas for each dose dispensed.

The gas may be air or an inert gas.

In one embodiment, the medicament dispenser may be in the form of an active dry powder inhaler in which a "puff" of compressed air or gas (e.g. helium) is delivered from the release means, such as an aerosol container, to aerosolize a dose of released dry powder medicament.

In another embodiment, the medicament dispenser is in the form of a needleless injection system in which compressed air or gas (e.g. helium) is delivered at high velocity from the release means (e.g. an aerosol container) to propel a dose of dry powder medicament for injection into the skin.

Thus, suitably the aerosol container, which as used herein refers to any suitable container for comprising liquefied gas under pressure, comprises a compressed air or gas (e.g. helium).

In another aspect, the medicament container may be arranged for rupture in response to firing of the release means.

The climate control means may comprise means to (i) reduce moisture increase in the dispenser; and/or (ii) maintain ambient temperature; and/or (iii) dry the meter prior to actuation of the dispenser.

The climate control means may comprise a desiccant and/or a heater.

The climate control means may comprise a temperature and/or a moisture sensor.

The dispenser of the invention is suitable for dispensing medicament, particularly for the treatment of respiratory disorders such as asthma and chronic obstructive pulmonary disease (COPD).

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

Medicaments can also be delivered in combinations. Preferred formulations containing combinations of active ingredients contain salbutamol (e.g., as the free base or the sulphate salt) or salmeterol (e.g., as the xinafoate salt) in combination with an antiinflammatory steroid such as a beclomethasone ester (e.g., the dipropionate) or a fluticasone ester (e.g., the propionate). A particularly

preferred combination comprises salmeterol xinafoate salt and fluticasone propionate.

Preferred medicaments are selected from albuterol, salmeterol, fluticasone propionate and beclomethasone dipropionate and salts or solvates thereof, e.g., the sulphate of albuterol and the xinafoate of salmeterol, and any mixtures thereof. Alternatively, the dispenser may be employed for dispensing vaccine.

The medicament container may comprise medicament in dry powder form.

Typically, a dry powder medicament includes a pharmaceutical excipient in dry powder form.

In one embodiment, the density of the dry powder medicament particles is reduced relative to standard dry powder medicament.

In another embodiment, the dry powder medicament particles are aerodynamically shaped to improve medicament delivery to the patient.

In another embodiment, the medicament container may comprise medicament in solution or suspension form.

The medicament container may comprise a suspension of a medicament in a propellant, for example, liquefied HFA134a, HFA-227, helium or carbon dioxide.

Alternatively, the medicament container may comprise a solution of a medicament in a solvent.

In one embodiment, the medicament is pre-metered prior to actuation of the access means by a patient.

Preferably, the medicament dispenser additionally comprises a safety mechanism to prevent unintended multiple actuations of the access means.

The safety mechanism may impose a time delay between successive actuations of the access means.

Preferably, the medicament dispenser comprises a manual override enabling manual actuation of the access means. The manual override may be designed to cover all situations in which the coupling does not actuate in the normal manner. These will include situations where actuation does not happen (e.g. due to power failure). Alternatively, this will include situations where actuation occurs, but reset of the coupling fails (e.g. due to power being in "continuous on" mode) and a manual reset, decoupling (e.g. by severing the coupling) or "circuit break" is employed.

Preferably, the medicament dispenser comprises a child resistance feature to prevent undesirable actuation thereof by children.

In another aspect, the invention provides an actuator for use in a medicament dispenser as described hereinabove.

In a further aspect, the invention provides an actuator for a medicament container comprising a housing, within said housing, a container seat for receipt of the medicament container; on the housing or connecting therewith, an exit channel for passage of the medicament to a patient and access means for directly or indirectly exposing the exit channel for use by the patient, wherein the access means comprises an access coupling, wherein the access coupling which is reversibly deformable in response to the application of non-mechanical energy thereto.

The actuator herein may be configured to include, as relevant, any of the above

described features of the medicament dispenser. In particular, the actuator may be configured to include an electronic data management system comprising control means for the actuation of the coupling.

Preferably, the non-mechanical energy comprises electric current flow through the coupling.

In one embodiment, the coupling comprises one or more wires which contract in response to application of non-mechanical energy thereto. More preferably, the one or more wires comprise an alloy which undergoes a phase transition on heating, for example in response to flow of electrical current therethrough. The alloy is for example, a nickel-titanium alloy.

In another embodiment, the one or more wires comprise an alloy which undergoes a phase transition on application of a magnetic field thereto (magnetic shape memory alloys).

Suitably, the actuator additionally comprises an electronic control system for controlling the supply of non-mechanical energy to the coupling. Suitably, the electronic control system is capable of providing pulses of non-mechanical energy to the coupling.

Suitably, the electronic control system is capable of receiving inputs from electronic sensors locatable on the dispenser. Suitably, the actuator additionally comprises an electronic sensor selected from the group consisting of a breath sensor, a shake sensor, a temperature sensor, an infrared sensor and a patient ID sensor.

In a further aspect, the invention provides a medicament container for use in the dispenser and/or the actuator as described hereinabove.

According to a further aspect of the present invention there is provided a laboratory test apparatus comprising at least one actuator as described above and a mounting (e.g. a bench mounting) for the at least one actuator. The laboratory test apparatus is designed for use in testing the performance of the medicament dispenser in a laboratory environment. Often, plural actuators will be mounted on a single mounting to enable simultaneous testing thereof. The laboratory test apparatus will typically be connected to various sensors and recording devices for monitoring aspects of the performance of the medicament dispenser.

According to a further aspect of the present invention there is provided a kit of parts comprising a medicament dispenser as described above in the form of a cartridge; and a housing shaped for receipt of said cartridge.

According to a further aspect of the present invention there is provided a kit of parts comprising an actuator as described above and, receivable by said actuator, a medicament container.

In a preferred commercial embodiment herein, the actuator is arranged for receipt of a refill cartridge. Typically, the actuator is in the form of a relatively complex device, including for example an electronic data management system and the cartridge is in the form of a medicament refill therefor.

In another aspect the cartridge comprises a medicament dispenser having a voltaic cell as an electrical energy source and the housing is provided with a mouthpiece for patient inhalation therethrough and electronic information display apparatus for displaying information to the patient.

The invention will now be described further with reference to the accompanying figures in which:-

Figure 1a shows an inhalation device according to the present invention;

Figure 1b shows the inhalation device of Figure 1a wherein the mouthpiece is in the in-use position;

Figure 1c shows the inhalation device of Figures 1a and 1b wherein the mouthpiece is in the storage position;

Figure 2a shows a sectional plan view of an inhalation device according to another embodiment of the invention; and

Figure 2b is a sectional side view of the inhalation device of Figure 2a.

Referring now to the figures, Figures 1a to 1c illustrate a cross-section of one embodiment of the invention in the form of inhalation device 2. The device 2 has a body 4 having an end cap 6, wherein the end cap 6 is reversibly attached to the body 4 by a snap fit mechanism 8, 10. Within the body 4 there is provided a medicament container 12, which is in communication with a hollow transition piece 14 also provided in said body 4.

A depressible button switch 16 is retainably mounted on the body 4 and linked to a power supply 18 and access means comprising an access coupling taking the form of a shape memory alloy (SMA) wire assembly 20, 22. The SMA wire 20, 22 assembly communicates with first and second rack pinion mechanisms 24, 26. Each of the first and second rack and pinion mechanisms 24, 26 (wherein, for clarity, only the first mechanism is shown in detail on Figues 1b and 1c) comprises a first rack 28, 30 attached to the SMA wire 20, 22 which communicates with a wheel 32, 34 axially mounted to the body 4, which wheel 32, 34 communicates with a curved second rack 36 which is mounted for communication with the mouthpiece 38.

Actuation of the device from the storage position (shown in Figure 1c) to the in-use position) (shown in Figures 1a and 1c) is achievable by the user holding the body 4 in a cupped palm and depression of the switch 16 to complete the circuit between the power supply 18 and the SMA wires 20, 22. The SMA wires rise in temperature due to the flow of electrical current and contract, drawing the first

rack 28 into engagement with wheel 32, which rotates and engages second rack 36, thereby moving the second rack 36 in the opposite direction. In turn, the movement of the second rack 36 causes the mouthpiece 38 to be moved to the in-use position, in which it protrudes from the body 4. In the in-use position it may be seen that the interior of the mouthpiece 38 communicates with the hollow interior of the transition piece 14, which itself communicates with the medicament container 12. Thus an inhalation passageway is provided from the mouthpiece 38 to the medicament container 12. Deactivation is achievable by the use of a second shape memory alloy wire assembly actuated by a second switch (not shown). Alternatively, deactivation may be actuated by removing pressure on the switch to break the circuit or by having a time delay after initial actuation to switch off the current to the SMA wire assembly.

Figures 2a and 2b 6b shows another inhalation device comprising a body 50, which is overall shaped for ease of grip in the hand of a user. Within the body 50 there is provided a medicament cartridge 52 and attached thereto mouthpiece 54, wherein the mouthpiece is comprised of a resiliently deformable elastomeric material. A shaped cover 56 is retainably mounted on first and second guide rails 58, 60 provided on the body 50 for slidable movement thereon.

Actuation of the device from the storage position (shown in Figure 2a) to the in-use position (shown in Figure 2b) is achievable by the user gripping the body 50 of the device in a partially cupped palm and depressing the switch 62. The switch 62 is linked to an electrical circuit comprising a power supply 64 and a SMA wire assembly 66. When the switch 62 is depressed, the circuit is completed sending an electrical current through the SMA wire assembly 66. The SMA wire assembly 66 heats and contracts drawing the cover 56 along the guide rails 58 and 60, thereby revealing the mouthpiece 54, which 'pops out' into its characteristic shape. Deactivation is achievable by, for example, the mechanisms described for Figure 1.

In another embodiment of the invention which is illustrated in Figure 3a and 3b, the exit channel 70 is reversibly covered by a removable plug 72. In this case, an SMA wire assembly 74 is linked to the plug 72 and to a patient actuable trigger such as a switch 76. In the storage position, the plug 72 is located close to the opening of the exit channel 70 and the airway 78 is covered. On depression of the switch 76, an electrical circuit (not shown) is completed and the SMA wire 74 heats and contracts. On contraction of the wire 74 , the SMA wire assembly draws the plug 72 away from the exit channel opening 70, and exposes the medicament within a medicament blister 80 for release, thus creating a free-flow passage from medicament to patient. On inhalation by the patient through the exit channel 70, air is drawn through the airway 78 and then through passage 82 to the blister 80 wherein the medicament is drawn out of the blister through the passage 84 and to the patient. To re-cover the opening with the plug, a second SMA wire assembly linked to another switch may be actuated (not shown).

It may be appreciated that any of the parts of the inhaler or actuator which contact the medicament suspension may be coated with materials such as fluoropolymer materials which reduce the tendency of medicament to adhere thereto. Any movable parts may also have coatings applied thereto which enhance their desired movement characteristics. Frictional coatings may therefore be applied to enhance frictional contact and lubricants used to reduce frictional contact as necessary.

It will be understood that the present disclosure is for the purpose of illustration only and the invention extends to modifications, variations and improvements thereto.

The application of which this description and claims form part may be used as a basis for priority in respect of any subsequent application. The claims of such

subsequent application may be directed to any feature or combination of features described therein. They may take the form of product, method or use claims and may include, by way of example and without limitation, one or more of the following claims:

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CLAIMS:

1. A medicament dispenser comprising a body, a medicament carrier, an exit channel for passage of the medicament to a patient, and access means for directly or indirectly exposing the exit channel for use by the patient, wherein the access means comprises an access coupling which is reversibly deformable in response to the application of non-mechanical energy thereto.

2. A medicament dispenser according to claim1 wherein the exit channel is a mouthpiece or nosepiece or skin-contacting channel or skin-penetrating channel.

3. A medicament dispenser according to claim 1 or claim 2 wherein the exit channel is movable relative to the body from a non-dispensing position to a dispensing position wherein a portion of the exit channel protrudes from the body and wherein it is in communication with the medicament carrier to allow passage of medicament therebetween.

4. A medicament dispenser according to claim 3 wherein the access means is coupled to the exit channel such that actuation of the access means moves the exit channel towards the non-dispensing position and deactuation of the access means moves the exit channel towards the dispensing position.

5. A medicament dispenser according to claim 3 or claim 4 wherein movement of the access means in a first direction moves the exit channel towards the non-dispensing position and movement of the access means in a second direction moves the exit channel towards the dispensing position.

6. A medicament dispenser according to any one of the preceding claims further comprising a protective cap or lid or cover or plug which covers the exit channel.

7. A medicament dispenser according to claim 6 wherein the protective cap/lid/cover/plug takes the form of a slide-cover and/or flip-top cover, and/or a shutter arrangement (e.g. as in a camera lens) and/or a plunger.

8. A medicament dispenser according to claim 6 or claim 7 wherein the access means is coupled to the cap/lid/cover/plug such that actuation of the access means reversibly removes the cap/lid/cover/plug from the exit channel and de-actuation of the access means re-covers the exit channel therewith.

9. A medicament dispenser according to any one of the preceding claims wherein the access means comprises a rack and pinion mechanism and/or a hinged lever mechanism and/or an electronic driven cam mechanism.

10. A medicament dispenser according to any one of the preceding claims wherein the medicament carrier is housed within the body or is attachable to exterior of the body.

11. A medicament dispenser according to any one of the preceding claims wherein the access means and the exit channel are directly coupled.

12. A medicament dispenser according to any one of the preceding claims wherein the exit channel is comprised of an elastic material.

13. A medicament dispenser according to any one of claims 6 to 12 wherein the exit channel is provided with a cover comprised of an elastic material.

14. A medicament dispenser according to any one of the preceding claims additionally comprising a curtain arrangement contractable by the exit channel

on movement of the exit channel from the non-dispensing to the dispensing position.

15. A medicament dispenser according to claim 14 wherein the curtain arrangement comprises a plurality of curtains comprised of an elastomeric material.

16. A medicament dispenser according to any one of the preceding claims wherein the access means is provided with a safety trigger mechanism to prevent accidental actuation thereof.

17. A medicament dispenser according to any one of the preceding claims wherein at least a portion of the access means is shaped for ease of grip by the user.

18. A medicament dispenser according to any one of the preceding claims wherein at least a portion of the access means has a friction-enhancing coating.

19. A medicament dispenser according to any one of claims 4 to 18 comprising no biasing means acting such as to bias the access means towards either the non-dispensing or the dispensing position.

20. A medicament dispenser according to any one of the preceding claims wherein the access means is actuable by a sliding thumb motion or a depressing motion.

21. A medicament dispenser according to any one of the preceding claims characterised in that the translational path definable by the movement of the exit channel from the non-dispensing position to the dispensing position does not bisect the rotational path defined by the rotation of the access means.

22. A medicament dispenser according to any one of the preceding claims wherein the access means is actuable by one-handed operation.

23. A medicament dispenser according to any of the preceding claims additionally comprising a reset mechanism for resetting the access means after actuation thereof.

24. A medicament dispenser according to claim 23, wherein the reset mechanism comprises a reset coupling which is reversibly deformable in response to the application of non-mechanical energy thereto.

25. A medicament dispenser according to any of claims 1 to 24, wherein said non-mechanical energy comprises electric current flow through the coupling.

26. A medicament dispenser according to any of claims 1 to 25, wherein the coupling comprises a wire, strip, coil or tube.

27. A medicament dispenser according to claim 26, wherein the coupling comprises multiple wires, strips, coils or tubes.

28. A medicament dispenser according to any of claims 1 to 27, wherein the coupling comprises one or more wires which contract in response to the application of non-mechanical energy thereto.

29. A medicament dispenser according to claim 28, wherein the coupling exhibits a degree of contraction of from 2% to 8% on application of non-mechanical energy thereto.

30. A medicament dispenser according to claim 29, wherein the coupling comprises an alloy which undergoes a phase transition on application of non-mechanical energy thereto.

31. A medicament dispenser according to claim 30, wherein said alloy is a nickel-titanium alloy.

32. A medicament dispenser according to claim 31, wherein said nickel-titanium alloy comprises from 5% to 95% nickel by weight and from 95% to 5% titanium by weight, preferably from 20% to 80% nickel by weight and from 80% to 20% titanium by weight.

33. A medicament dispenser according to either of claims 31 or 32, wherein said nickel-titanium alloy additionally comprises copper, niobium or any mixtures thereof.

34. A medicament dispenser according to claim 30, wherein the alloy is a copper-zinc-aluminium alloy or a copper-aluminium-nickel alloy.

35. A medicament dispenser according to claim 30, wherein the alloy has the composition defined as $Ni_{65-x-y}Mn_{20}+xGa_{15}+y$, where x is between 3 atomic % and 15 atomic % and y is between 3 atomic % and 12 atomic %.

36. A medicament dispenser according to claim 30, wherein the alloy has the composition defined as $(Ni_aFe_bCo_c)_{65-x-y}(Mn_dFe_eCo_f)_{20}+x(Ga_gSi_hAl_i)_{15}+y$, where x is between 3 atomic % and 15 atomic % and y is between 3 atomic % and 12 atomic %, and where a+b+c=1, where d+e+f=1, and g+h+i=1.

37. A medicament dispenser according to claim 30, wherein the alloy comprises an ion-exchange polymer composite.

38. A medicament dispenser according to claim 30, wherein the alloy comprises a contractile polymer.

39. A medicament dispenser according to any of claims 28 to 38, wherein said one or more wires have a diameter from 30 to 400 micrometers, preferably from 50 to 150 micrometers.

40. A medicament dispenser according to any of claims 28 to 39, wherein the coupling comprises from two to twenty, preferably six to twelve wires which contract in response to heating or application of a magnetic field thereto.

41. A medicament dispenser according to any of claims 1 to 40, wherein said strip comprises multiple layers of different metals.

42. A medicament dispenser according to claim 41, wherein the strip comprises a bimetallic strip.

43. A medicament dispenser according to either of claims 41 or 42, wherein the strip comprises at least one piezoelectric material.

44. A medicament dispenser according to any of claims 1 to 43, wherein the coupling is deformable in response to heating arising from electrical current flow in the range from 0.01A to 100A, preferably from 0.1A to 5A.

45. A medicament dispenser according to any of claims 1 to 43, wherein the coupling is deformable in response to a magnetic field of from 0.01 to 100 Tesla.

46. A medicament dispenser according to any of claims 1 to 45, additionally comprising an electrical energy source.

47. A medicament dispenser according to claim 46, wherein said electrical energy source comprises a voltaic cell or battery of voltaic cells.

48. A medicament dispenser according to claim 47, wherein said voltaic cell or battery of voltaic cells is rechargeable.

49. A medicament dispenser according to claim 46, wherein said electrical energy source comprises a photovoltaic cell or battery of photovoltaic cells.

50. A medicament dispenser according to claim 46, wherein said electrical energy source comprises a converter for converting mechanical energy into electrical energy.

51. A medicament dispenser according to any of claims 46 to 50, additionally comprising a controller for controlling the amount of electrical current flow through the coupling or to an electromagnet to provide a magnetic field.

52. A medicament dispenser according to any of claims 46 to 51, additionally comprising a timer for controlling the duration of electrical current flow through the coupling or to an electromagnet to provide a magnetic field.

53. A medicament dispenser according to any of claims 46 to 52 additionally comprising a local electrical energy store.

54. A medicament dispenser according to any one of claims 46 to 53 wherein the additional energy source is mechanically-generated.

55. A medicament dispenser according to claim 54 wherein the energy source comprises a biasable resilient member.

56. A medicament dispenser according to claim 55 wherein the biasable resilient member is a spring.

57. A medicament dispenser according to claim 54 wherein the energy source comprises a source of compressed fluid, preferably compressed gas.

58. A medicament dispenser according to claim 54 wherein the energy source comprises a chemical energy store, preferably a chemical propellant or ignition mixture.

59. A medicament dispenser according to claim 54 wherein the energy source comprises a physically explosive energy source.

60. A medicament dispenser according to any of claims 1 to 59, wherein flow of electrical current through the coupling and hence, actuation of the access means is responsive to a patient-actuable mechanism.

61. A medicament dispenser according to claim 60, wherein said mechanism comprises a button, switch or lever arrangement.

62. A medicament dispenser according to any of claims 1 to 61, in the form of an inhaler for the delivery of inhalable medicament.

63. A medicament dispenser according to claim 62, wherein heating arising from flow of electrical current through the coupling and hence, actuation of the transport means is responsive to a patient-actuable mechanism comprising a sensor which senses the breath of a patient.

64. A medicament dispenser according to claim 62 or 63, wherein the coupling is exposable to the airflow arising from inhalation or expiration of the

patient to assist in the cooling of the coupling post-actuation of the access means.

65. A medicament dispenser according to any of claims 1 to 64 comprising an actuation counter for counting the number of actuations of the access or a dose counter for counting the number of doses delivered.

66. A medicament dispenser according to claim 65, wherein the actuation counter is independent of the coupling.

67. A medicament dispenser according to any of claims 1 to 66 additionally comprising an electronic control system for controlling the supply of non-mechanical energy to the coupling.

68. A medicament dispenser according to claim 67, wherein the electronic control system is capable of providing pulses of non-mechanical energy to the coupling.

69. A medicament dispenser according to either of claims 67 or 68, wherein the electronic control system is capable of receiving inputs from electronic sensors locatable on the dispenser.

70. A medicament dispenser according to claim 69, additionally comprising an electronic sensor selected from the group consisting of a breath sensor, a shake sensor, a temperature sensor, an infrared sensor and a patient ID sensor.

71. A medicament dispenser according to any one of the preceding claims further comprising dose-metering means and/or transport means and/or climate control means

72. A medicament dispenser according to claim 71 wherein at least one of the dose-metering means and/or transport means and/or climate control means are directly or indirectly actuable by the access means

73. A medicament dispenser according to any one of the preceding claims wherein actuation of the access means is remote and/or voice activated.

74. A medicament dispenser according to any one of the preceding claims wherein actuation of access means primes the dispenser to release a dose of medicament.

75. A medicament dispenser according to any one of the preceding claims wherein the medicament container comprises medicament in dry powder form.

76. A medicament dispenser according to claim 75 wherein the dry powder medicament includes a pharmaceutical excipient in dry powder form.

77. A medicament dispenser according to claim 75 or claim 76 wherein the density of the dry powder medicament particles is reduced relative to standard dry powder medicament.

78. A medicament dispenser according to claims 75 to 77 wherein the dry powder medicament particles are aerodynamically shaped to improve medicament delivery to the patient.

79. A medicament dispenser according to any one of claims 75 to 78 wherein the medicament container takes the form of a dry powder reservoir.

80. A medicament dispenser according to any one of claims 1 to 74 wherein the medicament container comprises medicament in solution or suspension form.

81. A medicament dispenser according to claim 80, wherein said medicament container comprises a suspension of a medicament in a propellant.

82. A medicament dispenser according to claim 81, wherein, said propellant comprises liquefied HFA134a, HFA-227, helium or carbon dioxide.

83. A medicament dispenser according to claim 80, wherein said medicament container comprises a solution of a medicament in a solvent.

84. A medicament dispenser according to any of the preceding claims wherein the medicament is pre-metered prior to actuation of the access means by a patient.

85. A medicament dispenser according to any one of the preceding claims wherein the medicament is selected from the group consisting of albuterol, salmeterol, fluticasone propionate, beclomethasone dipropionate, salts or solvates thereof and any mixtures thereof.

86. A medicament dispenser according to any one of the preceding claims wherein the dry powder medicament includes a pharmaceutical excipient in dry powder form.

87. A medicament dispenser according to any one of the preceding claims wherein the density of the dry powder medicament particles is reduced relative to standard dry powder medicament.

88. A medicament dispenser according to any one of the preceding claims wherein the dry powder medicament particles are aerodynamically shaped to improve medicament delivery to the patient.

89. A medicament dispenser according to any one of the preceding claims additionally comprising a safety mechanism to prevent unintended multiple actuations of the inhaler.

90. A medicament dispenser according to claim 89 wherein the safety mechanism imposes a time delay between successive actuation of the inhaler.

91. A medicament dispenser according to any of the preceding claims comprising a manual override enabling manual actuation of the access means.

92. A medicament dispenser according to claim 91 comprising a child resistance feature to prevent undesirable actuation thereof by children.

93. Use of a medicament dispenser according to any one of claims 1 to 92 for dispensing medicament.

94. An actuator for use in a medicament dispenser according to any one of claims 1 to 92.

95. An actuator for a medicament container comprising a housing, within said housing, a container seat for receipt of the medicament container; on the housing or connecting therewith, an exit channel for passage of the medicament to a patient and access means for directly or indirectly exposing the exit channel for use by the patient, wherein the access means comprises an access coupling, wherein the access coupling which is reversibly deformable in response to the application of non-mechanical energy thereto.

96. An actuator according to either of claims 94 or 95, wherein said non-mechanical energy comprises electric current flow through the coupling.

97. An actuator according to any of claims 94 to 96, wherein the coupling comprises one or more wires which contract in response to the application of non-mechanical energy thereto.

98. An actuator according to any of claims 94 to 97, wherein said coupling comprises an alloy which undergoes a phase transition on the application of non-mechanical energy thereto.

99. An actuator according to claim 98, wherein said alloy is a nickel-titanium alloy.

100. An actuator according to any of claims 94 to 99 additionally comprising an electronic control system for controlling the supply of non-mechanical energy to the coupling.

101. An actuator according to claim 100, wherein the electronic control system is capable of providing pulses of non-mechanical energy to the coupling.

102. An actuator according to either of claims 100 or 101, wherein the electronic control system is capable of receiving inputs from electronic sensors locatable on the dispenser.

103. An actuator according to claim 102, additionally comprising an electronic sensor selected from the group consisting of a breath sensor, a shake sensor, a temperature sensor, an infrared sensor and a patient ID sensor.

104. An actuator according to claims 94 to 103 further comprising release means.

105. A dry powder medicament container for use in the dispenser according to claims 1 to 92 and/or the actuator of claims 94 to 104.

106. Laboratory test apparatus for testing a medicament container having transport means comprising at least one actuator according to any of claims 94 to 104 and a mounting for said at least one actuator.

107. Kit of parts comprising a medicament dispenser according to any of claims 1 to 92 in the form of a cartridge; and a housing shaped for receipt of said cartridge.

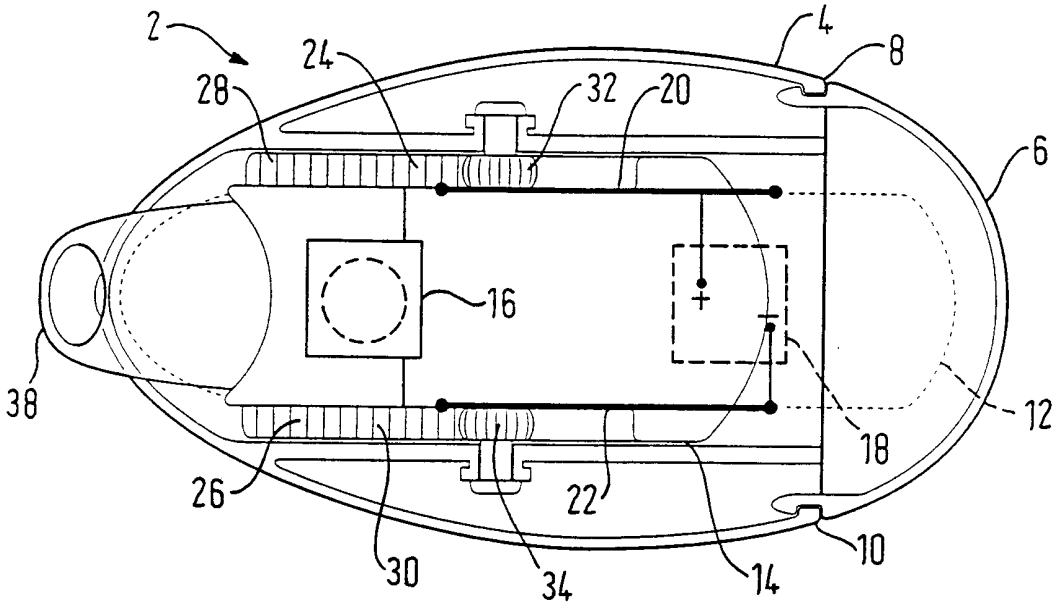


FIG. 1a

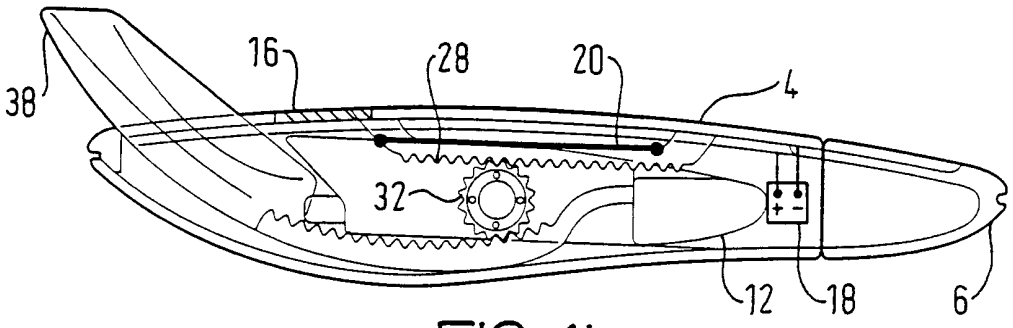


FIG. 1b

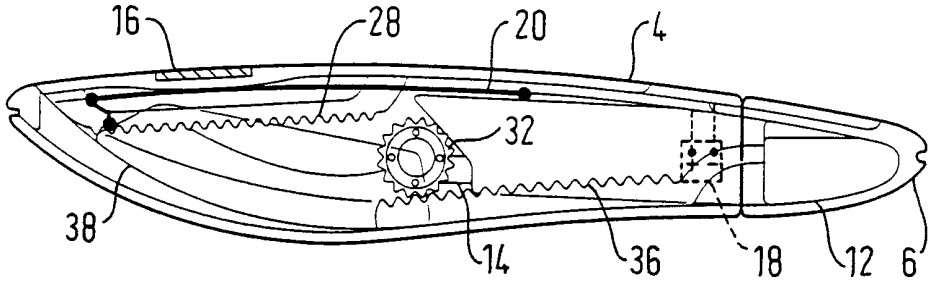


FIG. 1c

FIG. 2b

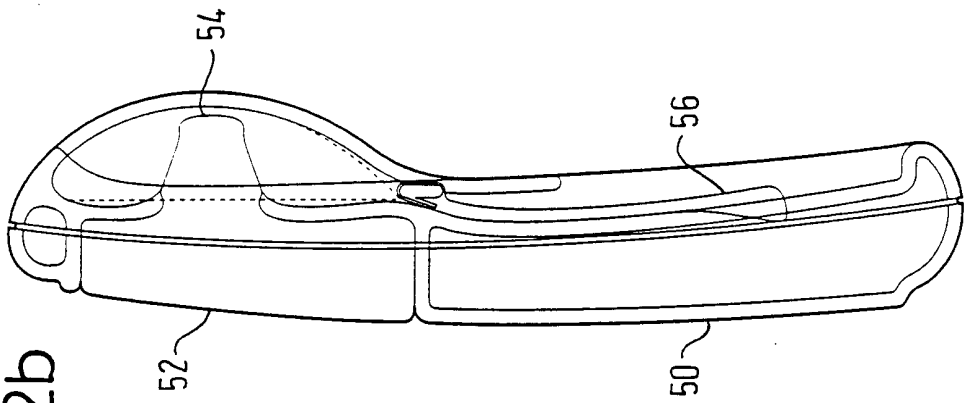
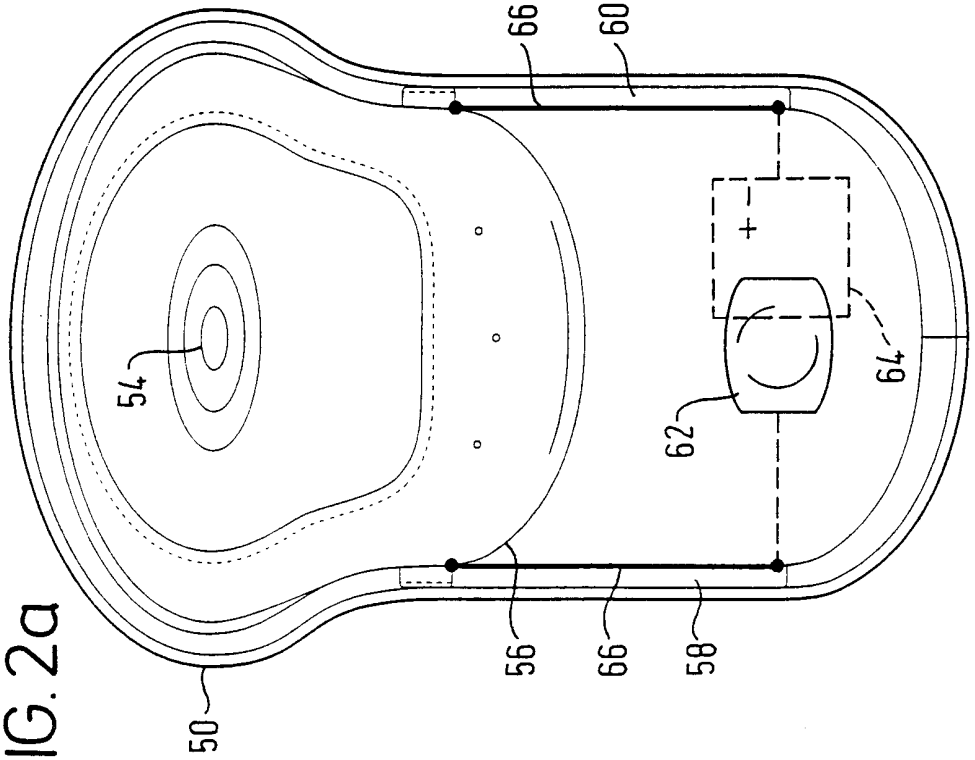


FIG. 2a



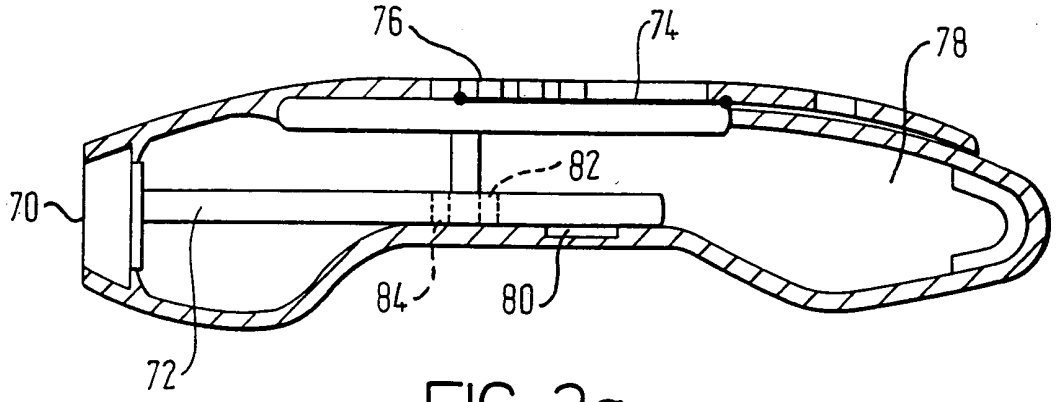


FIG. 3a

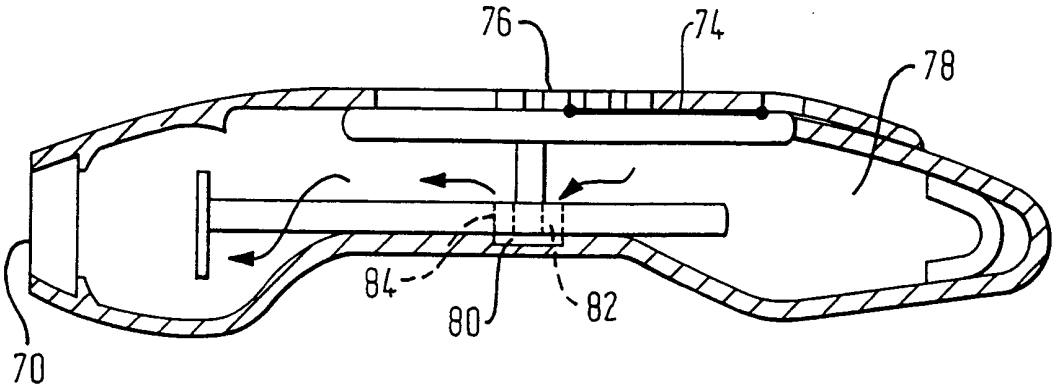


FIG. 3b

INTERNATIONAL SEARCH REPORT

Interna ..al Application No
PCT/EP 00/12391

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61M15/00

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

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A61M

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

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

EPO-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 0 461 281 A (ATOCHEM NORTH AMERICA) 18 December 1991 (1991-12-18) column 3, line 6 -column 8, line 2; figures 1-3 ---	1-5, 10-12, 16-20, 22-49, 60-107
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[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

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

"E" earlier document but published on or after the international filing date

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

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

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

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
6 April 2001	18/04/2001

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Zeinstra, H

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Form PCT/ISA/210 (second sheet) (July 1992)

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A	US 5 743 250 A (GONDA IGOR ET AL) 28 April 1998 (1998-04-28) column 28, line 20 - line 24 column 46, line 2 - line 24; figure 14	1-107

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