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(54) Title: DIRECT VESSEL HEATING FOR DISSOLUTION TESTING

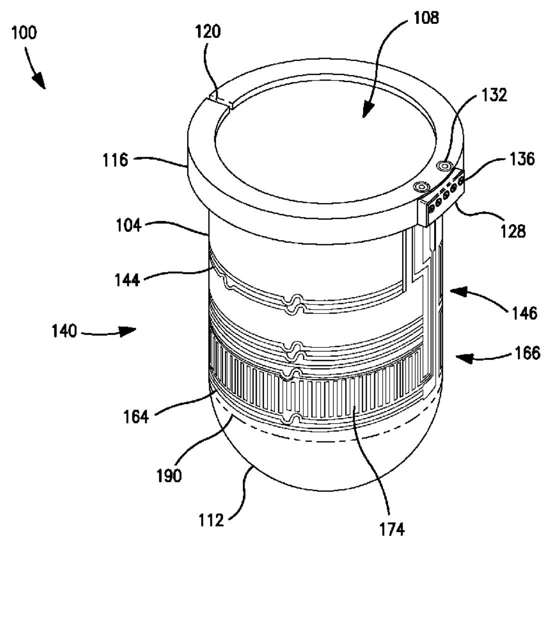

FIG. 1

(57) Abstract: A dissolution test vessel configured for direct vessel heating includes a lateral wall, a resistive heating element, and a temperature-sensing element. The resistive heating element and the temperature-sensing element are bonded directly to the lateral wall, and may be formed by dispensing flowable materials onto the lateral wall. The resistive heating element includes a contiguous first heating element end, heating element section, and second heating element end. The temperature-sensing element includes a contiguous first sensing element end, sensing element section, and second sensing element end. The vessel may communicate with a heater control system, which may be provided with a dissolution test apparatus at which the vessel is mounted.

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DIRECT VESSEL HEATING FOR DISSOLUTION TESTING

FIELD OF THE INVENTION

[0001] The present invention relates generally to dissolution testing of analyte-containing media. More particularly, the invention relates to heating and monitoring the temperature of media contained in test vessels of a dissolution test apparatus by utilizing a direct vessel heating technique, and to test vessels that integrally include direct vessel heating components.

BACKGROUND OF THE INVENTION

[0002] Dissolution testing is often performed as part of preparing and evaluating soluble materials, particularly pharmaceutical dosage forms (e.g., tablets, capsules, and the like) consisting of a therapeutically effective amount of active drug carried by an excipient material. Typically, dosage forms are dropped into test vessels that contain dissolution media of a predetermined volume and chemical composition. For instance, the composition may have a pH factor that emulates a gastro-intestinal environment. Dissolution testing can be useful, for example, in studying the drug release characteristics of the dosage form or in evaluating the quality control of the process used in forming the dose. To ensure validation of the data generated from dissolution-related procedures, dissolution testing is often carried out according to guidelines approved or specified by certain entities such as United States Pharmacopoeia (USP), in which case the testing must be conducted within various parametric ranges. The parameters may include dissolution media temperature, the amount of allowable evaporation-related loss, and the use, position and speed of agitation devices, dosage-retention devices, and other instruments operating in the test vessel.

[0003] As a dosage form is dissolving in the test vessel of a dissolution system, optics-based measurements of samples of the solution may be taken at predetermined time intervals through the operation of analytical equipment such as a spectrophotometer. The analytical equipment may determine analyte (e.g. active drug) concentration and/or other properties. The dissolution profile for the dosage form under evaluation--i.e., the percentage of analytes dissolved in the test media at a certain point in time or over a certain period of time--can be calculated from the measurement of analyte concentration in the sample taken. In one specific method employing a spectrophotometer, sometimes referred to as the sipper method, dissolution media samples are pumped from the test vessel(s) to a sample cell contained within the spectrophotometer, scanned while residing in the sample cell, and in some procedures then returned to the test vessel(s). In another more recently developed method, sometimes referred to as the *in situ* method, a fiber-optic "dip probe" is inserted directly in a test vessel. The dip probe includes one or more optical fibers that communicate with the spectrophotometer. In the *in situ* technique, the spectrophotometer thus does not require a sample cell as the dip probe serves a similar function. Measurements are taken directly in the test vessel and thus optical signals rather than liquid samples are transported between the test vessel and the spectrophotometer via optical fibers.

[0004] During the course of dissolution testing, it is desirable and often required to heat the media residing in the vessels of the dissolution test apparatus, and control the temperature of this media at a constant level or according to a predetermined temperature profile. For instance, when operating in accordance with certain USP guidelines, the media must be maintained at 37 ± 0.5°C. One way to control the temperature of the media is to provide a water bath with the dissolution test apparatus. The dissolution test vessels are supported by the dissolution test apparatus such that the vessels are at least partially immersed in the water bath. Heated water is circulated through the water bath and thus into thermal contact with each vessel, whereby heat is transferred from the water bath to the media contained in the vessels. Another way to control media temperature is by way of Direct Vessel Heating (DVH™) technology developed by Varian, Inc., Palo Alto, California. In this latter case, a heating element is attached to each vessel. The heating element is a multi-layered structure that includes resistive heating elements and temperature-sensing elements sandwiched between polymeric layers. Accordingly, the heating of each vessel of the dissolution system is independently controllable and the need for a water bath and associated components (water heater, pump, plumbing, etc.) is eliminated. Examples of vessels provided with this type of heating element are described in U.S. Patent Nos. 6,303,909 and 6,727,480, assigned to the assignee of the present disclosure and incorporated herein by reference in their entireties.

[0005] While vessels provided with heating elements of the type noted above generally perform well, there is a need for further improvements in the direct heating of vessels. The known heating elements require several layers of material, and must first be fabricated as a complete article and then applied to the vessels. Typically, the as-constructed heating elements are manually applied with the use of adhesives, which may result in variations in performance from one vessel to another. Moreover, the various materials required and fabrication process are costly. Therefore, there is a need for providing directly heated vessels that are fabricated more consistently, function more precisely, and are less costly.

SUMMARY OF THE INVENTION

[0006] To address the foregoing problems, in whole or in part, and/or other problems that may have been observed by persons skilled in the art, the present disclosure provides methods, processes, systems, apparatus, instruments, and/or devices, as described by way of example in implementations set forth below.

[0007] According to one implementation, a dissolution test vessel configured for direct vessel heating is provided. The dissolution test vessel includes a lateral wall, a resistive heating element, and a temperature-sensing element. The lateral wall is disposed about a longitudinal axis of the vessel and includes an upper end, a lower end axially spaced from the upper end, and an outside surface extending from the upper end to the lower end. The resistive heating element is bonded directly to the outside surface and includes a first heating element end, a second heating element end, and a heating element section contiguously running from the first heating element end, over a heating zone of the lateral wall and to the second heating element end. The heating element section runs along at least two different directions. The temperature-sensing element is bonded directly to the outside surface and includes a first sensing element end, a second sensing element end, and a sensing element section contiguously running from the first sensing element end, over a temperature sensing zone of the lateral wall and to the second sensing element end. The sensing element section runs along at least two different directions.

[0008] According to another implementation, a dissolution test apparatus configured for direct vessel heating is provided. The dissolution test apparatus includes a vessel support member having an aperture, a heater control system, and a vessel mounted at the vessel support member. The vessel includes a resistive heating element bonded directly an outside surface of the vessel, and a temperature-sensing element bonded directly to the outside surface. The resistive heating element and the temperature-sensing element communicate with the heater control system.

[0009] According to another implementation, a method is provided for fabricating a dissolution test vessel. The method includes depositing a first flowable material directly on an outside surface of a lateral wall of a vessel to form a resistive heating element. A second flowable material is deposited directly on the outside surface to form a temperature-sensing element. A contact block is attached to the vessel and placed in communication with the resistive heating element and the temperature-sensing element. A clear film may be applied directly to the outside surface wherein the film covers at least a portion of the resistive heating element and the temperature-sensing element.

[0010] Other devices, apparatus, systems, methods, features and advantages of the invention will be or will become apparent to one with skill in the art upon examination of the following figures and detailed description. It is intended that all such additional systems, methods, features and advantages be included within this description, be within the scope of the invention, and be protected by the accompanying claims.

BRIEF DESCRIPTION OF THE DRAWINGS

[0011] The invention can be better understood by referring to the following figures. The components in the figures are not necessarily to scale, emphasis instead being placed upon illustrating the principles of the invention. In the figures, like reference numerals designate corresponding parts throughout the different views.

[0012] Figure 1 is a perspective view of an example of a vessel provided in accordance with the teachings of the present disclosure.

[0013] Figure 2 is an elevation view of the vessel illustrated in Figure 1.

[0014] Figure 3 is another elevation view of the vessel illustrated in Figure 1.

[0015] Figure 4 is a detailed view of the region designated “A” in Figure 2.

[0016] Figure 5 is a cross-sectional elevation view of a portion of the vessel illustrated in Figures 1 to 3.

[0017] Figure 6 is an elevation view of the vessel illustrated in Figures 1 to 3 mounted to a vessel support member and communicating with a vessel heating control system.

[0018] Figure 7 is a schematic view of an example of a vessel heating control system according to the teachings of the present disclosure.

[0019] Figure 8 is a schematic view of a vessel being fabricated according to an example taught in the present disclosure.

[0020] Figure 9 is a perspective view of an example of a dissolution test apparatus at which one or more vessels taught in the present disclosure may be operated.

DETAILED DESCRIPTION OF THE INVENTION

[0021] An example of a vessel with integral direct vessel heating capability will now be described with reference to Figures 1-6.

[0022] Figure 1 is a perspective view and Figures 2 and 3 are elevation views of an example of a vessel **100** according to the present teachings. Typically, the vessel **100** has a cylindrical shape relative to a central or longitudinal axis **202** (Figure 2) of the vessel, but more generally the vessel **100** may have any shape suitable for containing dissolution media and receiving a stirring device and/or other types of *in situ* operative components. The vessel **100** generally includes a lateral wall or section **104** generally parallel with the central axis **202**. The lateral wall **104** terminates at an upper end **108**, which is open to the interior of the vessel **100** unless a vessel cover (not shown) is provided. Opposite to the upper end **108**, the lateral wall **104** includes a lower end at which a bottom section **112** of the vessel **100** adjoins the lateral wall **104**. The bottom section **112** may be hemispherical or rounded as illustrated or may have any other suitable shape. Typically, the bottom end **112** is completely closed but in other implementations may include an opening and an accompanying closure device, valve, or the like.

[0023] The vessel **100** may include a flanged section **116** (e.g., rim, flange, etc.), the outermost diameter of which is greater than the outermost diameter of the lateral wall **104**. The flanged section **116** facilitates the mounting of the vessel **100** at a vessel support member such as may be provided with a dissolution test apparatus. Typically, the vessel support member is provided in the form of a plate that has a plurality of apertures serving as vessel mounting sites supporting a plurality of respective vessels. The flanged section **116** may also be configured to facilitate centering of the vessel **100** within the aperture of the vessel support member. For this purpose, the flanged section **116** may be a separate component in the form of a collar or ring that is attached to the lateral wall **104** at the upper end **108**. As an example, the flanged section **116** may include a gap **120** (Figure 1) and one or more bores **324** (Figure 3) leading to the gap **120**. A screw or other fastener, tangentially oriented relative to the curvature of the vessel **100**, may be inserted through the bore(s) **324** and across the gap **120** to secure the flanged section **116** to the lateral wall **104**. The flanged section **116** may be similar to the TruCenter™ vessel commercially available from Varian, Inc., Palo Alto, California, or to embodiments disclosed in U.S. Patent Nos. 6,562,301 and 6,673,319, assigned to the assignee of the present disclosure. As an alternative to the illustrated two-piece design of the vessel **100**, the flanged section **116** may be a rim integrally formed with the lateral wall **104**.

[0024] The vessel **100** may further include a contact block (or contact element) **128**. The contact block **128** may be attached to or form a part of the flanged section **116**, as described further below. In the illustrated example, the contact block **128** is removably attached to the flanged section **116** by way of screws **132**. The contact block **128** may include a first set of contacts (not shown) located at the underside of the contact block **128**, and a second set of contacts **136** located at an outer surface of the contact block **128**. As illustrated in Figures 1 and 3, the contact block **128** may protrude radially outward from the flanged section **116** relative to the central axis **202** (Figure 2). The function of the contact block **128** is described below.

[0025] The vessel **100** includes a direct vessel heating area **140**. The direct vessel heating area **140** may be fabricated over a large portion of the outside surface of the lateral wall **104**. For instance, the direct vessel heating area **140** may span over a large portion of the axial length of the lateral wall **104** (i.e., in the direction of the central axis **202**), and fully circumscribe the lateral wall **104** to ensure uniform heating and temperature control of the media contents of the vessel **100**.

[0026] Referring to Figure 1, the direct vessel heating area **140** may include a continuous, first resistive heating element **144** configured to provide heat over a first heating zone **146** of the direct vessel heating area **140**. By "resistive" is meant that the material of the first heating element **144** is electrically resistive and thus dissipates heat in response to electrical current.

[0027] Referring to Figure 2, to provide heat throughout the first heating zone **146**, the first resistive heating element **144** includes a first heating element end **248**, a first main heating element section **250**, and a second heating element end **252**. The material constituting the first resistive heating element **144** is contiguous from the first heating element end **248**, to the first main heating element section **250**, and to the second heating element end **252**. Hence, establishing an electrical current from the first heating element end **248**, through the first main heating element section **250**, and to the second heating element end **252** generates heat. A majority of the heat is generated from first main heating element section **250** and thus in the first heating zone **146** defined thereby. For this purpose, the first main heating element section **250** may be configured or arranged in any suitable pattern. Generally, the first main heating element section **250** includes portions that run in at least two directions to provide sufficient heating coverage over the first heating zone **146**. In the illustrated example, the first main heating element section **250** includes horizontal portions **254** and vertical portions **256**. Moreover, again as an example, more than one horizontal portion **254** and/or vertical portion **256** may branch off of the first heating element end **248** and/or the second heating element end **252**. Alternative patterns may include, as examples, a sawtooth pattern, a square wave pattern, a trapezoidal pattern, a sinusoidal pattern, other serpentine patterns, and combinations of the foregoing. The first main heating element section **250** may also include fuse links **258**, which by example are illustrated as short sinusoidal portions.

[0028] Referring to Figure 1, in the present example, the direct vessel heating area **140** also includes a continuous, second resistive heating element **164** configured to provide heat over a second heating zone **166** of the direct vessel heating area **140**.

[0029] Referring to Figure 2, to provide heat over the second heating zone **166**, the second resistive heating element **164** includes a third heating element end **268**, a second main heating element section **270**, and a fourth heating element end. In the illustrated example, the fourth heating element end and the second heating element end **252** (associated with the first resistive heating element **144**) are one and the same, i.e., a single termination common to both the first resistive heating element **144** and the second resistive heating element **164** is provided. The configuration, patterning or arrangement, and operation of the second resistive heating element **164** may be the same or similar as described above regarding the first resistive heating element **144**.

[0030] The dual-zone heating design of the illustrated vessel **100** is useful for accommodating the operation of the vessel **100** when utilizing different levels of media during different tests. The dual-zone heating design is illustrated as an example. In other implementations, the direct vessel heating area **140** may include a single resistive heating element and corresponding single heating zone, or may include more than two resistive heating elements and correspondingly distinct heating zones.

[0031] The direct vessel heating area **140** may further include a continuous temperature-sensing element **174** configured to measure media temperature. In the illustrated example, the temperature-sensing element **174** runs over a temperature sensing zone that may be located within the second heating zone **166**. The second heating zone **166** is the lower of the two heating zones **146** and **166** and media is most likely to be filled at least to an elevation level coextensive with the second heating zone **166**. Alternatively, the temperature-sensing element **174** may be located within the upper or first heating zone **146**, or in both heating zones **146** and **166**, or two temperature-sensing elements may be located in the respective heating zones **146** and **166**. Also in the illustrated example, the temperature-sensing element **174** is located "within" the second heating zone **166** so as to facilitate fabrication of both the second resistive heating element **164** and the temperature-sensing element **174**. Alternatively, the temperature-sensing element **174** may overlap into both heating zones **146** and **166**. To provide an accurate measurement of media temperature, the temperature-sensing element **174** may cover a large portion of the direct vessel heating area **140**. In the illustrated example, the temperature-sensing element **174** covers a large portion of the second heating zone **166**.

[0032] Referring to Figure 2, the temperature-sensing element **174** includes a first sensing element end **278**, a main sensing element section **280**, and a second sensing element end **282**. The material constituting the temperature-sensing element **174** is contiguous from the first sensing element end **278**, to the main sensing element section **280**, and to the second sensing element end **282**. In this example, the resistivity of the material constituting the temperature-sensing element **174** varies with temperature and thus the temperature of the media, which is in thermal contact with the temperature-sensing element **174** across the lateral wall **104** of the vessel **100**, may be measured by sensing a change in the electrical current through the temperature-sensing element **174** or in the voltage across the temperature-sensing element **174**. The main sensing element section **280** may be configured or arranged in any suitable pattern. Generally, as in the case of the resistive heating elements **144** and **164**, the main sensing element section **280** includes portions that run in at least two directions to provide sufficient temperature-measurement coverage over the second heating zone **166**. In the illustrated example, the main sensing element section **280** includes horizontal portions and vertical portions arranged in a sinusoidal or serpentine pattern. Alternative patterns may be utilized, as noted above in the case of the resistive heating elements.

[0033] Figure 4 is a detailed view of the region designated "A" in Figure 3. As best shown in Figure 4, the heating element ends **248**, **252**, **268** and the sensing element ends **278** and **282** may be located proximate to each other and to the contact block **128**. By this configuration, relatively short jumper wires or other types of electrical interconnections (e.g., a flexible ribbon cable) may be provided to electrically interconnect the heating element ends **248**, **252**, **268** and the sensing element ends **278** and **282** respectively to the first set of contacts (not shown) located at the underside of the contact block **128**, and thus to the second set of contacts **136** located at an outer surface of the contact block **128**. To facilitate making the electrical contact with jumper wires or the like, each of the heating element ends and the sensing element ends may terminate at a respective bond pad **486**.

[0034] All portions of the resistive heating element(s) **144** and **164** and the temperature-sensing element(s) **174**, including their respective ends **248**, **252**, **268**, **278**, **282**, main sections **250**, **270**, **280**, and bond pads **486**, are directly bonded to the outer surface of the lateral wall **104** of the vessel **100**. That is, no intervening layers of material exist between the resistive heating element(s) **144** and **164** and the temperature-sensing element(s) **174** and the lateral wall **104**. Accordingly, these components comprising the direct vessel heating area **140** of the vessel **100** are formed integrally with the vessel **100**, as opposed to comprising a separate, multi-layered article that must be applied to the vessel **100** through the use of adhesives or other means. The resistive heating element(s) **144** and **164** and the temperature-sensing element(s) **174** are not removable from the lateral wall **104**; all of these components are part of the same unitary structure (i.e., the vessel **100**) as an end product ready for use. Moreover, the various components of the resistive heating element(s) **144** and **164** and the temperature-sensing element(s) **174** may all be formed on the lateral wall **104** at the same radial distance relative to the central axis **202**, thus forming a single level of circuitry. That is, for instance, the resistive heating element(s) **144** and **164** do not need to be located at a different radial distance from the temperature-sensing element(s) **174**. Moreover, the resistive heating element(s) **144** and **164** and the temperature-sensing element(s) **174** do not need to be sandwiched between different layers of material. The resistive heating element(s) **144** and **164** and the temperature-sensing element(s) **174** may be formed as part of the vessel **100** by any suitable technique. In some implementations, the resistive heating element(s) **144** and **164** and the temperature-sensing element(s) **174** are formed by dispensing a liquid or paste of an electrically conductive material onto the lateral wall **104** according to a desired pattern. Examples of dispensing include, but are not limited to, ink printing, pad printing, and silk screening. The compositions of the resistive heating element(s) **144** and **164** and the temperature-sensing element(s) **174** may depend on the fabrication technique utilized, but generally will be materials exhibiting an amount of electrical resistivity or conductivity suitable for transferring heat to the vessel **100** or sensing temperature. Examples of compositions of the resistive heating element(s) **144** and **164** and the temperature-sensing element(s) **174** include, but are not limited to, conductive or resistive inks, epoxies, or the like, and generally any material that may be applied to the lateral wall **104** according to a desired pattern or arrangement and yield a desired electrical conductivity or resistivity. The composition may include a metal or a conductive polymer. A specific example is a silver-containing ink such as the product designated 118.41 commercially available from Creative

Materials, Tyngsboro, Massachusetts. The lateral wall **104** may have any composition suitable for dissolution testing and compatible with the direct bonding of the resistive heating element(s) **144** and **164** and the temperature-sensing element(s) **174**, examples including various glasses and polymers.

[0035] The only other material that may be desired to be added as part of the direct vessel heating area **140** is a protective layer **190**, the boundaries of which are indicated by dashed lines in Figures 1-4. The protective layer **190** is likewise bonded directly to the components of the resistive heating element(s) **144** and **164** and the temperature-sensing element(s) **174**, and to the regions of the outer surface of the lateral wall **104** between these components. The protective layer **190** may cover all or a portion of the direct vessel heating area **140**. The protective layer **190** may be composed of any material that provides desired types of protections for these components (e.g., electrical insulation, thermal insulation, protection from oxidation, etc.). Examples of materials suitable for the protective layer **190** include, but are not limited to, clear dielectric coatings, clear PVC coatings such as may be employed as adhesives for medical devices, or the like. A specific example is the product designated 1-20323 commercially available from Dymax Corporation, Torrington, Connecticut.

[0036] Figure 5 is a cross-sectional elevation view of a portion of the vessel **100**. Representative sections of the resistive heating element **144** (or **164**) and the temperature-sensing element **174** are bonded directly to the lateral wall **104** of the vessel **100**, at the same radial distance from the lateral wall **104**. A representative section of the protective layer **190** is bonded directly to the resistive heating element **144**, the temperature-sensing element **174** and the lateral wall **104**. Accordingly, the direct vessel heating area **140** is a single-layer device that forms an integral part of the vessel **100**, with the protective layer **190** optionally added.

[0037] Figure 6 is an elevation view of the vessel **100** mounted in the aperture of a vessel support member **602** that is typically provided as part of a dissolution test apparatus. The vessel support member **602** typically includes a plurality of apertures **604** so that a like number of vessels **100** may be mounted and operated during a given dissolution test. The illustrated vessel support member **602** includes a recess **606** or like feature that receives the contact block **128** that extends from the flanged section **116** of the vessel **100**. The vessel support member **602** may include a set of contacts **608**, such as for example pins, which are configured for connection to the second set of contacts **136** of the contact block **128** during installation of the vessel **100**. By way of this interconnection and a wired or wireless communication link **610**, the electrical components of the vessel **100** may communicate with a vessel heating control system **612** that may be provided with the dissolution test apparatus. The use of the contact block **128** and corresponding features of the vessel support member **602** also ensure that the vessel **100** is precisely installed on the vessel support member **602** in the same location from one dissolution test to another, thereby ensuring consistency and validation of data acquisition.

[0038] Figure 7 is a general schematic diagram of an example of vessel heating control system **700** that may be provided with a dissolution test apparatus such as described above to interface with one or more vessels **100** with integral direct vessel heating capability as described above, and optionally also with temperature probes **704** insertable into the vessels **100**. The vessel heating control system **700**

generally includes an electronic controller **708** that communicates with various other components via suitable electrical lines or other types of communication links. That is, in the present schematic context, the illustrated communication lines represent wires or other physical types of electrical conduits or, alternatively, wireless transmissions of electromagnetic signals. Each vessel **100** includes one or more resistive heating element(s) **744** and temperature-sensing element(s) **774** as described above. The vessel heating control system **700** may include circuitry for presenting readouts of media temperature values based on measurement signals received from the temperature-sensing elements **774** of each vessel **100** and/or temperature probes **704** inserted in respective vessels **100** if temperature probes **704** are also provided. The vessel heating control system **700** may also include vessel heating control circuitry that communicates with or is part of the electronic controller **708**. As appreciated by persons skilled in the art, the electronic controller **708** may be processor-based and include analog and/or digital attributes as well as hardware, firmware and/or software attributes. The vessel heating control system **700** may also communicate with main control circuitry **712** of the dissolution testing apparatus over a dedicated communication link and hence can be housed within a suitable control unit of the dissolution testing apparatus such a head assembly.

[0039] The electronic controller **708** communicates the resistive heating elements **744** of the respective vessels **100** to heat the media contained in the vessels **100** by controlling the power supplied thereto. The electronic controller **708** is thus able to independently control the heating of each vessel **100**. The electronic controller **708** also communicates with each temperature-sensing element **774**, and each temperature probe **704** if provided, associated with each vessel **100**, and thus is able to monitor the temperatures of the respective volumes of media contained in each vessel **100** at any given instance of time based on measurement signals received from the temperature-sensing elements **774** and/or temperature probes **704**. The electronic controller **708** may be configured to continuously monitor media temperatures in real time, thus providing temperature readouts and heater control on a real-time basis or any other temporal or event-driven basis desired by the user. The temperature probe **704** may be utilized to provide feedback of temperature data for purposes complementary to the temperature-sensing elements **774**. As an example, the temperature probe **704** may be utilized to monitor start-up conditions. Once the set-point temperature in the vessel **100** has been reached and the system is stabilized, the temperature probe **704** may be removed from the vessel **100** and all further temperature monitoring handled by the temperature-sensing element **774** of the vessel **100**. The temperature probe **704** may also be utilized on an as-needed basis to verify that the temperature-sensing element(s) **774** and/or resistive heating element(s) **744** of a given vessel **100** are operating properly. Each temperature probe **704** may be inserted into and subsequently removed from the respective vessel **100** manually or by automated means provided by the dissolution test apparatus. In other implementations, the temperature-sensing elements **774** of the vessels **100** provide all temperature-monitoring tasks and separate temperature probes **704** are not utilized.

[0040] In the illustrated example, the electronic controller **708** also communicates with a peripheral readout or display device **716** such as an LCD screen or the like that is configured to display temperature readings taken from the vessels **100**, and may also display other information pertinent to the vessel heating process. The electronic controller **708** may also communicate with a peripheral input device **720** such as a keypad for enabling user input of vessel media set-point temperature, a variable or incremental temperature curve, and other appropriate system parameters for each vessel **100**.

[0041] In operation during a dissolution test, the user may operate the peripheral input device **720** to enter a set point temperature value, or a programmed temperature profile, according to which the media temperature in the vessels **100** installed at the dissolution test apparatus is to be maintained. The user has the additional option of setting different operating temperatures for each vessel **100** or each defined group of vessels **100**. The electronic controller **708** controls the operation of the heating elements **744** to ensure that an appropriate amount of power is being provided to maintain media temperature at the predetermined value. The temperature-sensing elements **774** measure and monitor media temperature in the vessels **100** by generating measurement signals periodically, continuously, or according to some other user-defined temporal or event-driven basis as described above, and transmit the measurement signals to the electronic controller **708**. In this manner, the electronic controller **708** is able to monitor the rise in media temperature in each vessel **100**, determine whether the media temperature in a given vessel **100** has stabilized at the previously inputted set point, and determine whether the media temperature has deviated from the set point or predetermined varying profile by greater than some predetermined error tolerance (e.g., +/- 0.05 °C) over some predetermined period of time (e.g., 10 seconds). When vessel media temperature needs to be adjusted to correct for a deviation, or needs to vary according to a predetermined profile, the electronic controller **708** transmits appropriate control signals to the heating elements **744** so that an appropriate amount of heat energy is transferred to the media. The electronic controller **708** may also utilize the measurement signals received from the temperature-sensing elements **774** and/or temperature probes **704** to determine whether a heating element **744** has malfunctioned, such as by failing to heat the vessel **100** or heating the vessel **100** in an excessive or uncontrolled manner. If such alert conditions are detected, the electronic controller **708** may operated to shut the heating system **700** down.

[0042] Figure 8 illustrates an example of a method for fabricating a vessel **800** with direct vessel heating capability according to one implementation of the present disclosure. The vessel **800** is mounted to a lathe **804** capable of moving the vessel **800** in two or more directions. For example, the lathe **804** may translate the vessel **800** linearly in a direction **806** along the axis of the vessel **800** and rotate the vessel **800** in a direction **810** about the axis. A printing or drawing system **814** is utilized in this example. The printing system **814** may include a supply and transport device **818** (e.g., pump, reservoir, etc.) that fluidly communicates with a dispensing device **822** (e.g., a pen, hollow stylus, nozzle, etc.) to supply a flowable medium (electrical conductive ink or paste, etc.) to the hollow tip of the dispensing device **822**. The vessel **800** is positioned such that the tip of the dispensing device **822** is proximate to the outer surface of the vessel **800**. Flow of the flowable medium is established and the lathe **804** is operated to move the vessel **800** along two or more directions. Movement of the lathe **804** is programmed such that the dispensing device **822** prints a resistive heating element or temperature-sensing element **826** onto the vessel **800** in a desired pattern. In alternative implementation, the dispensing device **822** is also movable in two or more dimensions, or the dispensing device **822** is movable while the lathe **804** or other means for mounting the vessel **800** remains stationary during the printing process.

[0043] Figure 9 is a perspective view of an example of a dissolution test apparatus **900** according to an implementation of the present disclosure. The dissolution test apparatus **900** may include a frame assembly **902** supporting various components such as a main housing, control unit or head assembly **904**, and a vessel support member (e.g., a plate, rack, etc.) **906** below the head assembly **904**. The vessel support member **906** supports a plurality of vessels **100** arranged in a desired array at a plurality of vessel mounting sites **912**. Each vessel **100** includes a direct vessel heating area **140** that forms an integral part of the vessel **100** and is configured as described above. Figure 1 illustrates eight vessels **100** by example, but it will be understood that more or less vessels **100** may be provided. The vessels **100** may be locked and centered in place on the vessel support member **906** by means such as ring lock devices or clamps (not shown). Alternatively, the vessels **100** themselves may be configured to have centering capability as noted above. Vessel covers (not shown) may be provided to prevent loss of media from the vessels **100** due to evaporation, volatility, etc.

[0044] The head assembly **904** may include mechanisms for operating or controlling various components that operate in the vessels **100** (*in situ* operative components). For example, the head assembly **904** typically supports stirring elements **914** that include respective motor-driven spindles and paddles operating in each vessel **100**. Individual clutches **916** may be provided to alternately engage and disengage power to each stirring element **914** by manual, programmed or automated means. The head assembly **904** also includes mechanisms for driving the rotation of the stirring elements **914**. The head assembly **904** may also include various other *in situ* operative components, two such operative components **918** and **920** being illustrated by example, and mechanisms for operating or controlling these operative components **918** and **920**. As examples, the operative components **918** and **920** may include, for any given vessel **100**, an optional temperature probe as described above, a fiber-optic probe for measuring analyte concentration in the media, media transport cannulas for dispensing and/or aspirating media to and from the vessel **100**, a pH detector, a dosage form holder (e.g., USP-type apparatus such as a basket, net, cylinder, disk, etc.), a video camera, etc. A dosage delivery module **926** may be utilized to preload and drop dosage units (e.g., tablets, capsules, or the like) into selected vessels **100** at prescribed times and media temperatures. Additional examples of mechanisms for operating or controlling various *in situ* operative components are disclosed for example in above-referenced U.S. Patent No. 6,962,674, assigned to the assignee of the present disclosure.

[0045] The head assembly **904** may include a programmable systems control module for controlling the operations of various components of the dissolution test apparatus **900** such as those described above. As also noted above in conjunction with Figure 7, the head assembly **904** may also include a vessel heating control system (module, circuitry, etc.) that interfaces with the components of the direct vessel heating area **140** of each vessel **100** as well as with a temperature probe if provided. Peripheral elements may be located on the head assembly **904** such as an LCD display **932** for providing menus, status and other information; a keypad **934** for providing user-inputted operation and control of spindle speed, temperature, test start time, test duration and the like; and readouts **936** for displaying information such as RPM, temperature, elapsed run time, vessel weight and/or volume, or the like.

[0046] The dissolution test apparatus **900** may further include one or more movable components for lowering operative components **914**, **918**, **920** into the vessels **100** and raising operative components **914**, **918**, **920** out from the vessels **100**. The head assembly **904** may itself serve as this movable component. That is, the entire head assembly **904** may be actuated into vertical movement toward and away from the vessel support member **906** by manual, automated or semi-automated means. Alternatively or additionally, other movable components **938** such as a driven platform may be provided to support one or more of the operative components **914**, **918**, **920** and lower and raise the components **914**, **918**, **920** relative to the vessels **100** at desired times.

[0047] In a typical operation, each vessel **100** is filled with a predetermined volume of dissolution media by pumping media to the media dispensing cannulas from a suitable media reservoir or other source (not shown). One of the vessels **100** may be utilized as a blank vessel and another as a standard vessel in accordance with known dissolution testing procedures. Dosage units are dropped either manually or automatically into one or more selected media-containing vessels **100**, and each stirring element **914** (or other agitation or USP-type device) is rotated within its vessel **100** at a predetermined rate and duration within the test solution as the dosage units dissolve. In other types of tests, a cylindrical basket or cylinder (not shown) loaded with a dosage unit is substituted for each stirring element **914** and rotates or reciprocates within the test solution. For any given vessel **100**, the temperature of the media may be maintained at a prescribed temperature (e.g., approximately 37 +/- 0.5 °C) if certain USP dissolution methods are being conducted or according to a predetermined temperature profile as described above. Media temperature is maintained by operating the components of the direct vessel heating area **140** of each vessel **100** as described above. The various operative components **914**, **918**, **920** provided may operate continuously in the vessels **100** during test runs. Alternatively, the operative components **914**, **918**, **920** may be lowered manually or by an automated assembly **904** or **938** into the corresponding vessels **100**, left to remain in the vessels **100** only while sample measurements are being taken at allotted times, and at all other times kept outside of the media contained in the vessels **100**. During a dissolution test, sample aliquots of media may be pumped from the vessels **100** via the media aspiration cannulas and conducted to an analyzing device (not shown) such as, for example, a spectrophotometer to measure analyte concentration from which dissolution rate data may be generated. In some procedures, the samples taken from the vessels **100** are then returned to the vessels **100** via the media dispensing cannulas (if provided) or separate media return conduits (if provided). Alternatively, sample concentration may be measured directly in the vessels **100** by providing fiber-optic probes as appreciated by persons skilled in the art. After a dissolution test is completed, the media contained in the vessels **100** may be removed via the media aspiration cannulas or separate media removal conduits.

[0048] In general, terms such as "communicate" and "in . . . communication with" (for example, a first component "communicates with" or "is in communication with" a second component) are used herein to indicate a structural, functional, mechanical, electrical, signal, optical, magnetic, electromagnetic, ionic or fluidic relationship between two or more components or elements. As such, the fact that one component is said to communicate with a second component is not intended to exclude the possibility that additional components may be present between, and/or operatively associated or engaged with, the first and second components.

[0049] It will be further understood that various aspects or details of the invention may be changed without departing from the scope of the invention. Furthermore, the foregoing description is for the purpose of illustration only, and not for the purpose of limitation—the invention being defined by the claims.

WHAT IS CLAIMED IS:

1. A dissolution test vessel configured for direct vessel heating, comprising:

a lateral wall disposed about a longitudinal axis of the vessel and comprising an upper end, a lower end axially spaced from the upper end, and an outside surface extending from the upper end to the lower end;

a resistive heating element bonded directly to the outside surface wherein the resistive heating element is integral with the lateral wall and non-removable therefrom, the resistive heating element comprising a first heating element end, a second heating element end, and a heating element section contiguously running from the first heating element end, over a heating zone of the lateral wall and to the second heating element end, the heating element section running along at least two different directions; and

a temperature-sensing element bonded directly to the outside surface wherein the temperature-sensing element is integral with the lateral wall and non-removable therefrom, the temperature-sensing element comprising a first sensing element end, a second sensing element end, and a sensing element section contiguously running from the first sensing element end, over a temperature sensing zone of the lateral wall and to the second sensing element end, the sensing element section running along at least two different directions.

2. The dissolution test vessel of claim 1, further comprising a clear film bonded directly to the outside surface and covering at least a portion of the resistive heating element and the temperature-sensing element

3. The dissolution test vessel of claim 1, further comprising a plurality of bond pads electrically connected to the respective first heating element end, the second heating element end, the first sensing element end, and the second sensing element end.

4. The dissolution test vessel of claim 1, further comprising an electrical contact element disposed at the upper end and comprising a first set of electrical contacts and a second set of electrical contacts, the first set of electrical contacts communicating with the respective first heating element end, the second heating element end, the first sensing element end, and the second sensing element end, and the second set of electrical contacts communicating with the first set of electrical contacts and configured for connection to a heater control circuit external to the dissolution test vessel.

5. The dissolution test vessel of claim 1, further comprising a flanged section disposed about the longitudinal axis and circumscribing the upper end, the flanged section comprising an electrical contact element, the electrical contact element comprising a first set of electrical contacts and a second set of electrical contacts, the first set of electrical contacts communicating with the respective first heating element end, the second heating element end, the first sensing element end, and the second sensing

element end, and the second set of electrical contacts communicating with the first set of electrical contacts and configured for connection to a heater control circuit external to the dissolution test vessel.

6. The dissolution test vessel of claim 5, wherein the electrical contact element is removably attached to the flanged section.

7. The dissolution test vessel of claim 5, wherein the electrical contact element extends radially outward from an outermost diameter of the flanged section relative to the longitudinal axis.

8. The dissolution test vessel of claim 1, wherein the resistive heating element is a first resistive heating element, the heating element section is a first heating element section, and the heating zone is a first heating zone, and further comprising a second resistive heating element bonded directly to the outside surface and comprising a third heating element end, a fourth element end, and an elongated second heating element section contiguously running from the third heating element end, over a second heating zone of the lateral wall and to the fourth heating element end, the second heating element section running along at least two different directions.

9. The dissolution test vessel of claim 8, wherein the first heating zone is disposed axially above the second heating zone, and the temperature sensing zone is disposed at least partially within the second heating zone.

10. A dissolution test apparatus configured for direct vessel heating, comprising:

a vessel support member having an aperture;

a heater control system; and

a vessel mounted at the vessel support member, the vessel comprising:

a lateral wall disposed about a longitudinal axis of the vessel and comprising an upper end, a lower end axially spaced from the upper end, and an outside surface extending from the upper end to the lower end;

a resistive heating element bonded directly to the outside surface wherein the resistive heating element is integral with the lateral wall and non-removable therefrom, the resistive heating element comprising a first heating element end in signal communication with the heater control system, a second heating element end in signal communication with the heater control system, and an elongated heating element section contiguously running from the first heating element end, over a heating zone of the lateral wall and to the second heating element end, the heating element section running along at least two different directions; and

a temperature-sensing element bonded directly to the outside surface wherein the temperature-sensing element is integral with the lateral wall and non-removable therefrom, the temperature-sensing element comprising a first sensing element end in signal communication with the heater control system, a second sensing element end in signal communication with the heater control system, and an elongated sensing element section contiguously running from the first sensing element end, over a temperature sensing zone of the lateral wall and to the second sensing element end, the sensing element section running along at least two different directions.

11. The dissolution test apparatus of claim 10, further comprising a clear film bonded directly to the outside surface and covering at least a portion of the resistive heating element and the temperature-sensing element.

12. The dissolution test apparatus of claim 10, wherein the vessel further comprises an electrical contact element disposed at the upper end and comprising a first set of electrical contacts and a second set of electrical contacts, the first set of electrical contacts communicating with the respective first heating element end, the second heating element end, the first sensing element end, and the second sensing element end, and the second set of electrical contacts communicating with the first set of electrical contacts and with the heater control system.

13. The dissolution test apparatus of claim 10, wherein the vessel further comprises a flanged section disposed on the vessel support member and circumscribing the upper end, the vessel alignment ring comprising an electrical contact element, the electrical contact element comprising a first set of electrical contacts and a second set of electrical contacts, the first set of electrical contacts communicating with the respective first heating element end, the second heating element end, the first sensing element end, and the second sensing element end, and the second set of electrical contacts communicating with the first set of electrical contacts and with the heater control system.

14. The dissolution test apparatus of claim 13, wherein the vessel support member comprises a set of vessel support member electrical contacts in signal communication with the heater control system, and the second set of electrical contacts of the electrical contact element are removably connected to the respective vessel support member electrical contacts.

15. The dissolution test apparatus of claim 10, wherein the electrical contact element extends radially outward from an outermost diameter of the flanged section relative to the longitudinal axis and into a recess of the vessel support member.

16. The dissolution test apparatus of claim 10, wherein the vessel support member includes a plurality of apertures, the vessel is one of a plurality of vessels mounted at the respective apertures, each vessel includes a respective resistive heating element and a temperature-sensing element, and each resistive heating element and temperature-sensing element is in signal communication with the heater control system.

17. A method for fabricating a dissolution test vessel, the method comprising:

depositing a first flowable material directly on an outside surface of a lateral wall of a vessel to form a resistive heating element integral with and non-removable from the lateral wall, the resistive heating element comprising a first heating element end, a second heating element end, and an elongated heating element section contiguously running from the first heating element end, over a heating zone of the lateral wall and to the second heating element end, the heating element section running along at least two different directions;

depositing a second flowable material directly on the outside surface to form a temperature-sensing element integral with and non-removable from the lateral wall, the temperature-sensing element comprising a first sensing element end, a second sensing element end, and an elongated sensing element section contiguously running from the first sensing element end, over a temperature sensing zone of the lateral wall and to the second sensing element end, the sensing element section running along at least two different directions; and

attaching a contact block to an upper end of the vessel and placing the contact block in electrical communication with the resistive heating element and the temperature-sensing element.

18. The method of claim 17, further comprising applying a clear film directly to the outside surface wherein the film covers at least a portion of the resistive heating element and the temperature-sensing element.

19. The method of claim 17, wherein the first flowable material and the second flowable material are selected from the group consisting of conductive inks, resistive inks, conductive epoxies, and resistive epoxies.

20. The method of claim 17, further comprising attaching a flanged section to the upper end, wherein the contact block is attached to the flanged section.

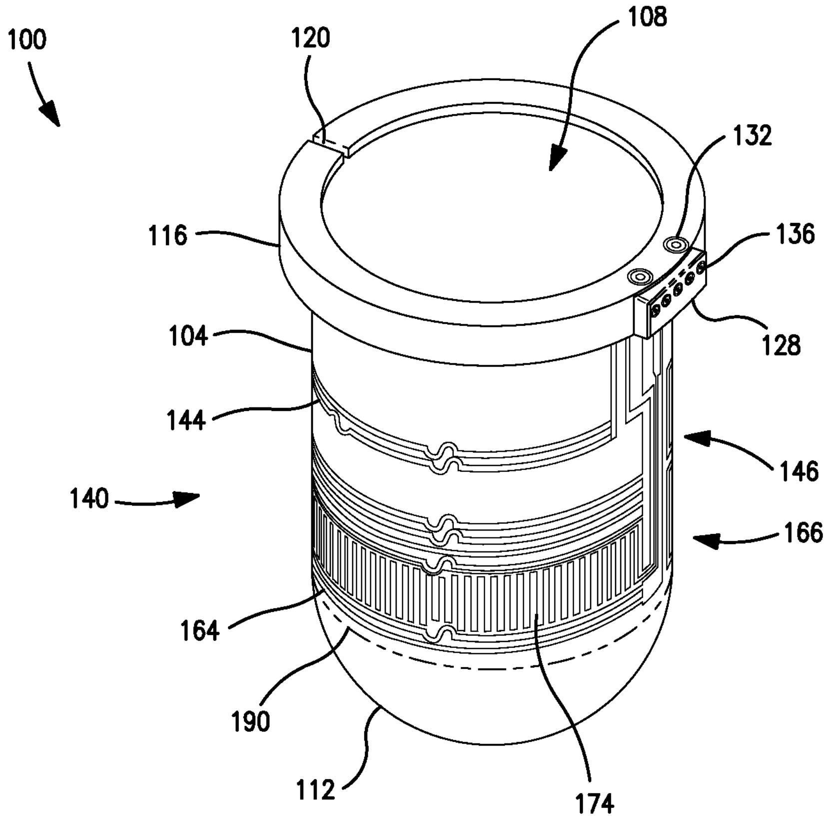

FIG. 1

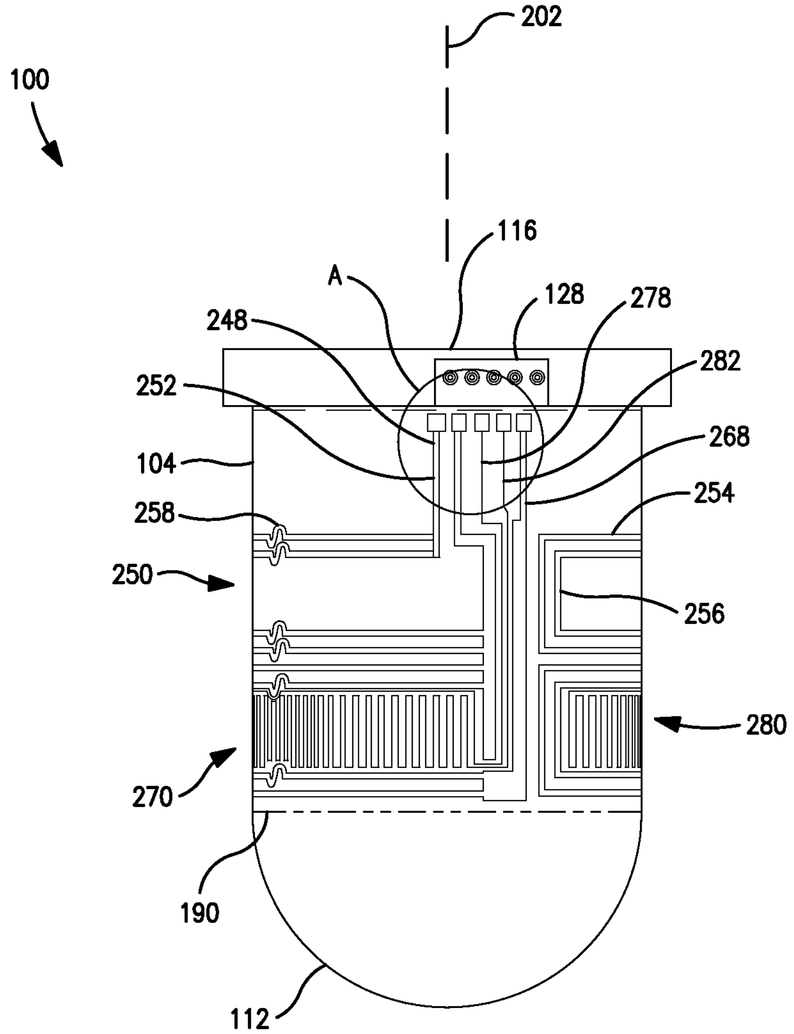
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FIG. 2

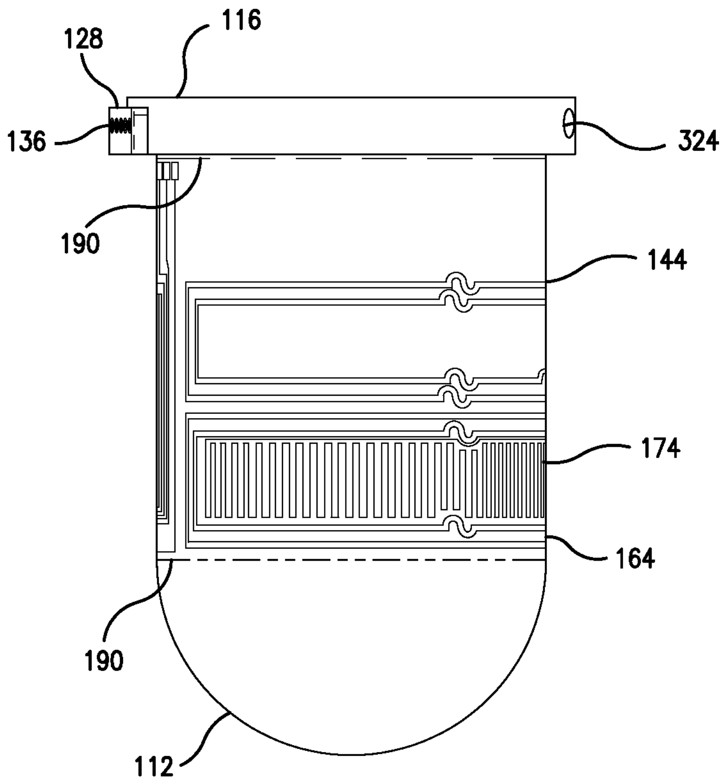

FIG. 3

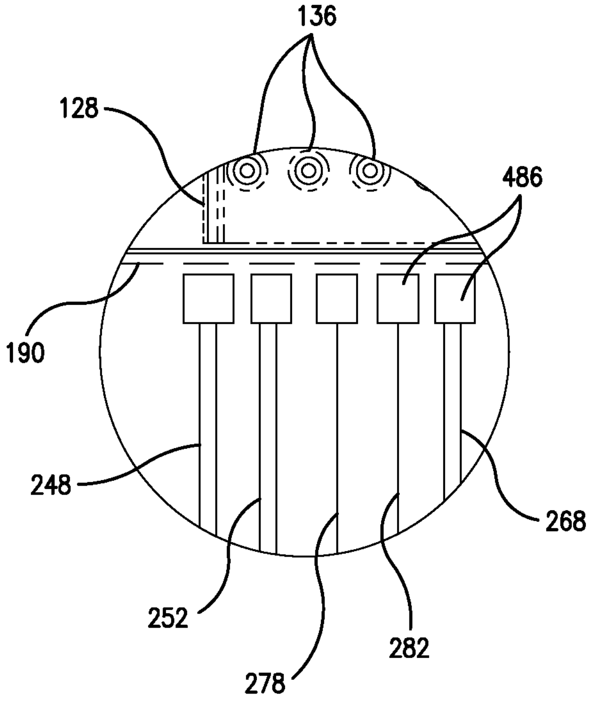

FIG. 4

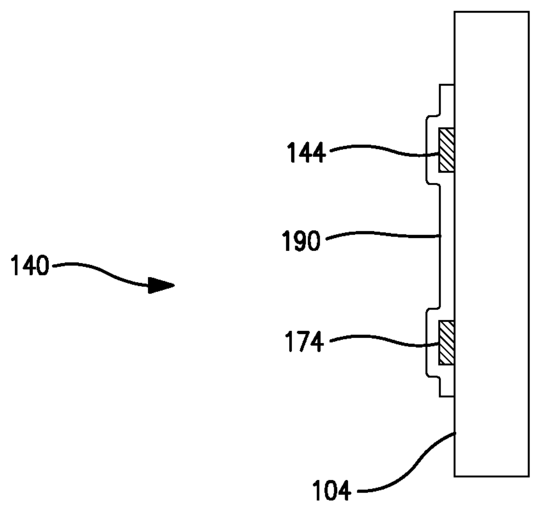

FIG. 5

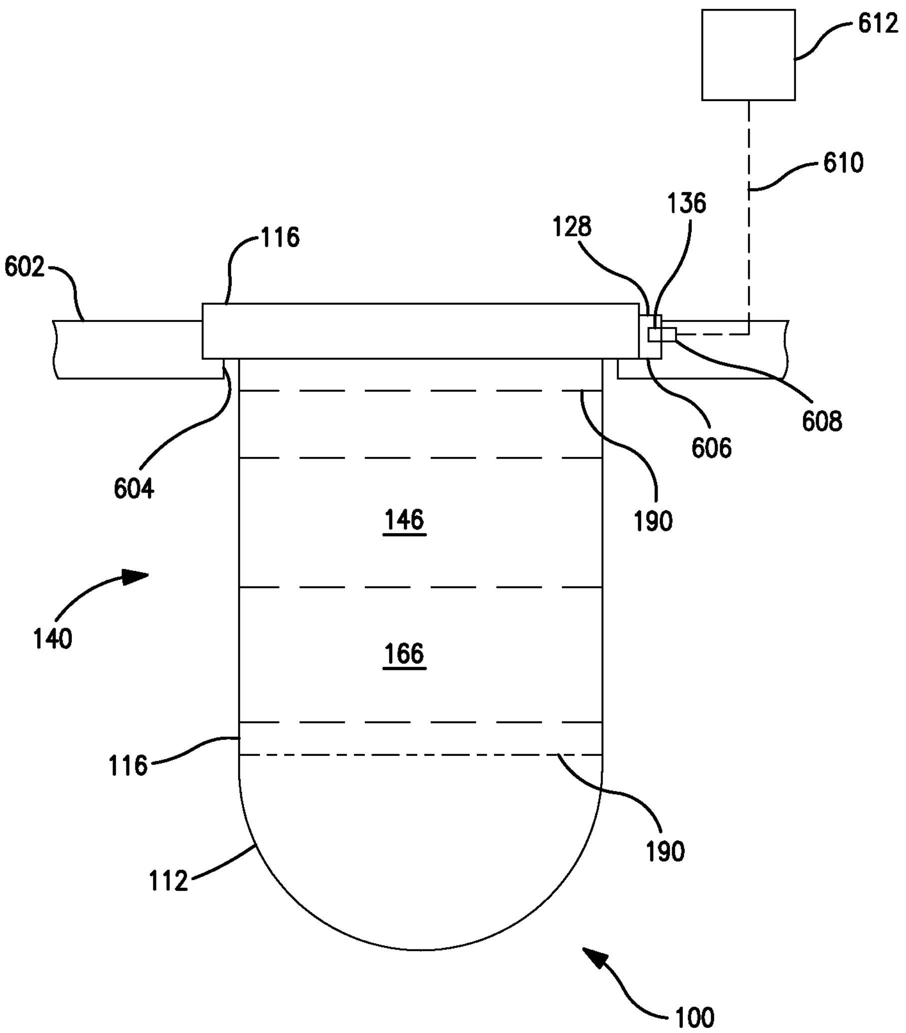
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FIG. 6

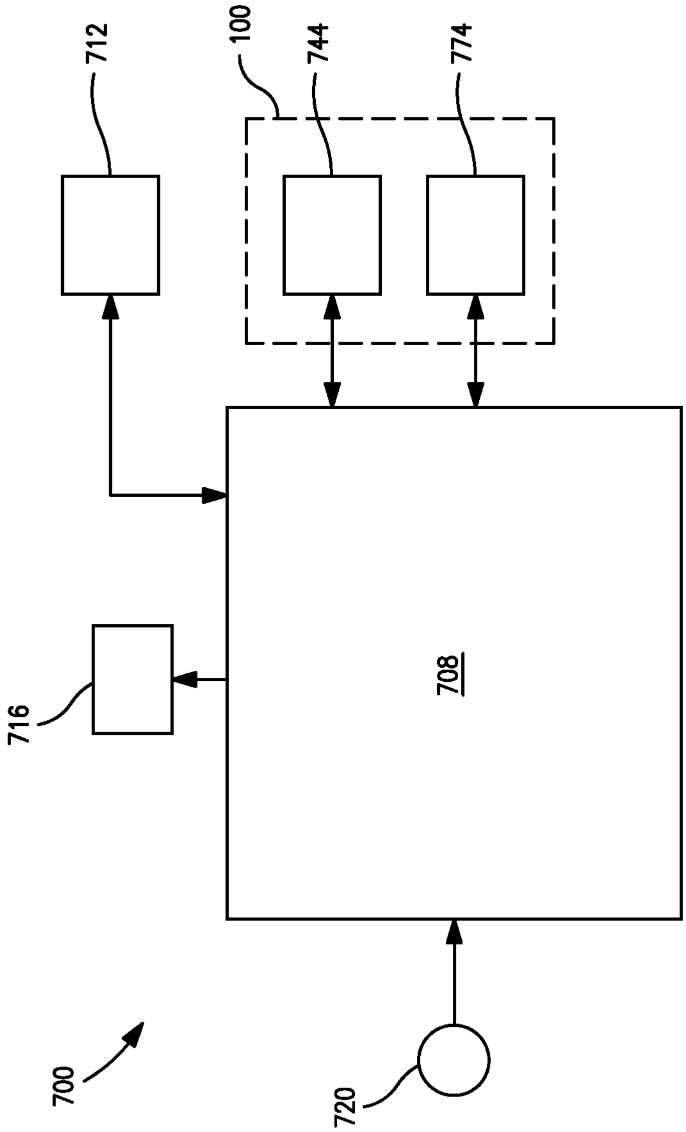

FIG. 7

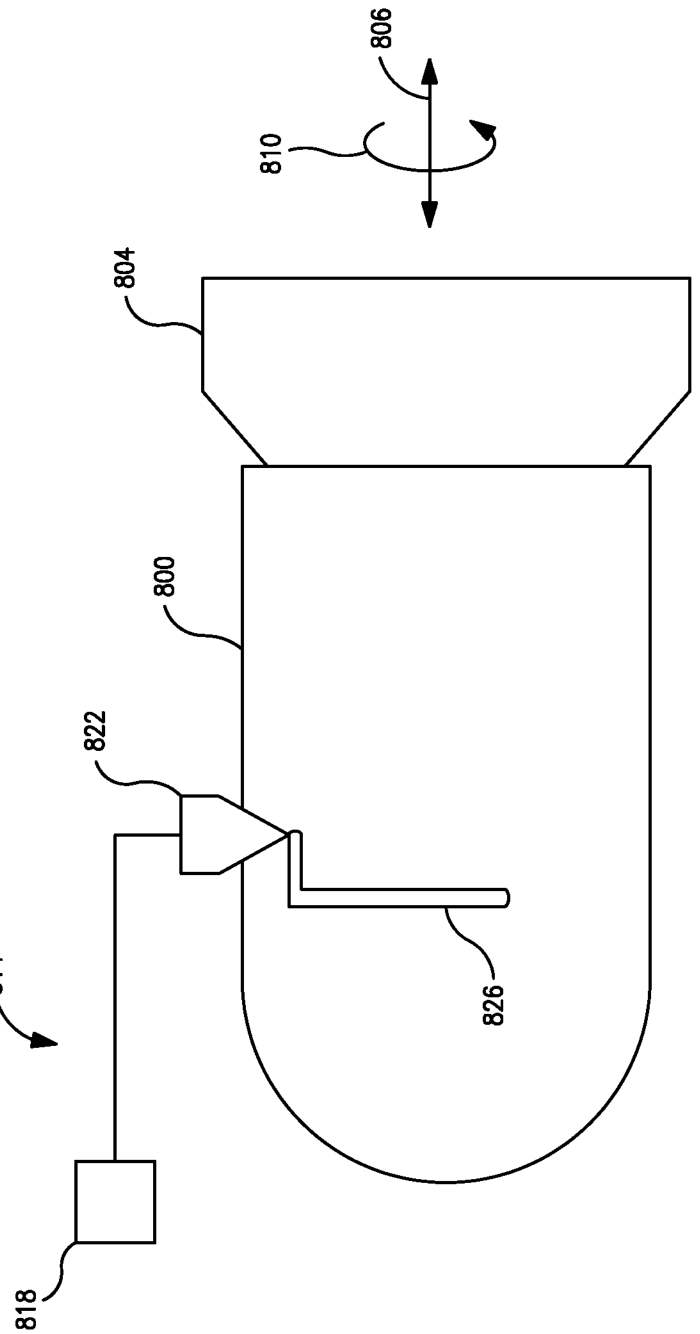

FIG. 8

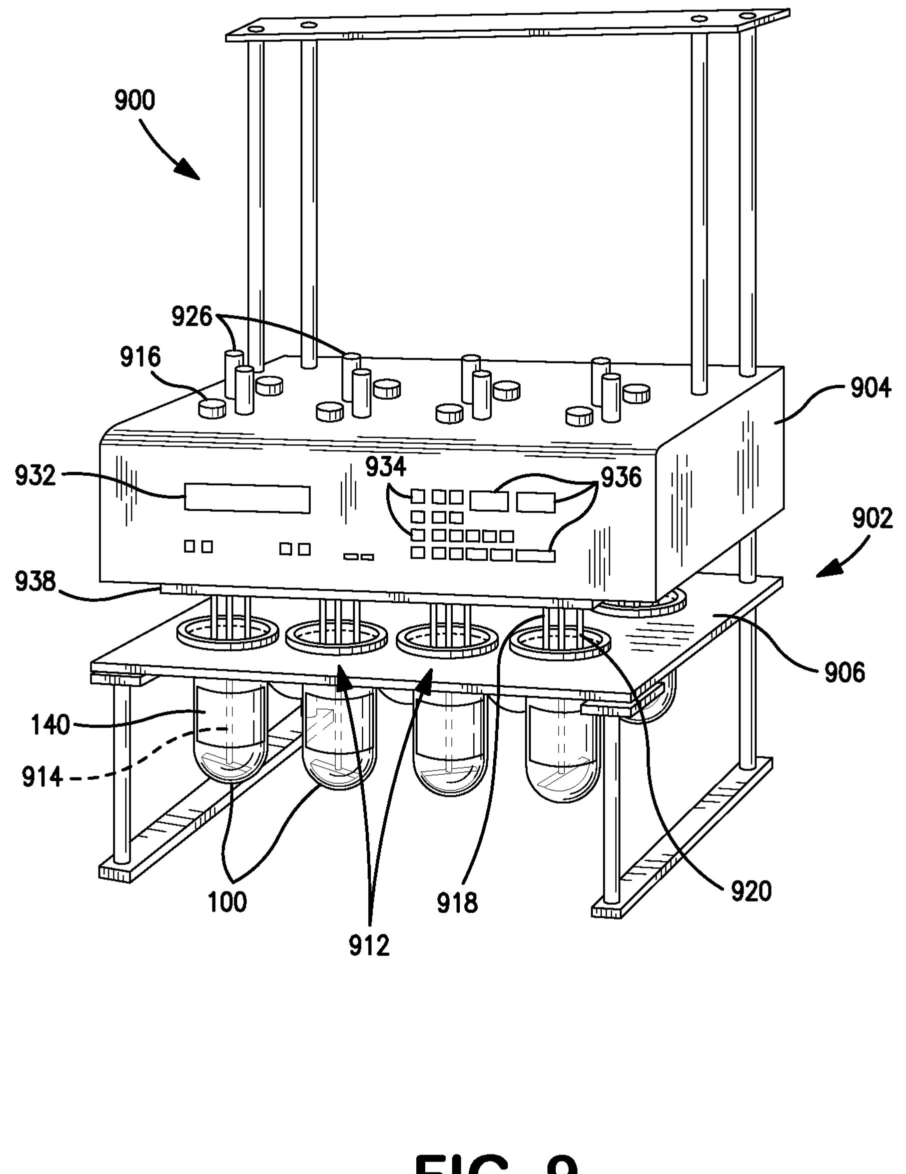

FIG. 9