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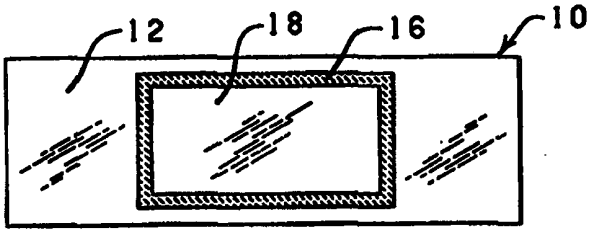
(54) Title: ANALYTIC PLATE AND METHOD

(57) Abstract

An analytical plate such as a microscope slide (10) having an upper surface (12) and a lower surface (14). Disposed upon a portion of the upper surface (12) is a liquid containment border (16).



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ANALYTIC PLATE AND METHOD

BACKGROUND

The present invention relates generally to the field of analytic plates such as microscope slides or diagnostic plates and more particularly to such analytic plates having borders thereon.

Standard microscope slides and diagnostic glass plates are thin rectangular sheets of glass or plastic. In use, a sample comprising an aqueous or non-aqueous liquid, liquid reagent, biological fluid and/or biological tissue section(s) is placed upon a portion of the slide or diagnostic glass plate. Before analysis, the sample on the slide or plate may be dried, placed in a fixative, or remain fresh prior to treatment for enhanced visualization by light, electron, or fluorescent microscopy, and/or including gross analysis with the human eye. The sample may be analyzed in its natural state or may need treatment with one or more liquid dyes to enhance visualization. Further treatment with molecular biological techniques may include, for example, treatment by monoclonal, polyclonal antibodies, in-situ hybridization by molecular probes, and/or their liquid detection reagents. During routine analysis or manipulation of a slide or plate, the sample or liquid reagent may spill from the slide, run or migrate onto other portions of the slide, and/or "wick off" if the slide touches another object, thus resulting in a loss of all or part of the liquid sample or reagent. It is desirous to avoid such inadvertent

or undesired mixing or contamination of different samples or liquid reagents.

It is therefore beneficial for the slide to have means to confine the sample or liquid used in treating the sample to a specific area on the slide or plate. This has been accomplished previously by creating a slide or plate having one or more depressions, or "wells" therein. Alternatively, a physical barrier or hydrophobic material may be applied to the slide surface in a bordered pattern to confine the liquid applied to the plate within the area surrounded by the border. Such borders may comprise a coating of teflon, paint, wax, paraffin, epoxy resin, or other resinous material, or a paint. Each of these materials results in a border having a thickness resulting in a raised border extending a distance above the surface of the glass, for example, a teflon layer is generally from about 0.00254 to about 0.00635 cm (about .001 to about .0025 inches) high. These raised areas are generally opaque and the end result is a loss of the transparent nature of the slide. In spite of the fact that these raised borders may be somewhat effective in confining the liquid, there continues to be a need for a slide or plate which achieves confinement of the liquid upon a slide while maintaining transparency of the glass or plate. It is the object of the present invention to provide such a slide.

SUMMARY OF THE INVENTION

The present invention contemplates an analytic plate such as a microscope slide or a diagnostic plate having a containment border for inhibiting migration of liquids or liquid samples thereon, wherein the border is substantially transparent and is substantially flush with the surface of the slide or plate and which covers only a portion of the surface of the slide or plate.

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1A is a plan view of a microscope slide constructed in accordance with the present invention.

Figure 1B is a side view of the slide of Figure 1A.

Figure 2A is a plan view of another version of a microscope slide constructed in accordance with the present invention.

Figure 2B is a side view of the slide of Figure 2A.

Figure 3 is a plan view of another version of a microscope slide constructed in accordance with the present invention.

Figure 4 is a plan view of another version of a microscope slide constructed in accordance with the present invention.

Figure 5 is a plan view of another version of a microscope slide constructed in accordance with the present invention.

Figure 6 is a plan view of another version of a microscope slide constructed in accordance with the present invention.

Figure 7 is a plan view of a pen used in accordance with the present invention.

DETAILED DESCRIPTION OF THE INVENTION

The present invention contemplates an analytic plate such as a microscope slide or a diagnostic plate having a containment border for inhibiting migration of liquids or liquid samples thereon, wherein the border is substantially transparent and is substantially flush with the surface of the slide or plate and which covers only a portion of the surface of the slide or plate.

Where used herein, the term "analytic plate" refers to those types of plates such as microscope slides and diagnostic plates which are used, for example, in microscopic analysis or diagnostic analysis or comparison of samples. Analytic plates are generally comprised of clear glass or plastic but may also comprise ceramic materials. When used herein, the terms, "plate" and "slide" are intended to be interchangeable.

Referring now to Figures 1A and 1B, a glass microscope slide having the general reference numeral 10 is shown. The slide 10 has a conventional length, width and thickness as is well known to one of ordinary skill in the art. The slide 10 has an upper surface 12 and a lower surface 14. Disposed upon a portion of the upper surface 12 is a liquid containment border 16 which in the version of Figure 1A has a rectangular shape. Where used herein the term "liquid containment border" or "containment border" refers to a transparent border which prevents passage of an aqueous or non-aqueous liquid thereacross. The containment border 16 surrounds a containment area 18 of the upper surface 12 of the slide 10. The containment border 16 forms a liquid barrier about the containment

area 18. When a liquid or liquid sample (not shown) is placed upon the containment area 18 of the slide 10 for analysis, the containment border 16 prevents the spreading, leakage or migration of the liquid or liquid sample from the containment area 18, thus causing the sample to be retained in a discrete and confined location upon the slide 10. Where used herein, the term liquid or liquid sample is intended to refer to a liquid material, or a liquid biological sample (e.g., blood, urine, plasma, or cerebrospinal fluid) which is desired to be localized on the slide.

The coating material which is used to form the containment border 16 comprises a material which when applied to the slide 10 is preferably transparent or clear although it may have a color to indicate its position on the slide or have printed, by one of ordinary skill in the art, on the lower surface 14 and/or upper surface 12 of the slide 10 information (lines or numbers or symbols) indicating the position of the liquid border 16 on the upper surface 12. The border 16 forms a molecular layer when dry and therefore is substantially flush (level) with the upper surface 12 of the slide 10. The border 16 is therefore not raised above the upper surface 12 to a degree that is visible to the naked eye. In fact, the containment border 16 preferably has a thickness of less than about 0.0000254 cm (about 0.00001 inches). After the coating is applied to the slide thereby forming the containment border and the slide is dried, the slide may be buffed or treated chemically (e.g., by xylene, alcohol, or acetone or other commonly used laboratory solvents) wherein the containment border is rendered clear and invisible

whereby the border leaves the refractive index of the slide unaltered when viewed through a microscope.

In a preferred embodiment the coating material which forms the containment border 16 is a composition comprising a liquid repellant compound dissolved in a volatile solvent. In a particularly preferred version, the composition comprises an alkyl polysiloxane and a mineral acid mixed with a solvent in a manner well known in the art. Such a mixture is described in U.S. Patent No. 3,579,540, the specification of which is hereby incorporated herein by reference in its entirety. Other polysiloxanes, silicones and silicon fluids which can permanently or at least substantially permanently bond to a glass surface and function in accordance with the present invention are also contemplated and are well known in the art, and are available commercially for use herein. Although a polysiloxane acid mixture is particularly preferred, it will be understood by one of ordinary skill in the art that any material which can adhere to the surface of at least one of a glass, plastic or ceramic slide or plate and which forms a substantially non-raised molecular layer as described and claimed herein and is suitable for use in the present invention.

The coating can be applied to the slide 10 in any manner known in the art for applying a liquid to a surface, for example, by brushing, wiping, by using a stamping device, by spraying or by application from a device (pen-like) filled with the coating to be applied to the slides or plates (described in more detail below).

In an alternative method of application of the coating for the containment border 16, the analytic slide may be provided with a removable raised layer of a material such as a silicone rubber which is applied as a raised strip on a portion of the upper surface 12 of the slide 10 (not shown). Prior to the application of the liquid or liquid sample for treatment, the raised silicone strip is peeled away from the upper surface 12 of the slide 10, leaving a residual coating comprising a containment border 16 in accordance with the present invention. After the raised silicone rubber strip has been peeled away leaving the containment border 16, the analytic plate can be used in accordance with the present invention.

It is another distinctive characteristic of the present invention that after the coating is applied to the slide 10 to form the containment border 16 and the coating material has dried thereon, the containment border 16 is highly resistant to abrasion and to chemical removal and physical removal by washing, scrubbing, soaking in acids, alkalis, organic solvents, and aqueous solvents. The slide 10 can therefore be used repeatedly without losing its functionality.

The containment border 16 of the present slide 10 is further distinguished from prior art slides with borders which have teflon borders or other physical barriers because the surface of such prior art slides must be treated before the teflon coating can adhere to the slide (e.g., using an adhesive) thus causing solvents to dissolve the adhesive and the subsequent loss of the border's

efficiency due to peeling and/or loss of the liquid confinement integrity of the border. The borders of slides using coatings of teflon, epoxy, or paint are generally opaque and are raised above the surface of the slide, unlike the borders on the slides of the present invention. In the present invention, there is no intervening layer (e.g., an adhesive) between the glass and the coating comprising the containment border 16. Further, borders of such prior art slides also suffer from non-specific binding of reagents along their edges thereby causing interference with the specimen. An example is interference from non-specific fluorescence.

Although the microscope slide of the present invention may consist solely of a slide 10 with the containment border 16 thereon, in some embodiments the slide may further have a distinct marking surface thereon for writing upon or for attaching a label thereto. Figures 2A and 2B show such a slide, designated therein by the general reference numeral 10a. The slide 10a has a marking surface 20 which is a "frosted" portion of the slide 10a (i.e., a portion of the slide 10a which has been etched off or abraded). In an alternative version of such a slide, the marking surface 20 may be an opaque epoxy or painted coating. Other means of forming a marking surface will be apparent to one of ordinary skill in the art. Figure 2A further shows an alternative version of the invention wherein the containment border, designated by the general reference numeral 22 comprises a pair of strips extending from one edge of the slide to another, rather than forming a box pattern as

shown in slide 10a. Figure 3 shows a slide 10b which is essentially the same as slide 10a except the containment border is a border 24 which forms an entire "box" on the surface 12 of the slide 10b. Figure 4 shows an alternative embodiment of the invention, a slide 10c having a containment border 26 which comprises a pair of separate containment areas 28. The separate containment areas 28 can therefore contain separate samples which are prevented from mixing by the portion 30 of the containment border 26 which separates the two containment areas 28. Although not specifically shown in the figure, the slide 10c may be constructed to comprise a plurality of separate containment areas 28 greater than two for holding a plurality of samples, as will be understood by a person of ordinary skill in the art. Figure 5 shows a slide 10d having a pair of circular containment borders 32 which surround containment areas 34. Alternative versions of slide 10d may have only a single circular containment border 32, or may have a plurality of circular containment borders 32. Figure 6 shows a slide 10e comprising a containment border 36 having a diagonal border 38 extending thereacross forming a pair of triangle shaped containment areas 40. Alternative versions of the slide 10e may have only a single triangle shaped containment area 40, or may have a plurality of areas 40. Further, it will be understood by a person of ordinary skill in the art that the shapes of the containment areas are not limited only to those shown in the figures herein. The containment areas may have other shapes, such as ovals, stars, ellipses, pentagons, hexagons, trapezoids, or even

non-geometric or fanciful shapes. Further, a single slide may have more than one particular shape of containment border disposed thereon, for example, a circle and a box or a pair of circles and a pair of boxes.

As is evident from the above, each slide contemplated herein has only a portion of the surface thereof coated with the coating material, with the specific purpose for retaining a liquid or liquid sample upon a discrete and predetermined portion of the slide.

In an alternative embodiment of the invention, one or more of the microscope slides or plates contemplated herein may be supplied as a kit along with other components used in microscopic analysis of samples. Said other components may comprise stains and reagents commonly used by those of ordinary skill, including but not limited to, stains, dyes, molecular biological reagents including monoclonal and polyclonal antibodies, and molecular probes and their detection reagents, and other aqueous and non-aqueous processing reagents. Examples of aqueous and non-aqueous processing reagents include xylene, toluene, acetone, and other organic and inorganic solvents, and alcohols, biological buffers, and aqueous reagents for use with antibodies, and molecular probes and their detection reagents.

As noted above, the containment border may be applied via a pen, or pen-like device, an example of which is shown in Figure 7. The pen is designated by reference number 50 and comprises a body 52 having a reservoir therein (not shown) which contains a quantity

of the liquid coating described elsewhere herein (e.g., polysiloxane). The pen 50 further comprises an applicator end 54, and a cap 56 for inhibiting evaporation of the coating material or drying of the tip 54. The pen 50 or cap 56 may comprise means for clipping, e.g., to a pocket. The applicator end may be a brush, a swab, a rubber tip, or any other device known to one of ordinary skill in the art of applicator pens.

As contemplated herein, a user can use the pen 50 to custom make his own "bordered slides" having a containment border as described herein. The border applied in such a manner is substantially permanent and resistant to removal by organic solvents such as xylene, as described above. In use, the user applies a layer of the polysiloxane material to a slide, allows it to dry, then applies the aqueous or non-aqueous liquid or histological material, or other biological sample, and carries out various processing steps known in the art for analyzing the specimen (e.g., treating with stains and organic solvents). Treatment with organic solvents used in the processing steps has substantially no effect on the durable containment border as claimed herein. The pen applicator of the present invention differs from other pen applicators known in the art (e.g., PAP Pen) because such prior art pens are used only to apply a greasy or oily layer to the slide which is neither resistant to abrasion or rubbing nor resistant to organic solvents, i.e., the layer can be physically wiped or worn off and is not resistant to most organic solvents such as xylene. The containment borders provided by using the pen 50 described herein are resistant to abrasion or to removal by organic solvents.

The user may desire to apply the polysiloxane material to a slide previously treated with a coating which imparts a positive charge to the slide. Preferably before application of the polysiloxane, such a charged coating will be removed from that area of the slide upon which the containment border is desired to be located. The charged coating can be removed by physical abrasion or by chemical removal. The chemical for removing the charged coating (e.g., organic or inorganic+ acids, or bases) may be applied to the slide before application of the polysiloxane material. Alternatively, the chemical for removing the charged coating, and the polysiloxane, may be applied simultaneously. For example, the chemical for removing the coating and the polysiloxane may be applied together in a single composition.

The examples described herein are not intended to limit the scope of the invention.

Changes may be made in the construction and the operation of the various components, elements and assemblies described herein or in the steps or the sequence of steps of the methods described herein without departing from the scope of the invention as defined in the following claims.

What is claimed is:

1. An analytic plate, comprising:

a glass, plastic, or ceramic plate having an upper surface and lower surface and having a containment border on a portion of said upper surface, the containment border surrounding a containment area for containing an aqueous or non-aqueous liquid or liquid sample and which substantially prevents the migration of the aqueous or non-aqueous liquid or liquid sample from the containment area to portions of the upper surface of the plate outside of the containment border, and wherein the containment border has a thickness of less than about 0.0000254 cm (about 0.00001 inches).

2. The analytic plate of claim 1 wherein the containment border is transparent.

3. The analytic plate of claim 2 wherein the containment border is colored.

4. The analytic plate of claim 1 wherein the containment border is invisible.

5. The analytic plate of claim 1 wherein the containment border comprises a coating comprising a polysiloxane composition.

6. The analytic plate of claim 5 wherein the polysiloxane composition comprises an alkyl polysiloxane.

7. The analytic plate of claim 1 wherein the containment border does not alter the refractive index of the analytic plate when viewed through a microscope.

8. The analytic plate of claim 1 wherein the containment border is abrasion resistant and resistant to removal by organic solvents.

9. The analytic plate of claim 1 wherein the containment border has a thickness of a molecular layer.

10. The analytic plate of claim 1 having printed information thereon indicating the position of the containment border, the printed information further comprising lines, numbers, or other symbols.

11. An analytic plate, comprising:

a glass, plastic, or ceramic plate having an upper surface and lower surface and having a containment border on a portion of said upper surface, the containment border surrounding a containment area for containing an aqueous or non-aqueous liquid or liquid sample and which substantially prevents the

migration of the aqueous or non-aqueous liquid or liquid sample from the containment area to portions of the upper surface of the plate outside of the containment border, and wherein the containment border has a thickness of less than about 0.0000254 cm (about 0.00001 inches) and wherein the refractive index of the plate is not altered by the containment border when viewed through a microscope.

12. A kit for microscopic analysis, comprising:

at least one analytic plate comprising:

a glass, plastic, or ceramic plate having an upper surface and having a containment border on a portion of said upper surface, the containment border surrounding a containment area for containing an aqueous or non-aqueous liquid or liquid sample and which substantially prevents the migration of the liquid or liquid sample from the containment area to portions of the upper surface of the plate outside of the containment border, and wherein the containment border has a thickness of less than about 0.0000254 cm (about 0.00001 inches); and

a reagent for treating a biological sample disposed upon the analytic plate.

13. The kit of claim 12 wherein the containment border of the analytic plate is transparent.

14. The kit of claim 12 wherein the containment border of the analytic plate comprises a coating comprising a polysiloxane composition.

15. The kit of claim 14 wherein the polysiloxane composition comprises an alkyl polysiloxane.

16. The kit of claim 12 wherein the containment border of the analytic plate is colored.

17. The kit of claim 12 wherein the containment border of the analytic plate is invisible.

18. The kit of claim 12 wherein the containment border of the analytic plate does not alter the refractive index of the analytic plate when viewed through a microscope.

19. The kit of claim 12 wherein the containment border of the analytic plate is abrasion resistant and resistant to removal by organic solvents.

20. The kit of claim 12 wherein the containment border of the analytic plate has a thickness of a molecular layer.

21. The kit of claim 12 wherein the containment border of the analytic plate has printed information thereon indicating the position of the containment border, the printed information further comprising lines, numbers or other symbols.

22. The kit of claim 12 wherein the reagent is selected from a group of stains and biological reagents consistent with medical diagnosis comprising stains, dyes, aqueous and non-aqueous processing reagents, and molecular biological reagents and their detection reagents.

23. The kit of claim 22 wherein the aqueous and non-aqueous processing reagents further comprise xylene, toluene, acetone, alcohols, biological buffers, monoclonal and polyclonal antibodies, molecular probes and their detection reagents.

24. A method of using an analytic plate, comprising:

providing a glass, plastic, or ceramic plate having an upper surface and a lower surface and having a containment border on a portion of said upper surface and wherein the containment border surrounds a containment area for containing an aqueous or non-aqueous liquid or biological sample, the containment border able to substantially prevent the migration of the liquid or biological sample from the containment area to portions of the

upper surface of the plate outside of the containment area, and wherein the containment border has a thickness of less than about 0.0000254 cm (about 0.00001 inches); and

applying the liquid or biological sample to the containment area of the glass, plastic, or ceramic plate.

25. The method of claim 24 wherein the liquid or liquid sample applied to the plate is selected from a group of stains and biological reagents consistent with medical diagnosis comprising stains, dyes, aqueous and non-aqueous processing reagents, and molecular biological reagents and their detection reagents.

26. The method of claim 25 wherein the liquid or liquid sample is an aqueous or non-aqueous processing reagent selected from the group consisting of xylene, toluene, acetone, alcohols, biological buffers, monoclonal and polyclonal antibodies, molecular probes and their detection reagents.

27. An applicator device for applying a containment border to an analytic plate, the applicator device comprising:

a pen comprising a reservoir and an applicator end and the reservoir containing a quantity of a liquid polysiloxane, and wherein when the applicator end is appressed to a surface of a glass, plastic, or ceramic analytic plate, the liquid polysiloxane flows from the reservoir through the applicator end to the surface of the analytic plate, and wherein the pen is sized to be held by a user's hand.

28. A method of applying a containment border to an analytic plate, comprising:

providing a glass, plastic, or ceramic analytic plate;

providing a pen comprising a reservoir and an applicator end and a quantity of a liquid contained within the reservoir; and

manually holding the pen and appressing the applicator end to a surface of the analytic plate and applying a containment border to the surface, wherein the containment border after drying is substantially flush with the surface of the plate, is resistant to abrasion and is resistant to removal by organic solvents.

29. A method of applying a containment border to an analytic plate, comprising:

providing a glass, plastic, or ceramic analytic plate;

providing a pen comprising a reservoir and an applicator end and a quantity of a liquid polysiloxane contained within the reservoir; and

manually holding the pen and appressing the applicator end to a surface of the analytic plate and applying a containment border to the surface, wherein the containment border after drying is substantially flush with the surface of the plate.

30. A method of using an analytic plate, comprising:

providing a glass, plastic, or ceramic plate having an upper surface and a lower surface and having a raised silicone layer upon a portion of the upper surface, wherein the raised silicone layer is removable;

removing the raised silicone layer thereby leaving a containment border on the upper surface and wherein the containment border surrounds a containment area for containing an aqueous or non-aqueous liquid or liquid sample, the containment border able to substantially prevent the migration of the liquid or liquid sample from the containment area to portions of the upper surface of the plate outside

of the containment area, and wherein the containment border has a thickness of less than about 0.0000254 cm (about 0.00001 inches); and

applying the liquid or liquid sample to the containment area of the glass, plastic, or ceramic plate.

31. The method of claim 30 wherein the liquid or liquid sample applied to the plate is selected from a group of stains and biological reagents consistent with medical diagnosis comprising stains, dyes, aqueous and non-aqueous processing reagents, and molecular biological reagents and their detection reagents.

32. The method of claim 31 wherein the liquid or liquid sample is an aqueous or non-aqueous processing reagent selected from the group consisting of xylene, toluene, acetone, alcohols, biological buffers, monoclonal and polyclonal antibodies, molecular probes and their detection reagents.

33. An analytic plate, comprising:

a plate having an upper surface and lower surface and having a containment border on a portion of said upper surface, the containment border surrounding a containment area for containing a liquid or a sample.

34. An analytic plate, comprising:

a plate having an upper surface and lower surface and having a containment border on a portion of said upper surface, the containment border surrounding a containment area for containing a liquid or a sample, and wherein the refractive index of the plate is not altered by the containment border.

35. A kit for microscopic analysis, comprising:

at least one analytic plate comprising:

a plate having an upper surface and having a containment border on a portion of said upper surface, the containment border surrounding a

containment area for containing a liquid or a sample; and

a reagent for treating a sample disposed upon the analytic plate.

36. A method of using a plate, comprising:

providing a plate having an upper surface and a lower surface and having a containment border on a portion of said upper surface and wherein the containment border surrounds a containment area for containing a liquid or a sample; and

applying the liquid or the sample to the containment area of the plate.

37. An applicator device for applying a containment border to a plate, the applicator device comprising:

a pen comprising an applicator end, and wherein when the applicator end is near a surface of a plate, liquid flows through the applicator end to the surface of the plate.

38. A method of applying a containment border to a plate, comprising:

providing a plate;

providing a pen comprising an applicator end; and

positioning the applicator end near a surface of the plate and applying a containment border to the surface.

39. A method of applying a containment border to a plate, comprising:

providing a plate;

providing a pen comprising an applicator end; and

positioning the applicator end near a surface of the plate and applying a containment border to the surface, wherein the containment border is substantially flush with the surface of the plate.

40. A method of using a plate, comprising:

providing a plate having an upper surface and a lower surface and having a raised layer upon a portion of the upper surface, wherein the raised layer is removable;

removing the raised layer thereby leaving a containment border on the upper surface and wherein the containment border surrounds a containment area for containing a liquid or a sample; and

applying the liquid or the sample to the containment area of the plate.

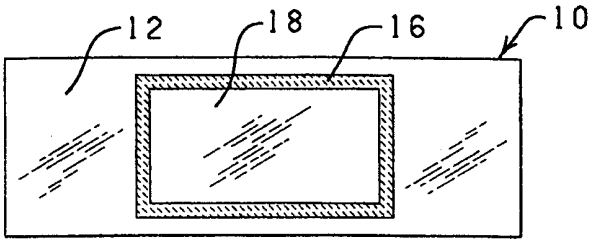

Fig. 1A

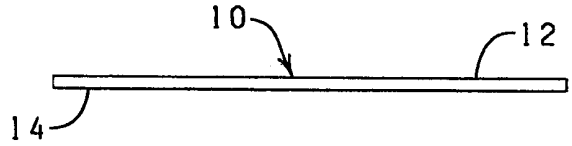

Fig. 1B

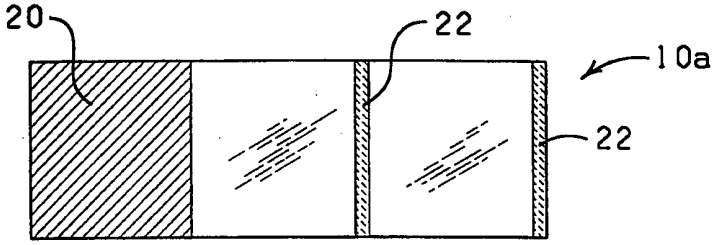

Fig. 2A

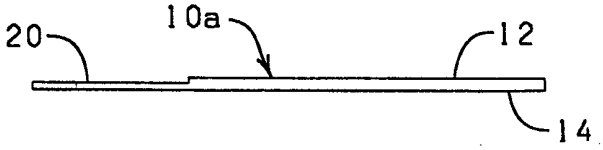

Fig. 2B

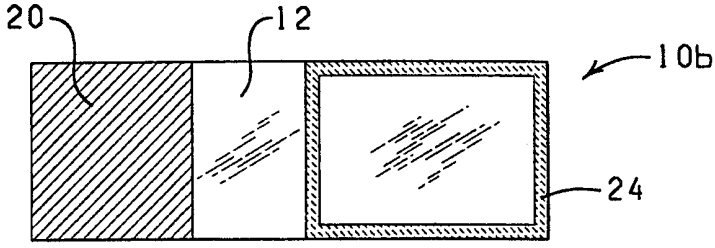

Fig. 3

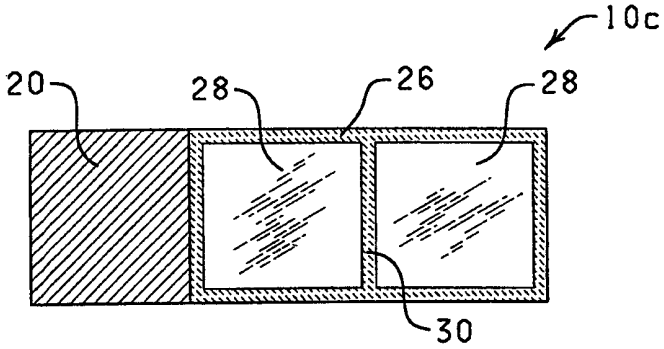

FIG. 4

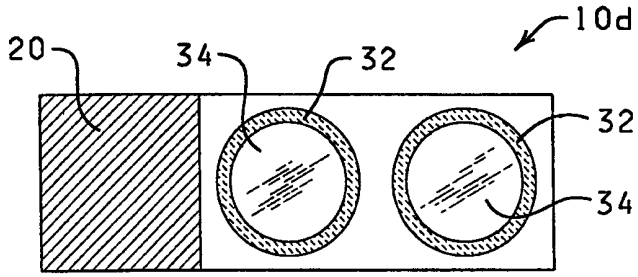

FIG. 5

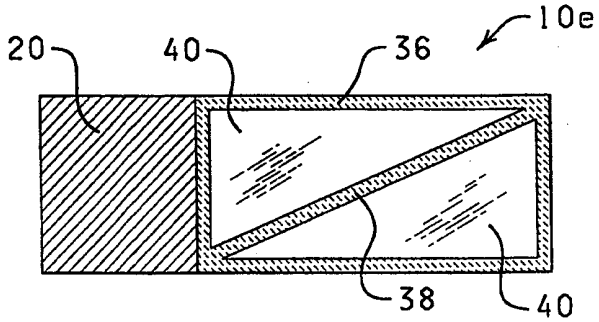

FIG. 6

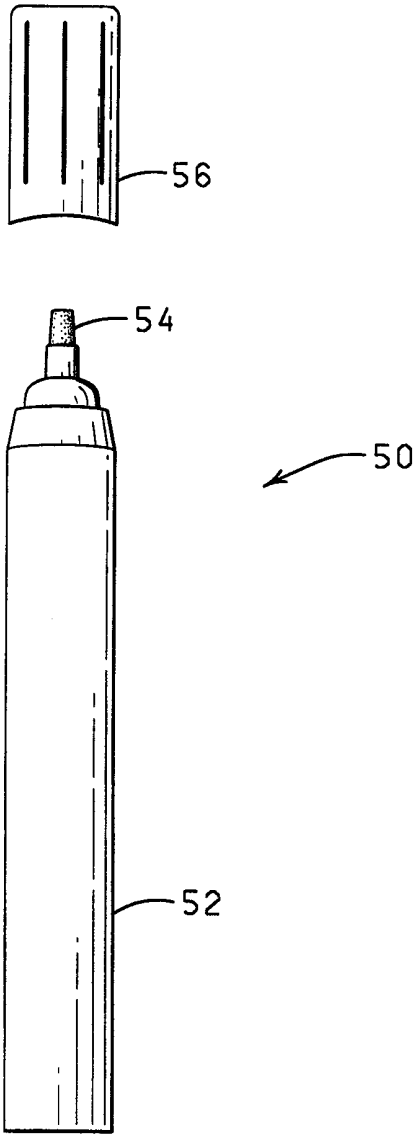

FIG. 7

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US99/02854

A. CLASSIFICATION OF SUBJECT MATTER

IPC(6) : G01N 33/48
US CL : 422/61

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).

U.S. : none

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

none

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

NONE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	"Introducing Lab Tek II- TheNext Generation" Brochure, Nalge Nunc International, Naperville, IL. Aug. 3,1996	1-40

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

*	Special categories of cited documents:	"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
"A"	document defining the general state of the art which is not considered to be of particular relevance	"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
"E"	earlier document published on or after the international filing date	"Y"	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"L"	document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"&"	document member of the same patent family
"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		

Date of the actual completion of the international search 22 April 1999	Date of mailing of the international search report 07 MAY 1999
Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703)305-3230	Authorized officer LYLE A. ALEXANDER Telephone No. (703)308-0651

Form PCT/ISA/210 (second sheet)(July 1992)★