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(54) Title: MULTI-TIERED PIPETTE TIP HOLDER AND EJECTION MECHANISM FOR A DYNAMIC BROAD VOLUMETRIC RANGE PIPETTE

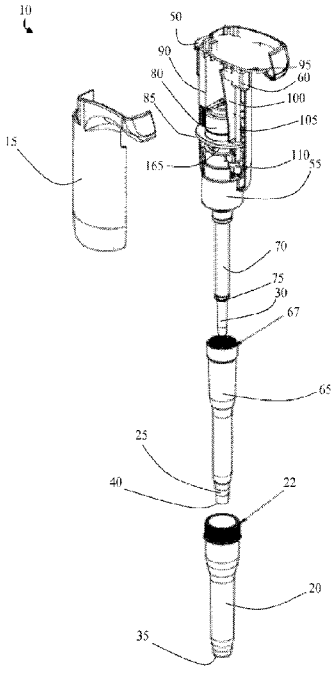


FIG. 3A

(57) Abstract: Broad volumetric range pipettes with multi-tiered pipette tip holder and ejection assemblies and methods of using such pipettes are disclosed herein. These pipettes typically include a concentric cylinder arrangement with each outer cylinder configured for contacting and dislodging a pipette tip attached to the tip holder portion of the immediately adjacent inner cylinder. In this manner, different sized pipette tips can be used on a single device. In addition, a locking mechanism is described for locking the large tip holder into a downward position to minimize the extension of the small tip holder and thereby enabling attachment of large, filtered pipette tips and reducing/eliminating the risk that the liquid being transferred will contaminate the pipetting device.

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MULTI-TIERED PIPETTE TIP HOLDER AND EJECTION MECHANISM FOR A DYNAMIC BROAD VOLUMETRIC RANGE PIPETTE

CROSS-REFERENCE TO RELATED APPLICATIONS

This application claims the benefit of the filing date of U.S. Provisional Application No. 63/402,858, filed August 31, 2022, the entire contents of which is incorporated by reference herein.

FIELD OF THE INVENTION

The present invention generally relates to pipetting devices capable of dispensing liquids across a broad range of volumes. In particular, described herein is pipetting device with a multi-tiered pipette tip holder design and concentric cylinder ejection mechanism to enable the use of pipette tips of different sizes on a single device.

BACKGROUND OF THE INVENTION

Pipettes and other similar liquid dispensing devices are commonly used in laboratories and in field research for dosage of liquids. Typical pipettes include a piston movable in a cylinder and serving to aspire liquid into and dispense liquid from a disposable pipette tip attached to the dispensing end of the pipette. The liquid volume is usually adjustable. The piston is moved by manual actuation (*e.g.*, force applied to a button) or by means of an electric motor and an associated control system. Electronic pipettes have a control system and associated user interface for setting, *e.g.*, the volume and other necessary pipette functions and for giving commands for performing operations. When the desired function has been selected and the volume and other settings have been entered, depression of an operating switch automatically carries out the actuation of the piston.

Pipettes are commonly used to dispense volumes of liquids that are generally less than about 1 mL and in the range from about 0.5 µl to about 1 mL. However, as will be understood by the skilled artisan, current pipette technology does not allow dispensing liquid volumes across this entire range using a single fluid displacement device — at least not without sacrificing

accuracy and precision. Typical wet lab work requiring the dispensing of liquids across this range will require the use of three to four different pipetting devices, each optimized for accurate and precise aspiration/dispensing of a subset of this volumetric range. For instance, a researcher will commonly use a 20 µl pipette for dispensing fluid volumes ranging from about 2 µl to about 20 µl, a 200 µl pipette for dispensing fluid volumes ranging from about 20 µl to about 200 µl, and a 1,000 µl pipette for dispensing fluid volumes ranging from about 100 µl to about 1,000 µl. Moreover, each pipette will have a tip holding portion with an outer circumferential diameter particularly suitable for the attachment of disposable pipette tips of a certain size (and volumetric capacity). Having to use multiple devices leads to cluttering of the work area and drives up costs. As such, not only must pipetting devices be designed for accurate volumetric range aspiration of liquids, but such a pipette will need to be able to accommodate pipette tips of different sizes to achieve accurate and precise broad volumetric range capabilities in a single device.

There is a need, therefore, for a single pipetting device capable of using pipette tips of different sizes to ensure accuracy and precision of transferring liquids across a broad range of volumes.

SUMMARY OF THE INVENTION

Described herein is a broad volumetric range pipetting device with a multi-tiered pipette tip holder and concentric cylinder pipette tip ejection design. In particular, the device disclosed herein preferably employs a dispensing unit portion comprised of two or more cylindrical housings disposed over the chamber cylinder that contains the piston and vacuum chamber. Each cylinder or cylindrical housing will taper slightly near the bottom end, and each cylinder will preferably have an inner diameter that is at least slightly larger than the outer circumferential diameter of the adjacent cylinder over which it is disposed (*i.e.*, a concentric arrangement) and be configured for movement along the axis of the adjacent inner cylinder (*i.e.*, movement up and down in relation to the adjacent inner cylinder). In addition, the inner cylinders will tend to extend beyond the bottom edge of the adjacent outer cylinder to provide for a pipette tip attachment surface. In this manner, the concentric arrangement of cylinders provides for a multi-tiered pipette tip holder surface for attachment of pipette tips having different sizes – the cylinders with the smaller outer circumferential diameters configured for attachment of smaller

pipette tips, and the cylinders with the larger outer circumferential diameters configured for attachment of larger pipette tips. Further, the bottom edge of each outer cylinder can contact and dislodge a pipette tip attached to the tip holding portion of the adjacent inner cylinder over which it is disposed. Further, the pipetting device will include an ejector element that can be used to apply force to the concentric cylinders and eject the pipette tips. In some embodiments, the pipetting device also includes a locking mechanism to prevent contamination of the dispensing end when certain pipette tips are being used.

In one aspect, the invention features a pipette with a multi-tiered pipette tip holder and ejection mechanism. The device includes a pipette body with an upper drive unit section and a lower dispensing section. On the lower dispensing section is a small tip holder portion and a chamber cylinder with a fluid inlet to enable fluid to be drawn into the chamber cylinder or discharged therefrom. The device also includes an ejection assembly comprising an ejector element, ejection rod, a first dispenser cylinder having a large tip holder portion and a small tip ejection edge, and a second dispenser cylinder having a large tip ejection edge. The first dispensing cylinder is disposed over the chamber cylinder and configured to move up and down in relation to the chamber cylinder, while the second dispensing cylinder is disposed over the first dispensing cylinder and configured to move up and down in relation to the first dispensing cylinder. In this aspect, the ejection rod is configured to contact the second dispensing cylinder and move the second dispensing cylinder to a first position wherein the large tip ejection edge contacts and ejects a large pipette tip from the large tip holder portion when a first force is applied to the ejector element, or cause the first dispensing cylinder to move to a second position wherein the small tip ejection edge contacts and ejects a small pipette tip from the small tip holder portion with a second force is applied to the ejector element. In an embodiment, the fluid is air.

In one embodiment, the pipette further includes a biasing element disposed circumferentially around a portion of the ejection rod and configured to bias the ejection rod in an upwards position. In another embodiment, the large tip holder portion has an outer diameter that is greater than the outer diameter of the small tip holder portion. In a preferred embodiment, the ejector element is disposed on the upper drive unit section.

In some embodiments, the pipette includes a first ejector member connected to the first dispensing cylinder, and both a second ejector member and the ejection rod connected to the

second dispensing cylinder such that the second ejector member can contact and move the first ejector member to the second position when the second force is applied to the ejector element. In another embodiment, the first ejector member and second ejector member are positioned within the upper drive unit section with the first dispensing cylinder and second dispensing cylinder forming part of the lower dispensing section.

In some aspects, the pipette also includes a piston slidably positionable within the chamber cylinder between an open position and a closed position, and a motor disposed within the upper drive unit portion and operably connected to the piston and configured to actuate the piston between the open position and the closed position within the chamber cylinder. Accordingly, the actuation of the piston to the open position defines a liquid volume to be aspirated by the pipette in an amount approximately equivalent to a fluid volume displaced by the movement of the piston. In yet other embodiments, the small tip holder portion is configured for attachment of a pipette tip having a maximum liquid capacity in the range from about 2 µl to about 200 µl; preferably, about 20 µl to about 200 µl. In still other embodiments, the large tip holder portion is configured for attachment of a pipette tip having a maximum liquid capacity in the range from about 200 µl to about 5,000 µl; preferably, about 200 µl to about 1,000 µl.

In another embodiment, the pipette further includes a locking mechanism comprising a trigger, biasing element, and locking rod movable between a locking position and unlocking position. The movement of the second dispensing cylinder and first dispensing cylinder to the second position causes the locking rod to move to the locking position and prevent upwards movement of the first dispensing cylinder. Further, the force applied to the trigger against the biasing element causes the locking rod to move to the unlocking position whereby the locking rod no longer prevents upwards movement of the first dispensing cylinder. In one embodiment, the locking rod contacts a bottom side of the trigger when in the locking position.

In other embodiments, the pipette further includes a printed control board for controlling the motor in response to an end-user volume input and a sensor in electronic communication with a printed control board. In this embodiment, the sensor is configured to detect when the first dispensing cylinder is unlocked and prevents the motor from causing the piston to move upwards to the open position to the extent that it defines a liquid volume to be aspirated by the pipette that exceeds the maximum liquid capacity of a small pipette tip. The sensor can also detect when the first dispensing cylinder is locked and allows the motor to cause the piston to

move upwards to the open position to the extent that it defines a liquid volume to be aspirated by the pipette that exceeds the maximum liquid capacity of a small pipette tip.

Another aspect of the invention features a method of replacing a pipette tip on the pipette described above that includes the step of applying force to the ejector element until the small tip ejection edge contacts and dislodges the small pipette tip from the small tip holder portion or applying force to the ejector element until the large tip ejection edge contacts and dislodges the large pipette tip from the large tip holder portion, depending on whether a small pipette tip or a large pipette tip is attached to the corresponding tip holder portion. In one embodiment, the method includes the step of inserting the small tip holder portion into a pipette receiving end of a small pipette tip so as to create an interference fit. In another embodiment, the method includes the step of inserting the large tip holder portion into a pipette receiving end of a large pipette tip so as to create an interference fit. In yet another embodiment, the method includes the step of holding the trigger down when applying force to the ejector element.

Another aspect of the invention features a pipetting device with a multi-tiered pipette tip holder and ejection mechanism that includes an elongated pipette body comprising an air inlet at a dispensing end, an ejector element, and a concentric cylinder assembly. The concentric cylinder assembly includes a chamber cylinder in fluid communication with the fluid inlet, a small tip ejection cylinder having a small tip ejection edge and a large tip holder portion, and a cylindrical dispenser housing having a large tip ejection edge. Further, the chamber cylinder is concentrically received within the small tip ejection cylinder, the small tip ejection cylinder is concentrically received within the cylindrical dispenser housing and configured to move up and down in relation to the chamber cylinder, and the cylindrical dispenser housing is configured to move up and down in relation to the small tip ejection cylinder. In this aspect, the pipetting device also includes an ejection rod in mechanical communication with the ejector element and configured to cause the cylindrical dispenser housing to move to a first position wherein the large tip ejection edge contacts and ejects a large pipette tip from the large tip holder portion when a first force is applied to the ejector element, or cause the small tip ejection cylinder to move to a second position wherein the small tip ejection edge contacts and ejects a small pipette tip from the small tip holder portion with a second force is applied to the ejector element.

In one embodiment, the pipetting device also includes a first ejection member connected to the small tip ejection cylinder, and a second ejection member connected to the ejection rod

and to the cylindrical dispenser housing. As such, the ejection rod moves the second ejection member and the cylindrical dispenser housing to the first position when a first force is applied to the ejector element, or the ejection rod causes the second ejection member to contact and move the first ejection member and small tip ejection cylinder to the second position when the second force is applied to the ejector element. In another embodiment, the pipetting device includes a locking mechanism comprising a trigger, biasing element, and locking rod movable between a locking and unlocking position. The movement of the cylindrical dispenser housing and small tip ejection cylinder to the second position causes the locking rod to move to the locking position and prevent upwards movement of the small tip ejection cylinder.

In another embodiment, force applied to the trigger against the biasing element causes the locking rod to move to the unlocking position whereby the locking rod no longer prevents upwards movement of the small tip ejection cylinder. In yet another embodiment, the locking rod contacts a bottom side of the trigger when in the locking position.

In some embodiments, the pipetting device includes a piston slidably positionable within the chamber cylinder between an open position and a closed position and a motor operably connected to the piston and configured to actuate the piston between the open position and the closed position within the chamber cylinder. As such, the actuation of the piston to the open position defines a liquid volume to be aspirated by the pipette in an amount approximately equivalent to a fluid volume displaced by the movement of the piston. In one embodiment, the motor is mechanically connected to a threaded piston, wherein the threaded piston is connected to the piston by one or more magnets. In another embodiment, the pipetting device may include a printed control board for controlling the motor in response to an end-user volume input and a sensor in electronic communication with a printed control board, such that the sensor detects: (i) when the small tip ejection cylinder is unlocked and prevents the motor from causing the piston to move upwards to the open position to the extent that it defines a liquid volume to be aspirated by the pipette that exceeds the maximum liquid capacity of a small pipette tip; and/or (ii) when the small tip ejection cylinder is locked and allows the motor to cause the piston to move upwards to the open position to the extent that it defines a liquid volume to be aspirated by the pipette that exceeds the maximum liquid capacity of a small pipette tip.

Other features and advantages of the invention will be apparent by reference to the drawings, detailed description, and examples that follow.

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. 1 depicts a side view of an embodiment of the pipetting device described herein.

FIG. 2A depicts a side view of an embodiment of the pipetting device with the locking mechanism disengaged for small pipette tip attachment.

FIG. 2B depicts a side view of an embodiment of the pipetting device with the locking mechanism engaged for large pipette tip attachment.

FIG. 2C depicts a close-up view of the pipette dispensing end with the locking mechanism disengaged for small pipette tip attachment.

FIG. 2D depicts a close-up view of a small pipette tip attached to the small tip holder portion.

FIG. 2E depicts a close-up view of the pipette dispensing end with the locking mechanism engaged for large pipette tip attachment.

FIG. 2F depicts a close-up view of a large pipette tip attached to the large tip holder portion of the large tip cylinder.

FIG. 2G depicts an internal view of an exemplary ejection mechanism and locking mechanism with the locking mechanism disengaged.

FIG. 2H depicts an internal view of an exemplary ejection mechanism and locking mechanism with the locking mechanism engaged.

FIG. 2I depicts a bottom perspective internal view of an exemplary ejection mechanism and locking mechanism with the locking mechanism engaged.

FIG. 3A is an exploded view of an exemplary pipetting device.

FIG. 3B is an exploded view of an exemplary pipetting device.

FIG. 3C is an exploded view of the drive unit of an exemplary pipetting device.

FIG. 3D is an exploded view of the drive unit of an exemplary pipetting device.

FIG. 3E is an exploded view of the drive unit of an exemplary pipetting device.

FIG. 3G is an exploded view of the drive unit of an exemplary pipetting device.

FIG. 4 is a cross-sectional diagram depicting an exemplary pipetting device.

FIG. 5A is a cross-section diagram depicting an alternative embodiment of the locking mechanism.

FIG. 5B is a perspective view of the alternative locking mechanism.

DETAILED DESCRIPTION OF THE INVENTION

The pipetting devices described herein utilize a multi-tiered pipette tip holder and ejection assembly to enable the use of different sized pipette tips with a single pipette, which, in turn, enables the accurate and precise transfer of a large range of liquid volumes. The multi-tiered pipette tip holder and ejection assembly includes a dispensing unit with a nested, concentric cylinder design. In general, the innermost cylinder will typically be a chamber cylinder containing the vacuum chamber and piston for causing the aspiration of liquids. Connected to the bottom (or integral with the chamber cylinder) will be the dispensing end of the pipetting device, which would also include the small tip holder portion. Next, two or more cylinders will be disposed over the chamber cylinder and small tip holder portion in a concentric arrangement with inner cylinder extending beyond the bottom edge of the immediately adjacent outer cylinder to provide a pipette tip attachment portion or surface. As such, it is preferable that each adjacent outer cylinder have an inner diameter that is slightly larger than the outer circumferential diameter of the adjacent inner cylinder. Moreover, each outer cylinder will be configured to move up and down in relation to the immediately adjacent inner cylinder, and each outer cylinder will preferably have a bottom edge to serve as an ejection edge to dislodge a pipette tip from the tip holder portion of the immediately adjacent inner cylinder.

An ejector element and rod mechanism may be incorporated to enable the end-user to manually or, via a motor-controlled actuator mechanism, apply downward force on one or more of the ejector cylinders to eject a small or large pipette tip. In this manner, the multi-tiered, concentric cylinder design enables the use of both small and large pipette tips on a single pipetting device and allows ease of ejection from the multi-tiered pipette tip attachment portion. Further, a locking mechanism can be incorporated into the design to maintain the large tip holder cylinder in the downward position and reduce the extension of the small tip holder beyond the small tip ejection edge of the large tip holder cylinder thereby enabling attachment of a large pipette tip while minimizing or eliminating the potential for contamination with the liquid being aspirated. The pipetting device and ejection assembly is described in detail below.

Unless defined otherwise, all technical and scientific terms used herein have the same meaning as those commonly understood by one of ordinary skill in the art to which this invention belongs. Standard techniques are used unless otherwise specified. Although methods and materials similar or equivalent to those described herein can be used in the practice or testing of

the present disclosure, suitable methods and materials are described below. The materials, methods and examples are illustrative only, and are not intended to be limiting. All publications, patents and other documents mentioned herein are incorporated by reference in their entirety.

As used herein, the singular forms "a," "an," and "the" include the plural referents unless the context clearly indicates otherwise.

The term "about" refers to the variation in the numerical value of a measurement, *e.g.*, diameter, area, length, volume, etc., due to typical error rates of the device used to obtain that measure. In one embodiment, the term "about" means within 5% of the reported numerical value.

The term "approximately equivalent" is used herein to refer to the volume of fluid displaced by the device as compared to the volume of liquid aspirated by the device and means that the volume of fluid (*e.g.*, air) displaced by movement of the plunger element within the vacuum chamber is not exactly equal to the volume of liquid aspirated into the tip attached to the end of the device due to the difference between the density of the fluid and the density of the liquid. The device design is calibrated taking into account this factor and is well within the purview of the skilled artisan.

The terms "interference fit" or "friction fit" are used interchangeably herein and refer to a fastening between two parts that is achieved by friction after the parts are pushed together.

The designations "up" and "down," "upward" and "downward," and "horizontal" and "vertical" as used herein refer to an orientation of the pipette device in which the pipette housing and dispenser portion are oriented with the actuating element or handle at the top and the dispensing end at the bottom (*see, e.g.*, FIG. 1). In this orientation, a pipette tip fastened or attached onto the dispensing end of the pipetting device can be directed towards a vessel situated thereunder, in order to aspirate or deliver a liquid.

The terms "outer diameter" or "outer circumferential diameter" are used herein to refer to the diameter across a cylindrical component measured from one point on the outer surface of the cylinder wall to another point on the outer surface of the cylinder wall. The term "inner diameter" is used herein to refer to the diameter across a cylindrical component measured from one point on the inner surface of the cylinder wall to another point on the inner surface of the cylinder wall.

Air-displacement style pipettes are commonly used in the art. While the exemplary embodiments described herein disclose a single piston and motor driven air-displacement pipetting device, other pipette designs, such as a dual motor nested plunger design and manually-operated plunger designs, can be adapted for use with the pipette tip ejection assembly and locking mechanism. As will be understood in the art, the single piston air-displacement design utilizes the movement of a piston within a cylindrical vacuum chamber to enable the aspiration and dispensing of liquid volumes. In general, a disposable pipette tip of the appropriate size is attached to the dispensing end of the pipetting device. The end of the pipette tip can then be placed in a liquid to be transferred. Movement of the piston upwards within the vacuum chamber expands the size of the chamber thereby creating a vacuum that causes an influx of fluid (*e.g.*, air). This fluid displacement facilitates the aspiration of an approximate equivalent volume of liquid into the attached pipette tip. Movement of the piston downwards within the vacuum chamber then forces the fluid (*e.g.*, air) out of the chamber and causes dispensing of the liquid out of the pipette tip. By precisely controlling the movement of the piston within the vacuum chamber, the end-user can precisely and accurately control the volume of liquid being transferred. However, to better ensure accuracy and precision of the liquid being transferred, disposable pipette tips having the appropriate volumetric capacity need to be selected for use. Larger pipette tips capable of accurately transferring larger volumes of liquid will tend to have a larger attachment circumference than pipette tips optimized for the transfer of smaller volumes of liquid thus highlighting the need for pipetting device dimensions capable of attaching a large range of pipette sizes.

Exemplary pipetting device designs are shown in FIGS. 1-4. While the piston-driven air-displacement pipette design shown in the drawings is capable of a broad volumetric range (*e.g.*, from about 1 µl to about 1,000 µl), such a broad volumetric range will require the use of both small disposable pipette tips (*e.g.*, with maximum liquid transfer capacities of up to about 5 µl, 20 µl, 100 µl, or 200 µl) and large disposable pipette tips (*e.g.*, with a maximum liquid transfer capacity of up to about 1,000 µl). As one having ordinary skill in the art will recognize, the small pipette tips will require a tip holder circumference for interference/friction fit that is smaller than the tip holder circumference required for the attachment of large pipette tips. As such, provided herein is a concentric cylinder design where the increasing outer circumferential diameters of the successive cylinders create a multi-tiered tip holding system with each

successive cylinder having a larger outer circumferential diameter for attaching larger pipette tips. These attachment portions or seats preferably are designed to have an outer diameter of the appropriate size to enable a sufficient interference fit for either small pipette tips or large pipette tips. In a preferred embodiment, each of the small tip holder and larger tip holder will taper slightly from the top portion to the bottom portion to enable ease of attachment by insertion of the tip holder into the open end of a disposable pipette tip. As disposable pipette tips of standard sizes are well known in the art, the design of the small tip holder and large tip holder shape and size to enable optimal attachment of the appropriate pipette tip is well within the purview of the skilled artisan.

For instance, a small tip holder portion suitable for attachment of a small pipette tip may have an outer diameter that tapers from about 5 mm to about 6 mm (preferably, from about 5.2 mm to about 5.6 mm) at the top portion down to about 4 mm to about 5.2 mm (preferably, from about 4.7 mm to about 5.1 mm) at the bottom portion. In an exemplary embodiment, the large tip holder portion suitable for attachment of a large pipette tip may have an outer diameter that tapers from about 7.5 mm to about 8.5 mm (preferably, from about 7.5 mm to about 7.8 mm) at the top portion down to about 6.5 mm to about 8 mm (preferably, from about 7 mm to about 7.5 mm) at the bottom portion. For instance, the exemplary embodiment depicted in the examples has a small tip holder portion having an outer diameter of about 5.6 mm at the top portion that tapers to about 4.9 mm at the bottom portion, whereas the large tip holder portion has an outer diameter of about 8.06 mm at the top portion that tapers to about 7.3 mm at the bottom portion. A suitable fluid opening at the dispensing end of the device may have a diameter ranging from about 1.3 mm to about 2 mm (preferably, from about 1.5 mm to about 1.8 mm). The multi-tiered arrangement of concentric cylinders provide pipette tip attachment portions or seats suitable for accommodating different sized pipette tips.

The small tip holder portion is suitable for attachment of a small disposable pipette tip having a maximum liquid transfer capacity of about 2 µl to about 200 µl, *e.g.*, 2 µl, 5 µl, 10 µl, 20 µl, 100 µl, or 200 µl; or the small tip will have a maximum liquid transfer capacity of about 20 µl to about 200 µl. The large tip holder portion is suitable for attachment of a large disposable pipette tip having a maximum liquid transfer capacity of about 200 µl to about 5,000 µl; preferably, between about 200 µl about 1,000, *e.g.*, 200 µl, 500 µl, or 1,000 µl.

In other embodiments, the outer diameter of the large tip holder and/or the outer diameter of the small tip holder can be designed to accommodate disposable pipette tips having a maximum liquid transfer capacity greater than 1,000 µl or a maximum liquid transfer capacity less than 2 µl, respectively. For instance, the outer diameter of the large tip holder can be increased to a diameter suitable for accommodating disposable pipette tips having a maximum liquid transfer capacity of about 1,000 µl to about 5,000 µl, *e.g.*, 1,000 µl, 1,500 µl, 2,000 µl, 2,500 µl, 3,000 µl, 3,500 µl, 4,000 µl, 4,500 µl, or 5,000 µl (*e.g.*, a P5,000 disposable pipette tip). Likewise, the outer diameter of the small tip holder can be decreased to a diameter suitable for accommodating disposable pipette tips having a maximum liquid transfer capacity of equal to or less than about 2 µl, or equal to or less than about 1 µl (*e.g.*, P2 disposable pipette tip). Alternatively, rather than altering the outer diameter of the large tip holder and/or small tip holder, tip holders of larger or small outer diameters can be added to the multi-tier tip holder design to provide an even greater range of pipette tip sizes that can be accommodated.

In a preferred design, a large tip cylinder (also referred to as the small tip ejection cylinder or first dispenser cylinder) will have an inner diameter that is at least slightly larger than the outer circumferential diameter of the chamber cylinder and will be disposed over the chamber cylinder. The large tip cylinder will function to provide the attachment surface for the large pipette tip as well as the ejection edge for a small pipette tip. The chamber cylinder includes, or is attached to, a small tip holder portion suitable for attaching small pipette tips to the dispensing end of the pipetting device. In this arrangement, the small tip holder portion will extend or protrude beyond the ejection edge of the large tip cylinder. At its farthest, the small tip holder portion may extend or protrude beyond the ejection edge of the large tip cylinder by about 5 mm to about 10 mm, *e.g.*, 5 mm, 5.1 mm, 5.2 mm, 5.3 mm, 5.4 mm, 5.5 mm, 5.6 mm, 5.7 mm, 5.8 mm, 5.9 mm, 6 mm, 6.1 mm, 6.2 mm, 6.3 mm, 6.4 mm, 6.5 mm, 6.6 mm, 6.7 mm, 6.8 mm, 6.9 mm, 7 mm, 7.1 mm, 7.2 mm, 7.3 mm, 7.4 mm, 7.5 mm, 7.6 mm, 7.7 mm, 7.8 mm, 7.9 mm, 8 mm, 8.1 mm, 8.2 mm, 8.3 mm, 8.4 mm, 8.5 mm, 8.6 mm, 8.7 mm, 8.8 mm, 8.9 mm, 9 mm, 9.1 mm, 9.2 mm, 9.3 mm, 9.4 mm, 9.5 mm, 9.6 mm, 9.7 mm, 9.8 mm, 9.9 mm, or 10 mm; preferably, it extends or protrudes beyond the ejection edge of the large tip cylinder by about 6 mm to about 9 mm. In one exemplary embodiment, the small tip holder portion may extend or protrude beyond the ejection edge of the large tip cylinder by about 9 mm. Since the large tip cylinder is disposed over the chamber cylinder and configured to move parallel along the vertical

axis of and in relation to the chamber cylinder (*i.e.*, up and down), when force is applied to the ejection element and rod mechanism, the large tip cylinder will be moved downward such that the small tip ejection edge will contact and dislodge a small pipette tip if a small pipette tip is attached to the small tip holder portion.

The next cylinder in the arrangement is the cylindrical dispenser housing (or second dispenser cylinder), which will have an inner diameter that is at least slightly larger than the outer circumferential diameter of the large tip cylinder and will be disposed over the large tip cylinder and configured to move parallel along the vertical axis of and in relation to the large tip cylinder (*i.e.*, up and down). The cylindrical dispenser housing will have a large tip ejection edge. Since the cylindrical dispenser housing is disposed over the large tip cylinder and configured to move up and down in relation to the large tip cylinder, when force is applied to the ejection element and rod mechanism, the cylindrical dispenser housing will be moved downward such that the large tip ejection edge will contact and dislodge a large pipette tip if a large pipette tip is attached to the large tip holder portion.

The pipetting devices described herein may also have a locking mechanism for preventing upwards movement of the large tip cylinder (*i.e.*, locking the large tip cylinder into the downward position) when large pipette tips are to be used. This locking mechanism reduces the length of the chamber cylinder and small tip holder portion that will extend or protrude beyond the small tip ejection edge of the large tip cylinder. In the locked position, the small tip holder portion may extend or protrude beyond the ejection edge of the large tip cylinder by about 0 mm to about 3 mm, *e.g.*, 0 mm, 0.1 mm, 0.2 mm, 0.3 mm, 0.4 mm, 0.5 mm, 0.6 mm, 0.7 mm, 0.8 mm, 0.9 mm, 1 mm, 1.1 mm, 1.2 mm, 1.3 mm, 1.4 mm, 1.5 mm, 1.6 mm, 1.7 mm, 1.8 mm, 1.9 mm, 2 mm, 2.1 mm, 2.2 mm, 2.3 mm, 2.4 mm, 2.5 mm, 2.6 mm, 2.7 mm, 2.8 mm, 2.9 mm, or 3 mm; preferably, it extends or protrudes beyond the ejection edge of the large tip cylinder by about 0 mm to about 1.5 mm. In one exemplary embodiment, when in the locked position, the small tip holder portion may extend or protrude beyond the ejection edge of the large tip cylinder by about 1.3 mm. Thus, when a large pipette tip or large filtered pipette tip is attached to the large tip holder portion, there is reduced risk of contaminating the dispenser opening of the pipetting device as liquid is drawn up into the large pipette tip. Moreover, this locking design will allow the attachment of large, filtered pipette tips as the extension of the small tip holder

portion will not contact the filter component and prevent secure interference fit of the large, filtered pipette tip to the large tip holder portion.

An exemplary embodiment of the multi-tiered, concentric pipette tip holder and ejection design on a pipetting device is depicted in FIGS. 1-4. While a single piston, air-displacement type pipetting device is shown, the ejector mechanism described herein can be adapted for use with many other types of pipetting devices available in the art, such as concentric, dual-piston designs and others. Moreover, manually-operated piston designs are also suitable. As shown in FIG. 1, the pipetting device **10** generally has an elongated or rod-like shape with a top, upper drive unit section that contains the drive unit and all of the associated components encased in a pipette housing **15**. The pipetting device **10** also generally includes a bottom, lower fluid displacement and dispensing section, which includes a cylindrical dispenser housing **20** disposed over two or more inner cylinders and majority of the dispensing components. In particular, the dispensing section of the pipetting device **10** is comprised of concentric cylinders or housings that work in cooperation to form the multi-tiered pipette tip attachment portions and tip ejector mechanism as will be explained in detail below. The dispensing section has an opening **45** at the dispensing end, a large tip holder **25**, and a small tip holder **30**. As shown in FIG. 3A, the large tip holder **25** is part of the bottom portion of the large tip cylinder bottom **65** closest the opening **45**, and the small tip holder **30** is attached to the end of the chamber cylinder **70**. The dispenser housing **20**, large tip cylinder **65**, and small tip holder **30**/chamber cylinder **70** form a concentric cylinder configuration such that the large tip holder **25** extends from the dispenser housing **20** beyond the large tip ejection edge **35**, and the small tip holder **30** extends from the large tip cylinder **65** beyond the small tip ejection edge **40** as shown in, *e.g.*, FIG. 1. This forms a multi-tiered tip holder design, where the outer circumference of the device at the large tip holder **25** is larger than the outer circumference at the small tip holder **30**. The tiered design allows for fitting or fastening of tips of different sizes via interference or friction fit, which exploits the circular force of the pipette tip against the tip holder portion of the pipetting device to secure a large pipette tip (*e.g.*, a 1,000 ul pipette tip) onto the large tip holder **25** or a small tip (*e.g.*, 10 ul, 20 ul, 100 ul, or 200 ul pipette tip) onto the small tip holder **30**. Thus, the pipetting device **10** is capable of aspirating and dispensing a liquid in a range of volumes from between about 0.1 µl to about 1,500 µl, *e.g.*, about 0.1 µl, 0.2 µl, 0.3 µl, 0.4 µl, 0.5 µl, 1.0 µl, 1.5 µl, 2.0 µl, 2.5 µl, 3.0 µl, 4.5 µl, 5.0 µl, 10 µl, 15 µl, 20 µl, 25 µl, 30 µl, 40 µl, 50 µl, 60 µl, 70 µl, 80 µl, 90 µl,

100 µl, 110 µl, 120 µl, 130 µl, 140 µl, 150 µl, 160 µl, 170 µl, 180 µl, 190 µl, 200 µl, 210 µl, 220 µl, 230 µl, 240 µl, 250 µl, 260 µl, 270 µl, 280 µl, 290 µl, 300 µl, 350 µl, 400 µl, 450 µl, 500 µl, 550 µl, 600 µl, 650 µl, 700 µl, 750 µl, 800 µl, 850 µl, 900 µl, 950 µl, 1,000 µl, 1,100 µl, 1,200 µl, 1,300 µl, 1,400 µl, or 1,500 µl. In a particular embodiment, the pipetting device **10** is capable of aspirating and dispensing a liquid in the range of volumes from between about 0.5 µl and about 1,000 µl.

As one having ordinary skill in the art will appreciate, typical pipettes utilize disposable pipette tips and must be quickly removed and replaced in between the handling of different liquid samples to prevent contamination or unwanted mixture of liquids. Thus, ejector mechanism of the instant disclosure utilizes the concentric cylinder design for quickly and easily removing both large and small pipette tips without the user having to touch the tips themselves.

Both the dispenser housing **20** and the large tip cylinder **65** have ejection edges at the end closes to the opening **45** – the large tip ejection edge **35** and small tip ejection edge **40**, respectively. The pipetting device **10** includes an ejector element **50** at the top of the device that can be pressed downward to activate the pipette tip ejection mechanism. As the user pushes down on the ejector element **50**, the dispenser housing **20** moves downwards in relation to the large tip cylinder **65**, large tip holder **25**, and small tip holder **30**. The large tip ejection edge **35** will contact and dislodge any large pipette tip that is attached to the large tip holder **25**. As the user continues to push down the ejector element **50**, both the dispenser housing **20** and the large tip cylinder bottom move downwards in relation to the small tip holder **30**. The small tip ejection edge **40** will contact and dislodge any small pipette tip that is attached to the small tip holder **30**. While the ejection mechanism in this embodiment is manually-operated, motor-driven designs are also contemplated and work in a similar manner.

As shown in FIG. 2A, the small tip holder **30** extends beyond the small tip ejection edge **40** of the large tip cylinder **65** (*i.e.*, by about 9 mm) thereby providing an attachment surface for a small pipette tip to be securely attached to the small tip holder **30**. FIG. 2C and FIG. 2D depict close-up views of the small tip holder **30**. A small tip **ST** is attached to the small tip holder **30** by interference fit (*see* FIG. 2D). When the end-user aspirates liquid and wishes to change the tip, the ejector element **50** is manually (or, in alternative embodiments, electronically by a motor) moved downwards, which moves the dispenser housing **20** downward. As the dispenser housing is continued to be moved downward, the large tip cylinder **65** is then also moved downward as

the small tip ejection edge **40** contacts the small pipette tip **ST** and dislodges the small pipette top **ST** from the small tip holder **30**. As shown in FIG. 2B and FIG. 2E, the small tip holder **30** now extends only slightly beyond the small tip ejection edge **40** (*i.e.*, by about 1.3 mm, or less) as compared to when the large tip cylinder **65** is in the upward position. In some embodiments, when in the locked position, the small tip holder **30** extends beyond the small tip ejection edge **40** by between about 0 mm to about 3 mm; preferably, less than about 2 mm; more preferably, less than about 1.3 mm.

The ejector mechanism of the invention may also include a locking mechanism that is configured to maintain the large tip cylinder **65** in the downward position. In this manner, the small tip holder **30** will no longer extend significantly beyond the small tip ejection edge **40** (*see* FIG. 2E). The extension of the small tip holder **30** may contact the liquid being aspirated when a large tip is attached to the large tip holder **25** (for example, if a large volume of liquid is being aspirated) or prevent attachment of large pipette tips containing filter components. To solve this problem, the locking mechanism is configured to maintain the large tip cylinder **65** in the downward position. As shown in FIG. 2F, a large, filtered pipette tip **ST** can now be attached to the large tip holder **25** without the small tip holder **30** being an impediment. When the end-user wishes to switch back to using small pipette tips, the locking trigger **60** is pressed, which releases the large tip cylinder **65** back to the upward position (*see* FIG. 2A and FIG. 2C). In this manner, the end-user can easily switch from using large pipette tips to small pipette tips, and from small pipette tips to large pipette tips by using the locking trigger **60**.

FIGS. 3A-3F depict various exploded views of an exemplary pipetting device that includes both the ejection mechanism and locking mechanism. Part of the pipette housing **15** is removed to reveal the drive section components. FIGS. 3A-3F also reveal the various dispensing section components. The motor **80** is powered by rechargeable battery **90**, controlled by the printed circuit board **95**, and disposed on a motor holder **85**. The motor **80** moves a threaded piston rod **155** and piston **115**. The threaded piston rod **155** is connected to the piston **115** by way of a pair of magnets **130** that compensate for misalignment of the system, it being understood, however, that other embodiments may not require the magnets. In this particular embodiment, the motor **80** is a stepper motor. However, other suitable motors can include servo motors, DC motors, or other linear actuator-type motors. As shown in the drawings, the pair of magnets **130** are connected to the threaded piston rod **155** by the top magnet holder **125** and to

the piston **115** by the bottom magnet holder **135**. The exemplary magnets may be made from any suitable material, such as, but not limited to, any type of neodymium, while the magnet holders may be made of magnetic or non-magnetic materials including, but not limited to, steel, stainless steel, aluminum, plastic, and the like. The motor **80** moves the piston **115** up and down with the chamber cylinder **70**. As the piston **115** is moved upwards within the chamber cylinder **70**, a vacuum is created that forces air into the dispensing unit of the device, which, in turn, forces liquid into the pipette tip attached to the pipetting device. As the piston **115** is moved downwards within the chamber cylinder **70**, air is forced out of the dispensing unit, which, in turn, forces the liquid out of the pipette tip. The chamber cylinder **70** is attached to the bottom of the motor holder **85** by mating threads **87**, **72**. Further, an O-ring **120** may be included to create an airtight seal between the piston **115** and the chamber cylinder **70** to prevent air from escaping as the piston **115** is moved up and down. The small tip holder **30** is attached to the bottom of the chamber cylinder **70** by threads **74**. Another O-ring **75** can be included to create an airtight seal between the small tip holder **30** and the large tip cylinder bottom **65**.

FIG. 3A illustrates the concentric configuration of the chamber cylinder **70**, the large tip cylinder **65**, and dispenser housing **20**. The large tip cylinder **65** is disposed over the chamber cylinder **70** and attached to the small tip ejector member **165** by way of threads **67**, **175** (*see also* FIG. 3F for best view of the small tip ejector member **165**). The dispensing housing **20** is then disposed over the large tip cylinder **65** and attached to the large tip ejector member **55** by threads **22**. The ejector element **50** is connected to the ejection rod **140**. A biasing element **145** (*e.g.*, spring) is circumferentially disposed around the ejection rod **140** to bias the ejection rod in the upwards position. The ejection rod **140** is passed through a hole **86** in a flange on the motor holder **85** and connected large tip ejector member **55** by insertion into a hole **57**. A c-washer **160** and washer **150** may be included to hold the biasing element **145** in position. As the ejection element **50** is pressed down, it moves the ejection rod **140** against the biasing element **145**. The ejection rod **140** moves the large tip ejector member **55** and dispenser housing **20** downwards in relation to the large tip holder **25**. When a large pipette tip is attached to the large tip holder **25**, the large tip ejection edge **35** of the dispenser housing **20** contacts the large pipette tip and dislodges it from the large tip holder **25**. While the large tip cylinder **65** and the small tip ejection member **165** are separate components in the exemplary embodiments for easier disassembly and cleaning, they can be integral or part of the same component. Likewise, while

the dispenser housing **20** and the large tip ejection member **55** are separate components in the exemplary embodiments for easier disassembly and cleaning, they can be integral or part of the same component

When a small tip is attached to the small tip holder **30** and needs to be ejected, the end-user continues to press the ejector element **50**. As the large tip ejector member **55** continues to be moved downward, a spacer **110** beneath the spacer arms **112** of the large tip ejector member **55** contacts a seat **114** of the small tip ejector member **165**. As the large tip ejector member **55** and small tip ejector member **165** are moved together, the small tip ejector member **165** moves the large tip cylinder **65** downwards. The small tip ejection edge **40** of the large tip cylinder **65** contacts the small pipette tip and dislodges it from the small tip holder **30**. As the ejector element **50** is released, the biasing element **145** moves the ejection rod **140** upwards to reset the cylinder positions. In this manner, the concentric cylinder design of the ejector mechanism enables the ejection of both small and large tips.

The locking mechanism is also shown in FIGS. 2G-2I and 3A-3F. As explained above, the locking mechanism can maintain the large tip cylinder **65** in the downward position to prevent contamination when large pipette tips are used and enables the use of large pipette filter tips. The locking mechanism embodiment shown in the drawings includes a locking trigger **60** with trigger projection **62** and a locking rod hole **108** through the bottom **109** of the trigger projection **62**, a biasing element **100** (*e.g.*, a leaf spring), and a locking rod **105** with a top surface **107**. While this embodiment shows the ejection mechanism and locking mechanisms at opposite positions of the device, they can be positioned closer to each other or on the side of the device. The locking rod **105** is passed through a hole in the spacer element **110** and inserted into a hole **170** on the seat **114** of the small tip ejector member **165**. As shown in FIG. 2G, when in the upward and unlocked position, the top surface **107** of the locking rod **105** is passed through the locking rod hole **108** in the trigger projection **62**. The biasing element **100** biases the locking trigger **60** to the lateral and outward position in relation to the pipette housing **15** in both the locked and unlocked positions of the trigger **60**. In the unlocked position, the locking trigger projection **62** pushes inward on the contact area **102** of the face of the biasing element **100**, which simultaneously opposes this force. At the same time, the locking rod **105** prevents the locking trigger **60** from being moved outward due to the opposing force of the biasing element **100** against the locking trigger projection **62**. As the ejector element **50** and ejection rod **140** are

forced downward against the biasing element **145**, the large tip ejector member **55** continues to be moved downward until the spacer **110** contacts the seat **114** of the small tip ejector member **165** and moves the small ejector member **165** downwards.

The downward position of the small ejector member **165** moves the locking rod **105** downward such that the top end **107** of the locking rod moves out of the locking hole **108** and clears the obstacle of the locking trigger **60**, which allows the locking trigger **60** to snap into the horizontal/outward locked position as the top of the locking rod **107** contacts the bottom **109** of the locking trigger projection **62** (*see* FIGS. 2H and 2I). The contact between the top of the locking rod **107** and the bottom **109** of the locking trigger projection **62** prevents the upward movement of the small ejector member **165** and, in turn, the large tip cylinder **65**. As such, the small tip holder **30** does not extend significantly beyond the small tip ejection edge **40** (*see* FIG. 2E).

To release the locking mechanism, the end-user presses the locking trigger **60** to force the lateral movement of the locking trigger projection **62** against the biasing element **100**. The trigger projection **62** slides across the top surface **107** of the locking rod **105** until the top surface of **107** meets the locking rod hole **108** in the trigger project **62** and is no longer in direct contact with the bottom **109** of the trigger projection **62**. The top surface **107** of the locking rod **105** will then slide up into the locking rod hole **108** by the upward force applied to the small tip ejector member **165** and large tip cylinder **65** by the biasing element **145**. When the locking rod **105** is back in the upwards position, the device is returned to the small tip configuration, which means that the small tip ejector member **165** and large tip cylinder **65** are moved upwards (*see also* FIG. 2C).

FIG 4. is a diagram of an exemplary pipetting device **10** with the concentric cylinder ejection mechanism and locking mechanism. The dispensing unit of the pipetting device **10** includes an opening **45** in fluid communication with a fluid path **180** that leads into a vacuum chamber **185** within the chamber cylinder **70**. When a small pipette tip is being used, the small pipette tip (*e.g.*, a 200 µl capacity tip) is attached to the small tip holder **30**. In some embodiments, the pipetting device **10** includes an LCD screen and interface to enable the end-user to input the desired dispensing volume. In other embodiments, the pipetting device **10** may include volume control buttons or knobs as is known in the art. For the motor-controlled embodiment, the user then presses the actuator element **17**, which sends a signal via the

instrument control PCB **95** to the motor **80**. The motor moves the threaded piston rod **155** and piston **115** upwards. As the piston **115** moves upwards within the vacuum chamber **185**, the volumetric capacity of the vacuum chamber **185** increases and creates the vacuum necessary to cause a corresponding displacement of air into the fluid path **180**, which air displacement draws a corresponding volume of liquid into the small pipette tip (*e.g.*, about 1µl to about 200 µl) pipette tip not shown). The end-user then presses the actuator element **17** again to cause the downward movement of the piston **115** and dispensing of the liquid out of the small pipette tip.

To eject the small pipette tip, the end-user then presses the ejector element **50**, which moves the ejection rod **140** against the biasing element **145**. The large tip ejector member **55** and dispenser housing **20** are moved downward until the spacer **110** contacts the seat **114** of the small tip ejector member **165**. The small tip ejector member **165** and large tip cylinder **65** are then moved downwards so that the small tip ejection edge **40** dislodges the small pipette tip from the small tip holder **30**. The end-user can then attach another small pipette tip and repeat the process, or switch to a large pipette tip. To use another small pipette tip, the end-user presses the locking trigger **60** against the biasing element **105** to let the locking rod **105** pass through the locking rod hole **108** in the locking trigger projection **62** thereby moving the small tip ejector member **165** and large tip cylinder **65** upwards.

If the end-user desires to use a large pipette tip (*e.g.*, a pipette tip with a 1,000 µl capacity), the end-user first will press the ejector element **50** all the way down to let the locking rod **105** be locked into the downward position while not pressing/holding the locking trigger **60**. As such, the locking trigger **60** will move outwards, and the locking trigger projection **62** will engage the top surface **107** of the locking rod **105** to prevent the upward movement of the locking rod **105**, the small tip ejector member **165**, and the large tip cylinder **65**. In the locking configuration, the small tip holder **30** does not significantly extend beyond the small tip ejection edge **40**, which enables attachment of the large pipette tip while preventing potential contamination of the fluid path **180** with liquid or enabling the attachment of a large pipette tip with a filter component.

The end-user then adjusts the volume settings as needed and presses the actuator element **17** to move the piston **115** upwards within the vacuum chamber **185** to force liquid to be drawn up the large pipette tip as described above (*e.g.*, about 100 µl to about 1,000 µl). The liquid will then be dispensed when the actuator element **17** is pressed a second time. The end-user then

presses the ejector element **50** to move the ejection rod **140** against the biasing element **145** thereby moving the large tip ejector member **55** and dispenser housing **20** downward until the large tip ejection edge **35** of the dispensing housing **20** dislodges the large pipette tip. To switch back to using small pipette tips, the end user presses the locking trigger **60** against the biasing element **100** to force the locking rod **105** back to the up position.

While the above depicts a leaf spring as the biasing element **100**, other suitable embodiment employs a compression spring as the biasing element **100** that can be positioned between the locking trigger **60** and the locking rod **105**, or between the locking trigger **60** and the pipette housing **15**. FIGS. 5A and 5B depict an embodiment of the locking mechanism that includes a compression spring as the biasing element **100** placed between the locking trigger **60** and the locking rod **105**. In this embodiment, the biasing element **100** (*e.g.*, compression spring) is disposed within a bore **63** of the locking trigger **60**. An end **101** of the biasing element **100** contacts the locking rod **105** to bias the locking trigger **60** to the lateral and outward position. Other designs suitable for maintaining pressure on the locking trigger **60** include a spring under tension, elastic material, or other suitable biasing element.

To further prevent contamination of the fluid path by liquid, some embodiments of the device will include an electronic sensor, such as, but not limited to an optic sensor, and a microcontroller programmed to recognize when the large tip cylinder is in the downward and locked position relative to the small tip holder or when the locking trigger is engaged. In this manner, the electronic sensor can detect when the small tip holder is exposed and therefore prevent the end-user from selecting an aspirating volume that is beyond the capacity of small pipette tips, for example, volume selections above 200 µl. Further, when the locking mechanism is engaged, the electronic sensor will enable the selections of volumes up to the large tip pipette capacity, such as up to 1,000 µl. Thus, the electronic sensor will provide an additional mechanism to prevent contamination caused by aspirating an amount of liquid beyond the small tip capacity, which would flood the fluid path with the overflow liquid. In some embodiments, the sensor can be mounted on the bottom of the PCB (or elsewhere) and can detect the position of the locking trigger. The locking trigger may include a small flange ("flag") that moves in and out of the optical sensor detection path. In this manner, when the optical sensor is blocked by the flag, the optical sensor will send a signal to the microcontroller, which will cause the display

screen (*e.g.*, LCD) of the device to provide options for only the relevant volume range and will further prevent the motor command for moving the motor more than the relevant volume.

References

10 – pipetting device
15 – pipette housing
17 – actuator element
18 – hand rest
20 – dispenser housing
22 – threads
25 – large tip holder
30 – small tip holder
35 – large tip ejection edge
40 – small tip ejection edge
45 - opening
50 – ejector element
55 – large tip ejector member
57 – hole
60 – locking trigger
62 – trigger projection
63 – bore (locking trigger)
65 – large tip cylinder
67 – threads
70 – chamber cylinder
72 – threads
74 – threads
75 – O-ring
80 – motor
85 – motor holder
87 – hole
87 – threads

90 – rechargeable battery

95 – printed circuit board

100 – biasing element

101 – biasing element end (for contacting locking rod)

102 – contact area

105 – locking rod

107 – top of locking rod

108 – locking rod hole

109 – bottom of the trigger projection

110 – spacer

112 – spacer arms

114 – spacer seat

115 – piston

120 – O-ring

125 – top magnet holder

130 – magnet

135 – bottom magnet holder

140 – ejection rod

145 – biasing element

150 – washer

155 – piston rod

160 – c washer

165 – small tip ejector member

170 – hole for locking rod

175 – threads

180 – fluid path

185 – vacuum chamber

CLAIMS

We claim:

1. A pipette with a multi-tiered pipette tip holder and ejection mechanism comprising:

a pipette body comprising an upper drive unit section and a lower dispensing section, the lower dispensing section comprising a small tip holder portion and a chamber cylinder and having a fluid inlet to enable fluid to be drawn into the chamber cylinder or discharged therefrom; and

an ejection assembly comprising an ejector element, ejection rod, a first dispenser cylinder having a large tip holder portion and a small tip ejection edge, and a second dispenser cylinder having a large tip ejection edge, wherein the first dispensing cylinder is disposed over the chamber cylinder and configured to move up and down in relation to the chamber cylinder, and wherein the second dispensing cylinder is disposed over the first dispensing cylinder and configured to move up and down in relation to the first dispensing cylinder;

wherein the ejection rod is configured to:

(i) contact the second dispensing cylinder and move the second dispensing cylinder to a first position wherein the large tip ejection edge contacts and ejects a large pipette tip from the large tip holder portion when a first force is applied to the ejector element; or

(ii) cause the first dispensing cylinder to move to a second position wherein the small tip ejection edge contacts and ejects a small pipette tip from the small tip holder portion with a second force is applied to the ejector element.

2. The pipette of claim 1, wherein the fluid is air.

3. The pipette of claim 1 or claim 2, further comprises a biasing element disposed circumferentially around a portion of the ejection rod and configured to bias the ejection rod in an upwards position.

4. The pipette of any one of claims 1-3, wherein the large tip holder portion comprises an outer diameter that is greater than the outer diameter of the small tip holder portion.

5. The pipette of any one of claims 1-4, wherein the ejector element is disposed on the upper drive unit section.

6. The pipette of any one of claims 1-5, further comprising a first ejector member connected to the first dispensing cylinder, and a second ejector member connected to the second dispensing cylinder, wherein the ejection rod is connected to the second dispensing cylinder, and wherein the second ejector member contacts and moves the first ejector member to the second position when the second force is applied to the ejector element.

7. The pipette of claim 6, wherein the first ejector member and second ejector member are positioned within the upper drive unit section, and wherein the first dispensing cylinder and second dispensing cylinder form part of the lower dispensing section.

8. The pipette of any one of claims 1-7, further comprising:

a piston slidably positionable within the chamber cylinder between an open position and a closed position; and

a motor disposed within the upper drive unit portion and operably connected to the piston and configured to actuate the piston between the open position and the closed position within the chamber cylinder;

wherein the actuation of the piston to the open position defines a liquid volume to be aspirated by the pipette in an amount approximately equivalent to a fluid volume displaced by the movement of the piston.

9. The pipette of any one of claims 1-8, wherein the small tip holder portion is configured for attachment of a pipette tip having a maximum liquid capacity in the range from about 2 µl to about 200 µl.

10. The pipette of claim 9, wherein the small tip holder portion is configured for attachment of a pipette tip having a maximum liquid capacity in the range from about 20 µl to about 200 µl.

11. The pipette of any one of claims 1-10, wherein the large tip holder portion is configured for attachment of a pipette tip having a maximum liquid capacity in the range from about 200 µl to about 5,000 µl.

12. The pipette of claim 11, wherein the large tip holder portion is configured for attachment of a pipette tip having a maximum liquid capacity in the range from about 200 µl to about 1,000 µl.

13. The pipette of any one of claims 1-12, further comprising a locking mechanism comprising a trigger, biasing element, and locking rod movable between a locking and unlocking position, wherein movement of the second dispensing cylinder and first dispensing cylinder to the second position causes the locking rod to move to the locking position and prevent upwards movement of the first dispensing cylinder.

14. The pipette of claim 13, wherein force applied to the trigger against the biasing element causes the locking rod to move to the unlocking position whereby the locking rod no longer prevents upwards movement of the first dispensing cylinder.

15. The pipette of claims 13 or claim 14, wherein the locking rod contacts a bottom side of the trigger when in the locking position.

16. The pipette of any one of claims 13-15, further comprising a printed control board for controlling the motor in response to an end-user volume input and a sensor in electronic communication with a printed control board, wherein the sensor detects:

(i) when the first dispensing cylinder is unlocked and prevents the motor from causing the piston to move upwards to the open position to the extent that it defines a liquid volume to be aspirated by the pipette that exceeds the maximum liquid capacity of a small pipette tip; or

(ii) when the first dispensing cylinder is locked and allows the motor to cause the piston to move upwards to the open position to the extent that it defines a liquid volume to be aspirated by the pipette that exceeds the maximum liquid capacity of a small pipette tip; or

(iii) both (i) and (ii).

17. A method of replacing a pipette tip on a pipette, the method comprising:

(a) providing the pipette of any one of claims 1-16, wherein a small pipette tip is attached to the small tip holder portion, and applying force to the ejector element until the small tip ejection edge contacts and dislodges the small pipette tip from the small tip holder portion; or

(b) providing the pipette of any one of claims 1-16, wherein a large pipette tip is attached to the large tip holder portion, and applying force to the ejector element until the large tip ejection edge contacts and dislodges the large pipette tip from the large tip holder portion.

18. The method of claim 17, further comprising the step of inserting the small tip holder portion into a pipette receiving end of a small pipette tip so as to create an interference fit.

19. The method of claim 17, further comprising the step of inserting the large tip holder portion into a pipette receiving end of a large pipette tip so as to create an interference fit.

20. The method of claim 17, further comprising holding the trigger down when applying force to the ejector element.

21. A pipetting device with a multi-tiered pipette tip holder and ejection mechanism comprising:

an elongated pipette body comprising an air inlet at a dispensing end;

an ejector element;

a concentric cylinder assembly comprising (i) a chamber cylinder in fluid communication with the fluid inlet, (ii) a small tip ejection cylinder having a small tip ejection edge and a large

tip holder portion, and (iii) a cylindrical dispenser housing having a large tip ejection edge, wherein:

(i) the chamber cylinder is concentrically received within the small tip ejection cylinder;

(ii) the small tip ejection cylinder is concentrically received within the cylindrical dispenser housing and configured to move up and down in relation to the chamber cylinder;

(iii) the cylindrical dispenser housing is configured to move up and down in relation to the small tip ejection cylinder.

an ejection rod in mechanical communication with the ejector element and configured to:

(i) cause the cylindrical dispenser housing to move to a first position wherein the large tip ejection edge contacts and ejects a large pipette tip from the large tip holder portion when a first force is applied to the ejector element; or

(ii) cause the small tip ejection cylinder to move to a second position wherein the small tip ejection edge contacts and ejects a small pipette tip from the small tip holder portion with a second force is applied to the ejector element.

22. The pipetting device of claim 21, further comprising a first ejection member connected to the small tip ejection cylinder, and a second ejection member connected to the ejection rod and to the cylindrical dispenser housing, wherein:

(i) the ejection rod moves the second ejection member and the cylindrical dispenser housing to the first position when a first force is applied to the ejector element; or

(ii) the ejection rod causes the second ejection member to contact and move the first ejection member and small tip ejection cylinder to the second position when the second force is applied to the ejector element.

23. The pipetting device of claim 21 and 22, further comprising a locking mechanism comprising a trigger, biasing element, and locking rod movable between a locking and unlocking position, wherein movement of the cylindrical dispenser housing and small tip ejection cylinder to the second position causes the locking rod to move to the locking position and prevent upwards movement of the small tip ejection cylinder.

24. The pipetting device any one of claims 21-23, wherein force applied to the trigger against the biasing element causes the locking rod to move to the unlocking position whereby the locking rod no longer prevents upwards movement of the small tip ejection cylinder.

25. The pipetting device of any one of claims 21-24, wherein the locking rod contacts a bottom side of the trigger when in the locking position.

26. The pipetting device of any one of claims 21-25, further comprising:

a piston slidably positionable within the chamber cylinder between an open position and a closed position; and

a motor operably connected to the piston and configured to actuate the piston between the open position and the closed position within the chamber cylinder;

wherein the actuation of the piston to the open position defines a liquid volume to be aspirated by the pipette in an amount approximately equivalent to a fluid volume displaced by the movement of the piston.

27. The pipetting device of any one of claims 21-26, wherein the motor is mechanically connected to a threaded piston, wherein the threaded piston is connected to the piston by one or more magnets.

28. The pipetting device of any one of claims 21-27, further comprising a printed control board for controlling the motor in response to an end-user volume input and a sensor in electronic communication with a printed control board, wherein the sensor detects:

(i) when the small tip ejection cylinder is unlocked and prevents the motor from causing the piston to move upwards to the open position to the extent that it defines a liquid volume to be aspirated by the pipette that exceeds the maximum liquid capacity of a small pipette tip; or

(ii) when the small tip ejection cylinder is locked and allows the motor to cause the piston to move upwards to the open position to the extent that it defines a liquid volume to be aspirated by the pipette that exceeds the maximum liquid capacity of a small pipette tip; or

(iii) both (i) and (ii).

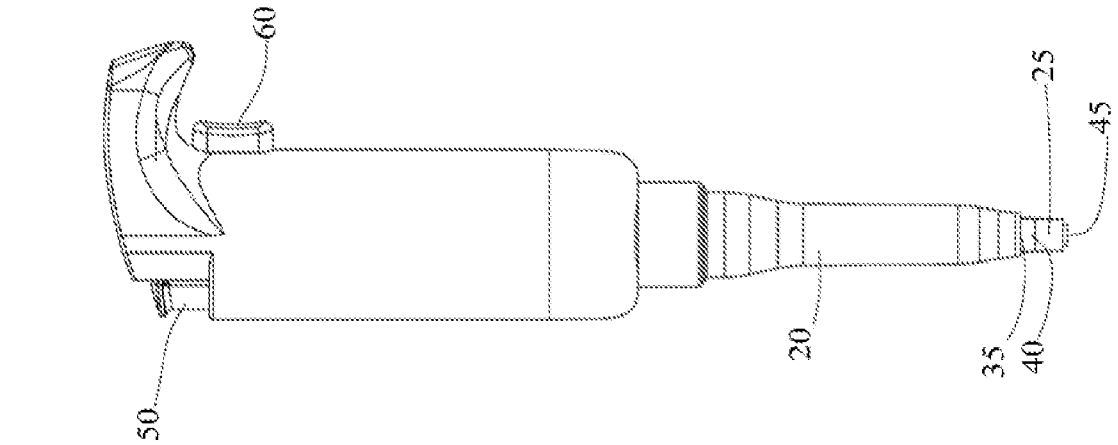


FIG. 2B

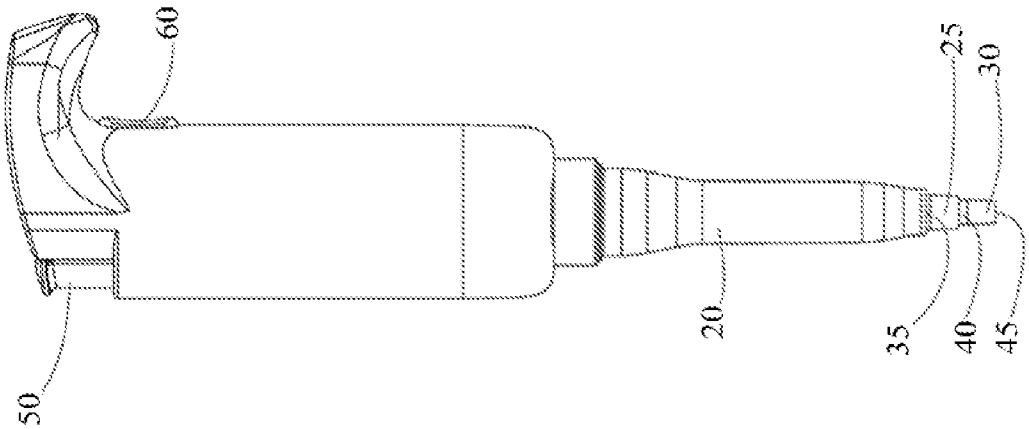


FIG. 2A

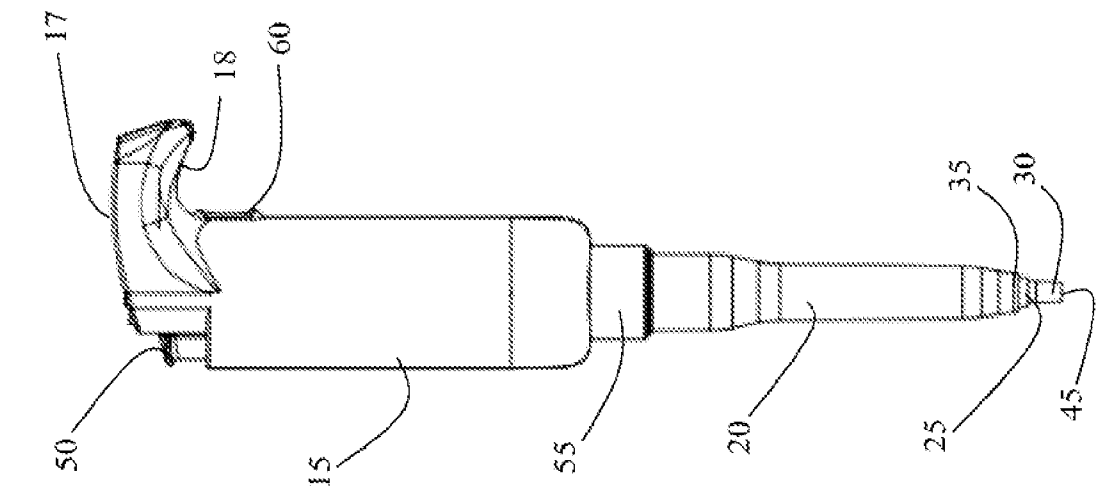


FIG. 1

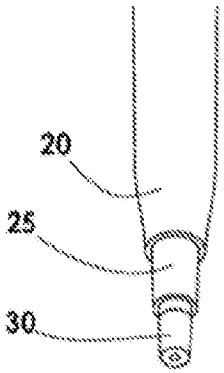


FIG. 2C

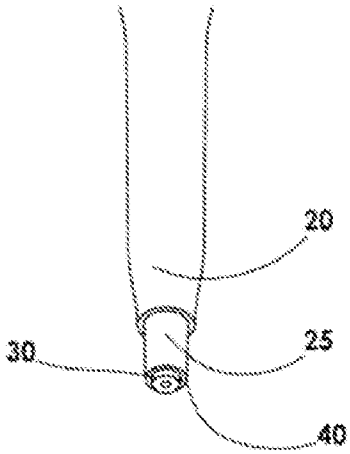


FIG. 2E

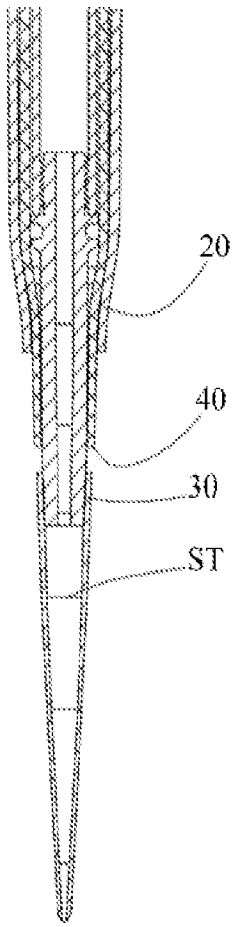


FIG. 2D

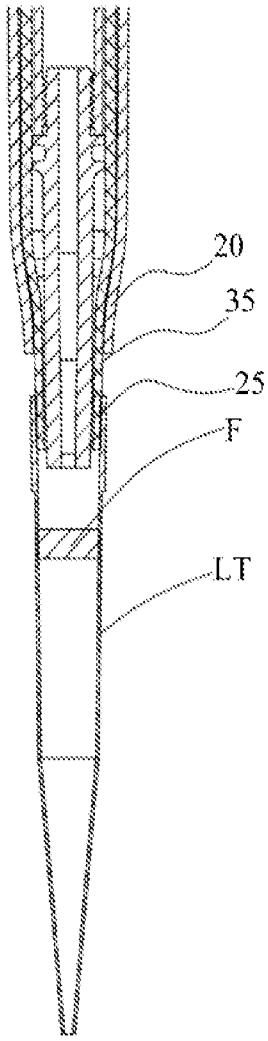


FIG. 2F

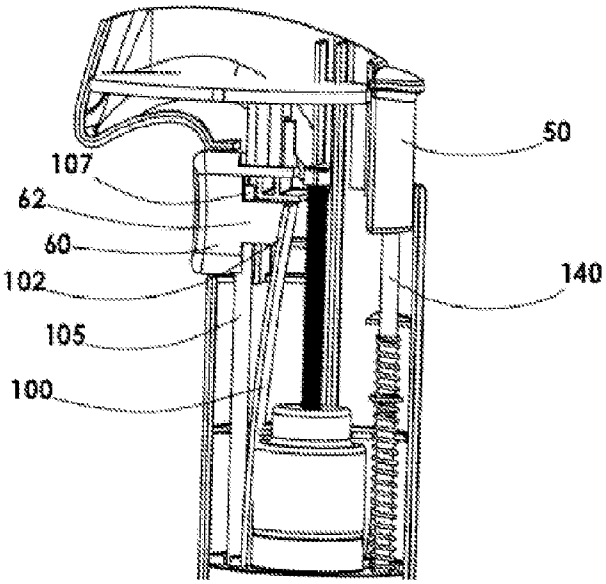


FIG. 2G

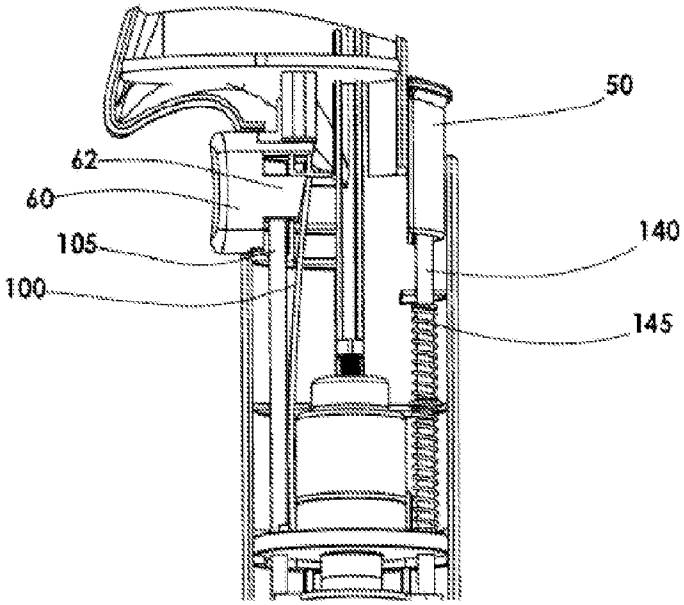


FIG. 2H

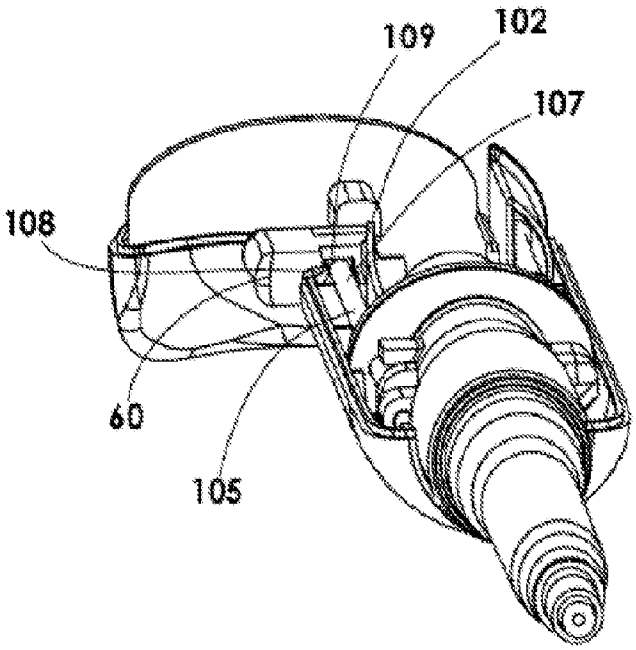


FIG. 2I

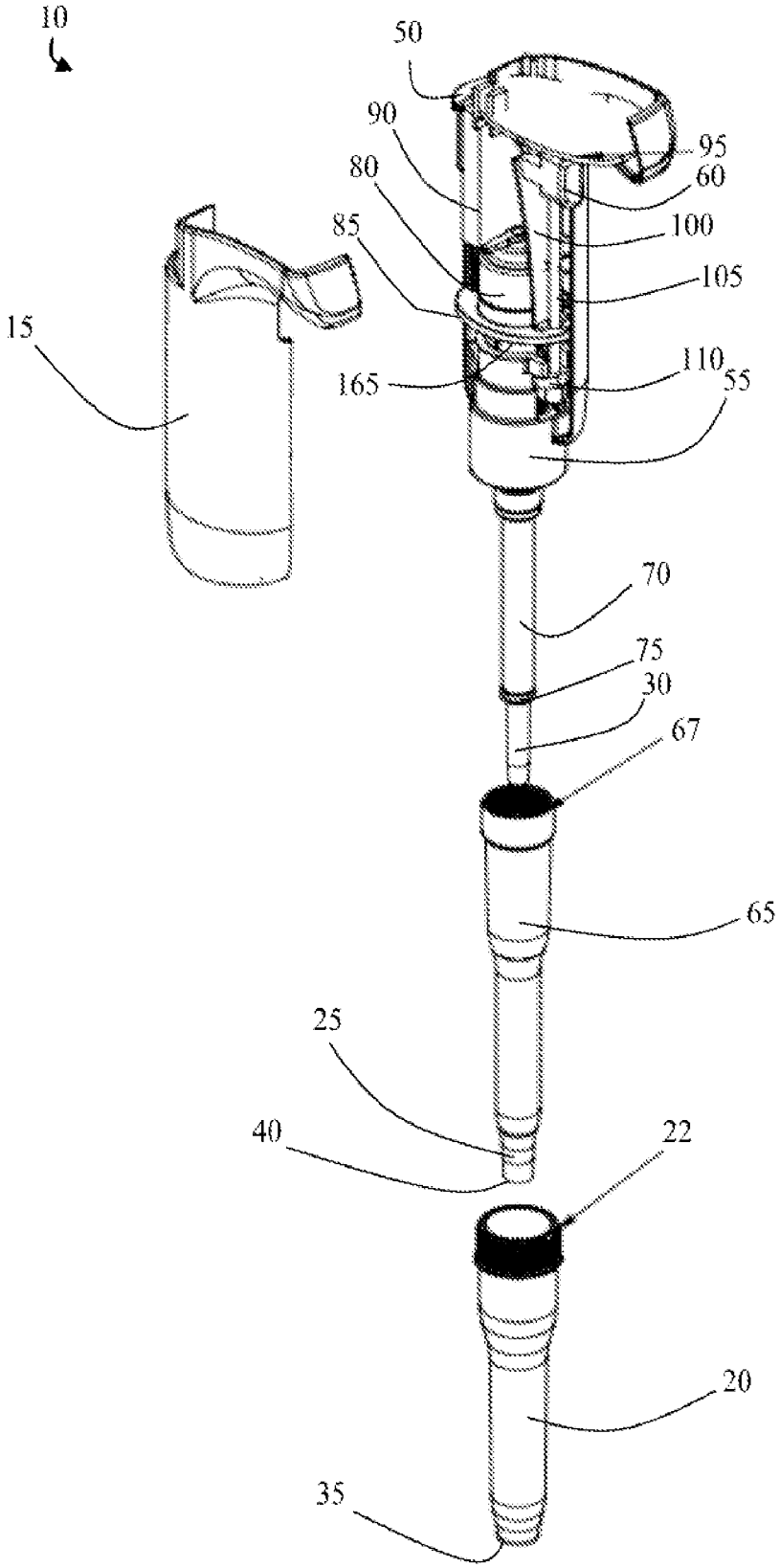

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FIG. 3A

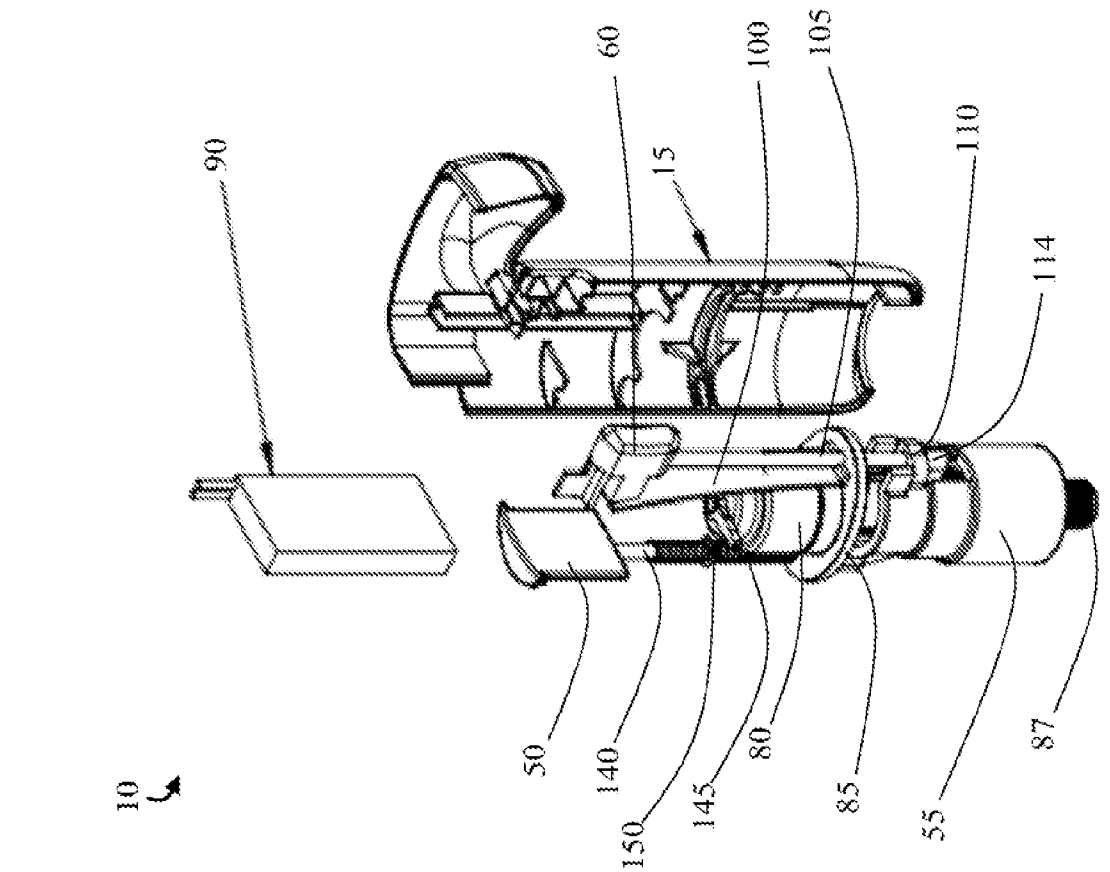

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FIG. 3C

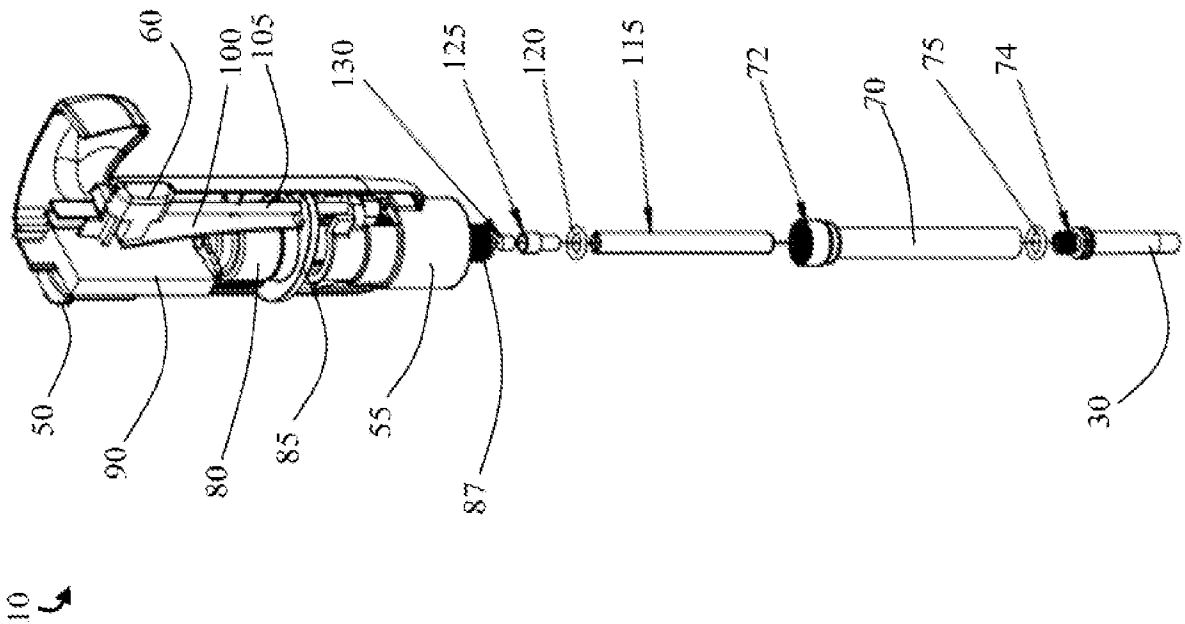

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FIG. 3B

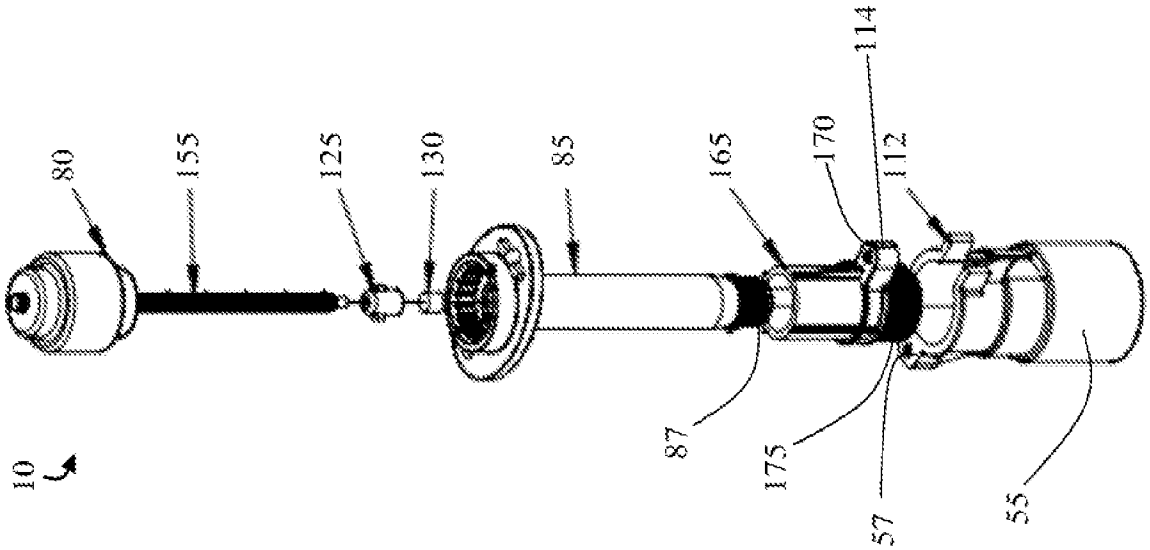


FIG. 3F

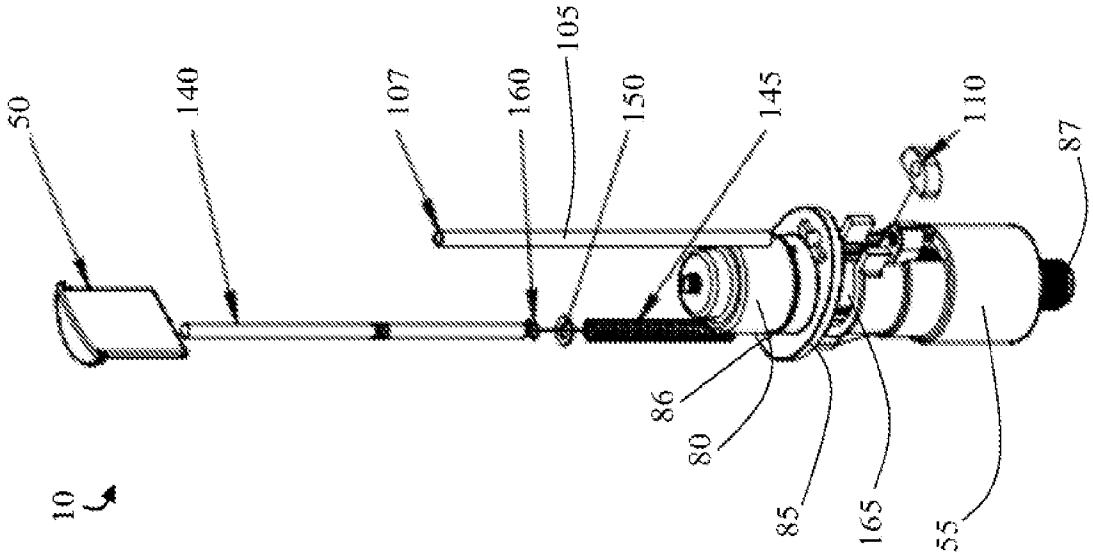


FIG. 3E

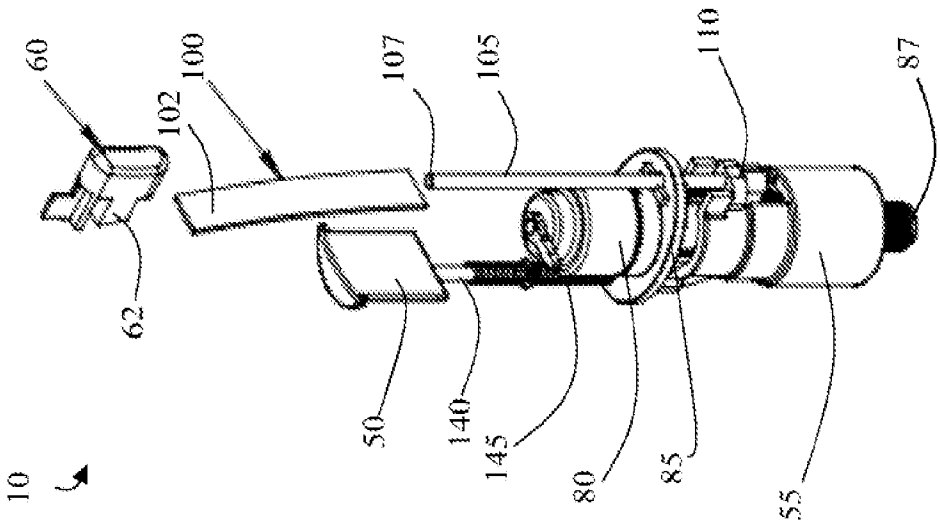


FIG. 3D

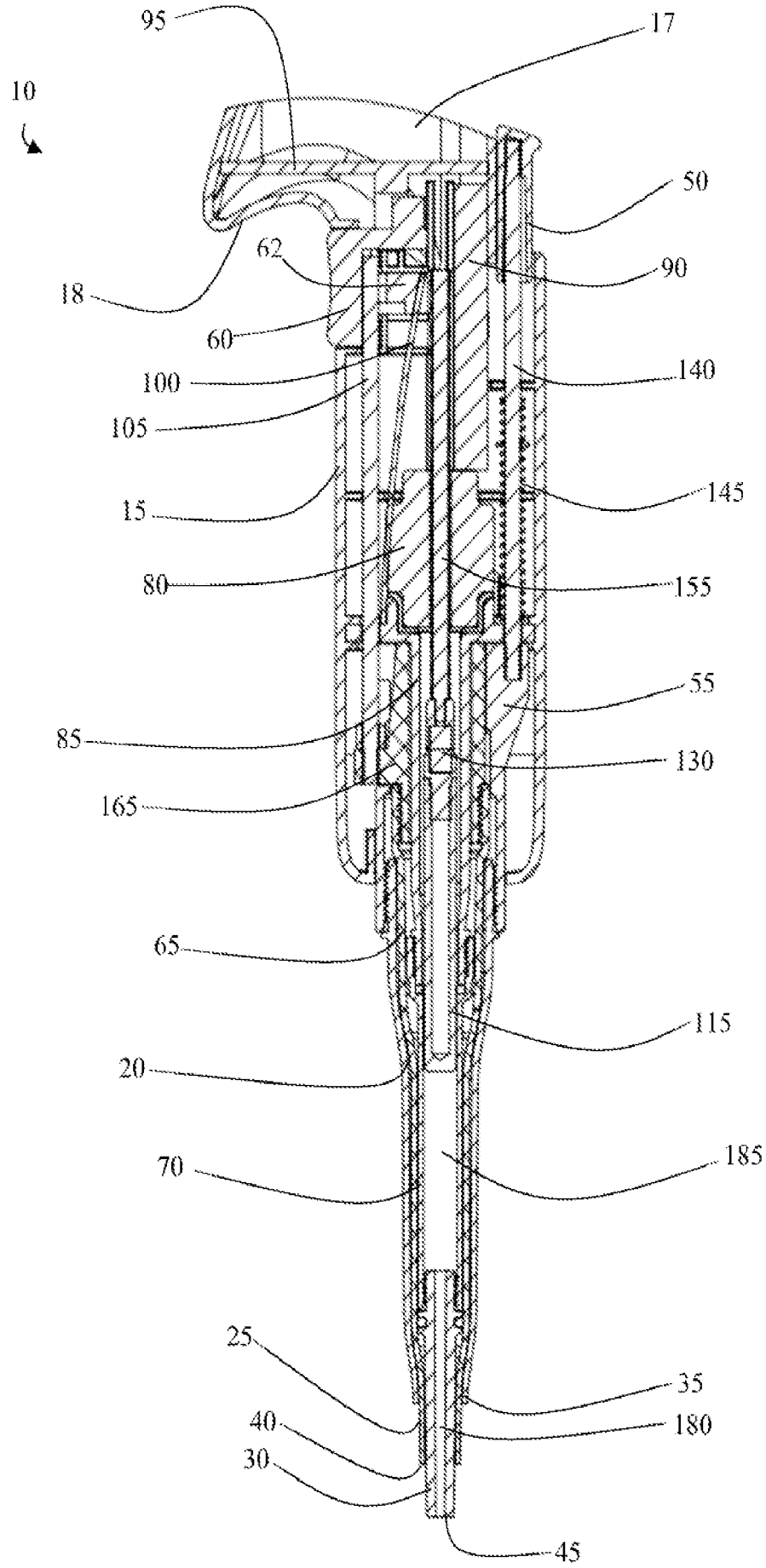

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FIG. 4

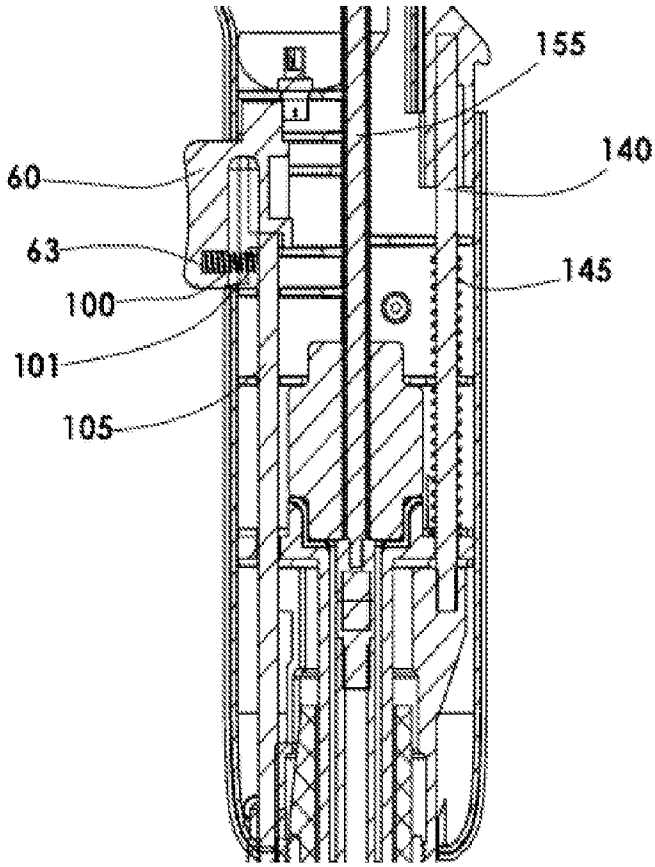


FIG. 5A

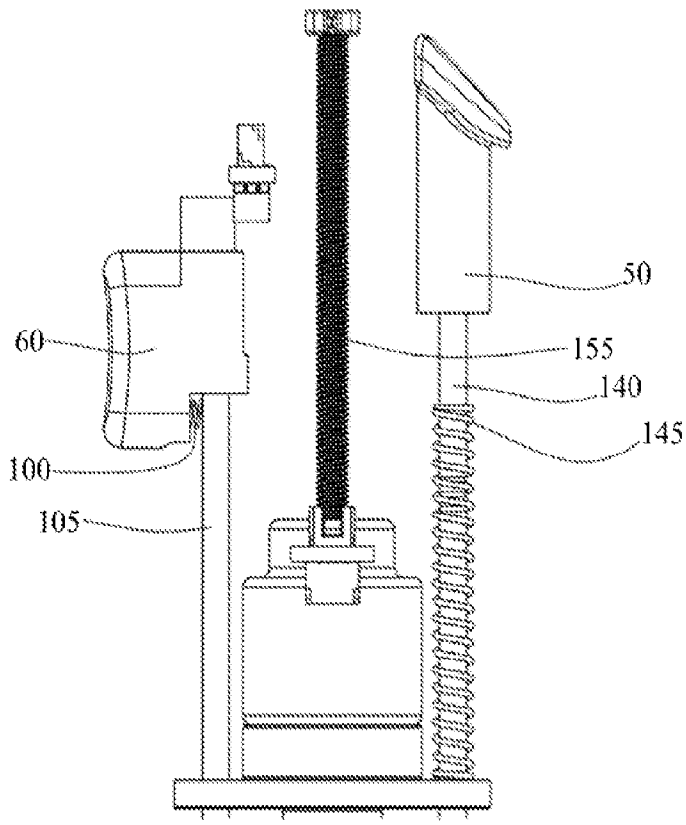


FIG. 5B

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2023/031425

A. CLASSIFICATION OF SUBJECT MATTER
INV. B01L3/02
ADD.

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)
B01L

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, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 1 688 180 A1 (ROCHE DIAGNOSTICS GMBH [DE]; HOFFMANN LA ROCHE [CH]) 9 August 2006 (2006-08-09) paragraphs [0009], [0016], [0023] - [0025], [0029]; figures 1-3	1-28
A	JP S61 212336 A (EASTMAN KODAK CO) 20 September 1986 (1986-09-20) the whole document	1-28
A	US 2021/252497 A1 (NEESE CHARLES [US] ET AL) 19 August 2021 (2021-08-19) paragraphs [0006] - [0008]; figure 6	1-28

☐ Further documents are listed in the continuation of Box C.

☒ See patent family annex.

* Special categories of cited documents :

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

"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	Date of mailing of the international search report
21 December 2023	15/01/2024

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

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INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/US2023/031425

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