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(71) Applicant: **LIFE TECHNOLOGIES CORPORATION**
[US/US]; 5823 Newton Drive, Carlsbad, California 92008 (US).

(72) Inventor: **GORDON, Michael**; c/o Life Technologies Corporation, 5823 Newton Drive, Carlsbad, California 92008 (US).

(74) Agent: **HIERHOLZER, Matthew**; c/o Life Technologies Corporation, 5823 Newton Drive, Carlsbad, California 92008 (US).

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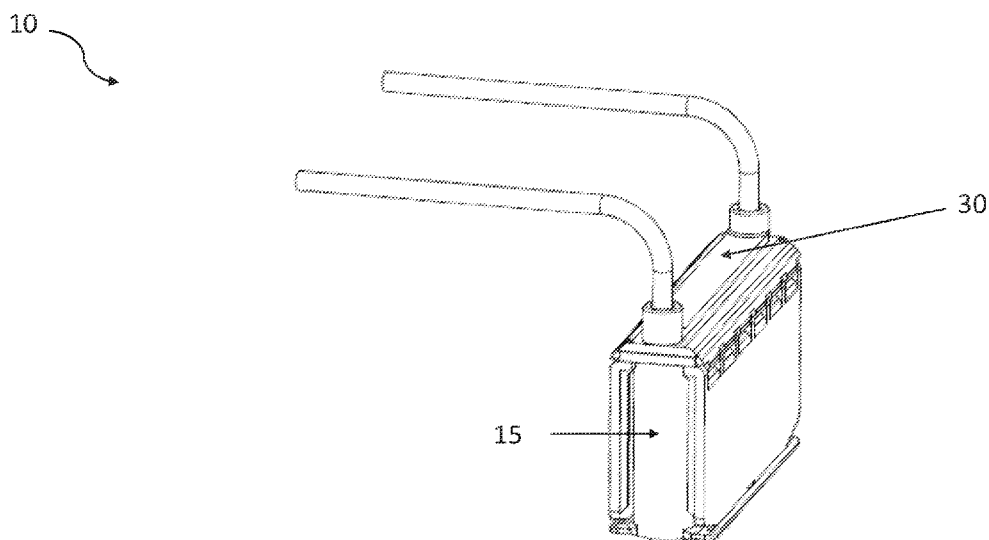


FIG. 1

(57) Abstract: Assemblies, methods, and systems for delivering a fluid into a fluidic flow. An assembly includes: a dispenser body having an interior wall defining a lumen having a longitudinal axis and a diameter; a cap configured to traverse the diameter of the lumen, the cap having an upper surface and a lower surface; a piston disposed within the lumen, the piston having a top surface and a bottom surface, the top surface together with the interior wall and the lower surface of the cap defining a working volume of the lumen, wherein the piston is movable along the longitudinal axis to change the working volume; an outlet in fluid connection with the working volume; and a fluid conduit extending between a first portion of the fluid conduit and a second portion of the fluid conduit, the fluid conduit being in fluid connection with the working volume via the outlet between the first and second portions of the fluid conduit.

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ASSEMBLY AND SYSTEM FOR CONTROLLED DISPENSING OF FLUID

CROSS REFERENCE TO RELATED APPLICATION(S)

[0001] This application claims the benefit of priority to U.S. Provisional Patent Application No. 63/523,331, filed June 26, 2023, the disclosure of which is considered part of, and incorporated in its entirety by reference in the disclosure of this application.

BACKGROUND

FIELD

[0002] This disclosure relates generally to fluid delivery, and more particularly to an assembly and system for controlled dispensing of a fluid, as well as methods of use for dispensing a fluid into a fluid conduit to perform a process in a fluidic workflow.

BACKGROUND INFORMATION

[0003] Syringes are popularly used for the manipulation of samples in research, medical, and diagnostic settings. A syringe typically consists of a needle attached to one end of a hollow cylinder and a plunger connected to a sliding piston. Fluid is drawn into the hollow cylinder from the needle by pulling on the plunger. Fluid can be injected or dispensed from the hollow cylinder by pushing on the plunger causing the piston to push out the fluid from the needle. The syringes can be filled with a desired sample just before using the syringe, or the syringes can be pre-filled with desired sample.

[0004] In several applications, pre-filled syringes transport samples from one point to another (e.g., within a laboratory or one geographical location to another). Such pre-filled syringes have plungers attached to the piston that typically extend well beyond the top of the hollow cylinder.

A disadvantage of using a syringe is that when the plunger is accidentally pushed or bumped, the fluid can dispense at an undesired time and/or location.

[0005] Another disadvantage of using a syringe is the risk of accidental needle punctures to technicians using the syringe. This is a particular concern in applications that involve risk of exposure of a technician to a biological sample, such as a patient sample, caused by a needle puncture.

[0006] Thus, there exists a need for an improved device for controlled dispensing of fluid that enables transport of fluid contained in the device without risk to a technician of an accidental needle puncture or accidental discharge of fluid from the device upon transport.

BRIEF SUMMARY

[0007] One aspect of the present disclosure provides an assembly for dispensing fluid. In embodiments, the assembly includes:

- a dispenser body having an interior wall defining a lumen having a longitudinal axis and a diameter;

- a cap configured to traverse the diameter of the lumen, the cap having an upper surface and a lower surface;

- a piston disposed within the lumen, the piston having a top surface and a bottom surface, the top surface together with the interior wall and the lower surface of the cap defining a working volume of the lumen, wherein the piston is movable along the longitudinal axis to change the working volume;

- an outlet in fluid connection with the working volume; and

a fluid conduit extending between a first portion of the fluid conduit and a second portion of the fluid conduit, the fluid conduit being in fluid connection with the working volume via the outlet between the first and second portions of the fluid conduit.

[0008] In embodiments, the assembly has a first configuration in which the cap does not traverse the diameter of the lumen and the lumen is fluidically unsealed, and a second configuration in which the cap traverses the diameter of the lumen and the lumen is fluidically sealed. In some embodiments, movement of the piston along the longitudinal axis causes fluid flow through the outlet when the assembly is in the second configuration when the lumen is fluidly sealed.

[0009] In some embodiments, the dispenser body includes one or more additional interior walls defining separate additional lumens, each having a longitudinal axis and a diameter. In some embodiments, the additional lumens each include a piston defining a working volume, and each piston is movable along the respective longitudinal axes to change the respective working volumes of each lumen. In some embodiments, the fluid conduit is in fluid connection with the working volume of each lumen between an input port of the fluid conduit and an output port of the fluid conduit. In one embodiment, the assembly includes 2 to 10 lumens formed in the dispenser body, each having a working volume in fluid connection to the fluid conduit between the input port of the fluid conduit and the output port of the fluid conduit.

[0010] In another aspect, the disclosure provides a system for dispensing fluid including an assembly of the present disclosure. In embodiments, the system includes:

an assembly of the present disclosure; and

an actuator operably coupled to a lumen of the dispenser body configured to move a piston defining a working volume of the lumen along the longitudinal axis of the lumen to

decrease the working volume and cause fluid flow from the working volume into the fluid conduit when the assembly is in the second configuration in which the lumen is fluidically sealed.

[0011] In another aspect, the disclosure provides a system for dispensing fluid including an assembly of the present disclosure. In embodiments, the system includes:

one or more assemblies of the present disclosure having one or more dispenser bodies, each having one or more lumens with working volumes; and

one or more actuators operably coupled to each lumen of the one or more dispenser bodies configured to move a piston defining a working volume along a longitudinal axis of the lumen to decrease the working volume and cause fluid flow from the working volume into the fluid conduit when the assembly is in the second configuration in which the lumen is fluidically sealed.

[0012] In some embodiments, the system includes a first feedline fluidically coupled to an input port of a fluid conduit disposed upstream of the one or more dispenser bodies a second feedline fluidically coupled to an output port fluidically coupled to the fluid conduit disposed downstream of the one or more dispenser bodies to form a sterile and functionally closed system. In some embodiments, the system includes a cell processing system fluidically coupled to the first feedline and the second feedline.

[0013] In another aspect, the present disclosure provides a method of dispensing fluid from the assembly of the present disclosure. The method includes:

providing an assembly of the present disclosure;

loading a fluid into a working volume of a lumen of the dispenser body when the assembly is in the first configuration and the working volume of the lumen is fluidically unsealed;

transitioning the assembly to the second configuration in which the working volume of the lumen is fluidically sealed; and

advancing a piston disposed in the lumen along the longitudinal axis of the lumen to cause flow of the fluid from the working volume into a fluid conduit.

[0014] In yet another aspect, the disclosure provides a method of performing a fluidic workflow utilizing the assembly or system of the present disclosure. The method includes:

delivering a fluid from a working volume of the assembly or system of the present disclosure into a fluid flow contained within a functionally closed system; and

performing a fluidic workflow.

[0015] In some embodiments, the fluid includes a gene editing reagent and the fluid flow includes a cell, or component thereof. In some embodiments, the fluidic workflow includes a cell processing protocol, such as a protocol that includes transformation, transfection, transduction, activation, isolation, separation, imaging, labeling, and/or culturing of a cell, or portion thereof.

[0016] The forgoing general description of the illustrative implementations and the following detailed description thereof are merely exemplary aspects of the teachings of this disclosure, and are not restrictive.

BRIEF DESCRIPTION OF THE DRAWINGS

[0017] The accompanying drawings, which are incorporated in and constitute a part of the specification, illustrate one or more embodiments and, together with the description, explain these embodiments. The accompanying drawings have not necessarily been drawn to scale. Any

values dimensions illustrated in the accompanying graphs and figures are for illustration purposes only and can or cannot represent actual or preferred values or dimensions. Where applicable, some or all features cannot be illustrated to assist in the description of underlying features.

[0018] Figure 1 is an elevated perspective view showing an assembly in an embodiment of the present disclosure.

[0019] Figure 2 is a bottom perspective view of the assembly shown in Figure 1.

[0020] Figure 3 is a cross sectional front view of the assembly shown in Figure 1.

[0021] Figure 4 is a cross sectional elevated front view of the assembly shown in Figure 1.

[0022] Figure 5 is a cross sectional front view of the assembly shown in Figure 1.

[0023] Figure 6 is an exploded view of the cap and fluid conduit of the assembly shown in Figure 1.

[0024] Figure 7 is an exploded view of the cap and fluid conduit of the assembly shown in Figure 1.

[0025] Figure 8 is a cross sectional elevated side view of the assembly shown in Figure 1.

[0026] Figure 9 is a bottom perspective view of the assembly shown in Figure 1.

[0027] Figure 10 is an exploded view of the assembly shown in Figure 1.

[0028] Figure 11 is a perspective view of the assembly shown in Figure 1 before the cap is coupled to the dispenser body.

[0029] Figure 12 is a side view of the assembly shown in Figure 11.

[0030] Figure 13 is a side view of the assembly shown in Figure 11 with the cap contacting the dispenser body and attachment members uncoupled from the dispenser body.

[0031] Figure 14 is a side view of the assembly shown in Figure 13 with the cap contacting the dispenser body and attachment members being moved to couple with the dispenser body.

[0032] Figure 15 is a side view of the assembly shown in Figure 13 with the cap contacting the dispenser body and attachment members being moved to couple with the dispenser body.

[0033] Figure 16 is a side view of the assembly shown in Figure 13 with the cap contacting the dispenser body and attachment members being moved to couple with the dispenser body.

[0034] Figure 17 is a side view of the assembly shown in Figure 13 with the cap contacting the dispenser body and attachment members coupled with the dispenser body to prepare the assembly for dispensing fluid.

[0035] Figure 18 is a cross sectional front view of the assembly shown in Figure 1 with the pistons moved away from the cap thereby defining a positive working volume within each lumen.

[0036] Figure 19 is a cross sectional front view of the assembly shown in Figure 1 with the luminally disposed pistons moved toward the cap such that the working volume within each lumen is null.

[0037] Figure 20 is an elevated perspective view showing an assembly in an embodiment of the present disclosure.

[0038] Figure 21 is a side view of the assembly shown in Figure 20.

[0039] Figure 22 is a perspective view of the assembly shown in Figure 20 with the cap being moved to cover lumens of the dispenser body.

[0040] Figure 23 is a side view of the assembly shown in Figure 21.

[0041] Figure 24 is a perspective view of the assembly shown in Figure 20 with the cap moved to contact the dispenser body.

[0042] Figure 25 is a side view of the assembly shown in Figure 24.

[0043] Figure 26 is a perspective view of the assembly shown in Figure 20 with the cap having a fluid tight seal with the dispenser body.

[0044] Figure 27 is a side view of the assembly shown in Figure 26.

DETAILED DESCRIPTION

[0045] The description set forth below in connection with the appended drawings is intended as a description of various embodiments of the disclosed subject matter and is not necessarily intended to represent the only embodiment(s). In certain instances, the description includes specific details for the purpose of providing an understanding of the disclosed embodiment(s). However, it will be apparent to those skilled in the art that the disclosed embodiment(s) can be practiced without those specific details. In some instances, well-known structures and components can be shown in block diagram form in order to avoid obscuring the concepts of the disclosed subject matter.

[0046] Reference throughout the specification to “one embodiment” or “an embodiment” means that a particular feature, structure, or characteristic described in connection with an embodiment is included in at least one embodiment of the subject matter disclosed. Thus, the appearance of the phrases “in one embodiment” or “in an embodiment” in various places throughout the specification is not necessarily referring to the same embodiment. Further, the particular features, structures or characteristics can be combined in any suitable manner in one or more embodiments. Further, it is intended that embodiments of the disclosed subject matter cover modifications and variations thereof.

[0047] It is to be understood that terms such as “distal,” “proximal,” “top,” “bottom,” “front,” “side,” “length,” “lower,” “interior,” “inner,” “outer,” and the like that can be used herein merely

describe points of reference and do not necessarily limit embodiments of the present disclosure to any particular orientation or configuration. Furthermore, terms such as “first,” “second,” “third,” and the like, merely identify one of a number of portions, components, steps, operations, functions, and/or points of reference as disclosed herein, and likewise do not necessarily limit embodiments of the present disclosure to any particular configuration or orientation.

[0048] The terms “longitudinal,” “axial” or “axially” are generally longitudinal as used herein to describe the relative position related to a syringe, a delivery mechanism, and components of the system herein. The term “radial” generally refers to a direction perpendicular to the “axial” direction. For example, the term “radial” generally refers to a direction perpendicular to the axis “A”.

[0049] The term “fluid” refers primarily to a liquid, but also includes a suspension of solids diffused in the liquid, dissolved therein, or gas that coexists in the liquid inside the fluid-containing portion of the syringe. In the present disclosure, fluid is used as an example substance aspirated into a syringe for explaining the concepts. In many embodiments, samples can be dispensed (e.g., aspirated) without deviating from the scope of the present disclosure.

[0050] As used herein, the term “sample” refers to a liquid which may include one or more reagents, such as a biological molecule.

[0051] The term “biological molecule” or “biomolecule” is intended to generally refer to any organic or biochemical molecule that occurs in a biological system including a whole cell, a cellular component, a substrate, or any portions thereof.

[0052] As used herein, a “cellular component” is intended to include any component of a cell that may be at least partially isolated upon lysis of the cell. Cellular components include components that are recombinantly or synthetically produced which may be functionally and/or

structurally altered to include synthetically (e.g., chemically synthesized) derived components. Cellular components may be organelles, such as nuclei, perinuclear compartments, nuclear membranes, mitochondria, chloroplasts, or cell membranes; polymers or molecular complexes, such as lipids, polysaccharides, proteins (membrane, trans-membrane, or cytosolic); nucleic acids, viral particles, or ribosomes; or other molecules, such as hormones, ions, cofactors, or drugs.

[0053] In various embodiments, a sample includes a cell (e.g., a mammalian cell or a non-mammalian cell), cellular component, biomolecule, or other reagent (e.g., a reagent used in the development or manufacturing of cell and gene therapies). In some embodiments, the sample can be a fluid and loaded into an assembly of the disclosure through a needle, a tube, a vial, or other container(s). In some embodiments, the tube, vial or other container is single-use and composed of a material suitable for preparing, mixing, centrifuging, transporting and/or storing solid and liquid samples and reagents, such as quartz, glass, metal or a polymer (e.g., polypropylene, polyvinyl, polyurethane, polycarbonate and the like).

[0054] Systems used in cell-based or gene-based therapies (e.g., T-cell therapy or CAR T-cell therapy) involve numerous pieces of equipment performing multiple processes, and the addition of numerous reagents/cell culture components to various pieces of equipment, often in a specified sequence referred to as a workflow, or fluidic workflow.

[0055] In the field of cell and gene therapy, functionally-closed, sterile systems are highly desirable. “Open” steps (e.g., involving manual intervention) should be minimized to reduce the risk of biological contamination.

[0056] Presently, when electroporation, a common technique used in gene editing, is used to deliver a payload (e.g., biomolecule, such as a nucleic acid or protein, or other reagent), cells are

concentrated and resuspended in electroporation buffer (e.g., electrically conductive fluid) within a bag or rigid vessel. Once resuspended, additional reagents can be added to the cells in a specific sequence. At present time, this is achieved within a biosafety cabinet and is considered to be an open step, which carries some risk of contamination. Ideally, this step occurs outside of a biosafety cabinet and within an automated closed system, however, current solutions for automatic injection of different fluids are inadequate, especially for low volume fluids (e.g., <1ml). Following the addition of the payload and requisite additional reagents, the bag or other storage medium containing the cells is then coupled to an electroporation platform to electroporate the cells.

[0057] Arrangement of syringes and automatic injection devices for delivering fluid (e.g., a fluid including a payload) into a fluidic workflow can be associated with problems including, for example, dead volumes, priming issues, needle punctures, or the accidental injection of liquid such as, for example, when a plunger is bumped or inadvertently depressed. The present disclosure solves several problems outlined above, and provides new assemblies, systems and methods for delivery of fluid samples (e.g., liquids, suspensions, and the like).

[0058] As discussed further herein, the assemblies 10 of the present disclosure generally include a cap and a dispenser body which are assembled after fluid is added to one or more lumens of the dispenser body by forming a hermetic fluid tight seal between the cap and the dispenser body to contain the added fluid within a working volume of the lumen. As such, the assemblies 10 have a first unassembled configuration and a second assembled configuration. In the first unassembled configuration, the cap is not in sealing engagement with the dispenser body and fluid may be added to the dispenser body. In the second assembled configuration, the cap is disposed over one or more lumens of the dispenser body and a fluidic seal is created between the

cap (and optionally an intervening sealing member) and the dispenser body to hermetically seal fluid contained within a lumen of the dispenser body.

[0059] As also discussed herein, assemblies 10 of the present disclosure may be configured for dispensing a single fluid from an assembly having a single fluid containing lumen or configured for dispensing multiple fluids from an assembly having multiple (e.g., 1, 2, 3, 4, 5, 6 or more) fluid containing lumens. The Figures illustrate embodiments of assemblies 10 configured to dispense multiple fluid samples (i.e., 6) into a fluidic flow path (e.g., fluid within a fluid conduit which may be operably coupled to a fluidic workflow). It will be appreciated that while the assemblies illustrated in the Figures are configured with a dispenser body having 6 lumens, the disclosure encompasses assemblies in which the dispenser body is configured to have any number of lumens, for example, a single lumen, or 2, 3, 4, 5, 6, 7, 8, 9, 10 or more lumens.

[0060] Figures 1-19 illustrate an embodiment of the assembly 10 which includes a dispenser body 15, a cap 30, a piston 45, and a fluid conduit 65. Example illustrations of the assembly 10 in the first unassembled configuration are shown in Figures 11-16 and illustrations of the assembly 10 in the second assembled configuration are shown in Figures 1, 2 and 17.

[0061] In embodiments, the dispenser body 15 has an interior wall 20 defining a lumen 25 having a longitudinal axis (A-A') and a diameter (D). The cap 30 is configured to traverse the diameter of the lumen 25 and includes an upper surface 35 and a lower surface 40. The piston 45 is disposed within the lumen and includes a top surface 50 and a bottom surface 55. The top surface 50 together with the interior wall 20 and the lower surface 40 of the cap, optionally along with an intervening sealing member 95 (e.g., a gasket), defining a working volume (LQ) of the lumen (see Figure 5).

[0062] As shown in Figure 5, the assembly may further include an outlet 60 in fluid connection with the working volume (LQ). The outlet provides a fluid pathway to the fluid conduit 65 which extends between a first portion 70 of the fluid conduit and a second portion 75 of the fluid conduit such that the fluid conduit is in fluid connection with the working volume via the outlet between the first and second portions of the fluid conduit.

[0063] In the assembly 10 illustrated in Figures 1-19, a region of the fluid conduit 65 disposed between the first portion 70 of the fluid conduit and the second portion 75 of the fluid conduit is defined by a channel 90 formed within the upper surface 35 of the cap and a cover member 100 disposed over the channel 90. It will be appreciated that the cap 30 and the cover member 100 may be formed from two or more discrete parts which are coupled together to form the region fluidic conduit with the channel 90 being formed in the cover member 100, the upper surface 35 of the cap, or a combination thereof. Alternatively, the cap 30 and cover member 100 may be formed as a single unitary part. In some embodiments, the channel 90 is formed entirely within the volume of the cap 30 such that internal surfaces of the fluid conduit 65 disposed between the first portion 70 of the fluid conduit and the second portion 75 of the fluid conduit are disposed within the volume of the cap material (e.g., the channel traverses through the cap).

[0064] As discussed herein, the assembly 10 has a first unassembled configuration in which the cap may, or may not, traverse the diameter D of the lumen 25 and the lumen is fluidically unsealed (see Figures 11-16) and a second assembled configuration in which the cap traverses the diameter D of the lumen 25 and the lumen is fluidically sealed (see Figures 1, 2 and 17).

[0065] In embodiments, the assembly 10 further includes one or more attachment members 105 configured to engage the dispenser body 15 and secure the cap 30 to the dispenser body when the assembly is in the second assembled configuration. For example, the assembly 10

shown in Figures 1-19 includes 2 attachment members hingably connected to the cap 30. Each attachment member 105 includes features that engage features of the dispenser body 15 to facilitate securement of the cap to the dispenser body. In some embodiments, each attachment member may include one or more engagement elements that interact with one or more engagement surfaces of the dispenser body.

[0066] Figures 11-16 show transition of the assembly from the first unassembled configuration to the second assembled configuration. During assembly, the cap 30 is disposed over the lumens of the dispenser body 15 and subsequently the attachment members 105 are moved downward to contact the sides of the dispenser body. As the attachment members 105 are moved downward, engagement elements 110 contact engagement surfaces 115 which presses the central portion of the cap disposed over the lumens downward onto the dispenser body such that a hermetic fluid tight seal is created (see Figures 13-16). During the final step of assembly, one or more distal tip surfaces 120 of each attachment member 105 are received by one or more corresponding slots 125 disposed on the dispenser body 15 to secure the cap 30 to the dispenser body and form the completed assembly 10 (see Figure 1).

[0067] It will be appreciated that while Figures 1-19 illustrate an embodiment of assembly 10 which includes a particular configuration of elements to facilitate attachment of the cap to the dispenser body, attachment may be achieved using a number of different connectors. For example, attachment may be achieved using fasteners, latches, snap type connections, threaded engagements and the like. Similarly, it will be appreciated that the cap and the dispenser body can be configured in a variety of ways to achieve a hermetic fluid tight seal between the cap and the dispenser body to form the completed assembly.

[0068] For example, Figures 20-27 illustrate an embodiment of the assembly 10 which includes a single attachment member hingably connected to both the dispenser body and the cap. As shown in Figures 20-27, in this embodiment, the assembly 10 includes the dispenser body 15, the cap 30 and attachment member 105 hingably connected to the dispenser body and the cap. Figures 20-25 show the assembly 10 in the first unassembled configuration in which the attachment member 105 is not engaged with the dispenser body 15 such that a hermetic fluid tight seal is created between the cap 30 and the dispenser body 15. During assembly, the attachment member 105 is rotated about the hinges such that the cap 30 covers the lumens of the dispenser body 15 (see Figure 24). The attachment member 105 is then moved downward to contact and engage the side of the dispenser body 15. As the attachment member 105 is moved downward, engagement elements 110 contact engagement surface 115 which presses the central portion of the cap disposed over the lumens downward onto the dispenser body such that a hermetic fluid tight seal is created. During the final step of assembly, one or more distal tip surfaces 120 of the attachment member 105 are received by one or more corresponding slots 125 disposed on the dispenser body 15 to secure the cap 30 to the dispenser body and form the completed assembly 10 (see Figure 26).

[0069] In various embodiments, the piston is movable along the longitudinal axis of the lumen to change the working volume. For example, in the embodiment shown in Figures 1-19, moving the piston 45 along the length of the lumen 25 to increase the distance between the upper surface 50 of the piston and the cap 30 increases the working volume (LQ). Alternatively, moving the piston 45 along the lumen 25 to decrease the distance between the upper surface 50 of the piston and the cap 30 decreases the working volume (LQ), e.g., to dispense fluid contained within the working volume into the fluid conduit.

[0070] During use, fluid is added to one or more lumens while the assembly is in the first unassembled configuration and the lumen is oriented toward the bottom portion of the dispenser body to provide a working volume. Next, the assembly is transitioned from the first configuration to the second assembled configuration to complete assembly. These steps can be performed in a sterile environment, such as a biosafety cabinet or laminar flow hood, to avoid contamination. The assembly is then fluidly connected to a fluid workflow by fluidly coupling the input port and the output port to feedlines in fluidic connection with a fluidic workflow, e.g., a closed loop electroporation assembly. Additionally, the assembly is operably coupled to one or more actuators configured to provide automated control of movement of individual pistons within their respective lumens, e.g., to advance the piston along the length of the lumen toward the outlet to reduce the working volume and dispense fluid into the fluid conduit. Fluid is then dispensed from respective lumens into the fluid conduit by controlled movement of individual pistons. Dispensing from different lumens may be performed independently, or in unison, at a controlled rate via manual or automated operation of the one or more actuators.

[0071] Accordingly, the disclosure further provides a system for dispensing fluid including an assembly of the present disclosure. In embodiments, the system includes an assembly of the present disclosure; and an actuator operably coupled to a lumen of the dispenser body configured to move a piston defining a working volume of the lumen along the longitudinal axis of the lumen to decrease the working volume and cause fluid flow from the working volume into the fluid conduit when the assembly is in the second configuration in which the lumen is fluidically sealed.

[0072] In another aspect, the disclosure provides a system for dispensing fluid including one or more assemblies of the present disclosure. In embodiments, the system includes one or more

assemblies of the present disclosure having one or more dispenser bodies, each having one or more lumens with working volumes; and one or more actuators operably coupled to each lumen of the one or more dispenser bodies configured to move a piston defining a working volume along a longitudinal axis of the lumen to decrease the working volume and cause fluid flow from the working volume into the fluid conduit when the assembly is in the second configuration in which the lumen is fluidically sealed.

[0073] In some embodiments, the system includes a first feedline fluidically coupled to an input port of a fluid conduit disposed upstream of the one or more dispenser bodies a second feedline fluidically coupled to an outlet port fluidically coupled to the fluid conduit disposed downstream of the one or more dispenser bodies to form a sterile and functionally closed system. In some embodiments, the system includes a cell processing system, such as a transfection assembly, fluidically coupled to the first feedline and the second feedline.

[0074] In various embodiments, the actuator for controlling movement of the piston can include a pneumatic mechanism, a lead screw mechanism, a loaded spring mechanism, or other driving mechanism.

[0075] In some embodiments, the dispenser body 15 is made from material that enables visual detection of contents within the lumen, e.g., transparent plastic, transparent glass, and the like. The dispenser body can be marked with a measurement scale to enable visualization of the amount of contents contained in the lumen. For example, the measurement scale can be configured to measure a volume of contents aspirated in the lumen in milliliters (ml), microliters (μ l), ounces (oz), or other measurement units. In some embodiments, the dispenser body is composed from any known material typically used for dispensing a fluid containing a biomolecule, such as a non-bioreactive plastic, glass or other material that does not react with the

contents to be dispensed. In some embodiments, the dispenser body is composed of, or includes a bioreactive material that preserves or otherwise stabilizes the contents of the lumen to maintain extended longevity.

[0076] In various embodiments, the piston can be made of compliant material e.g., elastic material such as a rubber material or silicone or other resiliently deformable material. The terms “elastic” and “elastic material” mainly refer to cross-linked thermoset polymers, such as silicone or rubber-like polymers, which are more easily deformable than plastics. Such material is, e.g., biologically and chemically inert/non-reactive and thus suitable for use with reactive or biological fluids and is not easily affected by leaching or gas movement under ambient temperature and pressure.

[0077] Once the desired amount of contents (e.g., a fluid, a sample, and the like) is loaded into one or more lumens, the assembly can be used in different applications, such as preparing for a gene editing step of T-cell therapy workflow. Accordingly, it will be appreciated that depending upon the particular application, multiple lumens can be filled with different types of contents, such as biomolecules (e.g., Cas9 protein, guide RNA, and donor DNA, respectively for gene editing applications). Advantageously, as the assemblies can be easily transported and handled without accidentally discharging or mixing of fluids. Additionally, the input port and output port of the fluid conduit may be hermetically sealed such that the fluid contents of the assemblies are not exposed to risks of contamination when transported out of a sterile environment.

[0078] In some embodiments, the output port is connected (e.g., in a closed, sterile manner) to a system such as an electroporation or other transfection system (e.g., as described in International Patent Application No. PCT/US2020/05713, which is incorporated by reference herein in its entirety), or culture system. As such, the systems described herein may be used for

generating a cell therapy or treatment using genetically modified cells, T cells, CAR T cells, NK cells, stem cells, and the like.

[0079] While certain embodiments have been described, these embodiments have been presented by way of example only, and are not intended to limit the scope of the present disclosures. Indeed, the novel methods, assemblies and systems described herein can be embodied in a variety of other forms; furthermore, various omissions, substitutions and changes in the form of the methods, apparatuses and systems described herein can be made without departing from the spirit of the present disclosures. The accompanying claims and their equivalents are intended to cover such forms or modifications as would fall within the scope and spirit of the present disclosures.

[0080] Exemplary Subject Matter of the Invention is represented by the following clauses:

[0081] Clause 1: An assembly comprising: a dispenser body having an interior wall defining a lumen having a longitudinal axis and a diameter; a cap configured to traverse the diameter of the lumen, the cap having an upper surface and a lower surface; a piston disposed within the lumen, the piston having a top surface and a bottom surface, the top surface together with the interior wall and the lower surface of the cap defining a working volume of the lumen, wherein the piston is movable along the longitudinal axis to change the working volume; an outlet in fluid connection with the working volume; and a fluid conduit extending between a first portion of the fluid conduit and a second portion of the fluid conduit, the fluid conduit being in fluid connection with the working volume via the outlet between the first and second portions of the fluid conduit, wherein the assembly has a first configuration in which the cap does not traverse the diameter of the lumen and the lumen is fluidically unsealed and a second configuration in

which the cap traverses the diameter of the lumen and the lumen is fluidically sealed, and wherein movement of the piston along the longitudinal axis causes fluid flow through the outlet when the assembly is in the second configuration.

[0082] Clause 2: The assembly of clause 1, wherein the fluid conduit has an input port adjacent the first portion of the fluid conduit and an output port adjacent the second portion of the fluid conduit, and wherein movement of the piston along the longitudinal axis toward the cap causes fluid to flow from the working volume into the fluid conduit via the outlet when the assembly is in the second configuration.

[0083] Clause 3: The assembly of clause 2, wherein the input port and the output port are hermetically sealed.

[0084] Clause 4: The assembly of clause 1, wherein an internal surface of the fluid conduit is defined by a channel formed within a volume of the cap or on the upper surface of the cap between the first portion of the fluid conduit and the second portion of the fluid conduit.

[0085] Clause 5: The assembly of clause 1, wherein at least a region of the fluid conduit between the first portion of the fluid conduit and the second portion of the fluid conduit is defined by a channel formed from the upper surface of the cap and a cover member disposed over the channel.

[0086] Clause 6: The assembly of clause 1, wherein the cap comprises a channel formed through the cap defining a portion of the fluid conduit between the first portion of the fluid conduit and the second portion of the fluid conduit.

[0087] Clause 7: The assembly of clause 1, further comprising a sealing member disposed between the lower surface of the cap and the dispenser body.

[0088] Clause 8: The assembly of clause 1, wherein the cap is hingably attached to the dispenser body.

[0089] Clause 9: The assembly of clause 8, wherein the cap comprises a first attachment member configured to reversibly engage the dispenser body, and wherein when the assembly is in the second configuration the first attachment member is engaged with the dispenser body.

[0090] Clause 10: The assembly of clause 1, wherein the cap comprises a first attachment member and a second attachment member configured to reversibly engage the dispenser body, and wherein when the assembly is in the second configuration the first attachment member and the second attachment member are engaged with the dispenser body.

[0091] Clause 11: The assembly of clause 10, wherein the first attachment member and the second attachment member are hingably attached to a central portion of the cap.

[0092] Clause 12: The assembly of clause 1, wherein the outlet comprises a valve.

[0093] Clause 13: The assembly of clause 12, wherein the valve is configured to allow flow of fluid through the outlet from the working volume and into the fluid conduit and prevent flow of fluid through the outlet from the fluid conduit and into the working volume.

[0094] Clause 14: The assembly of clause 1, wherein the dispenser body comprises a second interior wall defining a second lumen having a longitudinal axis and a diameter.

[0095] Clause 15: The assembly of clause 14, wherein the second lumen comprises a second piston defining a working volume of the second lumen, and wherein the second piston is movable along the longitudinal axis to change the working volume.

[0096] Clause 16: The assembly of clause 15, wherein the fluid channel is in fluid connection with the working volume of the lumen and the working volume of the second lumen.

[0097] Clause 17: The assembly of clause 1, wherein the dispenser body comprises at least 4-6 lumens, each being defined by a different interior wall of the dispenser body and having a longitudinal axis and a diameter.

[0098] Clause 18: The assembly of clause 17, wherein the diameter of each lumen is the same or different and a length of each lumen is the same or different.

[0099] Clause 19: The assembly of clause 17, wherein each lumen comprises a piston defining a working volume of each lumen, and wherein each piston is movable along the longitudinal axis of each lumen to change the working volume.

[0100] Clause 20: The assembly of clause 19, wherein each lumen comprises an outlet.

[0101] Clause 21: The assembly of clause 20, wherein the fluid channel is in fluid connection with each of the working volumes via the outlet of each lumen, and wherein each outlet is disposed between the first and second portions of the fluid conduit.

[0102] Clause 22: A system comprising: an assembly according to any one of clauses 1-21; and an actuator operable to move the piston along the longitudinal axis thereby decreasing the working volume of the lumen and causing fluid flow from the working volume into the fluid conduit when the assembly is in the second configuration.

[0103] Clause 23: The system of clause 22, wherein the actuator is operable to dispense all, or any portion of the working volume in a single operation.

[0104] Clause 24: The system of clause 23, wherein the actuator is configured to dispense a portion of the working volume in one or more timed intervals.

[0105] Clause 25: The system of clause 22, wherein the assembly comprises a plurality of lumens, and wherein the working volume of each of the plurality of lumens is independently controlled by a separate actuator.

[0106] Clause 26: The system of clause 25, wherein the separate actuators are operable to independently or simultaneously, dispense all, or any portion of their respective working volume in a single operation.

[0107] Clause 27: The system of clause 26, wherein the separate actuators are configured to dispense a portion of their respective working volume in one or more timed intervals.

[0108] Clause 28: The system of clause 22, wherein a first feedline is fluidically coupled to the input port and a second feedline is fluidically coupled to the output port forms a sterile and functionally closed system.

[0109] Clause 29: The system of clause 28, further comprising a cell processing system fluidically coupled to the first feedline and the second feedline.

[0110] Clause 30: The system of clause 22, wherein the input port is fluidically coupled to a fluid source.

[0111] Clause 31: The system of clause 30, wherein the fluid source is liquid.

[0112] Clause 32: The system of clause 30, wherein the fluid source is a gas.

[0113] Clause 33: The system of clause 32, wherein the gas is pressurized.

[0114] Clause 34: The system of clause 33, wherein the gas is pressurized via an inline pump.

[0115] Clause 35: The system of clause 33, wherein the gas is from a vessel containing pressurized gas.

[0116] Clause 36: A method of dispensing a fluid, comprising: an assembly according to any one of clauses 1-21 or the system according to any one of clauses 22-35; loading a fluid into the working volume of the lumen when the assembly is in the first configuration; transitioning the assembly to the second configuration; and advancing the piston along the longitudinal axis of the lumen to cause flow of fluid from the working volume into the fluid conduit.

[0117] Clause 37: The method of clause 36, wherein loading of the fluid is performed under sterile conditions.

[0118] Clause 38: The method of clause 36, further comprising fluidically coupling the first portion of the fluid conduit and the second portion of the fluid conduit to one or more fluid lines before advancing the piston.

[0119] Clause 39: The method of clause 38, wherein fluidically coupling the first portion of the fluid conduit and the second portion of the fluid conduit to the one or more fluid lines forms a sterile and functionally closed system.

[0120] Clause 40: A method of performing a fluidic workflow, comprising: delivering a fluid from the working volume of the assembly according to any one of clauses 1-21, or the system according to any one of clauses 22-35, into a fluid flow contained within a functionally closed system; and performing a fluidic workflow.

[0121] Clause 41: The method of clause 40, wherein the fluid comprises a gene editing reagent and the fluid flow comprises a cell.

[0122] Clause 42: The method of clause 41, wherein the fluidic workflow comprises a cell processing protocol.

[0123] Clause 43: The method of clause 42, wherein the cell processing protocol comprises transformation, transfection, transduction, activation, isolation, separation, imaging, labeling, and/or culturing of the cell, or portion thereof.

[0124] Clause 44: Use of the assembly according to any one of clauses 1-21, or the system according to any one of clauses 22-35, to dispense a fluid into a fluidic workflow.

[0125] Clause 45: Use of the assembly according to any one of clauses 1-21, or the system according to any one of clauses 22-35, in a workflow to generate a genetically modified cell.

[0126] Clause 46: Use of the assembly according to any one of clauses 1-21, or the system according to any one of clauses 22-35, in a workflow to generate a cell or gene therapy.

CLAIMS

What is claimed is:

1. An assembly comprising:

a dispenser body having an interior wall defining a lumen having a longitudinal axis and a diameter;

a cap configured to traverse the diameter of the lumen, the cap having an upper surface and a lower surface;

a piston disposed within the lumen, the piston having a top surface and a bottom surface, the top surface together with the interior wall and the lower surface of the cap defining a working volume of the lumen, wherein the piston is movable along the longitudinal axis to change the working volume;

an outlet in fluid connection with the working volume; and

a fluid conduit extending between a first portion of the fluid conduit and a second portion of the fluid conduit, the fluid conduit being in fluid connection with the working volume via the outlet between the first and second portions of the fluid conduit,

wherein the assembly has a first configuration in which the cap does not traverse the diameter of the lumen and the lumen is fluidically unsealed and a second configuration in which the cap traverses the diameter of the lumen and the lumen is fluidically sealed, and

wherein movement of the piston along the longitudinal axis causes fluid flow through the outlet when the assembly is in the second configuration.

2. The assembly of claim 1, wherein the fluid conduit has an input port adjacent the first portion of the fluid conduit and an output port adjacent the second portion of the fluid conduit, and wherein movement of the piston along the longitudinal axis toward the cap causes fluid to flow from the working volume into the fluid conduit via the outlet when the assembly is in the second configuration.

3. The assembly of claim 2, wherein the input port and the output port are hermetically sealed.

4. The assembly of claim 1, wherein an internal surface of the fluid conduit is defined by a channel formed within a volume of the cap or on the upper surface of the cap between the first portion of the fluid conduit and the second portion of the fluid conduit.
5. The assembly of claim 1, wherein at least a region of the fluid conduit between the first portion of the fluid conduit and the second portion of the fluid conduit is defined by a channel formed from the upper surface of the cap and a cover member disposed over the channel.
6. The assembly of claim 1, wherein the cap comprises a channel formed through the cap defining a portion of the fluid conduit between the first portion of the fluid conduit and the second portion of the fluid conduit.
7. The assembly of claim 1, further comprising a sealing member disposed between the lower surface of the cap and the dispenser body.
8. The assembly of claim 1, wherein the cap is hingably attached to the dispenser body.
9. The assembly of claim 8, wherein the cap comprises a first attachment member configured to reversibly engage the dispenser body, and wherein when the assembly is in the second configuration the first attachment member is engaged with the dispenser body.
10. The assembly of claim 1, wherein the cap comprises a first attachment member and a second attachment member configured to reversibly engage the dispenser body, and wherein when the assembly is in the second configuration the first attachment member and the second attachment member are engaged with the dispenser body.
11. The assembly of claim 10, wherein the first attachment member and the second attachment member are hingably attached to a central portion of the cap.
12. The assembly of claim 1, wherein the outlet comprises a valve.

13. The assembly of claim 12, wherein the valve is configured to allow flow of fluid through the outlet from the working volume and into the fluid conduit and prevent flow of fluid through the outlet from the fluid conduit and into the working volume.
14. The assembly of claim 1, wherein the dispenser body comprises a second interior wall defining a second lumen having a longitudinal axis and a diameter.
15. The assembly of claim 14, wherein the second lumen comprises a second piston defining a working volume of the second lumen, and wherein the second piston is movable along the longitudinal axis to change the working volume.
16. The assembly of claim 15, wherein the fluid channel is in fluid connection with the working volume of the lumen and the working volume of the second lumen.
17. The assembly of claim 1, wherein the dispenser body comprises at least 4-6 lumens, each being defined by a different interior wall of the dispenser body and having a longitudinal axis and a diameter.
18. The assembly of claim 17, wherein the diameter of each lumen is the same or different and a length of each lumen is the same or different.
19. The assembly of claim 17, wherein each lumen comprises a piston defining a working volume of each lumen, and wherein each piston is movable along the longitudinal axis of each lumen to change the working volume.
20. The assembly of claim 19, wherein each lumen comprises an outlet.
21. The assembly of claim 20, wherein the fluid channel is in fluid connection with each of the working volumes via the outlet of each lumen, and wherein each outlet is disposed between the first and second portions of the fluid conduit.

22. A system comprising:
an assembly according to any one of claims 1-21; and
an actuator operable to move the piston along the longitudinal axis thereby decreasing the working volume of the lumen and causing fluid flow from the working volume into the fluid conduit when the assembly is in the second configuration.
23. The system of claim 22, wherein the actuator is operable to dispense all, or any portion of the working volume in a single operation.
24. The system of claim 23, wherein the actuator is configured to dispense a portion of the working volume in one or more timed intervals.
25. The system of claim 22, wherein the assembly comprises a plurality of lumens, and wherein the working volume of each of the plurality of lumens is independently controlled by a separate actuator.
26. The system of claim 25, wherein the separate actuators are operable to independently or simultaneously, dispense all, or any portion of their respective working volume in a single operation.
27. The system of claim 26, wherein the separate actuators are configured to dispense a portion of their respective working volume in one or more timed intervals.
28. The system of claim 22, wherein a first feedline is fluidically coupled to the input port and a second feedline is fluidically coupled to the output port forms a sterile and functionally closed system.
29. The system of claim 28, further comprising a cell processing system fluidically coupled to the first feedline and the second feedline.
30. The system of claim 22, wherein the input port is fluidically coupled to a fluid source.

31. The system of claim 30, wherein the fluid source is liquid.
32. The system of claim 30, wherein the fluid source is a gas.
33. The system of claims 32, wherein the gas is pressurized.
34. The system of claim 33, wherein the gas is pressurized via an inline pump.
35. The system of claim 33, wherein the gas is from a vessel containing pressurized gas.
36. A method of dispensing a fluid, comprising:
 - an assembly according to any one of claims 1-21;
 - loading a fluid into the working volume of the lumen when the assembly is in the first configuration;
 - transitioning the assembly to the second configuration; and
 - advancing the piston along the longitudinal axis of the lumen to cause flow of fluid from the working volume into the fluid conduit.
37. The method of claim 36, wherein loading of the fluid is performed under sterile conditions.
38. The method of claim 36, further comprising fluidically coupling the first portion of the fluid conduit and the second portion of the fluid conduit to one or more fluid lines before advancing the piston.
39. The method of claim 38, wherein fluidically coupling the first portion of the fluid conduit and the second portion of the fluid conduit to the one or more fluid lines forms a sterile and functionally closed system.
40. A method of performing a fluidic workflow, comprising:

delivering a fluid from the working volume of the assembly according to any one of claims 1-21 into a fluid flow contained within a functionally closed system; and performing a fluidic workflow.

41. The method of claim 40, wherein the fluid comprises a gene editing reagent and the fluid flow comprises a cell.

42. The method of claim 41, wherein the fluidic workflow comprises a cell processing protocol.

43. The method of claim 42, wherein the cell processing protocol comprises transformation, transfection, transduction, activation, isolation, separation, imaging, labeling, and/or culturing of the cell, or portion thereof.

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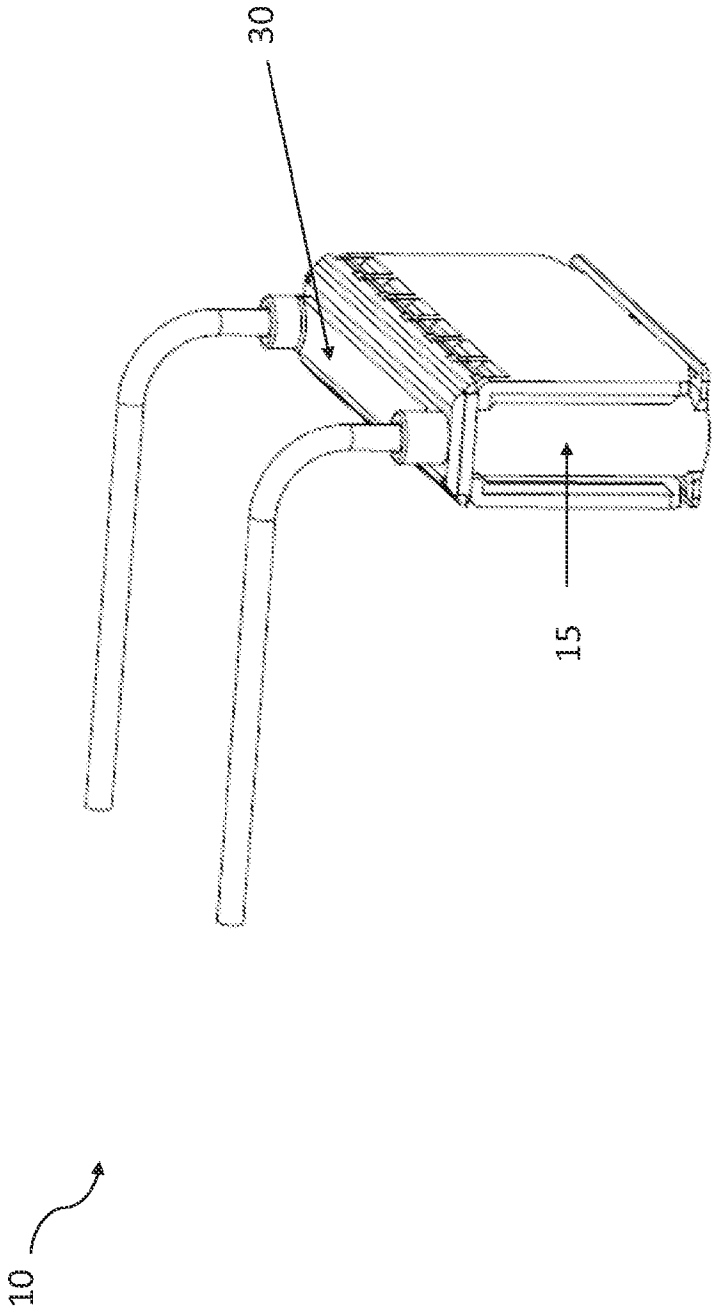


FIG. 1

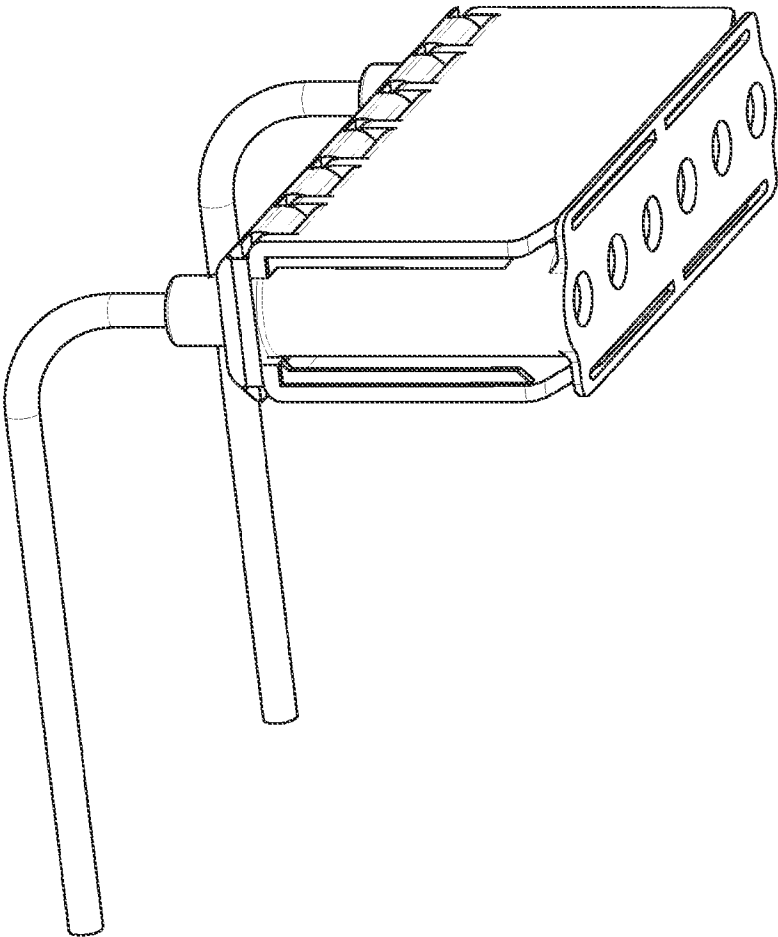


FIG. 2

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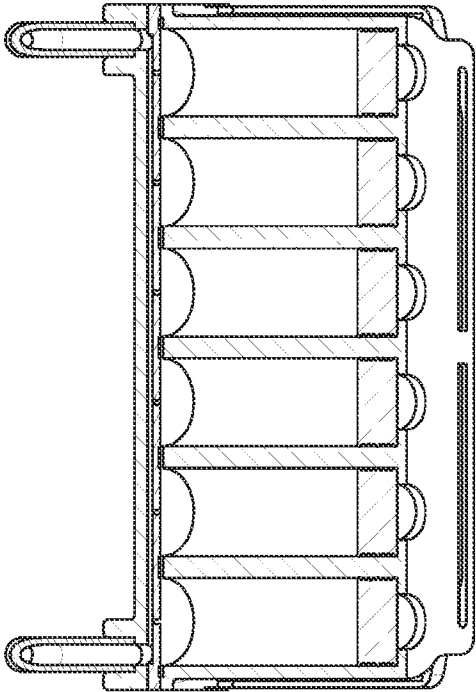


FIG. 3

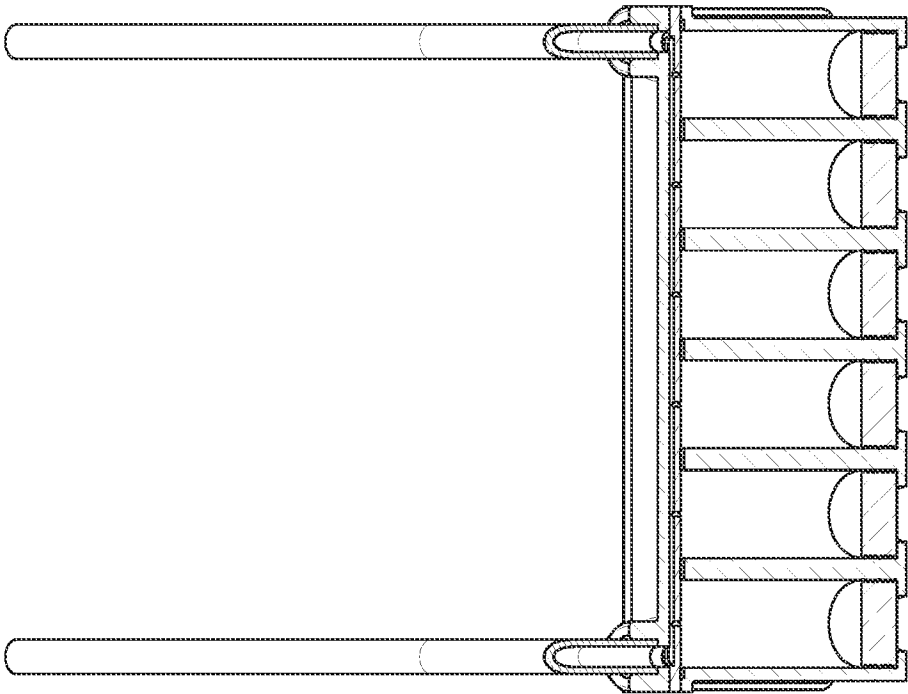
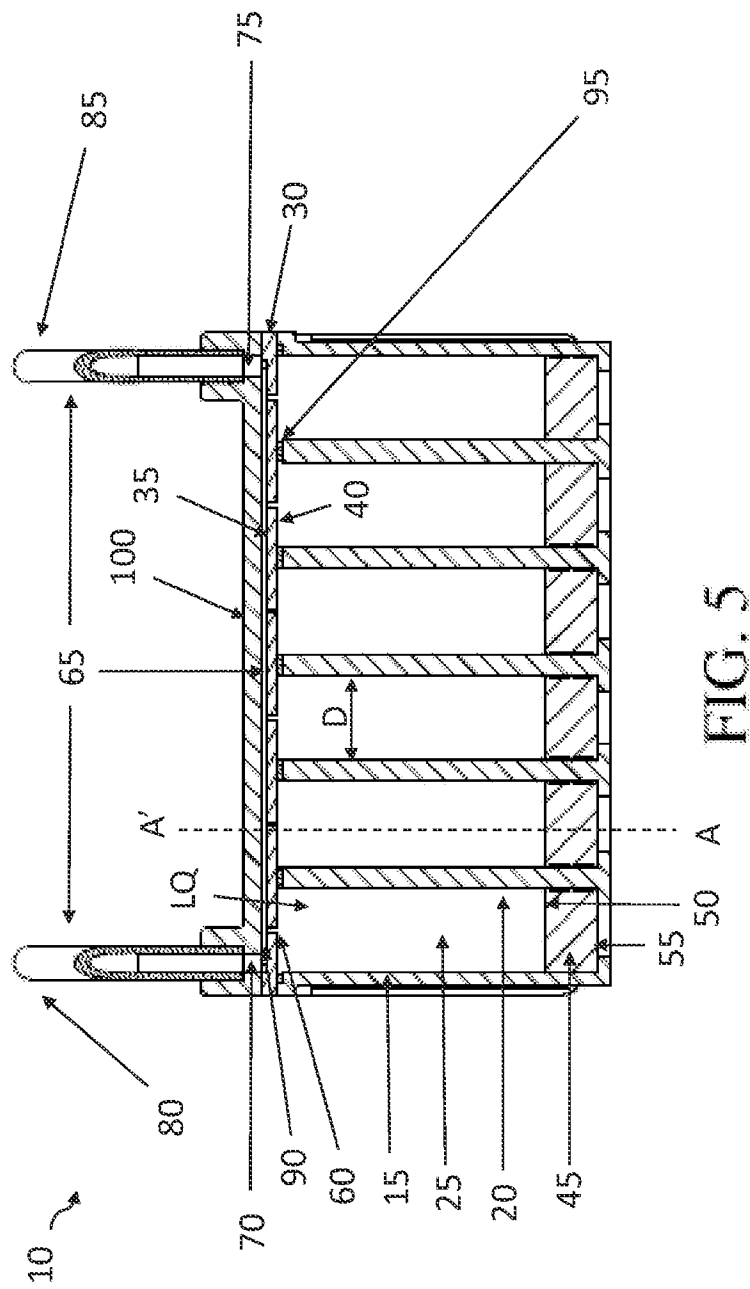


FIG. 4



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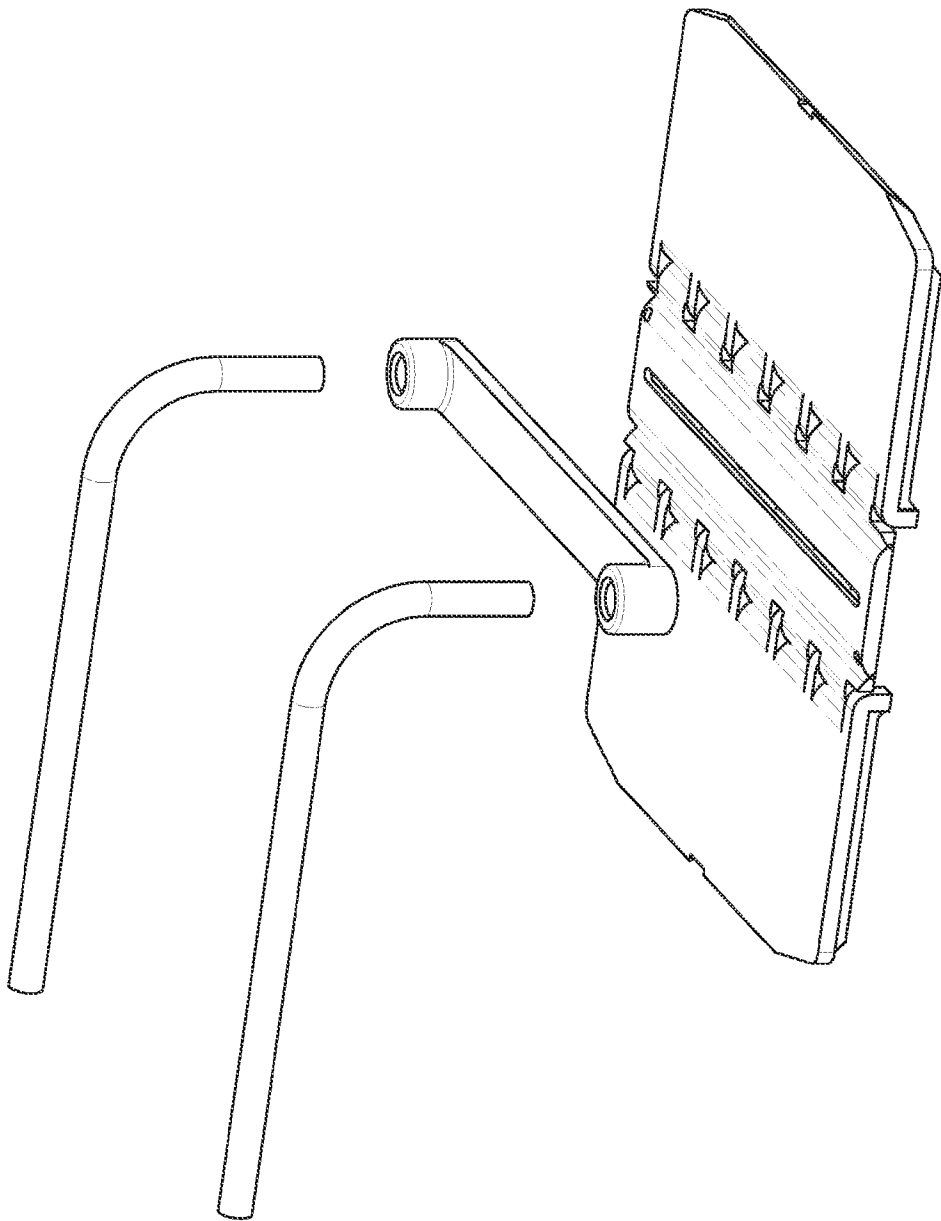


FIG. 6

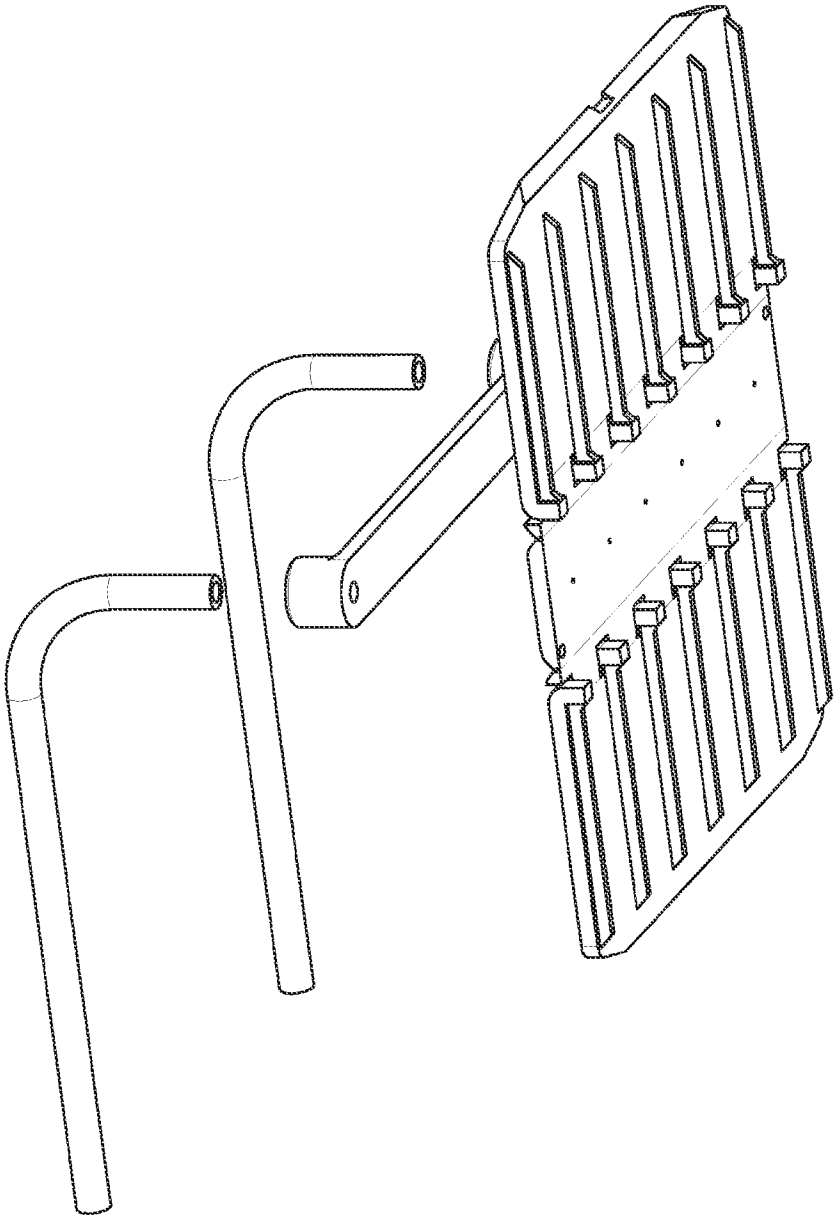


FIG. 7

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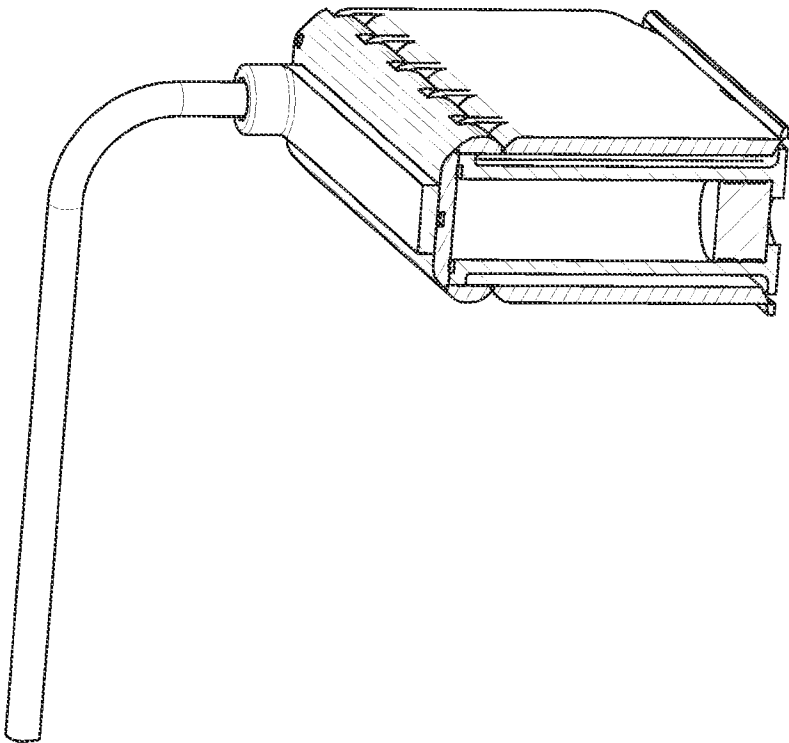


FIG. 8

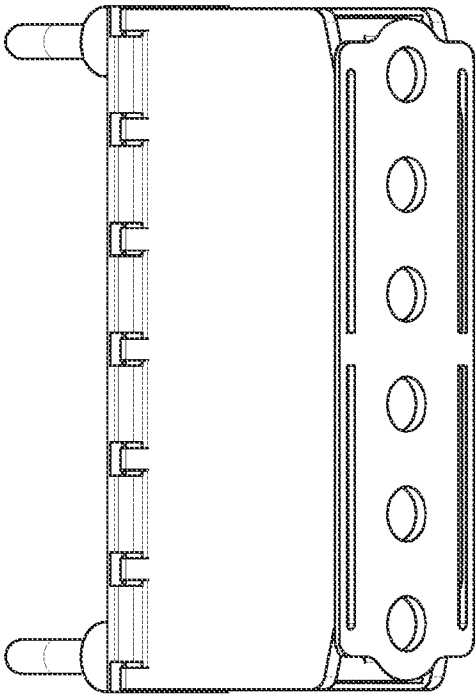


FIG. 9

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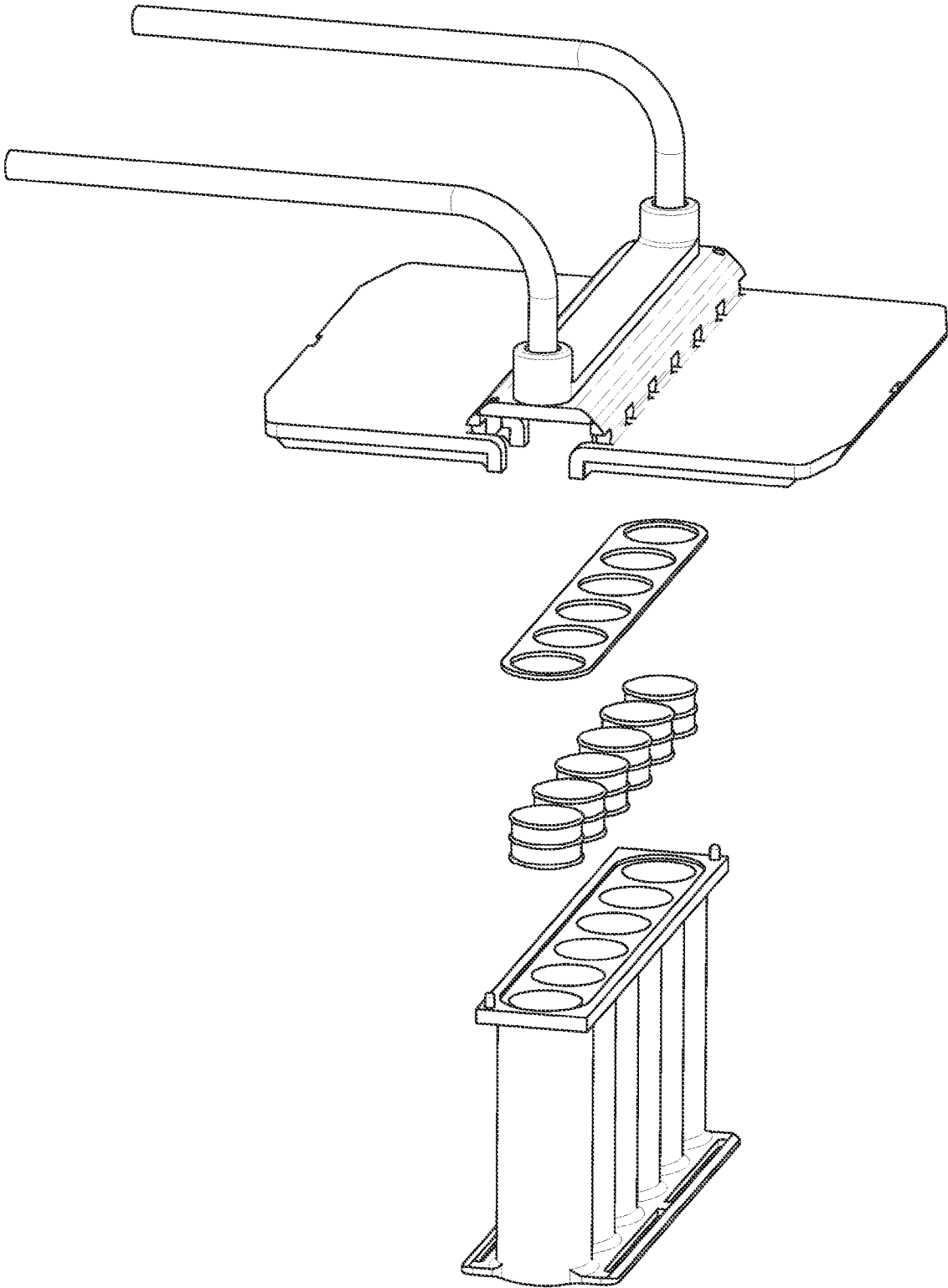


FIG. 10

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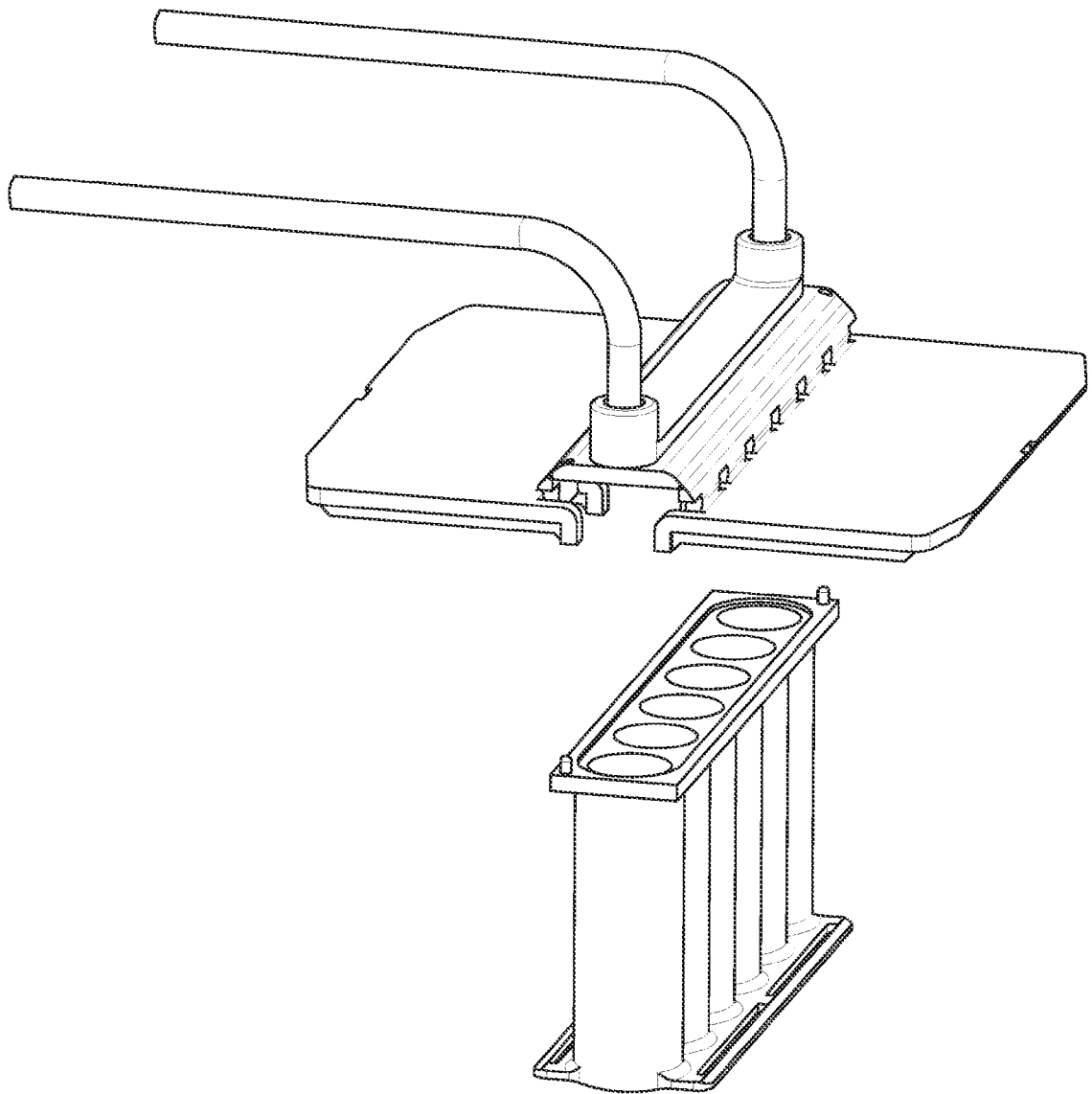


FIG. 11

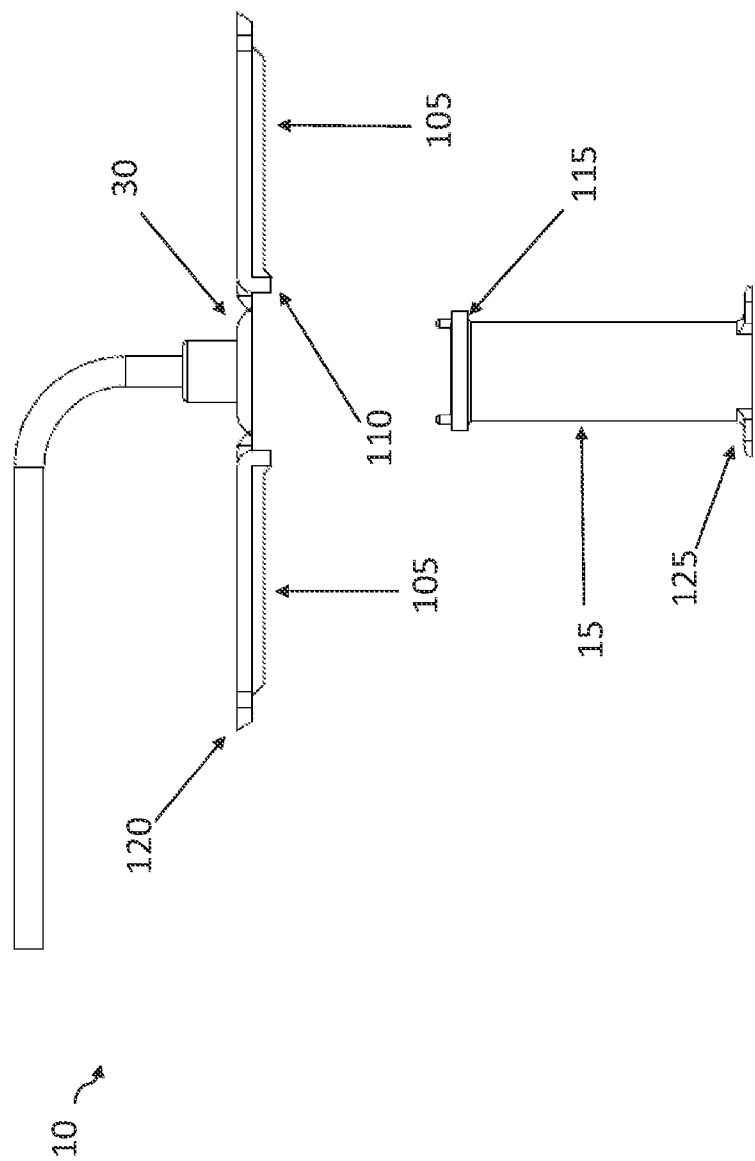


FIG. 12

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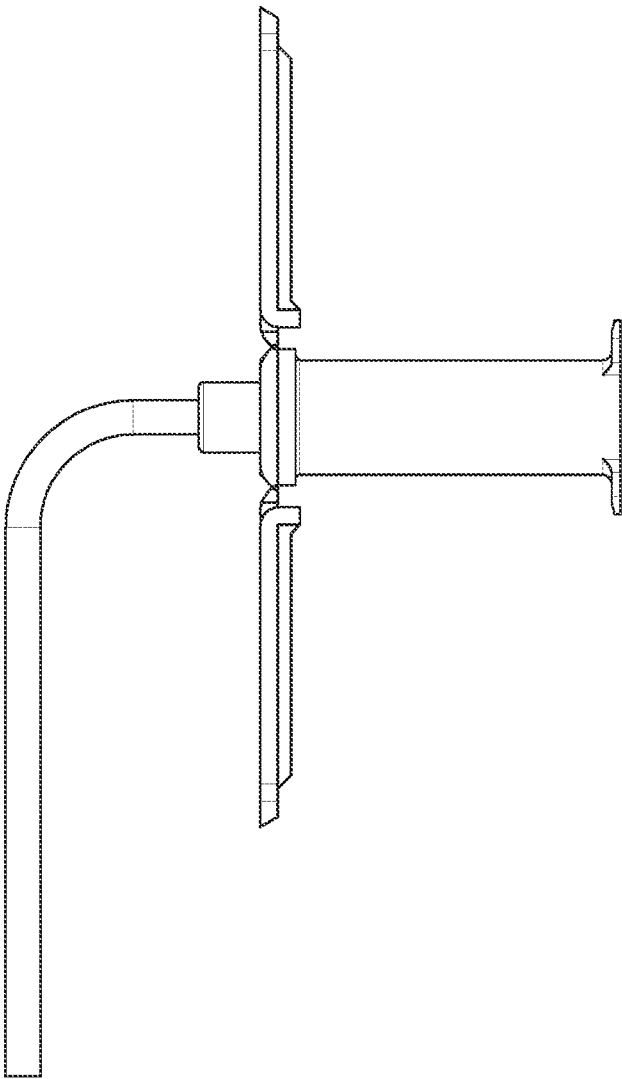


FIG. 13

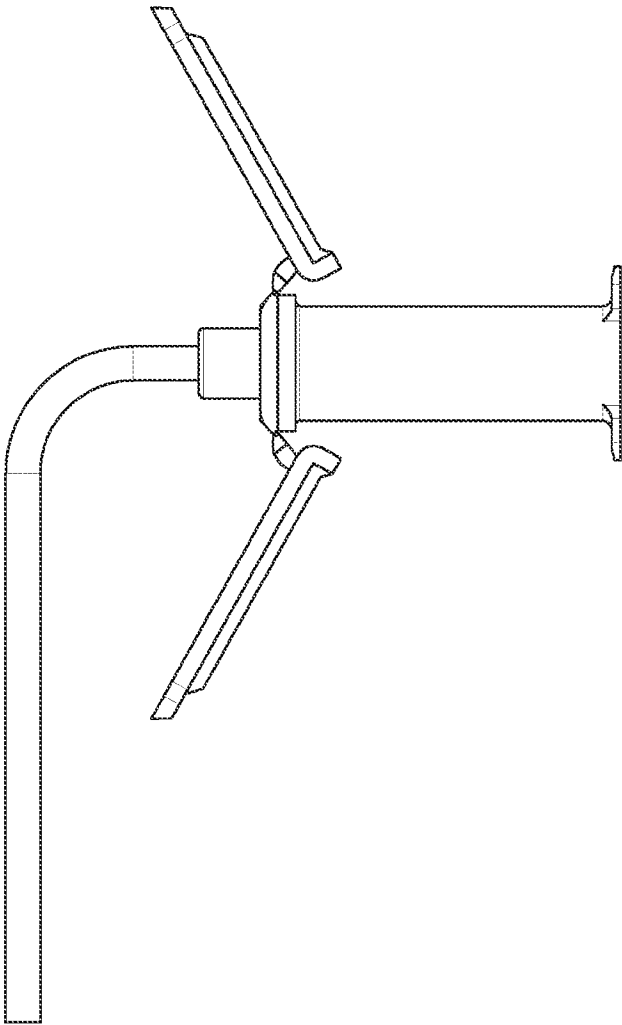


FIG. 14

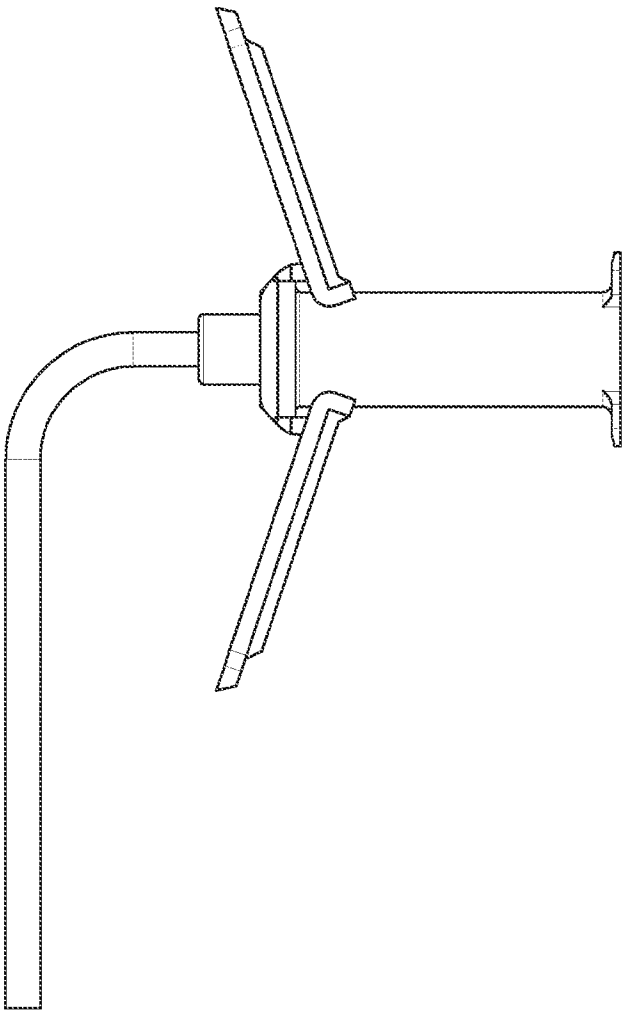


FIG. 15

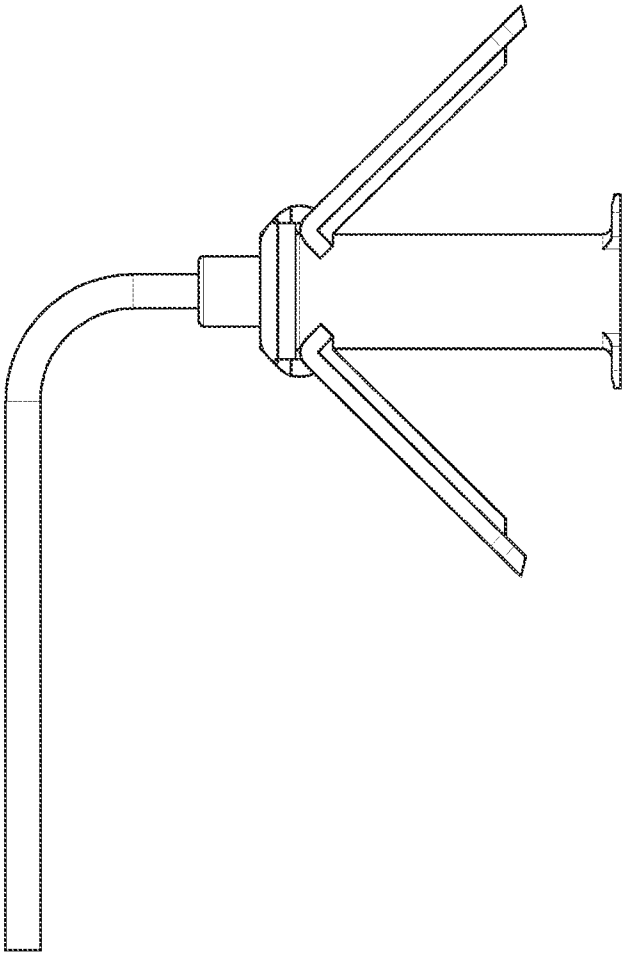


FIG. 16

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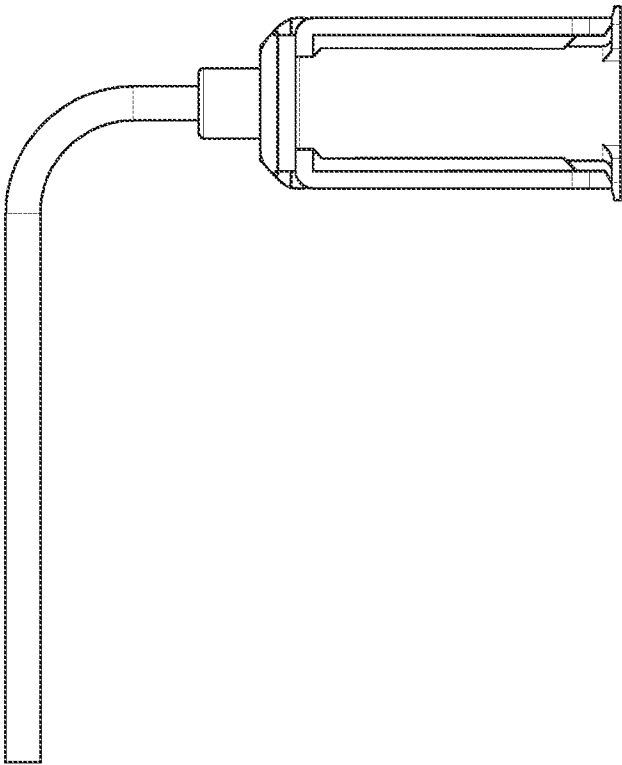


FIG. 17

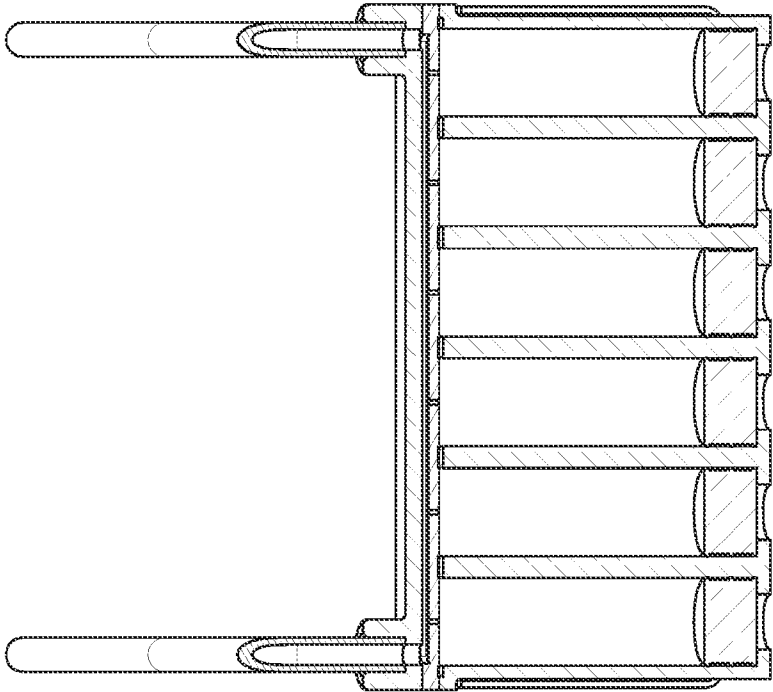


FIG. 18

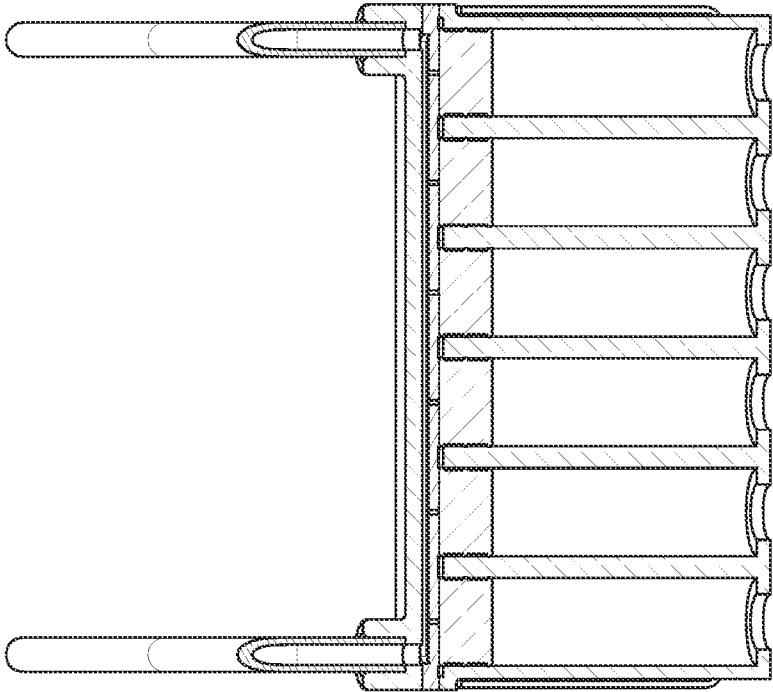


FIG. 19

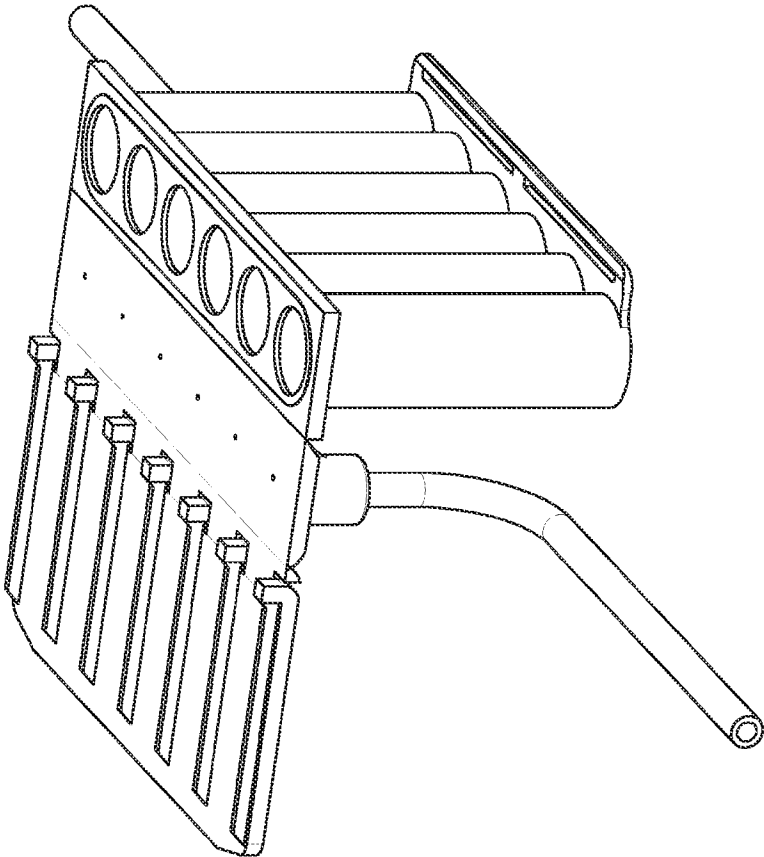


FIG. 20

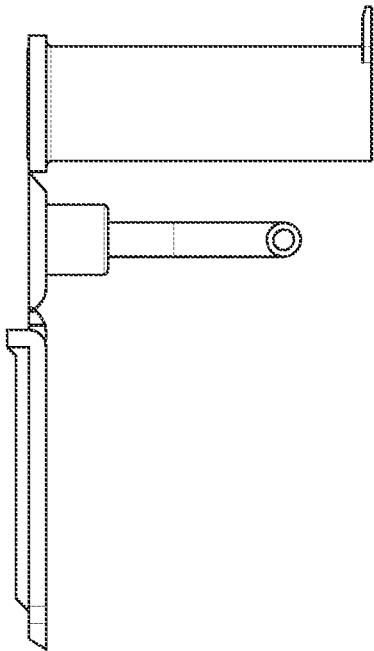


FIG. 21

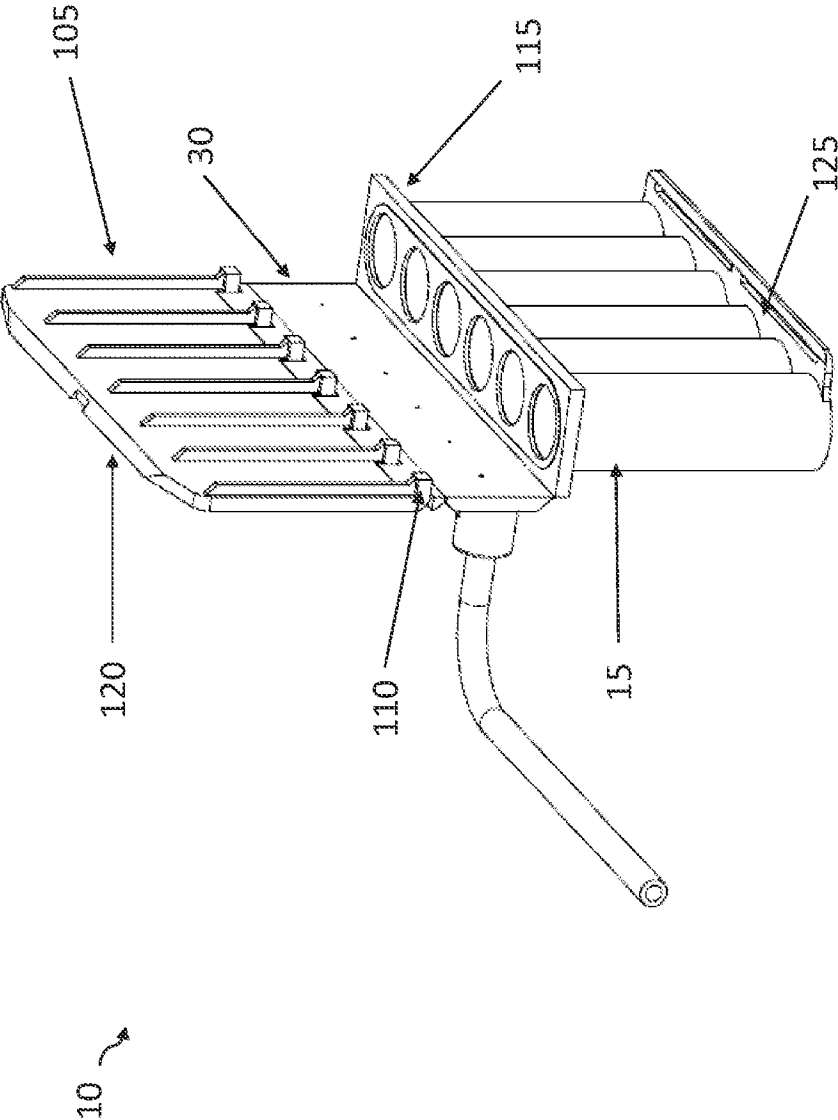


FIG. 22

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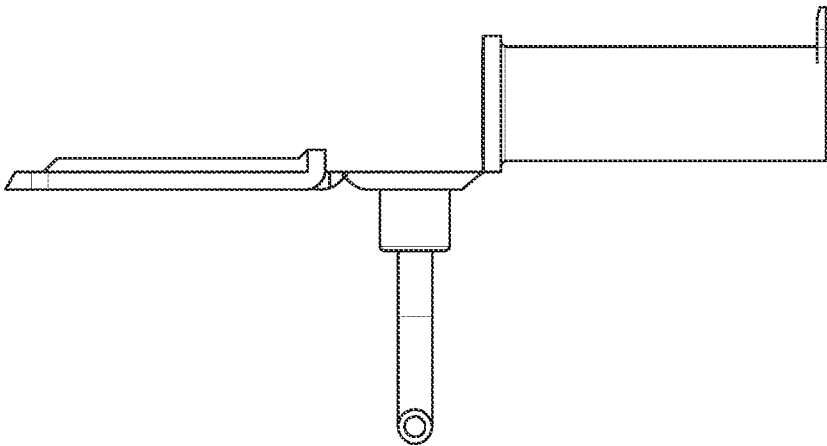


FIG. 23

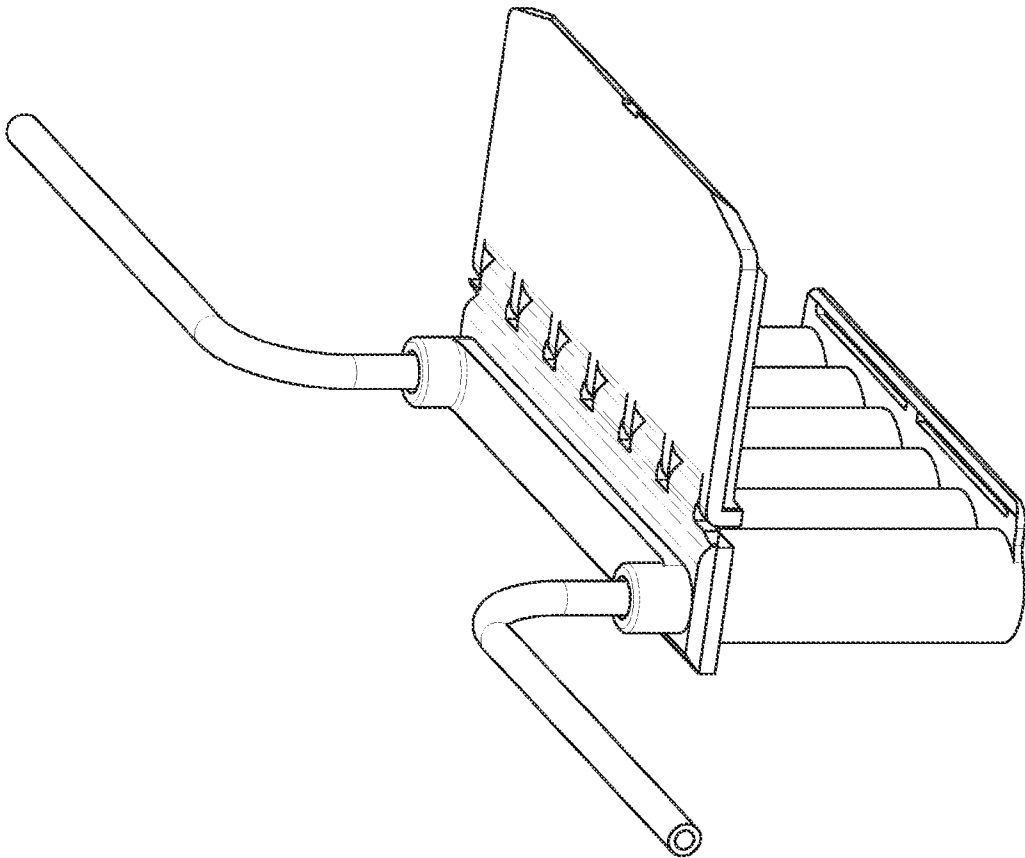


FIG. 24

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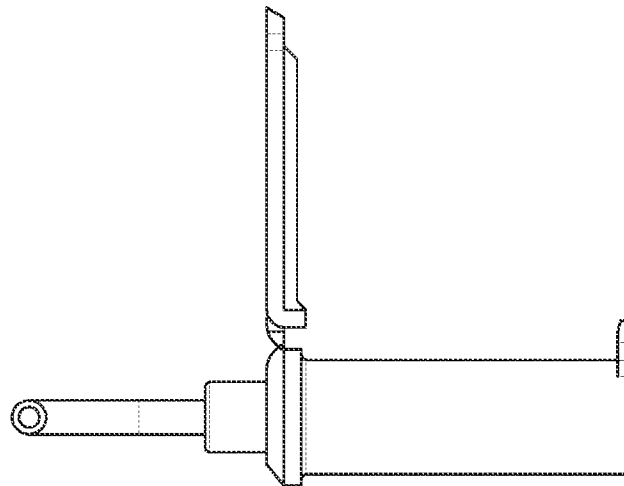


FIG. 25

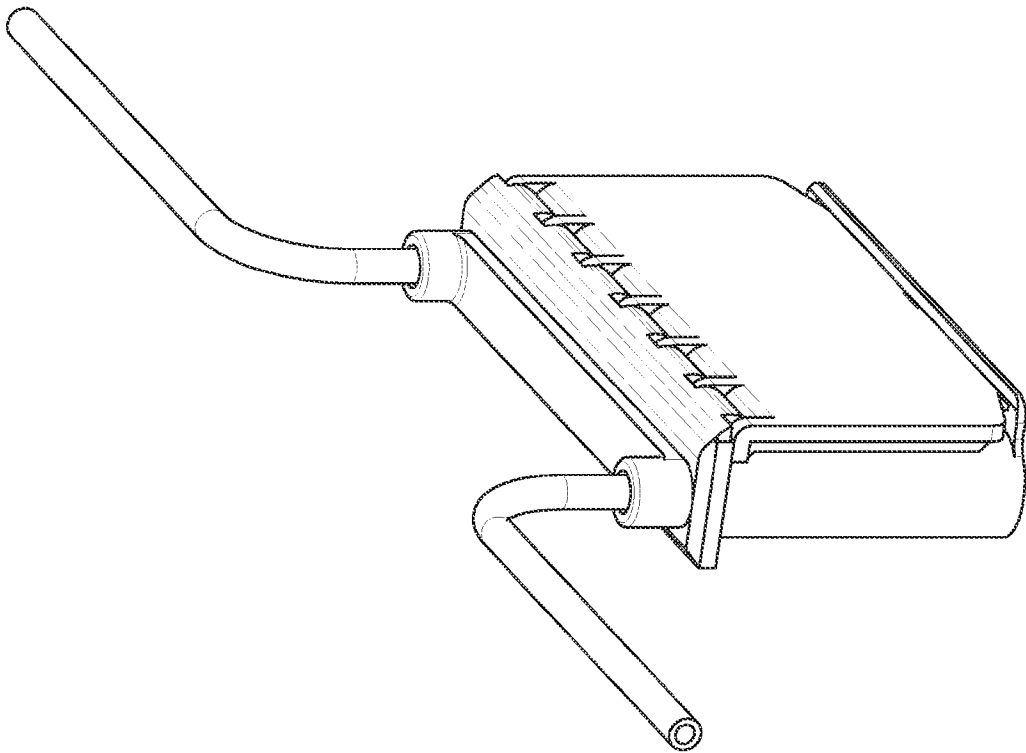


FIG. 26

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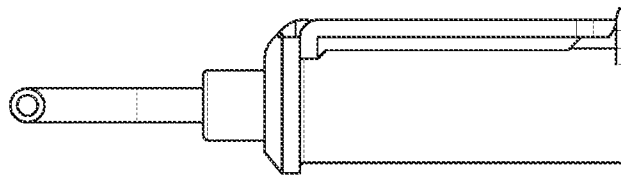


FIG. 27

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2024/035522

A. CLASSIFICATION OF SUBJECT MATTER

INV.	A61M5/14	A61J1/14	A61M5/19	A61M5/24	A61M5/20
	A61M5/31	A61M39/00	B01L3/00	C12M1/00	A61J1/05
	A61M5/168	A61M5/145	A61M39/20		

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

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

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

EPO-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2011/015640 A1 (HESS BRIAN J [US] ET AL) 20 January 2011 (2011-01-20) paragraph [0052] - paragraph [0055]; figure 3 -----	1,6-11, 22-24,36
X	US 2012/175384 A1 (GRETER ANDY [CH] ET AL) 12 July 2012 (2012-07-12) paragraph [0047] - paragraph [0050]; figure 3 paragraph [0027] -----	1,6-11, 14-24, 36,37
X	US 2017/143908 A1 (EGGERT ILONA [DE] ET AL) 25 May 2017 (2017-05-25) paragraph [0096] - paragraph [0102]; figure 10 ----- -/-	1,6-27, 31-38



Further documents are listed in the continuation of Box C.



See patent family annex.

* Special categories of cited documents:

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

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

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

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

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

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

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

"&" document member of the same patent family

Date of the actual completion of the international search

23 September 2024

Date of mailing of the international search report

04/10/2024

Name and mailing address of the ISA/

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040,
Fax: (+31-70) 340-3016

Authorized officer

Strömsdörfer, Daniel

INTERNATIONAL SEARCH REPORT

International application No

PCT/US2024/035522

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 2005/113763 A1 (REYNOLDS DAVID L [CA]) 26 May 2005 (2005-05-26) paragraph [0082] - paragraph [0083]; figures 1e-1f -----	1, 36
A	US 2014/224829 A1 (CAPONE CHRISTOPHER D [US] ET AL) 14 August 2014 (2014-08-14) paragraph [0131]; figures 1-10 -----	1-43

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/US2024/035522

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