(19) DANMARK

(10) DK/EP 2723647 T3

(12) Oversættelse af europæisk patentskrift

Patent- og Varemærkestyrelsen

(51) Int.Cl.: *B 65 D 47/06 (2006.01)* *B 65 D 41/04 (2006.01)* *B 65 D 51/00 (2006.01)* *B 65 D 51/24 (2006.01)* *B 65 D 53/04 (2006.01)* *B 65 D 53/06 (2006.01)*

(45) Oversættelsen bekendtgjort den: **2018-07-23**

(80) Dato for Den Europæiske Patentmyndigheds bekendtgørelse om meddelelse af patentet: **2018-05-09**

(86) Europæisk ansøgning nr.: **11868058.6**

(86) Europæisk indleveringsdag: **2011-06-22**

(87) Den europæiske ansøgnings publiceringsdag: **2014-04-30**

(86) International ansøgning nr.: **US2011041462**

(87) Internationalt publikationsnr.: **WO2012177250**

(84) Designerede stater: **AL AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HR HU IE IS IT LI LT LU LV MC MK MT NL NO PL PT RO RS SE SI SK SM TR**

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(54) Benævnelse: **Beholderlukninger og fremgangsmåder til anvendelse og fremstilling deraf**

(56) Fremdragne publikationer:
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DESCRIPTION

TECHNICAL FIELD

[0001] This disclosure relates generally to vessel closures and more specifically to vessel closures having inserts, such as tubing, extending through the vessel closure.

BACKGROUND

[0002] During certain manufacturing processes, vessels containing various fluids are used. Often it is necessary to transfer fluid into or out of a vessel during the process and do so in a substantially aseptic manner without breaching the closed nature of the system. In particular, the need to transfer fluid often arises in the manufacturing and processing of pharmaceuticals, biopharmaceuticals, or other biotechnology applications where processes are conducted in vessels of varying shapes and sizes. The need for fluid transfer into and out of a vessel arises in other applications and industries as well, including but not limited to the production of food, cosmetics, paint, chemicals, including hazardous chemicals, and the transfer and handling of semiconductor fluids.

[0003] Regardless of the industry, during transfers or sampling, the fluid in a vessel must remain substantially free of contaminants. In addition, when making such transfers, it is desirable to keep the environment surrounding a vessel free from contamination by the contents of the vessel or a sample taken therefrom. It is often the case that, throughout the manufacturing process, there is a need to maintain fluid communication with the interior of the vessel by way of, for example, tubing extending through a vessel closure from the exterior of the vessel into the interior of the vessel. To accomplish a substantially aseptic transfer, it is desirable to control the environment through which the fluid flows, for example, the pathway from a vessel to a sample container should be substantially aseptic along the entire pathway. Furthermore, it is desirable that the vessel closure be safe for use, reliable, and of low-cost construction.

[0004] It is also desirable to transfer fluid using a vessel closure which is pre-sterilized and disposable. A pre-sterilized, disposable vessel closure avoids the need for an operator to sterilize the vessel closure for use. Further, such sterilization can damage vessel closures and render them useless before their first use.

[0005] Known vessel closures utilize either thermoplastic or elastomeric tubing to create fluid communication with the interior of a vessel. Known vessel closures use for example, all elastomeric tubing, such as silicone tubing, or utilize all thermoplastic tubing, such as C-Flex® tubing. Vessel closures incorporating silicone tubing are often manufactured using insert injection molding at temperatures between 177° to 204° C (350° to 400° F). These

temperatures will melt or damage thermoplastic tubing. Further, vessel closures manufactured with silicone seals have not heretofore included thermoplastic tubing due to the lack of adhesion of silicone directly onto thermoplastic tubing.

[0006] WO 2005/084372 discloses a gasket, a container and a cap element. The cap element may be connected to a liquid transmitting mechanism, e.g., a spray nozzle, a pump assembly for selectively transmitting liquid retained by the container.

[0007] Thus, what is needed is a vessel closure with a seal capable of adhering to silicone tubing and other inserts. What is also needed is a vessel closure with a seal with both silicone and thermoplastic tubing within the same vessel closure wherein the tubing creates a substantially aseptic fluid pathway into and out of a vessel. What is further needed are manufacturing techniques for manufacturing a low cost, disposable vessel closure with both silicone and thermoplastic tubing wherein the tubing creates a substantially aseptic fluid pathway into and out of a vessel. What is also needed is a method of using the aforementioned vessel closures to circulate fluid into and out of a vessel while also having the option of controlling the temperature of the fluid.

SUMMARY

[0008] The present invention is defined by the features of the independent claims 1 and 12. Further preferred embodiments of the invention are defined in the dependent claims. Briefly described, a vessel closure comprising a body, one or more apertures extending axially through the body, one or more inserts extending axially through one or more apertures, and a cast seal disposed within the body and surrounding each insert. In one embodiment, the vessel closure may have one or more inserts comprising silicone tubing. In one embodiment, the cast seal is pourable, self-leveling silicone, such as room temperature vulcanizing ("RTV") silicone. The inserts in the vessel closure comprising one or more thermoplastic tubes extending axially through one or more apertures extending through the vessel closure; an anchor adhesively attached to a portion of each thermoplastic tube, the anchor capable of bonding with a casting agent; and a casting agent securing each anchor and thermoplastic tube through each aperture. The thermoplastic tubes may be C-Flex® tubing.

[0009] In another embodiment, briefly described, a tubing assembly in a vessel closure comprising flexible tubing extending through an aperture in the closure; a deformable sleeve adhesively attached to and surrounding at least a portion of the flexible tubing; the sleeve being formed of a material having plasticity such that pressure applied to the sleeve causes the sleeve to deform about and seal the flexible tubing and upon continued application of pressure to the sleeve, the sleeve and flexible tubing are cut and the sleeve retains a deformed shape substantially sealing the tubing; and a cast seal surrounding the sleeve.

[0010] In a further embodiment, briefly described, a vessel closure comprising a body, at least two apertures through the body, and flexible tubing passing through the at least two apertures

wherein the ends of the tubing are both directed into the interior of the vessel thereby forming a loop on the exterior of the vessel.

[0011] Also, briefly described, a method of manufacturing a vessel closure comprising a body, one or more apertures extending axially through the body, and an insert extending axially through one or more apertures. The method comprising creating one or more apertures in a body; inserting an insert axially through one or more apertures; casting a casting agent into the body; and curing the casting agent to form a seal around and bond to the one or more inserts.

[0012] In another embodiment, briefly described, a method of manufacturing a vessel closure, the vessel closure comprising one or more apertures through a body with tubing extending through the one or more apertures; the method comprising creating one or more apertures in a body; inserting silicone tubing through at least one aperture; inserting thermoplastic tubing through at least one other aperture wherein at least a portion of the thermoplastic tubing is surrounded by a sleeve adhesively attached to the tubing, wherein the outer surface of the sleeve is capable of bonding with a casting agent; casting a casting agent into the body; and curing the casting agent to form a seal around and bond to the silicone tubing and to the at least one sleeve surrounding the thermoplastic tubing. In one embodiment, the thermoplastic tubing may be C-Flex® tubing.

[0013] Also, briefly described, a method of circulating a fluid into and out of a vessel comprising sealing a vessel with a closure, the closure comprising a body, at least two apertures through the body, and flexible tubing routed through the at least two apertures so the ends of the tubing are both directed into the interior of the vessel thereby forming a loop on the exterior of the vessel; attaching circulating means to the loop on the exterior of the vessel and using circulating means to circulate fluid out of and into the vessel through the flexible tubing. In one embodiment, the fluid is circulated using a peristaltic pump.

[0014] Thus, vessel closures, methods of manufacturing the same, and methods of utilizing the same are disclosed that possess distinct attributes and represent distinct improvements over the prior art. These and other aspects, features, and advantages of the vessel closures of this disclosure will be better understood and appreciated upon review of the detailed description set forth below when taken in conjunction with the accompanying drawing figures, described briefly below. According to common practice- the various features of the drawings may not be drawn to scale. Dimensions and relative sizes of various features and elements in the drawings may be shown enlarged or reduced to illustrate more clearly the embodiments of the invention.

BRIEF DESCRIPTION OF THE DRAWINGS

[0015]

Fig. 1 is a perspective view of an illustrative vessel closure, cast seal, and three tubes.

Fig. 2 is a bottom view of an illustrative vessel closure, cast seal, and three tubes.

Fig. 3 is a cross section of an illustrative vessel closure, cast seal, and three tubes.

Fig. 4 is a cross section of a vessel closure according to the invention, with cast seal, three tubes, and three different anchors, illustrating a variety of anchors that may be used.

Fig. 5 is a side view of a vessel closure, cast seal, and two tubes, illustrating the seal pulled away from the interior of the vessel closure.

Fig. 6 is a cross-section of an illustrative vessel closure, cast seal, and two tubes, illustrating the invention in a relatively smaller vessel closure than shown in Fig. 1.

Fig. 7 is a cross-section of an illustrative vessel closure, cast seal, two tubes, illustrated in yet a different relatively smaller vessel closure.

Fig. 8 is a perspective view of an illustrative vessel closure, cast seal, and two tubes.

Fig. 9 is a cross-section of an illustrative vessel closure, cast seal, two tubes, and an aperture in the vessel closure sealed only by the cast seal, illustrating a pierceable section of the seal.

Fig. 10 is a cross-section of a vessel closure, cast seal, two tubes, and a puncture site, illustrating an embodiment according to the invention with an anchor attached to one tube, a tube with no anchor, and a specialized puncture site over one aperture in the vessel closure.

Fig. 11 is a cross-section of a vessel closure according to the invention, depicting a temperature probe, tube, and anchor.

Fig. 12 is a side view of a tube and anchor.

Fig. 13 is a perspective view of a vessel closure, temperature probe, tube, and anchor before the tube and anchor are connected to the vessel closure and before a seal is cast around the anchor, tube, and probe.

Fig. 14 is a cross-section of an illustrative vessel closure, two fittings, and a tube wherein the fittings shown are a male and female luer.

Fig. 15 is a perspective view of an illustrative tri-clamp closure, three tubes, and a cast seal.

Fig. 16 is a cross-section of an illustrative tri-clamp closure, three tubes, and a cast seal.

Fig 17 is a cross-section of an illustrative closure, a tube, and fitting wherein the fitting shown is a quick connect fitting.

Fig. 18 is a side view of an illustrative closure and two fittings wherein the fittings are a barbed fitting and a quick connect fitting.

Fig. 19 is a cross-section of an illustrative vessel closure and tubing, illustrating the tubing routed through the closure to form a loop on the exterior of the closure,

Fig. 20 is a cross-section of an illustrative vessel, vessel closure, seal, and silicone tube, illustrating the vessel closure sealed to the vessel.

DETAILED DESCRIPTION OF EXEMPLARY EMBODIMENTS

[0016] Next to embodiments that are described for illustrative purposes, certain exemplary embodiments of the present invention are described below and illustrated in the accompanying figures. The embodiments described are only for purposes of illustrating the present invention and should not be interpreted as limiting the scope of the invention, which of course, is limited only by the claims below. Referring now in more detail to the figures, wherein like reference numerals indicate like parts throughout the several views, Fig. 1 depicts a first illustrative vessel closure, in this case a vessel closure with multiple tubes extending through the vessel closure thereby creating fluid communication between the inferior and exterior of a vessel onto which the vessel closure may be placed. It should be understood that the vessel closure is not limited to use with any particular fluids but, depending on the size and composition of the inserts, may be used with fluids with particulates or having a high viscosity or with fluids having no or very little particulate content or low viscosity.

[0017] The vessel closure **100** illustrated in Fig. 1 generally depicts a body, inserts, and a seal shown assembled together to form a single vessel closure. The vessel closure **100** has a body **110**, discussed in more detail below, one or more apertures extending axially through the body, inserts **130** extending axially through each aperture, and a cast seal **120** disposed within the body and surrounding each insert. The vessel closure is not limited to this number of inserts, but may incorporate more or fewer inserts. The vessel closure is suitable for use with vessels that include without limitation: containers, beakers, bottles, canisters, flasks, bags, receptacles, tanks, vats, vials, tubes, and the like that are generally used to contain fluids, slurries, and other similar substances.

[0018] In the vessel closure illustrated in Fig. 1, the body is a cap. Suitable caps for the vessel closure include those commonly used in the field of pharmaceutical, biopharmaceutical, and biotechnology processing. Such caps include: a 38-430 cap with an outer diameter at the open end of approximately 42 mm and being approximately 29 mm tall (as depicted in Figs. 1, 4, 9, 10, and 17-19); a centrifuge cap having an outer diameter at the open end of approximately 34 mm and being approximately 13 mm tall (such as depicted in Figs. 5 and 6); a 20-415 cap with an outer diameter at the open end of approximately 24 mm and being approximately 14.6 mm tall (such as depicted in Figs. 7 and 8); and a GL-45 cap having an outer diameter at the open end of approximately 53.7 mm and being approximately 25.5 mm tall. The invention, however, is not limited to a cap of any particular dimensions. Bodies of vessel closures may be made from thermoplastics such as polyolefins, polypropylene, polyethylene, polysulfone, polyester, polycarbonate, and glass filled thermoplastics. The invention, however, is nor limited to a cap made from any particular material(s). The bodies may also be made from thermosets such as

epoxies, pheonolics, and novolacs. The body may also be a hygienic or sanitary clamp having dimensions disclosed in ASME BPE table DT-5-2 ("Hygiénic Clamp Ferrule Standard Dimensions and Tolerances") (2009), which is incorporated by reference herein in its entirety. The body is not limited to caps or hygienic clamps but may constitute any suitable closure that seals the interior of a vessel from the exterior environment.

[0019] Fig. 1 further depicts three inserts **130** extending axially through the body. The inserts extend through apertures in the body. The number of apertures in the body may correspond with the number of inserts to be placed in the body.

[0020] Also depicted in Fig. 1 is a cast seal **120.** In a preferred embodiment the cast seal is constructed from a self-leveling, pourable silicone such as room temperature vulcanizing ("RTV") silicone. The RTV silicone may be a two-component system (base plus curative) ranging in hardness from relatively soft to a medium hardness, such as from approximately 9 Shore A to approximately 56 Shore A. Suitable RTV silicones include Wacker® Elastocil® RT 622, a pourable, addition-cured two-component silicone rubber that vulcanizes at room temperature; and Blue Star Silicones Rhodorsil® RTV 1556, a two-component, high strength, addition-cured, room temperature or heat vulcanized silicone rubber compound. Both the Wacker® Elastocil® RT 622 and the Bluestar Silicones Rhodorsil® RTV 1556 have a viscosity of approximately 12,000 cP (mPa.s). The aforementioned silicones and their equivalents offer low viscosity, high tear cut resistance, high temperature and chemical resistance, excellent flexibility, low shrinkage, and the ability to cure a cast silicone seal at temperatures as low as approximately 24° C (75° F). In another embodiment, the casting agent is a perfluoropolyether liquid. A preferred perfluoropolyether liquid is Sifel 2167, available from Shin-Etsu Chemical Co., Ltd.

[0021] In an embodiment, the cast seal is disposed within the body of the vessel closure so that when the body is attached to a vessel opening, such as a bottle opening, the cast seal creates a seal between the interior of the vessel and the exterior environment. Preferably, the seal formed by the vessel closure between the interior of the vessel and the exterior environment is substantially aseptic. As best shown in Figs. 1 and 3, the cast seal **120** surrounds the inserts **130,** thereby creating a unified seal and insert subassembly. In an embodiment, the seal between the cast seal **120** and insert **130** is substantially aseptic

[0022] In one embodiment, the inserts are silicone tubing. For clarity, only a portion of the silicone tubing is shown in Fig. 1. The tubing may be of any length suitable and necessary for the desired process. In an embodiment, at least a portion of the silicone tubing is treated with a primer where the cast silicone surrounds the tubing. Suitable primers are SS-4155 available from Momentive™, Med-162 available from NuSil Technology, and Rodorsil® V-O6C available from Bluestar Silicones.

[0023] Referring now to Fig. 2, a bottom-view of an illustrative vessel closure shows the body **110,** the inserts **130,** and the cast seal **120** partially filling the body of the vessel closure and surrounding the exterior of the inserts extending through the apertures in the body. As shown

in Fig. 3, which is a cross-section of the vessel closure of Fig. 2, the body **110** contains the cast seal **120** and the inserts extend axially through the body **110** and the cast seal **120.**

[0024] Turning now to Fig. 4, a vessel closure according to the invention is shown with a variety of anchors **140, 150,** and **160.** For clarity, the selection and depiction of various anchors is for illustrative purposes only. The vessel closures may have any variety of different anchors or have all the same anchors. Specifically, Fig. 4 depicts three different anchors **140, 150,** and **160,** a body **110,** a cast seal **120,** and three inserts **130,** in this case, tubing. Anchor **140** is a retaining nut affixed in place around the silicone tube insert **130.** The retaining nut prevents the insert from being pulled out of a vessel. Anchor **150** has a retaining nut portion and a cone-shaped portion. (Anchor **150** is also shown as anchor **750** in Fig. 12.) The retaining nut portion is located on the interior of the body, while the cone-shaped section is on the exterior of the body. Anchor **150** prevents the insert from being pulled out of a vessel or being pulled into a vessel when, for example, a vacuum is placed on the interior of the vessel. Anchor **160** is a sleeve, also referred to herein as an anchor sleeve, that prevents the insert from being pulled out of the body. Anchor sleeve **160** also provides a surface to which the cast seal may bond. The cast seal may also bond to an anchor and the insert on which the anchor is placed. Regardless of the shape of the anchor, the cast seal **120** bonds to the anchor. The anchors may be constructed of such material that is particularly suitable for bonding with the cast seal, such as metal (aluminum, stainless steel, etc.). plastic, glass-filled plastic, ceramics, and composites. The anchors are adhesively attached to the inserts. Thus, when a vessel closure according to the invention is constructed, the anchor is adhesively attached to the insert, for example, a tube; the cast seal is bonded to the anchor, and the anchor secures the one or more tubes and cast seal to the body of the vessel closure.

[0025] In another embodiment, the cast seal **120** is also attached to the body by way of priming at least a portion of the body and adhesively attaching the cast seal to the body. In this embodiment, the cast seal will not pull away from the interior of the body. However, in other embodiments the cast seal need not necessarily be attached to the body. As best shown in the illustrative vessel closure of Fig. 5, a vessel closure **200** may have a body **210,** apertures extending axially through the body (not shown in Fig. 5), a cast seal **220,** and two inserts **230,** in this case, silicone tubing. The body shown in Fig. 5 represents a centrifuge cap. In Fig. 5, the cast seal **220** is shown pulled away from the body **210.** Upon placement of the body of the vessel closure to a vessel, for example, placing a cap on a bottle, the cast seal **220** will be seated within the body. Fig. 20 shows such an arrangement and is discussed in detail below. Fig. 6 shows the cast insert seated within the body **210** without the presence of a vessel. As with the vessel closure shown in Fig. 1, the vessel closure in Fig. 4 shows two inserts but any number of inserts could be used.

[0026] Returning to Fig. 4, the vessel closure may have only inserts such as the insert with anchor sleeve **160.** The anchor sleeve **160** adhesively attaches to the insert. In one embodiment, the insert is thermoplastic tubing, such as C-Flex® tubing. When anchor sleeves partially or completely surround each insert, the seal need not be constructed of cast silicone but may be made of any casting agent capable of bonding to the anchor sleeve. For example,

in applications involving solvents, a casting agent such as liquid perfluoropolyether could be used. Regardless of which casting agent is used, the casting agent is preferably aseptically sealed to the anchor.

[0027] In an embodiment, at least a portion of the anchors are treated with a primer where the anchor sleeve contacts the casting agent. In yet another embodiment, the vessel closure may contain inserts comprising elastomeric tubing wherein at least a portion of the tubing is surrounded by an anchor sleeve and silicone tubing extends through the body and seal. In such embodiment, the silicone tubing is not surrounded, either partially or wholly by an anchor sleeve. In this embodiment, the preferred casting agent is liquid silicone.

[0028] Again returning to Fig. 4, anchor sleeve **160** may be a deformable sleeve, such as those disclosed in PCT/US08/0488, owned by the assignee of the instant application. In an embodiment, the deformable sleeve surrounds and is adhesively attached to flexible tubing, In one embodiment, the deformable sleeve is attached to the flexible tubing at a location that facilitates substantially sealing, cutting, and detaching the deformable sleeve. In such embodiments, the sleeved is formed of a material having plasticity such that pressure applied to the sleeve causes the sleeve to deform about and seal the flexible tubing and upon continued application of pressure to the sleeve, the sleeve and flexible tubing are cut and the sleeve retains a deformed shape, thereby substantially sealing the tubing. In these embodiments, the flexible tubing is thermoplastic tubing, elastomeric tubing, or a combination of thermoplastic and elastomeric tubing. Further, when a deformable sleeve is used, the casting agent may adhere to and aseptically seal with the deformable sleeve.

[0029] Turning now to Figs. 7 and 8, an illustrative vessel closure **300** is shown representing a body **310** representative of a 20-415 cap, a cast seal **320,** and two inserts **330.** The inserts may be silicone tubing.

[0030] Fig. 9 illustrates an embodiment of an illustrative vessel closure **400** having a body **410,** a cast seal **420,** inserts **430,** and a pierceable recess **440** formed in the cast seal **420.** The pierceable recess **440** is a section of the cast seal **420** in which a removable insert was set during the casting and curing of the silicone and later removed to form an area of the cast seal **420** that is thinner than the remainder of the cast seal. In one embodiment the pierceable recess **440** is thin enough for a hypodermic needle to be inserted through the pierceable recess **440** thereby accessing the interior of a vessel so that fluid may be introduced into or removed from a vessel.

[0031] Fig. 10 illustrates another embodiment of a vessel closure **500** according to the invention having a body **510,** a cast seal **520,** inserts **530,** and a pierceable insert **540.** The pierceable insert **540** may be constructed from silicone or other suitable material that would allow a hypodermic or other similar needle to pierce the insert and thereby introduce or remove fluid from a vessel. Also shown in in Fig. 10 is an anchor sleeve **550,** Fig, 10 illustrates an example of a vessel closure potentially having three different inserts. The tubing without the sleeve may be silicone while the tubing with the sleeve could be elastomeric tubing, such as C-

Flex® tubing. Lastly, the pierceable insert **540** represents the third type of insert.

[0032] Fig. 11 depicts yet another embodiment of a vessel closure **600** according to the invention having a body **610,** a cast insert **620,** inserts **630** and **640,** and an anchor **650.** Insert **630** may be, for example, silicone tubing, and the anchor **650** is constructed with a retaining nut portion in the interior of the body **610** and a conical section on the exterior of the body **610,** thereby securing the insert **630** to body **610** by way of, for example, a friction fit. Insert **640** is a temperature probe. Various inserts may be used in the vessel closures including but not limited to: tubing (including but not limited to elastomeric and thermoplastic tubing), temperature probes, pH sensors, pierceable inserts, strain relief boots, dip tubes, barbed fittings, luers, and quick connect fittings. The invention is not limited to the aforementioned inserts. Inserts of any size, function, and construction may be used.

[0033] Further, check valves may be attached to tubing extending into the interior of a vessel. Use of such check vakes keeps fluids from entering a vessel until a requisite and sufficient force is applied to the fluid to open the check valve. Such force could be applied, for example, by a syringe or pump. In one embodiment, check valves such as Model #110 from Smart Products may be used

[0034] Fig. 12 illustrates an insert **700** comprised of tubing **730** and an anchor **750.** The anchor **750** is the same anchor as depicted in Fig. 11 and illustrates a how the anchor may be friction fit into an aperture in the body **610** by pressing the conical section into and through an aperture until the anchor snaps into place.

[0035] As shown best in Fig. 13, various inserts extend axially through apertures in the body during the manufacturing process before a casting agent is poured into the body of a vessel closure to form a seal. Specifically, Fig. 13 illustrates a perspective view of a vessel closure **800,** a body **810,** an insert **830,** a temperature probe **840,** an anchor sleeve **850,** and apertures **870** and **880** in the body. As shown in Fig. 13, the insert **830** and anchor sleeve **850** combination have not yet been fully inserted into aperture **870** in the body. In addition, the cast seal (not shown) has not yet been poured.

[0036] Fig. 14 shows an illustrative vessel closure **900,** a body **910,** a cast seal **920,** and three inserts **930, 940,** and **950.** In a preferred embodiment insert **930** is silicone tubing. Insert **940** is a male luer fitting and insert **950** is a female luer fitting.

[0037] Fig. 15 depicts an illustrative tri-clamp vessel closure **1000** comprising a body **1100,** a cast seal **1200,** and inserts **1300.** Fig. 16 shows a cross-section of the tri-clamp vessel closure **1000** comprising a body **1100,** a cast seal **1200,** and inserts **1300.** Tri-clamp closures may be made with inserts other than the tubing inserts shown in Figs. 15 and 16. Tubing is shown as merely an example of the type of insert that may be used.

[0038] Fig. 17 shows an illustrative vessel closure **2000,** a body **2100,** a cast seal **2200,** and two inserts **2300** and **2400.** In an embodiment insert **2300** is a silicone tube. Insert **2400**

depicts a male quick connect fitting. A quick connect fitting may be further secured to the body of the vessel closure by affixing a nut to the threaded portion of the insert that extends into the interior of the body. The body **2100** represents a 38-430 cap.

[0039] Fig. 18 depicts an illustrative vessel closure **3000,** a body **3100,** a cast seal **3200,** and two inserts **3300** and **3400.** Insert **3300** is a barbed fitting of the type that accepts flexible tubing, such as silicone or thermoplastic tubing. Insert **3400** is a male quick connect fitting. In an embodiment, the barbed insert may have a barbed extension extending into the interior of the body as well as extending away from the exterior of the body so that tubes may be attached extending into and out of a vessel.

[0040] Fig. 19 depicts an illustrative vessel closure **4000,** a body **4100,** a cast seal **4200.** and tubing **4300.** Body **4100** has at least two apertures so that tubing **4300** passes through each aperture and the ends of the tubing are both directed into the interior of a vessel thereby forming a loop on the exterior of the vessel. The loop shown in Fig. 19 is for illustrative purposes only and die loop on the vessel closure may be made in any length necessary to accommodate pumping or pumping and temperature control. The vessel closure illustrated in Fig. 19 may be used to circulate fluid into and out of a vessel without exposure to the environment outside of the vessel, thereby forming a closed system utilizing few components. In an embodiment, a peristaltic pump is connected to the loop of tubing outside the vessel and used to circulate the fluid. In yet another embodiment, a heat exchanger is used, instead of or in addition to a pump, to regulate the temperature of the fluid.

[0041] As best shown in Fig. 20, the cast seals disclosed herein may be sealingly compressed between the body of a vessel closure and a vessel by tightening the closure onto a vessel. Fig. 20 depicts an illustrative vessel closure body **5100** mechanically depressed to a vessel by the body being tightened to a vessel **5400** thereby compressing the cast seal **5200** against the vessel. In a preferred embodiment, the cast seal is aseptically sealed to the vessel.

[0042] The vessel closures may be manufactured by creating one or more apertures in a body. In an embodiment, the apertures may be made using a punch press. However, the apertures may be made using a drill, mill, laser, or any combination thereof. In another embodiment, the apertures are molded when the bodies are molded. Inserts are then inserted axially through the one or more apertures in the body. Silicone tubing is inserted through at least one aperture. Thermoplastic tubing is inserted through at least one other aperture so that the vessel closure has both silicone and thermoplastic tubing. A portion of the thermoplastic tubing is surrounded by an anchor adhesively attached to the thermoplastic tubing. The anchor is constructed of material capable of bonding with a casting agent. A casting agent is then cast into the body. The casting agent is cured to form a seal around and bond to the at least one anchor surrounding at least a portion of the thermoplastic tubing and to the silicone tubing. In an embodiment, the thermoplastic tubing is C-Flex® tubing. Preferred casting agents include liquid silicone and liquid perfluoropolyether.

[0043] In the aforementioned methods for manufacturing vessel closures, the liquid silicone

may be cast at temperatures much lower than required for insert and/or injection molding. Accordingly, components may be incorporated into the vessel closures that could not be incorporated into vessel closures manufactured using insert and/or injection molding. Such inserts include, but are not limited to, thermoplastic inserts such as C-Flex® tubing. Accordingly, the vessel closures may combine silicone and thermoplastic tubing within the same vessel closure. The vessel closures also allow for a variety of different inserts to be included in a single vessel closure, such as a variety of fittings, silicone tubing, C-Flex® tubing, temperature gauges, pH sensors, and others. The vessel closures are low cost and disposable but still capable of effectuating a substantially aseptic seal to a vessel while still allowing maximum flexibility in inserts. In addition, the methods of utilizing the vessel closures to circulate fluid into and out of a vessel provide systems with relatively few components all while maintaining a substantially aseptic system in which the fluid is located.

[0044] The vessel closures may be assembled and then the entire devices or components thereof may be rendered substantially aseptic by, for example, gamma radiation. Alternatively, the entire vessel closures or components thereof may be rendered substantially aseptic by exposure to steam above 121°C for a period of time long enough to eliminate microorganisms. The entire devices or components thereof may also be rendered aseptic by chemical treatment, such as with ethylene oxide (ETO). Once rendered substantially aseptic, the vessel closures may be appropriately packaged and stored to maintain the substantially aseptic state until ready for use.

[0045] The foregoing descriptions of vessel closures, methods of manufacturing vessel closures, and methods of utilizing vessel closures illustrate and describe various embodiments. As various changes can be made in the above embodiments without departing from the scope of the invention disclosed and claimed herein, it is intended that all matter contained in the above description or shown in the accompanying figures shall be interpreted as illustrative and not limiting. Furthermore, the scope of the invention covers various modifications, combinations, alterations, etc., of the above-described embodiments that all are within the scope of the claims. Additionally, the disclosure shows and describes only selected embodiments of the invention, but the invention is capable of use in various other combinations, modifications, and environments and is capable of changes or modifications within the scope of the inventive concept as expressed herein, commensurate with the above teachings, and/or within the skill or knowledge of artisans in the relevant art. Furthermore, certain features and characteristics of each embodiment may be selectively interchanged and applied to other illustrated and non-illustrated embodiments of the invention without departing from the scope of the invention.

REFERENCES CITED IN THE DESCRIPTION

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Patent documents cited in the description

- WO2005084372A [0006]
- US080488W [0028]

Patentkrav

1. Beholderlukning (100) omfattende et legeme (110), en eller flere åbninger, der strækker sig aksialt gennem legemet, en eller flere indsatser (130), der strækker sig gennem en eller flere åbninger, og en støbt tætning (120), som er anbragt indvendigt i legemet (110) og omgiver hver indsats, **kendetegnet ved, at** mindst én eller flere indsatser (130) omfatter termoplastisk rørledning, hvortil et anker (140, 150, 160) er klæbende fastgjort, den støbte tætning (120) er forbundet med ankeret (140, 150, 160), og ankret fastgør den ene eller flere indsatser (130) og den støbte tætning (120) til legemet.

2. Beholderlukning ifølge krav 1, hvor den ene eller flere af indsatserne (130) omfatter en rørledning i silikone.

3. Beholderlukning ifølge et hvilket som helst af kravene 1 til 2, hvor den støbte tætning (120) er fastgjort til legemet (110) ved hjælp af priming af mindst en del af legemet og klæbende fastgørelse af den støbte tætning (120) til legemet.

4. Beholderlukning ifølge et hvilket som helst af kravene 1 til 3, yderligere omfattende mindst én åbning i legemet (110) uden en indsats (130) og tætnet med den støbte tætning (120) for at danne en gennemtrængelig lukning over den mindst én åbning.

5. Beholderlukning ifølge et hvilket som helst af kravene 1 til 4, hvor den ene eller flere indsatser (130) er udvalgt fra gruppen bestående af en rørledning, en temperatursonde, en pH-sensor, en gennemtrængelig indsats, en trækaflastningsmuffe, et nedsænkningsrør, en beslag med modhager, en luer og et beslag til hurtig forbindelse.

6. Beholderlukning ifølge et hvilket som helst af kravene 1 til 5, hvor en eller flere reguleringsventiler er anbragt på rørledningen, som strækker sig ind i det

indvendige af en beholder, når beholderlukning (100) er anbragt på en beholder.

7. Beholderlukning ifølge krav 1, hvor den ene eller flere indsatser omfatter en fleksibel rørledning, hvor den fleksible rørledning passerer gennem to af åbningerne, således at enderne af den fleksible rørledning begge er rettet mod det indvendige af en beholder, når beholderlukningen er anbragt på en beholder, hvorved der dannes en sløjfe på den udvendige side af beholderen.

8. Beholderlukning ifølge et hvilket som helst af kravene 1 til 7, hvor ankeret (140, 150, 160) er konstrueret fra materiale, der er udvalgt fra gruppen bestående af metal, plastik, glasfyldt plastik, keramik og kompositter.

9. Beholderlukning ifølge krav 2, hvor det ene eller flere silikonerør er klæbende fastgjort til ét eller flere ankre; hvor ankrene fastgør det ene eller flere silikonerør til legemet.

10. Beholderlukning ifølge et hvilket som helst af kravene 1 til 9, hvor det ene eller flere termoplastiske rør omfatter en fleksibel rørledning, og hvor ankeret (140, 150, 160) omfatter en deformerbar muffe, som omgiver mindst en del af den fleksible rørledning,
hvor den deformerbare muffe dannes af et materiale, som har en sådan plasticitet, at det tryk, som påføres den deformerbare muffe, får den deformerbare muffe til at deformeres omkring og tætne den fleksible rørledning, og efter kontinuerlig påføring af tryk på den deformerbare muffe, skæres den deformerbare muffe og den fleksible rørledning, og muffen bevarer en deformeret form, som i det væsentlige tætner den fleksible rørledning,
hvor støbningsmidlet danner en støbt tætning, som omgiver den deformerbare muffe.

11. Beholderlukning ifølge et hvilket som helst af kravene 1 til 10, hvor støbningsmidlet er udvalgt fra gruppen bestående af flydende silikone og flydende

perfluoropolyether.

12. Fremgangsmåde til fremstilling af en beholderlukning (100) omfattende et legeme (110), en eller flere åbninger, der strækker sig aksialt gennem legemet, en eller flere indsatser (130), der strækker sig gennem en eller flere åbninger; hvor fremgangsmåden omfatter:
frembringelse af en eller flere åbninger i et legeme (110);
indføring af en eller flere indsatser (130) aksialt gennem den ene eller flere åbninger,
hvor den ene eller flere af indsatserne omfatter en termoplastisk rørledning, hvortil et anker (140, 150, 160) er klæbende fastgjort;
støbning af et støbningsmiddel til legemet; og
hærdning af støbningsmidlet for at danne en tætning (120) omkring og forbundet med ankeret (140, 150, 160), hvor ankeret fastgør den ene eller flere indsatser.

DRAWINGS

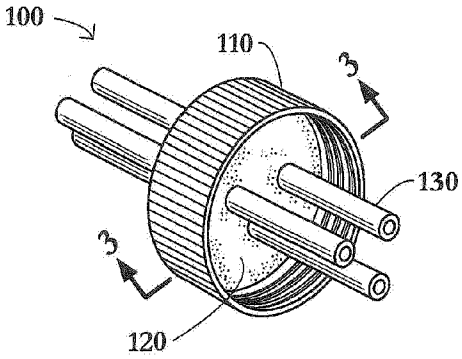


FIG. 1

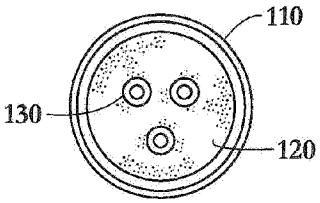


FIG. 2

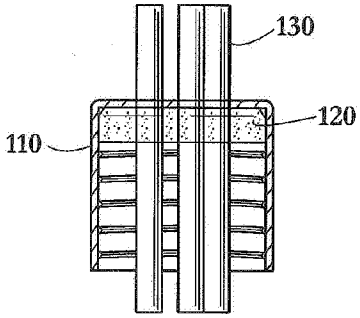


FIG. 3

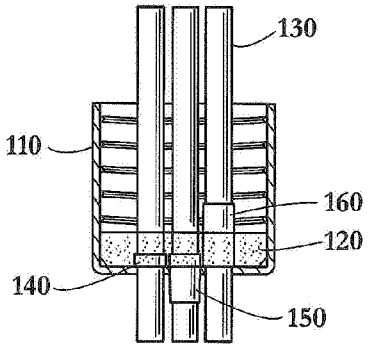


FIG. 4

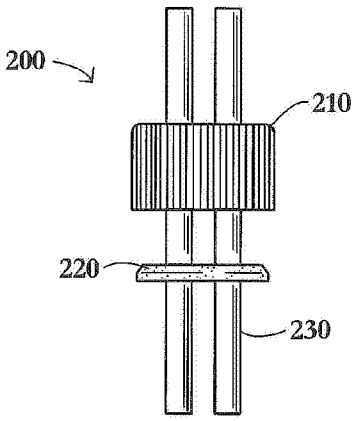


FIG. 5

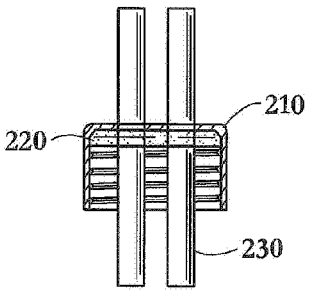


FIG. 6

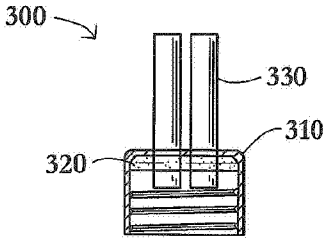


FIG. 7

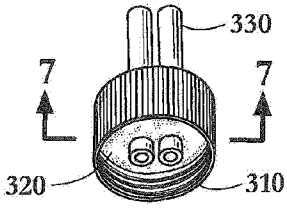


FIG. 8

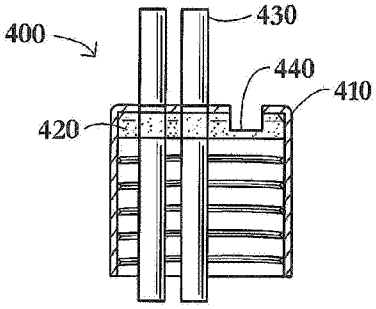


FIG. 9

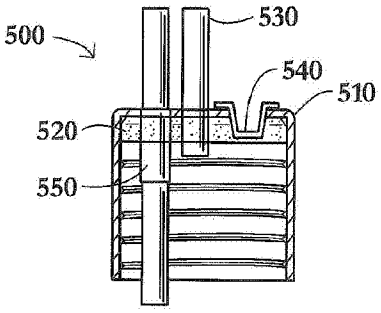


FIG. 10

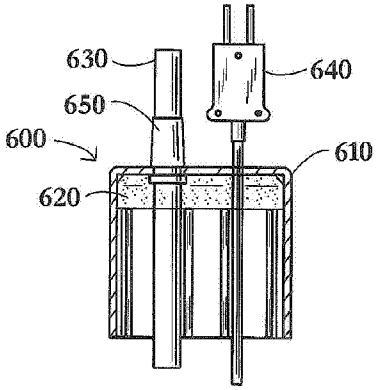


FIG. 11

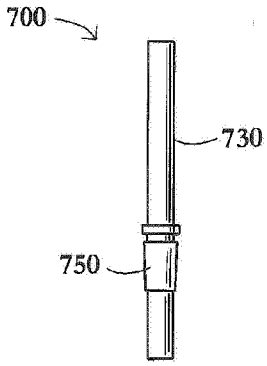


FIG. 12

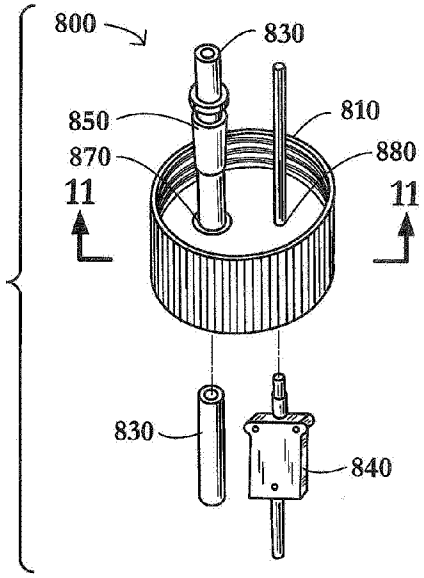


FIG. 13

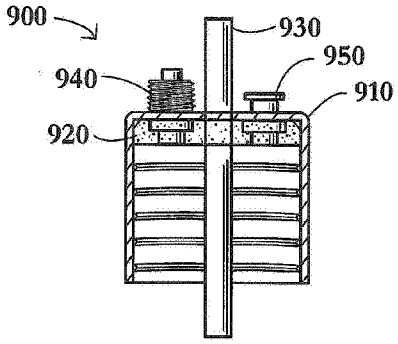


FIG. 14

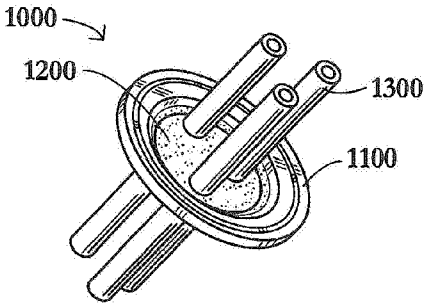


FIG. 15

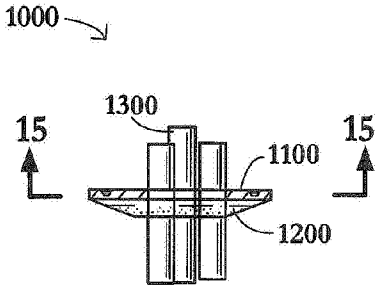


FIG. 16

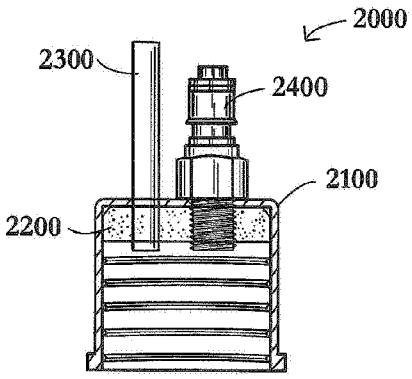


FIG. 17

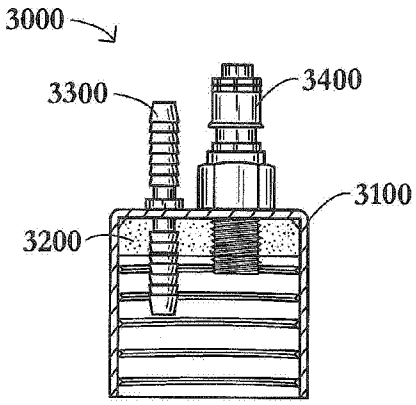


FIG. 18

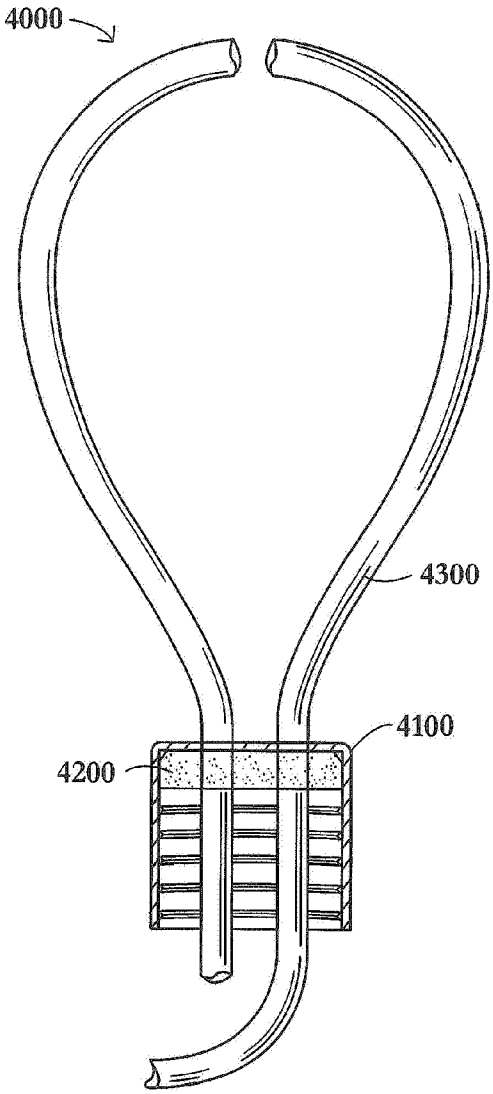


FIG. 19

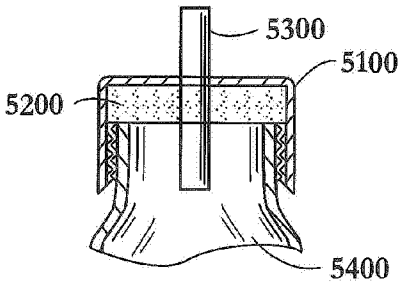


FIG. 20