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(54) **Title**: AIR TOLERANT IMPLANTABLE PISTON PUMP

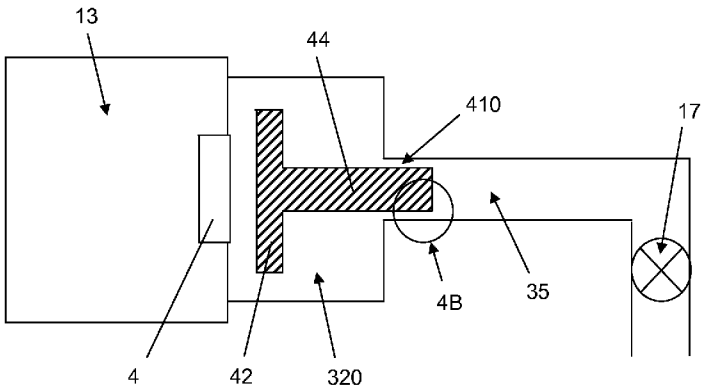

FIG. 4A

(57) **Abstract**: An implantable infusion device includes a reservoir (13) for housing an infusion medium and a drive mechanism having an inlet chamber (320), a piston (44) and a piston channel (35). The inlet chamber is in fluid communication with the reservoir. The piston channel is in fluid communication with the inlet chamber, and has a distal end and a proximal end, the proximal end being closer to the inlet channel than the distal end. The piston is axially moveable within the piston channel to drive infusion medium out of the distal end of the piston channel. The clearance (410) between the piston and the channel is sufficiently small to prevent undissolved gas in the inlet chamber from passing through the clearance. The inlet chamber may be sufficiently large to allow undissolved gas to accumulate without adversely affecting the performance of the infusion device.

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AIR TOLERANT IMPLANTABLE PISTON PUMP

FIELD

The present disclosure relates generally to implantable infusion devices; in particular to implantable infusion devices employing piston drive mechanisms.

BACKGROUND

Treatment of diseases and ailments of the body often benefit from short- or long-term infusion of therapeutic compositions. While such therapeutic compositions may be administered extracorporeally, e.g., via transcutaneous injection, many patients benefit from the consistent and repeatable dosage provided by an implantable infusion device. Such devices may employ a reservoir for storing an infusible therapeutic composition and a pumping mechanism coupled to the reservoir for discharging the infusible fluid through an outlet of the device. The discharge outlet is typically connected to flexible medical tubing, e.g., a catheter, leading to a targeted delivery site within the patient. The infusion device may further include electronics to control delivery of the therapeutic composition to the patient in accordance with a prescribed schedule.

Implantable infusion devices are typically implanted subcutaneously, e.g., in the chest or abdominal cavity. The device reservoir may be accessible via a self-sealing, needle-penetrable septum. Such devices are typically implanted so that the septum is located generally directly beneath the skin. The septum provides a fluid passageway that permits the reservoir to be refilled periodically via a transcutaneous injection. Accordingly, the pump reservoir can be filled or refilled without requiring surgical removal from the patient's body, and further without requiring any other significant surgical procedure.

During initial filling or refilling of the reservoir, gas bubbles or gas dissolved or entrained in the infusible therapeutic composition may be introduced into the reservoir. Formation or introduction of gas bubbles in the reservoir can potentially lead to problems with the pumping mechanism that can result in inaccurate delivery of the therapeutic composition or pump failure. For many infusion devices, it is recommended to vent or aspirate the reservoir prior to refilling to remove air trapped in the reservoir.

In some case, it is also recommended to degas the therapeutic composition prior to introducing the composition into the reservoir. Such processes can be time consuming and may not be fully effective, due in part to faulty technique.

While air bubbles can cause problems with many pumping mechanisms, with piston pumps air bubbles tend to cause inaccurate delivery of fluid due to the volume occupied by the air. Further many implantable infusion devices employing piston pumps include valves upstream or downstream of the piston. Air in the system may result in inoperability of the system due to inability to generate sufficient pressure to draw or force air through the valves or may require prolonged amounts of time to clear the air prior to resuming fully functional operation.

BRIEF SUMMARY

The present disclosure describes, among other things, implantable infusion devices employing piston pumps that can tolerate air bubbles. Such devices continue to function despite incomplete aspiration of the reservoir or degassing, if such procedures are warranted.

In various embodiments, an implantable infusion device includes a reservoir for housing an infusion medium and a drive mechanism having an inlet chamber, a piston and a piston channel. The inlet chamber is in fluid communication with the reservoir. The piston channel is in fluid communication with the inlet chamber, and has a distal end and a proximal end, the proximal end being closer to the inlet chamber than the distal end. The piston is axially moveable within the piston channel to drive infusion medium out of the distal end of the piston channel. The clearance between the piston and the channel is sufficiently small to prevent undissolved gas in the inlet chamber from passing through the clearance. For example, the clearance between the piston and the channel may be sufficiently small such that the infusion medium is retained in the clearance between the piston and the channel via capillary action and surface tension effects prevent the passage of undissolved gas through the clearance. The device may be configured to provide any suitably small clearance, such as a clearance between about 3 micrometers and about 10 micrometers.

The reservoir may be a positive pressure reservoir or a negative pressure reservoir, relative to ambient atmospheric pressure. For example, the reservoir, in some embodiments may be maintained at a pressure of, for example, greater than 5 psia, greater than 10 psia or between about 15 psia and 16 psia. Use of negative pressure reservoirs (e.g., abut 14 psia or less) presents special concerns, as the ability of a gas to dissolve in a solution, such as a fluid therapeutic composition, decreases as pressure decreases; thereby increasing the likelihood of air bubble formation within the reservoir and pumping mechanism. In such situations, it may be important to properly degas the therapeutic composition prior to delivering the composition to the reservoir. The ability to tolerate incomplete degassing would be desirable, as degassing procedures are time consuming and often suffer from improper technique.

Positive pressure reservoirs can also present special concerns. For example, proper functioning of a valves downstream of the piston channel are important in infusion devices employing positive pressure reservoirs. If the valve fails or is of too low of a cracking pressure, therapeutic fluid may be inadvertently pushed through the device and into the patient. However, due to concerns with air bubbles, the cracking pressure of such valves has been kept low to ensure that the drive mechanism can generate sufficient pressure to move the air bubble past the valve if such air bubbles are present and to maintain low energy consumption of the drive mechanism.

In various embodiments, regardless of whether the reservoir is a positive pressure or a negative pressure reservoir, the infusion devices described herein include a valve downstream, of the piston channel. The valve may have a cracking pressure that is between about 5 psi less than the reservoir pressure and about 5 psi more than the reservoir pressure. For example, the valve cracking pressure may be about the same as the reservoir pressure. If the reservoir pressure is between 15 and 19 psia, the valve cracking pressure may be 20 psia or greater to ensure that inadvertent or undesired administration of infusion medium is avoided. Similarly, infusion devices having negative pressure reservoirs (e.g. 14 psia or less) may also include a valve downstream of the piston channel to prevent undesired or inadvertent administration of a therapeutic fluid when subjected to lower atmospheric pressures, such as experienced at high elevations or on an airplane. With prior devices employing piston drive mechanisms, valves with high cracking pressures would not have been employed due to fear that if air

were to pass through the channel, the drive mechanism could not compress the air sufficiently to overcome the cracking pressure, causing the pump to effectively fail. However, with devices as described herein where undissolved air cannot pass through the channel, the piston drive mechanism can readily infuse a fluid medium through the channel to overcome the cracking pressure, open the valve, and force fluid out of the device. Accordingly, the devices described herein can employ safety valves that might not have been possible or practicable with prior infusion devices employing piston drive mechanisms.

The infusion device may also include a filter disposed between the inlet chamber and the reservoir, wherein the filter is configured to prevent microorganisms from entering the inlet chamber from the reservoir. Such a filter will generally and beneficially prevent undissolved gas from passing from the reservoir into the inlet chamber. However, gas dissolved in the infusion medium may pass through the hydrophilic filter, and over time, some of the dissolved or entrained gas will be freed or come out of solution and will form air bubbles in the inlet chamber. Such bubbles cannot pass through the filter into the reservoir and cannot be removed by aspiration when the reservoir is replenished with infusion medium. Accordingly, over time an increased volume of the inlet chamber may be occupied with air bubbles. For at least this reason, prior devices employing piston drive mechanism-avoided placement of a filter between the reservoir and the inlet chamber. Yet, it has been found, as described herein, that when the piston to channel clearance is sufficiently small to prevent undissolved free gas bubbles from passing through the clearance, 70% or more of the inlet chamber volume can be occupied by undissolved gas. Accordingly, infusion devices as described herein can include the beneficial effects of preventing contaminated infusion medium from reaching the inlet chamber and thus being delivered to the patient.

One or more embodiments of the infusion devices described herein may provide one or more advantages relative to previously manufactured or described devices. For example and in addition to the advantages of including a microbial filter and a valve as described above, the devices described herein can tolerate a good deal of error associated with degassing and aspiration associated with a refill procedure, which can often be a source of concern for implantable devices employing a piston drive

mechanism. These and other aspects and advantages will be apparent to one of skill in the art from the accompanying detailed description and drawings.

BRIEF DESCRIPTION OF THE DRAWINGS

Referring now to the drawings in which like reference numbers represent corresponding parts throughout:

FIG. 1 is a block diagram illustrating some components of a representative infusion device.

FIG. 2 is a block diagram illustrating some components of a representative drive mechanism.

FIGs. 3A-B are schematic diagrams of cross sections illustrating some representative components of a drive mechanism.

FIG. 4A is a schematic representative of selected components of an infusion device.

FIG. 4B is a schematic close-up view of the area within circle **4B** of **FIG. 4A**.

FIG. 5 is a schematic representative of selected components of an infusion device.

FIG. 6A is a schematic representative of selected components of an infusion device.

FIG. 6B is a schematic close-up view of the area within circle **6B** of **FIG. 6A**.

The drawings are not necessarily to scale. Like numbers used in the figures refer to like components, steps and the like. However, it will be understood that the use of a number to refer to a component in a given figure is not intended to limit the component in another figure labeled with the same number. In addition, the use of different numbers to refer to components is not intended to indicate that the different numbered components cannot be the same or similar.

DETAILED DESCRIPTION

In the following detailed description, reference is made to the accompanying drawings that form a part hereof, and in which are shown by way of illustration several specific embodiments of devices, systems and methods. It is to be understood that other embodiments are contemplated and may be made without departing from the scope of spirit of the present invention. The following detailed description, therefore, is not to be taken in a limiting sense.

All scientific and technical terms used herein have meanings commonly used in the art unless otherwise specified. The definitions provided herein are to facilitate understanding of certain terms used frequently herein and are not meant to limit the scope of the present disclosure.

As used in this specification and the appended claims, the singular forms "a", "an", and "the" encompass embodiments having plural referents, unless the content clearly dictates otherwise. As used in this specification and the appended claims, the term "or" is generally employed in its sense including "and/or" unless the content clearly dictates otherwise.

As used herein, undissolved gas means gas not dissolved or entrained in an infusion medium. It will be understood that gas may transition from being dissolved or entrained in an infusion medium to being in a free undissolved state. When in a free and undissolved state and surrounded by infusion medium, the gas will tend to form bubbles. Gas and air are generally used herein interchangeably.

As used herein, "about" means +/- 10% of the enumerated numerical value that it precedes. For example, "about" may mean +/- 5%, or +/- 3% of the enumerated numerical value that it precedes.

The present disclosure describes, among other things, implantable infusion devices employing piston pumps that can tolerate air bubbles. It has been found that piston pumps having a piston to bore clearance sufficiently small to prevent undissolved gas (i.e., gas not dissolved in infusion medium) from passing through a radial clearance channel formed between the piston and the bore. For example, it has been found that if

the clearance is sufficiently small such that infusion medium flows through the clearance channel via capillary action, undissolved gas bubbles do not pass through the clearance channel. Further, it has been shown that placement of an antimicrobial filter, such as a 0.22 micron filter, between a reservoir and an inlet chamber for the piston drive mechanism can be tolerated. Previously, infusion devices employing piston pumps would not include such filters due to fear that they might trap air bubbles within the piston inlet chamber causing pump inaccuracy or malfunction. In addition, such a filter generally prevents removal of the air bubbles from of the inlet chamber via aspiration during refilling of the reservoir. However, as described herein, it has been discovered that a large amount of undissolved gas can be tolerated within the pump inlet chamber (e.g., 70% or more of the volume of the chamber) without any significant adverse consequences.

Prior to describing details regarding piston pump infusion devices configured to tolerate air bubbles, a general discussion of representative infusion devices and drive mechanisms is provided with regard to **FIGS. 1, 2, 3A** and **3B**. Additional details regarding configurations for tolerating air bubbles are provided in the discussion related to **FIGS. 4A, 4B, 5, 6A** and **6B**.

Referring to **FIG. 1**, a block diagram of some components of a representative infusion device **10** is shown. The device includes a housing **12**. Housing may be made of any suitable material, such as a rigid polymeric material or metallic material, such as titanium. If device **10** is configured to be implanted in a patient, the housing **12** is preferably hermetically sealed. In the depicted device **10**, a fluid flow path includes an inlet **18**, a reservoir **13**, a filter **4**, a drive mechanism **20**, and an outlet **16**. The flow path may also include a one-way valve **17** disposed between the drive mechanism **20** and the outlet **16**, as depicted. The inlet **18** is fluidly coupled with reservoir **13**, in which infusion medium may be stored. The inlet **18** may include a port through the housing **12** to allow access to the reservoir **18** or fluid path upstream of the reservoir. A septum may be disposed over the port to seal the inlet **18**. The reservoir **13** is fluidly coupled to the drive mechanism **20**, which may draw infusion medium from the reservoir **13**. The filter **4** is configured to prevent microorganisms that may be in the infusion medium stored in the reservoir **13** from passing into the drive mechanism **20**. The drive mechanism **20** is fluidly coupled to the outlet **16** and forces fluid drawn from the

reservoir **12** out of the device **12** via the outlet **16**. The outlet may include a port to which a catheter may be operably coupled. The infusion device **10** may include other components that are not shown in **FIG. 1**. For example, a one-way valve may be disposed between the inlet **18** and the reservoir **13** or between the reservoir **13** and the drive mechanism **20.**

Representative examples of reservoirs **13** which may be employed in embodiments of infusion devices are described in U.S. Published Patent Application 2003/0050623, published March 13, 2003, and entitled "Infusion Device and Reservoir for Same". However, further embodiments may employ other suitable reservoir configurations, including, but not limited to, those described in U.S. Pat. No. 5,514,103 and U.S. Pat. No. 5,176,644, each to Srisathapat et al, U.S. Pat. No. 5,167,633 to Mann et al., U.S. Pat. No. 4,697,622 to Swift and U.S. Pat. No. 4,573,994 to Fischell et al.

In various embodiments, the reservoir **13** is a positive pressure reservoir, which means the pressure in the reservoir is greater than atmospheric pressure, forcing out the fluid contents of the reservoir **13** into the drive mechanism **20**. A propulsion mechanism (not shown) may be operably coupled to the reservoir **13** to drive fluid out of the reservoir. Any suitable propulsion mechanism may be employed. By way of example, the reservoir **13** may be a bellows reservoir and the propulsion mechanism may contain a propellant chamber that contains a fluid whose vapor pressure is such that, under conditions of normal body temperature, pressure is exerted on the bellows to force liquid in the reservoir **13** to enter the drive mechanism **20**. Examples of such propulsion mechanisms are found in Medtronic Inc.'s SYNCHROMED and ISOMED implantable infusion devices. A mechanical spring may be readily substituted for the liquid propellant. Alternatively, the reservoir **13** may be formed, at least in part, of an elastomeric or resilient material biased in an empty configuration that expands when filled and forces fluid to exit reservoir **13** and enter the drive mechanism **20**. Thus, the propulsion mechanism and reservoir may, in some embodiments, be the same component. A positive pressure reservoir **13** may be maintained at any suitable positive pressure by the propulsion mechanism or the elastic or resilient properties of the reservoir **13**. Typically, ambient atmospheric pressure about 14.2 psia. In some embodiments, the positive pressure reservoir **13** is maintained at a pressure of greater

than or equal to 15 psia, between 15 psia and 19 psia, between about 15 and about 16 psia, or between about 15.2 psia and about 15.5 psia.

In some embodiments, the reservoir **13** is a negative pressure reservoir, which means the pressure in the reservoir is greater than atmospheric pressure. For example, the reservoir **13** may be maintained at a pressure of less than or equal to 14 psia, less than or equal to10 psia, or between 12 and 14 psia. In general, whether positive or negative pressure, the reservoir **13** may be maintained at a pressure of greater than 0 psia, greater than 5 psia, or greater than 10 psia, or greater than 15 psia.

Examples of inlet structures **18** that may be employed in embodiments of infusions devices **10** described herein are described in U.S. Pat. No. 7,186,236 to Gibson et al., entitled "Infusion Device And Inlet For Same;" U.S. Pat. No. 5,514,103 and U.S. Pat. No. 5,176,644, each to Srisathapat et al; U.S. Pat. No. 5,167,633 to Mann et al.; U.S. Pat. No. 4,697,622 to Swift; and U.S. Pat. No. 4,573,994 to Fischell et al.

Still referring to **FIG. 1**, the infusion device **10** includes electronics **19** and a power source **5** disposed in the housing **12**. The electronics **19** are operably coupled to the power source **18** and are configured to control the drive mechanism **20**. The power source **18** may include a battery, such as a rechargeable battery. Electronics **18** may include a processor for controlling the drive mechanism **20**; memory for storing instructions, recording diagnostics, or the like; a telemetry module for wireless communication; a diagnostics module; or the like. Such modules and electronic components are well known to those of skill in the art and may be readily included and employed as desired.

Referring now to **FIGS. 2-3**, representative components of piston drive mechanisms **20** are shown. In the block diagram of **FIG. 2**, the drive mechanism **20** includes an inlet **27**, an outlet **28**, and piston actuation mechanism **21**. The piston actuation mechanism **21** is disposed in the flow path between the inlet **27** and the outlet **28**. Some representative components of a piston drive mechanism **20** are shown in the schematic cross sectional views depicted in **FIGS. 3A-B**.

The drive mechanism **20** depicted in **FIGS. 3A-B**, includes and inlet **27**, an outlet **28**, a stationary portion **320** forming a channel **35**, and an actuator having a piston

44 and an armature **42**. In **FIG. 3A**, the piston **44** is in the retracted position. In **FIG. 3B**, the piston **44** is in the forward position. In various embodiments, the stationary portion **320** forming the channel **35** is integrally formed with a housing of the drive mechanism. The channel **35** has a proximal end **351**, nearer the inlet **27**, and a distal end **352**, nearer the outlet **28**. The piston **44** is positioned in, and axially movable within, the channel **35** to drive infusion medium out of the distal end **352** of the channel **35**. A clearance **410** is formed between the piston **44** and the channel **35**. Preferably, the clearance **410** is sufficiently small such that fluidic resistance between the piston **44** and the channel **35** causes a volume of infusion medium delivered during the forward portion of the pumping stroke to be greater than a volume of the infusion medium backflowing through the channel **35** during the retracting portion of the pumping stroke. As described in more detail below (e.g. with regard to **FIGS. 5-6**), the radial clearance **410** is sufficiently small to prevent sufficiently small to prevent undissolved gas in the inlet chamber **330** from passing through the radial clearance channel. The intended fluid flow path is indicated by arrows in **FIGs. 3A-B**. The armature **42** is operably coupled to the piston **44**. In various embodiments, piston **44** is integrally formed with armature **42**. The armature **42** and piston **44** together form an actuator.

As the piston **44** retracts (e.g., moves from the position shown in **FIG. 3B** to the position shown in **FIG. 3A**), infusion medium is drawn through inlet **27** to the piston channel **35**. As the piston **35** is advanced, infusion medium is forced out of the channel **35** and out of the outlet **28**. Electromagnetic energy causes the armature **42** to advance the piston **44** in the channel **35**. A coil or solenoid may be disposed in the stationary member **320** forming the channel **35** to provide such electromagnetic energy. A mechanical biasing member (not shown), such as a spring, or electromagnetic force may allow the piston **44** to retract.

The drive mechanism **20** or components thereof, such as the armature **42**, may be formed or configured in any suitable manner. In various embodiments, the drive mechanism or components thereof are drive mechanisms or components described in U.S. Patent Application Publication No. 2007/0168008, entitled "Implantable Therapeutic Substance Delivery Device Having a Piston Pump with and Anti-Cavitation Valve"; U.S. Patent Application Publication No. 2006/0206099, entitled "Low Profile Inlet Valve for a Piston Pump Therapeutic Substance Delivery Device"; US Patent No

6,997, 921, entitled "Infusion device and driving mechanism for same", or described in US Patent Application Publication No. 2009/0118711, published on May 7, 2009, entitled "Reduced-noise implantable infusion device".

Pistons and armatures as described herein may be made of any suitable material. For example, pistons or armatures may be formed from generally rigid, biocompatible and infusion medium compatible material, having a relatively high magnetic permeability such as, but not limited to, ferrous materials, ferritic stainless steel with high corrosion resistance, or the like. Pistons or armatures can also be fabricated with non-compatible materials and encased or plated in compatible materials. Pistons, armatures, or actuators may be molded, machined, or otherwise formed.

Referring now to **FIG. 4A**, a schematic drawing of some components of a representative implantable infusion device are shown. The implantable infusion device includes an actuator having a piston **44** for pumping fluid from the inlet chamber **320** through a channel **35**. A radial clearance **410** between the piston and channel is sufficiently small to prevent undissolved gas from passing from the inlet chamber **320** into the channel **35**. Referring to **FIG. 4B**, which represents the area within the circle labeled **4B** in **FIG. 4A**, the average distance **d** from a point on the exterior of the piston **44** to a closest point on the wall of the channel **35** in the clearance **410** is, in many embodiments, sufficiently small such that infusion media flows through the clearance **410** while undissolved air is prevented from passing through the clearance due to surface tension effects. The small clearance **410** provides fluidic resistance to prevent backflow and capillary retention of liquid to prevent passage of undissolved gas. While not intending to be bound by theory, it is believed that the liquid wets the surfaces of the clearance **410** and surface tension of the liquid prevents undissolved air from entering the channel **410**. In some embodiments, the distance **d** between the piston **44** and the channel **35** is between 3 micrometers and 10 micrometers, such as about 6 micrometers. By having a sufficiently small clearance **410**, where undissolved air or gas cannot escape between the piston **44** and the channel **35**, by-pass valves may be eliminated which have been previously proposed for dealing with potential transmission of air. Such by-pass valves may be complex and may only be partially effective in eliminating problems associated with passing air through the channel, such as inaccurate fluid delivery and pump malfunction.

Still with reference to **FIG. 4A**, the device may include a valve **17** in communication with and downstream of the channel **35**. In various embodiments, the valve **17** has a cracking pressure that is within about +/- 5 psi of the pressure of the reservoir **13**. In some embodiments, the valve **17** has a cracking pressure that is greater than the pressure of the reservoir **13**; e.g. 1, 2, 3, or 5 psi or more than the pressure of reservoir. Higher valve cracking pressures (whether within +/- 5 psi or greater than the reservoir pressure) may result in improved overall safety of the infusion device by preventing inadvertent or undesired leakage of infusion medium from the device. For example, if the reservoir **13** is a positive pressure reservoir and the piston **44** is in the retracted position relative to the channel **35**, the positive pressure of the reservoir **13** may force infusion medium through the channel **35** and out of the device outlet in the absence of the valve **17**. With prior devices employing piston drive mechanisms, valves with such a high relative cracking pressure would not have been employed due to fear that if air were to pass through the channel, the drive mechanism could not pump enough fluid to compress the air and overcome the cracking pressure, causing the pump to effectively fail. However, with devices as described herein where undissolved air cannot pass through the channel **35**, the piston drive mechanism can readily infuse a fluid medium through the channel to overcome the cracking pressure, open the valve **17**, and force fluid out of the device. In various embodiments, the reservoir **13** is a positive pressure reservoir maintained at between about 15 and 16 psia and the valve **17** has a cracking pressure of greater than 15 psi.

In various embodiments, the valve **17** has a cracking pressure that is 2 psi or greater than the reservoir **13** pressure minus the outlet pressure (ambient atmospheric pressure), when the difference is a positive number (i.e., the reservoir pressure is greater than ambient atmospheric pressure). As a patient with an implanted infusion device changes altitude, the pressure differential across the valve **17** changes. While the reservoir pressure remains fairly constant, the ambient pressure changes with altitude. If the valve cracking pressure is not sufficiently high to account for changes in altitude over a workable range, fluid from the reservoir may undesirably leak out of the device. For example, if the reservoir pressure is 15 psia and the ambient pressure is 10 psia, the pressure differential across the valve would be 5 psia. Accordingly, therapeutic fluid from the reservoir would leak across a valve having a cracking pressure of 5 psi or less

in such a situation. To prevent such undesirable leakage, the valve **17** may have, in various embodiments, a cracking pressure that is 2 psi or greater than the reservoir **13** pressure minus the outlet pressure over the range of use of the device. In some embodiments, the valve **17** has a cracking pressure that is 3 psi or greater or 5 psi or greater than the reservoir **13** pressure minus the outlet pressure (ambient pressure) to further prevent undesired leakage.

A table of atmospheric pressures at different altitudes is presented below:

Altitude (relative to sea level)	Pressure (psia)
-1,500 feet	15.5
0 feet	14.7
8,000 feet*	10.9
10,000 feet	10.1
15,000 feet	8.3

* Most airplanes in flight are pressurized to the equivalent of 8,000 feet

Thus, if a device is designed to safely operate at altitudes of 15,000 feet, the valve cracking pressure should be equal to or greater than: [2 + (reservoir pressure) – 8.3 psia], which equals: (reservoir pressure – 6.3 psia), if the reservoir pressure is greater than 8.3 psia. In many situations, a valve **17** having a cracking pressure of +/- 5 psi of the reservoir **13** pressure will have a cracking pressure that is 2 psi or greater than the reservoir **13** pressure minus the outlet pressure over the range of use of the device.

Still referring to **FIG. 4A**, the device also includes a reservoir **13** in fluid communication with an inlet chamber **320** of a drive mechanism. A filter **4** is disposed in the flow path between the reservoir **13** and the inlet chamber **320**. The filter **4** is configured to prevent microorganisms that may be present in the reservoir **13** from entering the inlet chamber **320**. Any suitable filter **4** may be employed. For example, a 0.22 micron filter is suitable for preventing microbes from passing from reservoir **13** into infusion chamber **320**. It may be desirable for the filter **4** to be hydrophilic to allow infusion medium to readily cross from the reservoir **13** into the infusion chamber **320** through the filter **4**. Examples of hydrophilic materials that may be used to form

suitable filters include nylon and polyvinylidene fluoride. A hydrophilic filter **4** will generally and beneficially prevent undissolved gas from passing from the reservoir **13** into the inlet chamber **320**. However, gas dissolved in the infusion medium may pass through the hydrophilic filter **4**. Over time, some of the dissolved or entrained gas will be freed or come out of solution and will form air bubbles in the inlet chamber **320**. Such bubbles cannot pass through the filter **4** into the reservoir **13** and cannot be removed by aspiration when the reservoir **13** is replenished with infusion medium. Accordingly, over time an increased volume of the inlet chamber **320** may be occupied with air bubbles.

Accordingly, it may be desirable for the volume of the inlet chamber **320** to be sufficiently large to accommodate a significant volume of undissolved gas that may accumulate over the service life of the infusion device. It has been found that when the clearance distance **d** between the piston **44** and the channel **35** is sufficiently small to prevent undissolved air from passing through the clearance **410**, 70% or more of the volume of the inlet chamber **320** can be occupied with undissolved gas and the pump continues to deliver accurate amounts of infusion medium. While not relevant to infusion accuracy, high volumes of undissolved gas in the inlet chamber **320** can result in increased noise resulting from contact of the armature **42** with the stationary portion of the drive mechanism surrounding the proximal end of the channel **35**. Armature designs configured to reduce noise, such as those described in US 2009/118711 (published on May 7, 2009, entitled REDUCED-NOISE IMPLANTABLE INFUSION DEVCE, may be employed. It should be noted that, while a large inlet chamber **320** volume may be desirable from the standpoint of providing for increased volumes of undissolved gas over the service life of the infusion device (e.g., longer service life would tend to result in larger volume), a large inlet chamber **320** volume may be undesirable for keeping the overall volume of the device small and because, in infusion devices employing bellows or collapsible reservoirs, infusion medium cannot be readily removed from the chamber **320** when the reservoir **13** is refilled due to the presence of the filter **4**. Thus, larger chamber volumes may lead to increased volumes of stale infusion medium that can reside in the chamber **320**. Accordingly, the size of the inlet chamber **320** should be balanced between the desire to maximize the volume of undissolved gas that the chamber can accommodate, the desire to reduce overall size of

the device, and the desire to minimize the volume of stale drug that may remain in the chamber. In various embodiments, the inlet chamber **320** has a volume of between about 100 microliters and about 300 microliters. Such a volume may be desirable in an infusion device having a reservoir volume of between about 20 milliliters to about 50 milliliters and a service life of about 8 to 10 years. For infusion devices having larger or smaller reservoir volumes or service lives, it may be desirable for the inlet chamber volume to be larger or smaller in light of the considerations discussed above.

Some of the concepts described above with regard to **FIG. 4A** are further discussed below with regard to **FIGS. 5-6,** in which selected portions or components of the device shown in **FIG. 4A** are shown. In **FIGS. 5-6**, a portion of the device including the filter **4**, the inlet chamber **320**, the piston **44** and the channel **35** is shown. Infusion medium **500** and an air bubble **600** are shown in the chamber **320**. In **FIG. 5**, the piston **44** is in the retracted position and in **FIG. 6A**, the piston **44** is approaching the forward position. As the armature and piston **44** approach the forward position, the air bubble **600** is moved slightly away from the channel **35** and is displaced with infusion medium (see, e.g., **FIG. 6B**, which a close-up view of the area identified by circle **6B** in **FIG. 6A**), allowing the infusion medium to enter the channel **35** while preventing the air bubble **600** or a portion thereof from entering the channel **35** due to the small clearance between the piston **44** and the channel **35**. The liquid will wet the inlet chamber **320** and move freely around the gas bubbles or gas pocket. The undissolved gas will not enter the clearance due to wetting effects of the walls of the clearance channel **35** and surface tension of the liquid retained in the clearance via capillary action. As discussed above, the air bubble **600** or undissolved gas may occupy 70% or more of the volume of the inlet chamber **320** without adverse consequences of inaccurate fluid delivery when the clearance between the piston **44** and the channel **35** is sufficiently small to prevent the undissolved gas from entering the channel **35** from the inlet chamber **320**.

Thus, embodiments of the AIR TOLERANT IMPLANTABLE PISTION PUMP are disclosed. One skilled in the art will appreciate that the present invention can be practiced with embodiments other than those disclosed. The disclosed embodiments are presented for purposes of illustration and not limitation, and the present invention is limited only by the claims that follow.

What is claimed is:

1. An implantable infusion device, comprising:

a reservoir for housing an infusion medium;

a drive mechanism having an inlet chamber, a piston and a piston channel,

wherein the inlet chamber is in fluid communication with the reservoir,

wherein the piston channel is in fluid communication with the inlet chamber, the piston channel having a distal end and a proximal end, the proximal end being closer to the inlet channel than the distal end,

wherein the piston is axially moveable within the piston channel to drive infusion medium out of the distal end of the piston channel,

wherein the piston is positioned and moveable within the channel such that a clearance between the piston and the piston channel is sufficiently small to prevent undissolved gas in the inlet chamber from passing through the clearance; and

a filter disposed between the inlet chamber and the reservoir, wherein the filter is configured to prevent microorganisms from entering the inlet chamber from the reservoir.

2. The implantable infusion device of claim 1, wherein the clearance between the piston and the piston channel is sufficiently small such that the infusion medium is retained in the piston channel via capillary action.

3. The implantable infusion device of claim 1, wherein the average clearance between the piston and the piston channel is between 3 micrometers and 10 micrometers.

4. The implantable infusion device of claim 1, wherein the filter is configured to filter particles larger than 0.22 microns in diameter.

5. The implantable infusion device of claim 1, wherein the volume of the inlet chamber is between 100 microliters and 300 microliters.

6. The implantable infusion device of claim 1, wherein the reservoir is maintained at a pressure of greater than 5 psia.

7. The implantable infusion device of claim 1, wherein the reservoir is maintained at a pressure of greater than 10 psia.

8. The implantable infusion device of claim 1, wherein the reservoir is maintained at a pressure of between 15 psia and 16 psia.

9. The implantable infusion device of claim 1, further comprising:

an outlet in fluid communication with the piston channel, the outlet being closer to the distal end of the piston channel than the proximal end of the piston channel; and

a valve in fluid communication with, and disposed between, the outlet and the piston channel, wherein the valve has a cracking pressure that is between 5 psi less than the pressure of the reservoir and 5 psi more than the pressure of the reservoir.

10. The implantable infusion device of claim 1, further comprising:

an outlet in fluid communication with the piston channel, the outlet being closer to the distal end of the piston channel than the proximal end of the piston channel; and

a valve in fluid communication with, and disposed between, the outlet and the piston channel, wherein the valve has a cracking pressure that is at least 2 psi greater than the difference of the reservoir pressure minus the outlet pressure at the lowest ambient atmospheric pressure that the device is designed to be subjected.

11. The implantable infusion device of claim 1, further comprising:

an outlet in fluid communication with the piston channel, the outlet being closer to the distal end of the piston channel than the proximal end of the piston channel; and

a valve in fluid communication with, and disposed between, the outlet and the piston channel, wherein the valve has a cracking pressure that is equal to or greater than the reservoir pressure minus 6.3 psia.

12. The implantable infusion device of claim 1, wherein the drive mechanism is capable of continued operation without undissolved gas exiting the distal portion of the piston channel when 70% of the volume of the inlet chamber is occupied by undissolved gas.

13. An implantable infusion device, comprising:

a reservoir for housing an infusion medium, the reservoir being maintained at a pressure of greater than 8 psia;

a drive mechanism having an inlet chamber, a piston and a piston channel,

wherein the inlet chamber is in fluid communication with the reservoir, the inlet chamber having a volume of between 100 microliters and 300 microliters,

wherein the piston channel is in fluid communication with the inlet chamber, the piston channel having a distal end and a proximal end, the proximal end being closer to the inlet channel than the distal end,

wherein the piston is axially moveable within the piston channel to drive infusion medium out of the distal end of the piston channel,

wherein the piston is positioned and moveable within the channel such that an average clearance between the piston and the piston channel is between 3 micrometers and 10 micrometers; and

a filter disposed between the inlet chamber and the reservoir, wherein the filter is configured to prevent microorganisms from entering the inlet chamber from the reservoir.

14. The implantable infusion device of claim 13, wherein the reservoir is maintained at a pressure of greater than 10 psia.

15. The implantable infusion device of claim 13, wherein the reservoir is maintained at a pressure of between 14 psia and 19 psia.

16. The implantable infusion device of claim 13, further comprising:

an outlet in fluid communication with the piston channel, the outlet being closer to the distal end of the piston channel than the proximal end of the piston channel; and

a valve in fluid communication with, and disposed between, the outlet and the piston channel, wherein the valve has a cracking pressure that is between 5 psi less than the pressure of the reservoir and 5 psi more than the pressure of the reservoir.

17. The implantable infusion device of claim 13, further comprising:

an outlet in fluid communication with the piston channel, the outlet being closer to the distal end of the piston channel than the proximal end of the piston channel; and

a valve in fluid communication with, and disposed between, the outlet and the piston channel, wherein the valve has a cracking pressure that is at least 2 psi greater than the difference of the reservoir pressure minus the outlet pressure at the lowest ambient atmospheric pressure that the device is designed to be subjected.

18. The implantable infusion device of claim 13, further comprising:

an outlet in fluid communication with the piston channel, the outlet being closer to the distal end of the piston channel than the proximal end of the piston channel; and

a valve in fluid communication with, and disposed between, the outlet and the piston channel, wherein the valve has a cracking pressure that is equal to or greater than the reservoir pressure minus 6.3 psia.

19. The implantable infusion device of claim 13, wherein the pump is drive mechanism is capable of continued operation without exiting the distal portion of the piston channel when 70% or more of the volume of the inlet chamber is occupied by undissolved gas.

20. An implantable infusion device, comprising:

a reservoir for housing an infusion medium;

a drive mechanism having an inlet chamber, a piston a piston channel,

wherein the inlet chamber is in fluid communication with the reservoir,

wherein the piston channel is in fluid communication with the inlet chamber, the piston channel having a distal end and a proximal end, the proximal end being closer to the inlet channel than the distal end,

wherein the piston is axially moveable within the piston channel to drive infusion medium out of the distal end of the piston channel,

wherein the piston is positioned and moveable within the channel such that an average clearance between the piston and the piston channel is between 3 micrometers and 10 micrometers;

a filter disposed between the inlet chamber and the reservoir, wherein the filter is configured to prevent microorganisms from entering the inlet chamber from the reservoir;

an outlet in fluid communication with the piston channel, the outlet being closer to the distal end of the piston channel than the proximal end of the piston channel; and

a valve in fluid communication with, and disposed between, the outlet and the piston channel, wherein the valve has a cracking pressure that is between 5 psi less than the pressure of the reservoir and 5 psi more than the pressure of the reservoir.

21. The implantable infusion device of claim 20, wherein the reservoir is maintained at a pressure of greater than 0 psia.

22. The implantable infusion device of claim 20, wherein the inlet chamber has a volume of between 100 microliters and 300 microliters.

23. An implantable infusion device, comprising:

a reservoir for housing an infusion medium;

a drive mechanism having an inlet chamber, a piston a piston channel,

wherein the inlet chamber is in fluid communication with the reservoir,

wherein the piston channel is in fluid communication with the inlet chamber, the piston channel having a distal end and a proximal end, the proximal end being closer to the inlet channel than the distal end,

wherein the piston is axially moveable within the piston channel to drive infusion medium out of the distal end of the piston channel,

wherein the piston is positioned and moveable within the channel such that an average clearance between the piston and the piston channel is between 3 micrometers and 10 micrometers;

a filter disposed between the inlet chamber and the reservoir, wherein the filter is configured to prevent microorganisms from entering the inlet chamber from the reservoir;

an outlet in fluid communication with the piston channel, the outlet being closer to the distal end of the piston channel than the proximal end of the piston channel; and

a valve in fluid communication with, and disposed between, the outlet and the piston channel, wherein the valve has a cracking pressure that is at least 2 psi greater than the difference of the reservoir pressure minus the outlet pressure at the lowest ambient atmospheric pressure that the device is designed to be subjected.

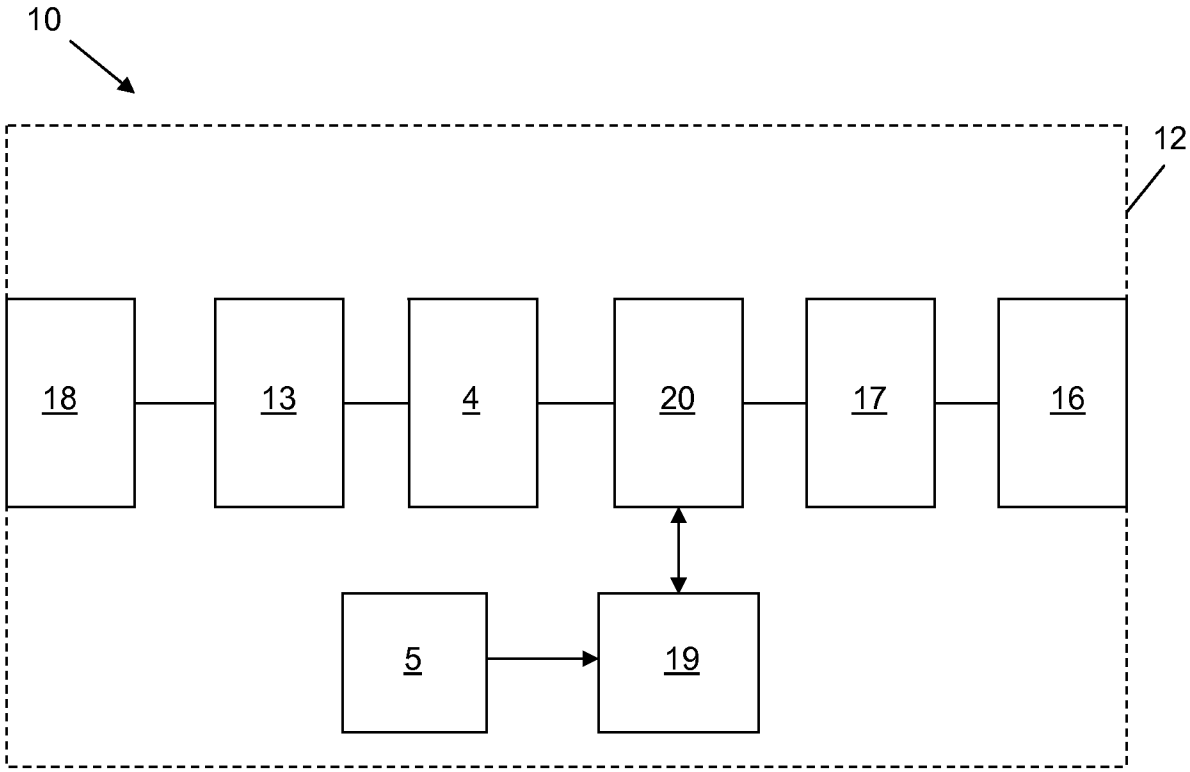

FIG. 1

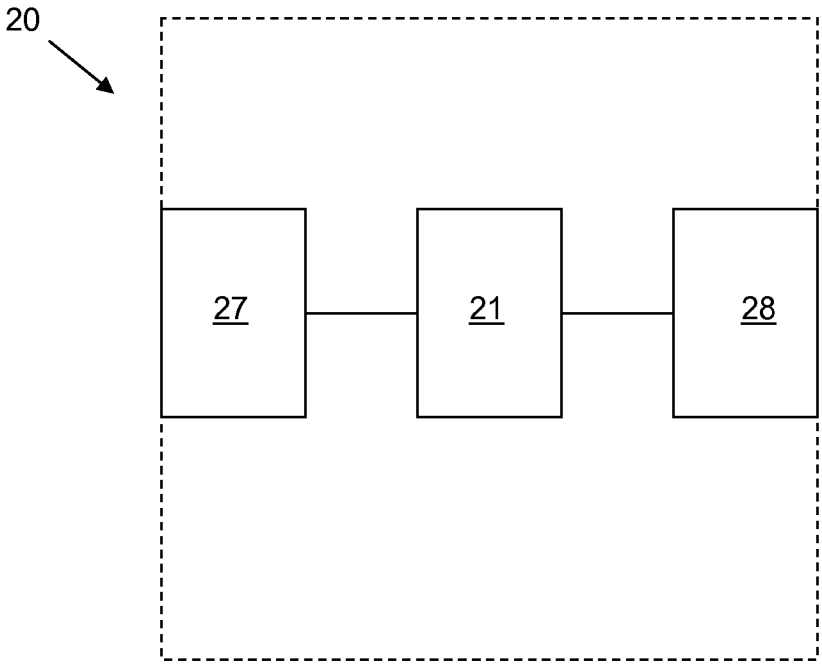

FIG. 2

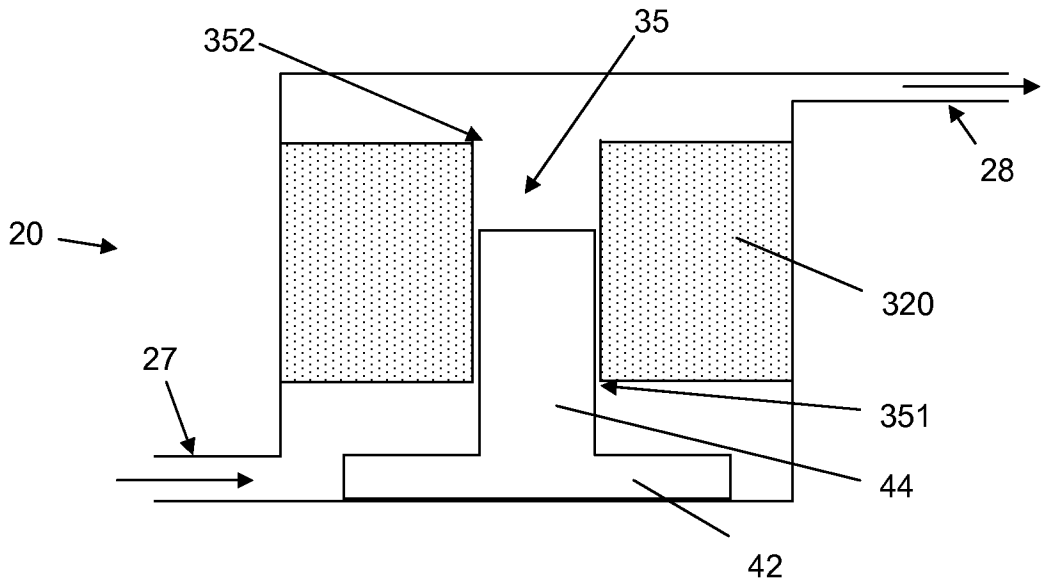

FIG. 3A

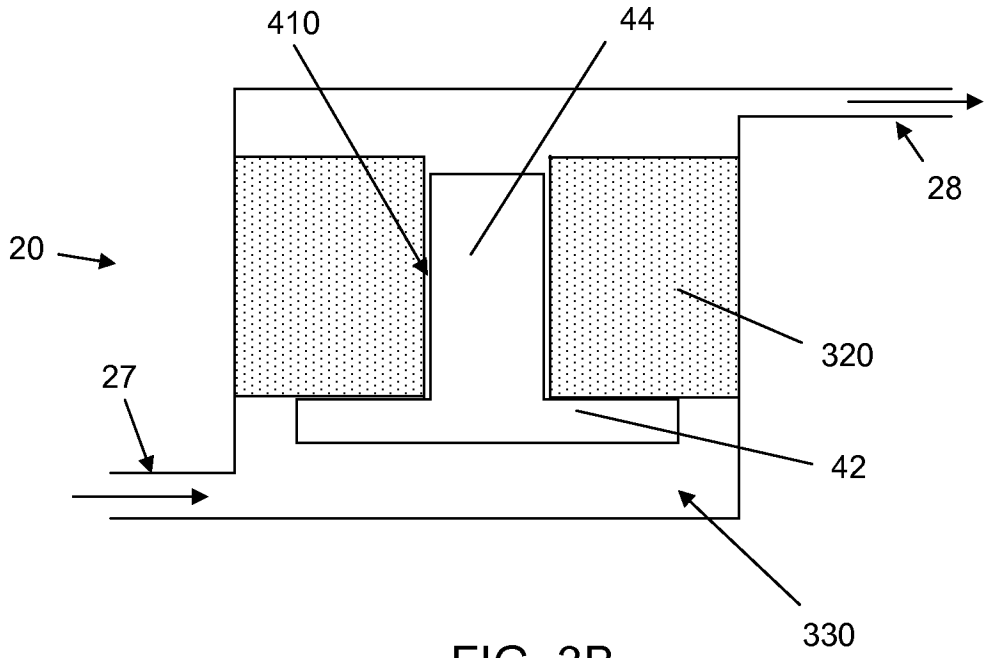

FIG. 3B

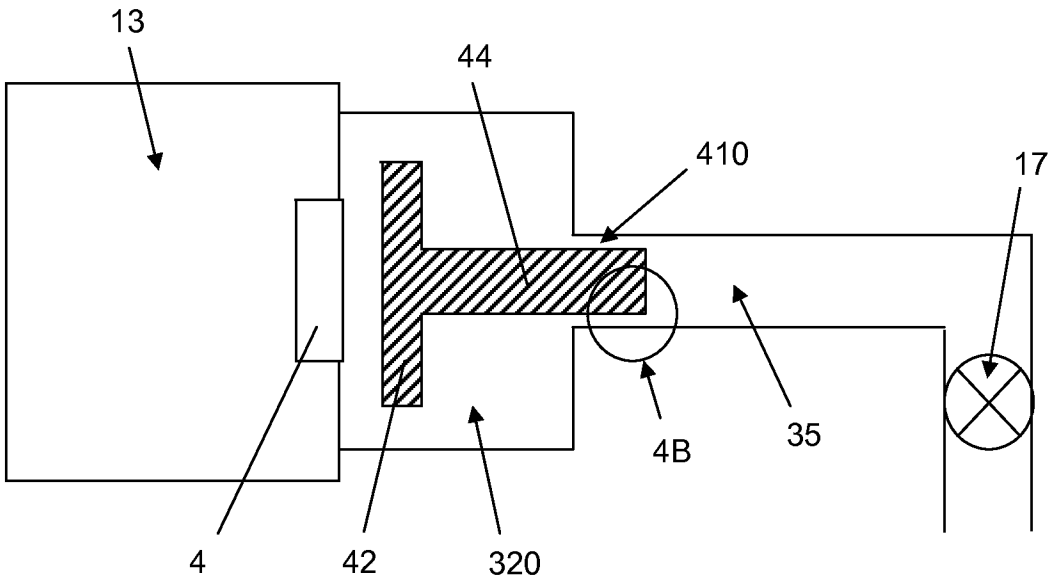

FIG. 4A

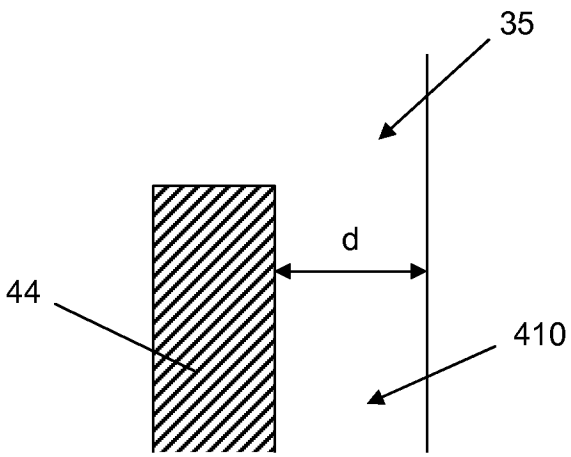

FIG. 4B

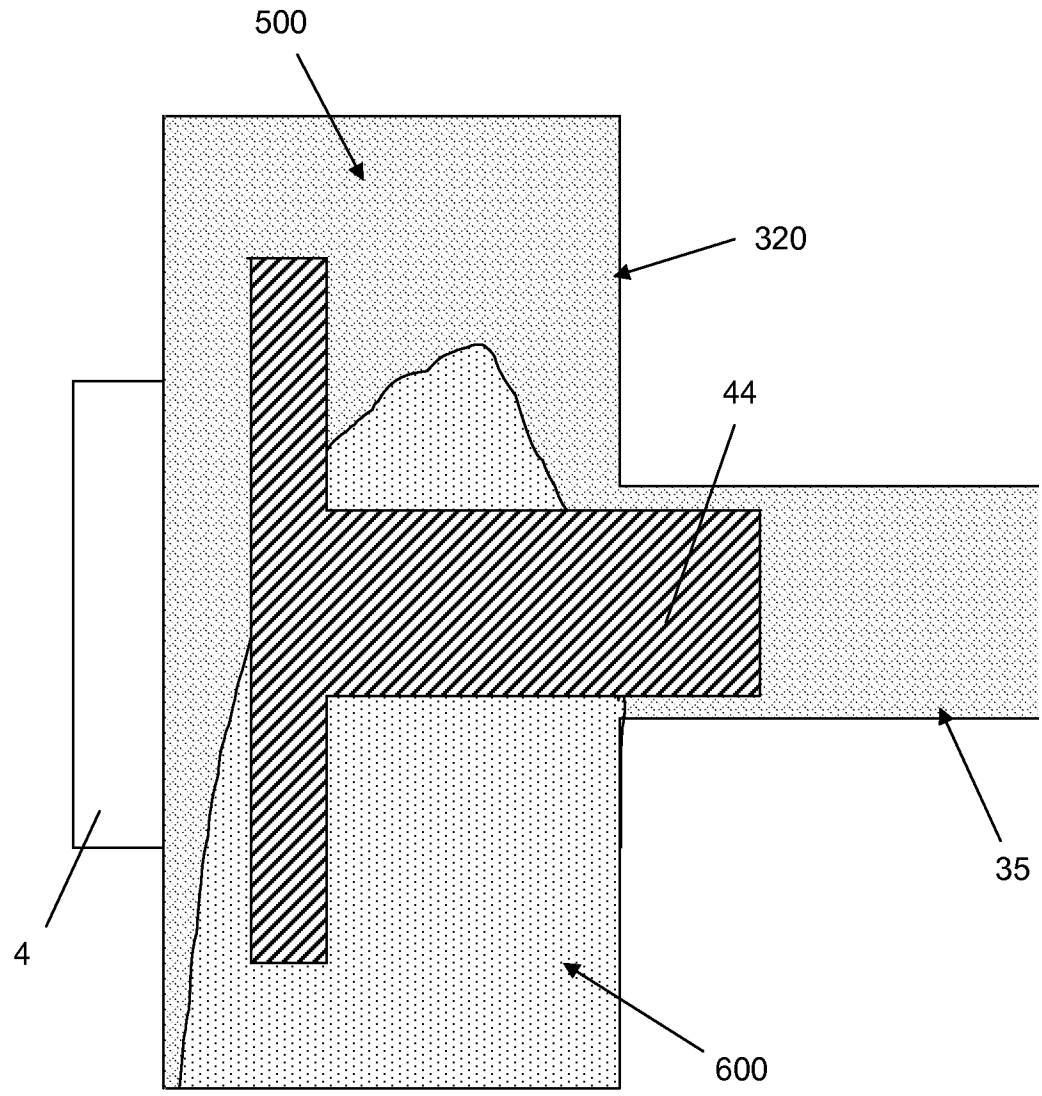

FIG. 5

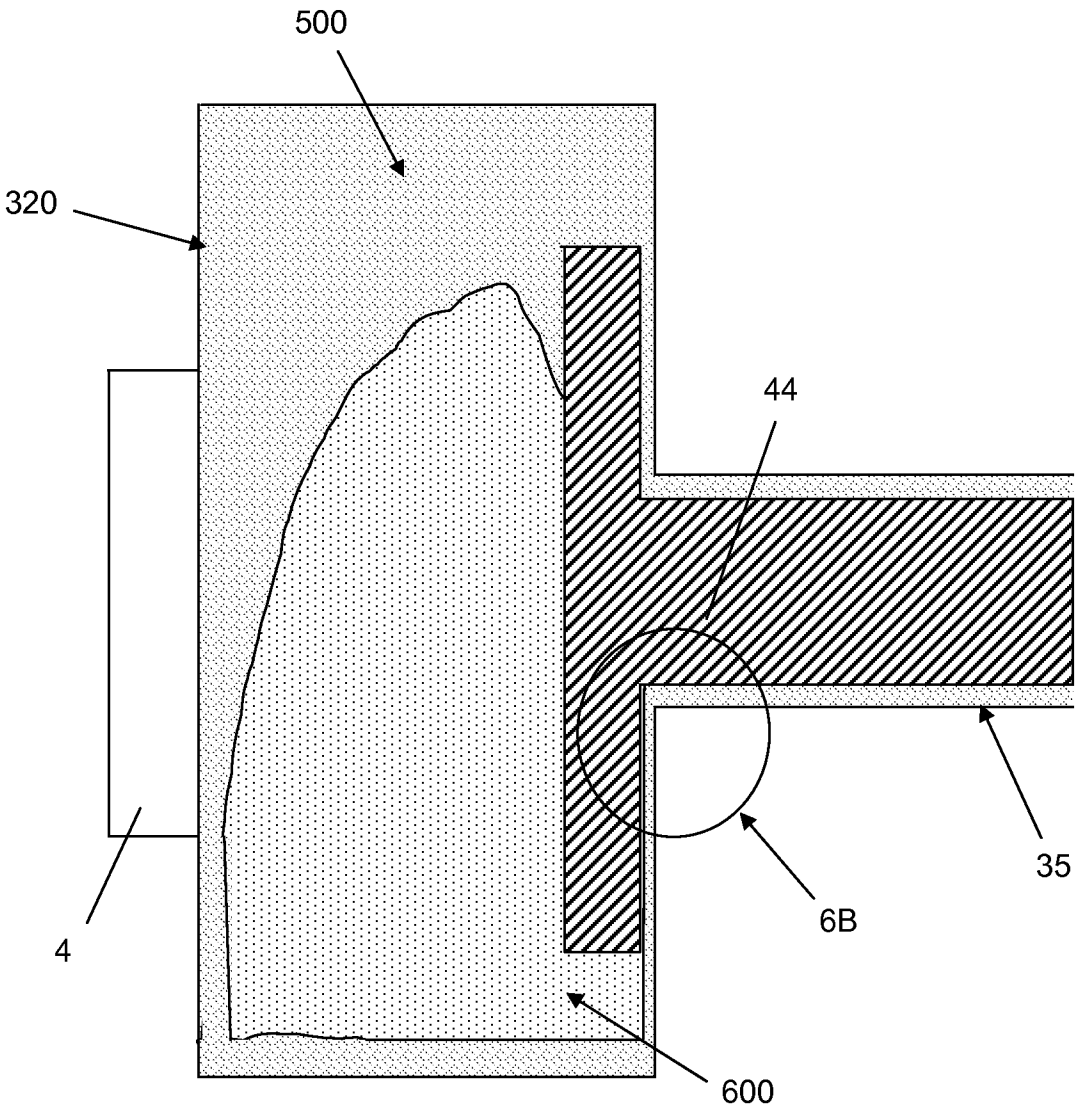

FIG. 6A

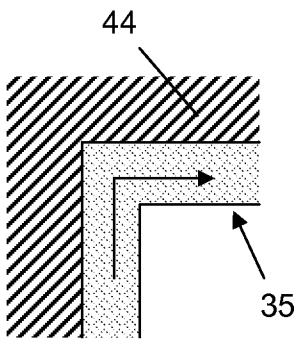

FIG. 6B

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2010/055781

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61M5/142 F04B53/00
ADD. A61M5/165

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

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
A61M F04B

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, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2009/118711 A1 (HAASE JAMES M [US] ET AL) 7 May 2009 (2009-05-07) * abstract; figures 1-3B,12 paragraphs [0029], [0030], [0033], [0035], [0036], [0045], [0058] - [0062], [0084], [0091] - [0092] -----	1-23
X	US 2004/127852 A1 (GRAY JOHN [US] ET AL) 1 July 2004 (2004-07-01) * abstract; figures 3,4 paragraphs [0019], [0025], [0072], [0073], [0088], [0110] claim 13 -----	1-23
X	US 4 636 150 A (FALK THEODORE J [US] ET AL) 13 January 1987 (1987-01-13) the whole document -----	1-23

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[X] Further documents are listed in the continuation of Box C.

[X] See patent family annex.

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

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"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
18 February 2011	25/02/2011

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

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INTERNATIONAL SEARCH REPORT

International application No
PCT/US2010/055781

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 2007/269322 A1 (FALK THEODORE J [US] ET AL) 22 November 2007 (2007-11-22) * abstract; figures 1-5 paragraphs [0074] - [0077], [0085] - [0093] -----	1-23
X	US 4 883 467 A (FRANETZKI MANFRED [DE] ET AL) 28 November 1989 (1989-11-28) the whole document -----	1-23

1

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/US2010/055781

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