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(71) Applicant: **MEDTRONIC, INC.** [US/US]; 710 Medtronic Parkway, NE, Minneapolis, Minnesota 55432 (US).

(72) Inventors: **MANDA, VenKatesh R.**; 11644 North McKusick Road, Stillwater, Minnesota 55082 (US). **GERBER, Martin T.**; 6384 Forestview Lane, Maple Grove, Minnesota 55369 (US). **HOBOT, Christopher M.**; 14895 Raspberry Drive, Rogers, Minnesota 55374 (US). **LURA, David B.**; 7817 Shenandoah Ln N, Maple Grove, Minnesota 55311-2672 (US). **MEYER, Thomas E.**; 9833 Primrose Ave N, Stillwater, Minnesota 55082 (US).

(74) Agents: **COLLIER, Kenneth** et al.; Medtronic, 60 Middletown Avenue, c/o Legal Mailstop MS54, North Haven, Connecticut 06473 (US).

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(54) Title: REGENERATIVE PERITONEAL DIALYSIS SYSTEM

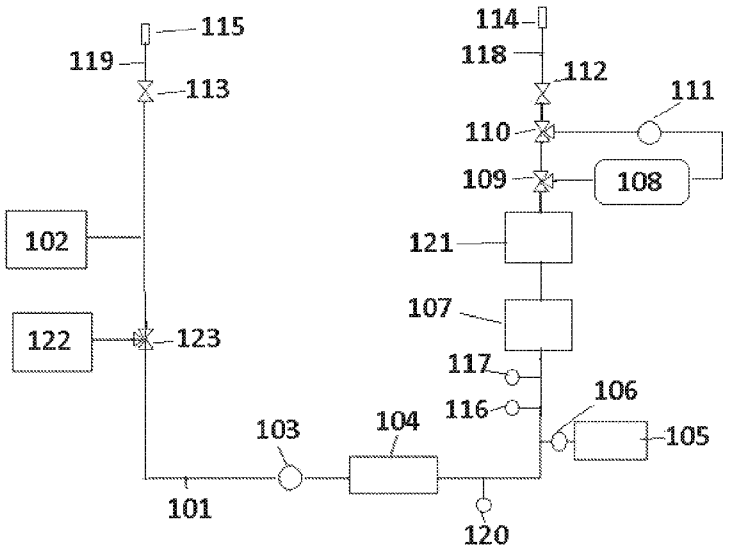

FIG. 1

(57) Abstract: Systems and methods of generating and regenerating peritoneal dialysate are provided. The systems and methods use a dialysate regeneration module (104), a sterilization module (107, 121) and concentrates (105) to prepare peritoneal dialysate from used peritoneal dialysate or source water (102). An optional integrated cycler for direct infusion of the generated peritoneal dialysate is included. Optional dialysate storage containers are provided for storage of the peritoneal dialysate prior to use.

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REGENERATIVE PERITONEAL DIALYSIS SYSTEM

FIELD OF THE INVENTION

[0001] The invention relates to devices, systems, and methods for generating a peritoneal dialysate having purity and sterility characteristics suitable for Peritoneal Dialysis (PD) and regenerating used fluid for subsequent use. The peritoneal dialysate can be generated or regenerated from water or used fluid of variable quality using a dialysate generation flow path containing a sterilization module. The sterilization module can be any one or more of an ultrafilter, Ultraviolet (UV) light source, microbial filter, dialyzer, and combinations thereof. The peritoneal dialysate generation system and related methods can automatically generate peritoneal dialysate fluid and deliver peritoneal dialysis therapy to a patient with an integrated cycler and regenerate a used fluid for subsequent use as fresh peritoneal dialysate.

BACKGROUND

[0002] Peritoneal Dialysis (PD), including Automated Peritoneal Dialysis (APD) and Continuous Ambulatory Peritoneal Dialysis (CAPD), is a dialysis treatment that can be performed at home, either by the patient alone or with a care-giver. PD differs from Hemodialysis (HD) in that blood is not removed from the body and passed through a dialyzer, but rather a catheter is placed in the peritoneal cavity and dialysate introduced directly into the peritoneal cavity. Blood is cleaned inside the patient using the patient's own peritoneum as a type of dialysis membrane. However, because fluid is directly introduced into a human body, the fluid used for peritoneal dialysate is generally required to be free of biological and chemical contaminants. The peritoneal dialysate should also contain specified concentrations of solutes buffer, osmotic agent, and cations for biocompatibility and for performing membrane exchange.

[0003] Peritonitis is a serious and common problem in the PD population that results in abdominal pain, fever, and cloudy dialysate. Peritonitis remains a leading complication of PD with around 18% of infection-related mortality in PD patients resulting from peritonitis (Fried *et al.*, "Peritonitis influences mortality in peritoneal dialysis patients," J. Am. Soc. Nephrol. 1996; 7:2176–2182). Moreover, peritonitis is a contributing factor to death in 16% of deaths on PD, and remains a major cause for patients discontinuing PD and switching to HD. Peritonitis and other peritoneal dialysis complications can often be traced to non-sterile techniques and/or contaminated starting dialysate.

[0004] The US FDA regulates pre-packaged dialysate for use in PD as a Class II drug if the pre-packaged dialysate is used in either a semi-automatic PD system or an automatic PD system (*e.g.*, cycler system). *See* 21 C.F.R. Sec. 876.5630. If the peritoneal dialysate is not pre-packaged, the US FDA requires the dialysate be prepared from a dialysate concentrate and "sterile purified water," which is defined by the FDA in 21 C.F.R. Sec. 165.110(a)(2)(iv) and (vii). Some possible contaminants present in water used to prepare dialysis fluid can be (i) particles, (ii) chemicals, and (iii) microbial contaminants such as bacteria, fungi and yeasts, and microbial derivatives or fragments (*e.g.*, endotoxins released during active growth and lysis of micro-organisms). In additional to meeting purity and sterility requirements, peritoneal dialysate must also contain specific and precise amounts of solutes, such as sodium chloride, sodium bicarbonate, and cation infusates.

[0005] Because traditional peritoneal dialysis systems require FDA-approved, pre-packaged dialysate, the dialysate can be expensive due to high manufacturing, shipping, and storage costs. Shortages can also occur. The problems are not mitigated by on-site dialysate preparation because the source water must still meet high fluid purity and sterility characteristics.

Such standards may be difficult to meet, particularly for continuous, automatic peritoneal dialysis machines designed for home use. Further, traditional systems usually require storage of hundreds of liters of dialysate bags, including 300 L or more of peritoneal dialysate and over 300 kg of fluid per month. Storage and shipping of the peritoneal dialysate is expensive, labor intensive, and requires significant storage space.

[0006] Known systems and methods require significant space to store peritoneal dialysate prior to use. Continuous ambulatory peritoneal dialysis (CAPD) traditionally uses 1-4 exchanges of peritoneal dialysate a day, with an overnight dwell. Because each exchange requires approximately 2-4 L of peritoneal dialysate, use of prepackaged dialysate requires storing about 8-16 L of dialysate per day, or 56-112 L of dialysate per week. Automated peritoneal dialysis uses a cycler to cycle peritoneal dialysis into and out of the peritoneal cavity of the patient, generally at night. APD generally uses 3-5 exchanges daily, requiring up to 20 L of dialysate per day and up to 140 L of dialysate per week. Tidal Peritoneal Dialysis (TPD) is similar to APD with the exception that a between 250 mL to 1000 mL of the peritoneal dialysate is left in the peritoneal cavity of the patient between infusions. As such, the known treatments require significant amounts of clean water, which can deter using known systems, particularly in areas where clean water is scarce.

[0007] Hence, there is a need for systems and methods that can regenerate and reuse peritoneal dialysate after a first treatment, lowering the requirements for fresh water and storage space. There is also a need for a system that can regenerate used peritoneal dialysate and reuse the peritoneal dialysate with an integrated cycler, reducing the number of components necessary for peritoneal dialysis.

SUMMARY OF THE INVENTION

[0008] The first aspect of the invention relates to a system. In any embodiment, the system can include a water source; a peritoneal dialysate generation flow path; wherein the peritoneal dialysate generation flow path is fluidly connectable to the water source; one or more peritoneal dialysate regeneration modules fluidly connectable to the peritoneal dialysate generation flow path; a concentrate source fluidly connectable to the peritoneal dialysate generation flow path; the concentrate source containing one or more solutes; and a sterilization module fluidly connectable to the peritoneal dialysate generation flow path.

[0009] In any embodiment of the first aspect of the invention, the peritoneal dialysate generation flow path can include connectors for connection to a cycler.

[0010] In any embodiment of the first aspect of the invention, the system can include an integrated cycler; the integrated cycler having a pump, an infusion line, and a drain line; wherein the infusion line is fluidly connected to the peritoneal dialysate generation flow path downstream of the sterilization module; and wherein the drain line is fluidly connected to the peritoneal dialysate generation flow path upstream of the peritoneal dialysate regeneration module.

[0011] In any embodiment of the first aspect of the invention, the system can have one or more dialysate containers fluidly connectable to the peritoneal dialysate generation flow path downstream of the sterilization module.

[0012] In any embodiment of the first aspect of the invention, the concentrate source can include one or more of an osmotic agent and an ion concentrate.

[0013] In any embodiment of the first aspect of the invention, the concentrate source can include at least an osmotic agent source and an ion concentrate source.

[0014] In any embodiment of the first aspect of the invention, the concentrate source can include multiple osmotic agent sources.

[0015] In any embodiment of the first aspect of the invention, the osmotic agent sources can contain osmotic agents selected from the group of dextrose, icodextrin, amino acids, and glucose.

[0016] In any embodiment of the first aspect of the invention, the ion concentrate source can include one or more from the group of sodium chloride, sodium lactate, magnesium chloride, calcium chloride, potassium chloride, and sodium bicarbonate.

[0017] In any embodiment of the first or second aspect of the invention, the concentrate source can include multiple ion concentrate sources.

[0018] In any embodiment of the first aspect of the invention, the system can have a concentrate pump positioned between the concentrate source and the peritoneal dialysate generation flow path for controlled addition of fluid from the concentrate source to the peritoneal dialysate generation flow path.

[0019] In any embodiment of the first aspect of the invention, the system can have a control system for controlling one or more pumps and valves to control movement of fluid through the system.

[0020] In any embodiment of the first aspect of the invention, the control system can include a timer wherein the timer causes the control system to generate peritoneal dialysate at a predetermined time.

[0021] In any embodiment of the first aspect of the invention, the control system can include a user interface, wherein the user interface causes the control system to generate peritoneal dialysate at a selected time.

[0022] In any embodiment of the first aspect of the invention, the sterilization module can include one or more ultrafilters; a UV light source; a heater, a flash pasteurization module, a microbial filter; or combinations thereof.

[0023] In any embodiment of the first aspect of the invention, the sterilization module can include the UV light source positioned downstream of the ultrafilter.

[0024] In any embodiment of the first aspect of the invention, the peritoneal dialysate regeneration module can include one or more selected from the group of a sorbent cartridge, activated carbon, an ion exchange resin, a reverse osmosis module, a carbon filter, and a nanofilter.

[0025] In any embodiment of the first aspect of the invention, the integrated cycler can have a heater.

[0026] In any embodiment of the first aspect of the invention, the integrated cycler can have at least one sensor selected from the group of a flow meter, a pressure sensor, a conductivity sensor, and a temperature sensor.

[0027] In any embodiment of the first aspect of the invention, the system can have a second ultrafilter in the peritoneal dialysate generation flow path.

[0028] In any embodiment of the first aspect of the invention, the integrated cycler can include a filter in the infusion line.

[0029] The features disclosed as being part of the first aspect of the invention can be in the first aspect of the invention, either alone or in combination, or follow a preferred arrangement of one or more of the described elements.

[0030] The second aspect of the invention is drawn to a method. In any embodiment of the second aspect of the invention, the method can include the steps of pumping fluid through a

peritoneal dialysate generation flow path having a peritoneal dialysate regeneration module; adding one or more concentrate solutions to the fluid in the peritoneal dialysate generation flow path; and pumping the fluid through a sterilization module.

[0031] In any embodiment of the second aspect of the invention, the fluid can be fluid returned to the peritoneal dialysate generation flow path from a peritoneal cavity of a patient.

[0032] In any embodiment of the second aspect of the invention, the method can include heating the fluid; pumping the fluid into a peritoneal cavity of a patient with an integrated cycler; and pumping the fluid from the peritoneal cavity of the patient into the peritoneal dialysate generation flow path.

[0033] In any embodiment of the second aspect of the invention, the method can include the step of pumping the fluid into one or more dialysate containers and pumping the fluid from the one or more dialysate containers into the peritoneal cavity of the patient.

[0034] In any embodiment of the second aspect of the invention, the step of adding one or more concentrate solutions to the fluid can include adding at least an osmotic agent and an ion concentrate to the fluid.

[0035] In any embodiment of the second aspect of the invention, the osmotic agent and ion concentrate can be added to the fluid from a single concentrate source.

[0036] In any embodiment of the second aspect of the invention, the osmotic agent and ion concentrate can be added from separate concentrate sources.

[0037] In any embodiment of the second aspect of the invention, the osmotic agent can be one or more selected from the group of glucose, dextrin, and icodextrin.

[0038] In any embodiment of the second aspect of the invention, the osmotic agent can include multiple osmotic agents.

[0039] In any embodiment of the second aspect of the invention, the multiple osmotic agents can be added from a single osmotic agent source.

[0040] In any embodiment of the second aspect of the invention, each of the multiple osmotic agents can be added from separate osmotic agent sources.

[0041] In any embodiment of the second aspect of the invention, the ion concentrate can be added from an ion concentrate source and can include one or more of sodium chloride, sodium lactate, magnesium chloride, calcium chloride, potassium chloride, and sodium bicarbonate.

[0042] In any embodiment of the second aspect of the invention, each of the ion concentrates can be added to the fluid from a single ion concentrate source.

[0043] In any embodiment of the second aspect of the invention, the ion concentrate source can include multiple ion concentrate sources; and each of the multiple ion concentrate sources can include different solutes.

[0044] In any embodiment of the second aspect of the invention, the step of adding one or more concentrate solutions to the fluid can include controlling an addition of concentrate from each of the ion concentrate sources to generate a peritoneal dialysate with a prescribed solute concentration.

[0045] In any embodiment of the second aspect of the invention, the method can be carried out by a peritoneal dialysate generation system having a control system.

[0046] In any embodiment of the second aspect of the invention, the peritoneal dialysate regeneration module can include one or more of a sorbent cartridge, activated carbon, a reverse osmosis module, a carbon filter and a nanofilter.

[0047] In any embodiment of the second aspect of the invention, the sterilization module can include one or more ultrafilters; a UV light source; a microbial filter; or combinations thereof.

[0048] In any embodiment of the second aspect of the invention, the sterilization module can include at least two ultrafilters.

[0049] The features disclosed as being part of the second aspect of the invention can be in the second aspect of the invention, either alone or in combination, or follow a preferred arrangement of one or more of the described elements.

BRIEF DESCRIPTION OF THE DRAWINGS

[0050] FIG. 1 shows a flow schematic of a regenerative peritoneal dialysate system.

[0051] FIG. 2 shows a detailed flow diagram of a regenerative peritoneal dialysate system.

[0052] FIG. 3 shows a detailed flow diagram for a regenerative peritoneal dialysate system with an integrated cycler.

[0053] FIG. 4 shows a system for adding concentrates to a peritoneal dialysate generation flow path.

[0054] FIG. 5 shows an overview of a system for generating, regenerating, and using peritoneal dialysate with a single concentrate source.

[0055] FIG. 6 shows an overview of a system for generating, regenerating, and using peritoneal dialysate with multiple concentrate sources.

[0056] FIG. 7A shows a perspective view of a peritoneal dialysate generation cabinet.

[0057] FIG. 7B shows a front view of a peritoneal dialysate generation cabinet.

[0058] FIG. 8 shows a perspective view of a peritoneal dialysate generation cabinet with door panels closed.

[0059] FIG.'s 9A-D show a peritoneal dialysate generation cabinet with a water reservoir and waste reservoir.

[0060] FIG. 10 shows a peritoneal dialysate generation cabinet connected to a faucet and drain.

[0061] FIG. 11 shows a dialysis caddy for use in a peritoneal dialysate generation flow path.

DETAILED DESCRIPTION OF THE INVENTION

[0062] Unless defined otherwise, all technical and scientific terms used have the same meaning as commonly understood by one of ordinary skill in the art.

[0063] The articles "a" and "an" are used to refer to one or to over one (*i.e.*, to at least one) of the grammatical object of the article. For example, "an element" means one element or over one element.

[0064] "Activated carbon" refers to a form of carbon processed to have small pores, increasing the surface area available for adsorption.

[0065] The term "amino acid," as used herein, refers to any nitrogen containing organic acid or peptide that can be used as an osmotic agent to generate peritoneal dialysate.

[0066] The term "calcium chloride source" refers to a source of calcium chloride in solid and/or solution form. The calcium chloride source can contain at least one fluid pathway and include components such as conduits, valves, filters or fluid connection ports, any of which are fluidly connectable to each other or to a fluid flow path. The calcium chloride source can either

be formed as a stand-alone enclosure or a compartment integrally formed with an apparatus for dialysis for containing a calcium chloride source.

[0067] A "carbon filter" is a bed of activated carbon.

[0068] The term "comprising" includes, but is not limited to, whatever follows the word "comprising." Use of the term indicates the listed elements are required or mandatory but that other elements are optional and may be present.

[0069] A "concentrate pump" is a pump configured to move fluid between a concentrate source and a flow path.

[0070] A "concentrate solution" is a solution of one or more solutes in water. The concentrate solution can have a solute concentration greater than that to be used in dialysis.

[0071] A "concentrate source" is a source of one or more solutes. The concentrate source can have one or more solutes that has a solute concentration greater than the solute concentration to be used for dialysis.

[0072] A "conductivity sensor" is device for measuring the electrical conductance of a solution and/or the ion, such as a sodium ion, concentration of a solution.

[0073] A "connector" and "for connection" describe the concept of forming a fluid connection between two components wherein fluid, gas, or mixture of both gas and fluid can flow from one component, through a connector or a component for connection, to another component. The connector provides for a fluid connection in its broadest sense and can include any type of tubing, fluid or gas passageway, or conduit between any one or more components of the invention. The connection can optionally be disconnected and then reconnected.

[0074] The term "consisting of" includes and is limited to whatever follows the phrase "consisting of." The phrase indicates the limited elements are required or mandatory and that no other elements may be present.

[0075] The term "consisting essentially of" includes whatever follows the term "consisting essentially of" and additional elements, structures, acts or features that do not affect the basic operation of the apparatus, structure or method described.

[0076] The terms "control," "controlling," or "controls" refers to the ability of one component to direct the actions of a second component.

[0077] A "control system" can be a combination of components that act together to maintain a system to a desired set of performance specifications. The control system can use processors, memory and computer components configured to interoperate to maintain the desired performance specifications. The control system can also include fluid or gas control components, and solute control components as known within the art to maintain the performance specifications.

[0078] The terms "controlled addition," to "control addition," or "controlling addition" refer to the ability to add one or more substances or fluids to a flow path or container in an accurately controllable amount.

[0079] The phrase "controlling the movement of fluid" refers to directing fluid through a flow path, container, receptacle, or reservoir of any type.

[0080] A "cycler" is a component for movement of fluid into and out of the peritoneal cavity of a patient.

[0081] The term "dextrose source" refers to a source of dextrose in solid and/or solution form. The dextrose source can interface with at least one other module found in systems for

dialysis. The dextrose source can contain at least one fluid pathway and include components such as conduits, valves, filters or fluid connection ports, any of which are fluidly connectable to each other or to a fluid flow path. The dextrose source can either be formed as a stand-alone enclosure or a compartment integrally formed with an apparatus for dialysis for containing a dextrose source.

[0082] The term "dialysate" describes a fluid into or out of which solutes from a fluid to be dialyzed diffuse through a membrane. Dialysate can differ depending on the type of dialysis to be carried out. For example, dialysate for peritoneal dialysis may include different solutes or different concentrations of solutes than dialysate for hemodialysis.

[0083] A "dialysate container" is any container capable of storing or containing dialysate for dialysis. The container any be of any suitable, size, geometry, or configuration.

[0084] The term "dialysis caddy" refers to a container detachably removable from a dialysis system, the caddy configured to hold one or more other containers. In any embodiment, the caddy can include one or more connectors for fluid connection from the containers to the dialysis system.

[0085] The term "downstream" refers to a position of a first component in a flow path relative to a second component wherein fluid will pass by the second component prior to the first component during normal operation. The first component can be said to be "downstream" of the second component, while the second component is "upstream" of the first component.

[0086] A "drain line" is a fluid line for carrying fluid to a drain such as a waste receptacle or drain. The drain line can be connected to a peritoneal cavity of a patient for draining fluid.

[0087] The term "filter" refers to a porous component through which fluid can pass, but that traps one or more materials within the fluid.

[0088] A "fitting feature" is any protrusion, indentation, groove, ridge, having any shape, size, or geometry that ensures that only a corresponding fitting feature complementary to the fitting feature can form a connection or fit to the corresponding fitting feature. The fitting feature can also include non-mechanical means for ensuring complementary connection such as magnets placed at particular locations, or visual or aural indicators such as color, lettering, or sound. The fitting feature can be affixed, integral, or labeled on a component or surface to ensure that a corresponding feature on a desired component or surface can mate or connect to the component or surface having the fitting feature.

[0089] A "flash pasteurization module" is a component or set of components capable of heating a fluid to a high temperature and recirculating the fluid for sterilization.

[0090] A "flow meter" is a device capable of measuring an amount or rate of fluid moving past or through a particular location.

[0091] The term "fluid" can be any substance that has no fixed shape that yields easily to external pressure such as a gas or a liquid. Specifically, the fluid can be water containing any solutes at any concentration. The fluid can also be dialysate of any type including fresh, partially used, or spent.

[0092] The terms "fluid connection," "fluidly connectable," or "fluidly connected" refer to the ability to pass fluid or gas from one point to another point. The two points can be within or between any one or more of compartments, modules, systems, and components, all of any type.

[0093] "Fluid returned to the peritoneal dialysate generation flow path from a peritoneal cavity of a patient" refers to fluid used in peritoneal cavity and then returned to the peritoneal dialysate generation flow path.

[0094] The terms "to generate peritoneal dialysate" or "peritoneal dialysate generation" refers to creating a peritoneal dialysate solution from constituent parts.

[0095] The term "glucose source" refers to a source of glucose in solid and/or solution form. The glucose source can interface with at least one other module found in systems for dialysis. The glucose source can contain at least one fluid pathway and include components such as conduits, valves, filters or fluid connection ports, any of which are fluidly connectable to each other or to a fluid flow path. The glucose source can either be formed as a stand-alone enclosure or a compartment integrally formed with an apparatus for dialysis for containing a glucose source.

[0096] A "heater" is a component capable of raising the temperature of a substance, container, or fluid.

[0097] The terms "heating" or to "heat" refer to raising the temperature of a substance, fluid, or container.

[0098] An "integrated cycler" is a component for movement of fluid into and out of the peritoneal cavity of a patient, wherein the integrated cycler forms a part of an overall system. For example, the integrated cycler can be contained in a housing with other components used for peritoneal dialysis and be in fluid and electrical connection with desired components.

[0099] An "infusion line" is a fluid line for carrying peritoneal dialysate into a body cavity or part of a patient such as a peritoneal cavity.

[00100] An "ion concentrate" refers to one or more ionic compounds. The ion concentrate can have one or more ionic compounds in the ion concentrate. Further, the ion concentrate can have an ion concentration greater than an ion concentration to be used in dialysis.

[00101] An "ion concentrate source" refers to a source of one or more ionic compounds. The ion concentrate source can be in water or solid form. The ion concentrate source can further have one or more ionic compounds that is at a higher ion concentration greater than generally used in dialysis.

[00102] The term "ion exchange resin" refers to a material capable of removing ions from a fluid and releasing different ions into the fluid.

[00103] The term "level of sterility" refers to an estimated probability of viable organisms surviving a sterilization process.

[00104] The term "magnesium chloride source" refers to a source of magnesium chloride in solid and/or solution form. The magnesium chloride source can interface with at least one other module found in systems for dialysis. The magnesium chloride source can contain at least one fluid pathway and include components such as conduits, valves, filters or fluid connection ports, any of which are fluidly connectable to each other or to a fluid flow path. The magnesium chloride source can either be formed as a stand-alone enclosure or a compartment integrally formed with an apparatus for dialysis for containing a magnesium chloride source.

[00105] The term "microbial filter" refers to a device inhibiting passage of microbes or fragments of microbes such as endotoxins in a fluid or solution while allowing the passage of the fluid or solution.

[00106] A "nanofilter" is a filter membrane having nanometer sized pores.

[00107] An "osmotic agent" is a substance dissolved in water capable of driving a net movement of water by osmosis across a semi-permeable membrane due to concentration differences of the osmotic agent on each side of the semi-permeable membrane.

[00108] An "osmotic agent source" refers to a source of osmotic agents in solid and/or solution form. The osmotic agent source can interface with at least one other module found in systems for dialysis. The osmotic agent source can contain at least one fluid pathway and include components such as conduits, valves, filters or fluid connection ports, any of which are fluidly connectable to each other or to a fluid flow path. The osmotic agent source can either be formed as a stand-alone enclosure or a compartment integrally formed with an apparatus for dialysis for containing an osmotic agent source.

[00109] The term "peritoneal cavity" refers to the space between the parietal peritoneum and visceral peritoneum of a patient.

[00110] "Peritoneal dialysate" is a dialysis solution that can to be used in peritoneal dialysis having specified parameters for purity and sterility. Peritoneal dialysate is not the same as dialysate used in hemodialysis although peritoneal dialysate may be used in hemodialysis.

[00111] A "peritoneal dialysate generation flow path" is a path that can be used in generating dialysate suitable for peritoneal dialysis.

[00112] A "peritoneal dialysate generation system" refers to a collection of components used to generate peritoneal dialysate.

[00113] The term "peritoneal dialysate regeneration module" refers to a component or components capable of removing waste products from a fluid.

[00114] "Peritoneal dialysis" is a therapy wherein a dialysate is infused into the peritoneal cavity, which serves as a natural dialyzer. In general, waste components diffuse from a patient's

bloodstream across a peritoneal membrane into the dialysis solution via a concentration gradient. In general, excess fluid in the form of plasma water flows from a patient's bloodstream across a peritoneal membrane into the dialysis solution via an osmotic gradient. Once the infused peritoneal dialysis solution has captured sufficient amounts of the waste components the fluid is removed. This cycle can be repeated for several cycles each day or as needed.

[00115] A "predetermined time" is a set time for an event to occur, such as a set time of day, or a set length of time from a previous event.

[00116] The term "prescribed solute concentration" refers to the concentration of one or more solutes in peritoneal dialysate intended for use by a patient.

[00117] The term "pressure sensor" refers to a device for measuring the pressure of a gas or liquid in a vessel, container, or fluid line.

[00118] The term "pump" refers to any device that causes the movement of fluids or gases by applying suction or pressure.

[00119] The terms "pumping fluid" or to "pump fluid" refer to moving a fluid through a flow path with a pump.

[00120] "Purified water" can be defined as water produced by distillation, deionization, reverse osmosis, or other suitable processes and that meets the definition of "purified water" in the United States Pharmacopeia, 23d Revision, January 1, 1995, and the FDA at 21 CFR Section §165.110(a)(2)(iv). Other criteria for purified water can be determined by those of skill in the art, particularly as relating to purified water suitable for peritoneal dialysis.

[00121] The terms "regenerative peritoneal dialysis" or to "regenerate peritoneal dialysate" refer to removing waste products from used peritoneal dialysate to generate a fluid reusable in peritoneal dialysis.

[00122] A "reverse osmosis module" is a set of components that act to drive fluid through one or more semipermeable membranes, wherein pressure is used to move the fluid from a side of the semipermeable membrane with a higher concentration of one or more solutes to a side of the semipermeable membrane with a lower concentration of the one or more solutes.

[00123] A "selected time" is a set time chosen by a user or algorithm.

[00124] A "sensor" is a component capable of determining or sensing the states of one or more variables in a system.

[00125] The term "sodium chloride source" refers to a source of sodium chloride in solid and/or solution form. The sodium chloride source can interface with at least one other module found in systems for dialysis. The sodium chloride source can contain at least one fluid pathway and include components such as conduits, valves, filters or fluid connection ports, any of which are fluidly connectable to each other or to a fluid flow path. The sodium chloride source can either be formed as a stand-alone enclosure or a compartment integrally formed with an apparatus for dialysis for containing a sodium chloride source.

[00126] The term "sodium lactate source" refers to a source of sodium lactate in solid and/or solution form. The sodium lactate source can interface with at least one other module found in systems for dialysis. The sodium lactate source can contain at least one fluid pathway and include components such as conduits, valves, filters or fluid connection ports, any of which are fluidly connectable to each other or to a fluid flow path. The sodium lactate source can either be formed as a stand-alone enclosure or a compartment integrally formed with an apparatus for dialysis for containing a sodium lactate source.

[00127] A "solute" is a substance dissolved in a solvent, such as water.

[00128] The term "sorbent cartridge" refers to a cartridge containing one or more sorbent materials for removing specific solutes from solution. The term "sorbent cartridge" does not require the contents in the cartridge be sorbent based, and the contents of the sorbent cartridge can be any contents that can remove solutes from a dialysate. The sorbent cartridge may include any suitable amount of one or more sorbent materials. In certain instances, the term "sorbent cartridge" refers to a cartridge which includes one or more sorbent materials besides one or more other materials capable of removing solutes from dialysate. "Sorbent cartridge" can include configurations where at least some materials in the cartridge do not act by mechanisms of adsorption or absorption.

[00129] A "sterilization module" is a component or set of components to sterilize a fluid by removing or destroying chemical or biological contaminants.

[00130] A "temperature sensor" is a sensor capable of determining the temperature of a fluid.

[00131] A "timer" is a device capable of determining the time of day, or the time elapsed between multiple events.

[00132] An "ultrafilter" is a semi permeable membrane through which a fluid can pass and that can remove one or more solutes or particles from the fluid.

[00133] The term "upstream" refers to a position of a first component in a flow path relative to a second component wherein fluid will pass by the first component prior to the second component during normal operation. The first component can be said to be "upstream" of the second component, while the second component is "downstream" of the first component.

[00134] A "user interface" is a component that allows a user to communicate information or instructions to a processor or a memory device and to receive information or instructions from the processor or memory device.

[00135] A "UV light source" is a component that uses ultraviolet light to kill biological contaminants in a fluid.

[00136] A "valve" is a device capable of directing the flow of fluid or gas by opening, closing or obstructing one or more pathways to allow the fluid or gas to travel in a path. One or more valves configured to accomplish a desired flow can be configured into a "valve assembly."

[00137] The term "water purification module" refers to a component or components capable of removing biological or chemical contaminants from water.

[00138] The term "water source" refers to a source from which potable or not potable water can be obtained.

Regenerative Peritoneal Dialysis System

[00139] The invention is drawn to systems and methods for regenerating and reusing peritoneal dialysate. FIG. 1 illustrates a block diagram of a flow path used in regenerating peritoneal dialysate. The flow path includes a peritoneal dialysate generation flow path **101**. Water source **102** can provide water for the initial preparation of peritoneal dialysate, as well as additional fluid as needed. System pump **103** provides a driving force for moving fluid through the peritoneal dialysate generation flow path **101**. The fluid in the peritoneal dialysate generation flow path **101** is pumped through a peritoneal dialysate regeneration module **104** to remove waste products and impurities. The water source **102** can be a source of potable water including a purified water source. Purified water can refer to water meeting the definition of "purified water" in the United States Pharmacopeia, 23d Revision, January 1, 1995.

Alternatively, purified water can refer to any source of water treated to remove at least some biological or chemical contaminants, whether or not the water meets the definition of purified water in United States Pharmacopeia, 23d Revision, January 1, 1995. In any embodiment of the first or second aspects of the invention, the water source **102** can be a non-purified water source, such as tap water, wherein the water from the water source **102** can be purified by the system as described. A non-purified water source can provide water without additional purification, such as tap water from a municipal water source, water that has undergone some level of purification, but does not meet the definition of "purified water" provided, such as bottled water or filtered water. In any embodiment, the water source can contain water meeting the WHO drinkable water standards provided in *Guidelines for Drinking Water Quality*, World Health Organization, Geneva, Switzerland, 4th edition, 2011. The water source **102** can be any size usable with the system, including between 3 and 20 L. A water source **102** of 6 L or less can generally generate the necessary peritoneal dialysate for multiple cycles when using a regenerative system. The peritoneal dialysate generation flow path **101** can also have a direct connection to a purified or non-purified water source. The water source **102** can be any source of water, whether from a tap, faucet, or a separate container or reservoir.

[00140] In any embodiment of the first or second aspects of the invention, the peritoneal dialysate regeneration module **104** can be a sorbent cartridge. The sorbent cartridge includes urease, a cation exchange material, an anion exchange material, and activated carbon. The urease can optionally be immobilized on alumina. The activated carbon operates to adsorb non-ionic molecules, organic molecules, and chlorine from the water, along with some endotoxins or bacterial contaminants. The activated carbon can be present in the sorbent cartridge in the form of a carbon filter or pad, or as a material layer in the sorbent cartridge. A carbon filter or pad is a

bed of activated carbon. The carbon filter can be in a self contained packaging, or present as a layer of activated carbon within the sorbent cartridge. The urease catalyzes the conversion of urea in the dialysate into ammonium ions. The cation exchange material, such as zirconium phosphate, can remove cationic species from the fluid, such as potassium, calcium, magnesium, the ammonium ions generated by the reaction of urea, or other cations, replacing the cationic species with hydrogen or sodium. The sorbent cartridge can include any cation exchange material capable of removing cations from the fluid. The anion exchange material, such as zirconium oxide, can remove anionic species from the fluid, such as phosphate or fluoride molecules, replacing the anionic species with acetate or hydroxide ions. The sorbent cartridge can have any anion exchange material known in the art capable of removing anionic species from the fluid. In any embodiment, the sorbent cartridge can include aluminum oxide for removal of fluoride and heavy metals. In any embodiment, the sorbent cartridge can have a layer of aluminum oxide, followed by a layer of activate carbon, a layer of urease, and then an ion exchange resin. The sorbent cartridge can purify up to 3 L of water or used peritoneal dialysate per exchange, with flow rates of up to 300 ml/min. A larger sorbent cartridge can be used when generating peritoneal dialysate for multiple infusions, including a sorbent cartridge that can purify between 3 and 20 L, between 3 and 5 L, between 3 and 10 L, between 5 and 12 L, between 10 and 15 L, or between 10 and 20 L of water, or more.

[00141] In any embodiment, the sorbent cartridge can be a single use component or a rechargeable component. Recharging can refer to the process of treating a sorbent material to restore the functional capacity of the sorbent material so as to put the sorbent material back into a condition for use or reuse in a new dialysis session. In some instances, recharging also includes treating a sorbent material so as to clean the sorbent material so that the sorbent material can be

stored and used in a subsequent dialysis session. In some instances, the total mass, weight and/or amount of "rechargeable" sorbent materials remain the same. In some instances, the total mass, weight and/or amount of "rechargeable" sorbent materials change. Without being limited to any one theory of invention, the recharging process may involve exchanging ions bound to the sorbent material with different ions, which in some instances may increase or decrease the total mass of the system. However, the total amount of the sorbent material will in some instances be unchanged by the recharging process. Upon a sorbent material undergoing "recharging," the sorbent material can then be said to be "recharged."

[00142] The sorbent cartridge can additionally include a microbial filter and/or a particulate filter. A microbial filter can further reduce the amount of endotoxins or bacterial contaminants present in the fluid. A particulate filter can remove particulate matter from the fluid. The sorbent materials described can be present in the sorbent cartridge in any order, or intermixed, so long as the zirconium phosphate is present downstream of the urease. The sorbent cartridge can be sized depending on the needs of the user, with a larger sized sorbent cartridge allowing for more exchanges before the sorbent cartridge must be replaced.

[00143] Alternatively, the peritoneal dialysate regeneration module **104** can be any component capable of removing contaminants from the fluid in the peritoneal dialysate generation flow path **101**, including any one or more of a sorbent cartridge, reverse osmosis module, nanofilter, an ion exchange resin, a combination of cation and anion exchange materials, activated carbon, silica, or silica based columns.

[00144] After passing through the peritoneal dialysate regeneration module **104**, the fluid is pumped to a concentrate source **105**, where necessary components for carrying out peritoneal dialysis can be added from the concentrate source **105**. The concentrates in the concentrate

source **105** are utilized to create a peritoneal dialysis fluid that matches a dialysis prescription. Concentrate pump **106** can control the movement of concentrates from the concentrate source **105** to the peritoneal dialysate generation flow path **101** in a controlled addition. The concentrates added from the concentrate source **105** to the peritoneal dialysate generation flow path **101** can include any component prescribed for use in peritoneal dialysate. Table 1 provides non-limiting exemplary ranges of commonly used components of peritoneal dialysate.

Table 1

Component	**Concentration**
Sodium chloride	132-134 mmol/L
Calcium chloride dehydrate	1.25-1.75 mmol/L
Magnesium chloride hexahydrate	0.25-0.75 mmol/L
Sodium Lactate	35-40 mmol/L
Dextrose (D-glucose) monohydrate	0.55-4.25 g/dL
pH	5-6
Osmolality	346-485 (hypertonic)

[00145] To reduce the glucose degradation products (GDP) formed, some peritoneal dialysate systems use a low GDP formulation. Exemplary peritoneal dialysate concentrations for low GDP formulations are provided in Table 2. Generally, the low GDP peritoneal dialysate is provided in two separate bags, with one bag containing calcium chloride, magnesium chloride and glucose maintained at low pH, and the second bag containing sodium chloride and the buffer components, including sodium lactate and sodium bicarbonate. The two bags are mixed prior to use to generate a peritoneal dialysate with a neutral pH. Alternatively, a two chamber bag is used, the chambers separated by a divider which is broken to mix the fluids prior to use.

Table 2

Low GDP peritoneal dialysate formulations

Component	**Concentration**
Sodium	132-134 mEq/L

Calcium	2.5-3.5 mEq/L
Magnesium	0.5-1.0 mEq/L
Lactate	0-40 mEq/L
Bicarbonate	0-34 mEq/L
pH	6.3-7.4
% glucose (g/dL)	1.5-4.25

[00146] One of skill in the art will understand that other components can be used in place of the components listed in Tables 1-2. For example, dextrose as listed in Table 1 is commonly used as an osmotic agent. In any embodiment of the first or second aspects of the invention, other osmotic agents can be used in addition to, or in place of, the dextrose, including glucose, icodextrin or amino acid solutions, including dialysate with multiple osmotic agents. Although the sources of sodium, calcium, and magnesium listed in Table 1 are chloride salts, other sodium, magnesium, and calcium salts can be used, such as lactate or acetate salts. Peritoneal dialysate may also contain buffers for maintaining pH of the peritoneal dialysate. Exemplary, non-limiting examples of suitable buffers include bicarbonate buffer, acetate buffer or lactate buffer. Although not generally used in peritoneal dialysis, potassium chloride can be used for hypokalemic patients who don't receive sufficient potassium through diet. The concentrate source **105** can contain one or more osmotic agents, as well as one or more ion concentrates, such as concentrated sodium chloride, sodium lactate, magnesium chloride, calcium chloride, and/or sodium bicarbonate. In any embodiment, the system can have a single concentrate that has all components mixed for a daytime or overnight treatment for use in a home by a single patient. The concentrate source **105** can include separate sources for any one or more of the solutes that are to be used in the peritoneal dialysate. Alternatively, the concentrate source **105** can include a separate osmotic agent source, and an ion concentrate source each with a separate concentrate pump to add each component needed to create the peritoneal dialysate. Concentrate pump **106**

pumps concentrated solutions from the concentrate source or sources **105** to the peritoneal dialysate generation flow path **101** in a controlled addition. Where more than one concentrate source is used, separate concentrate pumps can move each of the concentrates into the peritoneal dialysate generation flow path **101**, or a single concentrate pump can be used, with valves configured allow individual control over the movement of each of the concentrate solutions to the peritoneal dialysate generation flow path **101**.

[00147] One of skill in the art will understand that the peritoneal dialysate regeneration module **104** may not fully remove glucose, dextrose, icodextrin, or other osmotic agents. To control the amount of osmotic agent in the generated dialysate, the relative amounts of ionic solutes and osmotic agents required to be added may vary. To control the relative amounts of ions and osmotic agents in the dialysate where the peritoneal dialysate regeneration module **104** does not fully remove the osmotic agents, the concentrate source **105** can include a separate osmotic agent source and ion concentrate source. Refractive index sensor **120** determines the concentration of glucose or other osmotic agents in the dialysate downstream of the peritoneal dialysate regeneration module **104** and can control the addition of osmotic agents from the concentrate source **105**.

[00148] After addition of solutes from the concentrate source **105**, the fluid in the peritoneal dialysate generation flow path **101** can contain all the necessary solutes for peritoneal dialysis. Conductivity sensor **116** and refractive index sensor **117** are used to confirm the concentration of electrolytes and osmotic agents are within predetermined ranges.

[00149] The peritoneal dialysate should reach a level of sterility for peritoneal dialysis. The level of sterility can be any level that meets an applicable regulatory requirement, such as a sterility assurance level of 10^{-6} required by the FDA, meaning that the chance a viable organism

is present after sterilization is 1 in 1,000,000. The system can pump the fluid to a sterilization module for sterilization of the peritoneal dialysate. The sterilization module can include one or more of a first ultrafilter **107**, a second ultrafilter **121**, and a UV light source (not shown in FIG. 1). The sterilization module can be any component or set of components capable of sterilizing the peritoneal dialysate. In any embodiment, the sterilization module can be a single or multiple ultrafilters. Multiple ultrafilters provide further sterilization of the fluid and redundancy of the system to protect against sterilization failure. A secondary component, such as a UV light source or microbial filter (not shown in FIG. 1), can be used in the sterilization module to provide additional sterilization of the peritoneal dialysate. The UV light source can be positioned at any location in the peritoneal dialysate generation flow path **101**, including upstream of the first ultrafilter **107**, between ultrafilters **107** and **121** in a system using two ultrafilters, or downstream of the second ultrafilter **121**. The ultrafilters **107** and **121** used in the sterilization module can be replaced as necessary. In any embodiment, the ultrafilters **107** and **121** can have a 3-6 month lifetime before replacement. The ultrafilters **107** and **121** can be any ultrafilter known in the art capable of sterilizing the peritoneal dialysate. A non-limiting example of an ultrafilter that can be used in the systems described is the hollow fiber ForClean ultrafilter, available from Bellco, Mirandola (MO), Italy. In certain embodiments, the sterilization module can use heat sterilization. The sterilization module can include a heater (not shown) to heat the prepared dialysate. Alternatively or additionally, the sterilization module can include a flash pasteurization module (not shown) to sterilize the dialysate through flash pasteurization. The sterilization module can include both heat-based sterilization components and filtration based sterilization components, with the user adjusting the mode of sterilization based on the mode of use. For example, a heat based sterilization can be used when the peritoneal dialysate is

generated for later use, while a filtration based sterilization can be used when the peritoneal dialysate is generated for immediate use.

[00150] After passing through the sterilization module, the peritoneal dialysate can be used in peritoneal dialysis. A dialysate storage container **108** can store the peritoneal dialysate until used. The peritoneal dialysate can pass through valve **109** and into the dialysate storage container **108**. If ready for use, the peritoneal dialysate can be pumped from dialysate storage container **108**, through valve **110**, and back into the peritoneal dialysate generation flow path **101**. Pump **111** provides a driving force for the movement of the peritoneal dialysate from the dialysate storage container **108** to the peritoneal dialysate generation flow path **101**. Additional or alternative storage containers can be included at other locations in the peritoneal dialysate generation flow path **101**. A storage container can be included upstream of the sterilization module, and downstream of the water purification module. Before the fluid is utilized in the cycler stage, the fluid can be pumped through the sterilization module, eliminating issues related to storage of sterile fluid. The storage containers can be either upstream or downstream of the concentrate source **105**. Concentrates can be added to fluid before storing the fluid, or after storage of the fluid but prior to sterilization in the sterilization module. The peritoneal dialysate is then pumped through valve **112** and into infusion line **118**. Infusion line **118** can include a connector **114** for connection to any non-integrated cycler (not shown in FIG. 1), which can infuse the peritoneal dialysate into the patient. The direct connection to an external cycler can use any type of connector known in the art. The connectors can be single-use or reusable connectors and should provide for sterile transfer of fluids. The connectors should preferably be closed connectors, to avoid contact between the fluids and the external environment. A non-limiting example of a connector that can be used for a direct connection to an external cycler is

the INTACT® connectors provided by Medinstill Development LLC, Delaware, US. Alternatively, an integrated cycler (not shown in FIG. 1) can be provided, with direct infusion of the peritoneal dialysate from the peritoneal dialysate generation flow path **101** into the peritoneal cavity of the patient.

[00151] After a dwell time in the peritoneal cavity of the patient, the peritoneal dialysate can be drained from the peritoneal cavity of the patient by the cycler and returned to the peritoneal dialysate generation flow path **101** for fluid regeneration for subsequent cycles. Connector **115** on drain line **119** can connect to a drain line of a non-integrated cycler to return the used peritoneal dialysate back to the peritoneal dialysate generation flow path **101** through valve **113**. The fluid returned to the peritoneal dialysate generation flow path **101** from the peritoneal cavity of the patient can again be pumped through the peritoneal dialysate generation flow path **101** as described to regenerate the peritoneal dialysate for reuse in dialysis. A waste reservoir **122** can be fluidly connected to the peritoneal dialysate generation flow path **101** through valve **123** for removal of excess fluid drained from the peritoneal cavity of the patient.

[00152] The peritoneal dialysate regeneration system illustrated in FIG. 1 is a modular system that can be connected to any non-integrated cycler for infusion into and out of the peritoneal cavity of the patient. Alternatively, the dialysate storage container **108** can be detachable from the system, and separately connected to a non-integrated cycler. The dialysate storage container **108** can include one or more sterilized dialysate bags. The dialysate bags, once filled with peritoneal dialysate, can be stored until needed by the patient. The dialysate storage container **108** can alternatively be a reusable sterilized container or bag. The reusable container or bag can be cleaned and sterilized daily, or at set time periods. Alternatively, the dialysate storage container **108** can be any type of storage container, such as a stainless steel container.

The dialysate storage container **108** can store enough peritoneal dialysate for a single infusion of peritoneal dialysate into the patient, or enough peritoneal dialysate for multiple infusions into a patient. The connectors to the dialysate storage container **108** can be any type of connector known in the art. The connectors can be single use or disposable connectors that provide transfer of sterile fluids. A non-limiting example of connectors that can be used with the described system is the Lynx®-Millipore connectors available from Merck KGaA, Darmstadt, Germany.

[00153] As described, any number of concentrate sources can be included in the peritoneal dialysate generation flow path **101**. Table 3 provides exemplary non-limiting ranges of solutes that can be added from a single concentrate source **105** to the peritoneal dialysate generation flow path **101**, including the starting concentration of the solutes in the concentrate source, as well as exemplary final volumes of the solutes in the dialysate and the exemplary flow rates of both the solutes and the water in the dialysate generation flow path that will achieve those concentrations. The solutes shown in Table 3 are traditional peritoneal dialysate solutes. Table 4 shows exemplary ranges of solutes that can be used as a low GDP formulation. Table 5 shows exemplary ranges of solutes that can be used with icodextrin as the osmotic agent. Icodextrin is sometimes used as an osmotic agent for a long dwell period. If dextrose or glucose is used in a long dwell period, reabsorption of the ultrafiltrate can occur, reducing the net volume of fluid removed. Icodextrin results in a long sustained ultrafiltration, and can provide improved ultrafiltration efficiency over a long dwell period. One of skill in the art will understand that the concentrations of any of the solutes shown in Tables 3-5 can be altered by altering the flow rates of the system pump **103** or concentrate pump **106**. However, the ratio of the solutes included is fixed if using a single concentrate source **105**. If the ratio of the solutes needs to be altered for any reason, a new concentrate solution may be needed.

Table 3

Exemplary solutes for addition from a single concentrate source

Component	Concentration (g/l)	Solution volume (ml/L)	Flow rate (ml/min)
Glucose	100 – 850	50-400	1 – 18
Sodium Chloride	13 – 108	50-400	1 – 18
Sodium Lactate	11 – 90	50-400	1 – 18
$MgCl_2.6H_2O$	0.13 - 1.02	50-400	1 – 18
$CaCl_2.2H_2O$	0.6 - 5.1	50-400	1 – 18
Water		600-950	50-1000

Table 4

Exemplary solute ranges in a low GDP solution

Component	Concentration (g/l)	Solution volume (ml/L)	Flow rate (ml/min)
Glucose	100 - 900	50-400	1 – 18
Sodium Chloride	13 - 108	50-400	1 – 18
Sodium Lactate	11 - 90	50-400	1 – 18
$MgCl_2.6H_2O$	0.13 - 1.02	50-400	1 – 18
$CaCl_2.2H_2O$	0.6 - 5.1	50-400	1 – 18
Water		600-950	50-1000

Table 5

Exemplary solute ranges in icodextrin solution

Component	Concentration (g/l)	Solution volume (ml/L)	Flow rate (ml/min)
Icodextrin	100 – 850	100-400	2-37
Sodium Chloride	13 - 108	100-400	1 – 18
Sodium Lactate	11 - 90	100-400	2-37
$MgCl_2.6H_2O$	0.13 - 1.02	100-400	2-37
$CaCl_2.2H_2O$	0.6 - 5.1	100-400	2-37
Water		600-900	50-1000

[00154] Although using a single concentrate source in the system requires a fixed ratio of solutes in the generated peritoneal dialysate, a single concentrate source provides certain advantages. Storage requirements are decreased, as only a single concentrate solution needs to be stored for a given dialysate prescription. There is also a lower risk of patient error in adding solutes to the dialysate in the proper amounts. A single concentrate source also requires less supplies, less pumps, and less hardware. Further, because fewer containers are needed, the containers are easier to manage, clean, and disinfect. One of skill in the art will understand that a higher concentration of solutes in the concentrate source will allow minimization of the container size and maximization of the source water used in PD solution preparation, lowering costs. The limiting factor is mutual solubility of the components, which is generally limited by glucose or icodextrin solubility. The flow rate for the source water can be optimized to adjust the time required to prepare the solution. In the case of on-demand dialysate preparation, a high flow rate is desired to minimize the time needed to prepare the solution. The flow rate limit will be controlled by the metering accuracy of the concentrate pump at the rate required to match the water feed. With a single concentrate source, about 150 ml/exchange can be needed, corresponding to about 600 ml/day or 4.2 L/week. The concentrate source can be sized depending on the needs of the user, with a larger concentrate source requiring less frequent refilling.

[00155] FIG. 2 illustrates a detailed flow diagram of a regenerative peritoneal dialysate system. The initial peritoneal dialysate can be generated with water from water source **202**. Water pump **252** provides a driving force for moving water from water source **202** into the peritoneal dialysate generation flow path **201**. Filter **250** can remove any particulate matter from the water prior to entering the peritoneal dialysate generation flow path **201**. Valve **253** allows

for fast priming of the sorbent cartridge **204** and the peritoneal dialysate generation flow path **201**. Check valve **251** prevents back flow of fluid into the water source **202**. System pump **203** provides a driving force for moving fluid through the peritoneal dialysate generation flow path **201**. The water can pass through pressure sensor **254** to ensure the incoming water is within a predetermined pressure threshold. Conductivity sensor **255** measures the conductivity of the incoming water. The water passes through valves **256** and **249** and enters sorbent cartridge **204** for purification. Valve **249** can also direct fluid to waste reservoir **242** during disinfection at the beginning of each session. Filter **219** removes any particulate matter from the fluid after passing through sorbent cartridge **204**. The fluid is then pumped through valve **220** and degassed in degasser **216**. Degassing pump **217** provides a driving force for moving the fluid through degasser **216**. Pump **218** pumps fluid back into the peritoneal dialysate generation flow path **201**. Although shown as a degasser **216** with a degassing sprayer in FIG. 2, the degasser **216** can be any type of degasser known in the art. Vacuum pump **223** can create a vacuum to remove air from the top of the degassing vessel through valves **232** and **231**. Vent **233** allows the air to escape.

[00156] To generate the peritoneal dialysate, solutes are added from concentrate sources **205**, **206**, and **207**. As explained, any number of concentrate sources can be used. As illustrated in FIG. 2, the concentrate sources can include sodium chloride source **207**, ion concentrate source **206**, and osmotic agent source **205**. Concentrate pumps **208** and **209** provide a driving force for pumping concentrates into the peritoneal dialysate generation flow path **201**. Filters **212**, **213**, **214**, and **215** can remove particulate matter from the concentrates prior to entering peritoneal dialysate generation flow path **201**. Valves **210** and **211** control adding concentrates to the peritoneal dialysate generation flow path **201**. Valve **221** can direct the concentrates to a

location upstream of sorbent cartridge **204** during priming of the system. Conductivity sensor **225** determines the conductivity of the fluid after addition of sodium chloride and other concentrates. Mixing chamber **226** mixes the concentrates with the fluid in peritoneal dialysate generation flow path **201**. Conductivity sensor **227** determines the conductivity of the generated peritoneal dialysate. Flow meters **228** and **229** determine the flow rate of the fluid after addition of the concentrates. A pH and ammonia sensor **230** determines the pH of the peritoneal dialysate, and can determine the presence of ammonia or ammonium ions that remain in the peritoneal dialysate after passing through the sorbent cartridge **204**. Pressure sensor **234** measures the pressure of the fluid prior to sterilization and is used in the control circuit to control the pressure.

[00157] The generated peritoneal dialysate can be sterilized by pumping the peritoneal dialysate through a sterilization module, shown as two ultrafilters **235** and **237** in FIG. 2. The peritoneal dialysate can be pumped through a first ultrafilter **235**, through three-way valve **237** and then through an optional second ultrafilter **236**. Valve **238** can be used for back flushing the ultrafilters **235** and **237**. The sterilized peritoneal dialysate can be pumped through valve **243** to cycler connector **244**, which can connect to an infusion line of any non-integrated cycler (not shown). Alternatively, valve **248** can direct fluid into a dialysate container **246** for storage and later use. Pump **247** controls the movement of fluid into and out of dialysate container **246**. As described, additional or alternative storage containers can be included upstream of the sterilization module, either before or after addition of the concentrates. Storage of the fluid prior to the sterilization module may address potential sterilization issues associated with storage of sterilized dialysate during the storage phase. Dialysate stored in dialysate container **246** can be pumped back into the peritoneal dialysate generation flow path **201** by pump **247** and into cycler

connector **244** for infusion into a patient. Alternatively, dialysate container **246** can be detached from the system and separately used with any non-integrated cycler.

[00158] After the peritoneal dialysate is infused into the peritoneal cavity of a patient the peritoneal dialysate is held in the patient for a dwell period. After the dwell period, the peritoneal dialysate is drained from the patient. The fluid returned to the peritoneal dialysate generation flow path **201** from the peritoneal cavity of the patient is pumped through cycler connector **245** which can connect to a drain line of any non-integrated cycler (not shown). If a detachable dialysate container **246** is used, waste and storage reservoir **241** can be connected to collect used dialysate from the patient. After use, waste and storage reservoir **241** can be reconnected to the peritoneal dialysate generation flow path **201** and the used peritoneal dialysate pumped from the waste and storage reservoir **241** back into the peritoneal dialysate generation flow path **201**. Flow meter **222** determines the amount of fluid removed from the patient, and pressure sensor **224** monitors the draw pressure when removing fluid from the patient. The used peritoneal dialysate can be removed from the patient through valve **240** by pump **239** and pumped into storage reservoir **241**. The remaining used peritoneal dialysate can be pumped through the peritoneal dialysate generation flow path **201**, and back through the sorbent cartridge **204** to regenerate the peritoneal dialysis. Connectors **257**, **258**, and **259** can be used to disinfect the peritoneal dialysate generation flow path **201**.

[00159] FIG. 3 illustrates a detailed flow diagram for regeneration of peritoneal dialysate with an integrated cycler **345**. The initial peritoneal dialysate can be generated with water from water source **302**. Water pump **352** provides a driving force for moving water from water source **302** into the peritoneal dialysate generation flow path **301**. Filter **350** can remove any particulate matter from the water prior to entering the peritoneal dialysate generation flow path **301**. Valve

353 allows for fast priming of the sorbent cartridge **304** and the peritoneal dialysate generation flow path **301**. Check valve **351** prevents back flow of fluid into the water source **302**. System pump **303** provides a driving force for moving fluid through the peritoneal dialysate generation flow path **301**. The water can pass through pressure sensor **354**, which monitors pressure of fluid moving into sorbent cartridge **304**. If the pressure exceeds a defined pressure, the fluid flow rate can be slowed to maintain a maximum pressure. Conductivity sensor **355** measures the conductivity of the incoming fluid. The water passes through valves **356** and **357** and enters sorbent cartridge **304** for purification. Valve **356** can bypass the sorbent cartridge **304** during priming. Valve **357** can also drain fluid to waste reservoir **342** at the start of treatment. Filter **319** removes any particulate matter from the fluid after passing through sorbent cartridge **304**. The fluid is then pumped through valve **320** and degassed in degasser **316**. Degassing pump **317** provides a driving force for moving the fluid through degasser **316**. Pump **318** can pump fluid back into the peritoneal dialysate generation flow path **301**. Although shown as a degasser **316** with a degassing sprayer in FIG. 3, the degasser **316** can be any type of degasser known in the art. Vacuum pump **323** can create a vacuum to remove air from the top of the degassing vessel through valves **332** and **331**. Vent **333** allows the air to escape. After exiting the degassing vessel, the fluid can be heated by inline heater **322** to a desired temperature. The heater **322** can be placed at any location in the flow path prior to delivery to the patient **349**. In any embodiment, the heater **322** can be located after the exit of the sterilization module, particularly if fluid is stored prior to fluid passing through the sterilization module. Temperature sensor **324** can ensure the temperature of the fluid is within a predetermined range.

[00160] To generate the peritoneal dialysate, solutes are added from concentrate sources **305**, **306**, and **307**. As explained, any number of concentrate sources can be used. As illustrated

in FIG. 3, the concentrate sources can include sodium chloride source **307**, ion concentrate source **306**, and osmotic agent source **305**. Concentrate pumps **308** and **309** provide a driving force for pumping concentrates into the peritoneal dialysate generation flow path **301**. Filters **312**, **313**, **314**, and **315** can remove particulate matter from the concentrates prior to entering peritoneal dialysate generation flow path **301**. Valves **310** and **311** control adding concentrates to the peritoneal dialysate generation flow path **301**. Valve **321** can direct the concentrates to a location upstream of sorbent cartridge **304** during priming of the system. Conductivity sensor **325** determines the conductivity of the fluid after addition of sodium chloride and other concentrates. Mixing chamber **326** mixes the concentrates with the fluid in peritoneal dialysate generation flow path **301**. Conductivity sensor **327** determines the conductivity of the generated peritoneal dialysate. Flow meters **328** and **329** determine the flow rate of the fluid after addition of the concentrates. A pH and ammonia sensor **330** determines the pH of the peritoneal dialysate, and can determine the presence of ammonia or ammonium ions that remain in the peritoneal dialysate after passing through the sorbent cartridge **304**. Pressure sensor **334** determines the pressure of the fluid prior to sterilization.

[00161] The generated peritoneal dialysate can be sterilized by pumping the peritoneal dialysate through a sterilization module, shown as two ultrafilters **335** and **337** in FIG. 3. The peritoneal dialysate can be pumped through a first ultrafilter **335**, through three-way valve **337** and then through an optional second ultrafilter **336** and/or an optional UV light source (not shown). Valve **338** is used for back flushing the ultrafilters **335** and **337**. The sterilized peritoneal dialysate can be pumped through valve **343** to the integrated cycler **345**. Pressure sensor **344** ensures the peritoneal dialysate is at a safe pressure for infusion into the peritoneal cavity of the patient **349**. The pump **303** can use any safe pressure for infusing fluid into the

patient **349**. Generally, the pump pressures are on average set at ±10.3 kPa or 77.6 mmHg. If there is no fluid flow, the maximum pressure can increase to ±15.2 kPa or 113.8 mmHg for a short period, such as less than 10 seconds. Three-way valve **346** controls the infusion and drainage of peritoneal dialysate from the patient **349**. In any embodiment, an additional microbial filter (not shown) may be used to sterilize the peritoneal dialysis fluid immediately before the peritoneal dialysate enters the patient **349**. Connector **347** connects to catheter **348** for infusion and drainage of the peritoneal dialysate from the patient **349**. A filter (not shown) can be included between the three-way valve **346** and the catheter **348** for additional cleaning of the peritoneal dialysate. In any embodiment, the filter can be a disposable filter. Treatment, other than the first cycle of the day or night in APD or CAPD, generally begins with drainage of the peritoneal cavity of the patient **349**, prior to infusing the fresh peritoneal dialysate into the patient **349**. Overfill, or excessive solution in the peritoneal cavity beyond the target volume may present complications in therapy. Overfill can be caused by many factors, including failing to fully drain the peritoneal cavity prior to infusion of fresh peritoneal dialysate. In any embodiment, the integrated cycler **345** can start therapy with a drain step to ensure that no peritoneal dialysate remains in the peritoneal cavity. Monitoring both pressure and volume of peritoneal dialysate introduced to the patient **349** can avoid overfill. If the pressure rises to a certain point, the system can be programmed to end filling or send an alert to a user to complete filling of the peritoneal cavity at a desired level. The volume of peritoneal dialysate extracted from and introduced to the patient **349** can also be monitored with flow meters (not shown) to ensure proper volumes of exchanges. Draining the peritoneal cavity can be performed in a similar manner by monitoring the pressure and volume of the drained peritoneal dialysate.

[00162] After a dwell period, the peritoneal dialysate is drained from the patient **349**. The fluid is returned to the peritoneal dialysate generation flow path **301** from the peritoneal cavity of the patient **349**. Drain pump **339** provides a driving force for draining the peritoneal dialysate from the patient **349**. There is no set rate for draining peritoneal dialysate from the peritoneal cavity of the patient **349**, and any flow rate can be used with the integrated cycler **345**. A slow flow is defined as a drain flow rate of less than 50 mL/min for a standard fill, and less than 15 mL/min for a low fill. No flow is defined as a drain flow rate of less than 12 mL/min for a standard fill, and less than 3 mL/min for a low fill. If the detected flow rate of the drained dialysate is below the cutoffs, the system can generate an alarm. With the online generation of fluid described, a flow rate of 300 ml/min can support an exchange time of between 10 and 15 minutes for a full cycle of draining and filling the peritoneal cavity of a patient **349**. The fill/drain cycle can be performed in 10 to 15 minutes with 2 to 3 L of fluid moving in total, half of which is moved into the peritoneal cavity and half of which is moved out of the peritoneal cavity. The peritoneal cavity can be drained with a slight negative pressure of about 50 to 100 mbar created by the drain pump **339**. The drain rate can be up to 300 ml/minute or greater and can vary throughout the session. For example, a drain rate can be high such as at 300 ml/min, and then slow, such as to 100ml/min, as the cavity approaches an empty point. Similarly, a fill rate can be as high as 300 ml/min, and also vary throughout a session. In the case of power failure during treatment, the valves and pumps can be closed to prevent any dialysate flow. If power is returned quickly, the therapy can resume. With a longer power failure, an alert can be generated instructing the patient **349** to manually drain the peritoneal dialysate. In any embodiment, a battery backup can be included in the case of power failure.

[00163] The used peritoneal dialysate is pumped through three-way valve **346** and back into peritoneal dialysate generation flow path **301**. Flow meter **358** determines the amount of fluid removed from the patient **349**, and pressure sensor **359** monitors the draw pressure when removing fluid from the patient **349**. Peritoneal dialysate can be pumped through valve **340** into storage and waste reservoir **341** for storage of the removed fluid prior to starting delivery of regenerated fluid. The storage and waste reservoir **341** can be any size, including between 3-6 L. The remaining used peritoneal dialysate can be pumped through the peritoneal dialysate generation flow path **301**, and back through the sorbent cartridge **304** to regenerate the peritoneal dialysis. Connectors **360**, **361**, and **362** are used to disinfect the peritoneal dialysate generation flow path **301**.

[00164] For automated disinfection of the system, connector **347** can be connected to connector **360** to form a flow loop. Disinfectant can be circulated through the flow loop and heated. The disinfectant can be heated to any temperature capable of disinfecting the system, including temperatures of 90 °C or greater. The disinfectant can be introduced to the flow loop and recirculated at elevated temperatures to ensure complete disinfection. The disinfectant used can be any suitable disinfectant known in the art, including peracetic acid, citric acid, or bleach. The connectors and components of the system can be gamma and autoclave compatible to resist the high temperatures used during disinfection. The system can be primed by introducing a priming fluid to the peritoneal dialysate generation flow path **301** and integrated cycler **345**.

[00165] By generating and immediately using the peritoneal dialysate, the dialysate storage time can be reduced, reducing the possibility of bacterial growth. A user interface can be included on the peritoneal dialysis generation system in communication with the control system, allowing a patient **349** to direct the generation of peritoneal dialysate at a selected time as needed

at a selected time. Additionally, or alternatively, the peritoneal dialysate machine can include a timer, and the timer can cause the peritoneal dialysate machine to generate peritoneal dialysate at predetermined times according to the patient's **349** peritoneal dialysis schedule. Alternatively, the peritoneal dialysate generation machine can be equipped with wireless communication, such as Wi-Fi, Bluetooth, Ethernet, or any other wireless communication system known in the art to meet patient or clinic needs. The user can direct the peritoneal dialysis machine to generate peritoneal dialysate at a specified time from any location. By using a timer, user interface, or wireless communication to control the generation of peritoneal dialysate on demand, the peritoneal dialysate storage time can be reduced, lowering the chances of generating significant amounts of degradation products or allowing bacterial growth.

[00166] The peritoneal dialysate can be generated and used in real time, with direct infusion of the peritoneal dialysate into the patient through an integrated cycler. Alternatively, the peritoneal dialysate can be generated and stored prior to use with a non-integrated cycler. For real time generation and use of the peritoneal dialysate, the flow rate of fluid through the peritoneal dialysate generation flow path can be between 50 and 300 ml/min. If a dialysate storage container is used to store generated peritoneal dialysate, the flow rate of fluid through the peritoneal dialysate generation flow path can be any rate. The integrated or non-integrated cycler and the rest of the system can communicate for the purposes of generation and use of the peritoneal dialysate by any method known in the art, including Bluetooth, Wi-Fi, Ethernet, or direct hardware connections. Additional valves and regulators (not shown in FIG. 3) can be included to aid in connection and operation of the peritoneal dialysate generation flow path and an integrated or non-integrated cycler. The integrated or non-integrated cycler and the peritoneal

dialysate generation flow path can communicate directly, or can each communicate with a control system for control over the generation, regeneration, and use of the peritoneal dialysate.

[00167] In any embodiment of the first or second aspects of the invention, solutes can be added to a peritoneal dialysate generation flow path **401** from two or more separate concentrate sources, as shown in FIG. 4. The peritoneal dialysate generation flow path **401** can be fluidly connected to a water source and a peritoneal dialysate regeneration module upstream of the concentrate sources **402-406**, and fluidly connected to a sterilization module, an optional integrated cycler, and optionally a dialysate container downstream of the concentrate sources **402-406**, as illustrated in FIG.'s 1-3. For clarity, the components have been omitted from FIG. 4.

[00168] As illustrated in FIG. 4, the concentrate source can include one or more ion concentrate sources, such as sodium chloride source **402** containing sodium chloride to be added in a controlled addition to the peritoneal dialysate generation flow path **401** by concentrate pump **407** through valve **412**, sodium lactate source **403** containing sodium lactate to be added in a controlled addition to the peritoneal dialysate generation flow path **401** by concentrate pump **408** through valve **413**, magnesium chloride source **404** containing magnesium chloride to be added in a controlled addition to the peritoneal dialysate generation flow path **401** by concentrate pump **409** through valve **414**, and calcium chloride source **405** containing calcium chloride to be added in a controlled addition to the peritoneal dialysate generation flow path **401** by concentrate pump **410** through valve **415**. One of skill in the art will understand other ions can be used in formulation of peritoneal dialysate, and each can be contained in a separate ion concentrate source or combined into one or more combined ion concentrate sources. The concentrate source also includes one or more osmotic agent sources, such as dextrose source **406** containing dextrose to be added to the peritoneal dialysate generation flow path **401** by concentrate pump

411 through valve **416**. Any of the concentrate pumps **407-411** can include flow meters to control the addition of the solutes. A glucose source and/or an icodextrin source can be used in addition to, or in place of, dextrose source **406**. Multiple osmotic agents can be added to the peritoneal dialysate generation flow path **401** from one or more osmotic agent sources. One of skill in the art will understand other solutes can be used alternatively to, or in addition to, the solutes illustrated in FIG. 4. Any set of solutes used for peritoneal dialysate is within the scope of the invention. A control system in electronic communication with each of the concentrate pumps **407-411** can control the movement of fluid from the concentrate sources **402-406** to the peritoneal dialysate generation flow path **401**. The amount of each of the concentrates moved into the peritoneal dialysate generation flow path **401** can be controlled to result in peritoneal dialysate having a prescribed solute concentration, as determined by a doctor or health care provider. The valves **412-416** can optionally be replaced with hose T junctions with additional components for preventing backflow into the concentrate source line if that particular line is not being used. A hose T is a fluid connector in a T-shape, with a port at each end for fluid to enter or exit the hose T. Optional sensors **417**, **418**, **419**, and **420** ensure the solute concentration in the dialysate is at the correct level after each addition. The sensors **417-420** can be any type of sensor appropriate to confirm delivery of the concentrate, such as conductivity sensors. Optional pH sensor **421** ensures the pH is a proper level after addition of sodium lactate or other buffer. Optional refractive index meter **422** ensures the dextrose concentration in the dialysate is at the prescribed level. An additional sensor (not shown)can be included upstream of sodium chloride source **402** for sensing the conductivity of the water prior to addition of concentrates. One of skill in the art will understand that additional sensor arrangements can be used in the described system. Any number of sensors can be included to monitor the peritoneal dialysate

concentration, including 1, 2, 3, 4, 5, 6, 7, or more sensors. The concentrate sources can contain the solutes in either solid, powdered, or solution form. A solid or powdered source of solutes can be dissolved by the system by drawing fluid from the peritoneal dialysate generation flow path **401** into the concentrate source to generate a solution with a known concentration, such as a saturated solution of the solutes. The resulting solution is added to the peritoneal dialysate generation flow path as explained.

[00169] Although shown as a refractive index meter **422** in FIG. 4, one of skill in the art will understand that alternative methods of measuring the osmotic agent concentration can be used. In any embodiment, enzyme-based sensors can detect the concentration of the osmotic agent in the dialysate. Enzyme based sensors use an enzyme capable of oxidizing the osmotic agent, such as glucose or dextrose. The enzyme is immobilized on an electrode and covered in a membrane through which the osmotic agent can pass. The electrode is used to electrochemically measure the change in either the oxidant, such as oxygen, or the product of glucose oxidation, such as hydrogen peroxide. Alternatively, electron transfer between the electrode and the enzyme can be detected with mediators, such as ferrocene to facilitate electron transfer. The osmotic agents can alternatively be detected through pulsed amperometric detection (PAD). PAD can detect glucose by applying a positive potential to a sample, resulting in oxidation of the glucose. The oxidation products are adsorbed onto the electrode and then desorbed by applying a more positive potential. Applying the more positive potential results in formation of an oxide layer on the electrode leading to passivation of the electrode surface. The catalytic activity of the electrode is then restored by application of a more negative potential, resulting in dissolution of the oxide layer.

[00170] Although illustrated as a single concentrate source in FIG. 1, three concentrate sources in FIG.'s 2-3, and five separate concentrate sources in FIG. 4, one of skill in the art will understand that any number of concentrate sources can generate the peritoneal dialysate, including 1, 2, 3, 4, 5, 6, 7, or more concentrate sources. Any two or more of the separate concentrate sources illustrated in FIG. 4 can be combined into a single solute source, such as by combining all or some of the ion concentrate sources into a single ion concentrate source where the mixed contents do not cause precipitation of the mixed concentrates.

[00171] Although each concentrate source is illustrated in FIG. 4 with a separate concentrate pump and fluid line, one of skill in the art will understand that more than one concentrate source can use a single pump and fluid line, with valves arranged thereon for controlled addition to the peritoneal dialysate generation flow path **401**.

[00172] The concentrate sources **402-406** can be single use concentrate sources or disposable concentrate sources. The disposable concentrate sources are used in a single peritoneal dialysate generation process and then disposed. Multiple use concentrate sources are used repeatedly, and refilled as necessary with the solute.

[00173] Table 6 provides exemplary, non-limiting, ranges of solutes that can be added to the peritoneal dialysate using a separate osmotic agent source, glucose in Table 6, and a separate ion concentrate source containing sodium chloride, sodium lactate, magnesium chloride, calcium chloride and sodium bicarbonate. Because the glucose is added separately from the ion concentrates, the ratio of glucose to the other solutes can be varied depending on the needs of the patient.

Table 6

Exemplary ranges of solutes in a two-concentrate source system

Component	Concentration (g/l)	Solution volume (ml/L)	Dialysate composition
Part A			
Glucose	850	6 - 53	0.55-4.5 g/dL
Part B			
NaCl	269	20	92 mmol/L
Sodium Lactate	84	20	15 mmol/L
$MgCl_2.6H_2O$	5	20	0.5 mmol/L
$CaCl_2.2H_2O$	18	20	2.5 mmol/L
$NaHCO_3$	105	20	25 mmol/L
Water		927-979	56.10

[00174] By using multiple concentrate sources, greater individualization and therapy customization can be achieved for each patient. With a single concentrate source, all solutes in the generated peritoneal dialysate must be present in a fixed ratio. By using more than one concentrate source, the ratio of solutes used in the peritoneal dialysate can be altered as the concentration of each of the osmotic agent and ion solutes can be individually controlled. For example, as illustrated by Table 6, with a single ion concentrate source and a single osmotic agent source, peritoneal dialysate with greater or less osmotic agent per concentration of ions can be generated, providing the ability to adjust the tonicity of the peritoneal dialysate solution independently of the electrolyte composition to meet the UF needs of any patient with a single set of solutions and allowing greater control over ultrafiltration. The ultrafiltration rate that results from using the peritoneal dialysate solutions can be altered by altering the concentration of the osmotic agent independently of the ionic solutes, or by changing the osmotic agent used. For example, typical ultrafiltration volumes using dextrose as the osmotic agent vary with the dextrose concentration of the peritoneal dialysate. With a 1.5% dextrose solution, the typical ultrafiltration volume is about 150 mL. With a 2.5 % dextrose solution, the typical ultrafiltration

volume is about 250 mL. With a 4.25% dextrose solution, the typical ultrafiltration volume can exceed 600 mL. For a single exchange using separate concentrate sources for the ion concentrates and the osmotic agent, about 50 mL of the ion concentrate and 150 mL of the osmotic agent may be needed, corresponding to about 200 ml/day or 1.4 L/week of the ion concentrate and 600 ml/day or 4.2 L/week of the osmotic agent.

[00175] Because the system is not limited to discrete glucose or other osmotic agent concentrations like known commercial solutions; the system can customize the peritoneal dialysate solutions to meet the ultrafiltration needs of patient as determined by a healthcare provider. As illustrated in Table 6, the glucose level in the peritoneal dialysate solution can be varied from 0.55 g/dL to 4.5 g/dL, while maintaining the electrolytes and buffer components constant, allowing the system to cover the range of glucose formulations currently offered commercially using a single Part A and Part B composition.

[00176] In any embodiment of the first or second aspects of the invention, two osmotic agent sources can be used, such as a dextrose source and an icodextrin source. With two osmotic agent sources, one could use dextrose during the daytime exchanges for CAPD and icodextrin during the night dwell to take advantage of the higher UF removal from icodextrin. Conversely, dextrose could be used during the night dwell and icodextrin for the extended daytime dwell in APD systems.

[00177] By using separate concentrate sources for each solute, complete individualization of the concentrations and ratios of solutes in the peritoneal dialysate can be achieved. Table 7 provides exemplary ranges of solutes that can be used in peritoneal dialysate as made by a system with each solute in a separate concentrate source. An advantage of using separate concentrate sources for each solute is that virtually any peritoneal dialysate solution composition

can be prepared from a single set of component formulations. A system with separate concentrate sources for each solute is useful for patients whose prescriptions change periodically due to diet or other factors. Such patients would need to store multiple formulations if using only one or two concentrate sources, and the risk of errors would be increased.

Table 7

Exemplary dialysate composition from a multi-source system

Component	Concentration (g/l)	Solution volume (ml/L)	Dialysate composition
Part A: Glucose	850	6 – 53	0.55-4.5 g/dL
Part B: NaCl	320	15-18	132-134 mmol/L
Part C: Na Lactate	1000	2-4	15-40 mmol/L
Part D: MgCl2.6H2O	500	0.2-0.4	0.5 -1.0 mmol/L
Part E: CaCl2.2H2O	700	0.5-1.0	2.5-3.5 mmol/L
Part F: NaHCO3	85	0-34	0-34 mmol/L
Part G: Icodextrin	1000	0-75	0-7.5 g/dL
Water		820-971	

[00178] In any embodiment, the one or more concentrate sources can be detachable from the rest of the system for sterilization. The concentrate sources can also be sterilized each time the concentrate sources are filled with new concentrate solutions. Further, the concentrate sources can be sterilized after a set number of uses, or after a set period of time. Moreover, the concentrate sources and the rest of the peritoneal dialysate generation system can be sterilized without any of the components by passing a disinfection solution, such as a citric acid, peracetic acid, or bleach solution, through all of the lines and containers of the system. Disinfectant can be circulated through the peritoneal dialysate generation system and heated. The disinfectant can be heated to any temperature capable of disinfecting the system, including temperatures of at least

90 °C or greater. The disinfectant can be introduced to the peritoneal dialysate generation system and recirculated at elevated temperatures, as needed, to ensure complete disinfection.

[00179] FIG. 5 illustrates an overview of generating peritoneal dialysate in accordance with any embodiment of the first or second aspects of the invention. Fluid from a source **501** can be purified by a peritoneal dialysate regeneration module **502**, as explained. Concentrates from a single concentrate source **503**, which can contain both ion concentrates and one or more osmotic agents, can be added to the purified water to generate a non-sterile peritoneal dialysate solution **504**. The non-sterile peritoneal dialysate solution **504** is sterilized by a sterilization module **505**, which may include an ultrafilter. As explained, the peritoneal dialysate can be further purified by additional components in the sterilization module **506**, such as by ultrafiltration with a second ultrafilter, by a microbial filter, or by a UV light source, to generate a sterilized peritoneal dialysate **507**. The sterilized peritoneal dialysate **507** can be stored or used by any method described herein, including by immediately infusing the peritoneal dialysate into a patient **508** with an integrated cycler, or dispensing the peritoneal dialysate into a dialysate container for later use in peritoneal dialysis **509**, with either an integrated or non-integrated cycler. Regardless of the method of using the generated peritoneal dialysate, the spent peritoneal dialysate can be returned to the peritoneal dialysate generation flow path for regeneration and reuse.

[00180] FIG. 6 illustrates an overview of generating peritoneal dialysate with multiple concentrate sources. Fluid from a source **601** can be purified by a peritoneal dialysate regeneration module **602**, as explained. Concentrates from an ion concentrate source **603**, which can contain sodium, magnesium, calcium, and bicarbonate, as well as any other ions to be used in peritoneal dialysis, can be added to the purified fluid. An osmotic agent, such as dextrose, can

be added from a first osmotic agent concentrate source **604**. A second osmotic agent, such as icodextrin, can be added from a second osmotic agent concentrate source **605**. As illustrated in FIG. 4, any number of concentrate sources can be used for further individualization of the peritoneal dialysate, including separate sources for each of the ions used. After addition of the ion and osmotic agent concentrates, the fluid contains all necessary components for use in peritoneal dialysis as non-sterilized peritoneal dialysate **606**. The non-sterilized peritoneal dialysate solution **606** can be sterilized by a sterilization module **607**, which can include an ultrafilter or other sterilization components. The peritoneal dialysate can be further sterilized by the sterilization module **608**, either by ultrafiltration with a second ultrafilter, a microbial filter, or further sterilized with a UV light source, to generate a sterilized peritoneal dialysate **609**. The sterilized peritoneal dialysate **609** can be stored or used by any method described herein, including by immediately infusing the peritoneal dialysate into a patient with an integrated cycler **610**, or dispensing the peritoneal dialysate into a dialysate container for later use in peritoneal dialysis with either an integrated or non-integrated cycler **611**.

[00181] FIG.'s 7A-7B illustrate a non-limiting embodiment of a peritoneal dialysate generation cabinet **701**. FIG. 7A illustrates a perspective view of the peritoneal dialysate generation cabinet **701**, while FIG. 7B illustrates a front view of the peritoneal dialysate generation cabinet **701**. A fluid line **702** can connect a water source (not shown) to the peritoneal dialysate generation cabinet **701**. System pump **707** provides a driving force for the movement of fluid throughout the peritoneal dialysate generation flow path, as described with reference to FIG.'s 1-3. The water, or used peritoneal dialysate from a previous session, is pumped through the peritoneal dialysate generation cabinet **701** to a peritoneal dialysate regeneration module, shown as sorbent cartridge **704** in FIG.'s 7A-B. The fluid enters the

sorbent cartridge **704** through tubing (not shown) connected to the bottom of the sorbent cartridge **704** through the base of the peritoneal dialysate generation cabinet **701** and exits through tubing **715** at a top of the sorbent cartridge **704**. Concentrates from concentrate source **705** are added to the fluid through tubing **714** as described to generate non-sterilized peritoneal dialysate. A concentrate pump (not shown) can provide a driving force to move fluid from the concentrate source **705** into the peritoneal dialysate generation flow path inside of the cabinet. As described, more than one concentrate source can be used. The generated peritoneal dialysate is then pumped through a sterilization module, shown as ultrafilter **706**, for sterilization. The peritoneal dialysate enters the ultrafilter **706** through tubing **716** in a base of the ultrafilter **706** and exits through tubing **717** at a top of the ultrafilter **706**. A second ultrafilter, microbial filter, and/or UV light source (not shown in FIG. 7) can also be included. The peritoneal dialysate is then heated by a heater (not shown in FIG. 7) and pumped into the peritoneal cavity of a patient through infusion line **708** by metering pump **703**. Alternatively, infusion line **708** can be connected to any non-integrated cycler. After a dwell period, the peritoneal dialysate is drained from the patient through drain line **709** and back into the peritoneal dialysate generation flow path for regeneration. The patient tubing connected to infusion line **708** and drain line **709** can be a consumable or disposable patient tubing set, which can be replaced after each use. As described, the peritoneal dialysate generation flow path can include various sensors (not shown) for detection of conductivity, pH, refractive index, temperature, or other dialysate parameters. The sensors can be included either inside or outside of the body of the peritoneal dialysate generation cabinet **701**. The fluid lines and valves connecting the components of the peritoneal dialysate generation flow path can likewise be positioned inside of the cabinet body. As described, peritoneal dialysate generation cabinet **701** can have a graphical user interface

including screen **713** and keyboard **712**. Messages from the control system to the user, or from the user to the control system, can be generated and read through the graphical user interface. The user can direct the generation of peritoneal dialysate through keyboard **712**, and can receive messages from the system through screen **713**. The system can generate alerts to the user, including any problems detected by any of the sensors, as well as the progress of peritoneal dialysate generation. Any type of user interface can be used in place of the keyboard **712** and screen **713** in FIG.'s 7A-B. Alternatively, other interfaces can be included, such as lights, dials, buttons, switches or the like. In any embodiment, a single button can be used for directing the generation of peritoneal dialysate in place of the keyboard **712**. In any embodiment, either keyboard **712** or screen **713** can be used alone, as with a single touch screen for both data entry and display to enable simple operation. Although shown on table **718**, the peritoneal dialysate generation cabinet **701** can be used on any stable flat surface.

[00182] FIG. 8 illustrates the peritoneal dialysate generation cabinet **801** after being closed. If not in use, the concentrate source, the sorbent cartridge, and the tubing to and from the patient or non-integrated cycler (not shown in FIG. 8) can be removed, and the doors **802** and **803** of the peritoneal dialysate generation cabinet **801** can be closed to minimize storage space. Additionally, the screen **804** of the graphical user interface, as illustrated in FIG.'s 7A and 7B, can be folded down into the top of the peritoneal dialysate generation cabinet **801**, further minimizing storage space. The doors **802** and **803** can be open and closed by any method known in the art, including magnets, handles, indentations, hooks, or any other method of opening and closing the doors **802** and **803**. The peritoneal dialysate generation cabinet **801** can have a small size and portability optimized for in-home or beside use. Although shown on table **805**, the peritoneal dialysate generation cabinet **801** can be used on any stable flat surface.

[00183] FIG.'s 9A-D illustrate a non-limiting embodiment of the peritoneal dialysate generation system arranged as a peritoneal dialysate generation cabinet **901**. FIG. 9A illustrates a perspective view of the peritoneal dialysate generation cabinet **901**, FIG. 9B illustrates a front view of the peritoneal dialysate generation cabinet **901**, FIG. 9C illustrates a side view of the peritoneal dialysate generation cabinet **901**, and FIG. 9D illustrates a back view of the peritoneal dialysate generation cabinet **901**.

[00184] A fluid line **905** can connect a water source **904** to the peritoneal dialysate generation cabinet **901**. The fluid line **905** can enter through a connector **928** in a top **906** of the water source **904**. The fluid line **905** connects to the peritoneal dialysate generation flow path as described with reference to FIG.'s 1 and 5-6 through a back of the peritoneal dialysate generation cabinet **901** through connector **932** having a fitting **933** for holding the fluid line **905**, as illustrated in FIG. 9D. Any of the fluid lines illustrated can be disconnected and removed from the system for cleaning and replacement. A pump (not shown) can provide a driving force for the movement of fluid throughout the peritoneal dialysate generation flow path if required. Water is pumped through the peritoneal dialysate generation cabinet **901** to a water purification module, shown as sorbent cartridge **912** in FIG.'s 9A-B. The water can enter the sorbent cartridge **912** through tubing (not shown) connected to the bottom of the sorbent cartridge **912** within the peritoneal dialysate generation cabinet **901**. The water exits the sorbent cartridge **912** through connector **913** and tubing **914**. An osmotic agent from osmotic agent source **915** and an ion concentrate from an ion concentrate source **917** are added to the fluid as described to generate non-sterilized peritoneal dialysate. The osmotic agent concentrate is added to the fluid through paddle connector **916**. The ion concentrate is added to the fluid through paddle connector **918**. A concentrate pump (not shown) can provide a driving force to move fluid from

the concentrate sources **915** and **917** into the peritoneal dialysate generation flow path inside of the peritoneal dialysate generation cabinet **901**. As described, the system can use a single ion concentrate source in place of the two sources shown in FIG.'s 9A-B, or more than two concentrate sources. The generated peritoneal dialysate can then be pumped through a sterilization module (not shown), such as an ultrafilter. A second ultrafilter and/or a UV light source can also be included. An integrated cycler (not shown in FIG.'s 9A-D) can then pump the dialysate into infusion line **919** through connector **920** and into the patient. Fitting **925** allows the infusion line **919** to be removed from the system for cleaning or replacement. Waste fluids can be pumped out of the system through waste line **907**, which connects to the peritoneal dialysate generation cabinet **901** through connector **930** having fitting **931**. A separate drain line for returning used dialysate from the patient (not shown in FIG.'s 9A-D) can also connect to the peritoneal dialysate generation cabinet **901** for regeneration of the used dialysate. A waste line **907** disposing of waste fluids enters waste container **908** through a connector **929** in the top **909** of the waste container **908**. Handles **910** and **911** can be included on water source **904** and waste container **908** for easy movement and storage. Although the peritoneal dialysate generation cabinet **901** is illustrated on top of table **926** in FIG.'s 9A-D, the peritoneal dialysate generation cabinet **901** can be used on any stable flat surface.

[00185] As described, the peritoneal dialysate generation flow path can include various sensors for detection of conductivity, pH, refractive index, or other dialysate parameters. The sensors can be included either inside or outside of the body of the peritoneal dialysate generation cabinet **901**. The fluid lines and valves connecting the components of the peritoneal dialysate generation flow path can likewise be positioned inside of the cabinet body. As described, a top of the peritoneal dialysate generation cabinet **901** can have a graphical user interface **902**

including screen **903**. Messages from the control system to the user, or from the user to the control system, can be generated and read through the graphical user interface **902**. The user can direct the generation of peritoneal dialysate through the graphical user interface **902**, and can receive messages from the system through screen **903**. The system can generate alerts to the user, including any problems detected by any of the sensors, as well as the progress of peritoneal dialysate generation. A handle **924** can be included for opening the peritoneal dialysate generation cabinet **901** to allow access to components on the inside of the cabinet. Handles **921** and **923** can be included to hold the fluid lines and power cord when not in use.

[00186] Disinfection connector **922** illustrated in FIG.'s 9A and 9C can be included for disinfection of the waste line **907**. During disinfection, the waste line **907** can be disconnected from waste container **908** and connected to disinfection connector **922**. Disinfectant solution from a disinfectant source (not shown in FIG.'s 9A-D) can then be circulated through the waste line **907** to disinfect the waste line **907**. Disinfection connector **927** can be included for disinfection of fluid line **905**. Fluid line **905** can be connected to disinfection connector **922** and disinfection solution can be circulated through the fluid line **905**. Drain **934** on water source **904** and drain **935** on waste container **908**, allow the water source **904** and waste container **908** to be drained without inverting the containers.

[00187] FIG. 10 illustrates a peritoneal dialysate generation cabinet **1001** using a non-purified water source, faucet **1005** in sink **1004**. Although illustrated as faucet **1005** and sink **1004**, one of ordinary skill in the art will understand that any water source can be used. The ability to use municipal or other non-purified sources of water allow the peritoneal dialysate generation system to work at a patient's home without the need to store large amounts of purified water or dialysate. Fitting **1006** connects the water line **1007** to the faucet **1005** or other water

source, allowing the water line **1007** to be connected or disconnected as necessary. A pump (not shown) can provide a driving force for the movement of fluid throughout the peritoneal dialysate generation flow path as described with respect to FIG.'s 1 and 5-6. The water is pumped through the peritoneal dialysate generation cabinet **1001** to a water purification module, shown as sorbent cartridge **1011** in FIG. 10. The water enters the sorbent cartridge **1011** through tubing (not shown) connected to the bottom of the sorbent cartridge **1011** within the peritoneal dialysate generation cabinet **1001**. The water exits the sorbent cartridge **1011** through connector **1026** and tubing **1012**. An osmotic agent from osmotic agent source **1013** and an ion concentrate from an ion concentrate source **1014** are added to the fluid as described to generate non-sterilized peritoneal dialysate. The osmotic agent concentrate is added to the fluid through paddle connector **1016**. The ion concentrate is added to the fluid through paddle connector **1015**. A concentrate pump (not shown) can provide a driving force to move fluid from the concentrate sources **1013** and **1014** into the peritoneal dialysate generation flow path inside of the peritoneal dialysate generation cabinet **1001**. As described, the system can use a single ion concentrate source in place of the two sources shown in FIG. 10, or more than two concentrate sources. The generated peritoneal dialysate can then be pumped through a sterilization module (not shown), such as an ultrafilter. A second ultrafilter and/or a UV light source can also be included. An integrated cycler (not shown in FIG. 10) can then pump the dialysate into infusion line **1017** through connector **1018** and into the patient. Fitting **1019** allows the infusion line **1017** to be removed from the system for cleaning or replacement. Waste fluids can be pumped out of the system through waste line **1008**, which can connect to a drain **1009** shown in bathtub **1010**. A separate drain line (not shown) from the patient can be included to return used dialysate to the peritoneal dialysate generation cabinet **1001** for regeneration. Waste fluids can be disposed of in

drain **1009**. Although shown as a bathtub drain **1009** in FIG. 10, the waste fluids can be conveyed to any type of drain, or alternatively to a waste container as illustrated in FIG.'s 9A-D. Although the peritoneal dialysate generation cabinet **1001** is illustrated on top of table **1024** in FIG. 10, the peritoneal dialysate generation cabinet **1001** can be used on any stable flat surface. In certain embodiments, the peritoneal dialysate generation cabinet **1001** and the patient can be in the same room as the water source and drain **1009**. Alternatively, the patient and/or peritoneal dialysate generation cabinet **1001** can be in a separate room, with tubing long enough to reach patient. For longer distances, the tubing should be strong enough to withstand the pressures necessary in pumping fluid over longer distances.

[00188] As described, a top of the peritoneal dialysate generation cabinet **1001** can have a graphical user interface **1002** including screen **1003**. Messages from the control system to the user, or from the user to the control system, can be generated and read through the graphical user interface **1002**. The user can direct the generation of peritoneal dialysate through the graphical user interface **1002**, and can receive messages from the system through screen **1003**. The system can generate alerts to the user, including any problems detected by any of the sensors, as well as the progress of peritoneal dialysate generation. A handle **1020** can be included for opening the peritoneal dialysate generation cabinet **1001** to allow access to components on the inside of the cabinet. Handles **1021** and **1023** can be included to hold the fluid lines and power cord when not in use.

[00189] Disinfection connector **1022** can be included for disinfection of the waste line **1008**. During disinfection, the waste line **1008** can be disconnected from the drain **1009** and connected to disinfection connector **1022**. Disinfectant solution from a disinfectant source (not shown in FIG. 10) can then be circulated through the waste line **1008** to disinfect the waste line

1008. Disinfection connector **1025** can be included for disinfection of water line **1007**. The water line **1007** can be disconnected from faucet **1005** and connected to disinfection connector **1025**. Disinfectant solution can be circulate through the water line **1007** for disinfection.

[00190] In any embodiment of the first or second aspects of the invention, the solute sources included in the dialysate generation module can be provided in a dialysis caddy. A dialysis caddy is a container adapted to contain one or more other containers, each having one or more solute sources. One non-limiting example of a dialysis caddy is shown in FIG. 11. The dialysis caddy **1101** can contain some or all of the solute sources necessary for peritoneal dialysis. In any embodiment of the first or second aspects of the invention, the dialysis caddy **1101** can contain an ion concentrate source **1103**, osmotic agent source **1104**, and sodium chloride source **1105**. As explained, the ion concentrate source **1103** can contain any one or more of ion concentrates, such as magnesium chloride, calcium chloride or potassium chloride, or any other solutes used in peritoneal dialysis. Osmotic agent source **1104** can contain one or more osmotic agents, such as glucose, dextrose, or icodextrin. One of skill in the art will understand that any of the solutes can be contained in separate sources, and that the dialysis caddy **1101** can be adapted for any number of concentrate sources. In use, the dialysis caddy **1101** can be placed in a receiving slot of a dialysis system **1102**. As shown in FIG. 11, the dialysis caddy **1101** can be configured so each of the ion concentrate source **1103**, osmotic agent source **1104**, and sodium chloride source **1105** are aligned with connectors for connection to the peritoneal dialysate generation flow path, such as the connectors on paddle assemblies **1113** and **1114**. In any embodiment of the first or second aspect of the invention, the dialysis caddy **1101** can also contain a disinfectant source **1106**, which may contain a disinfectant, such as citric acid. To disinfect the system, the dialysis caddy **1101** can be turned so container connectors **1110** and

1111 on the disinfectant source **1106** can connect to the connectors on paddle assemblies **1113** and **1114**.

[00191] If the dialysis caddy **1101** is configured to generate peritoneal dialysate, container connector **1107** on ion concentrate source **1103** and container connector **1108** on osmotic agent source **1104** can connect to caddy connectors **1115** on paddle assembly **1113** and caddy connector **1116** on paddle assembly **1114**. Container connector **1109** on sodium chloride source **1105** can also connect to a caddy connector (not shown in FIG. 11). The paddles can form a part of paddle assembly **1112**. To connect the sources to the paddles, the paddles can be rotated downward on hinge **1117** and the caddy connectors **1115** and **1116** can connect to ion concentrate source **1103** and osmotic agent source **1104** respectively. In any embodiment of the first or second aspects of the invention, as shown in FIG. 11, the dialysis caddy **1101** and the sources within the caddy have one or more fitting feature to ensure the sources are connected to the correct paddle. The fitting features can also have the additional benefit of ensuring a tight fit within the dialysis caddy **1101**, and resist inadvertent movement. The one or more fitting features can ensure each source occupies a unique position within the dialysis caddy **1101**. Moreover, in any embodiment, the interior of the dialysis caddy **1101** can itself be a shaped fitting feature so each source can only be placed within a specific position or receiving compartment within the dialysis caddy **1101**. In any embodiment of the first or second aspects of the invention, fitting features can be included on any connection surface of the caddy, where any source contacts the interior of the caddy. The shape of a caddy surface can include fitting feature protrusion **1120**, which is a protrusion on the base of the dialysis caddy **1101**. The base of sodium chloride source **1105** can be designed with a corresponding complementary indentation, such as a similarly sized recess, while the other sources lack a complimentary

indentation. Sodium chloride source **1105** will be the only source that can properly fit into the position in the caddy above the fitting feature of protrusion **1120**. Similarly, fitting feature protrusion **1122** is a protrusion in the side of the dialysis caddy **1101** interior. The protrusion **1122** separates the sidewall of the dialysis caddy **1101** interior into two sections. Osmotic agent source **1104** can be the only source with the proper size, shape, or geometry to fit within one of the sections on the sidewall, whereas sodium chloride source **1105** can be the only source with the proper size, shape, or geometry to fit within the other section. Each concentrate source can be positioned in one particular location within the dialysis caddy **1101**. In any embodiment, the concentrate sources themselves can have fitting features to ensure the proper arrangement of the concentrate sources within the dialysis caddy **1101**. In FIG. 11 disinfectant (e.g. citric acid) source **1106** includes flange **1118**. Ion concentrate source **1103** has a corresponding slot. The disinfectant (e.g. citric acid) source **1106** can only be placed within the dialysis caddy **1101** at the precise position above ion concentrate source **1103**. By sizing and shaping the interior of the cavity and the concentrate sources, the concentrate sources can only be placed within the dialysis caddy **1101** in a single arrangement. If the dialysis caddy **1101** is attached to the rest of the dialysis system **1102**, the concentrate sources and connectors line up with the proper paddles for connection to the dialysis system, ensuring the proper solutes from the concentrate sources enter the dialysate flow path at the correct locations. The alignment also ensures the proper pumps and valves are controlling the correct solute additions. In any embodiment of the first or second aspects of the invention, handle **1121** can be included for easy of carrying and removal of the dialysis caddy **1101** from the dialysis system **1102**. During use, fluid lines, such as line **1119** in disinfectant (*e.g.* citric acid) source **1106**, can move fluids from the concentrate sources into the paddles.

[00192] Alternatively, any method of loading the peritoneal dialysate concentrates can be included in the described systems. For example, the peritoneal dialysate concentrates can be added using a disposable cassette. The disposable cassette can be multi-use or single-use with disposal of the cassette after therapy.

[00193] The connectors can include connectors for connection to reservoirs, containers, or a tap or faucet. The connectors can be any type of connector that can form a seal with a container, tap, or faucet that serve as the fluid sources in the system. The connectors can be screw-type connectors that screw onto the containers, faucet or tap, snap-type connectors that snap onto the containers, faucet, or tap, or any other type of connector known in the art. O-rings or other sealing members can be included in the connectors to form a water-tight seal with the containers, faucet, or tap.

[00194] For connection to a tap or faucet, the connectors should be able to form a seal with standard at-home faucets. The connectors can include an adjustable bore, wherein the size of the opening of the connector for connection to the tap or faucet can be increased or decreased to adjust to different size faucets. Nuts, screws, or other tightenable components can be included on the sides of the connectors allowing a user to tighten the connector around the faucet or tap regardless of the circumference of the faucet or tap. An o-ring or other sealing member can be placed on the faucet or tap to increase the effectiveness of the seal formed with the connectors.

[00195] Alternatively, a fitting can be screwed onto, or otherwise affixed to the faucet with a male end of the fitting extending outwardly from the faucet. The male end of the fitting can be inserted into the water line, and secured with an adjustable bolt, wire, or other tightening mechanism to ensure a proper seal.

[00196] For connection to a drain as illustrated in FIG. 9, the tubing for carrying waste fluids can simply be placed into the drain, bathtub, or other receptacle containing a drain for disposal. Alternatively, the tubing can include a connector for forming a sealable connection to a drain, ensuring that all waste fluids are directed into the drain.

[00197] One skilled in the art will understand that various combinations and/or modifications and variations can be made in the described systems and methods depending upon the specific needs for operation. Moreover, features illustrated or described as being part of an aspect of the invention may be used in the aspect of the invention, either alone or in combination, or follow a preferred arrangement of one or more of the described elements.

We claim:

1. A system, comprising:

a water source;

a peritoneal dialysate generation flow path; wherein the peritoneal dialysate generation flow path is fluidly connectable to the water source;

one or more peritoneal dialysate regeneration modules fluidly connectable to the peritoneal dialysate generation flow path;

a concentrate source fluidly connectable to the peritoneal dialysate generation flow path; the concentrate source containing one or more solutes; and

a sterilization module fluidly connectable to the peritoneal dialysate generation flow path.

2. The system of claim 1, wherein the peritoneal dialysate generation flow path comprises connectors for connection to a cycler.

3. The system of claim 1, further comprising an integrated cycler; the integrated cycler comprising a pump, an infusion line, and a drain line; wherein the infusion line is fluidly connected to the peritoneal dialysate generation flow path downstream of the sterilization module; and wherein the drain line is fluidly connected to the peritoneal dialysate generation flow path upstream of the peritoneal dialysate regeneration module.

4. The system of claim 1, further comprising one or more dialysate containers fluidly connectable to the peritoneal dialysate generation flow path downstream of the sterilization module.

5. The system of claim 1, wherein the concentrate source comprises one or more of an osmotic agent and an ion concentrate.

6. The system of claim 1, wherein the concentrate source comprises at least an osmotic agent source and an ion concentrate source.

7. The system of claim 6, wherein the concentrate source comprises multiple osmotic agent sources.

8. The system of claim 7, wherein the osmotic agent sources contain osmotic agents selected from the group consisting of dextrose, icodextrin, amino acids, and glucose.

9. The system of claim 6, wherein the ion concentrate source comprises one or more from the group consisting of sodium chloride, sodium lactate, magnesium chloride, calcium chloride, potassium chloride, and sodium bicarbonate.

10. The system of claim 6, wherein the concentrate source comprises multiple ion concentrate sources.

11. The system of claim 1, further comprising a concentrate pump positioned between the concentrate source and the peritoneal dialysate generation flow path for controlled addition of fluid from the concentrate source to the peritoneal dialysate generation flow path.

12. The system of claim 1, further comprising a control system for controlling one or more pumps and valves to control movement of fluid through the system.

13. The system of claim 12, wherein the control system comprises a timer, and wherein the timer causes the control system to generate peritoneal dialysate at a predetermined time.

14. The system of claim 12, wherein the control system comprises a user interface, wherein the user interface causes the control system to generate peritoneal dialysate at a selected time.

15. The system of claim 1, wherein the sterilization module comprises one or more from the group consisting of one or more ultrafilters, a UV light source, a heater, a flash pasteurization module, a microbial filter; and combinations thereof.

16. The system claim 15, wherein the sterilization module comprises a UV light source positioned downstream of an ultrafilter.

17. The system of claim 1, wherein the peritoneal dialysate regeneration module comprises one or more selected from the group consisting of a sorbent cartridge, activated carbon, a reverse osmosis module, a carbon filter, an ion exchange resin, and a nanofilter.

18. The system of claim 3, wherein the integrated cycler comprises a heater.

19. The system of claim 18, wherein the system further comprises at least one sensor selected from the group consisting of a flow meter, a pressure sensor, a conductivity sensor, and a temperature sensor.

20. The system of claim 15, wherein the sterilization module comprises at least two ultrafilters.

21. The system of claim 3, wherein the integrated cycler comprises a filter in the infusion line.

22. A method, comprising the steps of:

pumping fluid through a peritoneal dialysate generation flow path comprising a peritoneal dialysate regeneration module;

adding one or more concentrate solutions to the fluid in the peritoneal dialysate generation flow path; and

pumping the fluid through a sterilization module.

23. The method of claim 22, wherein the fluid is fluid returned to the peritoneal dialysate generation flow path from a peritoneal cavity of a patient.

24. The method of claim 22, further comprising the steps of:

heating the fluid;

pumping the fluid into a peritoneal cavity of a patient with an integrated cycler; and

pumping the fluid from the peritoneal cavity of the patient into the peritoneal dialysate generation flow path.

25. The method of claim 22, further comprising the step of pumping the fluid into one or more dialysate containers and pumping the fluid from the one or more dialysate containers into a peritoneal cavity of a patient.

26. The method of claim 22, wherein the step of adding one or more concentrate solutions to the fluid comprises adding at least an osmotic agent and an ion concentrate to the fluid.

27. The method of claim 26, wherein the osmotic agent and ion concentrate are added to the fluid from a single concentrate source.

28. The method of claim 26, wherein the osmotic agent and ion concentrate are added from separate concentrate sources.

29. The method of claim 26, wherein the osmotic agent is one or more selected from the group consisting of glucose, dextrin, and icodextrin.

30. The method of claim 26, wherein the osmotic agent comprises multiple osmotic agents.

31. The method of claim 30, wherein the multiple osmotic agents are added from a single osmotic agent source.

32. The method of claim 30, wherein each of the multiple osmotic agents are added from separate osmotic agent sources.

33. The method of claim 26, wherein the ion concentrate is added from an ion concentrate source and comprises one or more from the group consisting of sodium chloride, sodium lactate, magnesium chloride, calcium chloride, potassium chloride, and sodium bicarbonate.

34. The method of claim 33, wherein each of the ion concentrates are added to the fluid from a single ion concentrate source.

35. The method of claim 33, wherein the ion concentrate source comprises multiple ion concentrate sources; and wherein each of the multiple ion concentrate sources comprise different solutes.

36. The method of claim 35, wherein the step of adding one or more concentrate solutions to the fluid comprises controlling an addition of concentrate from each of the ion concentrate sources to generate a peritoneal dialysate with a prescribed solute concentration.

37. The method of claim 22, wherein the method is carried out by a peritoneal dialysate generation system.

38. The method of claim 22, wherein the peritoneal dialysate regeneration module comprises one or more selected from the group consisting of a sorbent cartridge, activated carbon, a reverse osmosis module, a carbon filter and a nanofilter.

39. The method of claim 22, wherein the sterilization module comprises one or more from the group consisting of one or more ultrafilters, a UV light source, a microbial filter, and combinations thereof.

40. The method of claim 39, wherein the sterilization module comprises at least two ultrafilters.

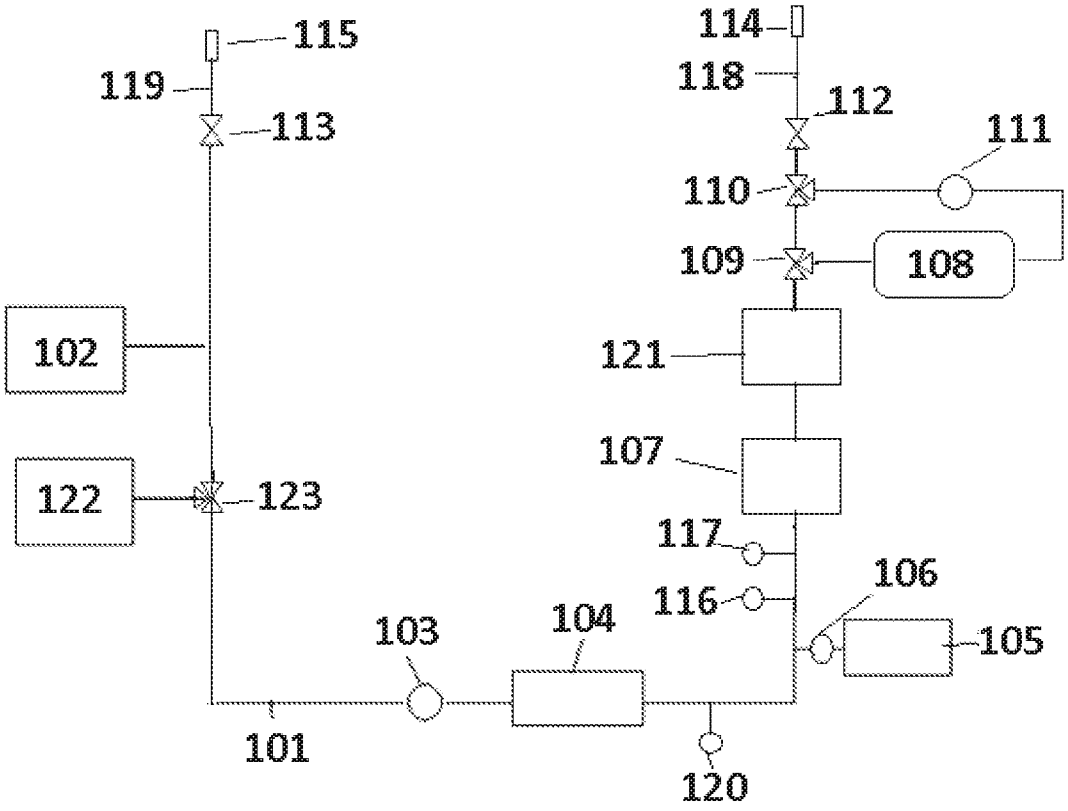
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FIG. 1

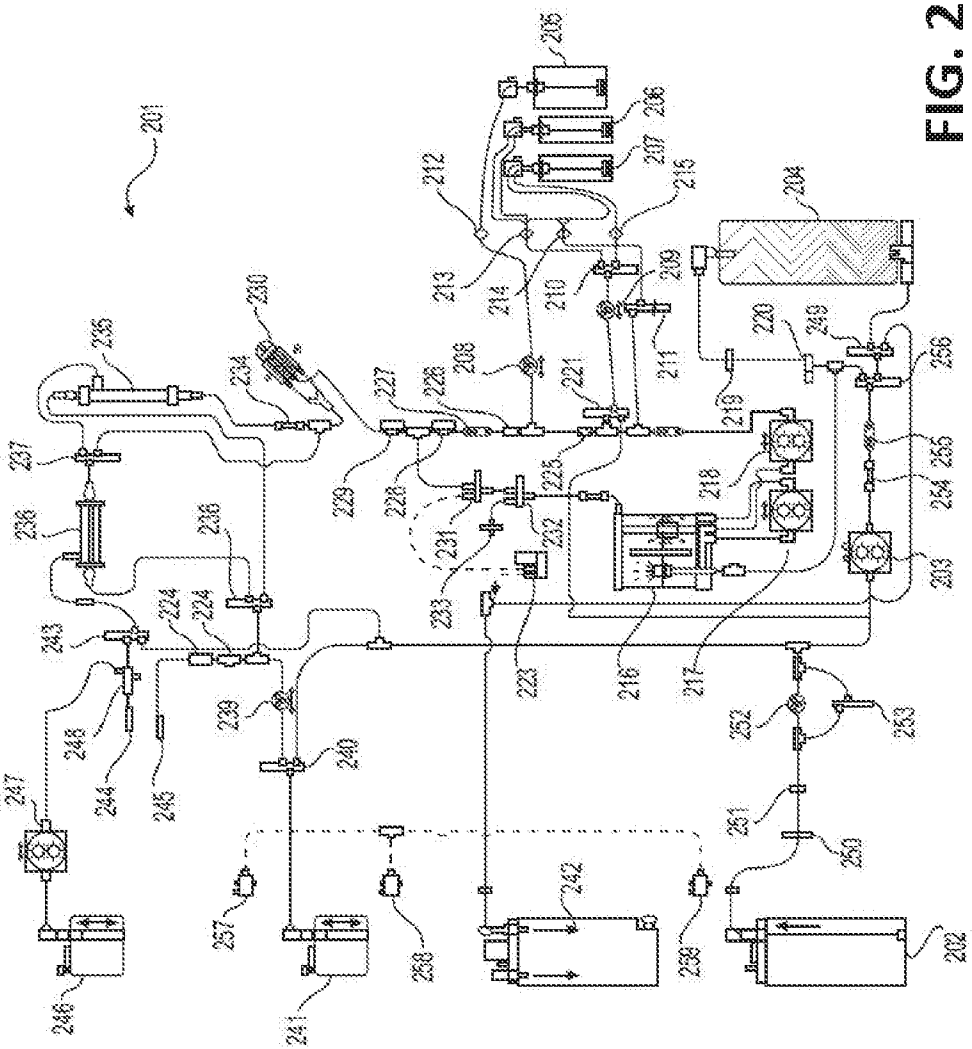
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FIG. 2

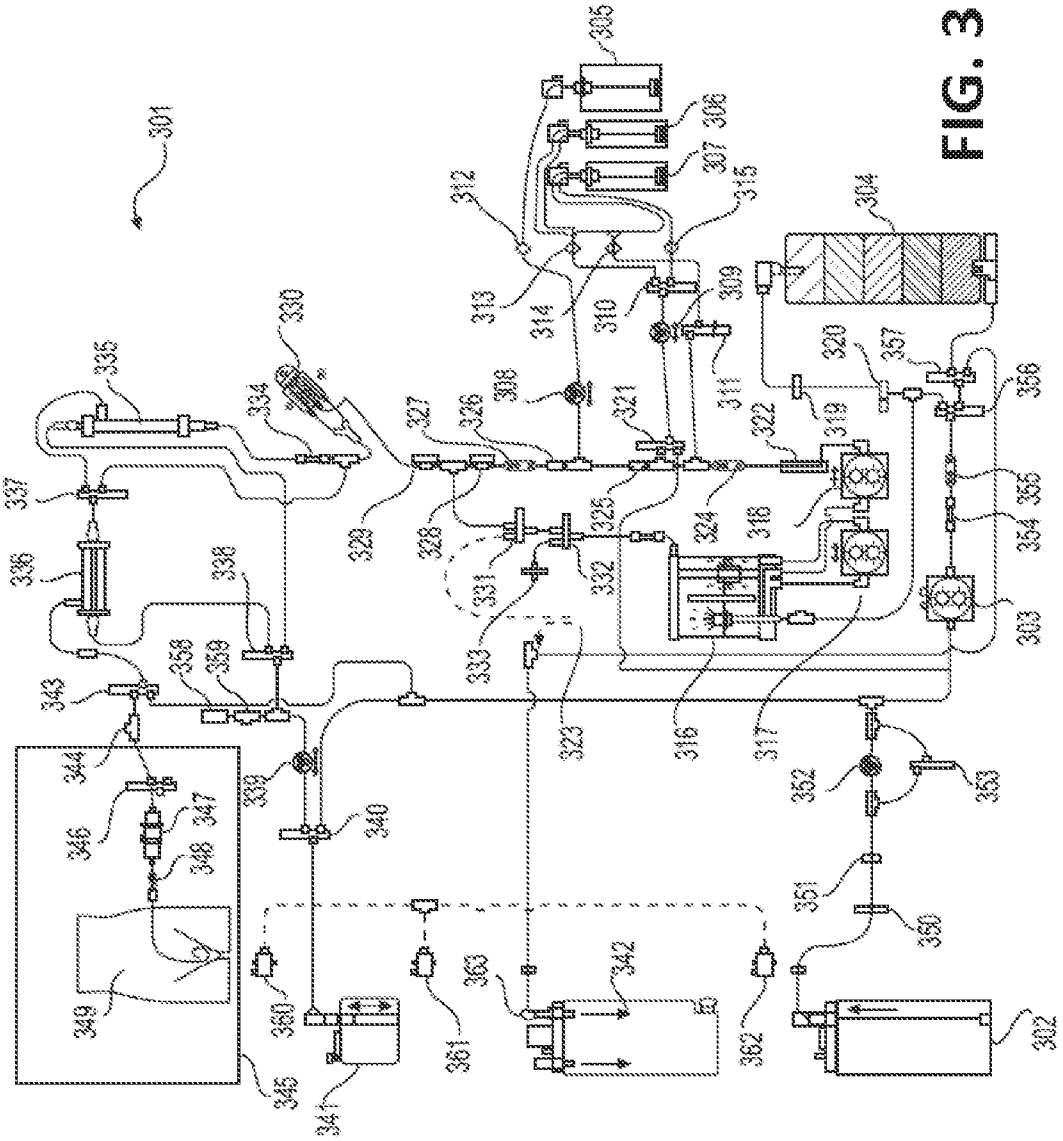
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FIG. 3

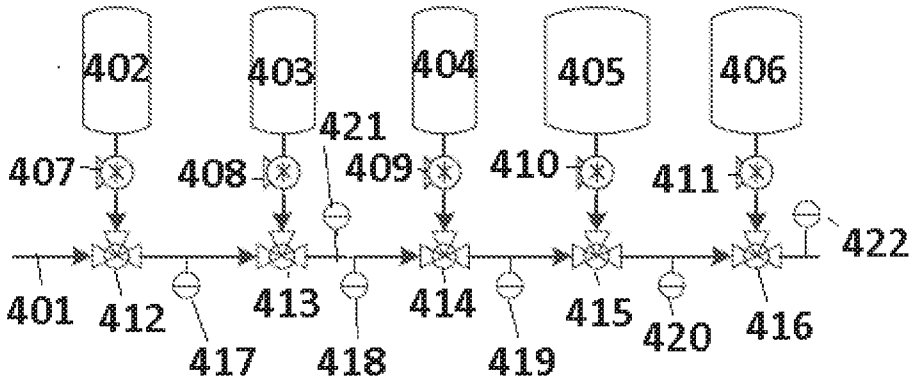
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FIG. 4

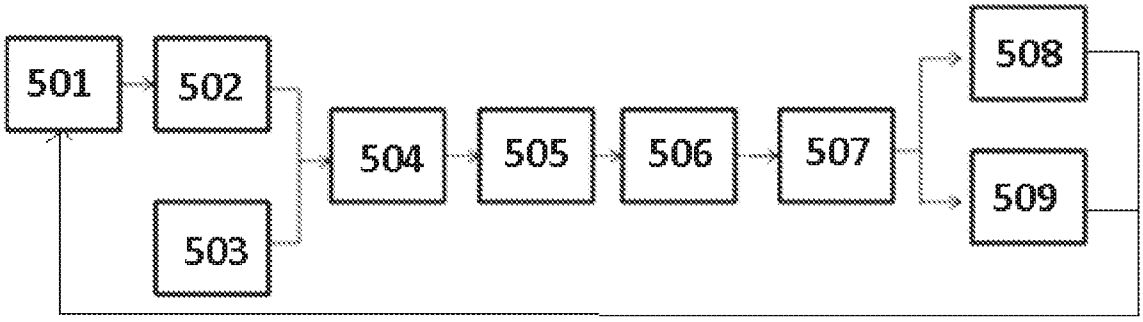
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FIG. 5

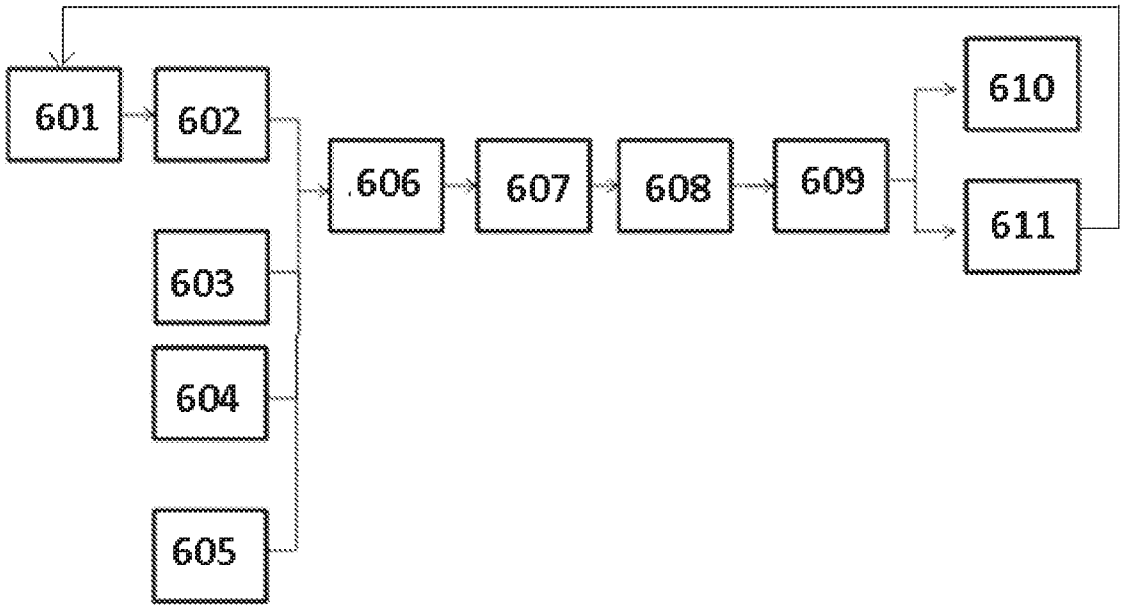

FIG. 6

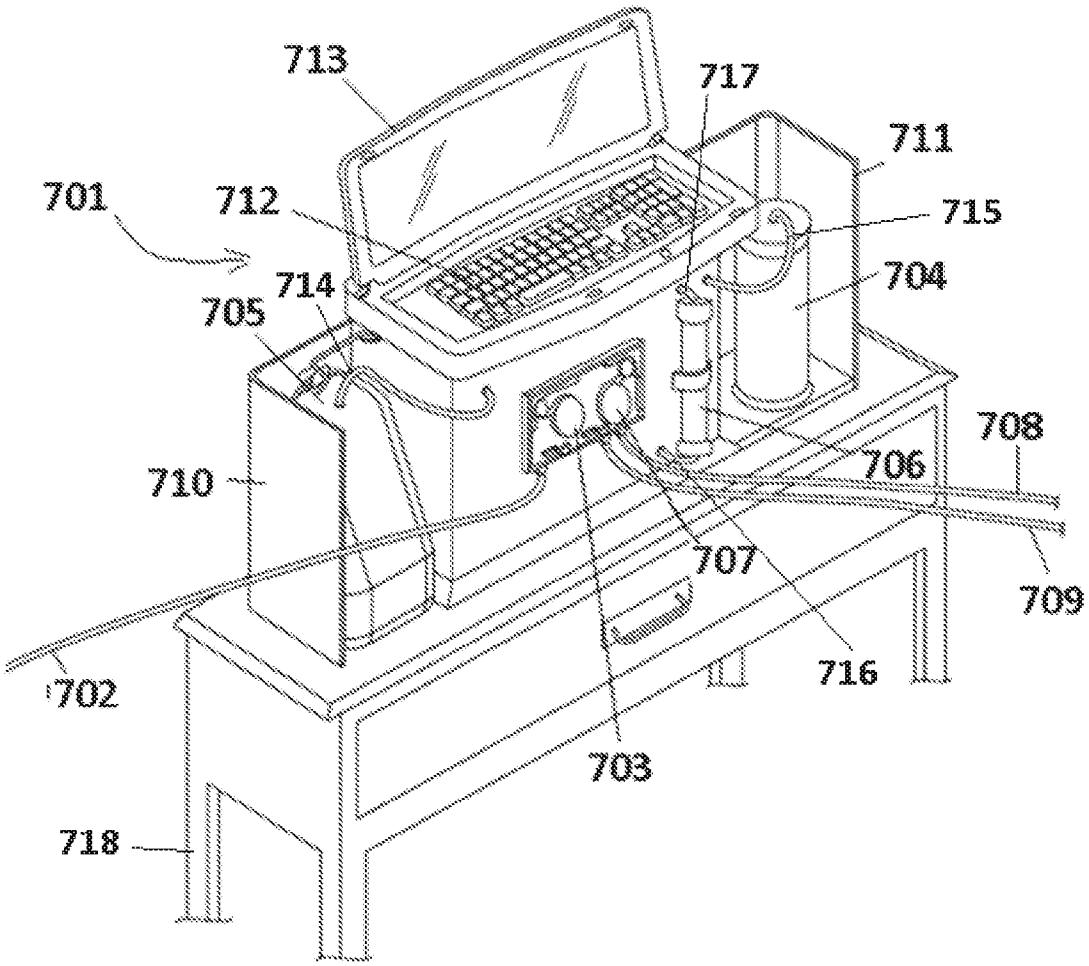
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FIG. 7A

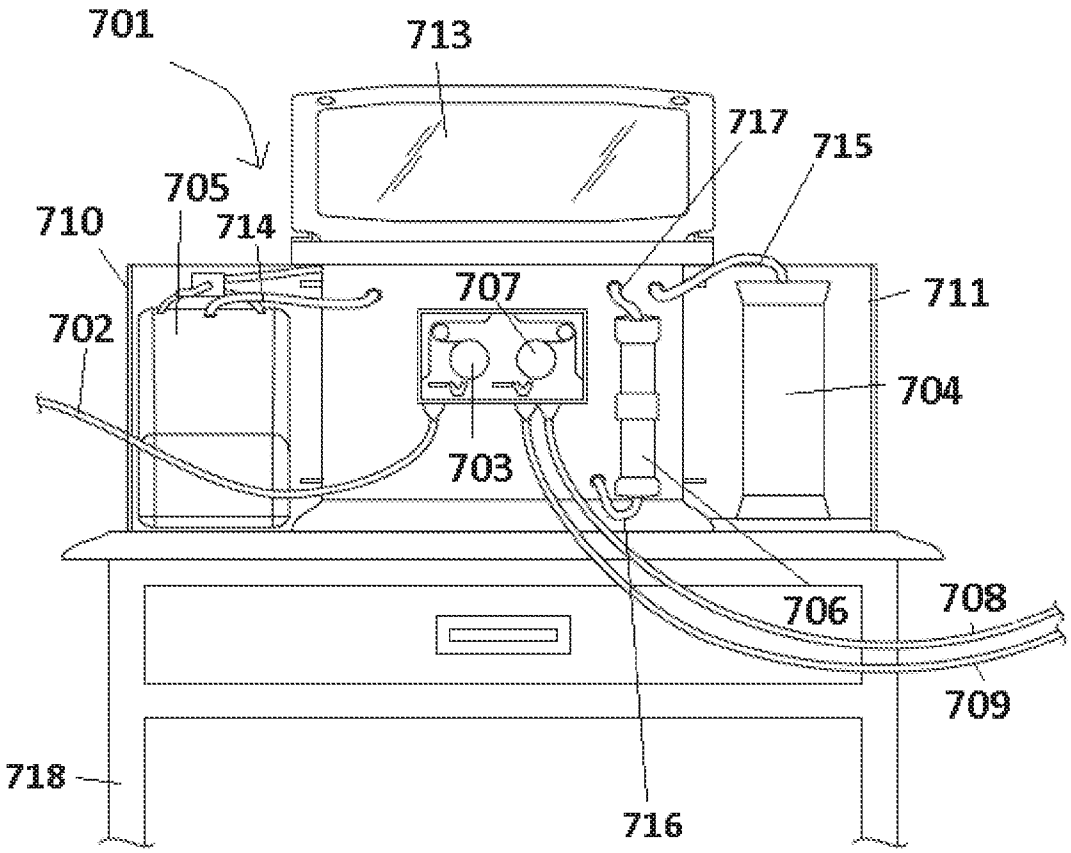
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FIG. 7B

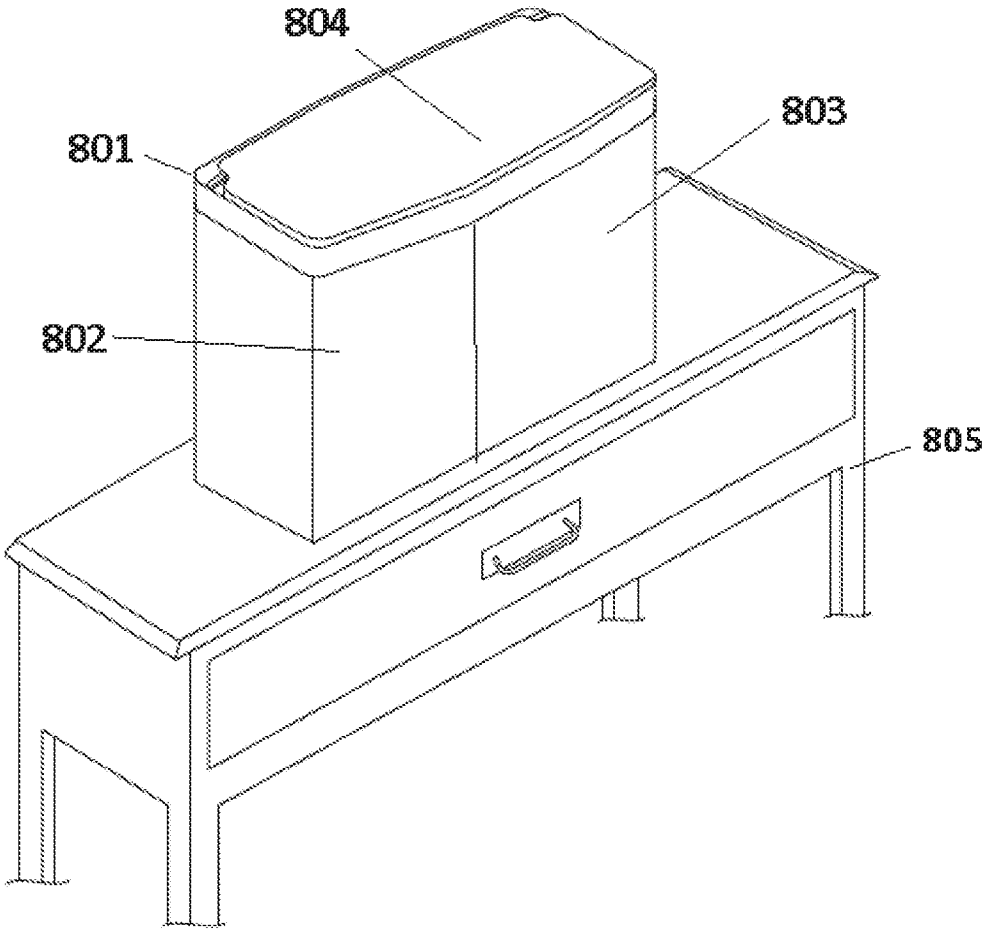

FIG. 8

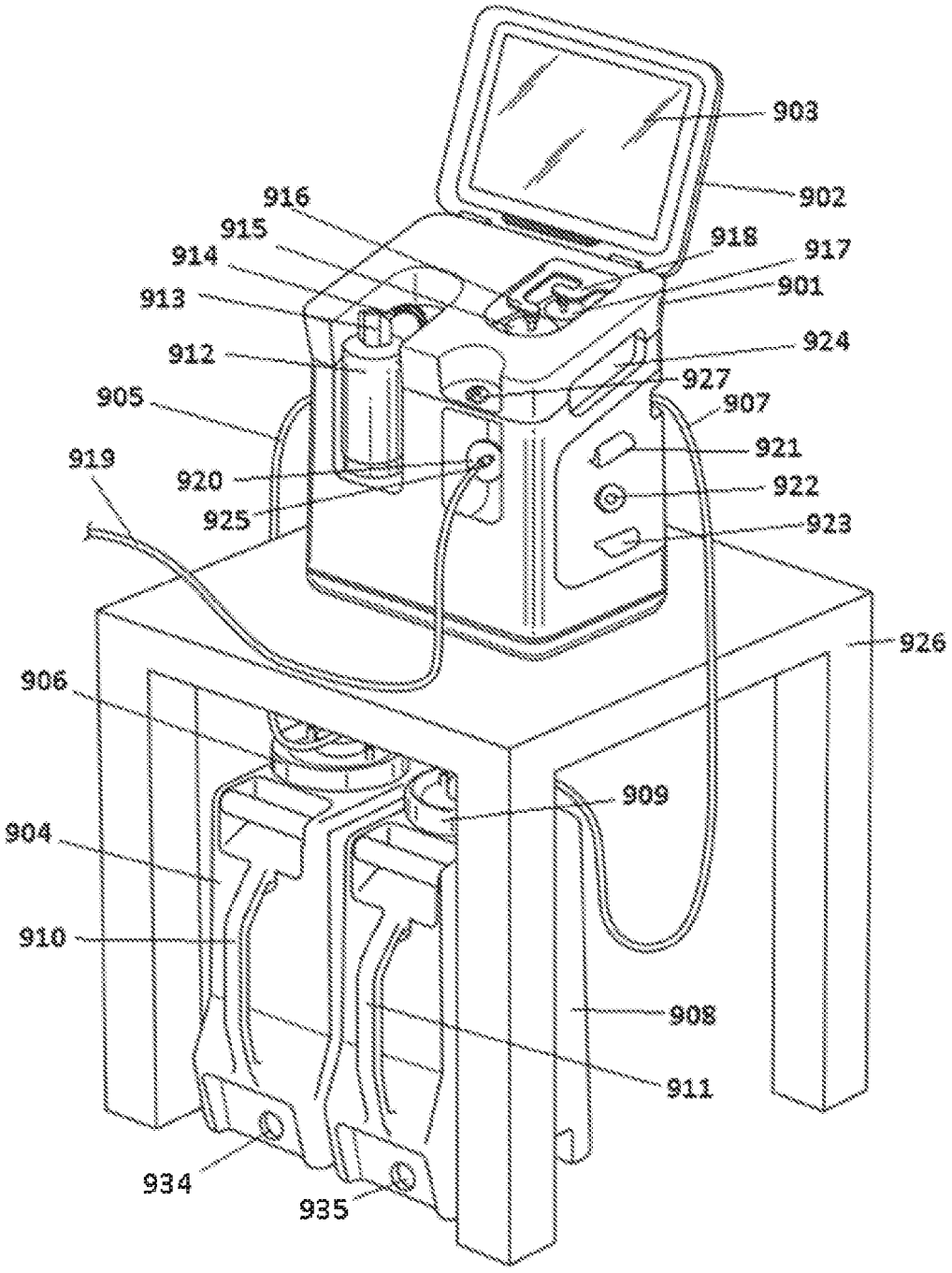
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FIG. 9A

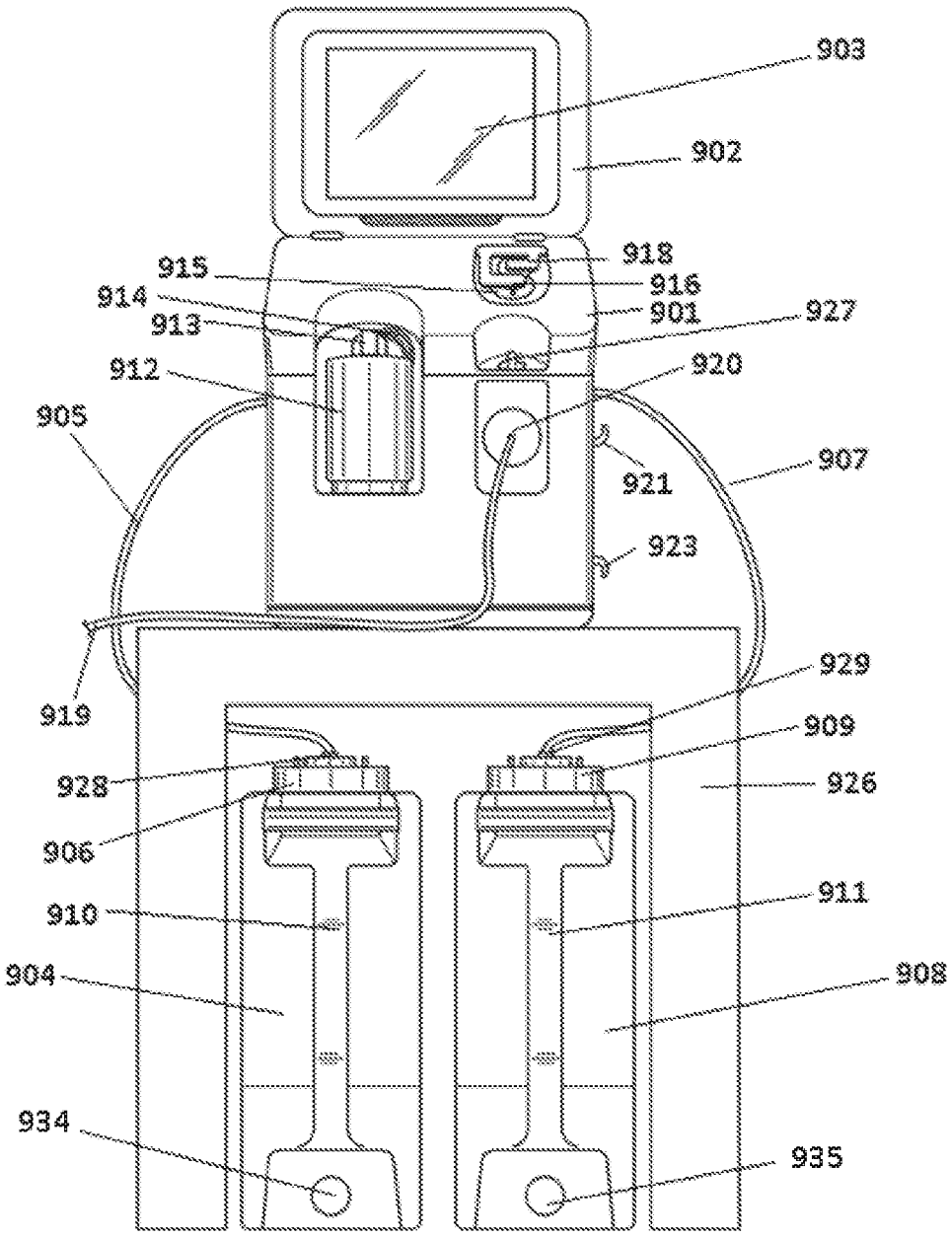
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FIG. 9B

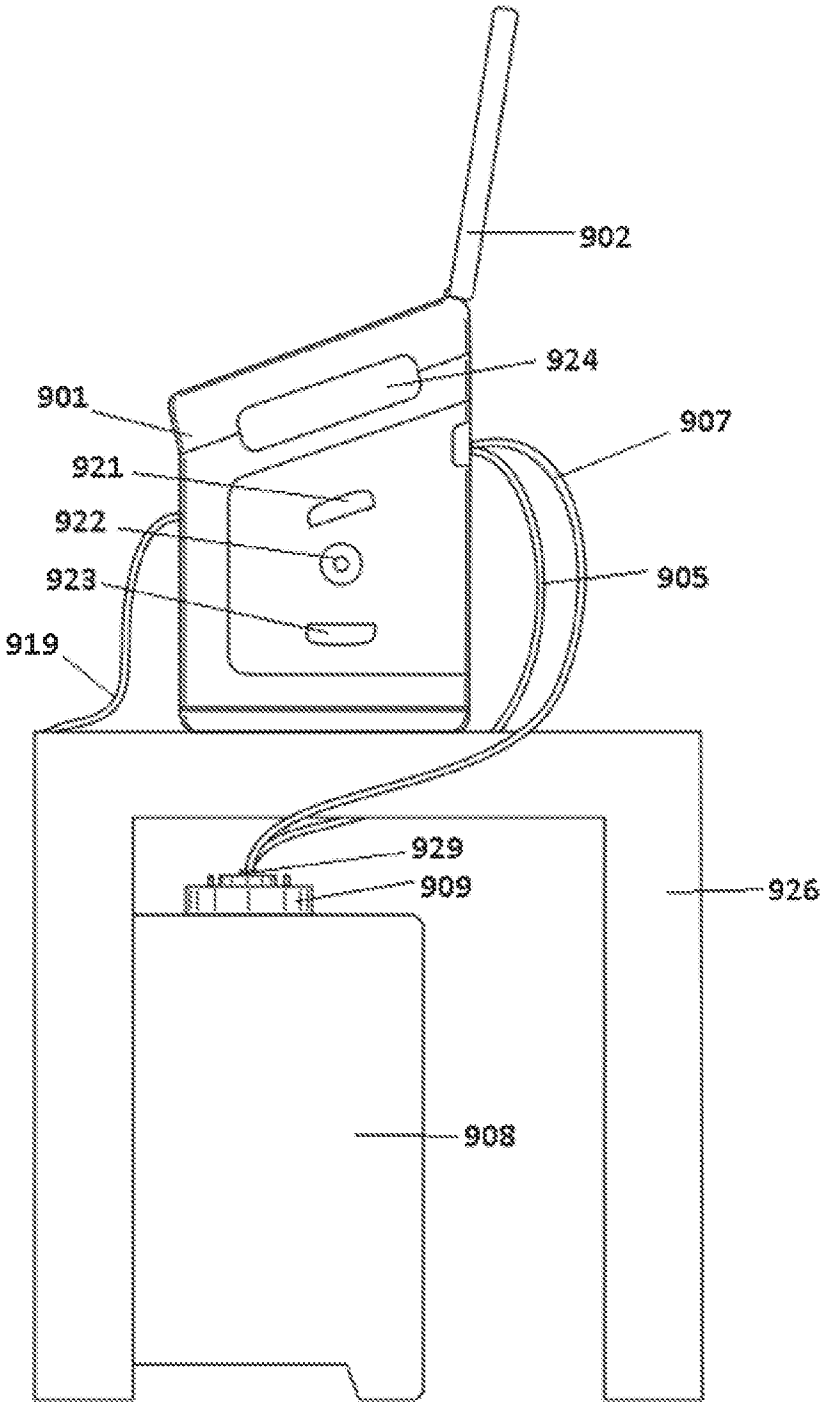

FIG. 9C

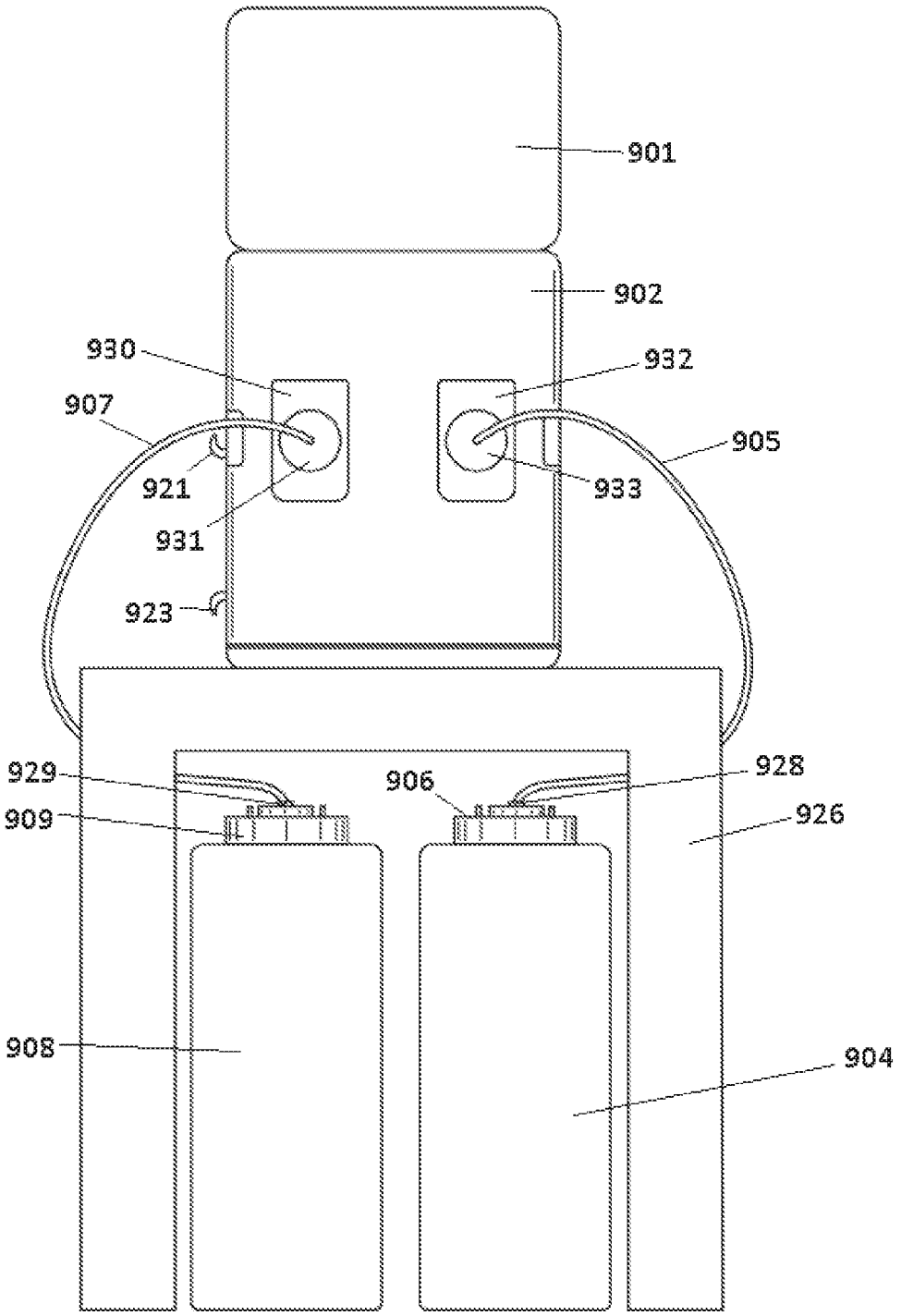
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FIG. 9D

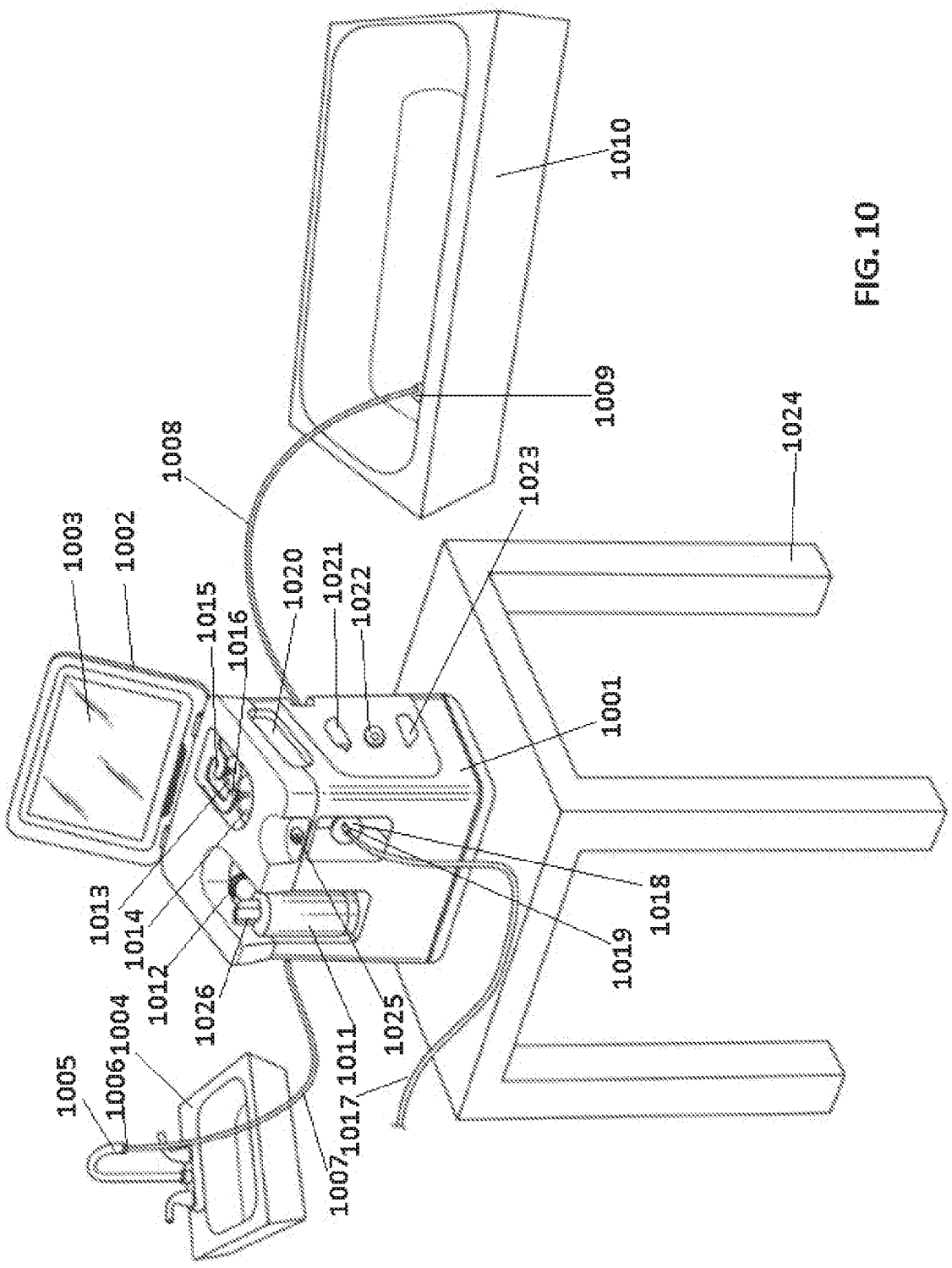
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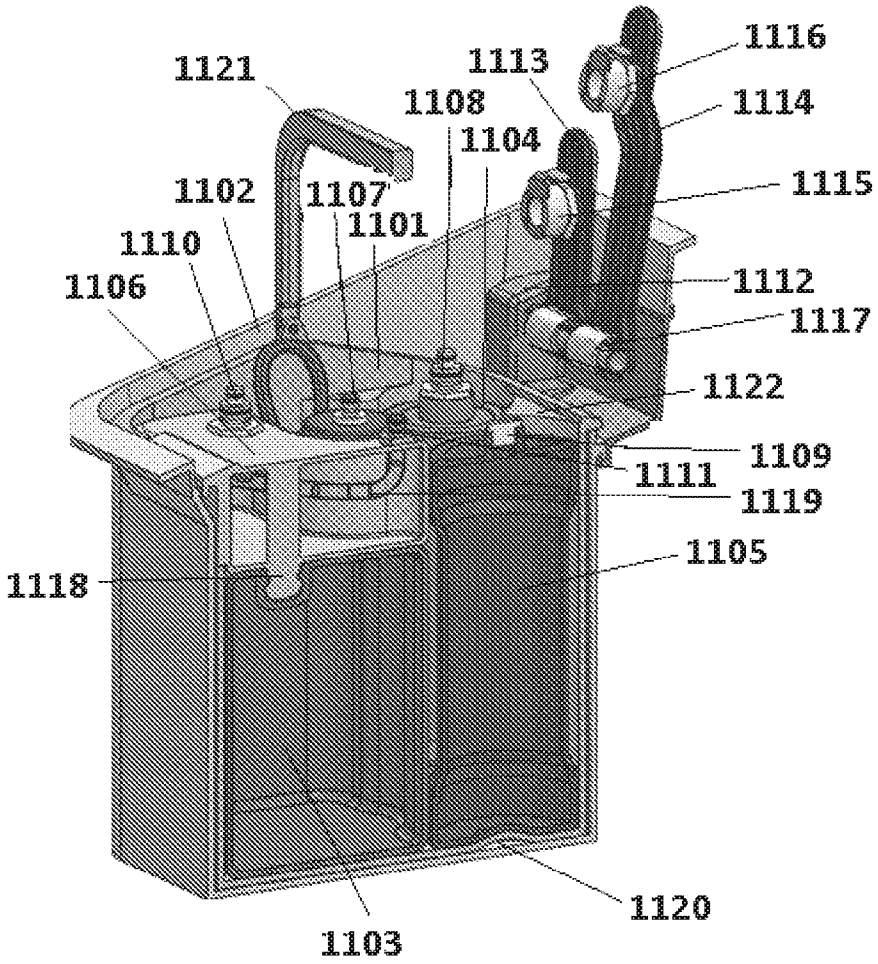
FIG. 10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1103

FIG. 11

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2017/025858

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61M1/16 A61M1/28 C02F1/00 C02F1/02 C02F1/28
C02F1/32 C02F1/44
ADD.
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
A61M C02F

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

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
EPO-Internal, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2010/312172 A1 (HOFFMAN JOSEF C A [US]) 9 December 2010 (2010-12-09)	1-6,9, 11-13, 15-19
Y	abstract; figures paragraphs [0035] - [0039], [0040] - [0041], [0091], [0098], [0108], [0110], [0123], [0129]	7,8,10, 14,20,21
X	US 5 141 493 A (JACOBSEN STEPHEN C [US] ET AL) 25 August 1992 (1992-08-25)	1-6,9, 11-13, 16,18,19
Y	abstract; figures column 3, line 21 - column 4, line 57 column 5, lines 27-60	7,8,10, 14,20,21

-/--

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

[X] See patent family annex.

* Special categories of cited documents :

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

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

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

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

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

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

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

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

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
19 June 2017	29/06/2017

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

Form PCT/ISA/210 (second sheet) (April 2005)

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2017/025858

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 2014/018727 A1 (BURBANK JEFFREY H [US] ET AL) 16 January 2014 (2014-01-16) abstract; figures 8A,9 paragraphs [0074], [0103], [0113], [0146]	7,8,14, 20
Y	WO 00/57935 A1 (GAMBRO LUNDIA A B [SE]) 5 October 2000 (2000-10-05) abstract; figures 3-5; table 2	10
Y	US 5 643 201 A (PEABODY ALAN M [US] ET AL) 1 July 1997 (1997-07-01) abstract; figure 1 column 5, lines 55-58	21

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2017/025858

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.: 22-40
because they relate to subject matter not required to be searched by this Authority, namely:

Rule 39.1(iv) PCT - Method for treatment of the human or animal body by therapy

2. [ ] Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. [ ] As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fees, this Authority did not invite payment of additional fees.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.

[ ] The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.

[ ] No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/US2017/025858

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
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