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Declarations under Rule 4.17:

— *as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))*

— *as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii))*

(54) Title: MEDICAL FLUID CONNECTORS AND METHODS FOR PROVIDING ADDITIVES IN MEDICAL FLUID LINES

(57) Abstract: Disclosed is a medical fluid connector configured to receive and dispense medical liquid. The medical connector can be structured to include an initial stage in which medical liquid is infused into the connector and dispensed out of the connector essentially unchanged. The medical connector also can be structured to include a subsequent stage in which medical liquid is not infused into the connector and a volume of therapeutic liquid is dispensed out of the connector. The therapeutic liquid can include a portion of the volume of the medical liquid that was infused into the connector in the initial stage plus a therapeutic additive.

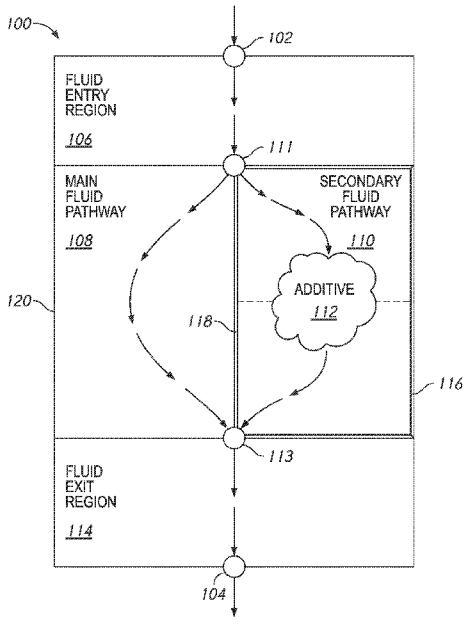

FIG. 1

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MEDICAL FLUID CONNECTORS AND METHODS FOR PROVIDING ADDITIVES IN MEDICAL FLUID LINES

PRIORITY CLAIM AND INCORPORATION BY REFERENCE

[0001] This application claims priority to U.S. Provisional Patent Application No. 62/492,887, filed on May 1, 2017, U.S. Provisional Patent Application No. 62/520,300, filed on June 15, 2017, U.S. Provisional Patent Application No. 62/558,618, filed on September 14, 2017, and U.S. Provisional Patent Application No. 62/662,149, filed on April 24, 2018, which are hereby incorporated by reference herein in their entireties, forming part of the present disclosure. Any feature, structure, material, method, or step that is described and/or illustrated in any embodiment in any of the foregoing provisional patent applications can be used with or instead of any feature, structure, material, method, or step that is described and/or illustrated in the following paragraphs of this specification or the accompanying drawings.

BACKGROUND

Field

[0002] This disclosure relates generally to medical fluid connectors, and specifically to medical fluid connectors for providing additives in medical fluid lines.

Description of the Related Art

[0003] In healthcare settings where an intravenous (IV) catheter is inserted into a patient, there is an ever-present risk of microbial invasion into the catheter, which can lead to a catheter-related bloodstream infection (CRBSI) in the patient. There are many negative effects of CRBSI's, including serious health risks and increased costs for additional patient treatment. It is common practice in situations where the risk of contracting a CRBSI is particularly high, such as in long-term uses of central venous catheters, to utilize an anti-microbial lock procedure to provide a static anti-microbial solution in the catheter when fluid is not being transferring to or from the patient through the catheter.

SUMMARY

[0004] Disclosed are embodiments of medical fluid connectors and/or fluid-modifying devices configured to receive, convey, and/or dispense medical liquid, methods of making the same, and methods of using the same. In some embodiments, the medical connector or fluid-modifying device can be structured to include an initial stage in which medical liquid is infused into the connector and at least a portion of the medical liquid (or all of the medical liquid) is dispensed out of the connector essentially unchanged. The medical connector or fluid-modifying device also can be structured to include a subsequent or final stage in which medical liquid is not infused into the connector and a volume of therapeutic liquid is dispensed out of the connector. In some embodiments, as illustrated, the connector or fluid-modifying device transitions automatically from the initial stage to the subsequent or final stage (e.g., without mechanical actuation or manipulation by a user of a switch or product setting or device configuration), such as by operation of fluid flow only and/or by one or more changes in a force propagated in or through a fluid. In some embodiments, the connector transitions from the initial stage to the subsequent stage by manual actuation by a user, such as by moving or changing a fluid pathway and/or opening a valve within or on the connector. The therapeutic liquid can include a portion of the volume of the medical liquid that was infused into the connector in the initial stage plus a therapeutic additive.

[0005] Some embodiments disclosed or claimed in this specification, or in any applications that claim priority to this specification, will overcome one or more of the identified shortcomings in the prior art. However, not all embodiments disclosed or claimed in this specification, or in any applications that claim priority to this specification, will overcome any or all of the identified shortcomings of the prior art, but can be useful for one or more other purposes.

BRIEF DESCRIPTION OF THE DRAWINGS

[0006] FIGURE 1 is a schematic illustration of a medical fluid connector;

[0007] FIGURE 2A is a front view of an example of a medical fluid connector of FIG. 1;

[0008] FIGURE 2B is a front view of another example of a medical fluid connector of FIG. 1;

[0009] FIGURE 2C is a front view of another example of a medical fluid connector of FIG. 1;

[0010] FIGURE 3A is an example cross-sectional view of the medical fluid connector of FIG. 2A, taken along the line 3A-3A of FIG. 2A;

[0011] FIGURE 3B is a cross-sectional view of the medical fluid connector of FIG. 2B, taken along the line 3B-3B of FIG. 2B;

[0012] FIGURE 3C is a cross-sectional view of the medical fluid connector of FIG. 2C, taken along line 3C-3C of Figure 2C;

[0013] FIGURE 3D is another example cross-sectional view of the medical fluid connector of FIG. 2A, taken along the line 3A-3A of FIG. 2A.

[0014] FIGURE 3E is another example cross-sectional view of the medical fluid connector of FIG. 2A, taken along the line 3A-3A of FIG. 2A.

[0015] FIGURE 3F is a cross-sectional view of the medical fluid connector of FIG. 3E, taken along the line 3F-3F of FIG. 3E.

[0016] FIGURE 4 is a front view of an internal fluid guide from the medical fluid connector of FIG. 2A;

[0017] FIGURE 5 is a front view of a fluid modifier from the medical fluid connector of FIG. 2A;

[0018] FIGURE 6A is an example cross-sectional view of the medical fluid connector of FIG. 3A with a cross-sectional view of a distal end of a syringe attached to an inlet end of the connector in a first stage of fluid flow;

[0019] FIGURE 6B is another example cross-sectional view of the medical fluid connector of FIG. 3D in a first stage of fluid flow;

[0020] FIGURE 6C is another example cross-sectional view of the medical fluid connector of FIGS. 3E-F in a first stage of fluid flow;

[0021] FIGURES 7 and 8 are example cross-sectional views of the medical fluid connector of FIG. 3A with a cross-sectional view of a distal end of a syringe attached to an inlet end of the connection in a second stage of fluid flow;

[0022] FIGURE 9 is an example cross-sectional view of the medical fluid connector of FIG. 3A with a cross-sectional view of a distal end of a syringe attached to an inlet end of the connection in a third stage of fluid flow;

[0023] FIGURE 10 is a cross-sectional view of the medical fluid connector of FIG. 2C with a cross-sectional view of a distal end of a syringe attached to an inlet end of the connector in a first stage of fluid flow;

[0024] FIGURES 11 and 12 are cross-sectional views of the medical fluid connector of FIG. 2C with a cross-sectional view of a distal end of a syringe attached to an inlet end of the connector in a second stage of fluid flow;

[0025] FIGURE 13 is a cross-sectional view of the medical fluid connector of FIG. 2C with a cross-sectional view of a distal end of a syringe attached to an inlet end of the connector in a third stage of fluid flow;

[0026] FIGURE 14 is a graph showing an example of an infusion of liquid through a connector of FIG. 2A, that illustrates a relationship between the concentration of additive as compared to infused volume; and

[0027] FIGURE 15 is a graph showing an example of an infusion of liquid through a connector of FIG. 2C, that illustrates a relationship between the concentration of additive as compared to infused volume.

DETAILED DESCRIPTION

[0028] Some embodiments disclosed herein pertain to medical connectors, fluid dispensers, and/or fluid modifiers. In some embodiments, the medical connectors include fluid modifiers that infuse a medical fluid with one or more additives, or permit the addition of one or more additives into a medical fluid, or modify a medical fluid in some other way, as the medical fluid passes through or is dispensed from the connector. In some embodiments, methods of making and/or using the disclosed connectors are provided. The following description provides context and examples, but should not be interpreted to limit the scope of the inventions covered by the claims that follow in this specification or in any other application that claims priority to this specification. No single component or collection of components is essential or indispensable. For example, some embodiments may not include a fluid modifier. Any feature, structure, component, material, step, or method that is described and/or illustrated in any embodiment in this specification can be used with or instead of any feature, structure, component, material, step, or method that is described and/or illustrated in any other embodiment in this specification. The relative sizes and dimensions of components shown in the drawings are not limiting if not present in a claim, but are intended to form part of the supporting disclosure in this specification when claimed.

[0029] While conventional procedures for achieving anti-microbial locks exist, those procedures are time-consuming, require the acquisition, storage, and use of multiple liquids, may be highly dependent on the techniques employed by healthcare

providers for successful outcomes (subject to human error or variation), and may not deliver the anti-microbial solution in an effective dosage or in a useful timing sequence. Some embodiments disclosed herein address one or more of these issues and/or other issues that can occur when using a catheter or while performing a conventional antimicrobial lock method with conventional equipment. In some embodiments, a medical fluid connector configured to provide an additive (e.g., an antimicrobial compound, etc.) to the catheter as a locking solution is provided. In some embodiments, as a medical fluid is passed through the connector, an initial volume of the medical fluid is unchanged or substantially unchanged, having little or no additive added to it, such that there is no clinically significant effect. In some embodiments, after the initial volume of medical fluid passes through the medical connector, the connector is configured to then permit removal of or distribute or expel (automatically, in some devices) an additive-infused or otherwise modified or different portion of medical fluid out of the connector and into the catheter. In some embodiments, a delayed release of additive into the medical fluid locks the catheter without infusing any (or substantially any or any clinically significant amount) of the locking solution (e.g., the additive-infused medical fluid) into the patient. For example, the initial liquid volume can be sufficient to flush the liquid container within the catheter into the patient (e.g., at least about 5 mL, or at least about 3 mL, or at least about 2 mL, etc.), and the volume of additive-infused liquid can be approximately equal to or less than the volume of liquid that is inside of the catheter in communication with the patient's blood flow (e.g., less than or equal to about 5 ml, or less than or equal to about 3 mL, or less than or equal to about 2 mL, etc.), or approximately equal to or less than the volume of liquid that is configured to be inside of the portion of the patient's catheter that is outside of the patient.

[0030] As illustrated in Figure 1, in some embodiments, a medical fluid connector 100 can comprise a housing 120, a fluid inlet or upstream connector 102, a fluid entry region 106, a main fluid pathway 108, a secondary fluid pathway 110, an additive 112, a fluid exit region 114, and a fluid outlet or downstream connector 104. As with all embodiments in this specification, any component(s) can be omitted. For example, a medical fluid connector 100 can omit the fluid entry region 106 and/or fluid exit region 114 (e.g., the fluid can enter or exit directly into or from another part of the connector 100. In the example illustrated, the connector 100 can be configured to: (a) receive a medical liquid in the inlet 102, such as saline or water or another medical

liquid (e.g., a glucose solution, a dextrose solution, a nutrient solution, a medicated or pharmaceutical solution, etc.); (b) permit a portion of the medical liquid to travel in the main fluid pathway 108 through to the fluid exit region 114 and out of the fluid outlet 104 without a clinically significant change to the liquid; and (c) permit another portion of the liquid to travel in the secondary fluid pathway 110 where it becomes mixed with an additive 112 and then moves into the fluid exit region 114 and out of the fluid outlet 104. In some embodiments, the medical liquid travelling through the secondary fluid pathway 110 can be offset in time, or out of phase, or delayed or advanced as compared to the medical liquid travelling through the main fluid pathway 108. In some embodiments, all or essentially all of the medical liquid infused into the connector is modified to include an additive, such as by first passing through a region of the connector containing a fluid modifier before exiting the connector. For example, in some embodiments, the main fluid pathway 108 and the secondary fluid pathway 110 are the same or overlap or are positioned in series flow rather than in parallel flow (as illustrated), such that all or essentially all of the medical liquid that is infused into the connector includes at least one additive before exiting the connector.

[0031] The main fluid pathway 108 and the secondary fluid pathway 110 can be separated by one or more physical barriers, or can constitute different portions of a single liquid flow being transported through the connector 100, or can represent a single liquid pathway in one or more different phases or configurations. In some embodiments, as shown, liquid that flows directly through the main fluid pathway 108, without deviating into the secondary fluid pathway 100, can be isolated or separated from the additive 112 or from a carrier, such as a matrix or substrate or other holder, of additive 112, during one or more phases, stages, or configurations of use. As illustrated, in some embodiments, the main fluid pathway 108 is essentially straight and/or is essentially co-linear or co-axial with the main central axis or longitude of the connector 200, while the secondary fluid pathway 110 can comprise at least a portion that is offset or spaced laterally from the main central axis or longitude of the connector 200, and/or non-parallel with the main central axis or longitude of the connector 200, and/or can include one or more turns or can follow a tortuous pathway through the connector 200. As shown, the secondary fluid pathway 110 can create more turbulence during fluid flow than the main fluid pathway 108, and/or can be configured to direct fluid through at least a portion of the secondary fluid pathway 110 in a direction that is different from or generally or completely opposite

from the direction of fluid flow through the main fluid pathway 108. In situations where the main fluid pathway 108 and the secondary fluid pathway 110 are separated by one or more physical barriers, a first diversion region 111 can be a location or a structure where the pathways 108, 110 separate or are caused to separate; and a second diversion region 113 can be a location or a structure where the separate pathways 108, 110 recombine or are caused to recombine. In many embodiments, either or both of the first and second diversion regions 111, 113 are omitted. In some embodiments, as shown in Figures 2A-3F and 6A-13, the first and second diversion regions 111, 113 can be positioned in the same location or substantially the same location (e.g., in or around a transitional region 274, 274A, 274B, 274C, 274D), and/or can exist or take effect at different times, depending on fluid-flow dynamics or changing configurations or positions of the structure of the connector 100. In some embodiments, as shown in Figure 1, the first and second diversion regions are not at the same location. In some embodiments, including those illustrated in Figure 2A, a carrier of the additive 112 or the additive 112 itself does not block or clog or impede the flow of fluid through the main fluid pathway 108 and/or the secondary fluid pathway 110 in a manner that would otherwise significantly diminish the fluid flow volume or rate.

[0032] Any of these steps and/or structures can be omitted. For example, in some embodiments, the connector 100 can be configured to permit all of the liquid to flow through a fluid pathway that includes one or more additives (e.g., if the additive is provided in the main fluid pathway and there is no secondary fluid pathway). In some embodiments, the one or more additives can be antimicrobial additives. As also described elsewhere herein, any other type of one or more additives can be used for any other type of patient therapy, with or without one or more antimicrobial additives.

[0033] As illustrated, in some embodiments, the connector 100 can comprise a fluid modifier 116 to alter one or more qualities of the liquid flow through the connector 100, such as by modifying the direction or size or shape of the liquid pathway through the connector 100 (e.g., in the secondary fluid pathway 110 and/or in the main fluid pathway 108), and/or by modifying the composition of the liquid flowing through the connector 100, such as by adding one or more additives 112 to the liquid flowing through the connector 100. A fluid modifier 116 may perform a single function or multiple functions. For example, in some embodiments, the fluid modifier 116 can: (a) permit the secondary fluid pathway to temporarily increase in size or volume or length; and/or (b) the fluid

modifier 116 can affect the timing or sequence of the passage of liquid through the secondary fluid pathway, such as by delaying the passage of liquid that enters and/or that travels through the secondary fluid pathway 110 as compared to the passage of liquid through the main fluid pathway 108 (e.g., liquid that passes by and/or does not travel through the secondary fluid pathway 110); and/or (c) the fluid modifier 116 can include a coating or a dusting or an impregnation or any other suitable application or placement or attachment of one or more additives on or in or underneath or covered by or surrounded by the fluid modifier 116 that can be dispersed from or by the fluid modifier 116 into the liquid passing through or around the fluid modifier 116 in a dosage, timing, and/or sequence that is clinically effective for a therapeutic use, such as for providing an anti-microbial lock.

[0034] For example, in some embodiments, the connector 100 can be configured to receive through the fluid inlet 102 a first medical liquid, such as saline or water or some other medical liquid, and to deliver out of the fluid outlet 104 a pre-determined initial volume of saline or water or some other medical liquid that has the same or essentially or substantially the same composition or the same or substantially the same clinical effect as the first medical liquid, and then subsequently to deliver out of the fluid outlet 104 a pre-determined secondary volume of a second medical liquid that is comprised of the first medical liquid plus a clinically significant concentration of one or more additives 112 that can be used to provide an effective therapy to a patient, such as an anti-microbial lock in a catheter line. Any other desired liquid delivery profile can be accomplished, such as an additional or alternative fluid delivery concentration or composition or sequence. For example, the first medical liquid can include a clinically significant concentration of one or more additives, followed by a second medical liquid that does not include a clinically significant concentration of one or more additives or that includes a different clinically significant concentration of one or more additives (e.g., if the main fluid pathway 108 and the secondary fluid pathway 110 both include one or more additives, or if there is an additional fluid pathway or if there are layers of additives positioned within the pathway); or a generally uniform concentration of one or more additives can be provided through substantially the entire period of infusion of liquid through the connector 100. In some embodiments, the fluid modifier 116 or the connector 100 does not include any additive 112, but may accomplish one or more other purposes,

such as performing a delay in the delivery of fluid or a pre-determine liquid-delivery sequence.

[0035] In some embodiments, as also described elsewhere herein, the secondary pathway 110 can fill as a result of, for example, a threshold volume and/or threshold rate of liquid passing into and/or through the main fluid pathway 108.

[0036] In some embodiments, the connector 100 comprises one or more additional fluid pathways (not shown) that fill before or after or while the secondary fluid pathway fills or is filled. In some embodiments, as described elsewhere herein, the additional pathways can fill as a result of, for example, a specific (e.g., threshold) volume and/or rate of liquid passing through the main fluid pathway and/or as a result of a specific (e.g., threshold) volume and/or rate of liquid passing through or into the secondary fluid pathway. In some embodiments, using a multistage configuration allows multiple infusion profiles or infusion profiles with multiple stages or changes to be obtained. In some embodiments, multiple connectors can be used (e.g., connected) serially or in any other way to achieve any of various clinically significant infusion profiles.

[0037] In some embodiments, there can be a boundary 118 that is in contact with or surrounding either or both of the main fluid pathway 108 and the secondary fluid pathway 110 or that is positioned between the main fluid pathway 108 and the secondary fluid pathway 100. The boundary can be configured to move, thereby changing either or both of the volumes or path lengths of the main fluid pathway 108 and the secondary fluid pathway 110, such as in a generally inverse relationship. In some embodiments, one or more valves can be provided between the main fluid pathway 108 and the secondary fluid pathway 110. For example, either or both of diversion regions 111, 113 can comprise a valve for selectively permitting or impeding fluid flow from the fluid entry region 106 and/or into the fluid exit region 114. The valve can transition between open and closed positions manually by a user or automatically (e.g., based upon a quantity of fluid flow or volume or a change in fluid pressure, or in some other way). In some embodiments, the valve or valves are responsive to a certain volume or force achieved in the main fluid pathway and/or in the secondary fluid pathway. In some embodiments, the connector 100 is configured to provide a desired dosage or concentration of one or more additives after a pre-determined period of time or after a pre-determined volume of liquid has passed through the connector 100, and/or during a pre-determined period of time or while a pre-

determined volume of liquid is passing through the connector, in the medical liquid that flows out of the fluid outlet 104 of the connector 100.

[0038] In some embodiments, the fluid modifier 116 can be omitted or can be configured to have no effect on the size, shape, and/or length of the fluid pathway. For example, in some embodiments, the size and/or length of the secondary fluid pathway 110 and the main fluid pathway 108 are both static, and/or the size and/or length of the secondary fluid pathway 110 can be greater than the main fluid pathway 108, thereby delaying the delivery of liquid through the secondary fluid pathway 110 as compared to the main fluid pathway 108. The secondary fluid pathway 110 can include one or more additives that can be dispersed into the liquid flowing through the connector 100, with or without a fluid modifier 116 to disperse the one or more additives into the liquid.

[0039] In some embodiments, the connector 100 is configured to deliver or to infuse a specific and/or adjustable volume of medical fluid with the additive. In some embodiments, as also described elsewhere herein, this volume is controllable depending on the length, volume, or other dimensions of the secondary fluid pathway 110. In some embodiments, the connector is configured to distribute sufficient additive-infused liquid to fill or substantially fill the catheter to which it is attached. In some embodiments, the connector is selected and/or configured to provide a volume of additive-infused liquid that fills only a portion of the catheter (e.g., a portion of tubing external to the patient's body) and/or a volume insufficient to overflow out of the catheter into the patient. For example, the volume of additive-infused liquid to be emitted from the connector 100 can be configured to be less than or approximately equal to the interior fluid-carrying volume of the patient's catheter or less than or approximately equal to a portion of the patient's catheter that is configured to be positioned outside of the patient's body during use. In some embodiments, the volume of additive-infused liquid is less than or equal to about: 0.25 mL, 0.5 mL, 2 mL, 5 mL, 10 mL, 25 mL, values between the aforementioned values, ranges spanning those values, or otherwise. In some configurations, the connector can be configured to receive a volume sufficient to fill or overfill the catheter and/or to deliver a small amount of additive or the entire volume of additive infused liquid into the patient (e.g., when the additive is a medicament, etc.). In some embodiments, in a multistage configuration or other configuration, a volume of additive-infused liquid can be delivered from the connector, followed by an additive-free (or substantially additive-free) volume of medical fluid. In some embodiments, for example, where a therapeutic agent and locking

agent are provided in a connector (or a series of connectors), the connector (or series) can be configured to deliver the therapeutic additive into the patient completely and to lock the catheter with the locking agent, which is retained or substantially retained in the catheter.

[0040] In some embodiments, the connector is configured to achieve one or more of the above-referenced volume distributions to the catheter when using any commercial catheter, including those selected from the group consisting of Hickman, Broviac, or Leonard tunneled catheters, including at least about 9 Fr or at least about 10 Fr Single or Double Lumen catheters, Double or Triple (e.g., red, blue, or white) Lumen catheters, at least about 12 Fr Double Lumen catheters, or at least about 12.5 Triple Lumen catheters. In some embodiments, the volume of additive-infused medical fluid distributed from (e.g., delivered out of) the connector is greater than or equal to about: 0.25 mL, 0.5 mL, 2 mL, 5 mL, values between the aforementioned values, ranges spanning those values, or otherwise. In some embodiments, the volume of additive-free medical fluid distributed from (e.g., delivered out of) the connector is greater than or equal to about: 0.25 mL, 0.5 mL, 2 mL, 5 mL, 10 mL, 25 mL, values between the aforementioned values, ranges spanning those values, or otherwise.

[0041] As also described in detail elsewhere herein, in some embodiments, at or near the termination of an infusion of medical liquid into the patient through the connector 100 (e.g., approximately at the point that the volume to be injected is achieved, the volume at which a plunger of a syringe used to infuse the fluid nears or reaches the terminal end of a syringe or bottoms out, at a point where the infusion is halted, etc.), the medical liquid in the secondary fluid pathway 110 exits the secondary fluid pathway 110 and passes through the fluid outlet 104. In some embodiments, this distribution of liquid from the secondary fluid pathway occurs automatically and/or without active manipulation of the connector by the user. In some embodiments, the medical fluid (e.g., the medical liquid without additive) and the additive-containing fluid (e.g., additive-infused liquid) mix at a location and/or time near or substantially at the end of the infusion of medical liquid through the connector 100 and/or form a locking solution at the fluid exit region 114 of the connector 100.

[0042] It is contemplated that any other embodiment that follows can include any feature, structure, component, material, step, or method of the connector 100 of Figure 1, whether or not explicitly described and/or illustrated in such other embodiment

for purposes of brevity. Nothing described or illustrated in connection with the connector 100 of Figure 1 is required or essential or indispensable in connector 100 or in any other embodiment in this specification.

[0043] As illustrated in Figure 2A, a connector 200 can include a fluid inlet 102 in the form of a first fluid-line attachment 202. The connector 200 can also include a cover cap 203, a housing 220, an air port 222, and a fluid outlet 104 in the form of a second fluid-line attachment 204. In some embodiments, the housing 220 can be formed of a rigid or substantially rigid material, such as polycarbonate. Either or both of the first or second fluid-line attachments can be closeable or resealable male or female connectors, such as a resealable female luer connector as the fluid inlet 202 and a resealable male luer connector with a male protrusion 205 as the fluid outlet 204, as shown. Any or all of the housing 220, the fluid guide 224, and/or the flexible carrier 232, and/or any other component or collection of components of the connector 200 can be made of, or can comprise a portion that is made of, a transparent or clear material to permit viewing of movement inside of the housing 220 or to permit viewing of liquid passing through the housing 220 or mixing with one or more additives inside of the housing 220. Any or all of the first fluid-line attachment 202, the housing 220, and the second fluid-line attachment 204 can be made of one or more rigid materials, such as polycarbonate or another form of plastic.

[0044] Figures 2B and 2C show other embodiments of medical connectors 200A, 200B. The embodiments of Figures 2B and 2C can include features that are the same as or that are different from features of the embodiment of Figure 2A. Figure 3A illustrates an example cross-section of the connector 200. Figures 3D-3E illustrate other example cross-sections of medical connectors 200C, 200D, although the connector 200C, 200D can have the same or substantially the same outer appearance as the connector 200 shown in Figure 2A. The embodiments of Figures 3D-3F can include features that are the same as or that are different from features of the embodiment of Figures 2A and 3A. Any feature, structure, component, material, step, or method that is described and/or illustrated in one of Figures 2A-2C and 3A-3F can be used with or instead of any feature, structure, component, material, step, or method that is described and/or illustrated in any other embodiment in this specification. Similar features (e.g., fluid guides, internal fluid pathways, etc.) for different embodiments of the connectors are shown with coinciding numerical values but labeled with either a letter or a different letter (e.g., no letter for

connector 200, the letter "A" for connector 200A, and the letter "B" for connector 200B, the letter "C" for connector 200C, and the letter "D" for connector 200D). For example, comparing the embodiment of Figure 2A to the embodiment of Figure 2B, the housing 220 of the connector 200 in Figure 2A coincides to the housing 220A of the connector 200A in Figure 2B. Likewise, comparing the embodiment of Figures 2A or 2B to the embodiment of Figure 2C, the housing 220 of the connector 200 in Figure 2A or the housing 220A of the connector 200A in Figure 2B coincides to the housing 220B of the connector 200B in Figure 2C.

[0045] For brevity, not every feature of the connector 200A of Figure 3B, the connector 200B of Figure 3C, the connector 200C of Figure 3D, or the connector 200D of Figures 3E-3F are numerically indicated, though certain features of the connector 200A, 200B, 200C, or 200D are apparent by comparing it with the connector 200 of Figure 3A and such features form part of the disclosure of Figures 3B-3F. In addition, just as the embodiments of Figures 3A-3F can have features that are the same or substantially the same, those embodiments can include one or more features that are different, as shown or otherwise. It should be appreciated that different features of the embodiments of Figures 3A-3F are for illustration only, and as disclosed elsewhere herein, any feature, structure, or component that is described and/or illustrated in one embodiment in this specification can be used with or instead of any feature, structure, or component that is described and/or illustrated in any other embodiment in this specification. Additionally, one or more of the features described for the illustrative embodiments herein can be excluded from other embodiments.

[0046] As illustrated in Figure 3A, an interior region of the connector 200 can comprise multiple components, including a fluid guide 224 with a proximal fluid port 228, a proximal cover region 256 (e.g., with a vent 225 (see also Figure 4)), an internal fluid pathway 226, a distal fluid port 230 (see also Figure 4), and a distal attachment region 250 (see also Figure 4); and a fluid modifying region 254 and a fluid modifier 116 in the form of a flexible carrier 232 with an internal region 248. In some embodiments, as shown, the fluid modifier 116 can be held in place at a plurality of points or regions inside of the connector 100. For example, a proximal edge 258 of the flexible carrier 232 can be securely held between an upper region 260 (e.g., forming a lip, a projection, a barb, etc.) of the housing 220 and an underside of the outer edge of the cover region 256 of the fluid guide 224; and a distal end region 262 of the flexible carrier 232 can be securely held

circumferentially in a fluid-tight manner in the distal attachment region 250 of the fluid guide 224, such as by forming a distal opening in the flexible carrier 232 that is slightly smaller than the outer circumference of the distal attachment region 250, causing the distal opening to exert a radially inwardly directed restoring force which tightly grips the distal attachment region 250 of the fluid guide 224. As shown, each of the connectors 200, 200A, 200B, 200C, 200D can be formed as a single integrated connector with any combination or all of the parts illustrated in the figures or described in the text permanently and non-removably attached to each other, and not configured to be attached together or removed from each other by a user in the normal course of use. Of course, in some embodiments, any components or combinations of components can be removable or attachable from each other by a user in suitable configurations, such as in modular configurations with different types of fluid modifiers that can be combined with different types of connector components. As illustrated in some embodiments, each of the connectors 200, 200A, 200B, 200C, 200D can be needle-free or needle-less or spike-less, without requiring an exposed metal or plastic needle or spike to pierce or penetrate a septum or seal or other structure to enable fluid flow.

[0047] As shown in Figures 3A, 3D, and 3E, the first fluid-line attachment 202, 202C, 202D can comprise an internal fluid channel 236, 236C, 236D that comprises a proximal female end 238, 238C, 238D (which in some embodiments can include an ISO 594-compliant luer taper) with a male-receiving region 234, 234C, 234D, and a male end 240, 240C, 240D that is coupled to the proximal fluid port 228, 228C, 228D of the fluid guide 224, 224C, 224D. In some embodiments, as shown in Figures 3A, 3D, and 3E, the proximal female end 238, 238C, 238D can be threaded. In some embodiments, the proximal female end is not threaded. The second fluid-line attachment 204, 204C, 204D can comprise an internal fluid channel 244, 244C, 244D, an internally threaded shroud 242, 242C, 242D, and a male luer protrusion 205, 205C, 205D (which in some embodiments can include an ISO 594-compliant luer taper). In some embodiments, the internal fluid pathway 226, 226C, 226D can have an internal diameter that is smaller than an internal diameter of the proximal internal fluid channel 236, 236C, 236D and/or an internal diameter of the internal fluid channel 244, 244C, 244D. In some embodiments, as shown in Figure 3C, any shroud provided herein can lack threading or, as shown in Figure 3B, any shroud provided herein can include threading. In some embodiments, any of the inlet or outlet adaptors (male or female) and shrouds disclosed herein can include

threading or lack threading. In some embodiments, as shown in the connector 200, 200C, 200D, the main fluid pathway 108 can be provided in the form of the combination of the internal fluid channel 236, 236C, 236D of the first fluid-line attachment and the internal fluid pathway 226, 226C, 226D of the fluid guide 224, 224C, 224D. In some embodiments, either or both of the first or second fluid-line attachments 202, 202C, 202D, 204, 204C, 204D can comprise closeable, resealable, and/or swabbable medical fluid connectors.

[0048] As shown in Figure 3B, in some embodiments, instead of a male connection, the connector 200A can include a fluid inlet 102 comprising a first fluid-line attachment 202A and a female luer connector 206A. In some embodiments, as shown in Figure 3B, the female luer connector 206A can include a male-receiving region 236A configured to receive a male protrusion (which in some embodiments can include an ISO 594-compliant luer taper). In some embodiments, the fluid inlet 102 is recessed as shown in Figure 3B. As shown, a recessed fluid-line attachment 202A can be disposed wholly within the connector and/or not protruding from the connector. In some embodiments, not shown, the fluid line attachment can be partially disposed in and/or partially protruding or exposed from the connector. Having a recessed fluid inlet 102 makes the connector 200A advantageously compact while still offering ease of manipulation by a user (e.g., providing a large area on the side of the connector for grasping between a finger and the thumb, allowing rotation and manipulation of the connector, for instance). In some embodiments, the recessed configuration facilitates bulk storage and/or transport of the connectors. In some embodiments, for example, the connectors 200A can be connected serially (e.g., end-to-end) and stored. As also disclosed elsewhere herein, serial connection or other connection of multiple connectors can advantageously be used to infuse more than one additive at a time. For instance, in some embodiments, where connectors are attached serially, each connector 200A in a series can comprise a different therapeutic and/or chemical agent. In some embodiments, during infusion of a medical fluid through serially linked connectors, different agents can be infused at once (e.g., with one infusion of medical fluid). In some embodiments, different connector configurations can be connected serially, in parallel, or in any other way to provide a desired additive infusion profile. The recessed configuration is also less bulky when in use, lowering chances that the connector is inadvertently contacted after insertion of the catheter into a patient, increasing the comfort level of the patient.

[0049] In some embodiments, as shown in Figure 3B, the recessed fluid inlet provides a receptacle 261A configured to receive a shroud of, for example, a syringe or another connector having a male luer fitting. In some embodiments, the receptacle 261A is configured to snuggly receive an interfacing shroud (e.g., is snug-fit). In some embodiments, the snug fitting within the receptacle provides added strength and/or stability to the connection between the coupling features. In some embodiments, this strength and/or stability can beneficially prevent movement, bending, or breakage of the coupled components. In some embodiments, interaction between the receptacle 261A and a shroud of a coupled device also provides stability in configurations where multiple connectors are attached serially by, for instance, preventing or substantially lowering the amount of movement between attached components (e.g., reducing bending, etc.).

[0050] In some embodiments, the connector has a length measured generally from a first end (e.g., from the inlet 102) to a second end (e.g., to the outlet 104) along the direction of fluid flow. In some embodiments, the connector also has a diameter measured across the connector transverse to the direction of fluid flow from a first side of the connector to a second side laterally (e.g., extending radially outward from the fluid pathway). In some embodiments, this diameter of the connector can be greater than an outer diameter of the fluid inlet and/or the fluid outlet. In some embodiments, this diameter can improve ease of gripping of the connector between fingers of a user.

[0051] As shown in Figures 3A, 3B, 3D, and 3E, in some embodiments, the length of the connector can be greater than the diameter (or equal to or greater than the diameter). As shown in Figure 3C, in some embodiments, the diameter can be greater than the length of the connector (or greater than or equal to the length).

[0052] In some embodiments, as also described elsewhere herein, having a length greater than the width of the connector also allows the user to easily grasp the connector and align it with the catheter during placement, replacement, or manipulation of the connector. In some embodiments, having a diameter greater than or equal to the length facilitates bulk storage and/or transport of the connectors. For example, as also described elsewhere herein, the connectors can be connected serially and stored or used (e.g., to infuse more than one additive or to infuse a greater quantity of additive). In some embodiments, in configurations where the diameter is greater than or equal to the length of the connector, serial or parallel connection and disconnection of the connectors is facilitated because the lateral sides of the connector protrude from the inlet and outlet

portions of the connector, allowing easier access to and manipulation of individual connectors.

[0053] As shown in Figure 3C, in some embodiments, any of the connectors disclosed herein can comprise traction features 221B to facilitate manipulation (e.g., placement, twisting, movement, etc.) of the connectors. For example, as shown in Figure 3C, the connector 200B can comprise grips 221B (e.g., roughenings, knurlings, traction pads, dimples, protrusions, ribs, etc.) around the periphery or portion of the periphery of the exterior of the connector 200B.

[0054] As shown in Figure 3C, in some embodiments, the connector 200B can include a fluid inlet 102 comprising a first fluid-line attachment 202B and a female luer connector 206B. As shown, the fluid inlet can lack a shroud. In some embodiments, as shown in Figure 3C, the female luer connector 206B can include a male-receiving region 236B configured to receive a male protrusion (which in some embodiments can include an ISO 594-compliant luer taper). In some embodiments, the fluid outlet of the connector 200B comprises a second fluid-line attachment 204B. In some embodiments, the second fluid-line attachment comprises one or more of an internal fluid channel 244B, a shroud 242 (e.g., a non-threaded shroud), and a male luer protrusion 205B (which in some embodiments can include an ISO 594-compliant luer taper). In some embodiments, the fluid outlet 104 lacks a shroud.

[0055] In some embodiments, the flexible carrier can be placed in an orientation that allows it to deform towards different portions of the connector 200, 200A, 200B, 200C, 200D. For example, in the embodiments of Figures 3A, 3B, 3D, and 3E, the flexible carrier 232, 232A, 232C, 232D is configured to deform upwardly and in a lateral direction that is towards the internal fluid pathway 226, 226A, 226C, 226D. In Figure 3C, the flexible carrier 232B configured to deform downwardly and laterally in a direction that is towards the housing 220B. In other embodiments, not shown, the flexible carrier can be placed in a position to deform in a direction towards the proximal end of the connector, or otherwise.

[0056] In some embodiments, such as shown in the embodiments of Figures 3A, 3D-3F, and 6A-9, the upwardly deforming configuration can advantageously utilize gravity as an additional restoring force when expelling the additive-infused liquid into the catheter. In other words, gravity (in addition to or instead of the elastic force of the fluid modifier) can provide a restoring force, pushing the additive-infused fluid out of the fluid

modifying region. In some embodiments, as shown in Figure 3C and 10-13, a downwardly deforming configuration (e.g., where the fluid contacting the flexible carrier enters at an upper portion of the flexible carrier and pushes the flexible carrier downward as the flexible carrier is deformed) can advantageously utilize gravity as an additional deforming force when infusing the medical liquid into the catheter. In other words, gravity (in addition to flow force of the fluid) can push against the flexible carrier, deforming it, and allowing infusion of the medical fluid with the additive. In some embodiments, during infusion, the user can manipulate the orientation of the connector (e.g., by holding it so the outlet faces upwardly or downwardly) to allow gravity to either or both aid in the deformation or restoration of the flexible carrier.

[0057] In some embodiments, such as shown in the embodiment of Figure 3C, the flexible carrier can be shaped in a manner that itself resists deformation. For example, the flexible carrier 232B of the embodiment of Figure 3C is cross-sectionally arch-shaped or substantially arch-shaped. The restorative force of one or more resiliently-shaped configurations (arch-shaped, arc-shaped, semi-circular, etc.) can advantageously provide additional restorative force to expel the additive-infused liquid from the fluid modifying region 254B.

[0058] As illustrated, in some embodiments, the first diversion region 111 of the embodiment of Figure 1 can be provided in the connector 200, 200A, 200B, 200D in the form of a plurality of alternative fluid pathways in the region between a distal end of the fluid guide 224, 224A, 224B, 224D and a constriction or diverter or divider 246, 246A, 246B, 246D, or near a distal end of the fluid guide 224C, with a diverter or divider 246C located proximal to the transitional region 274C. In some embodiments, the diverter or divider 246, 246A, 246B, 246C, 246D can comprise an opening that is narrower than the fluid pathway 226, 226A, 226B, 226C, 226D within the fluid guide 224, 224A, 224B, 224C, 224D. In some embodiments, the diverter or divider 246, 246A, 246B, 246C, 246D can include a constriction (such as shown in Figures 3A-3E), a manifold, a valve, or any other structure that can allow some but not all of the fluid from the fluid pathway 226, 226A, 226B, 226C, 226D to pass to the internal flow channel 244, 244A, 244B, 244C, 244D. The change in cross-sectional width between the fluid pathway 226, 226A, 226B, 226C, 226D within the fluid guide 224, 224A, 224B, 224C, 224D and the opening in the diverter or divider 246, 246A, 246B, 246C, 246D can cause some of the liquid that is passing through connector 200, 200A, 200B, 200C, 200D to be

diverted laterally into a lateral fluid region 252, 252A, 252B, 252C, 252D and then upwardly or downwardly into a fluid-modifying region 254, 254A, 254B, 254C, 254D such as a variable-volume fluid-modifying region 254, 254A, 254B, 254C, 254D between an interior wall 268, 268A, 268B, 268C, 268D of the housing 220, 220A, 220B, 220C, 220D and an exterior wall 264, 264A, 264B, 264C, 264D of the fluid modifier 116.

[0059] As shown in Figures 3A-3C, the transitional region 274, 274A, 274B can be located distal to the distal fluid port 230, 230A, 230B. The transitional region 274, 274A, 274B can include a gap separating a proximal end of the diverter or divider 246, 246A, 246B and a distal end 272, 272A, 272B of the fluid guide 224, 224A, 224B. The diverter or divider 246, 246A, 246B can be located distal to the transitional region 274, 274A, 274B. The transitional region 274, 274B in Figures 6A and 10 respectively can include the proximal opening of the diverter or divider 246, 246B and the lateral opening where the portion of the medical liquid 266, 266B is diverted laterally, and/or the space or volume located between these locations or structures. The lateral fluid region 252, 252A, 252B can extend radially and/or generally transverse to the fluid pathway 226, 226A, 226B.

[0060] As shown in Figure 3D, the diverter or divider 246C can be proximal to the transitional region 274C and can extend distally from the distal fluid port 230C to the transitional region 274C. The fluid guide 224C can have an outer surface 280C near the distal end 272C of the fluid guide 224C to interface with an inner surface 282C of the housing 220C near a proximal end of the second fluid-line attachment 204C. The interface can be impermeable to liquid such that liquid cannot pass through between the outer surface 280C and the inner surface 282C (for example, via a tight fit at the interface). The lateral fluid region 252C can be located near or at the distal fluid port 230C. The lateral fluid region 252C can extend generally transversely from the fluid pathway 226C to the variable-volume fluid-modifying region 254C and can comprise a generally uniform cross-section. In some embodiments, the cross-section of the lateral fluid region 252C can be generally circular.

[0061] The opening in the diverter or divider 246C can have a greater cross-sectional area than the lateral fluid region 252C. In some embodiments, the cross-sectional area of the opening in the diverter or divider 246C can be about four times that of the lateral fluid region 252C. In some embodiments, the opening in the diverter or divider 246C can have a greater internal diameter or width than the lateral fluid region

252C. In some embodiments, the internal diameter of the opening in the diverter or divider 246C can be at least about two times that of the lateral fluid region 252C. In some embodiments, the internal diameter of the opening in the diverter or divider 246C can be about 0.032" and the internal diameter of the lateral fluid region 252C can be about 0.016".

[0062] As shown in Figure 3E, the diverter or divider 246D can be located distal to the transitional region 274D so that the internal flow channel 244D extends distally from the diverter or divider 246D. The fluid guide 224D can have an outer surface 280D near the distal end 272D of the fluid guide 224D to interface with an inner surface 282D of the housing 220D near or at the proximal end of the second fluid-line attachment 204D. The interface can be liquid impermeable such that liquid cannot pass through between the outer surface 280D and the inner surface 282D (for example, via a tight fit at the interface). As shown in Figures 3E and 3F, the lateral fluid region 252D can be located to a lateral side of the transitional region 274D. The lateral fluid region 252D can be in fluid communication with the transitional region 274D at a distal end of the fluid region 252D, and can extend generally parallel to the fluid pathway 226D from the transitional region 274D to the variable-volume fluid-modifying region 254D. As shown in Figure 3E, the variable-volume fluid-modifying region 254D can include a portion between a distal end 286D of the fluid-modifying region 254D and a shoulder 284D of the fluid guide 224D. The lateral fluid region 252D can be in fluid communication with fluid-modifying region 254D at a location within this portion. In some embodiments, such as shown in Figures 3E and 3F, the lateral fluid region 252D can be adjacent the outer surface 280D near the distal end 272D of the fluid guide 224D. In other embodiments, the lateral fluid region can be located more laterally, with a tunnel connecting the lateral fluid region and the transitional region 274D.

[0063] The lateral fluid region 252D can have a generally uniform cross-section. As shown in Figure 3F, the lateral fluid region 252D can have a generally rectangular cross-section. In other embodiments, the cross section of the lateral fluid region 252D can have other shapes, such as semicircular, triangular, or others. The diverter or divider 246D can have an opening with a greater cross-sectional area than the lateral fluid region 252D. In some embodiments, the cross-sectional area of the opening in the diverter or divider 246D can be about four times that of the lateral fluid region 252D. In some embodiments, the opening in the diverter or divider 246D can have a

greater internal dimension than the lateral fluid region 252D. In some embodiments, the internal diameter of the opening in the diverter or divider 246D can be greater than a width of the cross-section of the lateral fluid region 252D. In some embodiments, the internal diameter of the opening in the diverter or divider 246D can be about 0.032" (resulting in a cross-sectional area of about 0.0008 square inch) and the lateral fluid region 252C can have cross-sectional dimensions such as 0.020" X 0.010", or any other dimensions resulting in a cross-sectional area of about 0.0002 square inch.

[0064] In some embodiments, such as shown in Figure 3A, at least a portion of the fluid modifying region 254 can be created by a separation or by an increase in distance between the flexible carrier 232 and another component of the connector 200, such as an inner wall 268 of the connector 200, producing a variable volume into which liquid can flow. The secondary fluid pathway 110 of the embodiment of Figure 1 can be provided in the connector 200, 200A, 200B, 200C, 200D of Figures 3A-3F in the form of the lateral fluid region 252, 252A, 252B, 252C, 252D and the fluid-modifying region 254, 254A, 254B, 254C, 254D, such as describedelsewhere herein. As illustrated in Figures 7-9 and Figures 11-13, the size or volume of the secondary fluid pathway 110 in the connector 200 (or 200C, 200D), 200B (or connector 200A, not shown) can be variable over time or variable as a function of the volume of fluid that has been infused into and/or out of the connector 200 (or 200C, 200D),, 200B. In some embodiments, as shown in Figures 3A-3E and 6-13, the fluid modifier 116 is a flexible carrier. In some embodiments, the fluid modifier 116 is a structure or device that does not significantly bend or flex to change the volume or direction of the fluid flow path, but instead merely permits an additive to be emitted or eluted or leached out into the fluid flow path, such as by dissolving into the fluid or releasing into the fluid or permitting the fluid to flow in, through, or around the fluid modifier 116 while the fluid modifier 116 itself remains essentially or entirely static.

[0065] In some embodiments, the connector comprises a fluid pathway with at least a portion that has a completely or at least substantially unobstructed pathway (e.g., through the entirety of the connector). For instance, while the constriction or diverter or divider 246, 246A, 246B, 246C, 246D can divert a portion of the medical fluid from the primary fluid path, a portion of fluid can travel directly through the opening in the diverter or divider or constriction unimpeded 266 (or 266C, 266D), 266B (as shown in Figures 6A-13). In some embodiments, the medical connector is configured to allow at least a

portion of the medical fluid to travel through it uninterrupted in a straight or substantially straight pathway and devoid (or substantially devoid) of additive. In some embodiments, as shown in Figures 3A-3E, the variable-volume fluid-modifying region 254, 254A, 254B, 254C, 254D is in fluidic communication with the fluid guide 224, 224A, 224B, 224C, 224D, the opening in the constriction or diverter or divider 246, 246A, 246B, 246C, 246D, and/or the internal fluid channel 244, 244A, 244B, 244C, 244D. Thus, while some embodiments can achieve certain objectives disclosed herein using a valve (e.g., to divert at least a portion of fluid into, for instance, a secondary fluid pathway of Figure 1), in other embodiments, the connector lacks a valve. In some embodiments, the infusion of additive containing fluid into the catheter happens by virtue of the elasticity of the flexible carrier, automatically and without additional infusion steps taken by a user.

[0066] As shown in Figure 5, in some embodiments, the flexible carrier 232 can be formed with a generally paraboloid shape, in which the exterior wall 264 comprises a wider proximal cross-sectional width and a narrower distal cross-sectional width. Any other suitable shape can be used (as shown in, for example, Figure 3C). In some embodiments, as shown, the flexible carrier 232 can be made of a flexible, resilient, deformable, and/or compressible material, such as silicone or another polymeric material. In some embodiments, the compressible material is porous or adherent to allow temporary uptake or reception of a therapeutic or antibacterial agent that can be subsequently released into the medical fluid. As shown, in some situations, the additive 112 can be provided on only one side of the flexible carrier 232 (or on any other carrier of additive 112), especially in situations when the medical fluid only contacts the flexible carrier 232 on one side. Of course, in many embodiments, the additive 112 can be provided on multiple sides of the flexible carrier 232 or the flexible carrier 232 can be provided with additive 112 embedded within and/or throughout its structure, such as when the flexible carrier 232 is a matrix or otherwise has passages through which the medical fluid passes or in which the medical fluid is temporarily absorbed. In some embodiments, the flexible carrier 232, 232A, 232B, 232C, 232D can be molded or otherwise made in a natural or native shape as shown in Figures 3A-3E and 5. In some embodiments, the flexible carrier is woven or otherwise formed. In some situations, when the flexible carrier 232, 232A, 232B, 232C, 232D is deformed or compressed or moved in some way that is different from its natural or native shape, it can be configured to exert a restoring force to return resiliently to its natural or native shape. In some

embodiments, the carrier can be formed of the additive 112 such that the carrier itself is partially or totally consumed or partially or totally dissolved away or leached into the medical fluid.

[0067] The flexible carrier 232, 232A, 232B, 232C, 232D can be configured to carry one or more additives 112 and to transfer the one or more additives 112 into the liquid that flows around or contacts the flexible carrier 232, 232A, 232B, 232C, 232D. In some embodiments, the one or more additives 112 can comprise any one or more of the following: an antimicrobial, an antibiotic, an antiseptic, an analgesic, an anesthetic, a blood-thinner, a chemotherapy drug, an immunosuppressive drug, a nutritional supplement, or any other therapeutic substance that is combinable with a liquid flowing through the connector 200, 200A, 200B, 200C, 200D. An example of an antimicrobial additive is chlorhexidine gluconate, which can be provided in powdered form and coated or dusted or positioned or otherwise placed around the outer surface of the exterior wall 264, 264A, 264B, 264C, 264D of the flexible carrier 232, 232A, 232B, 232C, 232D. In some embodiments, the one or more additives 112 can be temporarily adhered or bound or attached to the exterior wall 264, 264A, 264B, 264C, 264D of the flexible carrier 232, 232A, 232B, 232C, 232D, such as by electrostatic forces or in surface recesses or by a water-soluble or saline-soluble binder, such as glycerol. In some embodiments, the one or more additives 112 can be formed or trapped or bound to or into the structure of the exterior wall 264, 264A, 264B, 264C, 264D of the flexible carrier 232, 232A, 232B, 232C, 232D such as by being captured within a cross-linked matrix of the exterior wall 264, 264A, 264B, 264C, 264D in a manner that permits leaching out or eluting of the one or more additives into the liquid as the liquid flows around or through the flexible carrier.

[0068] In some embodiments, a degradable (e.g., biodegradable, water dissolvable, etc.) matrix is deposited on the exterior wall 264, 264A, 264B, 264C, 264D and/or on the flexible carrier 232, 232A, 232B, 232C, 232D. In some embodiments, the flexible carrier 232, 232A, 232B, 232C, 232D is a degradable matrix. In some embodiments, a portion of the degradable matrix dissolves upon exposure to medical fluid. In some embodiments, as the matrix degrades, sufficient additive is released into the medical fluid to permit locking of the catheter. In some embodiments, the degradable matrix can have a tailored or adjustable degradation rate and/or additive concentration such that the degradation rate and/or delivery concentration is sufficient to deliver an appropriate locking concentration throughout the estimated lifetime of the catheter or the

connector. For example, if a catheter is estimated to require locking about 15 times over its lifetime, the flexible carrier 232, 232A, 232B, 232C, 232D can be tailored to allow 1, 2, 10, 15 or more locks of the catheter line with sufficient therapeutic agent to, for example, avoid microbial growth in the catheter during the average lifetime use of the catheter.

[0069] In some embodiments, the additive (e.g. as disposed in, around, or near the variable-volume fluid-modifying region 254, 254A, 254B, 254C, 254D or elsewhere in the connector) comprises antibiotic. In some embodiments, the antibiotic is a gram-positive anti-bacterial, a gram negative antibacterial, or a combination thereof. In some embodiments, the additive comprises one or more of chlorhexidine, chlorhexidine gluconate, vancomycin, cefazolin, ceftazidime, ciprofloxacin, gentamicin, and/or ampicillin.

[0070] In some embodiments, the additive comprises an anti-coagulant. In some embodiments, the anti-coagulent is heparin. The anti-coagulant can be provided as the only additive or as an additive in combination with other additives described elsewhere herein. In some embodiments, the anti-coagulant is provided at a concentration of at least about: 100 units/mL, 2500 units/mL, 5000 units/mL, values between the aforementioned values, ranges spanning those values, or otherwise.

[0071] In some embodiments, the connector is configured to provide an additive infused solution with a concentration of equal to or at least about 0.2 mg/mL, 0.5 mg/mL, 1.0 mg/mL, 2.5 mg/mL, 5.0 mg/mL, 10 mg/mL, values between the aforementioned values, ranges spanning those values, or otherwise.

[0072] As illustrated in Figures 6A-9 (for the embodiment shown in Figure 2A, 3A, and 3D-3F) and Figures 10-13 (for the embodiment shown in Figure 2C and 3C), some embodiments of the connector 200, 200C, 200D, 200B can provide fluid flow in a plurality of different stages with different fluid flow characteristics and/or different liquid compositions. For example, in a first stage of the connector 200, 200C, 200D, 200B, as illustrated in Figures 6A-6C and 10, the flexible carrier 232, 232C, 232D, 232B can be in a first or initial phase in which its shape, orientation, and/or location is in a default or natural or native position. When moved or modified away from this position to a second or modified phase, the flexible carrier 232, 232C, 232D, 232B can be configured to exert one or more restoring forces to return to the first or initial phase. As shown, in the first or initial phase, the outer exterior wall 264, 264C, 264D, 264B of the flexible carrier 232,

232C, 232D, 232B can be in contact with, cover, and/or overlay at least a portion of, or nearly entirely, or all of, an interior wall of the region of the housing 220, 220C, 220D, 220B of the connector 200, 200C, 200D, 200B in which the flexible carrier 232, 232C, 232D, 232B is disposed.

[0073] As shown in Figures 6A-6C and 10, as a medical liquid 266, 266C, 266D, 266B (e.g., saline) is infused into the proximal end of the connector 200, 200C, 200D, 200B, such as from a syringe 270 (not shown in Figures 6B and 6C), 270B or other medical implement, the medical liquid passes through the first fluid-line attachment 202, 202C, 202D, 202B, into the internal pathway 226, 226C, 226D, 226B of the fluid guide 224, 224C, 224D, 224B, and then to the transitional region 274, 274C, 274D, 274B. The transitional region 274, 274D, 274B can be between the distal end 272, 274D, 272B of the fluid guide 224, 224D, 224B and the diverter or divider 246, 246D, 246B. The transitional region 274C can be distal of the distal end 272C of the fluid guide 224C and the diverter or divider 246C. As shown, the cross-sectional width or diameter of the constriction or opening in the diverter or divider 246, 246C, 246D, 246B is smaller than the cross-sectional width or diameter of the internal pathway 226, 226C, 226D, 226B of the fluid guide 224, 224C, 224D, 224B.

[0074] Some of the medical liquid 266, 266C, 266D, 266B passes from the transitional region 274, 274D, 274B directly through the constriction or opening in the diverter or divider 246, 246D, 246B, or from the internal fluid pathway 226C directly through the opening in the diverter or diverter 246C, into the interior of the male protrusion 205, 205C, 205D, 205B. In some embodiments, as illustrated, the portion of the medical liquid 266, 266C, 266D, 266B that passes directly through can be essentially unchanged; that is, it can have the same or essentially the same composition as before it entered the connector 200, 200C, 200D, 200B, and/or it can be therapeutically or clinically the same (e.g., the medical liquid can have no concentration of additive or clinically insignificant concentration, which can be a low enough concentration of additive dissolved in the medical liquid such that the medical fluid can be infused directly into a patient or otherwise be used as though it were completely additive-free). This essentially unchanged medical liquid 266, 266C, 266D, 266B passes very quickly through the connector 200, 200C, 200D, 200B, without a clinically significant delay, and emerges from and continues to be emitted from the second fluid-line attachment 204,

204C, 204D, 204B during an initial time period or over a period during which an initial volume of liquid is dispensed from the connector 200, 200C, 200D, 200B.

[0075] Generally simultaneously, another portion of the medical liquid 266, 266C, 266D, 266B is diverted laterally because the opening in the diverter or divider 246, 246C, 246D, 246B creates a lower flow rate (volume/time) of medical liquid 266, 266C, 266D, 266B entering from the wider internal fluid pathway 226, 226C, 226D, 226B of the fluid guide 224, 224C, 224D, 224B (and the transitional region 274, 274D, 274B) into the opening in the diverter or divider 246, 246C, 246D, 246B. As described above, the transitional region 274, 274D, 274B in Figures 6A, 6C, and 10 respectively can include the proximal opening of the diverter or divider 246, 246D, 246B and the lateral opening where the portion of the medical liquid 266, 266D, 266B is diverted laterally, and/or the space or volume located between these locations or structures. As described above, the lateral fluid region 252C and the diverter or divider 246C in Figure 6B can both be located proximal to the transitional region 274C. A ratio of the flow rate of medical fluid, and hence a volume of medical fluid, entering into the opening in the diverter or divider and into the lateral fluid region can be proportional to a ratio of the cross-sectional areas of the opening in the diverter or divider and the lateral fluid region. In some embodiments, such as shown in Figures 6B and 6C, the cross-sectional area of the opening in the diverter or divider 246C, 246D can be at least about three times or at least about four times that of the lateral fluid region 252C, 252D. When a volume of the medical fluid 266C, 266D enters the fluid pathway 226C, 226D, at least about 70% or at least about 80% of the volume of the medical fluid 266C, 266D enters the opening in the diverter or divider 246C, 246D, and less than or equal to about 30% or less than or equal to about 20% of the volume of the medical fluid 266C, 266D enters the lateral fluid region 252C, 252D. The ratio of the volume of medical fluid entering into the opening in the diverter or divider and into the lateral fluid region can be adjusted by adjusting the ratio of the cross-sectional areas of the opening in the diverter or divider and the lateral fluid region. In some embodiments, such as shown in Figures 6B and 6C, the ratio of the cross-sectional areas of the opening in the diverter or divider and the lateral fluid region can be adjusted by changing the size of the opening in the diverter or divider 246C, 246D, and/or the size of the lateral fluid region 252C, 252D.

[0076] In some embodiments, the diverted or laterally flowing liquid 276, 276C, 276D, 276B moves into the variable-volume fluid-modifying region 254, 254C,

254D, 254B and begins to: (a) exert a modifying force on the flexible carrier 232, 232C, 232D, 232B; and/or (b) contacts the exterior wall 264, 264C, 264D, 264B of the flexible carrier 232, 232C, 232D, 232B. In some embodiments of the connector 200, 200C, 200D, 200B, where the fluid modifier 116 is a flexible member but not a flexible carrier 232, 232C, 232D, 232B (e.g., because the fluid modifier 116 does not carry an additive 112), the variable-volume fluid-modifying region 254, 254C, 254D, 254B can contain the additive 112 or some other region or structure of the connector 200, 200C, 200D, 200B can contain or hold the additive 112 (e.g., a portion of a fluid-contacting inner wall 268, 268C, 268D, 268B of the housing 220, 200C, 200D, 220B or a portion of the fluid guide 224, 224C, 224D, 224B or one or more of any other structures or components of the connector 200, 200C, 200D, 200B, or any combination of structures or components). In some embodiments, the additive 112 can be omitted.

[0077] As shown in Figures 7-8 and 11-12, in a second stage of the connector 200, 200B, as more medical liquid 266, 266B is infused into the connector 200, 200B (such as by distally advancing and/or depressing a syringe plunger 277, 277B in the syringe 270, 270B), more medical liquid 266, 266B continues to pass through the diverter or divider 246, 246B and more liquid is forced into the variable-volume fluid-modifying region 254, 254B. The connector 200C, 200D can also have a second stage that can have substantially the same features as disclosed herein with reference to Figures 7 and 8 and that is not repeated for brevity. The additional liquid in the variable-volume fluid-modifying region 254, 254B causes the liquid to exert a force against the flexible carrier 232, 232B which causes at least a portion of the flexible carrier 232, 232B, such as a wall of the flexible carrier, to flex, bend, contract, collapse, deform, or otherwise move away from its default or natural or native position. The fluid-modifying region 254, or any component thereof, including the flexible carrier 232, 232B, can comprise a material that is softer, more pliable, more resilient, and/or more flexible than the material of the housing 220 of the connector 200. In some embodiments, at the same time, air contained within the internal region 248, 248B of the flexible carrier 232, 232B can be forced outside of the flexible carrier and through the vent 225, 225B and air port 222, 222B into the atmosphere. As shown, this escaping air can be sealed off from the flow of liquid through the connector 200, 200B. In some embodiments, the connector 200, 200B lacks a vent 225, 225B and the internal region 248, 248B is closed. In the illustrated embodiments, the mixing and emitting of additive into the medical liquid, and the fluid

flow within the connector 200, are not accomplished through erosion or dissolving or washing away of one or more layers that are configured to initially block mixing or emitting of the additive, but rather by a dynamic movement of one or more components of the connector that changes the direction, position, orientation, and/or volume of one or more fluid flow paths within the connector 200. Some embodiments can include one or more processes of mixing or emitting that include eroding or dissolving or washing away of one or more layers into the surrounding fluid.

[0078] As illustrated, in some embodiments, the movement of the flexible carrier 232, 232B can create a void between the exterior wall 264, 264B of the flexible carrier 232, 232B and the interior wall 268, 268B of the connector 200, 200B, which can increase the size of the variable-volume fluid-modifying region 254, 254B and temporarily store or retain liquid within the increasingly large fluid-modifying region 254, 254B. Once the flexible carrier 232, 232B begins to deform, it exerts a restoring force in opposition to the force of the entering liquid. In some embodiments, the force of the entering liquid is greater than the restoring force of the flexible carrier 232, 232B during the infusion stage. Simultaneously, the liquid in the fluid-modifying region 254, 254B can come into contact with and mix with one or more additives 112 on the flexible carrier 232, 232B or otherwise, transforming the liquid into a therapeutic liquid 278, 278B (e.g., an additive-containing liquid). In some embodiments, the therapeutic liquid 278, 278B can flow or swirl generally circumferentially around the interior of the housing 220, 220B of the connector 200, 220B in a general vortex pathway as medical liquid is infused into the connector 200, 200B, between the interior wall 268, 268B of the housing 220, 220B and the exterior wall 264, 264B of the flexible carrier 232, 232B, providing thorough mixing and consistency of concentration of additive 112 in the therapeutic liquid 278, 278B.

[0079] As shown in Figures 8 and 12, the second stage of the connector 200, 200B can end when the infusion of medical liquid 266, 266B into the connector 200, 200B ends, such as when the plunger 278, 278B of the syringe 270, 270B stops or bottoms out or moves to its distal end point within the syringe barrel. At this point, the fluid pressure within the main fluid pathway can decrease, and medical liquid 266, 266B can stop flowing from the first fluid-line attachment 202, 202B through the connector 200, 200B to the second fluid-line attachment 204, 204B.

[0080] As illustrated in Figure 9 and 13, a third stage of the connector 200, 200B can begin upon completion of the second stage, or at any other suitable time (such as after a delay after completion of the second stage). The connector 200C, 200D can also have a third stage that can have substantially the same features as disclosed herein with reference to Figure 9 and that is not repeated for brevity. In the third stage, the therapeutic liquid 278, 278B stored in the fluid-modifying region 254, 254B is no longer under pressure from the medical liquid 266, 266B that was previously being infused into the connector 200, 200B during stage two of the connector 200, 200B, and the restoring force exerted by the flexible carrier 232, 232B can then move the flexible carrier 232, 232B back toward its default or native or natural position in its first or initial phase. As the flexible carrier 232, 232B moves back toward its first or initial phase, the fluid modifying region 254, 254B shrinks or contracts or otherwise moves to decrease in size, and the therapeutic liquid 278, 278B in the fluid-modifying region 254, 254B is forced out, passing through the transitional region 274, 274B and the diverter or divider 246, 246B, into the male protrusion 205, 205B, and out of the connector 200, 200B. Thus, in some embodiments, the third stage can begin after infusion from the source (e.g., the syringe 270, 270B) of medical liquid 266, 266B stops, at which point a volume of therapeutic fluid 278, 278B is then dispensed from the distal end of the connector 200, 200B. In embodiments where the internal region of the connector is closed (e.g., in embodiments that lack a vent 225, 225B), the internal region increases in pressure upon deformation of the flexible carrier during depression of the syringe plunger. This pressure increase can be used to aid in forcing the additive-infused fluid out of the connector by exerting pressure on the flexible carrier, forcing the flexible carrier back into its original position.

[0081] Any of the first or second or third or other stages can be combined or eliminated. Any steps or methods that are described and/or illustrated in any particular stage can be performed additionally or alternatively in another stage. The descriptions and/or illustrations of stages are not intended to be exhaustive or limiting. In some embodiments, as illustrated, any transition from any stage to any other stage can be automatic. For example, one or more transitions between any stages can be governed by fluid-flow and/or fluid pressure parameters, not by one or more intentional or direct user adjustments or modifications of the connector. In some embodiments, one or more connector features can be manipulated and used collectively and/or singularly to adjust

and/or manipulate the ratio of medical fluid that remains substantially additive-free versus the amount of medical fluid infused with an additive (or additives). In some embodiments, multiple connector types with various features can be mixed and matched and attached serially for the infusion of multiple additives and/or to achieve multiple infusion profiles. As shown, in some embodiments, any of the connectors 200, 200A, 200B, 200C, 200D can be different from long-term medical pumps (e.g., bladder pumps or ambulatory pumps) in that the fluid-flow emitted from the downstream or outflow end or region of the connectors 200, 200A, 200B, 200C, 200D can terminate or stop generally simultaneously with or shortly after the fluid-flow infused or inserted into the upstream or inflow end or region of the connectors 200, 200A, 200B, 200C, 200D. For example, in some embodiments, as illustrated, the time between the beginning of fluid-flow infused or inserted into the upstream or inflow end or region of the connectors 200, 200A, 200B, 200C, 200D and the end of fluid-flow infused or inserted into the upstream or inflow end or region of the connectors 200, 200A, 200B, 200C, 200D can be generally equal to or greater than the time between the end of fluid-flow infused or inserted into the upstream or inflow end or region of the connectors 200, 200A, 200B, 200C, 200D and the end of fluid-flow emitted from the downstream or outflow end or region of the connectors 200, 200A, 200B, 200C, 200D, such that the connectors 200, 200A, 200B, 200C, 200D do not provide a long-term pumping function. Of course, in some embodiments, one or more structures, methods, functions, and/or components that are illustrated in the accompanying figures and/or described anywhere in this specification can be used in or with medical pumps or can be used as medical pumps with appropriate modifications.

[0082] In some embodiments, the cross-sectional area (e.g., diameter) of the internal fluid pathway is larger than the cross-sectional area of the fluid pathway through (or the opening in) the constriction or diverter or divider. In some embodiments, the diverter or divider can be a constriction. In some embodiments, the ratio of the cross-sectional area of the internal fluid pathway 226, 226A, 226B, 226C, 226D and the cross-sectional area of the opening in the diverter or divider or constriction 246, 246A, 246B, 246C, 246D can be changed from connector to connector to divert more or less liquid into the fluid modifying region. For example, if only a small volume of liquid is being infused, it may be advantageous to divert a larger volume of liquid into the fluid modifying region to allow sufficient additive to be infused into the medical fluid. As the cross-sectional area of the internal fluid pathway becomes larger relative to the cross-

sectional area of the fluid pathway at the diverter or divider or constriction, more fluid pressure builds at the diverter or divider or constriction diverting more fluid into the fluid modifying region. In some embodiments, the ratio of a cross-sectional area of the internal fluid pathway to the cross-sectional area of the fluid pathway through the diverter or divider or constriction is equal to or less than about: 5:4, 4:3, 2:1, 5:1, values between the aforementioned ratios, ranges spanning those ratios, or otherwise.

[0083] Alternatively or additionally, in some embodiments, the cross-sectional area of the entrance (e.g., the lateral fluid region) to the fluid modifying region is larger than the cross-sectional area of the fluid pathway through the diverter or divider or constriction. In some embodiments, the ratio of the cross-sectional area of the entrance of the fluid modifying region to the cross-sectional area of the opening in the diverter or divider or constriction can be different among a plurality of connectors to divert more or less liquid into the fluid modifying region, depending upon clinical needs. When the cross-sectional area of the entrance to the fluid modifying region is larger than the cross-sectional area of the fluid pathway at the diverter or divider or constriction, more fluid can be diverted into the fluid modifying region. In some embodiments, the ratio of a cross-sectional area of the entrance to fluid modifying region to the cross-sectional area of the fluid pathway through the diverter or divider or constriction is equal to or less than about: 2:1, 5:1, 10:1 values between the aforementioned ratios, ranges spanning those ratios, or otherwise.

[0084] In some embodiments, the volume of the secondary pathway can be adjusted and/or the volume of the primary fluid pathway can be adjusted. In some embodiments, the capacity of the secondary fluid pathway (e.g., the volume of liquid the secondary pathway can hold when filled) is equal to or at least about: 0.125 mL, 0.25 mL, 0.5 mL, 2 mL, 5 mL, values between the aforementioned values, ranges spanning those values, or otherwise. In some embodiments, capacity of the primary fluid pathway is equal to or at least about: 0.1 mL, 0.2 mL, 0.5 mL, 1 mL, values between the aforementioned values, ranges spanning those values, or otherwise. In some embodiments, by making the volume of the secondary fluid pathway 110 larger than the volume of the main fluid pathway 108, a larger volume of additive-infused medical liquid can be infused into the catheter. As shown in Figures 14 and 15, differing volume ratios of the main fluid pathway and secondary fluid pathway can be used to achieve different release profiles. In some embodiments, the ratio of the volume of the secondary fluid

pathway to the volume of the main fluid pathway is equal to or greater than about: 0.5:1, 1:1, 2:1, 4:1, ratios between the aforementioned ratios, ranges spanning those ratios, or otherwise. In some embodiments, the ratio of the length of the secondary fluid pathway to the length of the main fluid pathway can be adjusted. In some embodiments, the ratio of the length of the secondary fluid pathway to the length of the main fluid pathway is equal to or greater than about: 0.5:1, 1:1, 2:1, 4:1, ratios between the aforementioned ratios, ranges spanning those ratios, or otherwise. In some embodiments, the connector can be configured to have a low retained volume of fluid after the third stage is complete. In some embodiments, the retained volume of fluid in the connector after the third stage is less than or equal to about: 0.5 mL, 0.2 mL, 0.1 mL, values between the aforementioned values, ranges spanning those values, or otherwise.

[0085] In some embodiments, as discussed elsewhere herein, the medical fluid can enter the secondary fluid pathway 110 (or an additional fluid pathway) based in part on the rate and/or the volume of medical fluid injected into the connector 100. In some embodiments, for example, the amount of deformation of the flexible carrier and/or the amount of fluid that enters the secondary pathway depends on the rate at which a fluid is passed through main fluid pathway of the connector. In some embodiments, the secondary fluid pathway 110 is filled with medical fluid and/or the flexible carrier deforms when an infusion from, for example, a syringe into the connector reaches a rate of equal to, or at least, about: 0.25 mL/sec, 0.5 mL/sec, 2 mL/sec, 5 mL/sec, values between the aforementioned values, ranges spanning those values, or otherwise. In some embodiments, the additive can be completely or substantially distributed into the medical fluid with an infusion rate from a syringe (or other infusion device) of equal to, or at least, about: 0.25 mL/sec, 0.5 mL/sec, 2 mL/sec, 5 mL/sec, values between the aforementioned values, ranges spanning those values, or otherwise.

[0086] In some embodiments, the amount of deformation of the flexible carrier and/or the amount of fluid that enters the secondary pathway depends on the volume of fluid that is passed through the connector. In some embodiments, the secondary fluid pathway 110 is filled with medical fluid when an infusion volume is equal to or at least about: about: 2.5 mL, 5 mL, 10 mL, values between the aforementioned values, ranges spanning those values, or otherwise. In some embodiments, the additive can be completely or substantially completely distributed into the medical fluid using an

infusion volume of equal to or at least about: 2.5 mL, 5 mL, 10 mL, values between the aforementioned values, ranges spanning those values, or otherwise.

[0087] In some embodiments, the resiliency and/or the modulus of the flexible carrier can be selected to provide different release characteristics. In some embodiments, stiff materials deform less and result in less additive being added to the medical fluid but can expel the additive at a greater pressure and in less time. In some embodiments, the resilience of the flexible carrier is at least about: 0.1 J/m^3, 1 J/m^3, 10 J/m^3, 100 J/m^3, values between the aforementioned values, ranges spanning those values, or otherwise. In some embodiments, the modulus of the flexible carrier is greater than or equal to about: 0.01 GPa, 0.1 GPa, 1 GPa, 2 GPa, values between the aforementioned values, ranges spanning those values, or otherwise.

[0088] In some embodiments, a portion of the flexible carrier can comprise an indicator, for instance, a colored, luminescent, or fluorescent dye (not shown). In some embodiments, the indicator dissolves into the medical fluid with the additive. In some embodiments, the indicator is located on a portion of the flexible carrier that is away from or distal to the transitional region so that the indicator is only infused into the medical fluid after all or substantially all the additive is infused into the medical fluid. In some embodiments, where the indicator is present, the indicator only enters into the medical fluid when an appropriate rate and/or volume of medical fluid enters the variable-volume fluid-modifying region 254, 254A, 254B, 254C, 254D. In some embodiments, the indicator can be used to visually demonstrate that the additive has been appropriately infused into the medical fluid. In some embodiments, the indicator may also be used to visualize the distance that the lock solution (or any other therapeutic solution) has traveled in the catheter line.

[0089] In some embodiments, as shown in at least Figures 6A-9 and Figures 10-13, the connector 200, 200C, 200D, 200B can be structured and/or configured to: (a) initially direct liquid into the secondary fluid pathway 110 (e.g., the lateral fluid region 252, 252C, 252D, 252B and the variable-volume fluid-modifying region 254, 254C, 254D, 254B) in an entrance direction and then subsequently direct that same liquid, in a modified form, back out of the secondary fluid pathway 110, in a substantially or primarily opposite exit direction; (b) simultaneously provide a first fluid pathway through an interior or central region of the connector 200, 200C, 200D, 200B (e.g., internal fluid pathway 226, 226C, 226D, 226B) and a second fluid region or pathway (e.g., the lateral

fluid region 252, 252C, 252D, 252B and the variable-volume fluid-modifying region 254, 254C, 254D, 254B) through or around or into a peripheral or outer region of the connector 200, 200C, 200D, 200B; (c) simultaneously permit some portion of fluid conveyed within the connector 200, 200C, 200D, 200B to move primarily in a distal direction (e.g., in the fluid guide 224, 224C, 224D, 224B) and some portion of fluid conveyed within the connector 200, 200C, 200D, 200B to move primarily in a proximal direction (e.g., into the variable-volume fluid-modifying region 254, 254C, 254D, 254B); (d) provide a single fluid exit (e.g., diverter or divider or constriction 246, 246C, 246D, 246B) for both the main fluid pathway 108 and the secondary fluid pathway 110; (e) automatically continue emitting fluid out of the fluid exit region 114 (e.g., out of the male protrusion 205, 205C, 205D, 205B) for a clinically significant period of time after infusion of fluid into the fluid entry region 106 has stopped and/or produce an automatic delay in stopping the flow of fluid or permit a continuation in delivering or emitting a substantial or clinically significant amount of fluid (e.g., at least about 20% of the fluid-holding capacity of the overall connector 200, 200C, 200D, 200B or at least about 5 mL or at least about 10 mL) out of the fluid exit region 114 (e.g., male protrusion 205, 205C, 205D, 205B) after the infusion of fluid into the fluid entry region 106 (e.g., the first fluid-line attachment 202, 202C, 202D, 202B) has stopped; (f) provide an internal fluid pathway 226, 226C, 226D, 226B that does not move with respect to the housing 220, 220C, 220D, 220B of the connector 200, 200C, 200D, 200B; (g) provide a rigid internal fluid pathway (e.g., internal fluid pathway 226, 2226C, 226D, 226B) that extends across and/or within a flexible member (e.g., flexible carrier 232, 232C, 232D, 232B); (h) provide fluid flow both inside and outside of a flexible member (e.g., flexible carrier 232, 232C, 232D, 232B); (i) provide fluid contact and/or fluid flow across or around or on an outside surface of a flexible member; and/or (j) provide a rigid internal fluid pathway (e.g., internal fluid pathway 226, 226C, 226D, 226B) that extends across and/or within a flexible member (e.g., flexible carrier 232, 232C, 232D, 232B), the internal fluid pathway being longitudinally stationary with respect to the flexible member. Any of these features can be included in or omitted from any embodiment in this application.

[0090] Figures 14 and 15 provide examples of liquid dispensing profiles created by liquid flowing through and/or out of a fluid source, such as connector 200 (or connector 200C, 200D) and connector 200B, respectively. In the first stage, which in some embodiments can correspond to the condition of the connector 200, 200B shown in

Figures 6A and 10, medical fluid 266, 266B can pass into and out of the connector 200, 200B in an unchanged or essentially unchanged state such that the concentration of additive 112 is essentially non-existent or essentially zero or clinically insignificant. In the second stage, which in some embodiments can correspond to the condition of the connector 200, 200B shown in Figures 7-8 and 11-12, medical fluid 266, 266B can pass into and out of the connector with very little, if any change (e.g., not clinically significant), but some of the medical fluid can be internally mixing with additive 112 and can be temporarily retained or stored inside of the connector 200, 200B. In the second stage, medical fluid 266, 266B can also pass into and out of the connector in an unchanged or essentially unchanged state. Finally, in the third stage, which in some embodiments can correspond to the condition of the connector 200, 200B shown in Figures 9 and 13, medical fluid 266, 266B can stop being infused into the connector 200, 200B, and/or therapeutic fluid 278, 278B can be expelled or dispensed or emitted from a liquid storage or liquid retaining region inside of the connector 200, 200B with a high concentration of additive 112 in the therapeutic fluid 278, 278B, which is clinically significant (e.g., for an antimicrobial product, the concentration of antimicrobial additive can be sufficient to provide antimicrobial protection in a catheter that diminishes the risk of microbial invasion into the catheter to a level that is clinically acceptable according to one or more applicable industry standard practices or guidelines). For example, during the third or final stage, in some embodiments, the maximum concentration of additive can be at least about 3% or at least about 10% or at least about 30% of the total liquid volume or weight, and/or no more than about 5% or no more than about 12% or no more than about 40% of the total liquid volume or weight, depending upon the particular type of additive used and the therapeutic purposes of the treatment. As illustrated in Figures 14 and 15, the concentration of the additive can rapidly increase from essentially none (or a clinically insignificant amount) to any of the foregoing clinically significant concentrations (or any other clinically significant concentration) in a short time or while a small amount of liquid passes through the connector, such as within less than or equal to about 0.25 second or less than or equal to about1.0 second at an average fluid flow rate through a medical connector, or while less than or equal to about 1, 2, or 5 mL of liquid passes through the connector. In some embodiments, the percentage of concentration of additive, such as an antimicrobial additive and/or an antibiotic additive, can rise from essentially zero in the first stage to at least about 0.2% or at least about 1.5% in a

subsequent stage (e.g., the third stage). Many other different types and stages and concentrations of fluid-dispensing profiles can be provided, depending upon therapeutic needs. In some embodiments, the volume of liquid that is dispensed or expelled out of the connector during the first stage and/or the second stage (or any other initial or intermediate stage) can be greater than or equal to about the volume of liquid capacity of a catheter to which the connector is intended to be attached, such that the liquid dispensed or expelled out of the connector during the first stage and/or the second stage can provide a flush of basic, standard, non-therapeutic, non-pharmaceutical, or inert medical liquid (such as medical liquid without an additive, e.g. saline or other medical liquid without an additive) from the connector into the patient catheter to flush essentially the entire patient catheter before subsequent use. In some embodiments, the volume of liquid that is dispensed or expelled out of the connector during the third stage (or during any other intermediate or final stage or any stage that is subsequent to the first stage or to the second stage) can be less than or equal to about the volume of liquid capacity of the patient catheter to which the connector is intended to be attached, such that the liquid dispensed or expelled out of the connector during this stage does not become infused into the patient or does not become infused into the patient in any clinically significant volume, but rather is configured to remain in the catheter during a locking or antimicrobial phase. Many other different configurations can be used, including configurations that do not provide a locking or antimicrobial phase. The volumes in each stage can be designed or configured to fit a variety of different clinical needs or therapeutic purposes.

[0091] Some embodiments pertain to methods of using medical fluid connectors as disclosed herein. Any device or structure illustrated or described in this specification can be used with any method in this specification. In some embodiments, a method includes the step of obtaining a connector. In some embodiments, a method includes the step of attaching the connector to a catheter. In some embodiments, a method includes the step of obtaining a syringe or device capable of holding a medical fluid. In some embodiments, a method includes the step of attaching the syringe or other device to the connector. In some embodiments, a method includes the step of introducing medical fluid into the connector and/or the catheter using the syringe or other medical fluid carrying device. In some embodiments, a method includes the step of introducing an additive to the fluid as it passes through the connector. In some embodiments, a first portion of fluid that is substantially additive-free is introduced to the catheter. In some

embodiments, a second portion of fluid that contains additive is introduced to the catheter. In some embodiments, a first portion of fluid that contains additive (e.g., a therapeutic) is introduced to the catheter and/or passed through the catheter to the patient. In some embodiments, a second portion of fluid that is contains additive is introduced to the catheter. In some embodiments, the method includes the step of locking the catheter with an antimicrobial-containing medical fluid.

[0092] Some embodiments pertain to methods of preparing medical fluid connectors. In some embodiments, a method includes the step of obtaining one or more of a fluid guide, a proximal cover region (e.g., with a vent), and/or a distal fluid port. In some embodiments, a method includes the step of attaching a fluid modifier in place at a plurality of points or regions inside of the connector. In some embodiments, a method includes the step of affixing a proximal edge of the flexible carrier securely between an upper region (e.g., forming a lip, a projection, a barb, etc.) of the housing and an underside of the outer edge of a region of the fluid guide (e.g., a cover region). In some embodiments, a distal end region of the flexible carrier is fastened circumferentially (e.g., securely and/or in a fluid-tight manner) at the distal attachment region of the fluid guide, such as by affixing a distal opening in the flexible carrier that is slightly smaller than the outer circumference of the distal attachment region, causing the distal opening to exert a radially inwardly directed restoring force which tightly grips the distal attachment region of the fluid guide. In some embodiments, the fluid guide and/or the flexible carrier can be placed into the housing of the connector. In some embodiments, a cap can be placed over the fluid guide, securing it in place. In some embodiments, a first fluid line attachment can be affixed or placed on the fluid guide.

[0093] Certain features that are described in this disclosure in the context of separate implementations can also be implemented in combination in a single implementation. Conversely, various features that are described in the context of a single implementation also can be implemented in multiple implementations separately or in any suitable subcombination. Moreover, although features may be described above as acting in certain combinations, one or more features from a claimed combination can in some cases be excised from the combination, and the combination may be claimed as a subcombination or variation of a subcombination.

[0094] Any portion of any of the steps, processes, structures, and/or devices disclosed or illustrated in one embodiment, flowchart, or example in this disclosure can

be combined or used with (or instead of) any other portion of any of the steps, processes, structures, and/or devices disclosed or illustrated in a different embodiment, flowchart, or example. The embodiments and examples described herein are not intended to be discrete and separate from each other. Combinations, variations, and other implementations of the disclosed features are within the scope of this disclosure.

[0095] Some embodiments have been described in connection with the accompanying drawings. Moreover, while operations may be depicted in the drawings or described in the specification in a particular order, such operations need not be performed in the particular order shown or in sequential order, and/or one or more of the operations may be omitted entirely, to achieve desirable results. Other operations that are not depicted or described can be incorporated in the example methods and processes. For example, one or more additional operations can be performed before, after, simultaneously, or between any of the described operations. Additionally, the operations may be rearranged or reordered in other implementations. Also, the separation of various components in the implementations described above should not be understood as requiring such separation in all implementations, and it should be understood that the described components and systems can generally be integrated together in a single product or packaged into multiple products. Additionally, other implementations are within the scope of this disclosure.

THE FOLLOWING IS CLAIMED:

1. A medical fluid connector configured to receive and dispense medical liquid, the medical fluid connector comprising:

an initial stage in which medical liquid is infused into the connector and dispensed out of the connector essentially unchanged; and

a subsequent stage in which medical liquid is not infused into the connector and a volume of therapeutic liquid is dispensed out of the connector, the therapeutic liquid comprising a portion of the volume of the medical liquid that was infused into the connector in the initial stage plus a therapeutic additive.

2. The medical fluid connector of Claim 1 further comprising a fluid modifier.

3. The medical fluid connector of Claim 2 in which the fluid modifier is a flexible carrier.

4. The medical fluid connector of Claim 3 in which the flexible carrier comprises one or more additives.

5. The medical fluid connector of Claim 4 in which the one or more additives comprise an antimicrobial agent.

6. The medical fluid connector of Claim 5 in which the antimicrobial agent is chlorhexidine.

7. A medical fluid-modifying device configured to modify a medical fluid by inserting an additive into the medical fluid, the medical fluid-modifying device comprising:

an upstream connector;

a downstream connector;

a main fluid pathway; and

a secondary fluid pathway that is different from the main fluid pathway;

wherein the main fluid pathway is configured to convey unchanged a portion of the medical liquid that is inserted into the fluid-modifying device from the upstream connector to the downstream connector, and wherein the secondary fluid pathway is configured to add an additive into a portion of the medical liquid that is inserted into the fluid-modifying device.

8. The medical fluid-modifying device of Claim 7, wherein the unchanged portion of the medical liquid is conveyed through the medical fluid-modifying device before the portion of the medical liquid in which the additive is added.

9. The medical fluid-modifying device of Claim 8, wherein the unchanged portion of the medical liquid has a sufficient volume to be configured to flush out a patient catheter to be used with the medical fluid-modifying device before a clinically significant amount of additive is added to the medical liquid by the medical fluid-modifying device.

10. The combination of the medical fluid-modifying device of Claim 9 and the patient catheter.

11. The fluid-modifying device of Claim 7, wherein the secondary fluid pathway includes a carrier of additive.

12. The fluid-modifying device of Claim 11, wherein the carrier of additive is flexible.

13. The fluid-modifying device of Claim 12, wherein the flexible carrier of additive is configured to change the volume within the secondary fluid pathway.

14. The medical fluid-modifying device of Claim 7, wherein at a diversion region between the main fluid pathway and the secondary fluid pathway, the main fluid pathway has a first cross-sectional area and the secondary fluid pathway has a second cross-sectional area, the first cross-sectional area being greater than the second cross-sectional area.

15. The medical fluid-modifying device of Claim 15, wherein the first cross-sectional area is at least about four times larger than the second cross-sectional area.

16. A medical fluid connector configured to receive and dispense medical liquid, the medical fluid connector comprising:

an inlet configured to receive into the connector a first predetermined volume of a medical fluid; and

an outlet configured to dispense a second predetermined volume of the medical fluid out of the connector in at least a first stage and a second stage, the medical fluid connector being configured to move at least a portion of the medical fluid through the connector along a different fluid path in the second stage than in the first stage,

wherein in the first stage, the medical fluid is dispensed out of the connector without a therapeutic additive or at least without a clinically significant concentration of the therapeutic additive, and in the second stage, the medical fluid is dispensed out of the connector with a therapeutic additive of a clinically significant concentration, and

wherein transition from the first stage to the second stage takes place when a first dispensed volume of the medical fluid has been dispensed out of the connector that is smaller than the second predetermined volume.

17. The medical fluid connector of Claim 16, wherein a concentration of the therapeutic additive present in the dispensed medical fluid in the second stage initially increases with an increase in a volume of the medical fluid dispensed out of the connector.

18. The medical fluid connector of Claim 16 or 17, wherein the first dispensed volume is at least about 80% of the second predetermine volume.

19. The medical fluid connector of any of Claims 16-18, wherein the medical fluid connector is configured to dispense medical fluid during the second stage even after medical fluid is no longer being received into the connector.

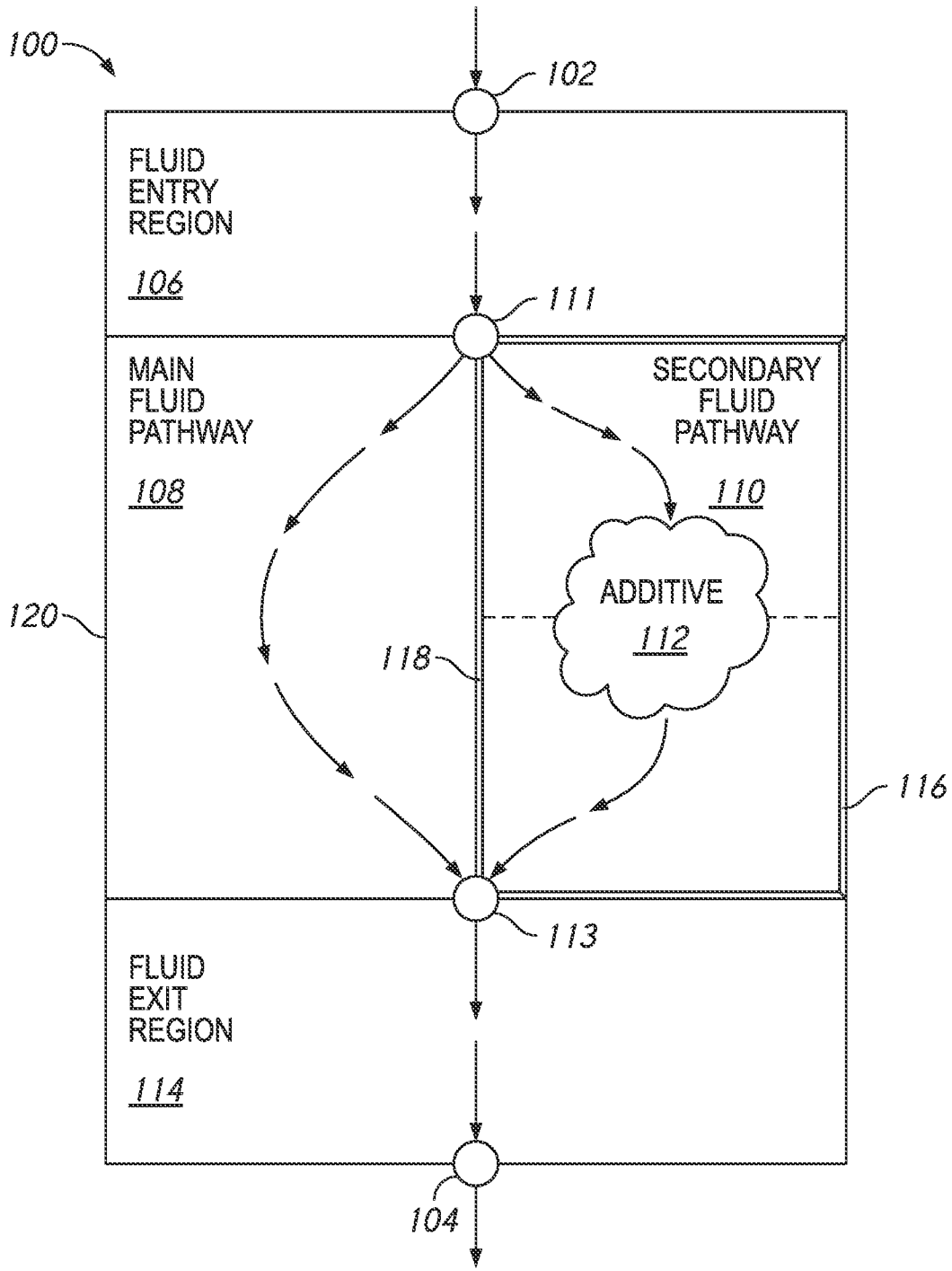
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FIG. 1

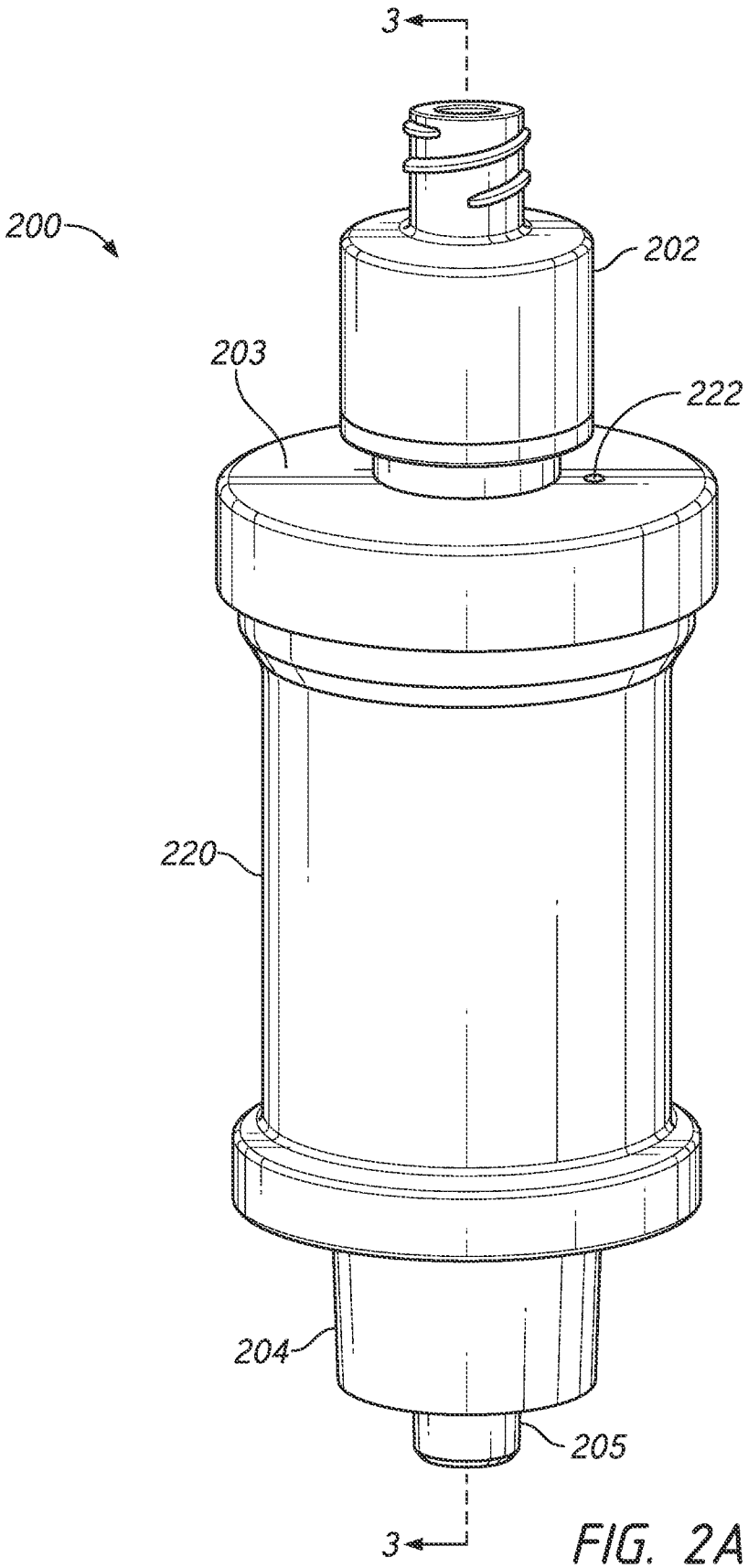

FIG. 2A

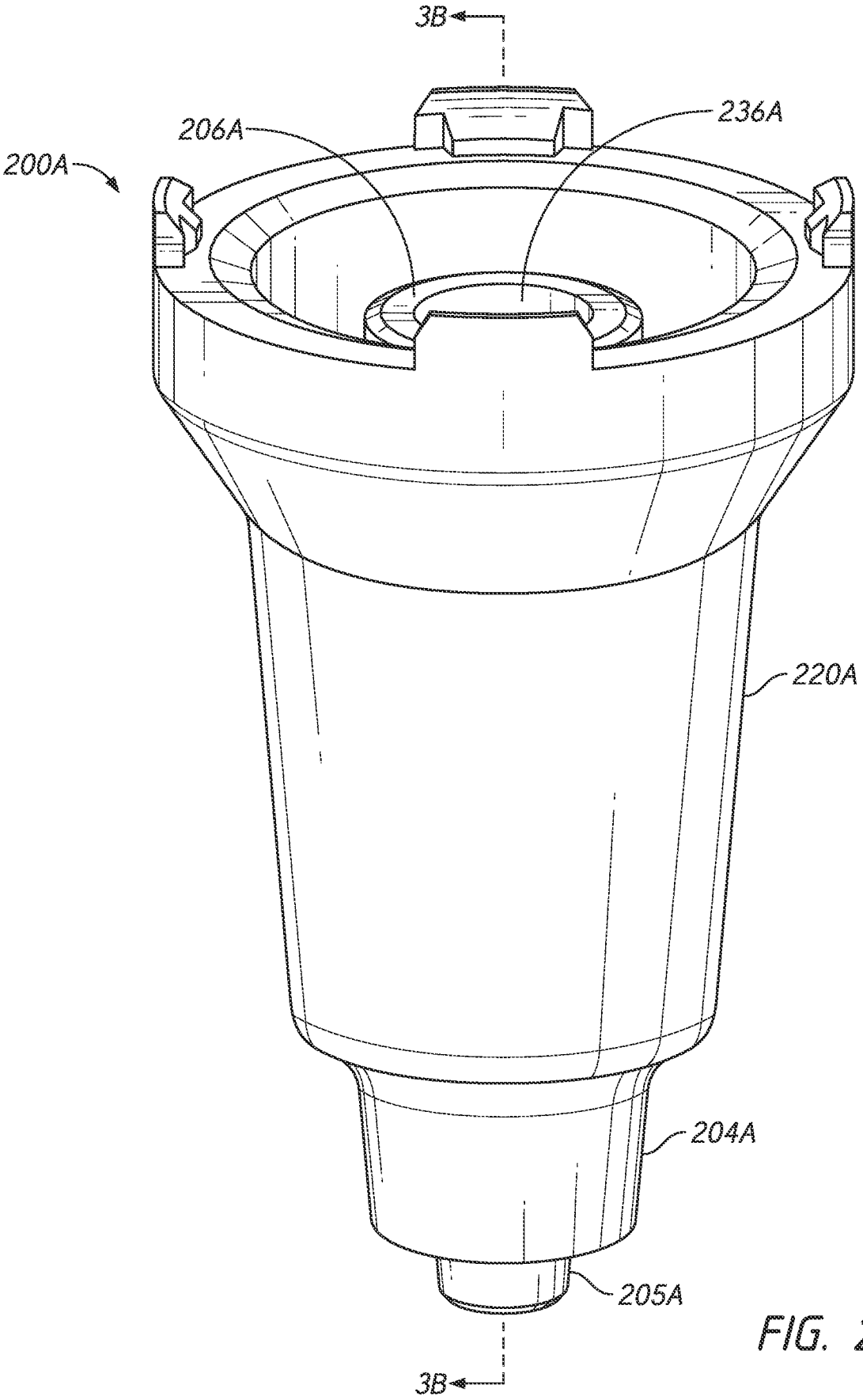

FIG. 2B

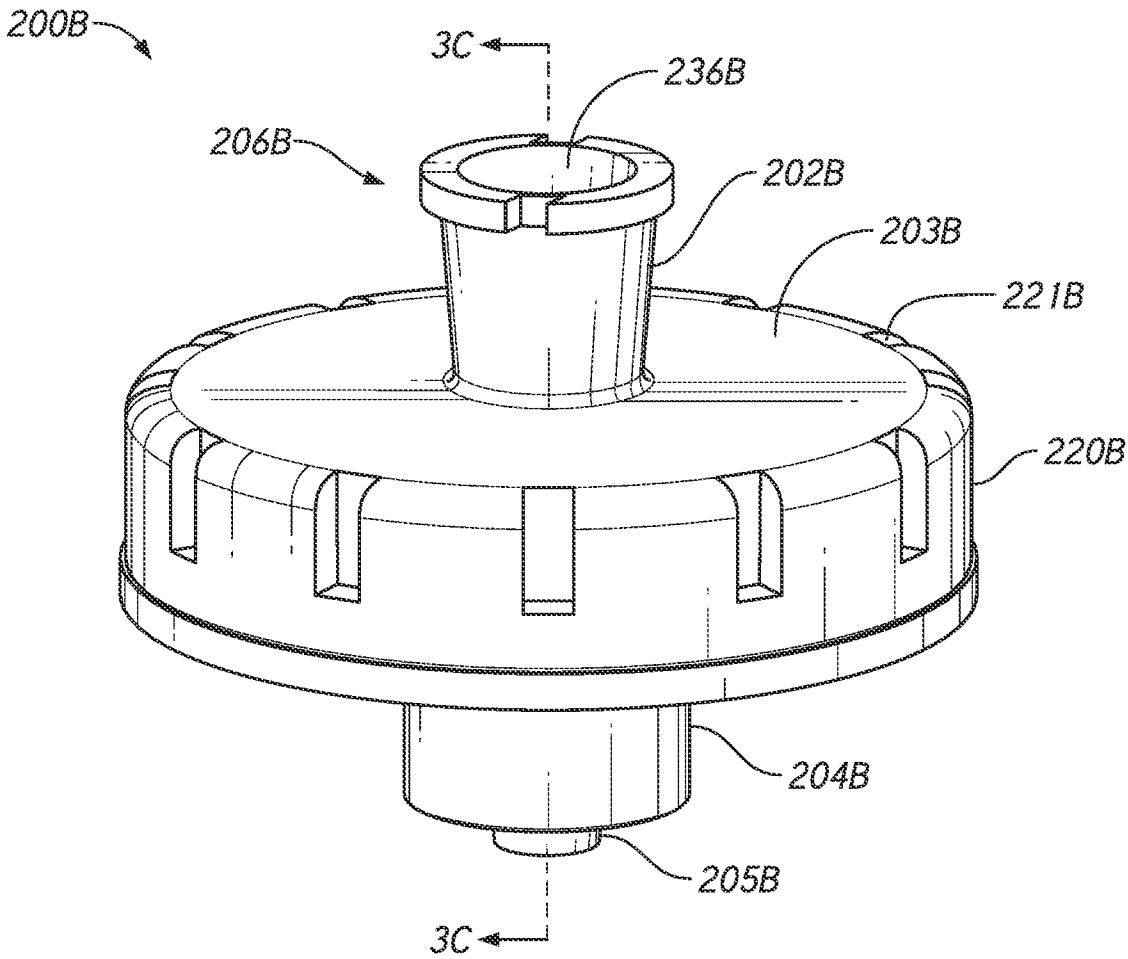

FIG. 2C

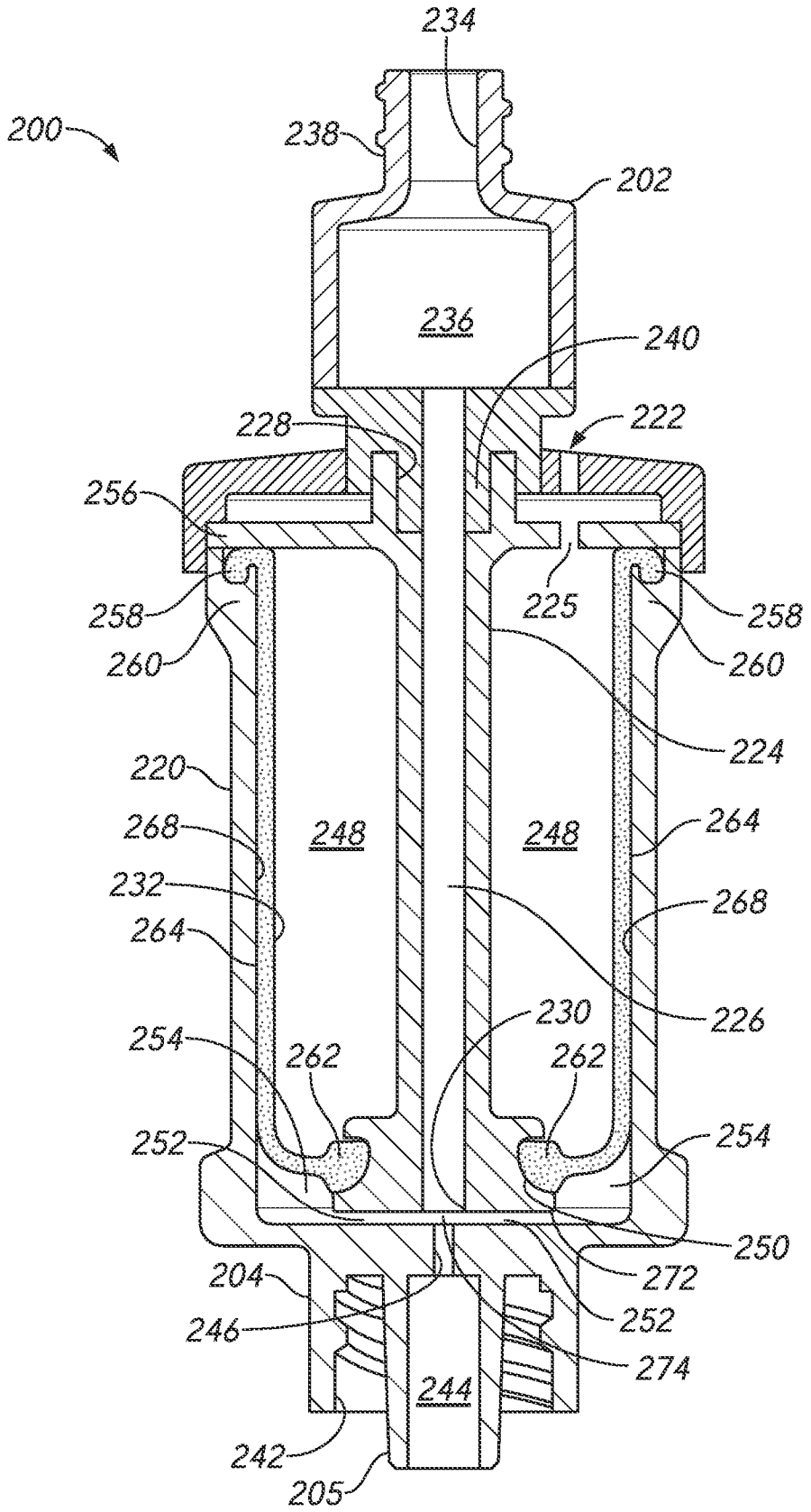
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FIG. 3A

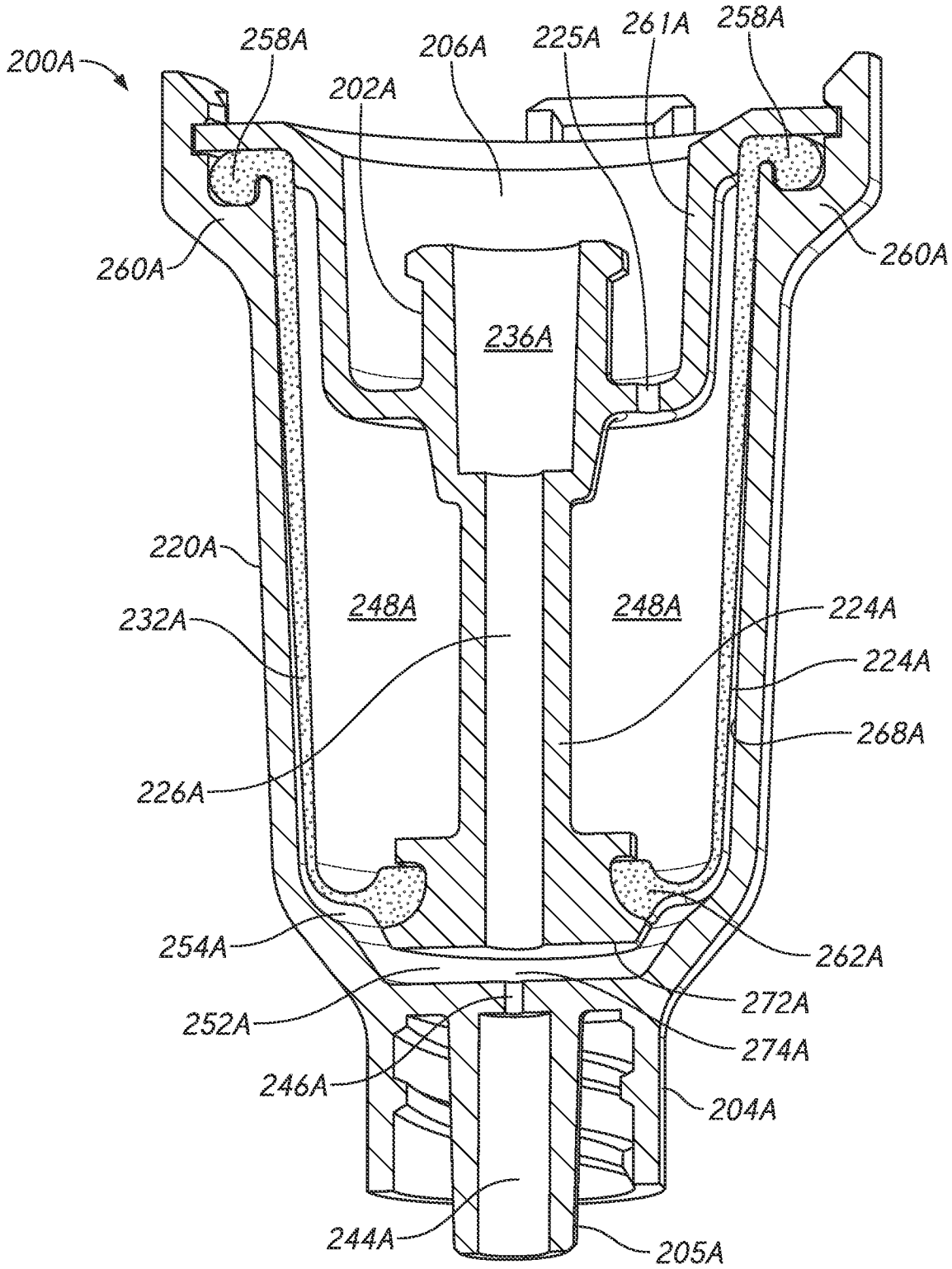
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FIG. 3B

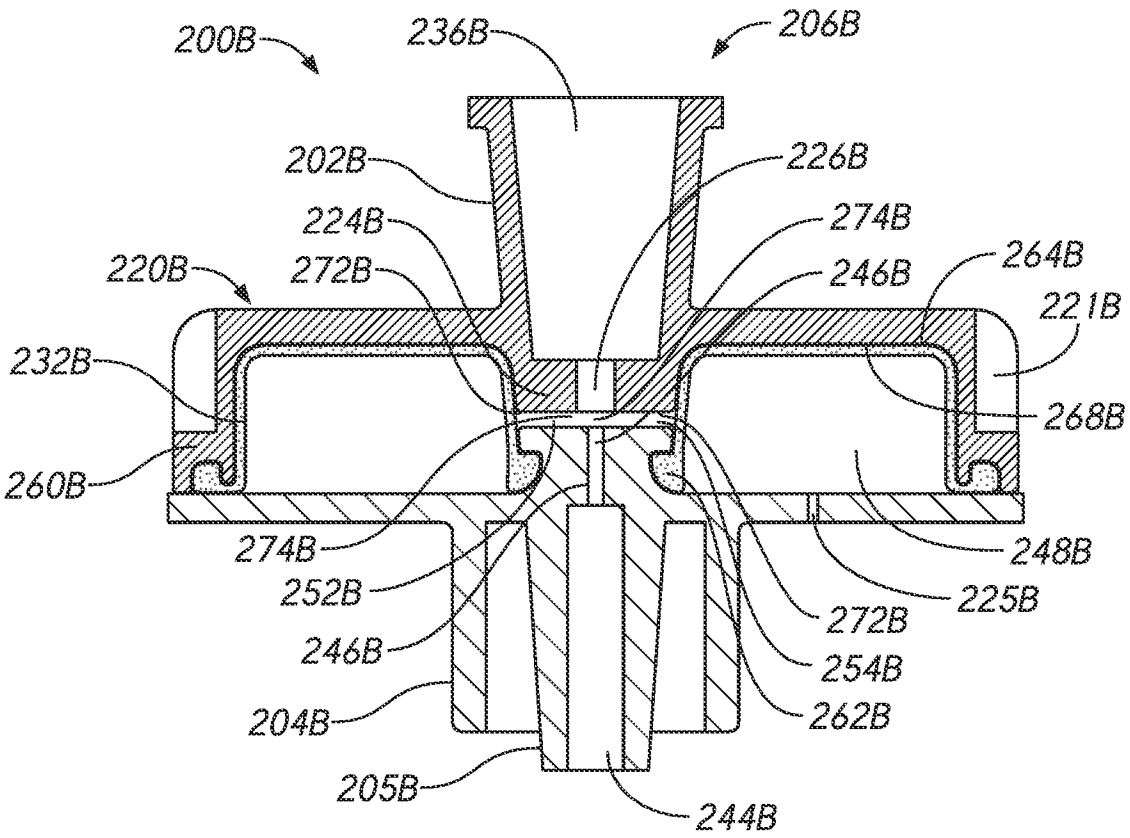
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FIG. 3C

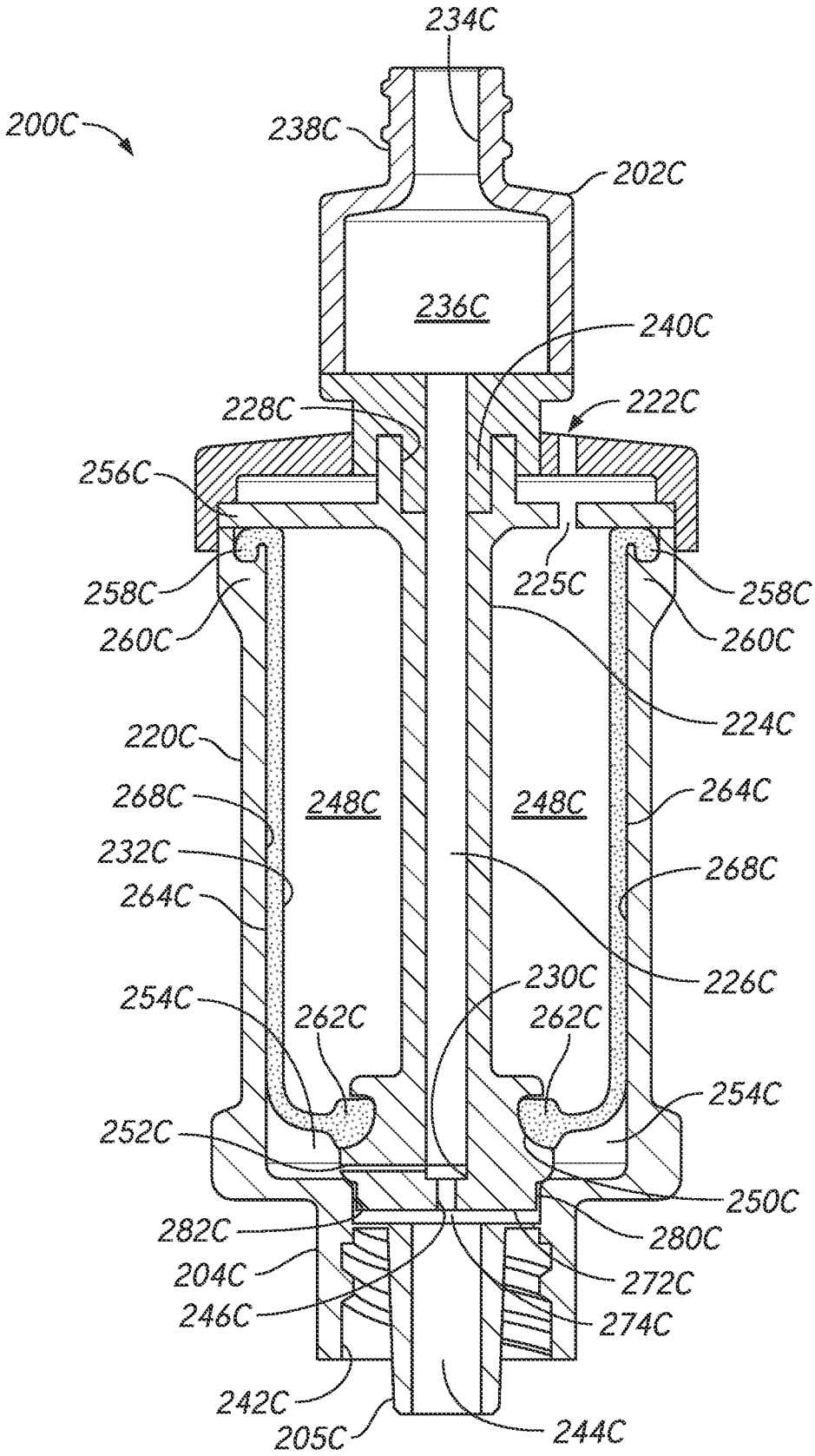
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FIG. 3D

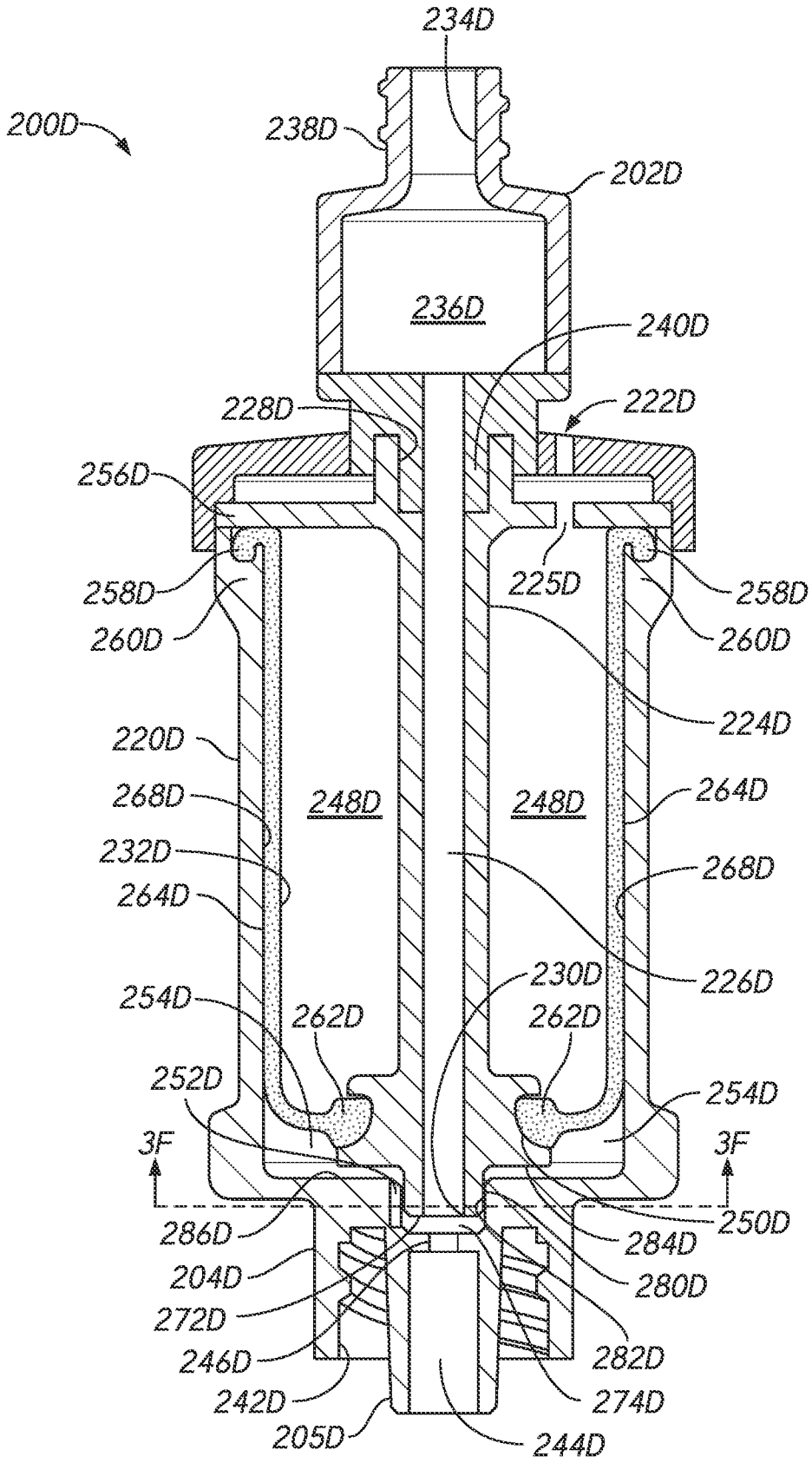
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FIG. 3E

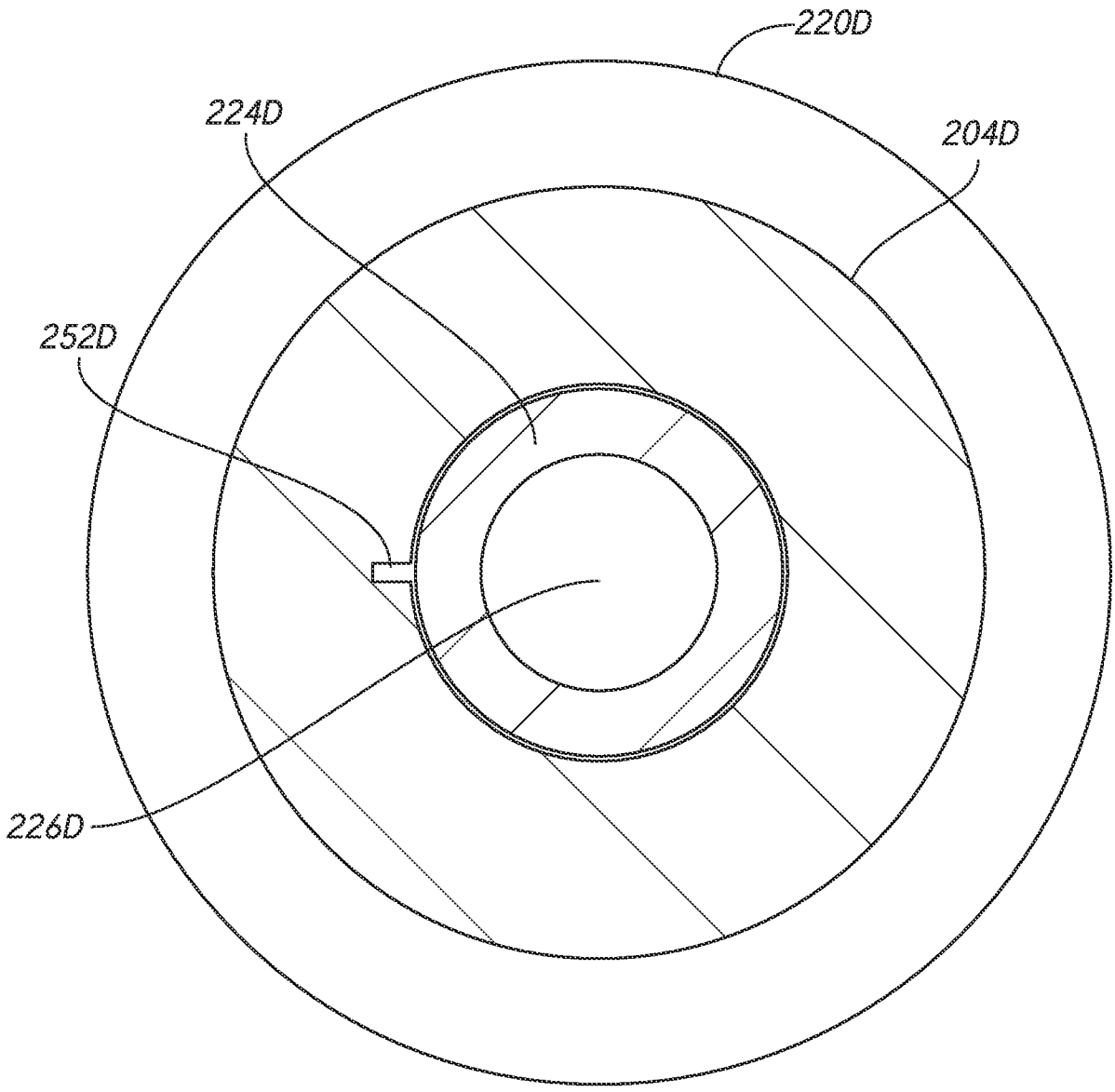
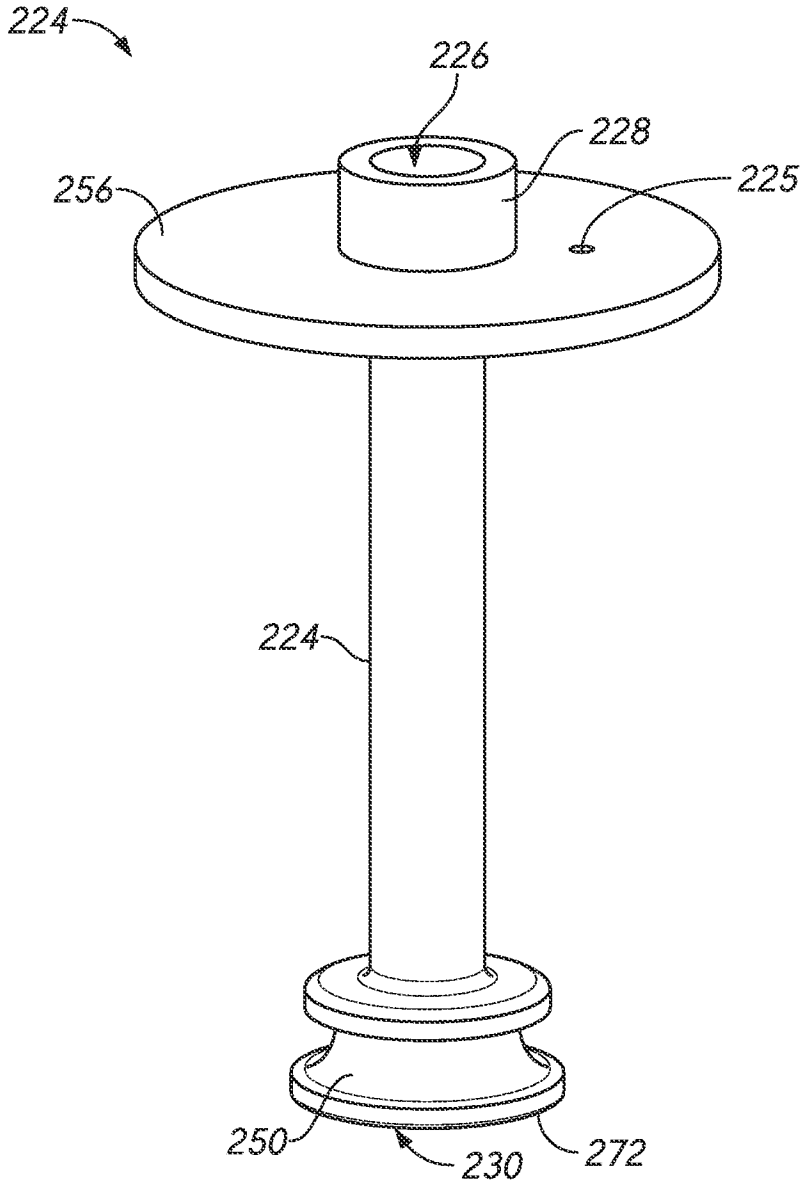


FIG. 3F



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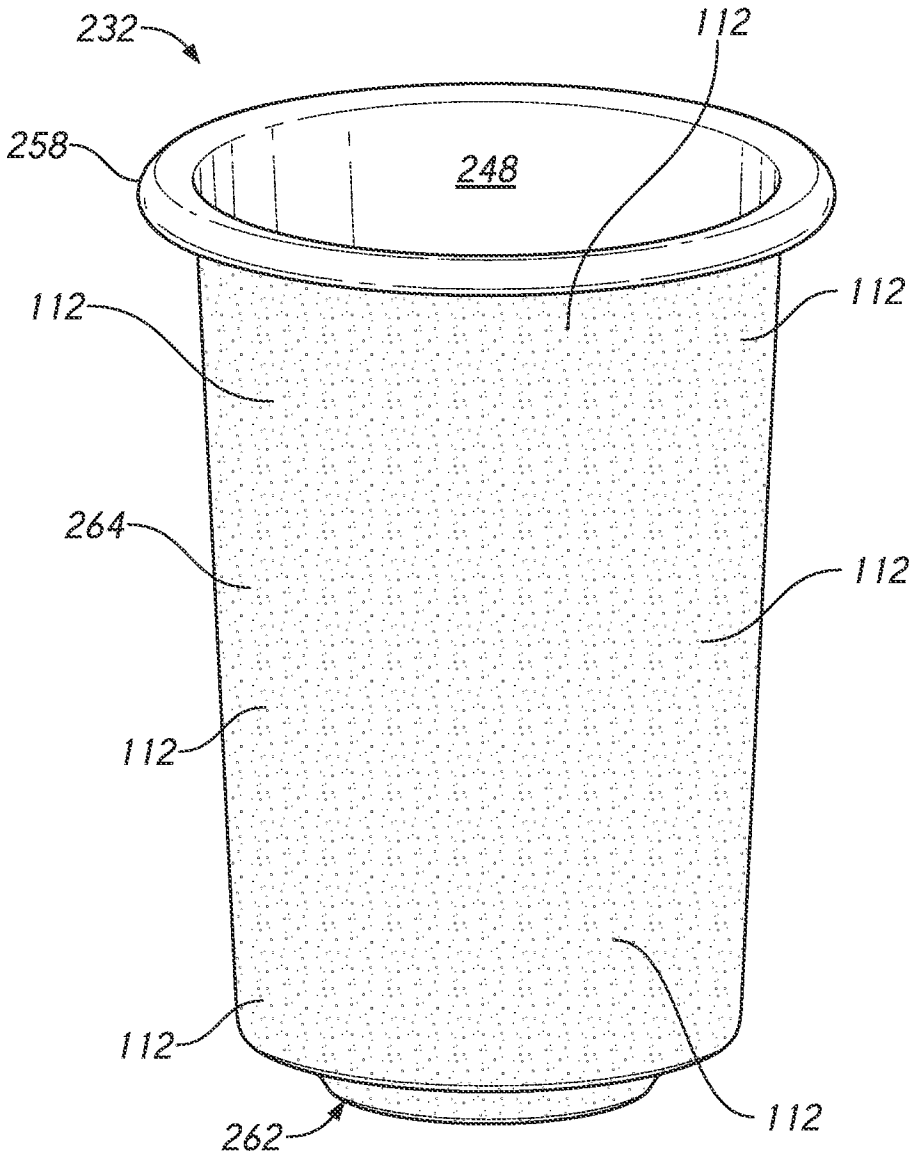

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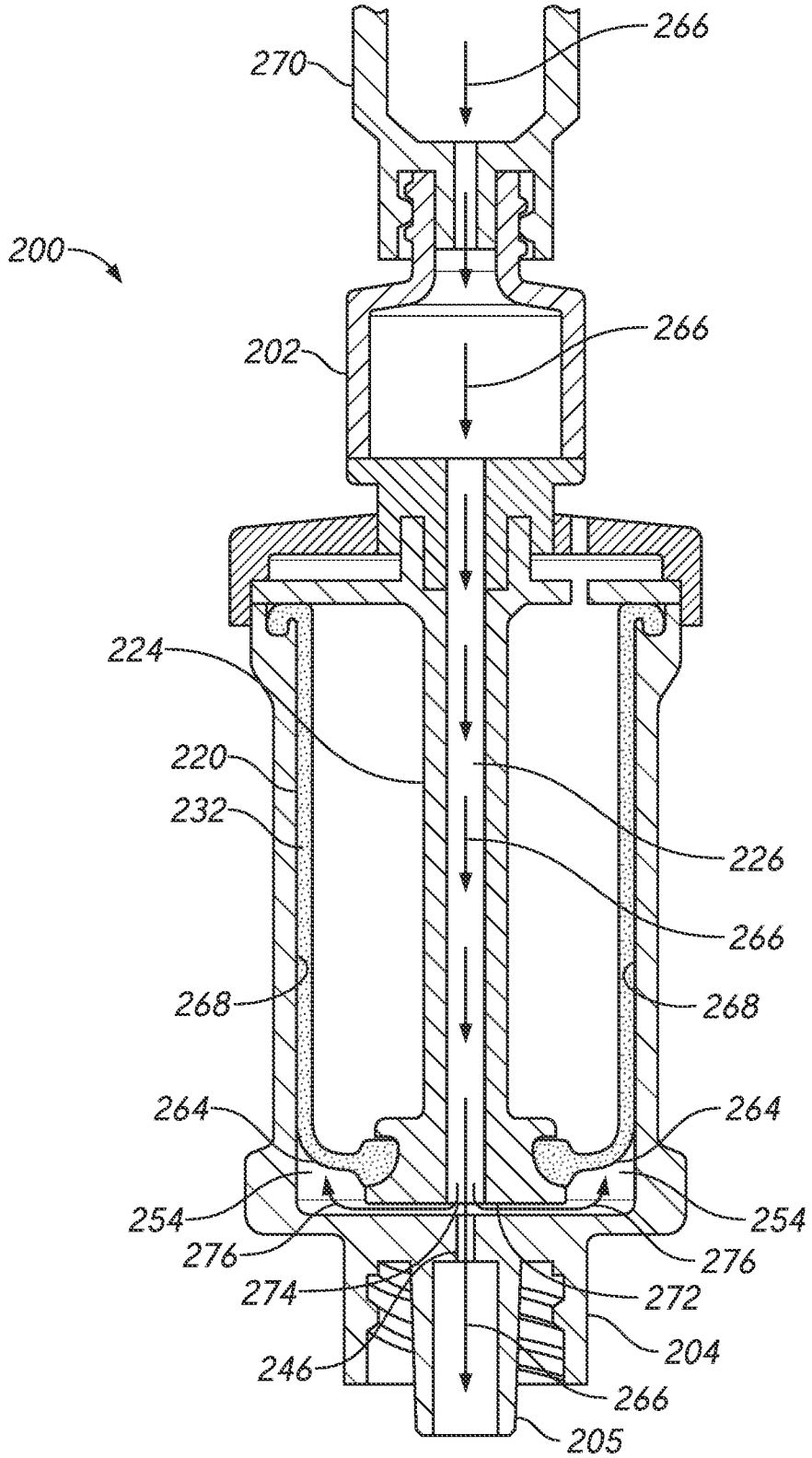
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FIG. 6A

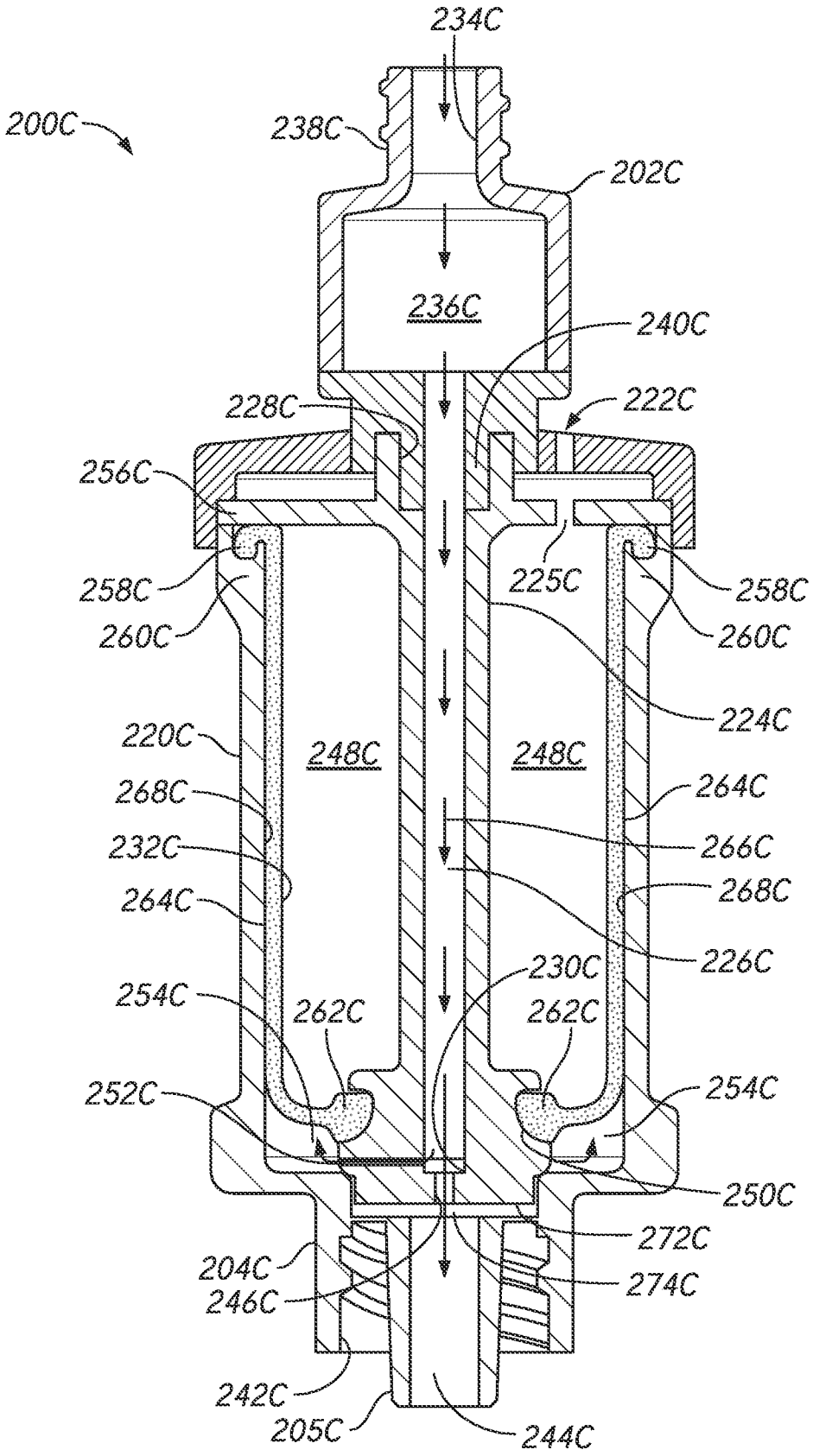
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FIG. 6B

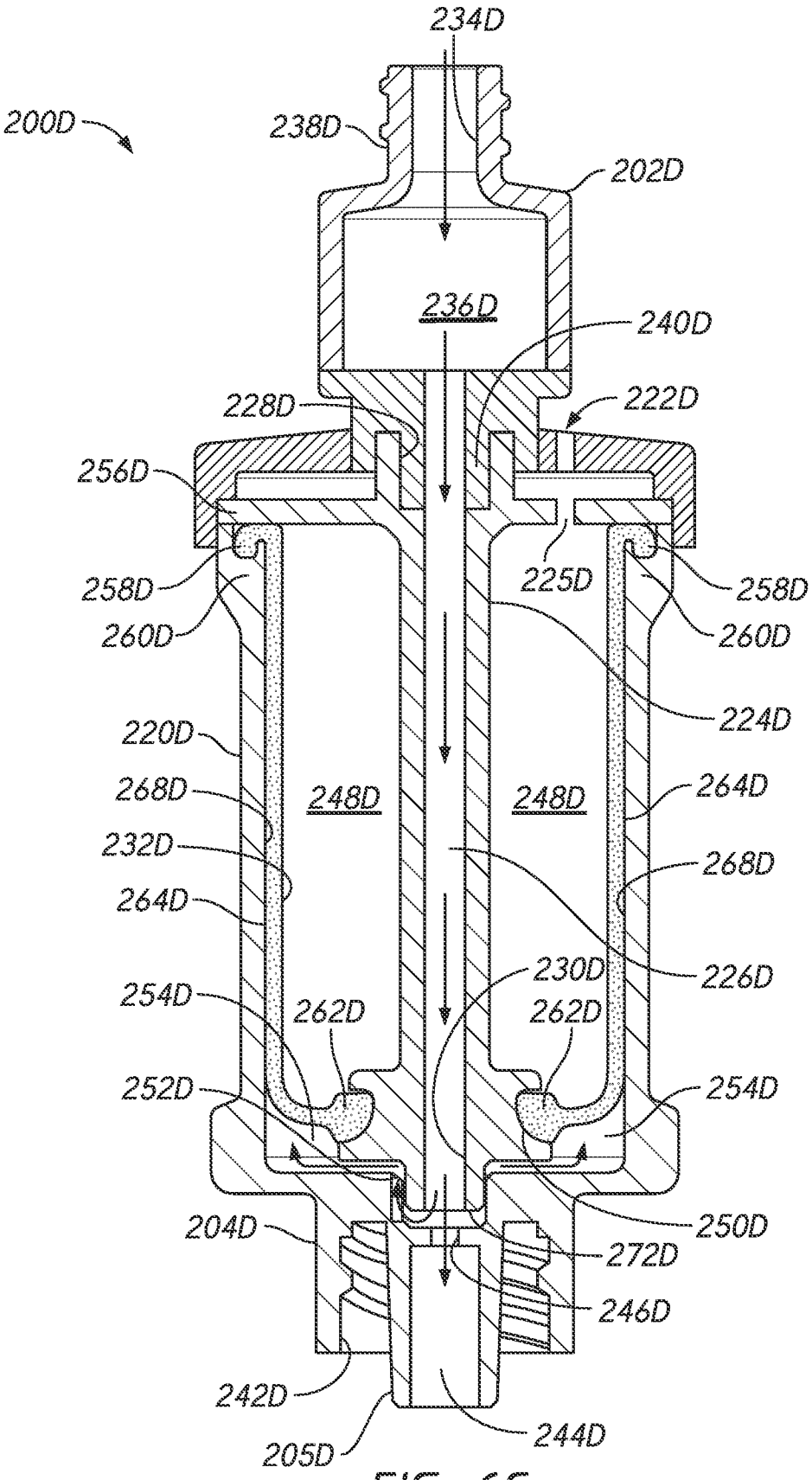
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FIG. 6C

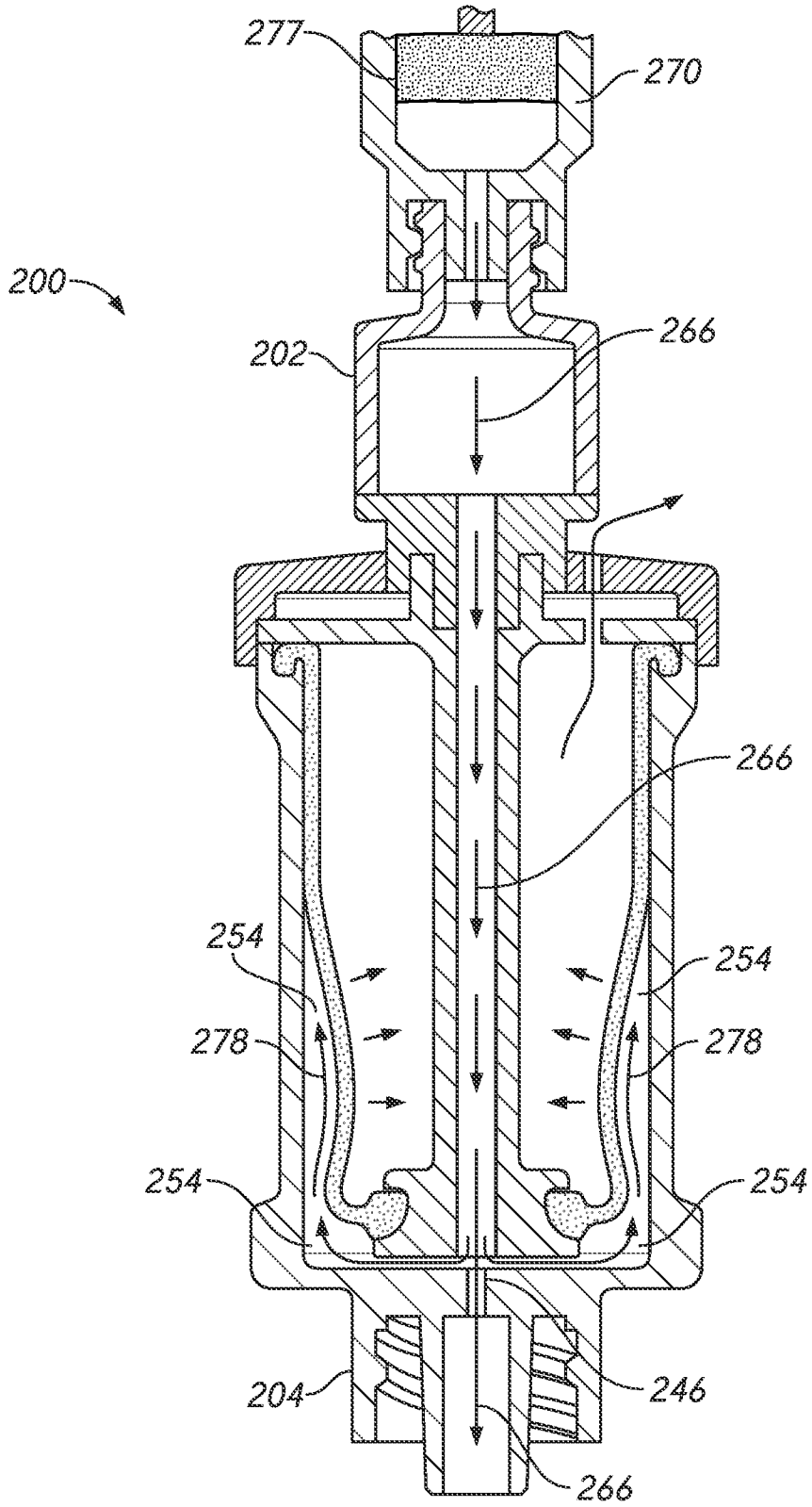

FIG. 7

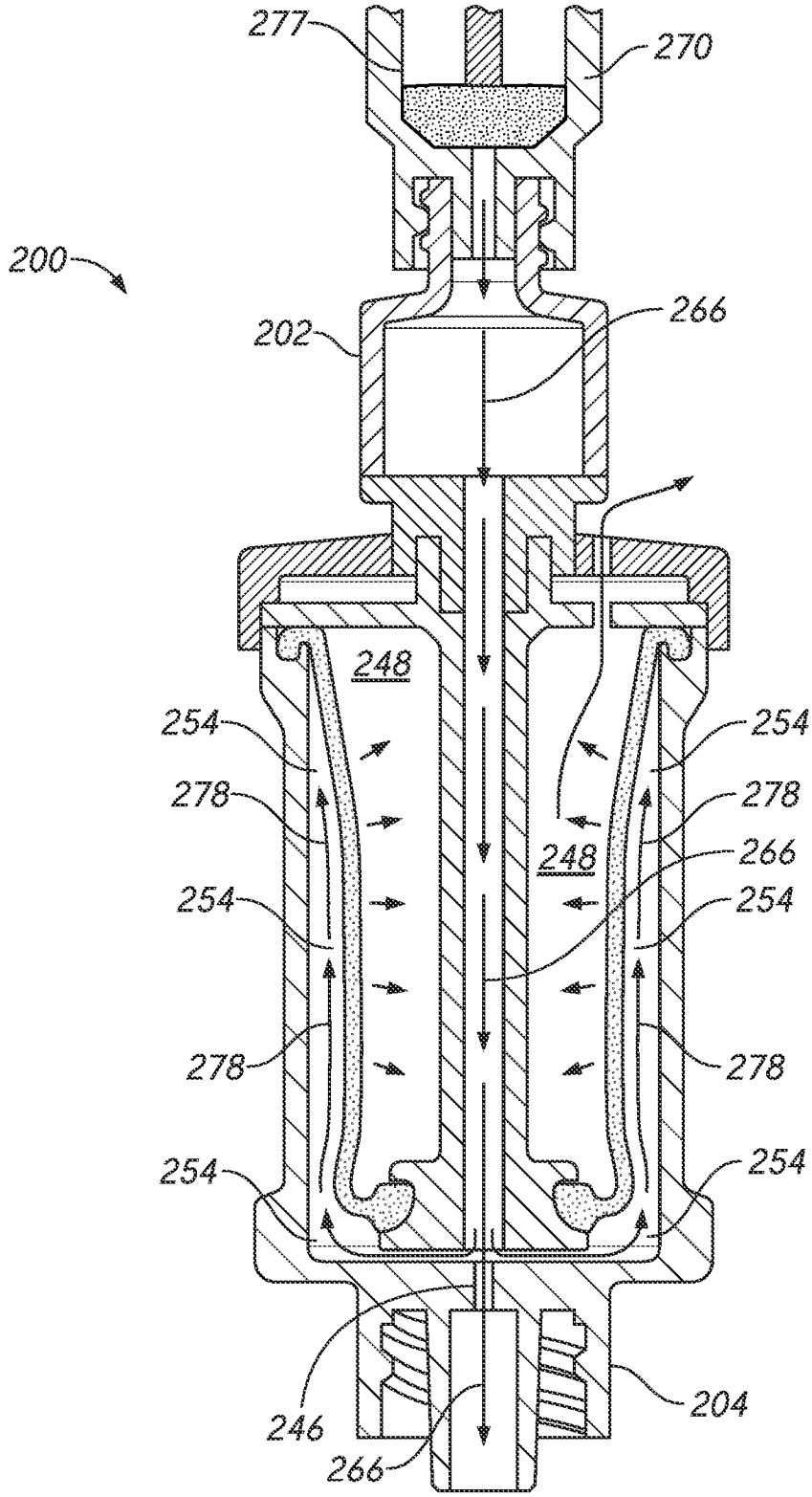
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FIG. 8

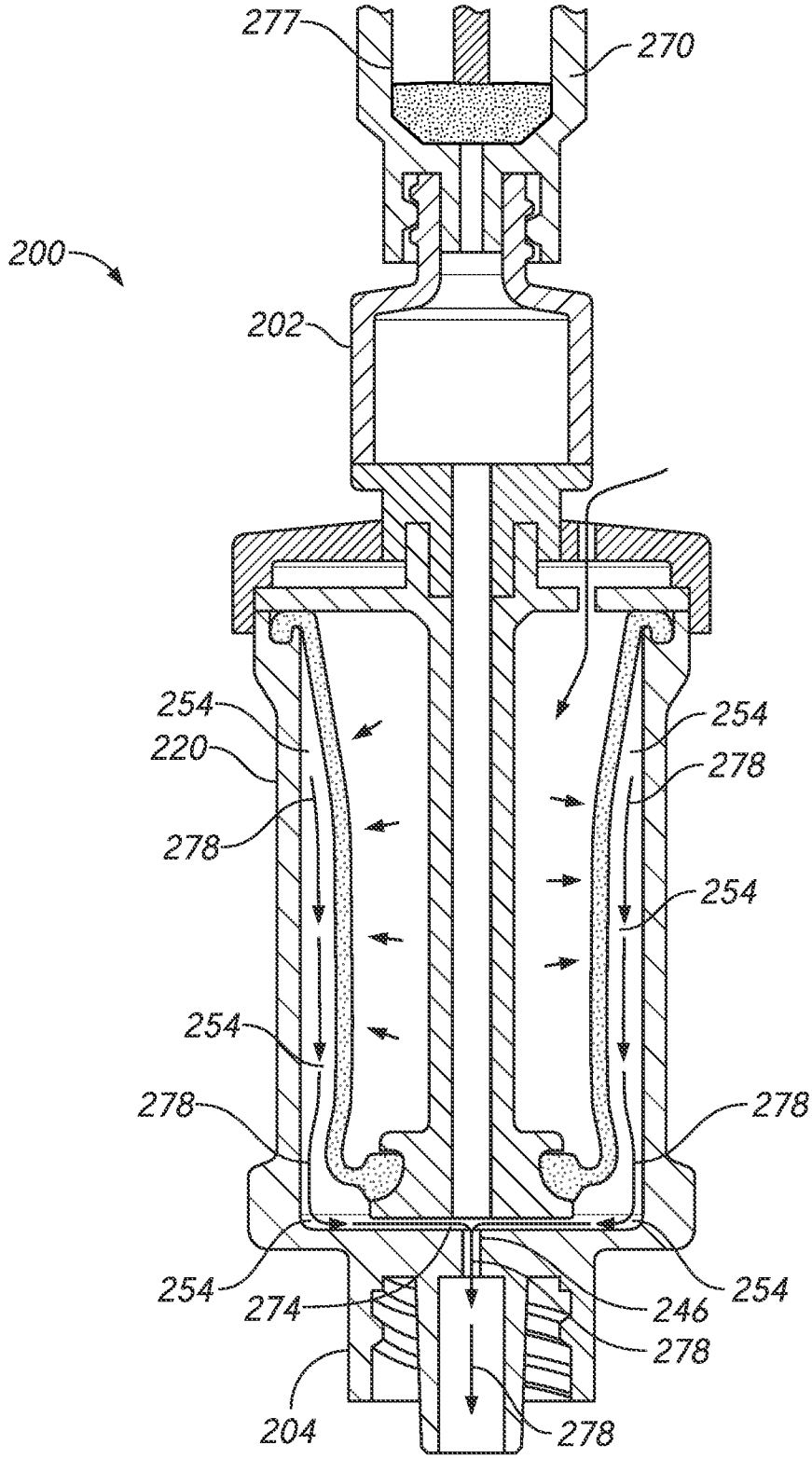
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FIG. 9

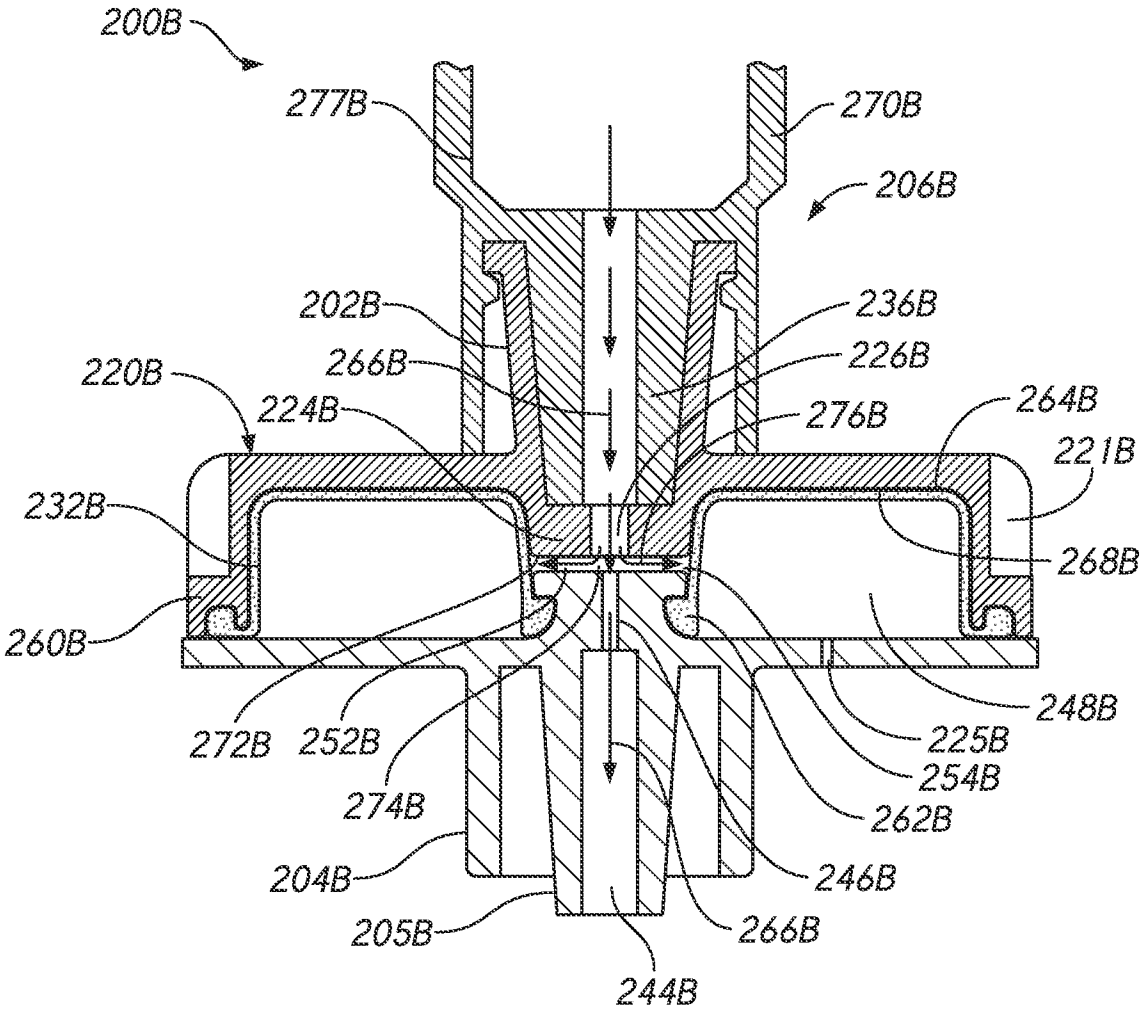
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FIG. 10

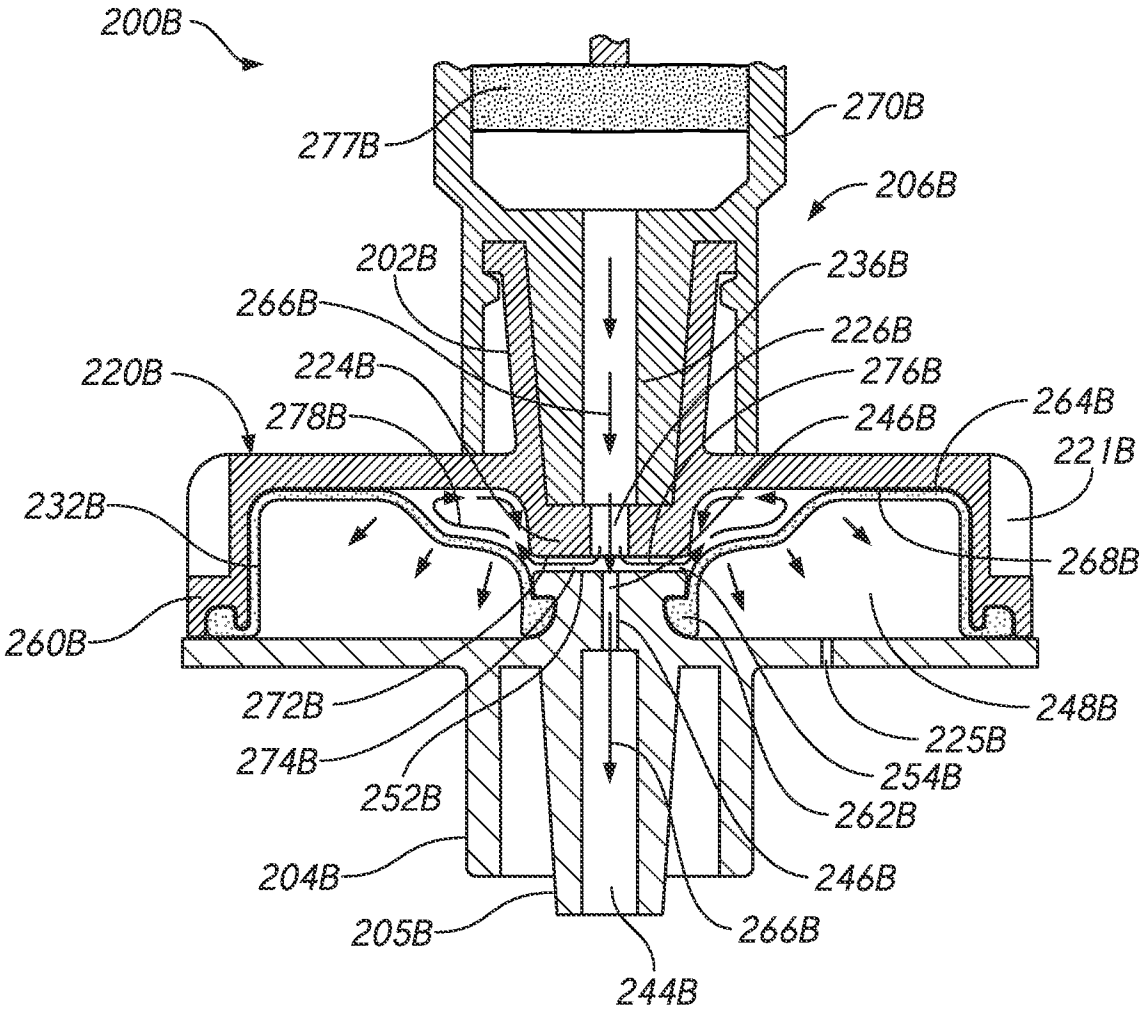
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FIG. 11

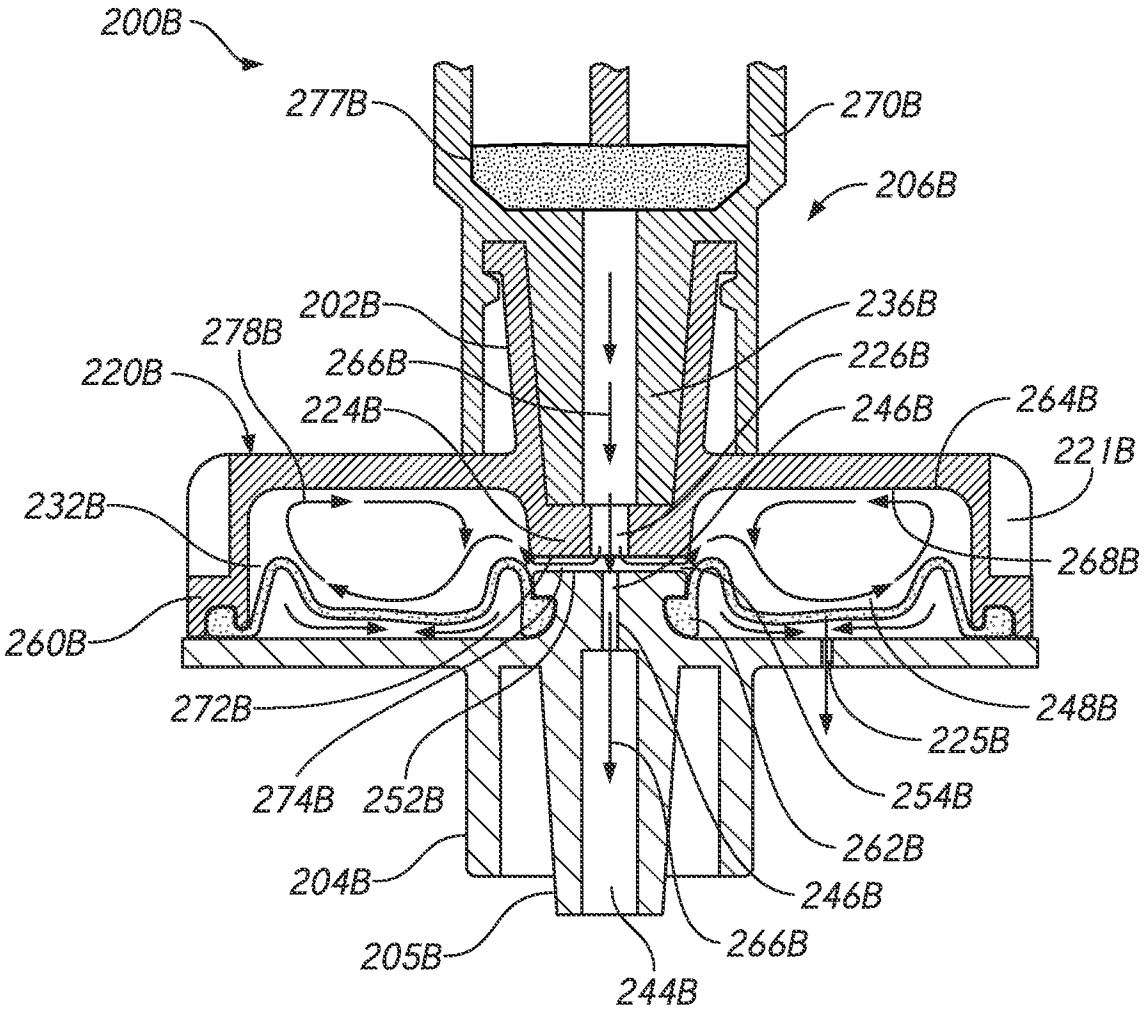
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FIG. 12

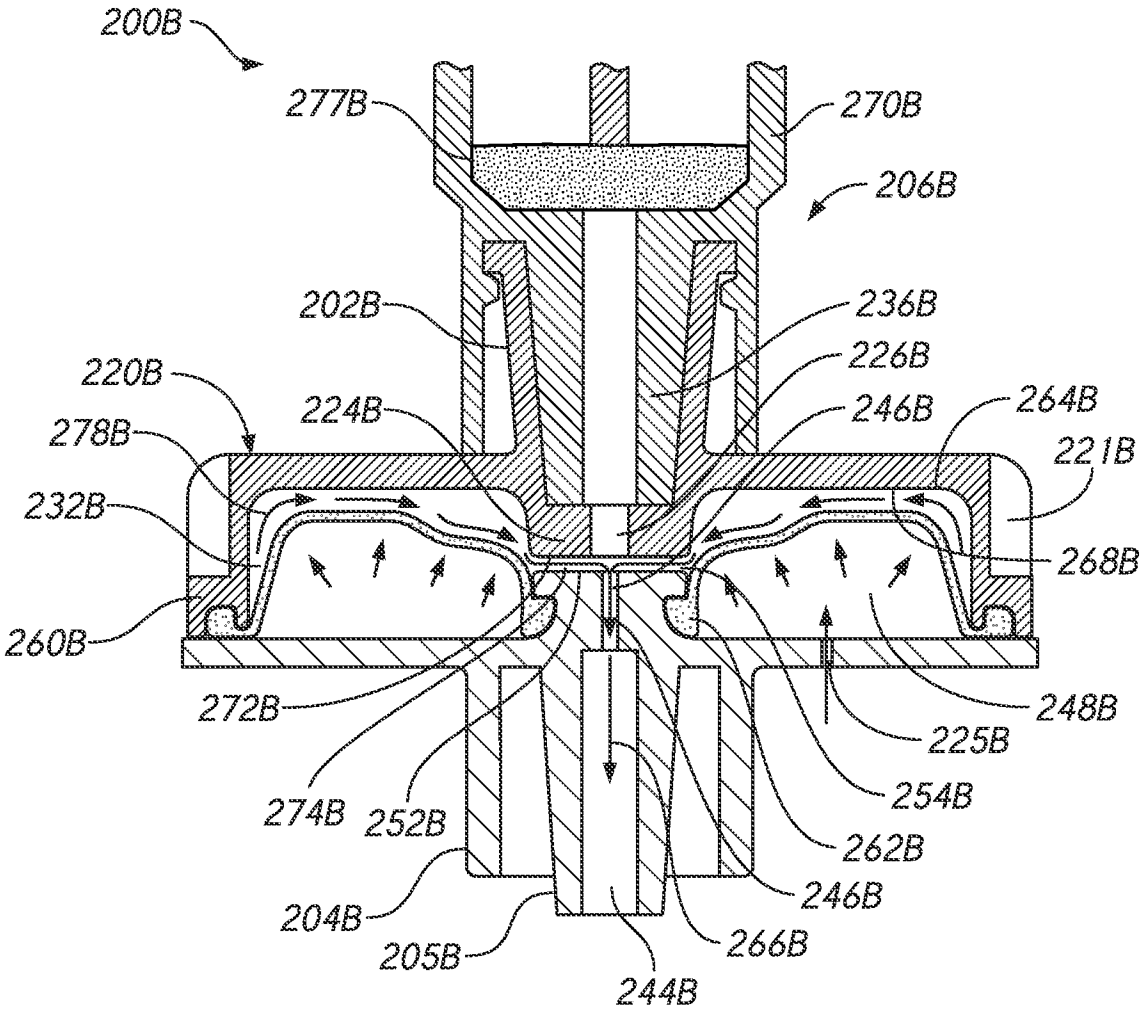
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FIG. 13

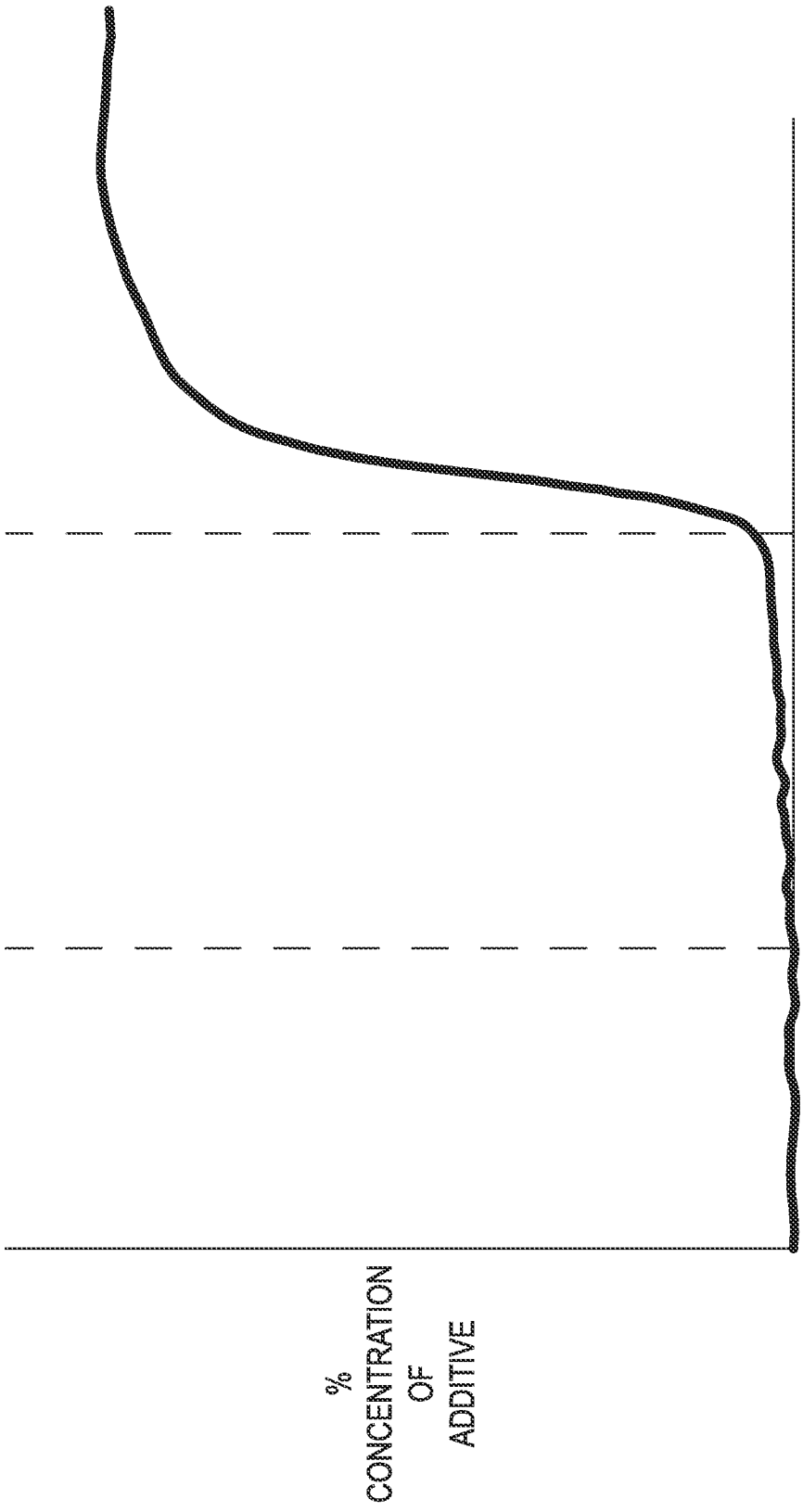

FIG. 14

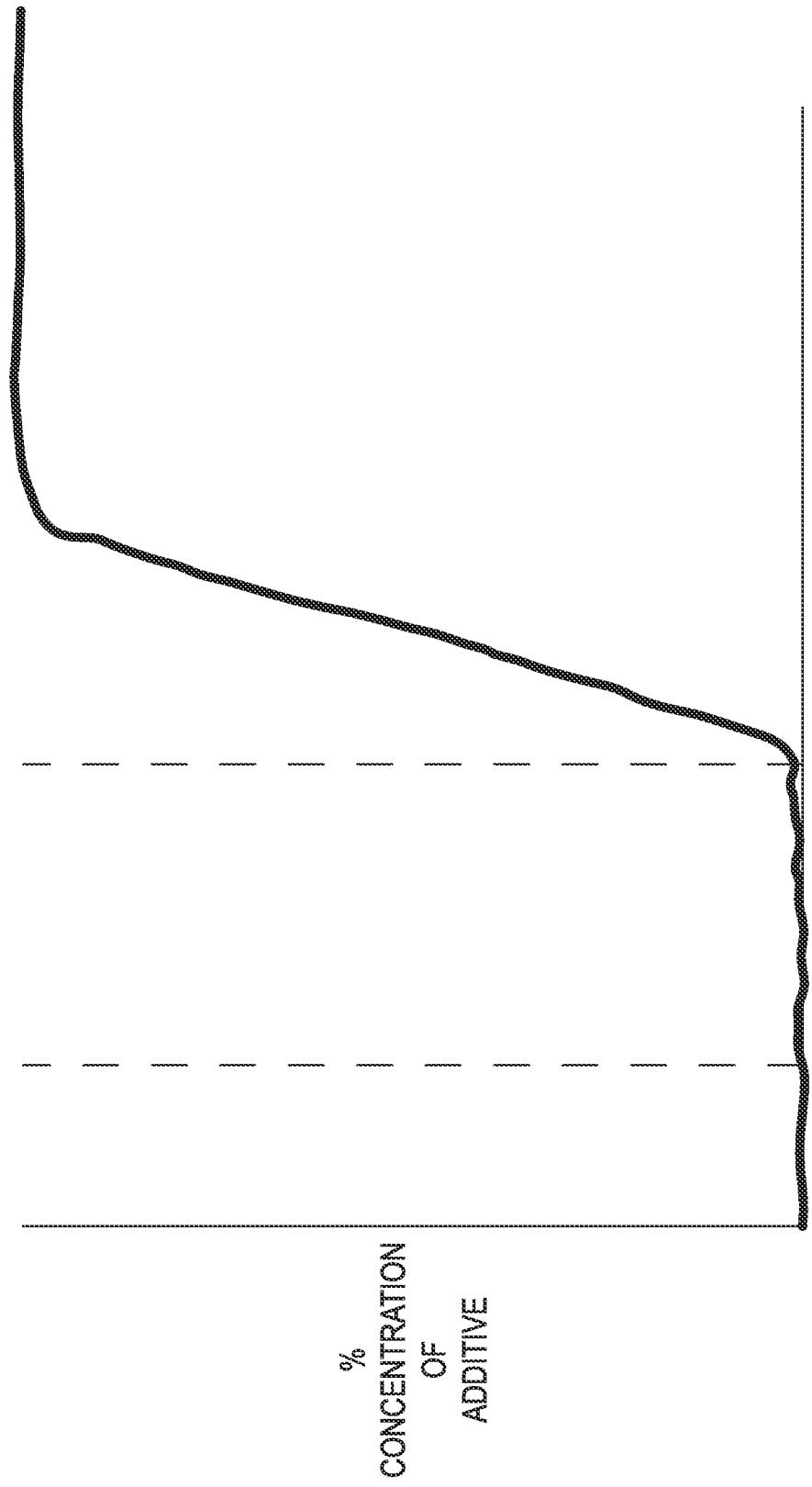

FIG. 15