US00RE38312E

(19) **United States**

(12) **Reissued Patent**

Gamble

(10) **Patent Number: US RE38,312 E**

(45) **Date of Reissued Patent: Nov. 11, 2003**

(54) **MICROPLATE ASSEMBLY AND CLOSURE**

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(21) Appl. No.: **09/829,824**

(22) Filed: **Apr. 10, 2001**

Related U.S. Patent Documents

Reissue of:

(64) Patent No.: **6,106,783**
Issued: **Aug. 22, 2000**
Appl. No.: **09/108,339**
Filed: **Jun. 30, 1998**

(51) **Int. Cl.**[7] **B01L 9/06**

(52) **U.S. Cl.** **422/102**; 422/99; 422/100; 422/101

(58) **Field of Search** 422/99, 100, 101, 422/102, 942, 948; 435/288.4, 305.2, 305.3, 305.4

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(57) **ABSTRACT**

A microplate assembly with closure comprises a microplate base **101** having a geometric array of wells **103**. Vials **113** of borosilicate glass inserted into the wells comprise flanges on the top portion of the vials. Closure **117** comprises an array of caps **119** having a complementary geometric pattern to the wells of the microplate base. The caps each comprises a septum and are connected by a thin membrane **121**. Each cap comprises a sidewall **403** having a vial engagement ring which snaps over the flange **115** of the vials. Septum openings **135** in the caps extend through the top of the caps and provide a means to fill and evacuate the vials with a penetration device passing through the septa of the caps of the closure.

12 Claims, 6 Drawing Sheets

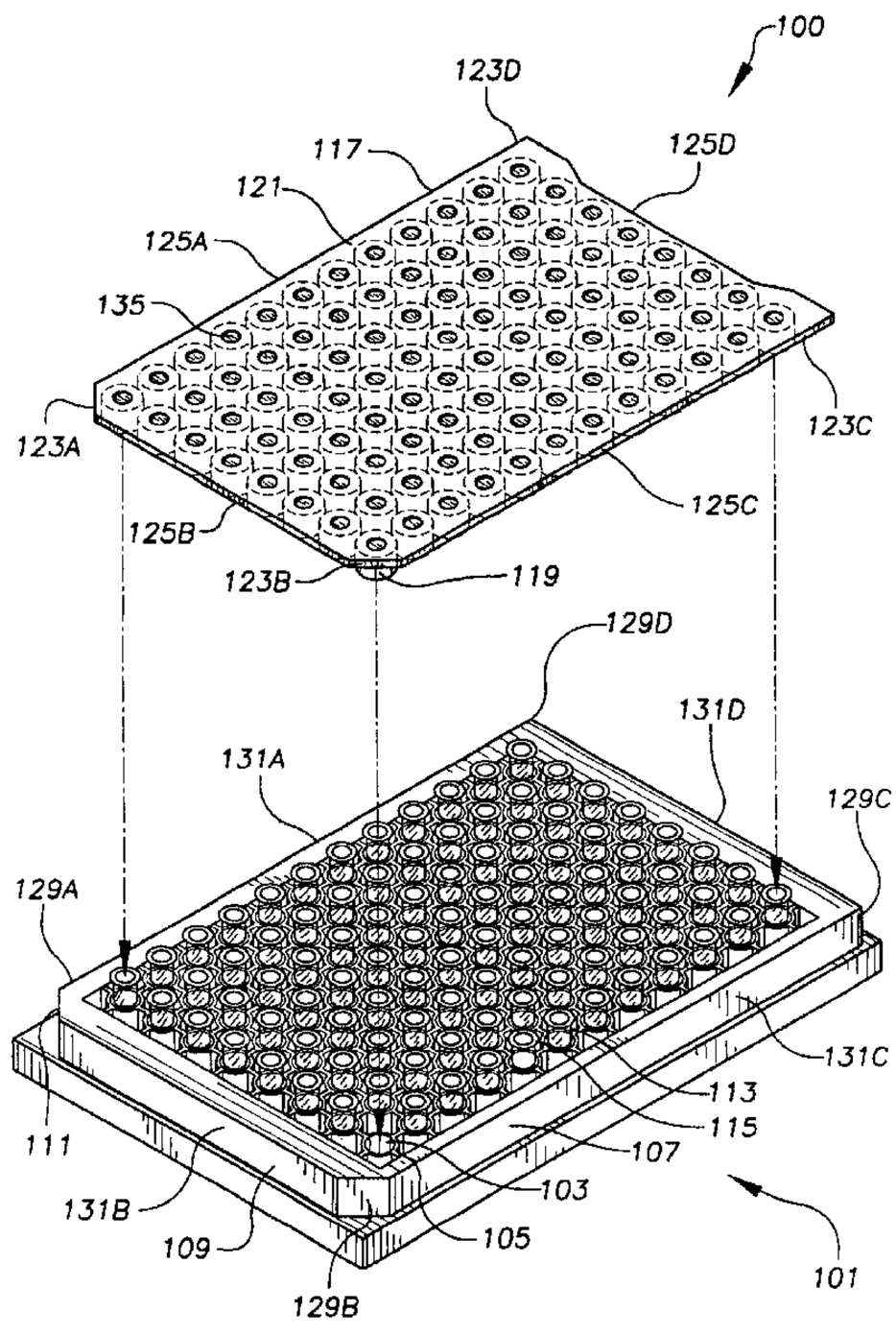


FIG. 1

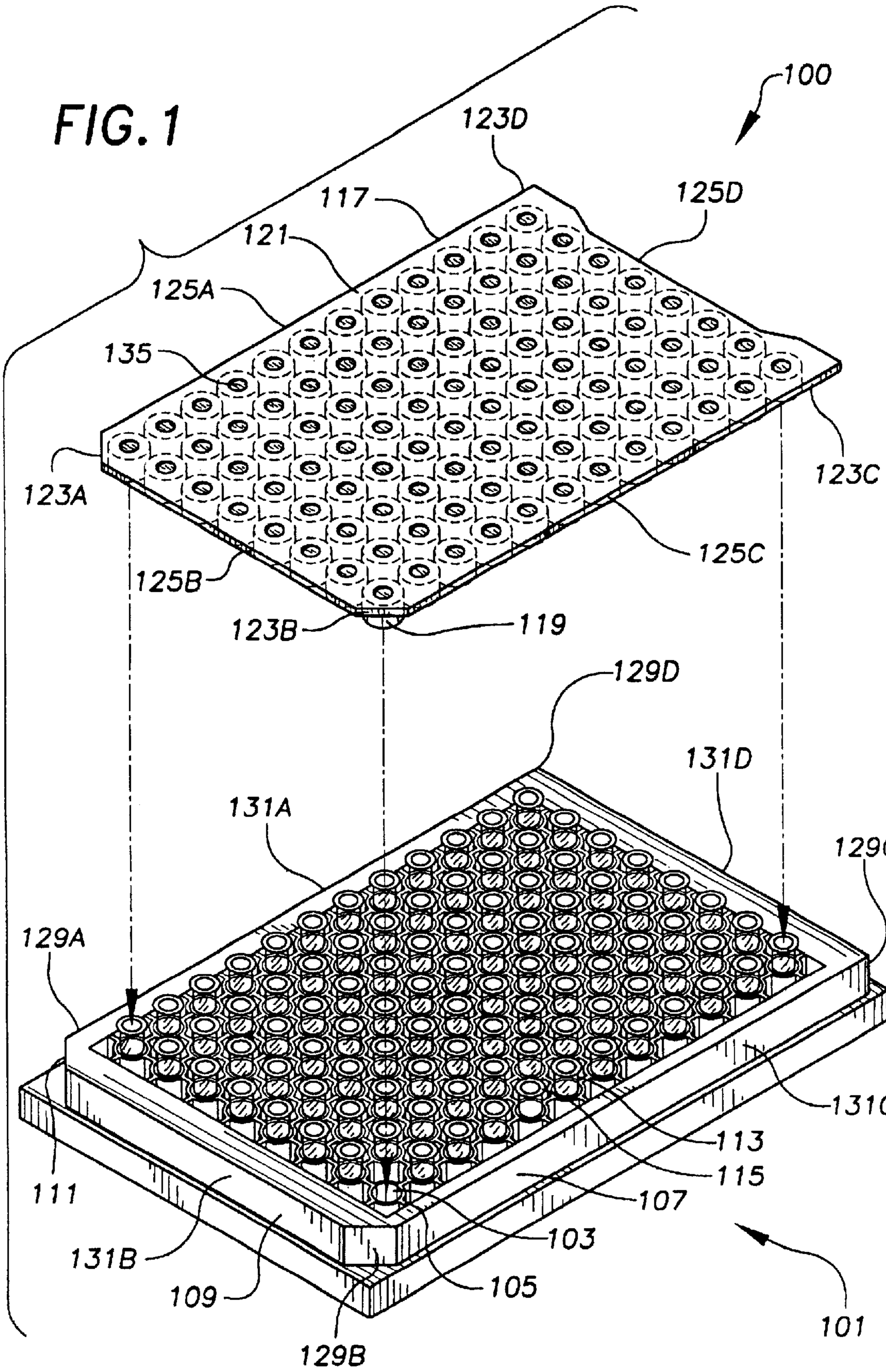

100
123D
117
125D
121
125A
135
123A
123C
125C
125B
123B
119
129D
131D
131A
129C
129A
131C
113
115
111
107
103
131B
109
105
101
129B

FIG.2

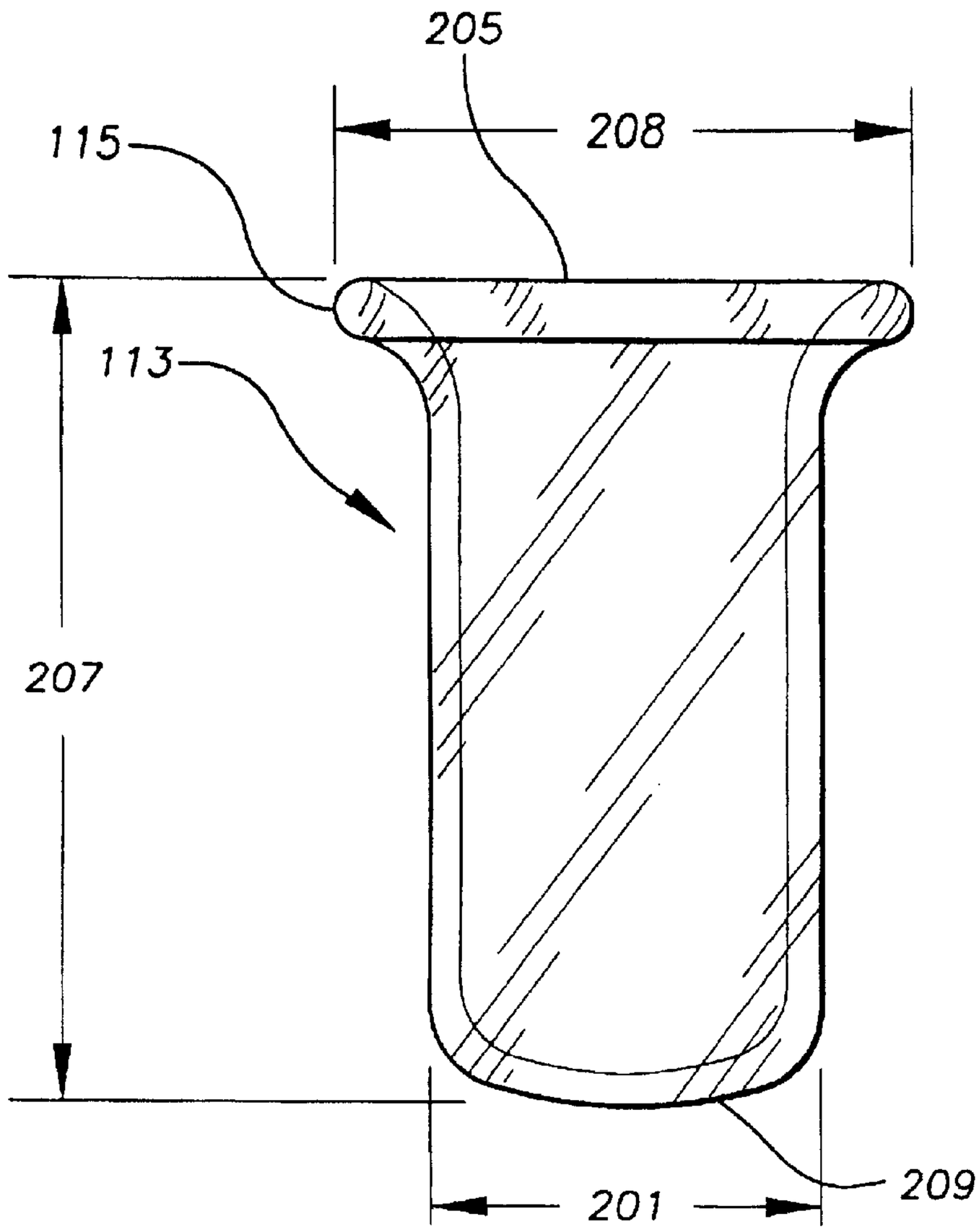
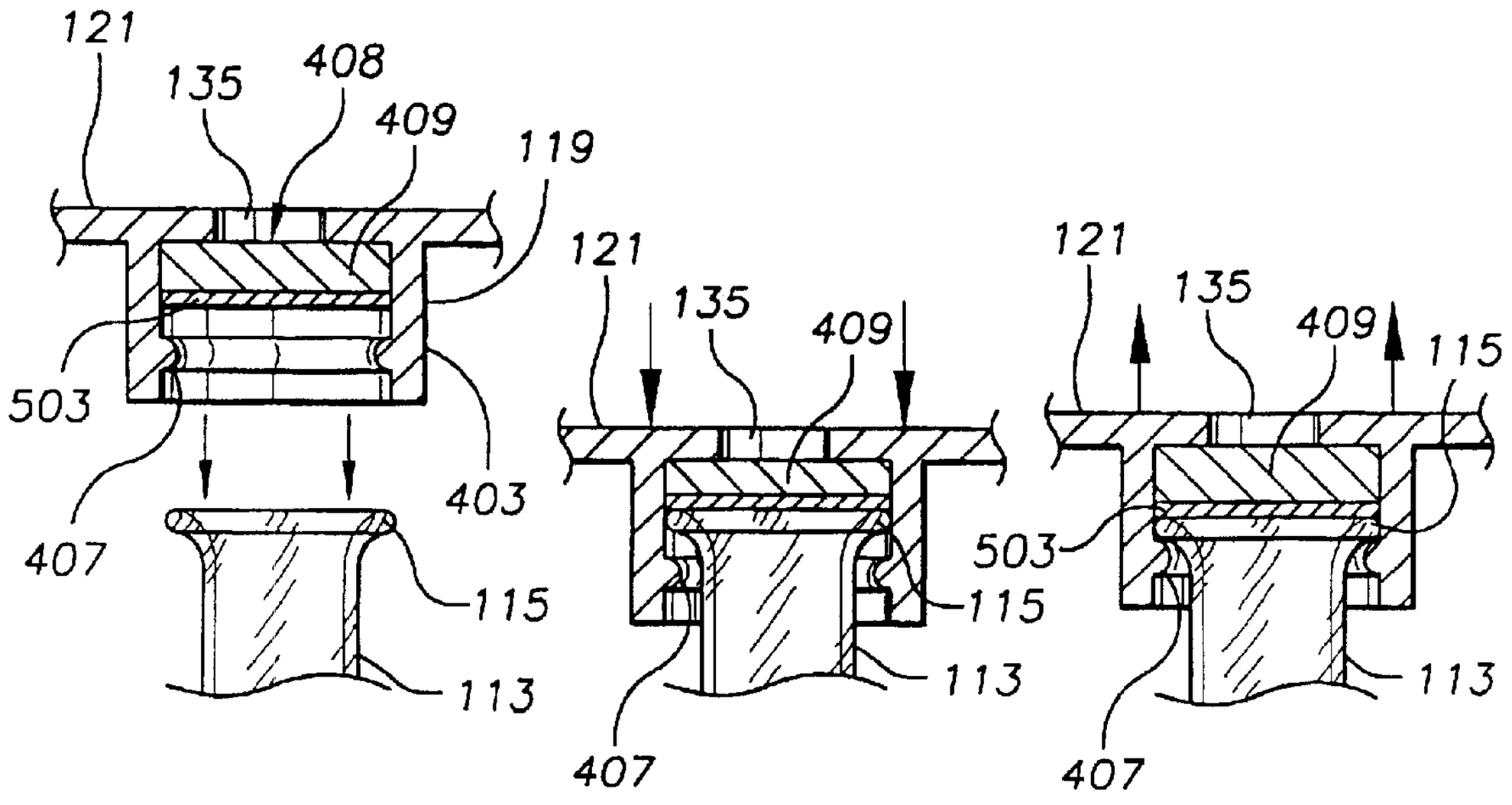


FIG.5A FIG.5B FIG.5C



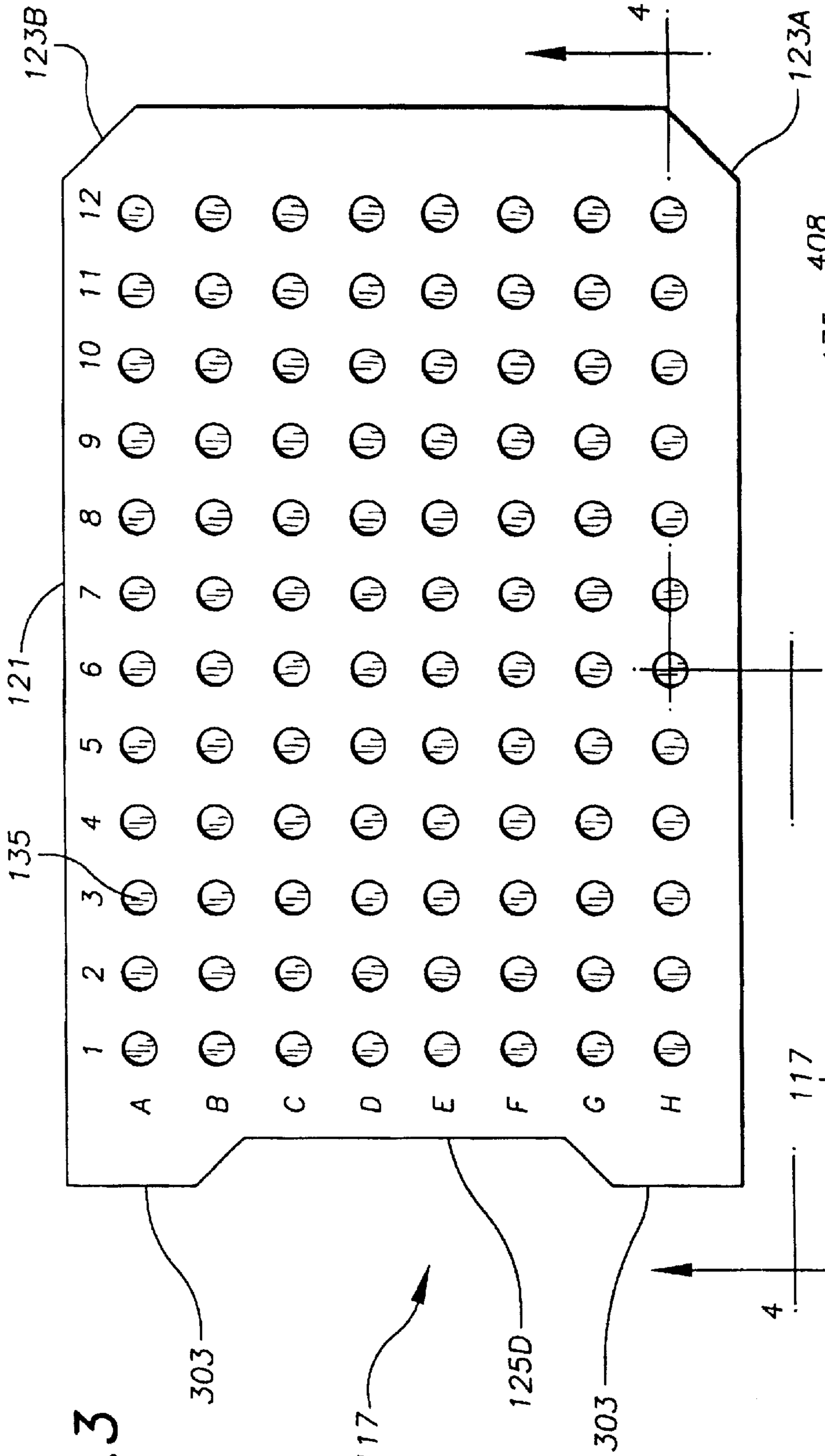

123B
4
123A
12
11
10
9
8
7
6
5
4
3
2
1
A
B
C
D
E
F
G
H
121
135
303
117
125D
303

FIG. 3

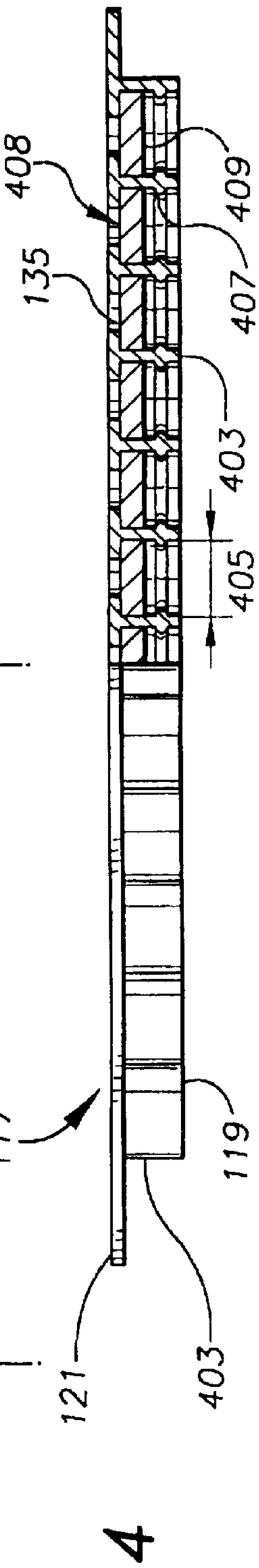

408
409
135
407
403
405
117
119
4
121
403

FIG. 4

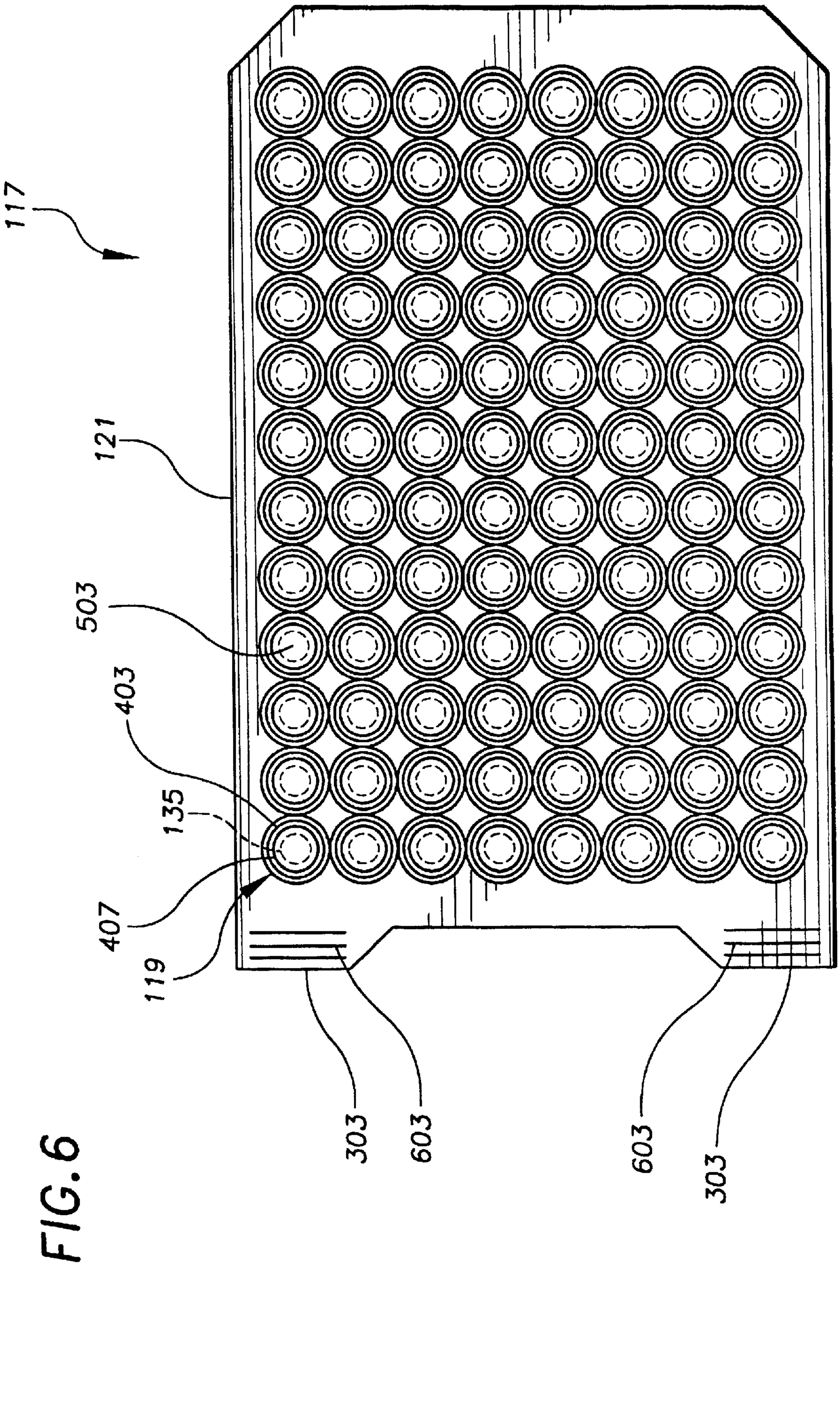


FIG. 6

FIG. 7

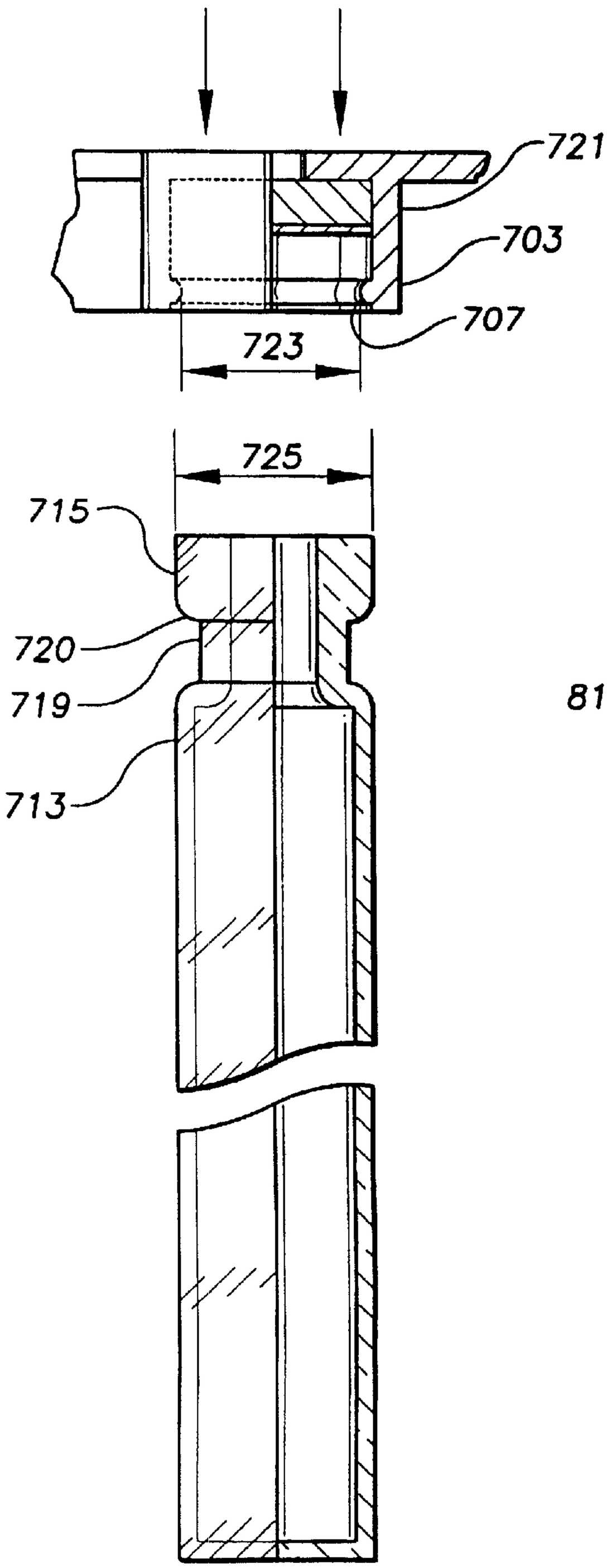


FIG. 8

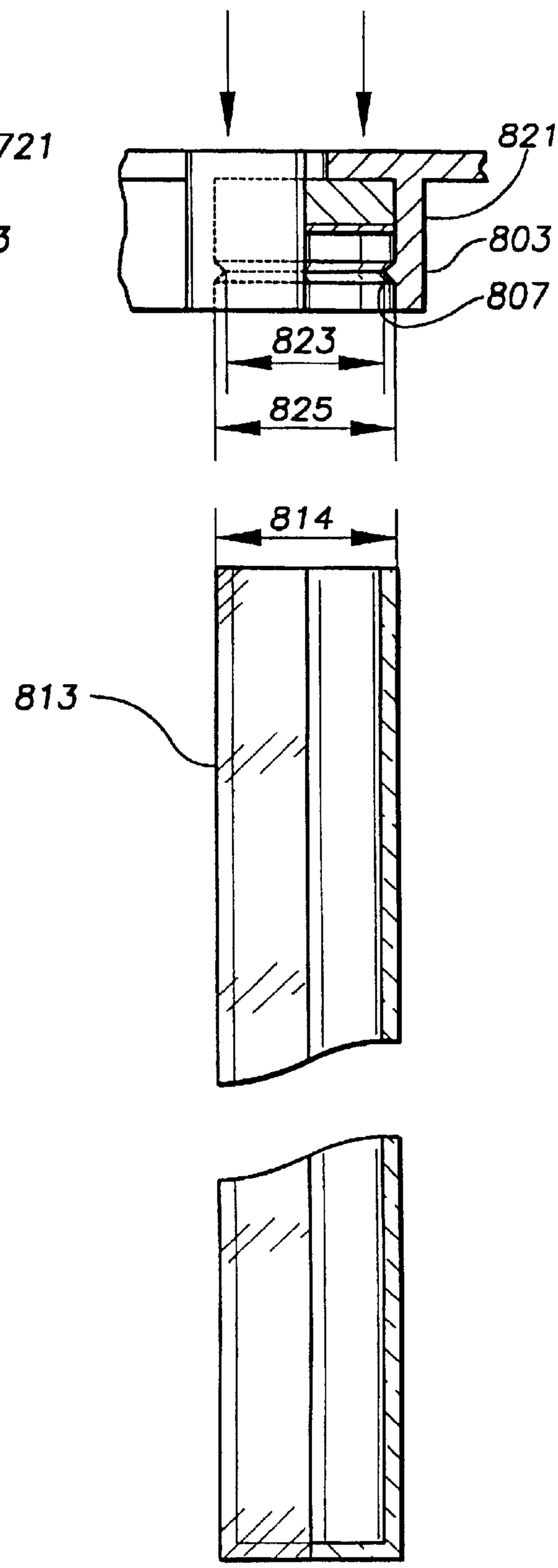


FIG.9

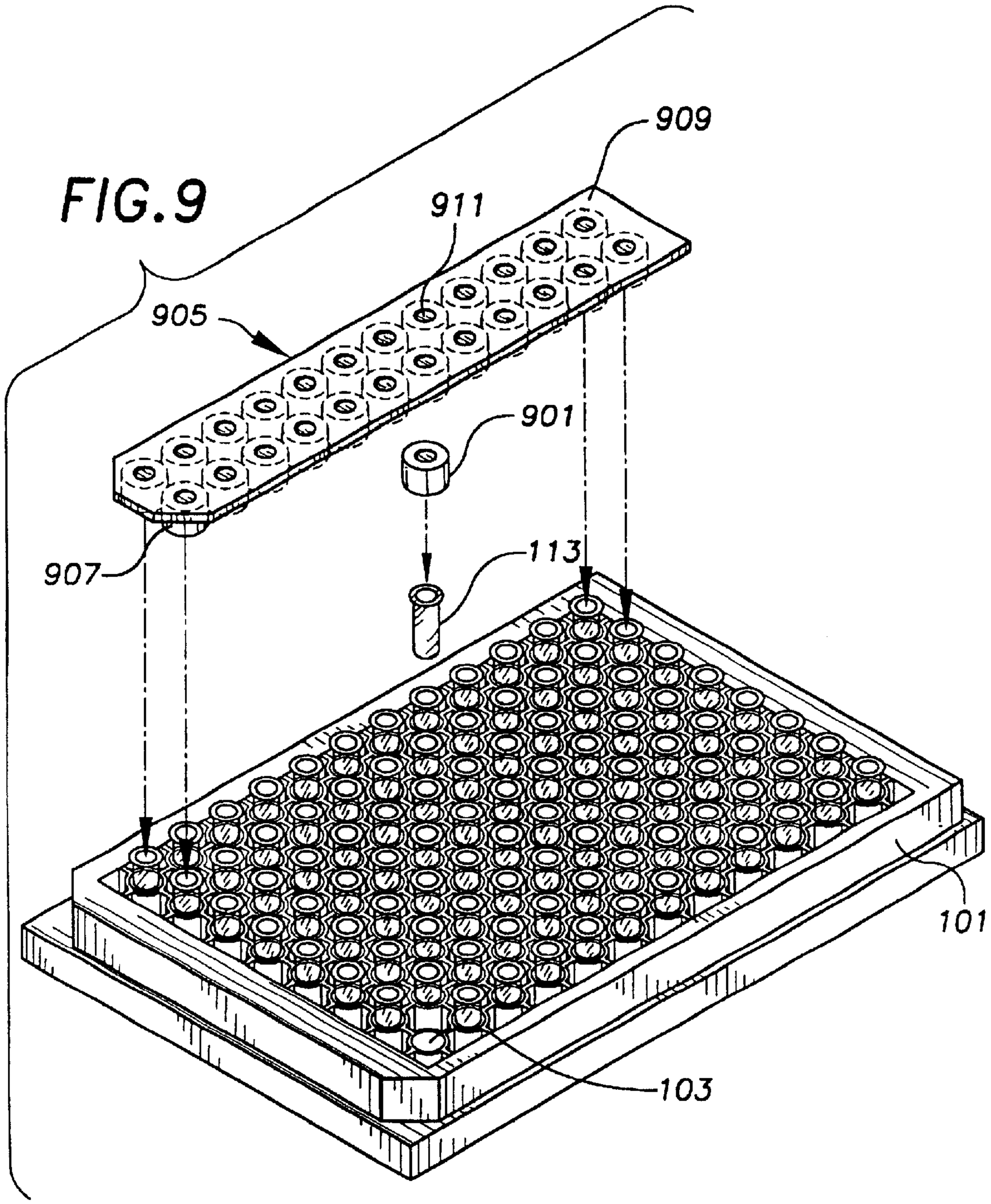
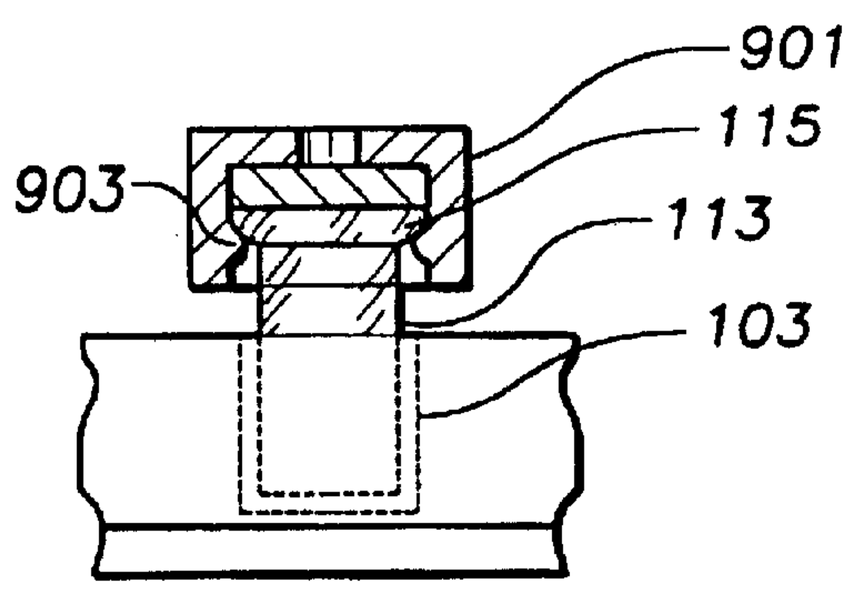


FIG.9A



MICROPLATE ASSEMBLY AND CLOSURE

Matter enclosed in heavy brackets [ ] appears in the original patent but forms no part of this reissue specification; matter printed in italics indicates the additions made by reissue.

BACKGROUND OF THE INVENTION

The present invention relates to sample handling and storing assemblies and, more particularly, to microplate assemblies.

The growth in medical and pharmaceutical research as well as diagnostic analysis and testing has created a need for equipment and procedures for low cost, efficient handing of samples. Automated equipment is available for filling and retrieval of samples from sample containers.

Microplates comprising a plurality of sample wells have provided a convenient means to store samples. Automated equipment is available to position microplates for sample filling, retrieving, and analysis. Despite improvements in sample handling equipment, many applications require manual labor when performing evolutions such as preparing sample containers or vials, or covering or uncovering the samples. This is especially the case when sample numbers are insufficient to justify design and building of custom automated equipment.

Normally the wells of microplates are used as the sample containers. One of the problems arising from this technique is cross contamination of samples due to the base of sample migration across the top surface of the microplate. Also, the use of adhesive web closures to cover multiple wells further increases cross contamination between wells. Due to the high cost of making microplates of glass, use of plastics has become common. These units suffer the additional problem of contamination of samples due to the fact that most plastics are less inert to sample solvents than glass.

OBJECTS AND SUMMARY OF THE INVENTION

Therefore and object of the present invention is to provide a microplate assembly with a closure which can be quickly and easily applied to a plurality of the sample containers of the microplate.

Another object of the present invention is to provide a microplate assembly with closure which reduces cross contamination of samples.

A further object of the present invention is to provide a microplate assembly with closure which improves chemical inertness as compared to using wells of plastic microplates.

Yet another object of the present invention is to provide a microplate assembly with closure which is low in cost, rugged and reliable.

The microplate assembly with closure of the present invention comprises a microplate base having a plurality of wells arranged in a geometric pattern. Glass vials having the quality of good chemical inertness are insertable into the wells of the microplate base. Caps, preferably integral with a flexible or semi-rigid membrane and in the geometric pattern of the microplate base wells, are placed over the vials. The caps comprise a sidewall. The inner diameter of the sidewall engages an outside surface of the glass vials. The caps have a septum opening and septum comprising a resealable portion and a barrier portion. The septum allows insertion of a probe such as a hypodermic needle for filling and retrieving samples while the caps are engaged on the vials. A vial seal of chemically inert material prevents contact of the sample and the septum seal.

In the preferred embodiment, a standard 96 well microplate base is utilized. Vials are made of borosilicate glass for inertness and long life. The vials have an outer diameter selected to make them insertable into the wells of the microplate base. The vials may be flanged, plain or serum finish. The closure comprises 96 caps arranged in the same geometric pattern as the wells of the microplate base. The caps are integrally formed with a membrane connecting the caps. The caps fit over the outer diameter of the vials and comprise a vial or flange engagement ring to retain the cap on the vial.

The microplate closure allows rapid capping or uncapping of a full complement of vials in the microplate simultaneously. In other embodiments, cap strips cover one or more rows or columns of vials. In yet another embodiment, single septum caps are utilized.

BRIEF DESCRIPTION OF THE DRAWINGS

These and other features, aspects and advantages of the present invention will become better understood with regard to the following description, appended claims and accompanying drawings where:

FIG. **1** is a perspective drawings of an embodiment of a microplate and closure assembly comprising a 96 well microplate, flanged vials, and a closure comprising 96 integral septum caps attached to a membrane;

FIG. **2** is a side elevation drawing of a flanged vial of the assembly of FIG. **1**;

FIG. **3** is a top view of the closure of FIG. **1** showing septum openings, alignment chamfers, and grip flap portions;

FIG. **4** is a side elevation and partial cutaway drawing taken along lines **4**—**4** of FIG. **3**;

FIG. **5**A is a detail of the flanged vial and a cutaway of a cap of the closure of FIG. **1** before the cap is inserted on the vial;

FIG. **5**B is a detail of the flanged vial and a cutaway of a cap of the closure of FIG. **1** when the cap is fully inserted on the vial with the flange of the vial compressing the septum seal of the cap;

FIG. **5**C is a detail of the flanged vial and a cutaway of a cap of the closure of FIG. **1** with the flange engagement ring of the cap engaging and retained by the flange of the vial;

FIG. **6** is a bottom view of the closure of FIG. **1** showing caps, membrane, flange engagement ring, flap portion and grip ribs, with the septum openings shown in phantom lines;

FIG. **7** is a side elevation and partial cutaway of a serum finish vial and cap of a closure the cap comprising a flange engagement ring for engaging the ledge of the flange;

FIG. **8** is a side elevation and partial cutaway of a flangeless vial and cap of a closure, the cap comprising a seal ring for engaging the outer diameter of the vial;

FIG. **9** is a perspective drawing of individual caps and cap strips for sealing single vials or strips of vials in a microplate; and

FIG. **9**A is detail cut-away drawing of a cap snapped over a flange of a vial.

DESCRIPTION OF THE PREFERRED EMBODIMENTS

The following is a description of the preferred embodiments of a microplate assembly with closure that provides for sealing and sampling a plurality of sample vials in the microplate.

FIG. **1** is a perspective drawing of embodiment **100** of the microplate assembly with closure. Microplate **101** comprises a plurality of wells **103** arranged in a geometric pattern. In the preferred embodiment, the geometric pattern is a rectangular array eight wells in width and 12 wells in length. In the preferred embodiment, wells **103** are 6.2 millimeters in diameter (nominal dimensions) and the spacing of wells **103** in the length and width directions is 9 millimeters. In other embodiments, microplates of different numbers of wells or geometric patterns of wells are used. In the preferred embodiment, microplate **101** is made of a plastic material such as polyethylene or polypropylene. In other embodiments, microplate **101** is made of metal, composites, or glass. Microplate **101** may be machined, die cast or injection molded. Microplate **101** may comprise ribs **105** which support wells **103** from longitudinal wall **107** and transverse wall **109** and from other wells. Chamfers **111** may be used to index or align the microplate for closure and for automatic sampling equipment (not shown). Microplates may be of either shallow well, as shown, or deep well as known in the art.

Wells **103** act as receptors for vials **113**. In the preferred embodiment, vials **113** are made of glass such as borosilicate glass and comprise a flange **115**. Glass vials provide a vial material which is inert to most sample materials. In the preferred embodiment, the diameter of vials **113** provide a loose fit in wells **103**, providing easy removal and replacement of vials **113**. In other embodiments, the outer diameter of vials **113** provide a snug or slight interference fit with wells **103**.

Closure **117** comprises a plurality of caps **119** attached to membrane **121**. Caps **119** are arranged in a geometric pattern similar to the geometric pattern of wells **103**. In the preferred embodiment, caps **119** form a rectangular array 8 caps wide by 12 caps in length. The similar geometric pattern of caps **119** and wells **103** provides alignment of caps **119** to vials **113** placed in wells **103**. When respective corners **123**A–D or edges **125**A–D, of closure **117** are aligned to respective corners **129**A–D and edges **131**A–D of microplate **101**, caps **119** are aligned with vials **113** placed in wells **103**.

In the preferred embodiment, caps **119** fit over flanges **115** of vials **113**. Pressing of closure **117** on vials **113** inserted in wells **103** engages caps **119** and respective vials **113**, sealing vials **113**. Hand or mechanical applicator pressure may be used to provide closure **117** engagement to vials **113**. Septum openings **135** provide access for insertion of injection needles.

FIG. **2** is a side elevation of vial **113** of FIG. **1**. In the preferred embodiment, vial **113** outer diameter **201** is 6.0 mm (nominal), allowing a loose fit with standard 96 well microplates having well inner diameter of 6.2 mm (nominal). Vial length **207** is typically 15±2 mm. In deep well microplates, vial length may be longer, for example 41±2 mm. Vial **113** comprises a flange **115** located at opening **205**. Flange **115** outer diameter **208** is 7.75 mm (nominal). In the preferred embodiment, vial bottom **209** is generally flat. In other embodiments, vial bottom **209** is cylindrical or tapered.

FIG. **3** is a top view of closure **117** showing an 8×12 array of septum openings **135** in membrane **121**. In the preferred embodiment, membrane **121** is made from a flexible polymeric material such as polyolefins. In other embodiments, membrane **121** is made of vinyl, natural or synthetic rubbers, or other elastomers. In the preferred embodiment, closure **117** is injection molded of polyethylene, resulting in caps (**119** of FIG. **1**) integral with membrane **121**. Flap portions **303** project along edge **125**D of closure **117**, providing a surface which is easily engaged with the fingers of the hand to remove and replace closure **117** on vials **113**. In other embodiments, flap portions or extended edge portions are provided on other edges of closure **117**. Corners **123**A and **123**B may be chamfered as shown to aid in alignment of closure **117** to microplate **101** of FIG. **1**. Chamfered corners also act as alignment means for storage and handling of groups of closures. In other embodiments, closure **117** is made of rigid polymeric material.

FIG. **4** is a side view and partial cross section of closure **117** taken at lines **4**—**4** of FIG. **3**. Caps **119** comprise sidewall portion **403**. Sidewall portion **403** is generally cylindrical and has an inner diameter **405** sufficient to fit over vials **113** of FIG. **1**. In the preferred embodiment, the inner diameter of caps **119** comprise a flange engagement ring **407** protruding inside sidewall **403** for engaging flanges **115** of vials **113** to retain caps **119** on vials **113**. Septum **408** comprising resealable portion **409** provides a seal between septum opening **135** and the vial (not shown).

FIG. **5**A is a detail cross section of cap **119** about to be engaged with vial **113**. Septum resealable portion **409** of septum **408** provides a seal between septum opening **135** and vial **113**. In this manner, a transfer device such as a hypodermic needle (not shown) may be inserted into septum opening **135** of membrane **121** and penetrate septum resealable portion **409** to fill or evacuate vial **113** with cap **119** engaged to vial **113**. Septum resealable portion **409** may be a self sealing compound such as soft butyl rubber. In other embodiments, septum resealable portion **409** is made of silicone, other elastomers or polymer materials. In still other embodiments, septum **408** may comprise a thin portion (not shown) of membrane **121** extending over septum opening **135**.

In the preferred embodiment, a barrier portion **503** disposed between septum resealable portion **409** and vial **113** provides a chemically resistant barrier seal for contents of vial **113**. In the preferred embodiment, barrier portion **503** is made of polytetrafluoroethylene (PTFE). In other embodiments, other polymers or metallic seals may be used.

FIG. **5**B is a detail cross section of cap **119** inserted over vial **113** so that flange **115** of vial **113** is inserted past engagement ring **407**. In the preferred embodiment, flange engagement ring **407** is made of a resilient material which deforms as flange **115** of vial **113** passes over flange engagement ring **407**. Septum resealable portion **409** compresses as cap **119** is inserted over flange **115** of vial **113**, allowing flange engagement ring **407** to expand after flange engagement ring **407** clears flange **115**. After cap **119** is released, septum resealable portion **409** expands to seat flange **115** against flange engagement ring **407** and barrier portion **503** seats the opening of vial **113** as shown in FIG. **5**C.

FIG. **6** is a bottom view of closure **117** showing caps **119** attached to membrane **121**. Flange engagement ring **407** is attached to the inner diameter of sidewall **403**. Barrier portion **503** and septum resealable portion **409** (not shown) cover septum opening **135**. Grip ribs **603** of flap portions **303** provide a grip surface to improve removal of closure **117** from microplate and vial assemblies.

FIG. **7** is a partial cutaway drawing of an embodiment of a vial and closure utilizing an 8 mm serum finish vial **713**. Crimp flange **715** provides a mount surface for a standard 8 mm crimp cap (not shown). Crimp recess **719** provides a ledge **720** on crimp flange **715** for the crimping portion of the crimp cap to grip. Serum finish vials may be used in square well or round well microplates.

Flange engagement ring **707** of cap **721** engages ledge **720** when cap **721** is pressed onto vial **713**. The inner diameter **723** of flange engagement ring **707** is less than the outer diameter **725** of flange **715**. Use of a resilient material for sidewall **703** of cap **721** and flange engagement ring **707** provides an expansion and contraction means of flange engagement ring **707**, allowing cap **721** to be pressed on vial **713**. Once flange engagement ring **707** is advanced to crimp recess **719**, flange engagement ring **707** expands inwardly and engages ledge **720** of flange **715**. Removal of cap **721** requires pulling of the cap sufficiently to expand flange engagement ring over flange **715**.

FIG. **8** is a partial cutaway drawing of another embodiment of vial and closure utilizing a flangeless vial **813**. In this embodiment, the inner diameter **823** of seal ring **807** is less than the outer diameter **814** of vial **813**. When pressed over vial **813**, seal ring **807** forms a tight fit with the outer diameter of vial **813**, sealing cap **821** and vial **813**. In other embodiments, seal ring **807** may have rectangular, semicircular, or trapezoidal cross sectional shapes. Or, several seal rings may be used. In still other embodiments, seal ring **807** is omitted, and the inner diameter **825** of cap **821** is less than outer diameter **814** of vial **813**. The resulting tight fit of sidewall **803** to the outer diameter **814** of vial **813** seals cap **821** to vial **813**. Resilient materials such as polyolefins for cap **821** allow adequate sealing with moderate (0.1 mm–0.5 mm) interference fits.

FIG. **9** is a perspective drawing of microplate **101** comprising 96 wells **103**. Individual septum caps **901** are snapped on flanged vials **113** and inserted into wells **103**. FIG. **9**A is a detail cutaway drawing of cap **901** snapped over flange **115** of vial **113**. Flange engagement ring **903** of cap **901** engages flange **115** to retain cap **901** on vial **113**. In the preferred embodiment, vial **113** is a loose fit in well **103**. In other embodiments, vial **113** forms a snug fit in well **103**.

Cap strip **905** comprises 16 integral caps **907** on membrane **909**, similar to those of FIGS. **1–6**. Caps **907** may comprises septum openings **911**. In other embodiments, cap strip **905** comprises one or more partial or full rows or columns of vial caps. Cap strip **905** allows a separate use of only a portion of the vials and wells of microplate **101**.

Accordingly the reader will see that the MICROPLATE ASSEMBLY AND CLOSURE provides fast closure and access to of a plurality of vials inserted into the wells of a microplate base. The device provides the following additional advantages:

The samples are housed in chemically inert vials;

Septa in the caps provide for filling and removal of samples while the caps are inserted on the vials;

Closure strips provide caps for selected rows or columns of vials; and

The device is simple and low in cost.

Although the description above contains many specifications, these should not be construed as limiting the scope of the invention but as merely providing illustrations of some of the presently preferred embodiments of this invention. Thus the scope of the invention should be determined by the appended claims and their legal equivalents, rather than by the examples given.

What is claimed is:

1. A microplate assembly with closure comprising:

a microplate base comprising a plurality of sample containable wells arranged in a geometric pattern;

a plurality of glass vials comprising dimensions providing a predetermined fit in said plurality of sample containable wells in the microplate base, each of said plurality of glass vials comprising a vial opening, a flange, and a closed vial bottom *and*;

a closure comprising a plurality of caps attached to a membrane, said plurality of caps arranged in the geometric pattern of said plurality of sample containable wells in the microplate base, each of said plurality of caps comprising a bottom cap opening, a top septum opening, a sidewall engageable to an outside surface of said each of said plurality of glass vials, the sidewall of each of said plurality of caps comprising a **[**vial**]** *flange* engagement ring on an inside surface of said sidewall for engaging the flange of each of said plurality of glass vials, *said flange engagement ring protruding inside of said sidewall,* and a septum between the top septum opening and the bottom cap opening.

2. The microplate assembly with closure of claim **1** wherein the microplate base is a 96 well base arranged in a twelve by eight array on nine millimeter centers.

3. The microplate assembly with closure of claim **1** wherein said plurality of glass vials are made of borosilicate glass.

4. A closure for a plurality of glass vials dimensioned for insertion into a plurality of sample containable wells of a microplate *arranged in a geometrical pattern*, the closure comprising:

a plurality of caps attached to a membrane, said plurality of caps arranged in the geometric pattern of said plurality of sample containable wells;

each of said plurality of caps comprising a cylindrically shaped sidewall, the sidewall comprising a bottom cap opening and comprising a **[**vial**]** *flange* engagement ring **[**on the**]** *protruding inside an* inner diameter of the sidewall, the **[**vial**]** *flange* engagement ring comprising a ring inner diameter sufficient to fit over and engage an outer diameter of *a flange of* each of said plurality of glass vials**[**,**]**; a top septum opening, and a septum between the bottom cap opening and the top septum *opening*.

5. The closure of claim **4** wherein the sidewall of said each of said plurality of caps comprises a flange engagement ring on the inner diameter of the sidewall for engaging a flange on said each of said plurality of glass vials.

6. The closure of claim **4** wherein the septum of each of said plurality of caps comprises a resealable portion for sealing the top septum opening and a barrier portion for sealing the resealable portion from each of said plurality of vials.

7. The closure of claim **6** wherein the barrier portion is PTFE.

8. The closure of claim **6** wherein the resealable portion comprises silicone.

[9. A microplate assembly with closure comprising:

a microplate base comprising a plurality of sample containable wells arranged in a geometric pattern;

at least one glass vial of dimensions providing a predetermined fit in said plurality of sample containable wells in the microplate base, said at least one glass vial comprising a vial top opening, a vial top flange comprising a top sealing surface, and a closed vial bottom; and

at least one snap cap insertable onto said at least one glass vial, said at least one snap cap comprising a top, a sidewall comprising a flange engagement element, and a septum comprising an upper resealable portion and a lower barrier portion, the septum disposed between the top and the flange engagement element;

whereby the barrier portion seals the top sealing surface of the glass vial when the flange engagement element engages the vial flange.]

[10. The microplate assembly with closure of claim 9 wherein the microplate base is a 96 well base arranged in a twelve by eight array on nine millimeter centers.]

[11. The microplate assembly with closure of claim 9 wherein said at least one glass vial is made of borosilicate glass.]

[12. A sample vial and cap assembly for insertion in a sample containable well of a microplate base, the sample vial and cap assembly comprising:

a glass vial of dimensions providing a predetermined fit in said sample containable well in the microplate base, the glass vial comprising a vial top opening, a vial top flange comprising a top sealing surface, and a closed vial bottom; and

a snap cap insertable onto said glass vial, the snap cap comprising a top, a sidewall comprising a flange engagement element, and a septum comprising an upper resealable portion and a lower barrier portion, the septum disposed between the top and the flange engagement element;

whereby the barrier portion seals the top sealing surface of the glass vial when the flange engagement element engages the vial flange.]

[13. The sample vial and cap assembly of claim 12 wherein the flange engagement element is disposed on the sidewall wherein the resealable portion of the septum is compressed to seal the barrier portion of the septum to the top sealing surface of the top flange of the vial when the flange engagement element is engaged to the top flange of the vial.]

[14. The sample vial and cap assembly of claim 13 wherein the flange engagement element is a flange engagement ring disposed on an inside surface of the sidewall and the flange engagement ring is made of a resilient material.]

15. The microplate assembly with closure of claim 1 wherein the closure comprises an alignment element for providing alignment to said microplate base.

16. The microplate assembly with closure of claim 15 wherein the alignment element is a chamfer on a corner of the closure.

17. The closure of claim 4 wherein the closure comprises an alignment element for providing alignment to a microplate.

18. The microplate assembly with closure of claim 17 wherein the alignment element is a chamfer on a corner of the closure.

* * * * *