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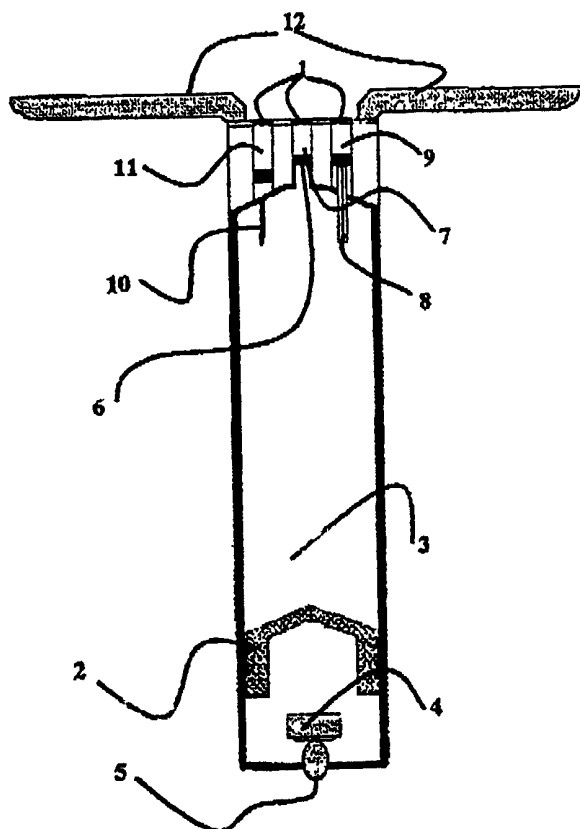
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- (71) Applicant (for all designated States except US): INTERAG [NZ/NZ]; 558 Te Rapa Road, Hamilton (NZ).
- (72) Inventors; and
- (75) Inventors/Applicants (for US only): BUNT, Craig, Robert [NZ/NZ]; 11 Queens Avenue, Hamilton (NZ). RATHBONE, Michael, John [GB/NZ]; 11 Walsh Street, Forest Lake, Hamilton (NZ). BURGGRAAF, Shane [GB/NZ]; 25 Richmond Street, Hamilton (NZ). OGLE, Colin, Roger [NZ/NZ]; 11 Jones Crescent, Hamilton (NZ).
- (74) Agents: PARK, A., J. et al.; Intellectual Property Lawyers and Patent Attorneys of Huddart Parker Building, 1 Post Office Square, Wellington (NZ).
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(54) Title: MULTIPLE MATERIAL DISPENSING



(57) Abstract: A device suitable for use as an intra vaginal device or as a bolus where, after initiation, a member (usually a plunger) moves with a known movement characteristic and is involved in the stagger release of multiple materials. That moving member is used to time the discharge of one or more material from its reservoir in the device (there being separate powering of the timed discharge) or is used to both time and indirectly power the discharge of one or more material from its reservoir, such discharges preferably being in a staggered manner. Optionally the moving member as a plunger may itself also directly discharge a material from a reservoir.

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“MULTIPLE MATERIAL DISPENSING”

THE CURRENT INVENTION

The present invention relates to dispensing apparatus for dispensing an agent or
5 its precursor(s), methods of use thereof and related means, methods and applications.

There are many instances where it is desired to activate or allow the activation
of the release of an active agent or its precursor(s) whether as a single dose, a
continuous dose or as a pulsile dose. Instances include microprocessor control
active delivery of agents as might be used to release a medicament into a body cavity
10 such as, for example, disclosed in PCT/NZ98/00011.

Many forms of such active delivery device (in addition to microprocessor or
other logic means capable of empowering the release) utilise a reservoir or barrel
having a membrane or piston that separates the formulation of the active agent or its
precursor(s) from a gas generating arrangement, eg, a hydrogel and its electrodes.

15 SUMMARY OF THE INVENTION

The present invention is directed to providing the timing mechanism for
dispensing apparatus (preferably which lends itself to an easier manufacturing
procedure (as will be described hereinafter in more detail)). It is an object of the
present invention to provide such apparatus and related means, methods and
20 procedures.

The present invention has found there can be an effective staggering of
materials to be delivered from a device (once initiated by some act) which thereafter
is to continue with its delivery regime without a need for further human input where
there is reliance on the movement (preferably rectilinearly) of a member or element
25 having a known movement profile or characteristic as the stagger timing mechanism.

In one aspect the invention is a **dispensing apparatus** capable of expressing
material, whether the same or different, from at least two reservoirs, the apparatus
being characterised in that actuation means for expressing material from an outlet of
a first of said reservoirs (hereafter “primary reservoir”) also directly or indirectly
30 expresses or times the expression of material from the outlet(s) of at least one other
said reservoir (hereafter “secondary reservoir(s)”) but only after a predetermined

state of expression of the material from said primary reservoir has occurred.

Preferably said actuation means for expressing material from said primary reservoir includes a piston (hereafter “primary piston”).

Preferably said at least one said secondary reservoir at least in part includes a
5 piston capable of expressing its material via its outlet.

In one embodiment said actuation means includes a gas generation unit the gas of which is capable of moving said primary piston.

Preferably said gas generation unit is a resistance circuit actuable to generate gas from the battery providing the powering therefor.

10 Preferably said gas generation unit includes a hydrogel electrolysed at least in part by a battery powered resistance circuit. In this respect see WO 94/01165, US Patent 5,402,42 and US Patent 5,741,275.

Preferably a switching mechanism is provided to allow the initiation of actuation of said gas generation unit.

15 In other embodiments said actuation means includes at least one of the group consisting of a spring, an osmotically expanding material, a chemical reaction, compressed gas, evolved or generated gas(es) and a motor.

Preferably said apparatus is capable of being inserted into a body cavity.

Preferably deployable members for retention in a target body cavity are
20 provided.

Preferably said apparatus is of a configuration for a target mammal with retention features for intra vaginal use. See, for example, US Patent 4,091,807, WO 99/07346, WO 95/13760, WO 98/33452 and WO 96/29025.

Preferably at least one of the materials to be expressed is a liquid or liquid
25 formulation.

Preferably at least one of the materials to be expressed is in the form of a solid or a solids formulation.

Preferably at least one of said outlets is sealed, plugged or otherwise closed yet is openable under the forces to act thereon as the associated material is pressed for
30 expression out of such outlet(s).

Preferably at least one of said secondary reservoirs has its material expressible

under the action of gas from said gas generation unit bypassing or ducting through said primary piston once the primary piston has moved a predetermined amount.

Preferably (at least) one of said secondary reservoirs has its material expressible under the action of said primary piston coming into contact with and driving a material expressing piston of a said secondary reservoir.

Preferably said primary piston carries a magnet capable of switch actuation for a circuit in turn, once actuated, to cause movement of means to express material from at least one said secondary reservoir.

Preferably said primary piston using a magnet/reed switch interaction can cause, using at least one of the group defined in claim 8, an expression of the material from at least one said secondary reservoir.

In another aspect the invention is as previously defined substantially as herein described with reference to any example thereof and/or any of the accompanying drawings.

In another aspect the invention is a **dispensing apparatus** comprising or including

an assembly defining partitioned chambers where the partitioning member can be moved by gas pressure increase(s) in one chamber to reduce the volume of the other chamber,

a battery powered circuit actuable to generate gas within or for said one chamber,

at least one assembly defining at least one material containing reservoir with an outlet (sealed, plugged or otherwise optionally closed) it or each capable of being reduced in volume by a piston,

wherein at least one said piston of a said material containing reservoir is moved to express the associated material only once, under the action of said gas generation, said partitioning member has moved a predetermined amount.

Preferably said partitioned chambers have a piston as its partitioning member.

Preferably said one chamber of said partitioned chamber to reduce in volume has an outlet (sealed or otherwise) and contains a material expressible out of said chamber as said volume is reduced.

In another aspect the invention is a **dispensing apparatus** comprising or including

an assembly defining partitioned chambers where the partitioning member can be moved to reduce the volume of the other chamber,

5 at least one assembly defining at least one material containing reservoir with an outlet (sealed, plugged or otherwise optionally closed) it or each capable of being reduced in volume by a piston,

wherein at least one said piston of a said material containing reservoir is moved to express the associated material only once said partitioning member has
10 moved a predetermined amount.

Preferably said partitioning member is movable by means of at least one of the group consisting of a spring, an osmotically expanding material, a chemical reaction, compressed gas, evolved or generated gas(es) and a motor.

Preferably a said piston of a said material containing reservoir is movable by
15 means of at least one of the group consisting of a spring, an osmotically expanding material, a chemical reaction, compressed gas, evolved or generated gas(es) and a motor.

Preferably said partitioned chambers have a piston as its partitioning member.

Preferably said one chamber of said partitioned chamber to reduce in volume
20 has an outlet (sealed or otherwise) and contains a material expressible out of said chamber as said volume is reduced.

In another aspect the invention is a **multiple material dispensing apparatus** having

a primary reservoir containing a first material expressible via an outlet under
25 the action of a primary piston, and

at least one secondary reservoir itself containing a material to be dispensed via an outlet under the action of a secondary piston, wherein said secondary piston is actuatable directly by said primary piston after an at least partial expression of the material of the primary reservoir.

30 In still another aspect the invention is a **dispensing apparatus** capable of expressing materials, whether the same or different, from at least two reservoirs, the

apparatus being characterised in that a piston (hereafter “primary piston”) in use will express or cause the expression at least some material from a reservoir and that piston, directly or indirectly, activates or causes the expression of at least some material from at least one other reservoir, the relative timing of the at least partial emptying of the reservoirs between or amongst the reservoirs being predetermined but nonetheless being dependent on said piston and its travel.

In still another aspect the invention is a **dispensing apparatus** capable of expressing material, whether the same or different, from at least two reservoirs in a delayed manner, the apparatus being characterised in that a member capable in use of moving or being set to move, can, upon predetermined movement occurring to provide the delay or delays, directly or indirectly express or time the expression of material from the outlet(s) of said at least two reservoirs.

Preferably each said reservoir includes a piston.

Preferably the apparatus is also apparatus of any one of claims 1 to 29.

Preferably said member in use capable of moving, moves under the influence of at least one of the group consisting of a spring, an osmotically expanding material, a chemical reaction, compressed gas, evolved or generated gas(es) and a motor.

Preferably in use said delays are staggered.

Preferably said member capable in use of moving or being set to move is a piston capable of expressing material from its own reservoir.

Preferably said apparatus is in the form of a bolus or intra vaginal device, eg; for use as a bolus.

In another embodiment said apparatus is adapted for release of active ingredients into an environment.

In another aspect the invention consists in a **dispensing apparatus** capable of expressing materials, whether the same or different, from at least two reservoirs, the apparatus being characterised in that a piston in use that can be initiated to move or which, in its in use site, can move, will express or cause the expression of at least some material from a reservoir and that primary piston also, directly or indirectly, activates or causes the expression of at least some material from at least one other reservoir.

Preferably the expression of at least some material from at least one other reservoir is under the action of a piston in turn moved, initiated to move or allowed to move by the state of movement of the primary piston.

In another aspect the invention consists in a **dispensing apparatus** capable of
5 expressing materials, whether the same or different, from at least two reservoirs, the apparatus being characterised in that a piston movable under the action of a generated gas in use will express or cause the expression at least some material from a reservoir and that primary piston also, directly or indirectly, activates or causes the expression of at least some material from at least one other reservoir.

10 In another aspect the invention consists in a **device for intraruminal, intra vaginal, or the like body cavity use capable of expressing materials**, whether the same or different, from at least two reservoirs, wherein the apparatus is characterised in that a piston in use will express at least some material from a reservoir and that piston directly or indirectly, activates or causes the expression of at least some
15 material from at least one other reservoir.

In another aspect the invention is an **intra vaginal device** having

- (i) a progesterone containing material in a primary reservoir, and
- (ii) oestradiol or an oestradiol containing material in a secondary reservoir, where, in use, a member which moves in a predetermined way provides a delay
20 in the release of (ii) with respect to (i).

Preferably said device has four reservoirs to release in sequence, reliant on said member's movement

- (a) a progesterone containing material,
- (b) oestradiol benzoate,
- 25 (c) cloprostenol sodium, and
- (d) oestradiol 17 β .

Preferably said device is also a device as previously defined.

In one embodiment said device is a bolus for use in a ruminant having in separate reservoirs a trace metal (eg; zinc) and an anthelmintic (eg; ivermectin)
30 which is also a device as previously defined.

In another aspect the invention is, in a plural reservoir (solids and/or liquid)

material dispensing apparatus, **the use** of a directly or indirectly (eg; through gas generation) driven member capable after initiation of progressive movement having predetermined travel characteristics as the initiator and/or force providing member for time staggered expression of material from the reservoirs.

5 In another aspect the invention is the **use** of a member initiatable to move (directly or indirectly under battery power) in a predetermined progressive manner to act as the timing element in the expression from material from different reservoirs in at least a staggered manner.

Preferably, in acting as the timing element said member applies directly or
10 indirectly force to an expression piston of at least one reservoir.

Preferably said member is itself an expression piston of a material containing reservoir.

In another aspect the invention is **a method of, at least in part, serially or sequentially expressing materials from a delivery device**, said method comprising
15 actuating a battery powered device to move an element thereof in a substantially known manner to thereby, with delay of such travel, to act, staggered with respect to time, upon a material expression component of each material containing reservoir to thereby express such material via an outlet.

In still another aspect the invention is **a method of stagger expressing**
20 **materials from a delivery device**, said method comprising setting, actuating or initiating the device to move an element thereof, firstly, to commence (directly or indirectly) material expression from a first reservoir of the device, and secondly, after the element has traveled a predetermined distance and as it continues to travel, to commence (directly or indirectly) material expression from another material
25 containing reservoir.

In another aspect the invention is **a method of patterning the delivery of plural materials into a body cavity of an animal** which comprises or includes the steps of

introducing into a said cavity a device containing said plural materials,
30 discharging at least one of said plural materials from a reservoir under the action of a plunger which reduces the volume of a reservoir available therefor

sometime after the initiation of the device, and,

by (direct or indirect) interaction with said plunger subsequently discharging at least one other material of the device from that material's reservoir within the device.

5 In one embodiment said device is an intra vaginal device.

In one embodiment said plunger is moved under the action of a gas generation unit.

Preferably said action with said plunger is by abutment with a piston to discharge said at least one other material.

10 Preferably said interaction with said plunger involves a bypass for a gas but moves said plunger to then in turn act directly upon a piston for discharging said at least one other material.

Preferably said interaction is indirect and involves magnetic switching.

15 Preferably said device is a bolus or an intra vaginal device and includes means of variable geometry deployable from an insertion condition to a retention condition.

Preferably said method is performed using, as said device, apparatus as previously defined.

In another aspect the present invention consists in a **dispensing apparatus** capable of expressing materials, whether the same or different, from at least two
20 reservoirs, the apparatus being characterised in that a piston in use will express or cause the expression at least some material from a reservoir and that piston, directly or indirectly, activates or causes the expression of at least some material from at least one other reservoir, the relative timing of the at least partial emptying of the reservoirs between or amongst the reservoirs being predetermined but nonetheless
25 being dependent on said piston and its travel.

Preferably the expressions are linked timewise to the travel of the piston.

Preferably the apparatus is for use as a bolus or as an intra vaginal device.

Other uses could be for timed release of actives into any environment, eg; fishtanks, lubricants into bearings, etc.

30 Preferably the expressions are linked timewise to the travel of the piston.

Preferments in respect of the dispensing apparatus or the bolus of the present

invention will now be described.

Preferably said apparatus is of a kind where the piston of said first reservoir advances without rotation. In other forms it may rotate.

Preferably the advancement of the piston of the first reservoir is under the
5 action of a gas and/or an activated electrical circuit.

Preferably the material of at least the first reservoir is a fluid. Preferably that fluid is a liquid. Preferably the liquid is or contains an active ingredient (whether solid or not). In other forms the material may be a gas or a mixture of a gas and liquid. Any such liquids may include a solids content and/or itself is a mixture of
10 multiple liquids. In some instances the material to be expressed from a reservoir can be a solid or almost a solid, eg loose powders, a gel, a capsule, or the like.

In some forms of the present invention at least one and preferably each of the reservoirs is provided with a closed outlet capable of being opened under the direct or indirect action on the contents of the associated reservoir, eg, as would be the case
15 with, for example, a waxed or frangible seal.

Preferably said apparatus has the piston thereof movable under the action of a gas which is generated upon the device being switch activated, eg, at the time of insertion.

In some forms of the present invention the gas may be generated from a
20 hydrogel or the like using an electrolysis dependent gas generation circuit capable of being activated. In still other forms preferably said gas is generated directly from the energisation of a circuit including a gas generation battery.

In some forms of the present invention the first reservoir may in turn discharge its content onto a down stream reservoir, eg utilising as a piston therebetween a seal
25 between the materials for the purpose of discharging first material from the second reservoir.

In still other arrangements there is a direct discharge through a rupturable or dischargeable seal of the material of the first chamber and a sequential movement of the piston towards at least one other reservoir until such time as there is interaction
30 therewith as a result of the pistons movement. Such interaction may be direct contact or penetration. For example, a needle type arrangement could penetrate the

piston of the first reservoir to thus allow the action of a gas that moves the first piston directly onto a piston or like member of such a second reservoir. In the same or different apparatus such interaction might mean there might equally be some extension of the piston into the reservoir of another material to itself act as a separate
5 delayed action thereof.

In still other interactions the piston may time (eg by magnetic interaction) some energisation of a release circuit forming part of a release arrangement of another reservoir.

BRIEF DESCRIPTION OF THE DRAWINGS

10 The invention consists in the foregoing and also envisages constructions of which the following gives examples.

In the accompanying drawings

Figure 1 shows a hybrid apparatus in accordance with the present invention where there can be an actuation of the device and some control of a discharge
15 sequence of materials from different reservoirs in a pre-determined manner,

Figures 2A to 2D shows a sequence of materials expression using a device substantially similar to that of Figure 1 with both a piston/needle and piston/piston interaction for the delayed deliveries,

Figures 3A to 3B in a similar manner to that of Figures 2A to 2D shows an
20 expression sequence again with a device similar to that of Figure 1 but this time with a primary piston interacting directly on a piston of at least two of the secondary reservoirs with stagger timing as to delivery therefrom,

Figure 4 shows the rate of vehicle delivery for a device of a kind as shown in Figure 1 in a simplified form,

25 **Figure 5** shows the effect of the needle and piston (diamond) or piston only (square) on delivery rate at 38°C of vehicle from an infusion reservoir of a device possessing the bolus reservoir option as depicted in the embodiments shown in Figures 2A to 2D,

Figure 6 shows the effect of short secondary piston (circle) or long secondary
30 piston (square) upon flow rate at 38°C of vehicle from the infusion reservoir of a device possessing piston/piston interaction options as shown in options of Figures

2A to 2D and more particularly 3A to 3D,

Figure 7 shows a plot to show the effect of the static resistance of the piston and seals of a primary bolus reservoir and the subsequent influence thereof on time lag between initiation of hydrogen production of a gas cell and release of a primary bolus reservoir dosage unit and vehicle from the infusion reservoir, Figure 7 showing the release of fluorescence from a primary bolus reservoir with a high static pressure piston,

Figure 8 is a similar plot to that of Figure 7 but in respect of a low static pressure piston,

Figure 9 shows the use of an interaction with the piston to time subsequent discharges,

Figures 10A through 10D show a device having (shown diagrammatically and not in an assembly) a sequence of three secondary reservoirs capable of being activated by passage past, for example, a reed switch of a magnet that moves as the moveable element or member, and

Figure 11 shows a most preferred form of the present invention having materials discharged from the primary reservoir under the action of a primary piston (moved by gas being generated after initiation), the primary piston subsequently, by abutment on piston extensions of two secondary reservoirs, leading to the staggered discharge from the secondary reservoirs.

While the preferred propulsion mechanism for the main piston is a gas generating or hydrogel cell, other mechanisms may be used.

Other mechanisms that may be employed to drive the main piston (or secondary pistons, especially following activations by a main piston via a magnet and reed switch) include;

- a spring,
- an osmotically expanding material, e.g. gelatin,
- chemical reaction, e.g. acid/base reaction resulting in the liberation of CO₂,
- compressed gas, e.g. a hydrocarbon, and
- a motor, e.g. a "watch" or turning screw.

Figure 1 shows a main barrel or reservoir having an outlet the upper end adjacent to smaller reservoirs. Preferably the formulations are protected within the barrel and smaller reservoirs by rupturable seals 1. A main piston 2 acts to dispense the contents from a main reservoir 3 as a result of an increase in pressure from a gas cell 4 that is activated by a switch 5. The contents of the main reservoir act upon the primary piston 6 of a primary reservoir 7 to dispense the primary reservoir contents after the rupture of the primary reservoir seal. The primary piston may also act directly upon the rod and piston 8 to dispense the contents of a terminal reservoir 9. The primary piston may also be pierced by a needle 10 thereby enabling gas to bypass the main piston and act upon a piston 11. Also present on the device are means by way of retention arms 12 for locating the device in a body cavity such as a vagina.

One configuration of the Figure 1 option is better presented in Figures 2A to 2D. As the infusion piston commences its migration towards the infusion reservoir orifice a dosage unit (e.g. tablet) located within the orifice (primary bolus reservoir) is expelled. Towards the end of the infusion pistons migration it acts upon a secondary piston whilst simultaneously being pierced by a needle. This action has two results;

- (1) a dosage unit in the secondary bolus reservoir is expelled, and
- (2) hydrogen from the gas cell is able to bypass the infusion piston in order to act upon the piston of the tertiary bolus reservoir and, once sufficient pressure has been reached, expel the contents of said reservoir.

A different configuration is presented in Figures 3A to 3D. As the infusion piston commences its migration towards the infusion reservoir orifice a dosage unit (e.g. tablet) located within the orifice (primary bolus reservoir) is expelled. Towards the end of the infusion pistons migration it acts upon a secondary piston and thereby a dosage unit in the secondary bolus reservoir is expelled. Following this action the infusion piston commences action upon a tertiary piston and thereby a dosage unit in the tertiary bolus reservoir is expelled.

Figure 4 shows the rate of vehicle delivery from a device similar to that represented in Figure 1 with the exception that the needle 10 and piston 11 are

absent.

The action of the infusion piston coming into contact with a secondary piston reduces the flow of vehicle from the infusion reservoir (Figure 5). However no additional reduction in flow of vehicle from the infusion reservoir is observed as a
5 result of the action of the infusion piston coming into contact with the needle as present in bolus reservoir mechanism of Figures 2A to 2D (see Figure 5).

In Figure 5 the arrow represents the time point at which the infusion piston comes into contact with the secondary piston and/or needle. The vehicle was aqueous 2% HPMC held at 38°C. The interaction between the needle and piston as
10 shown by the diamonds and the interaction between the piston with a piston is shown with the squares.

The action of the infusion piston coming into contact with a secondary piston reduces the flow of vehicle from the infusion reservoir (Figure 6). However selection of long (i.e. projecting further into the infusion reservoir) or short pistons
15 for the secondary bolus reservoir piston and altering the external resistor allows for control of the flow rate from the infusion reservoir (Figure 6).

In Figure 6 the vehicle is aqueous 4% HPMC at 38°C and the circles depict the effect of a short piston whilst the square depict the effect of a long piston. The piston options are those depicted as piston to piston interactions in Figures 2A to 2D and
20 3A to 3D.

The static resistance of the piston and seals of the primary bolus reservoir influences the time lag between initiation of hydrogen production by the gas cell and release of the primary bolus reservoir dosage unit and vehicle from the infusion reservoir (see Figure 7 and 8 and Table 1).

Table 1. Effect of high static pressure (2 points of contact between piston and reservoir walls) and low static pressure (1 point of contact between piston and reservoir walls) upon the lag between initiating hydrogen production by the gas cell and release of a dosage unit from the primary bolus reservoir.

5

Replicate	High friction	Low friction
1	655 – 660 mins	125 mins
2	Did not release	410 mins

10 Choice of appropriate rod lengths for the bolus chamber delivery mechanism and static pressure of the pistons within each individual reservoir would enable the selection of any desired delivery rate and profile.

Figure 7 shows the release of fluorescence from the primary bolus reservoir with a high static pressure piston whilst Figure 8 shows the release of fluorescence
15 from the primary reservoir with a low static pressure piston.

Figure 9 shows a main barrel or reservoir 1 in which a piston 2 containing a magnetic material 3 is enabled to migrate within the main barrel as a result of an increase in pressure from a gas cell 4. The magnet material is able to activate individual sensors 5 or sensor part or an array 6 which in turn control the action of a
20 device(s) 7 and/or 8.

In vivo performance of multiple material dispensing option of Figures 3A to 3D

An in vivo trial investigated the performance of bolus reservoir mechanism of Figure 3A to 3D. Devices were assembled as per Figures 3A to 3D, and inserted into
25 the vagina of normal cattle for 9 days. It was visually confirmed upon removal of the devices that all chambers were activated and the dosage units therein delivered.

Description of multiple material dispensing option of Figures 10A to 10D

The configuration of this option is presented in Figures 10A to 10D. As the
30 infusion piston commences its migration towards the infusion reservoir orifice dosage units (e.g. tablet) located within bolus reservoir are expelled due to the action of a magnet within the infusion piston activating sequential reed switches thereby

initiating the electrolytic production of gasses.

***In vitro* performance of multiple material dispensing option of Figures 10A to 10D**

5 Three devices as per Figures 10A to 10D and Figure 9 were constructed. Activation and expulsion of dosage units from all bolus reservoirs was visually confirmed.

10 ***In vivo* performance of multiple material dispensing option of Figures 10A to 10D**

 An in vivo trial investigated the performance of bolus reservoir mechanism of Figures 10A to 10D. Devices were inserted into the vagina of normal cattle for 9 days. It was visually confirmed upon removal of the devices that all chambers had been activated and the dosage units therein delivered.

15

Preferred multiple material dispensing option

 A preferred configuration is detailed in Figure 11 and Table 2. It consists of a cylinder that is divided by piston 13 in reservoir 14, containing the formulation, and part 15, containing the gas and the gas producing components. The action of piston 13 upon
20 the formulation contained in reservoir 14 causes piston 16 to expel the contents of reservoir 17 following the rupture of a seal 18.

 Following the expulsion of formulation piston 13 migrates towards the outlet of reservoir 17 thereby coming into contact with rod 19. Rod 19 acting under the influence of piston 13 drives piston 20 to expel the contents of reservoir 21
25 following the rupture of seal 22.

 Following further expulsion of formulation piston 13 migrates further towards the outlet of reservoir 17 thereby coming into contact with rod 23. Rod 23 acting under the influence of piston 13 drives piston 24 to expel the contents of reservoir 25 following the rupture of seal 26.

30

Table 2. Physical parameters of design brief for electronically modulated intravaginal synchrony device.

	Parameter	Specification
5	Gross physical dimensions	
	Delivery component outer diameter (cm)	2.5
	Delivery component length (cm)	13
	retention mechanism width (cm)	15
	Infusion reservoir (1)	
10	Volume (ml)	30
	Delivery rate (ml/day)	3.33
	Bolus reservoir one (5)	
	rod protrusion into infusion reservoir (%)	NA
	Volume (ml)	0.10
15	Bolus reservoir two (8)	
	rod protrusion into infusion reservoir (%)	11
	Volume (ml)	0.10
	Bolus reservoir two (11)	
	rod protrusion into infusion reservoir (%)	1
20	Volume (ml)	0.10

Example 1: RESERVOIR CONTENTS FOR INTRA VAGINAL PRODUCT

25 Main reservoir contents:

- 15 mg/ml progesterone dissolved in ethanol thickened with 4% hydroxypropyl methyl cellulose (P4)

Secondary reservoir contents:

- 30
- Primary - a tablet, liquid or semi-solid dosage unit of 10 mg oestradiol benzoate (ODB)
 - Secondary - a tablet, liquid or semi-solid dosage unit of 1000 mcg of cloprostenol sodium (PG)
 - Tertiary - a tablet, liquid or semi-solid dosage unit of 7.2 mg oestradiol
- 35 17beta (E17b)

Example 2: CONTENTS OF INTRARUMINAL PRODUCT

- Main reservoir contents - Zinc oxide liquid or semi-solid formulation
- Secondary reservoir(s) - tablet, liquid or semi-solid Ivermectin 60 mg

CLAIMS:

1. **Dispensing apparatus** capable of expressing material, whether the same or different, from at least two reservoirs, the apparatus being characterised in that actuation means for expressing material from an outlet of a first of said reservoirs
5 (hereafter “primary reservoir”) also directly or indirectly expresses or times the expression of material from the outlet(s) of at least one other said reservoir (hereafter “secondary reservoir(s)”) but only after a predetermined state of expression of the material from said primary reservoir has occurred.
2. Apparatus as claimed in claim 1 wherein said actuation means for expressing
10 material from said primary reservoir includes a piston (hereafter “primary piston”).
3. Apparatus as claimed in claim 1 or 2 wherein said at least one said secondary reservoir at least in part includes a piston capable of expressing its material via its outlet.
4. Apparatus as claimed in claim 2 or 3 wherein said actuation means includes a
15 gas generation unit the gas of which is capable of moving said primary piston.
5. Apparatus as claimed in claim 4 wherein said gas generation unit is a resistance circuit actuatable to generate gas from the battery providing the powering therefor.
6. Apparatus as claimed in claim 4 wherein said gas generation unit includes a hydrogel electrolysed at least in part by a battery powered resistance circuit.
- 20 7. Apparatus as claimed in claim 5 or claim 6 wherein a switching mechanism is provided to allow the initiation of actuation of said gas generation unit.
8. Apparatus of any one of claims 1 to 3 wherein said actuation means includes at least one of the group consisting of a spring, an osmotically expanding material, a chemical reaction, compressed gas, evolved or generated gas(es) and a motor.
- 25 9. Apparatus as claimed in any one of the preceding claims capable of being inserted into a body cavity.
10. Apparatus as claimed in claim 9 wherein deployable members for retention in a target body cavity are provided.
11. Apparatus as claimed in claim 9 or claim 10 of a configuration for a target
30 mammal with retention features for intra vaginal use.
12. Apparatus as claimed in any one of the preceding claims wherein at least one

of the materials to be expressed is a liquid or liquid formulation.

13. Apparatus as claimed in any one of the preceding claims wherein at least one of the materials to be expressed is in the form of a solid or a solids formulation.

14. Apparatus as claimed in any one of the preceding claims wherein at least one
5 of said outlets is sealed, plugged or otherwise closed yet is openable under the forces to act thereon as the associated material is pressed for expression out of such outlet(s).

15. Apparatus as claimed in claim 4, 5 or 6 wherein at least one of said secondary reservoirs has its material expressible under the action of gas from said gas
10 generation unit bypassing or ducting through said primary piston once the primary piston has moved a predetermined amount.

16. Apparatus as claimed in any one of claims 1 to 15 wherein (at least) one of said secondary reservoirs has its material expressible under the action of said primary piston coming into contact with and driving a material expressing piston of a said
15 secondary reservoir.

17. Apparatus of any one of claims 1 to 16 wherein said primary piston carries a magnet capable of switch actuation for a circuit in turn, once actuated, to cause movement of means to express material from at least one said secondary reservoir.

18. Apparatus of any one of claims 1 to 15 wherein said primary piston using a
20 magnet/reed switch interaction can cause, using at least one of the group defined in claim 8, an expression of the material from at least one said secondary reservoir.

19. Apparatus as claimed in any one of the preceding claims substantially as hereinbefore described with reference to any example thereof and/or any of the accompanying drawings.

25 20. **Dispensing apparatus** comprising or including
an assembly defining partitioned chambers where the partitioning member can be moved by gas pressure increase(s) in one chamber to reduce the volume of the other chamber,

30 a battery powered circuit actuatable to generate gas within or for said one chamber,

at least one assembly defining at least one material containing reservoir with an

outlet (sealed, plugged or otherwise optionally closed) it or each capable of being reduced in volume by a piston,

wherein at least one said piston of a said material containing reservoir is moved to express the associated material only once, under the action of said gas generation, said partitioning member has moved a predetermined amount.

21. Apparatus as claimed in claim 20 wherein said partitioned chambers have a piston as its partitioning member.

22. Apparatus as claimed in claim 20 or 21 wherein said one chamber of said partitioned chamber to reduce in volume has an outlet (sealed or otherwise) and contains a material expressible out of said chamber as said volume is reduced.

23. **Dispensing apparatus** comprising or including

an assembly defining partitioned chambers where the partitioning member can be moved to reduce the volume of the other chamber,

at least one assembly defining at least one material containing reservoir with an outlet (sealed, plugged or otherwise optionally closed) it or each capable of being reduced in volume by a piston,

wherein at least one said piston of a said material containing reservoir is moved to express the associated material only once said partitioning member has moved a predetermined amount.

24. Apparatus of claim 23 wherein said partitioning member is movable by means of at least one of the group consisting of a spring, an osmotically expanding material, a chemical reaction, compressed gas, evolved or generated gas(es) and a motor.

25. Apparatus of claim 23 or 24 wherein a said piston of a said material containing reservoir is movable by means of at least one of the group consisting of a spring, an osmotically expanding material, a chemical reaction, compressed gas, evolved or generated gas(es) and a motor.

26. Apparatus as claimed in any one of claims 23 to 25 wherein said partitioned chambers have a piston as its partitioning member.

27. Apparatus as claimed in any one of claims 23 to 26 wherein said one chamber of said partitioned chamber to reduce in volume has an outlet (sealed or otherwise) and contains a material expressible out of said chamber as said volume is reduced.

28. **A multiple material dispensing apparatus** having
a primary reservoir containing a first material expressible via an outlet under the action of a primary piston, and
at least one secondary reservoir itself containing a material to be dispensed via
5 an outlet under the action of a secondary piston, wherein said secondary piston is actuatable directly by said primary piston after an at least partial expression of the material of the primary reservoir.
29. **Dispensing apparatus** capable of expressing materials, whether the same or different, from at least two reservoirs, the apparatus being characterised in that a
10 piston (hereafter "primary piston") in use will express or cause the expression at least some material from a reservoir and that piston, directly or indirectly, activates or causes the expression of at least some material from at least one other reservoir, the relative timing of the at least partial emptying of the reservoirs between or amongst the reservoirs being predetermined but nonetheless being dependent on said
15 piston and its travel.
30. **Dispensing apparatus** capable of expressing material, whether the same or different, from at least two reservoirs in a delayed manner, the apparatus being characterised in that a member capable in use of moving or being set to move, can, upon predetermined movement occurring to provide the delay or delays, directly or
20 indirectly express or time the expression of material from the outlet(s) of said at least two reservoirs.
31. Apparatus as claimed in claim 30 wherein each said reservoir includes a piston.
32. Apparatus of claim 30 or 31 which is also apparatus of any one of claims 1 to 29.
- 25 33. Apparatus of claim 30 or 31 wherein said member in use capable of moving, moves under the influence of at least one of the group consisting of a spring, an osmotically expanding material, a chemical reaction, compressed gas, evolved or generated gas(es) and a motor.
34. Apparatus of any one of claims 30 to 33 wherein in use said delays are
30 staggered.
35. Apparatus of any one of claims 30 to 35 wherein said member capable in use of

moving or being set to move is a piston capable of expressing material from its own reservoir.

36. Apparatus of any one of claims 30 to 36 in the form of a bolus or intra vaginal device.

5 37. Apparatus as claimed in any one of claims 20 to 35 for use as a bolus.

38. Apparatus as claimed in any one of claims 20 to 35 for release of active ingredients into an environment.

39. **Dispensing apparatus** capable of expressing materials, whether the same or different, from at least two reservoirs, the apparatus being characterised in that a
10 piston in use that can be initiated to move or which, in its in use site, can move, will express or cause the expression of at least some material from a reservoir and that primary piston also, directly or indirectly, activates or causes the expression of at least some material from at least one other reservoir.

40. Apparatus as claimed in claim 39 wherein the expression of at least some
15 material from at least one other reservoir is under the action of a piston in turn moved, initiated to move or allowed to move by the state of movement of the primary piston.

41. **Dispensing apparatus** capable of expressing materials, whether the same or different, from at least two reservoirs, the apparatus being characterised in that a
20 piston movable under the action of a generated gas in use will express or cause the expression at least some material from a reservoir and that primary piston also, directly or indirectly, activates or causes the expression of at least some material from at least one other reservoir.

42. **A device for intraruminal, intra vaginal, or the like body cavity use**
25 **capable of expressing materials**, whether the same or different, from at least two reservoirs, wherein the apparatus is characterised in that a piston in use will express at least some material from a reservoir and that piston directly or indirectly, activates or causes the expression of at least some material from at least one other reservoir.

43. **An intra vaginal device** having
30 (i) a progesterone containing material in a primary reservoir, and
(ii) an oestradiol containing material in a secondary reservoir,

where, in use, a member which moves in a predetermined way provides a delay in the release of (ii) with respect to (i).

44. A device of claim 43 having four reservoirs to release in sequence, reliant on said member's movement

- 5 (a) a progesterone containing material,
 (b) oestradiol benzoate,
 (c) cloprostenol sodium, and
 (d) aestradiol 17 β .

45. A device of claim 43 or 44 which is also a device of any one of claims 1 to 35
10 and 39.

46. A **bolus** for use in a ruminant having in separate reservoirs a trace metal (eg; zinc) and an anthelmintic (eg; ivermectin) which is also a device of any one of claims 1 to 35 and 39.

47. In a plural reservoir (solids and/or liquid) material dispensing apparatus, **the**
15 **use** of a directly or indirectly (eg; through gas generation) driven member capable after initiation of progressive movement having predetermined travel characteristics as the initiator and/or force providing member for time staggered expression of material from the reservoirs.

48. **The use** of a member initiatable to move (directly or indirectly under battery
20 power) in a predetermined progressive manner to act as the timing element in the expression from material from different reservoirs in at least a staggered manner.

49. The use of claim 48 wherein in acting as the timing element said member applies directly or indirectly force to an expression piston of at least one reservoir.

50. The use of claim 48 or 50 wherein said member is itself an expression piston of
25 a material containing reservoir.

51. A **method of, at least in part, serially or sequentially expressing materials from a delivery device**, said method comprising actuating a battery powered device to move an element thereof in a substantially known manner to thereby, with delay of such travel, to act, staggered with respect to time, upon a material expression
30 component of each material containing reservoir to thereby express such material via an outlet.

52. **A method of stagger expressing materials from a delivery device**, said method comprising setting, actuating or initiating the device to move an element thereof, firstly, to commence (directly or indirectly) material expression from a first reservoir of the device, and secondly, after the element has traveled a predetermined
5 distance and as it continues to travel, to commence (directly or indirectly) material expression from another material containing reservoir.

53. A method as claimed in claim 52 wherein said device is a device as claimed in any one of claims 1 to 46.

54. **A method of patterning the delivery of plural materials into a body cavity**
10 **of an animal** which comprises or includes the steps of

introducing into a said cavity a device containing said plural materials,
discharging at least one of said plural materials from a reservoir under the action of a plunger which reduces the volume of a reservoir available therefor sometime after the initiation of the device, and,

15 by (direct or indirect) interaction with said plunger subsequently discharging at least one other material of the device from that material's reservoir within the device.

55. A method as claimed in claim 54 wherein said device is an intra vaginal device.

56. A method as claimed in claim 54 or 55 wherein said plunger is moved under
20 the action of a gas generation unit.

57. A method as claimed in any one of claims 54 to 55 wherein said action with said plunger is by abutment with a piston to discharge said at least one other material.

58. A method as claimed in any one of claims 54 to 56 wherein said interaction
25 with said plunger involves a bypass for a gas but moves said plunger to then in turn act directly upon a piston for discharging said at least one other material.

59. A method as claimed in any one of claims 54 to 56 wherein said interaction is indirect and involves magnetic switching.

60. A method as claimed in any one of claims 54 to 59 wherein said device is
30 a bolus or an intra vaginal device and includes means of variable geometry deployable from an insertion condition to a retention condition.

61. A method of any one of claims 54 to 60 when performed using, as said device, apparatus of any one of claims 1 to 46.

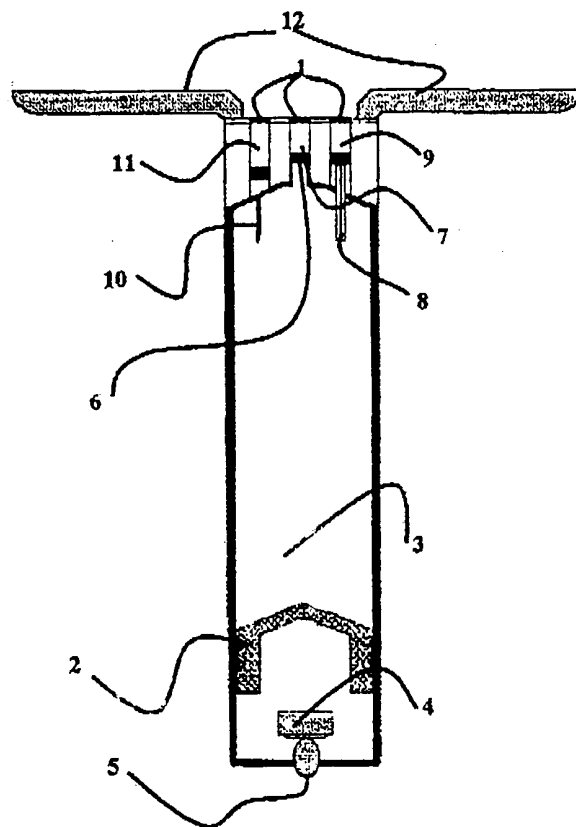


FIGURE 1

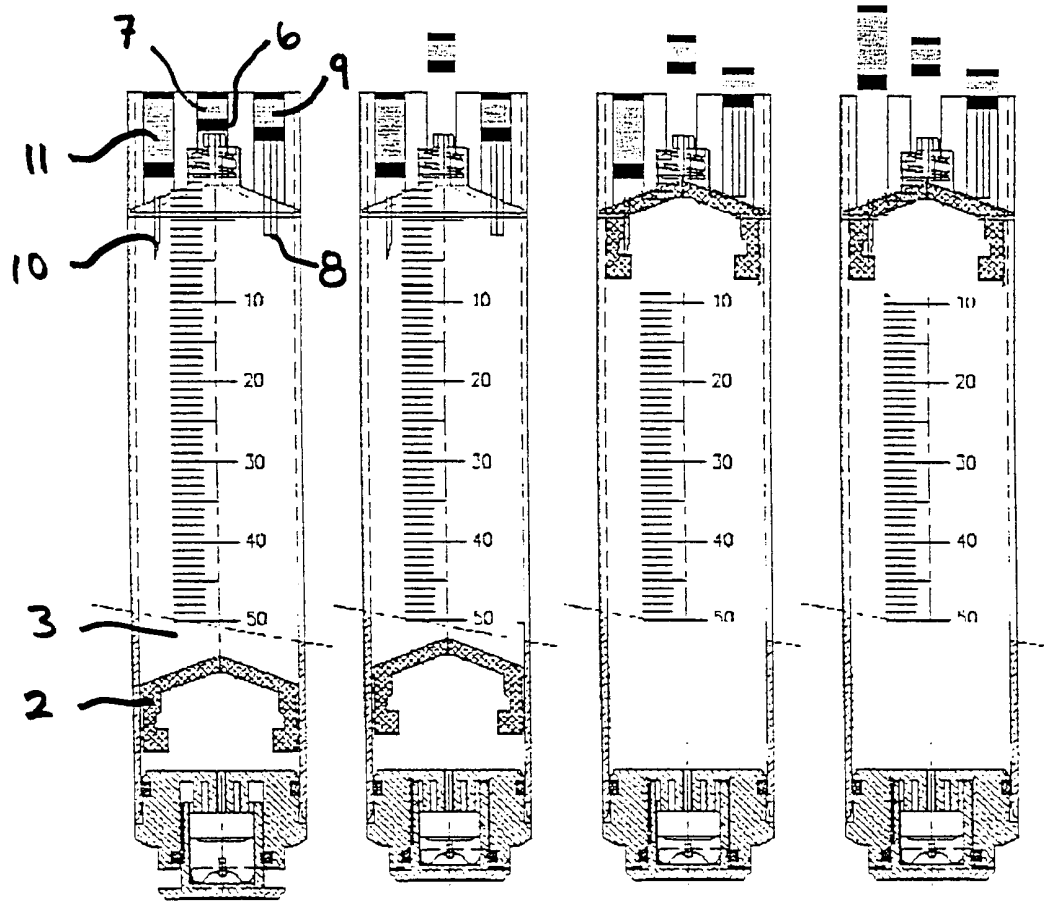


FIGURE 2A

FIGURE 2B

FIGURE 2C

FIGURE 2D

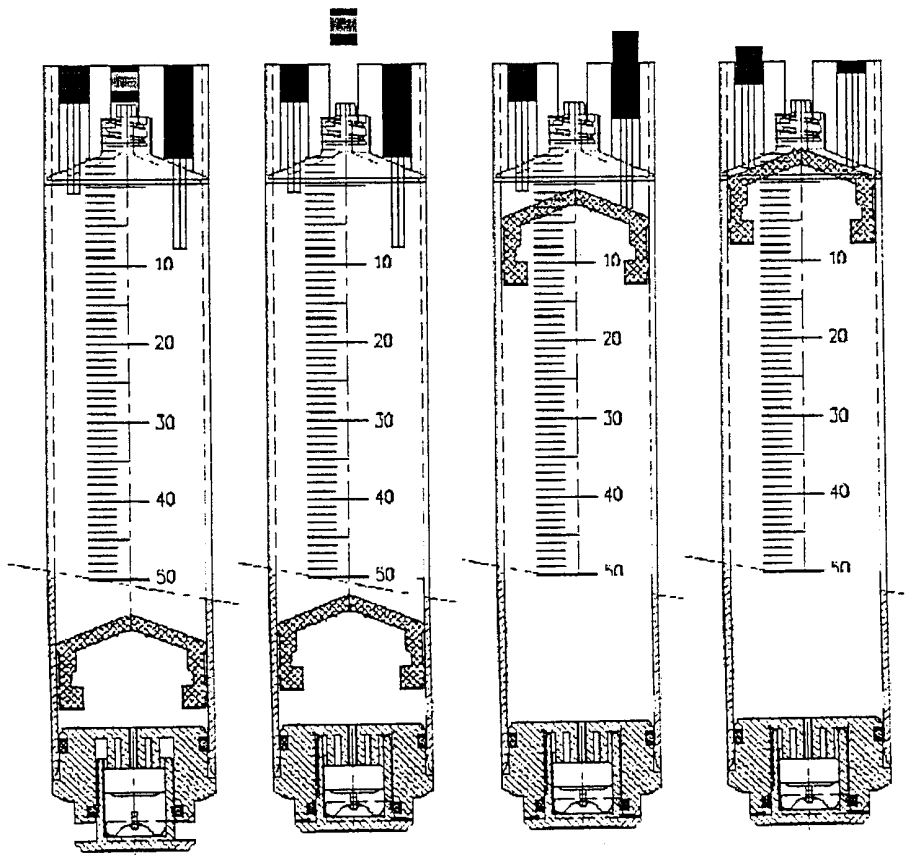


FIGURE 3A

FIGURE 3B

FIGURE 3C

FIGURE 3D

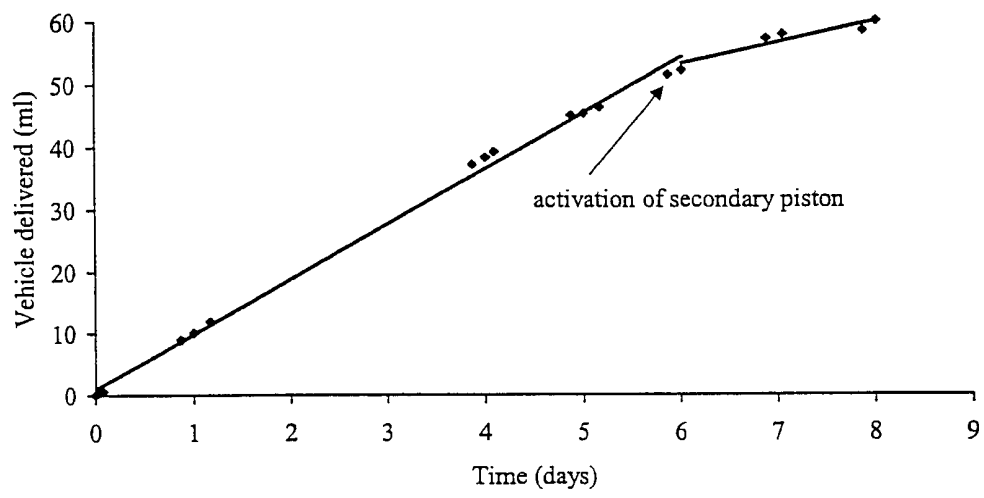


FIGURE 4

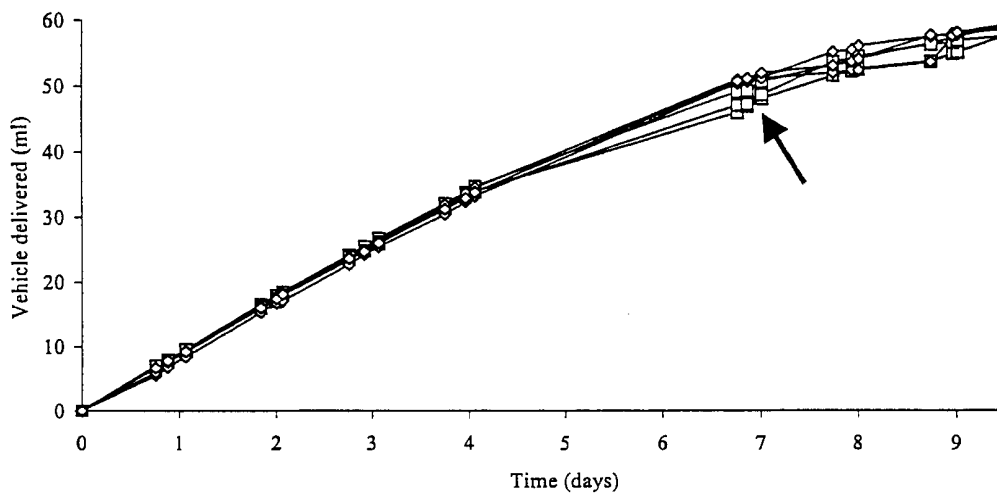


FIGURE 5

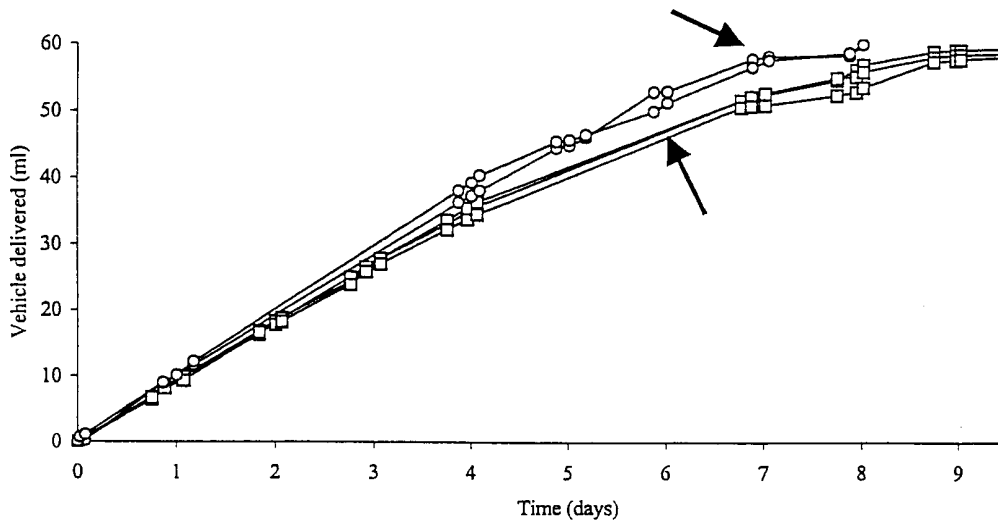


FIGURE 6

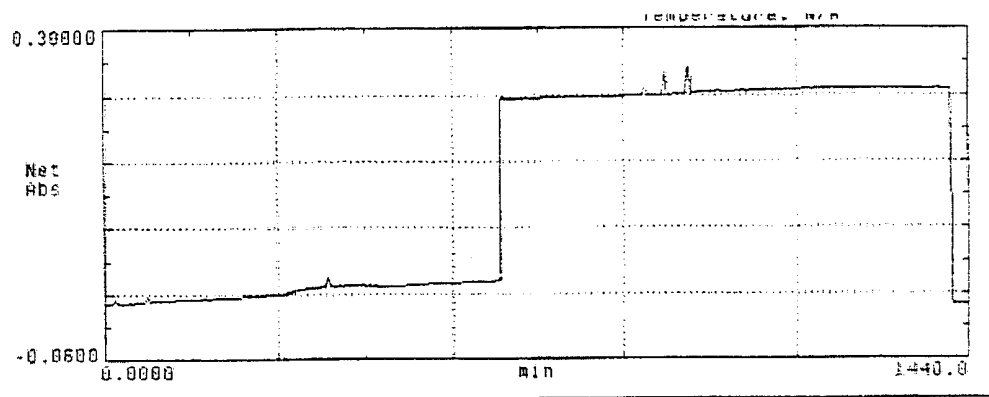


FIGURE 7

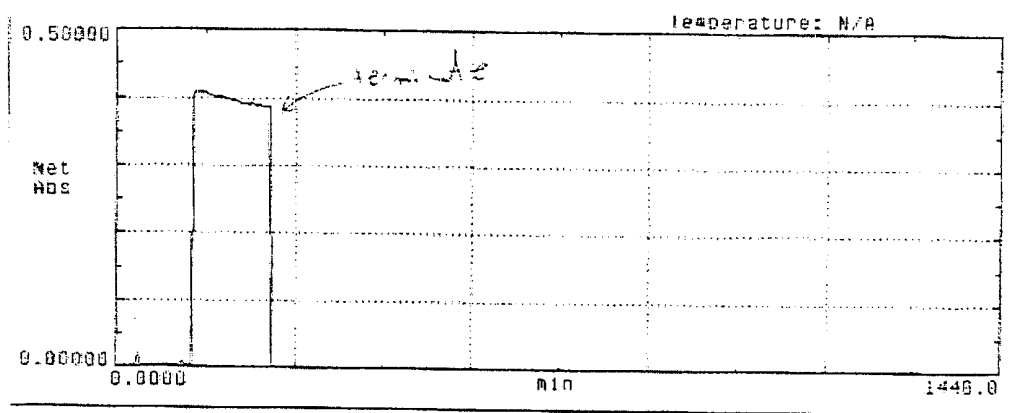


FIGURE 8

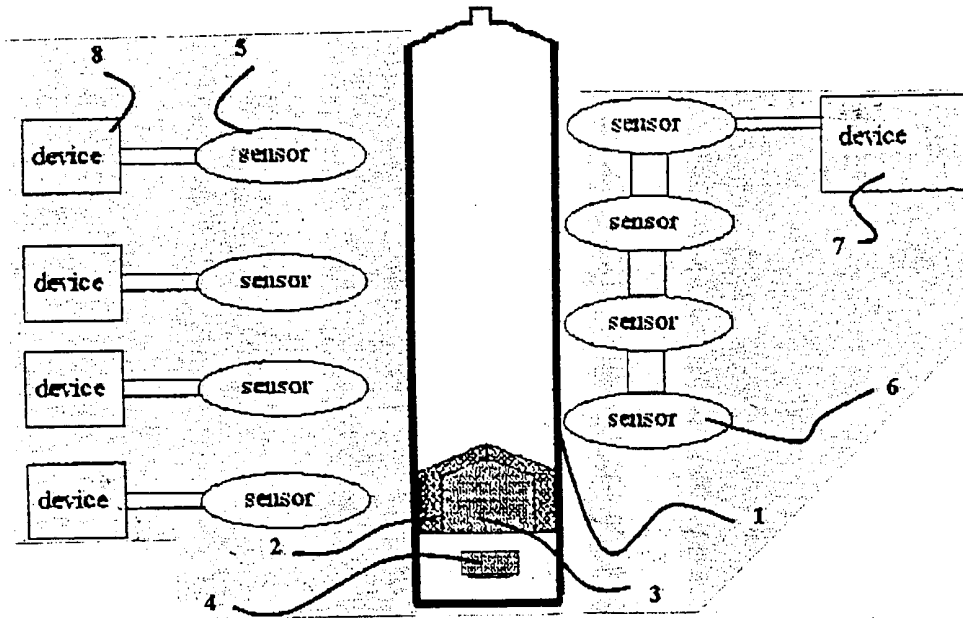


FIGURE 9

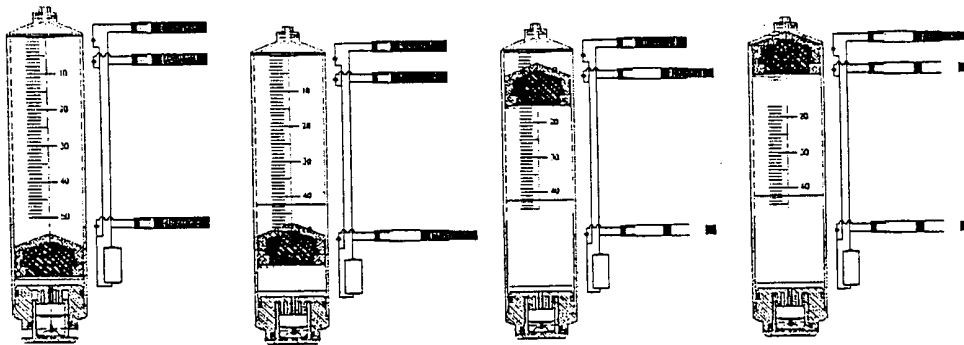


FIGURE 10A FIGURE 10B

FIGURE 10C FIGURE 10D

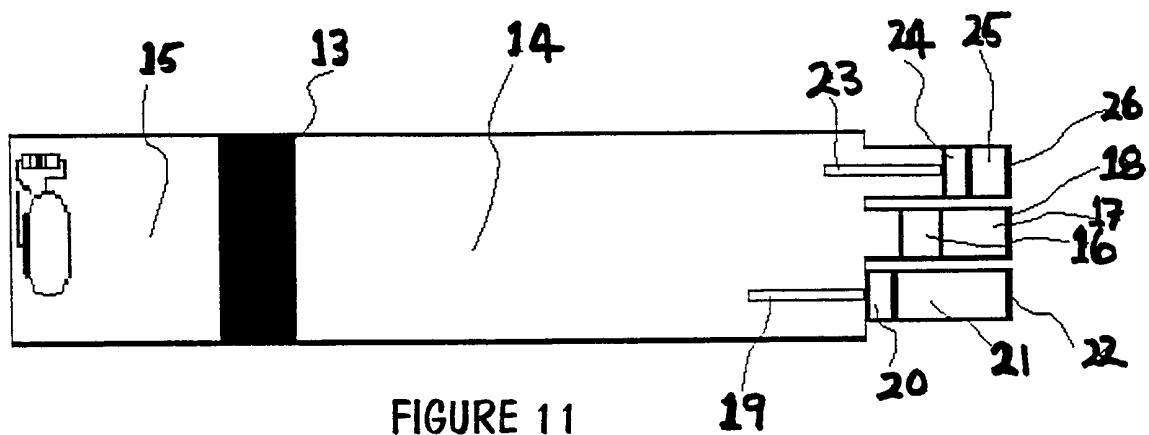


FIGURE 11

INTERNATIONAL SEARCH REPORT

International application No.
PCT/NZ00/00155

A. CLASSIFICATION OF SUBJECT MATTER		
Int. Cl. ⁷ : A61D 19/00, A61F 6/08, A61M 31/00, A61M 5/00		
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) A61D, A61M, A61K		
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 practicable, search terms used) DWPI: dispense, expel, express, deliver, introduce, pump, reservoir, chamber, barrel, compartment, 2, two, twin, second, multi, plural, dual, many, several, sequence, series, consecutive, successive, subsequent, delay, stagger, piston, plunger, amount, length, distance, timing, activate, cause, initiate, enable		
C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 4439184 A (WHEELER) 27 March 1984 ✓ Figures 1, 2, 4	1-3, 9, 12, 14, 16, 23, 26, 27, 29-31, 34, 35, 38, 39, 42, 43, 46-50, 52-55, 57, 61
Y		4-8, 10, 11, 20-22, 24, 25, 33, 36, 37, 41, 51, 56, 58, 60
X	US 5090963 A (GROSS ET AL.) 25 February 1992 Entire document	23, 23, 27
<input checked="" type="checkbox"/> Further documents are listed in the continuation of Box C <input checked="" type="checkbox"/> See patent family annex		
* Special categories of cited documents:		
"A"	document defining the general state of the art which is not considered to be of particular relevance	"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
"E"	earlier application or patent but published on or after the international filing date	"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
"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)	"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
"O"	document referring to an oral disclosure, use, exhibition or other means	"&" document member of the same patent family
"P"	document published prior to the international filing date but later than the priority date claimed	
Date of the actual completion of the international search 13 December 2000		Date of mailing of the international search report 15 DEC 2000
Name and mailing address of the ISA/AU AUSTRALIAN PATENT OFFICE PO BOX 200, WODEN ACT 2606, AUSTRALIA E-mail address: pct@ipaustrialia.gov.au Facsimile No. (02) 6285 3929		Authorized officer STEVEN WEISS Telephone No : (02) 6283 2466

INTERNATIONAL SEARCH REPORT

International application No.

PCT/NZ00/00155

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 3923058 A (WEINGARTEN) 2 December 1975 Figures 2-5	1-3, 9, 12, 14, 16, 23, 36, 37, 29-31, 34, 35, 38, 39, 42, 43, 46-50, 52-55, 57, 61
Y		4-8, 10, 11, 20-22, 24, 25, 33, 36, 37, 41, 51, 56, 58, 60
X	US 4413991 A (SCHMITZ ET AL.) 8 November 1983 Entire document	39, 40, 42
Y		41
X	US 5290259 A (FISCHER) 1 March 1994 Abstract Figure 1	39, 40, 42
Y		41
X	EP 737484 A2 (NISSHO CORPORATION) 16 October 1996 Figures 2 and 3	1-3, 9, 12, 14, 16, 23, 26, 27, 29-31, 34, 35, 38, 39, 42, 43, 46-50, 52-55, 57, 61
Y		4-8, 10, 11, 20-22, 24, 25, 33, 36, 37, 41, 51, 56, 58, 60
X	WO 91/16094 A1 (SURVIVAL TECHNOLOGY INC.) 31 October 1991 Entire document	1-3, 8, 9, 12, 14, 16, 23- 27, 29-31, 33-35, 38, 39, 42, 43, 46-50, 52-55, 57, 61
Y	WO 99/12593 A2 (BAXTER INTERNATIONAL INC.) 18 March 1999 Entire document	4-8, 20-22, 24, 25, 33, 41, 51, 56

INTERNATIONAL SEARCH REPORT

International application No.
PCT/NZ00/00155

C (Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	WO 00/37130 A1 (WINSEL) 29 June 2000 Entire document	1-9, 12, 15, 16, 20-31, 33-39, 41, 42, 47-58, 61
P,X	US 5989215 A (DELMOTTE ET AL.) 23 November 1999 Figure 4	39, 40
X	US 5599312 A (HIGASHIKAWA) 4 February 1997 Figures 1-5, 11-26, 28, 29	1-3, 9, 12-16, 23, 26-31, 34, 35, 38-40, 42, 43, 46-50, 52-55, 57, 61
Y		4-8, 10, 11, 20-22, 24, 25, 33, 36, 37, 41, 51, 56, 58, 60
Y	WO 97/40776 A1 (DEC INTERNATIONAL NZ LIMITED) 6 November 1997 Figures 1 and 3	10, 11, 36, 60
Y	WO 99/26556 A1 (DEC INTERNATIONAL NZ LIMITED) 3 June 1999 Figure 1	10, 11, 36, 60
X	WO 98/33452 A1 (DEC INTERNATIONAL NZ LIMITED) 6 August 1998 Entire document	39-42
Y		4-8, 10, 11, 20-22, 24, 25, 33, 36, 37, 51, 56, 58, 60
X	WO 96/37189 A1 (ALZA CORPORATION) 28 November 1996 Entire document	23
Y		8, 24, 25, 33, 36, 37
X	WO 92/07612 A1 (ALZA CORPORATION) 14 May 1992 Entire document	23
Y		8, 24, 25, 33, 36, 37
X	WO 96/08280 A1 (RIVER MEDICAL INC.) 21 March 1996 Entire document	1-4, 8, 12, 21-31, 33-35, 39, 41, 42, 47-50, 52, 54, 56, 57, 61

INTERNATIONAL SEARCH REPORT

International application No.

PCT/NZ00/00155

Box I Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. Claims Nos : 19
because they relate to subject matter not required to be searched by this Authority, namely:
They rely on references to the description or drawings which do not comply with PCT Rule 6.2(a).
2. Claims Nos : 32, 45
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
The scope of each claim is indeterminable.
3. Claims Nos :
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a)

Box II Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

Please see attached sheet.

1. As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims
2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

The additional search fees were accompanied by the applicant's protest.

No protest accompanied the payment of additional search fees.

Supplemental Box

(To be used when the space in any of Boxes I to VIII is not sufficient)

Continuation of Box No: 1

The international application does not comply with the requirements of unity of invention because it does not relate to one invention or to a group of inventions so linked as to form a single general inventive concept. In coming to this conclusion the International Searching Authority has found that there are different inventions as follows:

1. Claims 1-18, 28, 29, 37 and 38 (when appended to either claim 28 or claim 29), 43, 44, 47-52, 53 (when appended to any one of the aforementioned claims up to and including claim 44), 54-60, and 61 (when appended to any one of the aforementioned claims up to and including claim 44) are directed to sequential material delivery combined with multiple reservoirs or chamber dispensers. It is considered that the feature of sequential material delivery combined with multiple reservoirs or chambers, comprises a first "special technical feature".
2. Claims 20-27 include within their scope single reservoir dispensers. It is considered that the feature of a single reservoir comprises a second "special technical feature".
3. Claims 30, 31, 33-36 and 37 and 38 (when appended to any one of the aforementioned claims) are directed to parallel material delivery dispensers. Additionally, claims 39-42 include within their scope parallel material delivery combined with multiple reservoirs. It is considered that the feature of parallel material delivery comprises a third "special technical feature".

Since the abovementioned groups of claims do not share any of the technical features identified, a "technical relationship" between the inventions, as defined in PCT rule 13.2 does not exist. Accordingly the international application does not relate to one invention or to a single inventive concept, a priori.

INTERNATIONAL SEARCH REPORT
Information on patent family members

International application No.
PCT/NZ00/00155

This Annex lists the known "A" publication level patent family members relating to the patent documents cited in the above-mentioned international search report. The Australian Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

Patent Document Cited in Search Report		Patent Family Member					
US	4439184	NONE					
US	5090963	EP	481601	US	5242406	AU	89978/91
		CA	2057937	EP	494042	NZ	241218
		ZA	9110190	EP	385916	US	5062834
		US	5425706	IL	90816		
US	3923058	US	3896805				
US	4413991	NONE					
US	5290259	NONE					
EP	737484	JP	8280800	US	5720731		
WO	9116094	AU	76755/91	EP	525048	US	5092843
WO	9912593	AU	90407/98	EP	983101	EP	993835
		EP	993836	EP	1004324	NO	992161
		US	5971722				
WO	200037130	AU	17809/00	EP	1013296		
US	5989215	AU	45362/96	CA	2207992	EP	804257
		US	6074663	WO	9622115		
US	5599312	AU	55753/94	CA	2150255	CZ	9501415
		EP	695555	FI	952663	JP	8308928
		NO	952135	NZ	258210	SK	730/95
		US	5704918	WO	9412227		
WO	9740776	NONE					
WO	9926556	AU	16962/99	EP	1039843	ZA	9810651
		AU	45345/99	WO	9963967		
WO	9833452	AU	57838/98	NZ	314175	ZA	9800805
WO	9637189	AU	57927/96	CA	2215306	EP	828477
		US	5817335				
WO	9207612	AU	89206/91	MX	9101783	PT	99339
		US	5151093	ZA	9108527	US	5312389
ANNEX CONTINUED							

INTERNATIONAL SEARCH REPORT
Information on patent family members

International application No.
PCT/NZ00/00155

Patent Document Cited in Search Report		Patent Family Member					
WO	9608280	AU	36318/95	CA	2200057	EP	781147
		US	5578005	AU	75224/94	CA	2168336
		CN	1132498	EP	711243	US	5398851
		WO	9504691	US	5398850	US	5571261
		US	5588556	US	5553741	US	5558255
		AU	74823/94	CA	2168352	CN	1132481
		EP	713409	US	5397303	WO	9505211
		AU	19267/95	CA	2184168	EP	748252
		US	5398850	WO	9523641		
END OF ANNEX							