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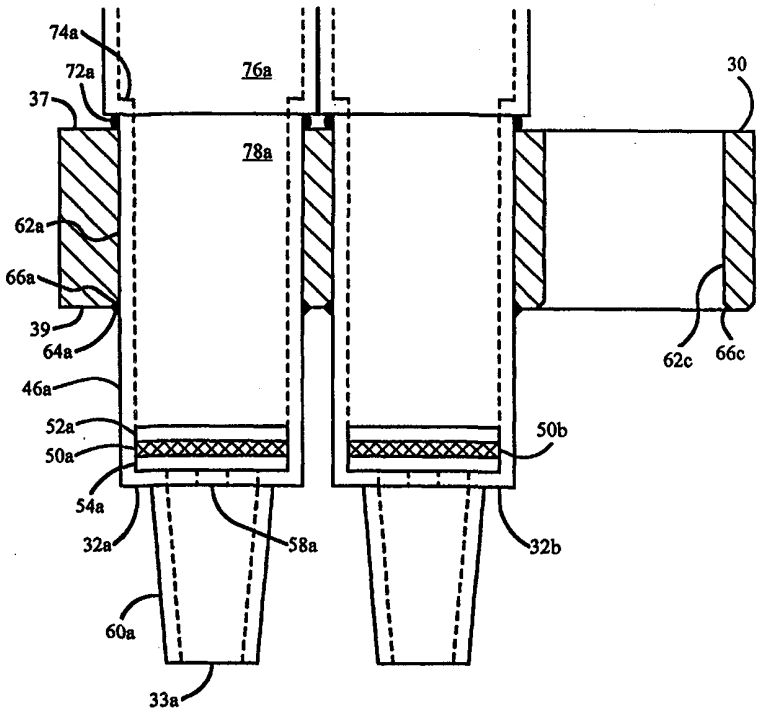
(54) Title: MODULAR SOLID PHASE EXTRACTION PLATE ASSEMBLY

(57) Abstract

A 96–well solid phase extraction (SPE) plate assembly comprises a common base plate having plural apertures (bores), and removable extraction cartridges (containers, tubes) extending through the bores. The plate assembly is mounted on a conventional 96–well plate vacuum manifold. The cartridges preferably snap into the base plate, but may also screw in. The apertures have annular counterapertures (counterbores) complementary to annular ridges protruding from the side walls of the cartridges. Each ridge snaps into a corresponding counteraperture. The modular design allows the end user to customize the extraction medium mix of the extraction plate assembly by inserting extraction containers having different sorbents into a common base plate. Gaskets are used to maintain a vacuum seal between the base plate and extraction cartridges, for maintaining a pressure gradient across the sorbents.



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MODULAR SOLID PHASE EXTRACTION PLATE ASSEMBLY

FIELD OF INVENTION

This invention relates to systems and methods for extracting solutes from solutions, and in particular to components and methods for solid phase extraction (SPE).

BACKGROUND OF THE INVENTION

In conventional solid phase extraction methods, solutes of interest are isolated from solution by running the solution through a solid phase extraction medium (sorbent) such as coated silica particles. A 96-well solid phase extraction plate is typically placed on a vacuum manifold. The vacuum manifold provides a pressure gradient over sorbents in the plate wells, driving the flow of liquid through the wells. The solutes of interest bind to the extraction medium, while the rest of the solution passes on to collection containers. The solutes of interest can then be recovered by running a suitable solvent through the extraction medium.

Typical extraction plates are monolithic 96-well plates having identical sorbents in all their wells. For descriptions of such plates see for example U.S. Patent Nos. 5,417,923, 5,047,215, 5,679,310, and European Patent Publication No. 0576602B1. The end user of a conventional monolithic plate cannot customize the sorbents in different wells of the plate in a practical manner. Thus, an end user investigating different assay methodologies and sorbents for a particular application may need a new 96-well extraction plate for each tested condition, even if only a few wells are required.

SUMMARY OF THE INVENTION

The present invention provides an extraction apparatus comprising a vacuum manifold connected to a vacuum source, defining a collection enclosure; a plurality of collection containers disposed in the collection enclosure; and an extraction plate assembly mounted on the manifold and covering the collection enclosure. The extraction plate assembly comprises a base plate mounted on the manifold, and a plurality of extraction cartridges mounted on the base plate.

The base plate has a top surface and a bottom surface. A plurality of apertures extend through the base plate from the top surface to the bottom surface. Each extraction cartridge has an inlet and an outlet. Each cartridge is removably locked in a corresponding aperture of the base plate with its inlet situated opposite its outlet relative to the base plate. Locking the extraction cartridges to the base plate allows the end user to reuse the base plate, replace used extraction cartridges, and customize the extraction media of the extraction plate assembly. Reusing the base plate allows the end user to reduce the amount of material discarded with each use.

Each cartridge comprises a solid-phase extraction medium disposed between its inlet and its outlet, for extracting solutes of interest from a liquid sample inserted into the cartridge through its inlet. Different cartridges of the extraction plate assembly may have different

extraction media. Each base plate aperture and cartridge outlet faces a corresponding collection container when the extraction plate assembly is mounted on the manifold, such that the collection container receives liquid from the cartridge outlet.

Each cartridge is preferably locked to the base plate through a snap-in lock. A snap-in lock allows relatively easy insertion and removal of cartridges from the base plate, and allows multiple linked cartridges to be removed from or inserted into the base plate simultaneously, in one motion. Preferably, the base plate has a counteraperture defined in the side wall of each aperture, and each extraction cartridge has a snap-in ridge for engaging a corresponding counteraperture to snap the cartridge into the base plate. Alternatively, each aperture may have a ridge defined in its side wall, and each cartridge may have a corresponding complementary depression for engaging the ridge.

The counteraperture is preferably situated at the bottom end of its corresponding aperture, along the bottom surface of the base plate, such that the snap-in ridge is positioned along the bottom surface when the cartridge is locked to the base plate. The counteraperture may also be situated within its corresponding aperture, such that the snap-in ridge is enclosed within the aperture when the extraction cartridge is locked to the base plate. Positioning the counteraperture at a base plate edge allows relatively close spacings between adjacent apertures, by relaxing the constraints imposed on the minimum inter-counteraperture spacing by base plate mechanical stability requirements. Closely spacing adjacent apertures allows increased cartridge fluid-holding volumes as a fraction of the total volume defined by the overall dimensions of the extraction plate assembly.

In an alternative embodiment, each cartridge is locked to the base plate through a screw-in lock. The base plate then has a helical groove defined in each aperture, and each cartridge has a helical thread complementary to the groove, for engaging the groove to screw the cartridge into the base plate.

The extraction plate assembly does not allow any substantial air paths therethrough other than through the extraction media. If the seal provided by the locking interface is not sufficient, a gasket may be used to establish a vacuum seal along an interface between each cartridge and the base plate. The gasket is preferably positioned between the top surface of the base plate and a lip of the cartridge. The gasket prevents gas flow through its corresponding base plate aperture, outside the cartridge.

The present invention further provides a method of making an extraction plate assembly and an extraction apparatus of the present invention. The base plate and extraction cartridges are individually manufactured by injection molding, extrusion, or other known techniques. The extraction cartridges are then locked into the base plate. The resulting extraction plate assembly if mounted onto the manifold, and positioned underneath a fluid-handling apparatus.

BRIEF DESCRIPTION OF THE DRAWINGS

Fig. **1-A** shows a perspective view of a preferred extraction apparatus of the present invention.

Fig. **1-B** shows a side sectional view of the apparatus of Fig. **1-A**.

Fig. **1-C** shows a top view of the apparatus of Fig. **1-A**.

Fig. **2-A** shows a side sectional view of two extraction containers locked in a base plate, according to the preferred embodiment of the present invention.

Fig. **2-B** shows a top view of one of the extraction containers of Fig. **2-A**.

Figs. **3-A** through **3-E** illustrate side sectional views of extraction containers locked in base plates, according to respective alternative embodiments of the present invention.

DETAILED DESCRIPTION OF THE INVENTION

In the following description, the term "vacuum" is understood to encompass partial vacuum pressures. The terms "top" and "bottom" are understood to be relative terms characterizing spatial relationships relative to a major plane of a base plate; the terms need not refer to the direction of gravity.

The following description illustrates embodiments of the invention by way of example and not necessarily by way of limitation.

Fig. **1-A** shows a perspective view of a preferred extraction apparatus **20** of the present invention. Figs. **1-B** and **1-C** show side sectional and top views of apparatus **20**, respectively. Apparatus **20** comprises a vacuum manifold **22**, and an extraction plate assembly **26** mounted on manifold **22**. Extraction plate assembly **26** comprises a base plate **30** mounted on manifold **22**, and a plurality of extraction cartridges (containers, tubes) **32** mounted on base plate **30**. Cartridges **32** are locked into base plate **30**, allowing an end user to replace selected cartridges **32** and reuse base plate **30**. Base plate **30** is hatched in Figs. **1-B** and **1-C** for clarity of presentation. Extraction plate assembly **26** preferably comprises 96 extraction cartridges **32**, each passing through an aperture in base plate **30**.

As illustrated in Fig. **1-B**, each extraction cartridge **32** has an inlet **31** and an outlet **33**. Each cartridge **32** further comprises a conventional extraction solid phase extraction medium (not shown) positioned in the fluid path between inlet **31** and outlet **33**. When cartridge **32** is mounted on base plate **30**, inlet **31** and outlet **33** are situated on opposite sides of base plate **30**. Inlet **31** is formed by an opening at the top of cartridge **32**, above base plate **30**. Outlet **33** is formed by a spout at the bottom of cartridge **32**, underneath base plate **30**. A conventional robotic sample-handling apparatus (not shown) is positioned to insert a sample through inlet **31**. The sample-handling apparatus may constrain the height of extraction apparatus **20** and cartridges **32**.

Manifold **22** may be a conventional vacuum manifold for holding 96-well collection plates. Manifold **22** comprises a manifold base **24a**, and a support part **24b** mounted on manifold base **24a**. An air conduit **36** is formed in one of the side walls of manifold base **24a**, for

connecting the interior of manifold **22** to a conventional vacuum source such as a vacuum pump (not shown). The direction of air flow through air conduit **36** is illustrated by the arrow **38**.

Support part **24b** has a rectangular top aperture for receiving base plate **30**. Base plate **30** is mounted on support part **24b**. Manifold **22** and extraction plate assembly **26** define a sealed enclosure **34** which is externally connected only through air conduit **36** and extraction containers **32**, as explained in more detail below. Gaskets (not shown) may be provided at the interfaces between manifold base **24a** and support part **24b**, and between support part **24b** and base plate **30**, for sealing enclosure **34**.

A collection plate **40** is positioned in manifold **22**, within enclosure **34**. Collection plate **40** can be a standard 96-well collection plate. Collection plate **40** comprises a plurality of collection containers **44** each positioned facing a corresponding aperture of base plate **30** and a corresponding outlet **33**. Each collection container **44** is positioned to receive liquid that has passed through a corresponding extraction cartridge **32**.

The vacuum pump connected to air conduit **36** establishes a partial vacuum within enclosure **34**. Liquid samples each comprising multiple solutes are inserted into inlets **31** by a conventional automatic pipetter (not shown). The pressure gradient across extraction cartridges **32** draws the samples through cartridges **32**. The extraction media within cartridges **32** capture solutes of interest from the samples, while the remaining solutes and solvent are transferred to collection containers **44** through outlets **33**. The solutes of interest can then be eluted from cartridges **32**.

Fig. **2-A** shows a more detailed side sectional view of part of extraction plate assembly **26**, illustrating part of two extraction cartridges **32a-b** and base plate **30**. Fig. **2-B** shows a top view of extraction cartridge **32a**. Cartridge **32b** is similar to cartridge **32a**. As illustrated in Fig. **2-A**, cartridge **32a** comprises a generally cylindrical fluid-holding body **46a**, and a tapered outlet spout **60a** extending downward from fluid-holding body **46a**. A disk-shaped or cylindrical solid-phase extraction medium **50a** is positioned in the fluid passage of cartridge **32a**, at the bottom of fluid-holding body **46a**. Extraction medium **50a** is a conventional solid phase extraction (SPE) silica- or polymer-based sorbent. Suitable surface functional groups for the sorbent include cyano, C1, C2, C4, C8, C18, cyclohexyl, phenyl, among others. Extraction medium **50a** is sandwiched between two conventional frit disks **52a**, **54a**. Extraction medium **50a** may be different from the extraction medium **50b** of cartridge **32b**.

The frit-sorbent composite formed by frit disks **52a, 54a** and extraction medium **50a** is pressed against the inside side wall of cartridge **32**. Extraction medium **50a** and frit disks **52a, 54a** are supported by a support structure **58a** extending into the fluid passage of cartridge **32a**, as illustrated in Fig. **2-B**. The transverse cross-section of support structure **58a** is preferably cross-shaped. Support structure **58a** prevents the frit-sorbent composite from sagging into outlet spout **60a** as liquid passes through cartridge **32a**.

As illustrated in Fig. **2-A**, cartridge **32a** is slidably mounted on base plate **30** through an aperture **62a**. Aperture **62a** extends through base plate **30** from a top surface **37** to a bottom surface **39** of base plate **30**. Top surface **37** and bottom surface **39** are preferably substantially planar, parallel surfaces, but may generally include recessed or protruding sections. Aperture **62a** is preferably a cylindrical bore having an inside diameter substantially equal to the outside diameter of the part of cartridge **32a** within aperture **62a**. Aperture **62a** may generally have a non-circular cross-section, such as a square, rectangular, or oval cross-section.

Aperture **62a** has an annular counteraperture (depression, recess) **66a** defined at the bottom end of its side wall, along bottom surface **39** of base plate **30**. Counteraperture **66a** lies in a plane perpendicular to the longitudinal axis of aperture **62a**. Cartridge **32a** has a snap-in ridge **64a** protruding from its side wall. Ridge **64a** is complementary to counteraperture **66a**. At least part of the surface of ridge **64a** engages counteraperture **66a** to snap-in cartridge **32a** into base plate **30**. Ridge **64a** preferably has a triangular longitudinal cross-section. The top planar surface of ridge **64a** abuts counteraperture **66a**, facilitating the locking and removal of cartridge **32a**. The bottom planar surface of ridge **64a** facilitates the insertion of cartridge **32a** into aperture **62a**. A free counteraperture **66c** is shown for an aperture **62c** in the absence of a corresponding extraction cartridge.

A PTFE (teflon) or rubber gasket **72a** is positioned between top surface **37** and a lip **74a** of cartridge **32a**. Gasket **72a** may be provided as part of base plate **30**, and may be attached to base plate **30** by an adhesive. Gasket **72a** may also be provided as part of cartridge **32a**. Gasket **72a** prevents gas flow through aperture **62a** outside cartridge **32a**, between the side walls of aperture **62a** and cartridge **32a**. Gasket **72a** establishes a vacuum seal along the interface between cartridge **32a** and base plate **30**, ensuring that the pressure gradient across base plate **30** efficiently drives the flow of fluid through cartridge **32a**. Lip **74a** is preferably defined by the interface between an upper section **76a** and a lower section **78a** of fluid holding body **46a**. Upper section **76a** has a larger transverse size than lower section **78a**.

Extraction cartridge **32a** is preferably made of a plastic such as polypropylene. Other suitable materials for cartridge **32a** include polyethylene or PTFE. Cartridge **32a** is preferably made by injection molding. Other suitable methods for forming cartridge **32a** include extrusion or machining.

For a 96-well extraction plate assembly, cartridge **32a** has a fluid-holding volume on the order of a few ml, typically between 1 ml and 5 ml, preferably about 2 ml . The center-to-center spacing between adjacent cartridges **32** on base plate **30** is on the order of mm to cm, preferably about 9 mm. The side wall of cartridge **32a** preferably has a constant thickness on the order of tenths of mm to mm, preferably about 0.5 mm. Upper section **76a** of fluid holding body **46a** has a length on the order of a few cm, preferably about 38 mm, an outside diameter on the order of mm, preferably about 9 mm, and an inside diameter on the order of mm, preferably about 8 mm. Lower section **78a** of fluid holding body **46a** has a length on the order of cm, preferably about

17 mm, an outside diameter on the order of mm, preferably about 8 mm, and an inside diameter on the order of mm, preferably about 7 mm. The diameter of aperture **62a** is equal to the outside diameter of lower section **78a**.

The distance between lip **74a** and the center of ridge **64a** is on the order of mm to cm, preferably about 6.5 mm. Ridge **64a** has a longitudinal dimension of about 1 mm. The sum of the thickness of gasket **72a** and the distance between upper surface **37** and lower surface **39** of base plate **30** is about equal to the distance between lip **74a** and the center of ridge **64a**. Ridge **64a** protrudes about 0.25 mm from the side wall of cartridge **32a**. Counteraperture **66a** preferably has a depth of about 0.35 mm, and forms angles of about 45° with respect to the side wall of aperture **62a** and with bottom surface **39** of base plate **30**. The extent of base plate **30** between cartridges **32a-b** is preferably about 1 mm along aperture **62a**, and at least 0.3 mm at the bottom of counteraperture **66a**.

The snap-in attachment of cartridges **32** to base plate **30** allows easy assembly of a heterogeneous extraction plate assembly **26** from cartridges having different extraction media. An end user may obtain extraction cartridges **32** separately from base plate **30**, and then choose the distribution of extraction media to use for extraction plate assembly **26**. A heterogeneous extraction plate assembly allows easily testing multiple extraction media simultaneously, thus facilitating method development, optimization studies, and comparisons or different extraction media. Furthermore, the end user may reuse base plate **30** with new cartridges **32**, or use base plate **30** with only a subset of its potential cartridges **32** by stoppering the unused apertures. By contrast, an end user constrained to use prior-art monolithic extraction plates would need a large number of different extraction plates for testing different extraction media. The end user may need a means of identifying used wells in the monolithic plate, or may need to discard an entire monolithic plate after each use even if a large number of wells within each monolithic plate are not needed for a particular testing method.

Placing counteraperture **66a** along an external surface of base plate **30** allows reducing the spacing between adjacent cartridges **32**. A counteraperture internal to the base plate may require larger spacings between adjacent cartridges, since the base plate internal side walls between adjacent counterapertures need to provide sufficient mechanical stability to the base plate. That is, mechanical stability concerns may require larger inter-counteraperture spacings for internal counterapertures than for external counterapertures.

Placing counteraperture **66a** along bottom surface **39** and gasket **72a** along top surface **37** allows easy insertion of cartridge **32a** from the top of base plate **30**. The transverse cross-sections of cartridge **32a**, aperture **62a**, and counteraperture **66a** are preferably circular for ease of manufacture of cartridge **32a** and base plate **30**, and for ease of insertion of cartridge **32a** into base plate **30**. A flat contact surface for the interface between ridge **64a** and counteraperture **66a** is preferred for ease of manufacture of cartridge **32a** and base plate **30**. Defining counteraperture **66a** in base plate **30** and ridge **64a** on cartridge **32** may allow the use of fewer

mold parts during the manufacture of cartridge **32** than defining a ridge in the base plate and a complementary depression in the cartridge.

Fig. **3-A** shows a side sectional view of part of an extraction cartridge **132** and a corresponding base plate **130**, according to an alternative embodiment of the present invention. Base plate **130** has an annular counteraperture **166** which is internal to its corresponding aperture **162**. In longitudinal cross-section (in the plane of Fig. **3-A**), counteraperture **166** has a curved shape. Cartridge **132** has an annular ridge **164** complementary to counteraperture **166**. The curved surface of the interface between ridge **164** and counteraperture **166** allows an improved fit between cartridge **132** and base plate **130**.

Fig. **3-B** shows a side sectional view of part of an extraction cartridge **232** and a base plate **230**, according to another alternative embodiment of the present invention. Base plate **230** comprises an aperture **262** extending therethrough. Aperture **262** comprises an upper section **262a** and a lower section **262b**. Upper section **262a** has a larger diameter than lower section **262b**. A counteraperture **266** is defined in lower section **262b**. Base plate **230** has a top surface **237** including a recessed portion **237'**.

Cartridge **232** comprises a fluid-holding body **246** and an outlet spout **260** extending downward from fluid-holding body **246**. Fluid holding body **246** defines a lip **274** at its interface with outlet spout **260**. Cartridge **232** further comprises a ridge **264** protruding from outlet spout **264.** Ridge **264** is complementary to counteraperture **266**, and engages counteraperture **266** to lock cartridge **232** to base plate **230**. A gasket **272** is sandwiched between lip **274** and recessed portion **237'**, sealing aperture **262** and preventing air flow outside cartridge **232**.

Cartridge **232** is part of a monolithic group of cartridges connected by a connection plate **235**. The cartridge group may be for example a strip of 8 or 12 cartridges having identical extraction media. The cartridge group may be collectively locked to and removed from base plate **230**. The cartridge group and connection plate **235** may be formed by an individual molded piece.

Fig. **3-C** shows a side sectional view of part of an extraction cartridge **332** and a corresponding base plate **330**, according to yet another alternative embodiment of the present invention. Base plate **330** has an aperture **362** extending therethrough. A helical groove **366** is defined in aperture **362**. Helical groove **366** extends through aperture **362**. Cartridge **364** has a helical thread **364** protruding from its side wall. Helical thread **364** is complementary to helical groove **366**, and engages helical groove **366** to screw cartridge **332** into plate **330**.

Fig. **3-D** shows a side sectional view of part of an extraction cartridge **432** and a corresponding base plate **430**, according to still another alternative embodiment of the present invention. Cartridge **432** has a helical thread **464** protruding from an outlet spout **460**. Helical thread **464** engages a complementary helical groove **466** defined in a lower section **462b** of an aperture **462**. Outlet spout **460** extends through lower section **462b**. A fluid-holding body **446**

of cartridge **432** extends through an upper section **462a** of aperture **462**. A gasket **472** rests on base plate **430** at the upper end of upper section **462**. A lip **474** of cartridge **432** is pressed down onto gasket **472**.

Fig. **3-E** shows a side sectional view of a part of an extraction cartridge **532** and a corresponding base plate **530**, according to yet another alternative embodiment of the present invention. Base plate **530** has an aperture **562** for receiving cartridge **532**. A ridge **564** protrudes from the side wall of aperture **562**. Cartridge **532** has an annular depression (recess, notch) **566** defined in its side wall, for engaging ridge **564** to snap cartridge **532** into base plate **530**.

It will be clear to one skilled in the art that the above embodiments may be altered in many ways without departing from the scope of the invention. For example, the base plate need not be a monolithic molded part, but may include two or more sandwiched flat sections. More than one counteraperture may be used. Various approaches may be suitable for locking the extraction cartridges to the base plate and providing a vacuum seal between the cartridges and the base plate, including for example press-fitting each cartridge into a corresponding tapered aperture in the base plate. Positive pressure may be used to drive the samples through the extraction cartridges, by connecting each cartridge through an individual tube to a positive pressure source. Accordingly, the scope of the invention should be determined by the following claims and their legal equivalents.

WHAT IS CLAIMED IS:

1. An extraction plate assembly for extracting solutes from liquid samples, comprising:

a) a base plate having a top surface and a bottom surface, and a plurality of apertures extending through said base plate from said top surface to said bottom surface, each of said apertures having a counteraperture defined therein; and

b) a plurality of snap-in extraction cartridges each having an inlet and an outlet, each of said cartridges being slidably mounted in a corresponding aperture of said base plate with said inlet situated opposite said outlet relative to said base plate, said each of said cartridges having:

a snap-in ridge for engaging a corresponding counteraperture to snap said each of said cartridges into said base plate, and

a solid phase extraction medium disposed between said inlet and said outlet, for extracting a solute from a liquid sample inserted into said each of said cartridges through said inlet.

2. The plate assembly of claim 1 wherein said corresponding counteraperture is situated substantially at a bottom end of said corresponding aperture, along said bottom surface of said base plate, such that said snap-in ridge is positioned along said bottom surface of said base plate when said each of said cartridges is locked to said base plate.

3. The plate assembly of claim 1 wherein said corresponding counteraperture is situated within said corresponding aperture, such that said snap-in ridge is enclosed within said corresponding aperture when said each of said extraction cartridges is locked to said base plate.

4. The plate assembly of claim 1 further comprising a gasket positioned between said top surface and a lip of said each of said cartridges, for preventing gas flow through said corresponding aperture outside said each of said cartridges.

5. The plate assembly of claim 1 wherein said plurality of cartridges comprises a first cartridge having a first solid phase extraction medium, and a second cartridge having a second solid phase extraction medium different from said first solid phase extraction medium.

6. An extraction plate assembly for extracting solutes from liquid samples, comprising:

a) a base plate having a top surface and a bottom surface, and a plurality of apertures extending through said base plate from said top surface to said bottom surface; and

b) a plurality of extraction cartridges each having an inlet and an outlet, each of said cartridges being removably locked in a corresponding aperture of said base plate with said inlet situated opposite said outlet relative to said base plate, said each of said cartridges

having a solid phase extraction medium disposed between said inlet and said outlet, for extracting a solute from a liquid sample inserted into said each of said cartridges through said inlet.

7. The plate assembly of claim 6 wherein:

a) said corresponding aperture has a counteraperture defined therein; and

b) said each of said cartridges has a snap-in ridge for engaging said counteraperture to snap said each of said cartridges into said base plate.

8. The plate assembly of claim 6 wherein:

a) said corresponding aperture has a helical groove defined therein; and

b) said each of said cartridges has a helical thread for engaging said groove to screw said each of said cartridges into said base plate.

9. The plate assembly of claim 6 wherein:

a) said corresponding aperture has a ridge protruding therefrom; and

b) said each of said cartridges has a depression for engaging said ridge to snap said each of said cartridges into said base plate.

10. The plate assembly of claim 6 further comprising a gasket positioned between said top surface and a lip of said each of said cartridges, for preventing gas flow through said corresponding aperture outside said each of said cartridges.

11. An extraction apparatus for extracting solutes from liquid samples, comprising:

a) a vacuum manifold connected to a vacuum source, defining a collection enclosure;

b) a plurality of collection containers disposed in said collection enclosure;

c) a base plate mounted on said vacuum manifold and covering said collection enclosure, said base plate having a top surface, a bottom surface, and a plurality of apertures extending through said base plate from said top surface to said bottom surface, each of said apertures being disposed substantially opposite one of said collection containers; and

d) a plurality of extraction cartridges each having an inlet and an outlet, each of said cartridges being removably locked in a corresponding aperture of said base plate with said inlet situated opposite said outlet relative to said base plate and with said outlet facing a corresponding collection container, said each of said cartridges comprising a solid phase extraction medium disposed between said inlet and said outlet, for extracting a solute from a liquid sample inserted into said each of said cartridges through said inlet.

12. The apparatus of claim 11 wherein:

a) said corresponding aperture has a counteraperture defined therein; and

b) said each of said cartridges has a snap-in ridge for engaging said counteraperture to snap said each of said cartridges into said base plate.

13. The apparatus of claim 12 wherein said counteraperture is situated substantially at a bottom end of said corresponding aperture, along said bottom surface of said base plate, such that said snap-in ridge is positioned along said bottom surface of said base plate when said each of said cartridges is locked to said base plate.

14. The apparatus of claim 12 wherein said counteraperture is situated within said corresponding aperture, such that said snap-in ridge is enclosed within said corresponding aperture when said each of said extraction cartridges is locked to said base plate.

15. The apparatus of claim 12 further comprising a gasket positioned between said top surface and a lip of said each of said cartridges, for preventing gas flow through said corresponding aperture outside said each of said cartridges.

16. The apparatus of claim 12 wherein said plurality of cartridges comprises a first cartridge having a first solid phase extraction medium, and a second cartridge having a second solid phase extraction medium different from said first solid phase extraction medium.

17. The apparatus of claim 10 wherein

a) said corresponding aperture has a helical groove defined therein; and

b) said each of said cartridges has a helical thread for engaging said groove to screw said each of said cartridges into said base plate.

18. The apparatus of claim 10 further comprising a gasket positioned between said top surface and a lip of said each of said cartridges, for preventing gas flow through said corresponding aperture outside said each of said cartridges.

19. A method of making an extraction plate assembly for extracting solutes from liquid samples, comprising:

a) providing a base plate having a top surface and a bottom surface, and a plurality of apertures extending through said base plate from said top surface to said bottom surface; and

b) providing a plurality of extraction cartridges each having an inlet and an outlet, each of said cartridges having a solid phase extraction medium disposed between said inlet and said outlet, for extracting a solute from a liquid sample inserted into said each of said cartridges through said inlet; and

c) locking each of said cartridges into a corresponding aperture of said base plate with said inlet situated opposite said outlet relative to said base plate.

20. The method of claim 19 wherein said locking said each of said cartridges comprises snapping-in said each of said cartridges into said corresponding aperture.

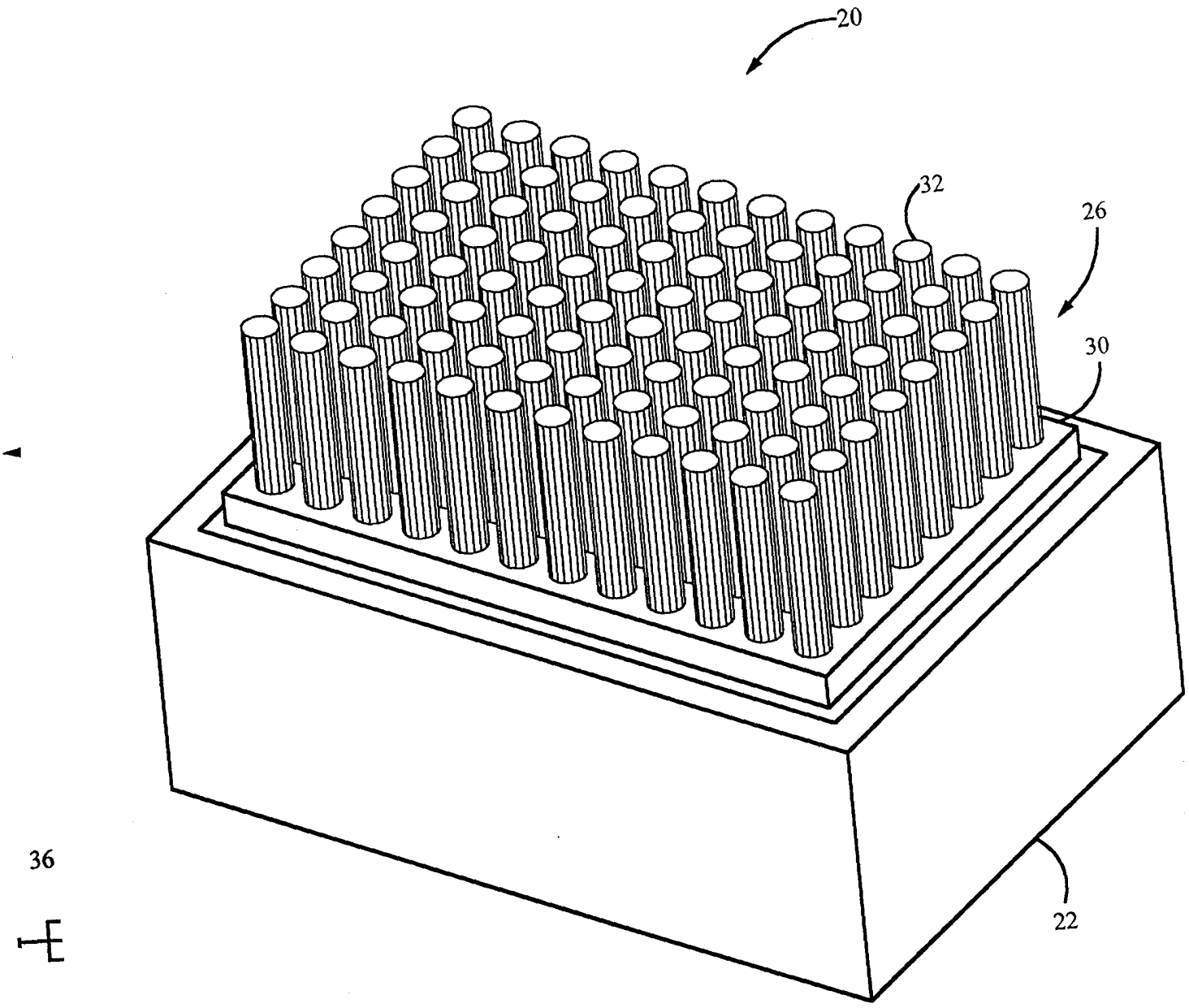
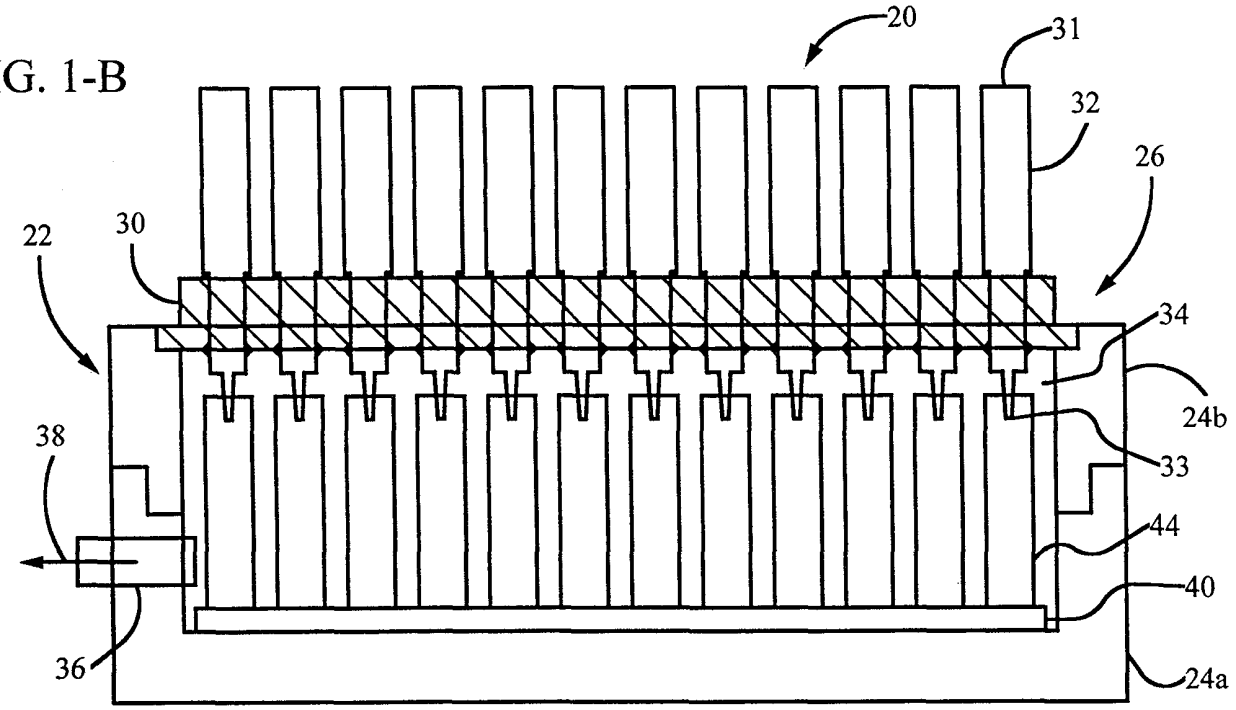


FIG. 1-A

FIG. 1-B



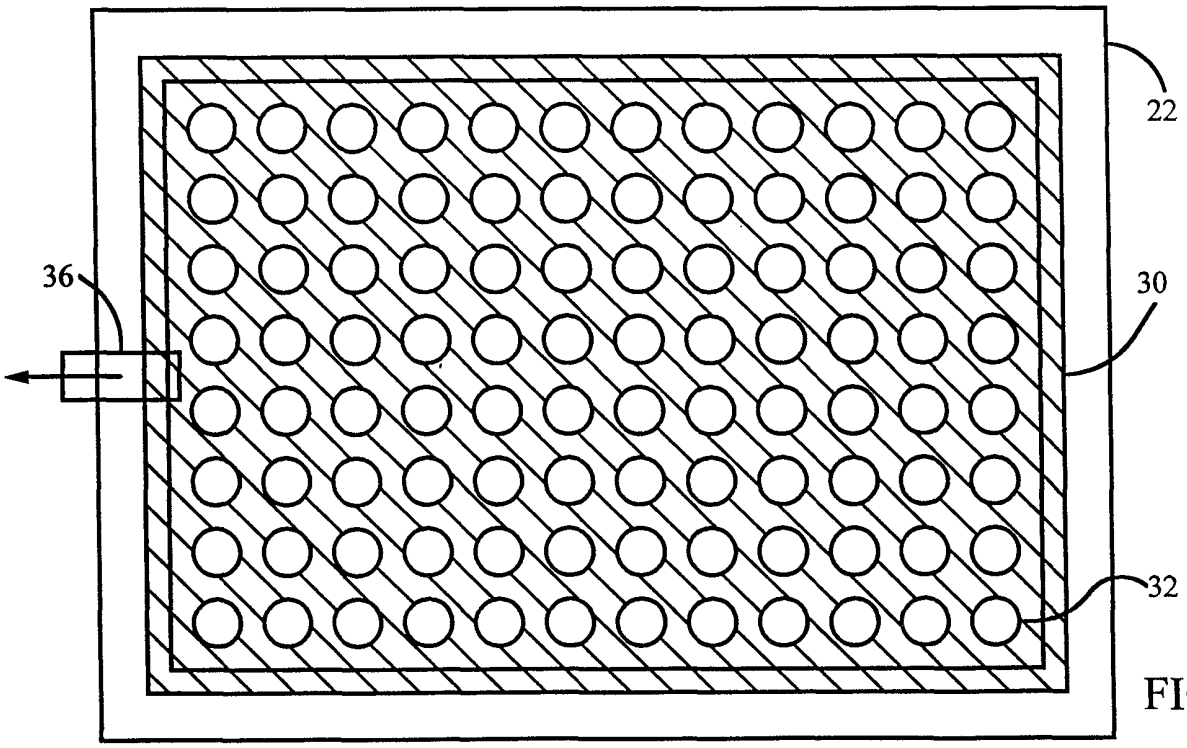
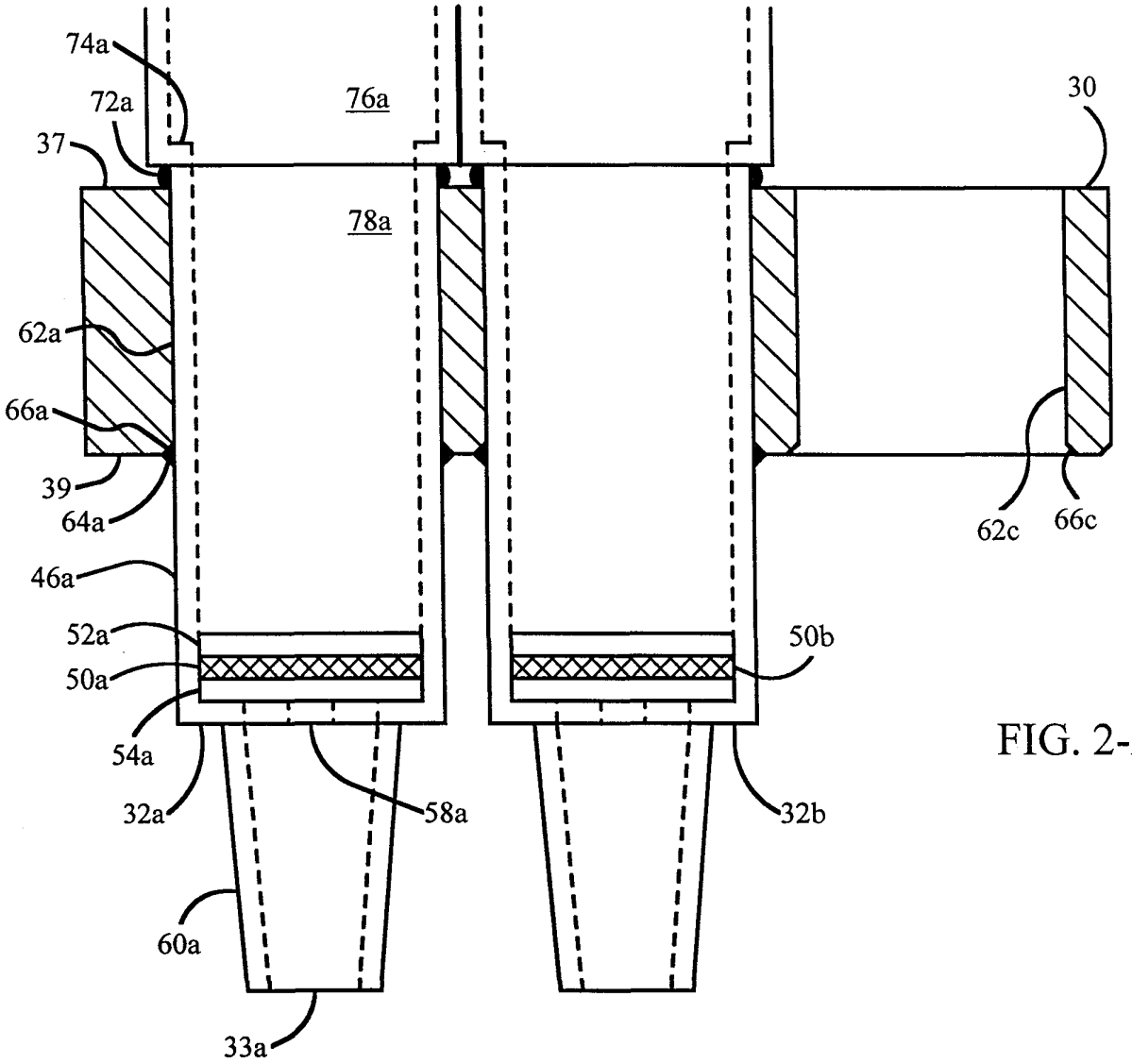


FIG. 1-C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76a
78a
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66a
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46a
52a
50a
54a
32a
58a
60a
33a
50b
32b
62c
66c

FIG. 2-A

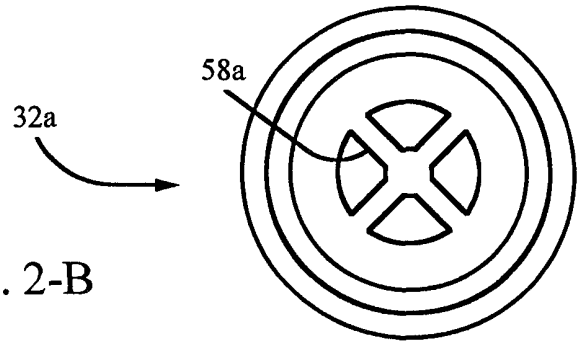
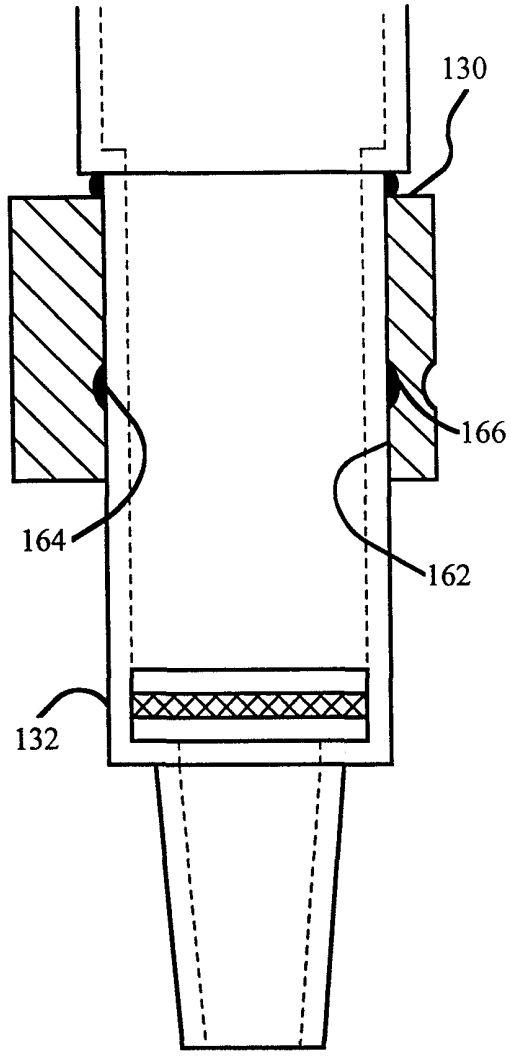

58a
32a

FIG. 2-B


130
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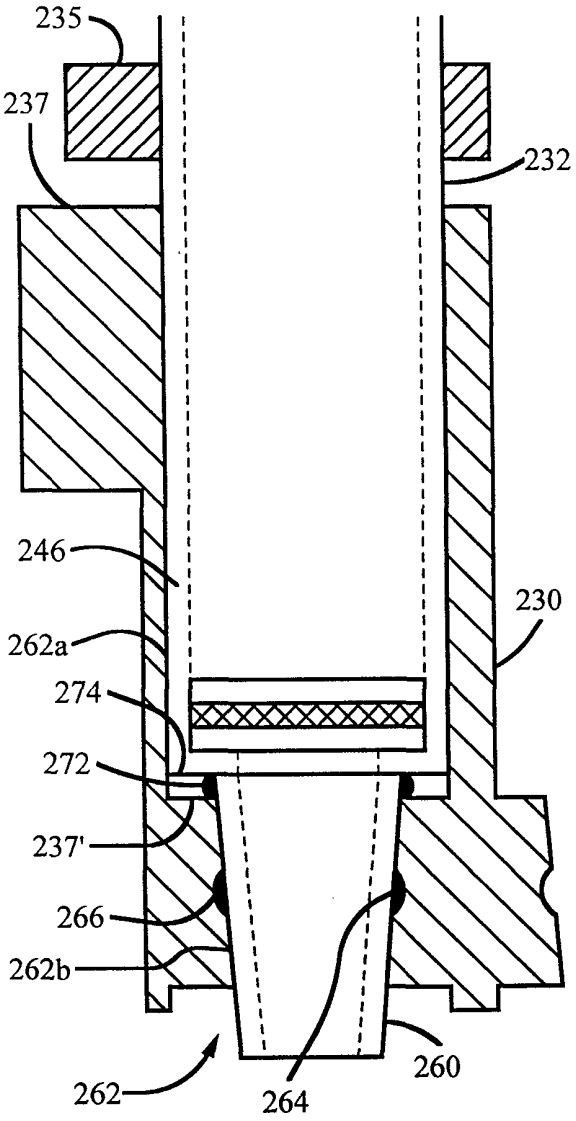
132

FIG. 3-A


235
237
232
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262a
274
272
237'
266
262b
262
264
260

FIG. 3-B

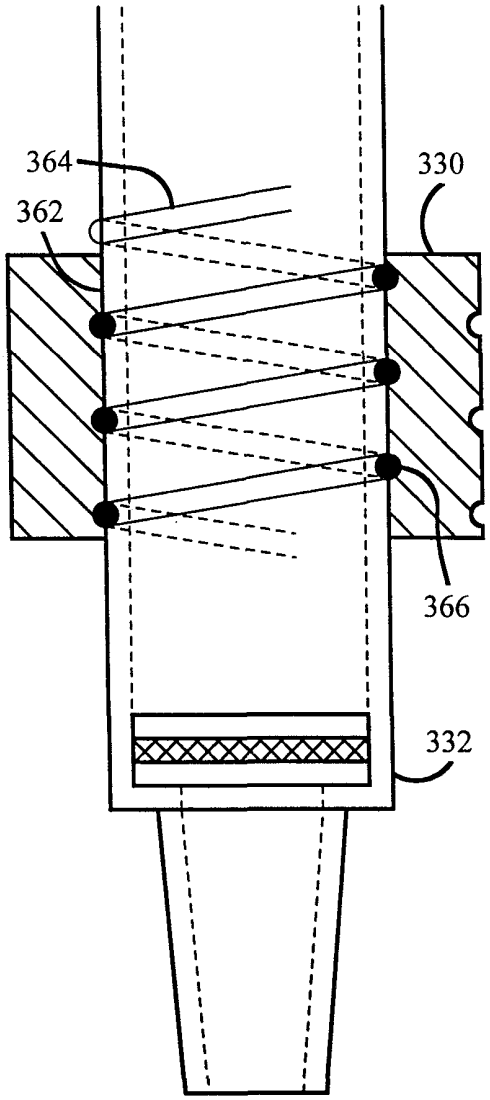

FIG. 3-C

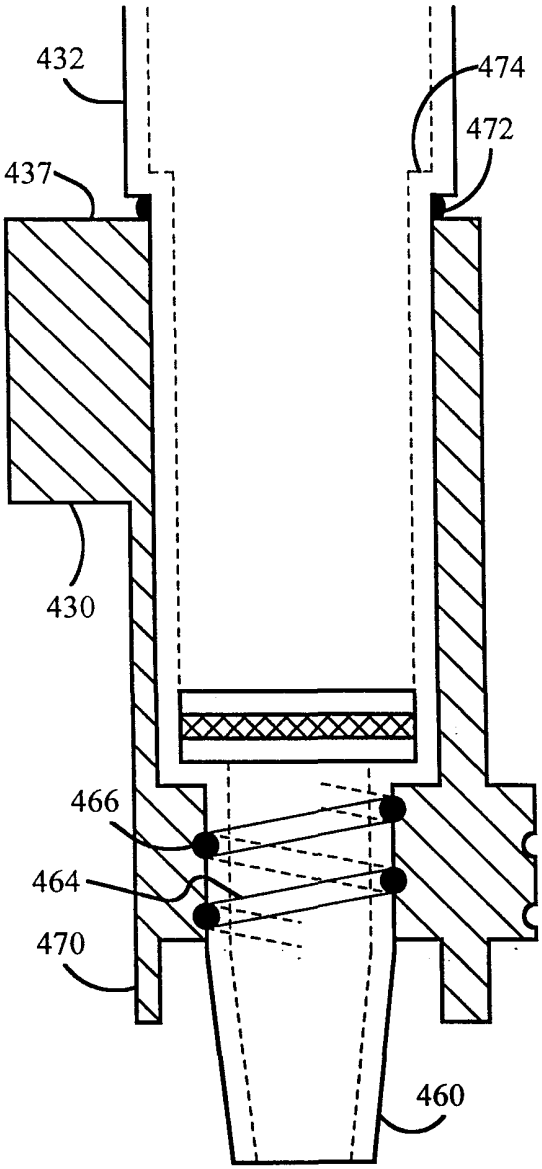

FIG. 3-D

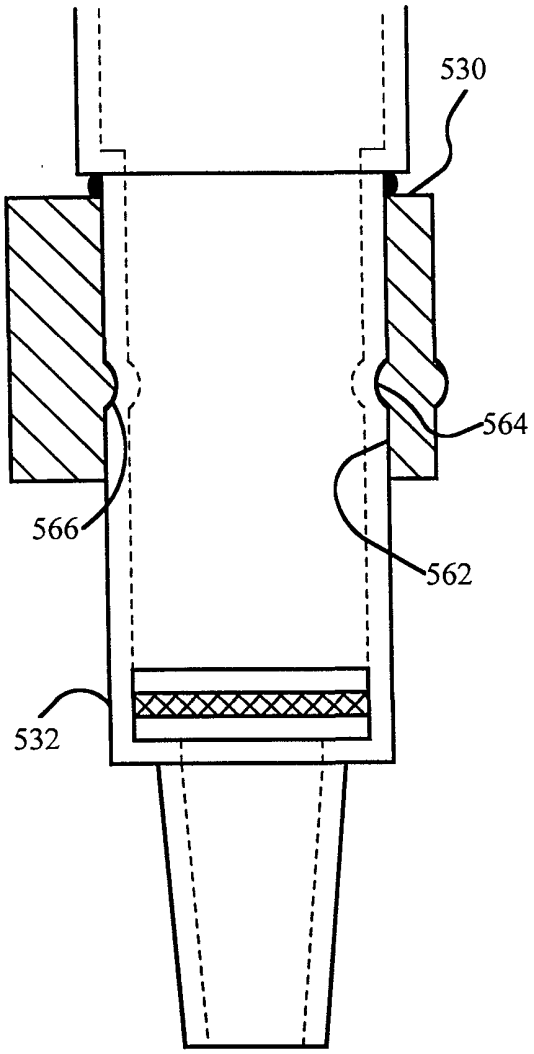

FIG. 3-E

INTERNATIONAL SEARCH REPORT

Inte. .ional Application No
PCT/US 99/28590

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 B01L3/00 G01N30/46

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)
IPC 7 B01L

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

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

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 5 603 899 A (FRANCISKOVICH PHILLIP P ET AL) 18 February 1997 (1997-02-18) column 2, line 53 -column 3, line 11; figures 1,3	1,5-7, 11,19
Y	column 4, line 2 - line 59; figure 5 column 5, line 21 - line 45; figure 6	8
Y	US 5 716 584 A (BAKER WILLIAM R ET AL) 10 February 1998 (1998-02-10) column 3, line 9 - line 30; figure 1B	8
P,X	US 5 846 493 A (BANKIER JACK D ET AL) 8 December 1998 (1998-12-08) column 4, line 47 - line 54 column 1, line 43 -column 2, line 18 column 5, line 40 - line 42 column 5, line 67 -column 6, line 10; figures 5,6	1,6,11, 19

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

[X] Patent family members are listed in annex.

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"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

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"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
20 April 2000	02/05/2000

Name and mailing address of the ISA	Authorized officer
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2

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INTERNATIONAL SEARCH REPORT

Int .tional Application No
PCT/US 99/28590

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication,where appropriate, of the relevant passages	Relevant to claim No.
A	US 5 800 784 A (HORN MARCUS J) 1 September 1998 (1998-09-01) column 12, line 12 - line 57; figures 3-8	1-20

Form PCT/ISA/210 (continuation of second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

Information on patent family members

Int\ ional Application No
PCT/US 99/28590

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		EP 0848721 A	24-06-1998
		JP 11502720 T	09-03-1999
		WO 9709353 A	13-03-1997
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