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- **Yamak, Maha**
Loveland, CO Colorado 80537-0599 (US)
- **Grenz, Robert Lee**
Loveland, CO Colorado 80537-0599 (US)
- **Downs, Wilford**
Loveland, CO Colorado 80537-0599 (US)
- **Hudson, William C.**
Loveland, CO Colorado 80537-0599 (US)

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(71) Applicant: **Agilent Technologies, Inc.**
Santa Clara, CA 95051 (US)

(74) Representative: **Grünecker, Kinkeldey, Stockmair & Schwanhäusser**
Leopoldstrasse 4
80802 München (DE)

(72) Inventors:
• **Hulka, Ivan**
Loveland, CO Colorado 80537-0599 (US)

(54) **Holding device for dried biological fluid spotting membrane and related methods**

(57) A holding device for a dried biological fluid spotting membrane includes a plastic top face, a plastic bottom face, and a pocket disposed between the top face and the bottom face. The plastic top face includes a window formed therein. The pocket is configured for receiving a dried biological fluid spotting membrane that is ac-

cessible through the window by a user during dried biological fluid spot testing. A method for assembling a holding device includes positioning the membrane within a pocket of a plastic membrane housing, and securing the membrane within the pocket. The holding device may be utilized for forming dried biological fluid spots and extracting samples therefrom for analysis.

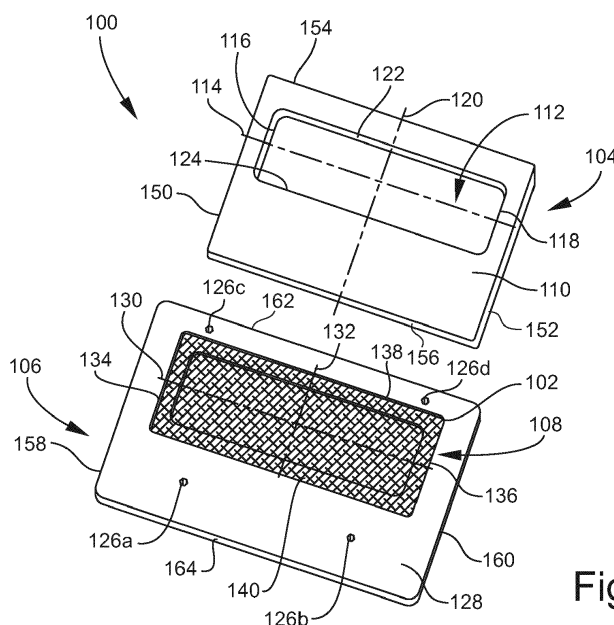


Fig. 1

Description

TECHNICAL FIELD

[0001] The present invention relates generally to dried biological fluid spot testing. More particularly, the present invention relates to devices and methods for holding dried biological fluid spotting membranes.

BACKGROUND

[0002] Dried biological fluid spot testing such as dried blood spot (DBS) testing is becoming increasingly popular for pharmaceutical companies in clinical trials. Collection sites for clinical trials may sample blood spots (or other types of biological fluid spots) in the field, allow the spots to dry, and then ship the spots at a lower cost than liquid samples due to the non-biohazard status of dried blood spots and the less rigorous requirements for temperature control. Blood spotting is also becoming useful in preclinical work as analytical chemists are required to store samples for Incurred Sample Reanalysis (ISR) studies, and dried blood spots have proven to be an effective way to stabilize the analytes and the matrix. Typically, DBS samples are prepared by applying drops of blood drawn from a finger or toe to an absorbent membrane or substrate (e.g., filter paper) of an appropriate composition. The blood saturates the membrane and is air dried for a period of time (e.g., several hours) sufficient to form an array of circular dried blood spots on the membrane. The spot-containing membrane (which, as described below, is typically housed in a cardboard holder) may then be stored in a plastic container and transported as needed without needing to be frozen. The dried blood spots may thereafter be separated from the bulk membrane by punching the dried blood spots to create individual dried blood spot disks. Analytes such as pharmaceutical compounds may then be extracted from the dried blood spots by any number of techniques and subjected to analytical testing. Other types of biological fluid samples may be dried and subsequently processed in an analogous manner.

[0003] Typically, the absorbent membrane is housed in a membrane holder that is made of cardboard or chipboard. The absorbent membrane is sandwiched between a top cardboard face and a bottom cardboard face. The top face is secured to the bottom face by adhesive. A user may access the absorbent membrane via a window that passes through the top face and/or the bottom face. Conventional cardboard holders have many problems. For instance, cardboard can bend or warp easily (during testing, handling, shipping, etc.) which can impede the uniformity of the absorbent membrane. As another example, chemicals in the adhesives used to secure the top cardboard face to the bottom cardboard face may contaminate blood samples on the absorbent membrane. Also, conventional cardboard holders are generally not reusable.

[0004] In view of the foregoing, there is a need for providing devices and methods specifically designed for effectively holding dried biological fluid spotting membranes. In particular, there is a need for providing a holding device for a dried biological fluid spotting membrane that is durable and effective in holding its form or shape (and thus the form or shape of the membrane) during testing (including automated testing), handling, shipping, etc. In addition, there is a need for providing a holding device for a dried biological fluid spotting membrane that minimizes (or eliminates) the use of chemical adhesives. There is also a need for providing a holding device for a dried biological fluid spotting membrane that is capable of being reused.

SUMMARY

[0005] To address the foregoing problems, in whole or in part, and/or other problems that may have been observed by persons skilled in the art, the present disclosure provides methods, processes, systems, apparatus, instruments, and/or devices, as described by way of example in implementations set forth below.

[0006] According to one implementation, a holding device for a dried biological fluid spotting membrane includes a plastic top face, a plastic bottom face, and a pocket disposed between the top face and the bottom face. The plastic top face includes a window formed therein, and the window has a length and a height. The pocket has a length and a height, and is configured for receiving a dried biological fluid spotting membrane that is accessible through the window by a user during dried biological fluid spot testing.

[0007] In some implementations, the length of the window is less than the length of the pocket, and the height of the window is less than the height of the pocket.

[0008] In some implementations, the window of the top face is a first window and the bottom face comprises a second window formed therein. The second window has a length that is substantially the same as the length of the first window, and a height that is substantially the same as the height of the first window.

[0009] In some implementations, the holding device includes a plastic laminate layer and a plastic body. The plastic laminate layer includes the top face. The plastic body includes the bottom face and an opposing inner face. The laminate layer is adhered to the inner face.

[0010] In some implementations, the holding device includes a plastic top piece and a plastic bottom piece. The plastic top piece includes the top face and a first inner face opposing the top face. The first inner face includes a plurality of male components extending from the first inner face. The plastic bottom piece includes the bottom face and a second inner face opposing the bottom face. The second inner face includes a plurality of female components extending into the second inner face. The female components are configured for detachably mating with the male components.

[0011] According to another implementation, a method is provided for assembling a holding device. A dried biological fluid spotting membrane is positioned within a pocket of a plastic membrane housing. The membrane is secured within the pocket, and is accessible by a user via a window formed in a top face of the plastic membrane housing.

[0012] In some implementations, securing the membrane within the pocket includes overmolding a top piece onto an inner face of the plastic membrane housing. The inner face includes the pocket formed therein, and the top piece includes the top face.

[0013] In some implementations, securing the membrane within the pocket includes adhering a plastic laminate layer to an inner face of the plastic membrane housing. The plastic laminate layer includes the top face.

[0014] In some implementations, securing the membrane within the pocket includes detachably mating male components extending from a first inner face of a top piece with female components extending into a second inner face of a bottom piece of the membrane housing. The top piece includes the top face and the first inner face opposing the top face. The bottom piece includes a bottom face and the second inner face opposing the bottom face. The second inner face includes the pocket formed therein.

[0015] According to another implementation, a method is provided for using a holding device in which a membrane is secured in a pocket of the holding device. A dried biological fluid spot is formed on the membrane by accessing the membrane via a window of the holding device, applying a drop of a biological fluid sample to the membrane to form a biological fluid spot, and allowing the biological fluid spot to dry.

[0016] In some implementations, the method includes accessing the dried biological fluid spot via the window and extracting a portion of the dried biological fluid spot formed on the membrane.

[0017] In some implementations, the method includes removing the top piece from the bottom piece by detaching male components from female components. The membrane may be removed from the pocket. The removed membrane may be replaced with a second dried biological fluid spotting membrane by positioning the second membrane within the pocket. The second membrane may be secured within the pocket by detachably mating the male components and the female components.

[0018] Other devices, apparatus, systems, methods, features and advantages of the invention will be or will become apparent to one with skill in the art upon examination of the following figures and detailed description. It is intended that all such additional systems, methods, features and advantages be included within this description, be within the scope of the invention, and be protected by the accompanying claims.

BRIEF DESCRIPTION OF THE DRAWINGS

[0019] The invention can be better understood by referring to the following figures. The components in the figures are not necessarily to scale, emphasis instead being placed upon illustrating the principles of the invention. In the figures, like reference numerals designate corresponding parts throughout the different views.

[0020] FIG. 1 is an exploded view of an example of a holding device for a dried biological fluid spotting membrane according to an implementation disclosed herein.

[0021] FIG. 2A is a plan view of a top face of a top piece of the holding device illustrated in FIG. 1.

[0022] FIG. 2B is a plan view of a first inner face opposite the top face illustrated in FIG. 2A.

[0023] FIG. 2C is a side cross-sectional elevation view of a male component illustrated in FIG. 2B.

[0024] FIG. 3A is a plan view of a second inner face of a bottom piece illustrated in FIG. 1, shown without the dried biological fluid spotting membrane.

[0025] FIG. 3B is a side cross-sectional elevation view of the bottom piece illustrated in FIG. 3A.

[0026] FIG. 4 is an exploded view of another example of a holding device for the dried biological fluid spotting membrane according to an implementation disclosed herein.

[0027] FIG. 5 is a perspective view of another example of a holding device for the dried biological fluid spotting membrane according to the present invention.

DETAILED DESCRIPTION

[0028] In the context of the present disclosure, the term "fluid" refers generally to liquid-phase materials and gas-phase materials, unless a liquid-phase material or a gas-phase material is specifically indicated. The terms "liquid-phase" and "liquid," and "gas-phase" and "gas," are used interchangeably. A liquid-phase material or liquid may be any liquid, such as a solution, suspension, slurry, multi-phase mixture or the like, and may include gaseous components (e.g., bubbles) and/or solid components (e.g., particles). A gas-phase material or gas may be any gas or vapor, and may include liquid components (e.g., droplets) and/or solid components (e.g., particles). A "dried fluid sample" or a "dried fluid spot" refers generally to a material that was initially provided in the liquid phase and was thereafter dried, such as by air drying.

[0029] In the context of the present disclosure, the term "analyte" refers generally to any sample molecule of interest—that is, a molecule on which an analysis is desired such as, for example, a chromatographic analysis.

[0030] Examples of implementations of the subject matter disclosed herein will now be described in more detail with reference to FIGS. 1-5.

[0031] FIG. 1 is an exploded view of an example of a holding device (or "membrane housing") **100** for a dried biological fluid spotting membrane (or "substrate," or "card") **102** according to an implementation of the present

teachings. Examples of biological fluids that may be formed into dried biological fluid spots using the membrane **102** include, but are not limited to, blood-based samples such as whole blood, plasma or serum. In these cases, the spot-containing membrane **102** is often termed a dried blood spotting card. It will be appreciated, however, that biological fluids formable into dried spots are not limited to blood-based samples. The membrane **102** may be made of any composition suitable for use as a spotting card, non-limiting examples of which include various types of cellulosic filter papers, glass fiber/cellulose composites, cellulose-free glass fiber paper, polyamides (e.g., nylon), propylene, nitrocellulose, polyether-sulfone, etc. Further examples of membrane compositions are described in U.S. Patent Application No. 12/860,669, titled DRIED BLOOD SPOTTING PAPER DEVICE AND METHOD, filed August 20, 2010, which is incorporated by reference herein in its entirety. Preferably, the membrane **102** material is able to uniformly absorb a biological fluid sample to form a homogeneous circular spot. Indicia such as dashed circles may be provided on the membrane **102** for assisting in placement of multiple biological fluid samples when it is desired to form an array of dried biological fluid spots. The indicia may include printed matter, perforations and/or scoring.

[0032] As illustrated in FIG. 1, the holding device **100** may include a plastic top piece **104**, a plastic bottom piece **106**, and a pocket **108** configured for receiving the membrane **102**. The top piece **104** and the bottom piece **106** may generally be made of any suitable plastic material capable of being injection molded or formable by any other suitable fabrication technique. Examples of suitable plastic materials include, but are not limited to, polypropylene, polyethylene, other polyolefins, polyamide, polyacrylate, and the like. As injection molding of plastic materials is widely known to those of skill in the art, a detailed discussion of the injection molding process will not be discussed in detail in the present disclosure. The top piece **104** may include a top face **110**, a first inner face (see FIG. 2B, element **220**) opposing the top face **110** and a first window **112** formed between the top face **110** and the first inner face **220**. As used herein, the phrase "a first window **112** formed between the top face **110** and the first inner face **220**" is not intended to limit the method by which the first window **112**, the top face **110**, or the first inner face **220** is formed. For example, in the injection molding process, a mold for the top piece **104** may be designed such that when the plastic material is injected into the mold, a protrusion in the mold may form the first window **112** between the top face **110** and the first inner face **220**. As another example, after the injection molding process, appropriate tools may be used to cut the first window **112** between the top face **110** and the first inner face **220**. It will be understood that the present disclosure encompasses various components formed into a surface or between two or more surfaces, as well as a surface or surfaces formed so as to provide various components therein or therethrough.

[0033] The first window **112** has a length and a height. To more easily describe dimensions of various components of the present invention, lengths and heights of the various components will be described in relation to horizontal and vertical axes. Although the cross-sections of the holding devices **100** (and holding devices **400** and **500** discussed below in conjunction with FIGS. 4-5) described herein are rectangular in shape, it will be understood that the cross-sections of the holding devices **100**, **400** and **500** (as well as the shapes of windows described herein) may be any suitable shape, such as circular, polygonal, elliptical, etc. The length of the first window **112** is measured along a horizontal axis **114**, and is the distance between a first side wall **116** and a second side wall **118** of the first window **112**. The height of the first window **112** is measured along a vertical axis **120**, and is the distance between a top wall **122** and a bottom wall **124** of the first window **112**. The first window **112** allows a user to access the membrane **102** when the top piece **104** is secured to the bottom piece **106**.

[0034] FIG. 2A is a plan view of the top face **110** of the holding device **100** illustrated in FIG. 1. FIG. 2B is a plan view of the first inner face **220**, which is opposite the top face **110** illustrated in FIG. 2A. The first inner face **220** may include a plurality of male components **226a** - **226d** extending from the first inner face **220**. The male components **226a** - **226d** are configured for detachably mating with corresponding female components (see FIGS. 1 and 3A-3B, elements **126a** - **126d**) extending into a second inner face **128**. In some implementations, the male components **226a** - **226d** may not be visible from the top face **110**. The broken lines formed into circles on the top face **110** in FIG. 2A illustrate where the male components **226a** - **226d** are positioned on the first inner face **220** relative to the top face **110**. Although the holding device **100** in the present implementation includes four male components **226a** - **226d** and four corresponding female components **126a** - **126d**, it will be understood that the holding device **100** may include any suitable number of male components **226a** - **226d** and corresponding female components **126a** - **126d**, and the male components **226a** - **226d** and female components **126a** - **126d** may be positioned in any suitable place on the first inner face **220** and the second inner face **128**, respectively. In some implementations, the first inner face **220** may include female components **126a** - **126d** extending into the first inner face **220**, and the second inner face **128** may include male components **226a** - **226d** extending from the second inner face **128**.

[0035] FIG. 2C is a side cross-sectional elevation view of the male component **226c** illustrated in FIG. 2B. As shown in FIG. 2C, the male component **226c** may include a compressible portion **230** such as a collar that is configured for compressing as the male component **226c** is pressed or otherwise detachably secured within the corresponding female component **126c**. For example, as the male component **226c** is positioned within the female component **126c**, the compressible portion **230** may be

compressed by force imparted by the inner wall(s) of the female component **126c**, which may result in an interference fit, friction fit, press fit, or the like between the male component **226c** and the corresponding female component **126c**. As shown in FIG. 2C, in some implementations the compressible portion **230** may include two or more segments separated by a gap that are movable relative to each other when force is imparted to one or more of the segments. The other male components **226a**, **226b** and **226d** may be configured substantially identical to male component **226c**.

[0036] Returning to FIG. 1, the bottom piece **106** of the holding device **100** includes the second inner face **128** and a bottom face (see FIG. 3B, element **340**). As discussed above, the second inner face **128** may include the female components **126a** - **126d** extending into the second inner face **128**. In the present example, the female components **126a** - **126d** have hexagonal cross-sections. It will be understood that the female components **126a** - **126d** may include any suitable cross-sectional shape, so long as the female components **126a** - **126d** are configured for detachably receiving the corresponding male components **226a** - **226d**. In some implementations, the female components **126a** - **126d** may extend into the second inner face **128** a selected depth. In some implementations, the female components **126a** - **126d** may extend through the bottom piece **106**, i.e., from the second inner face **128** to the bottom face **340**.

[0037] As shown in FIG. 1, the pocket **108** may be formed in the second inner face **128**, and is configured for receiving the membrane **102**. The pocket **108** is shown more clearly in FIG. 3A. FIG. 3A is a plan view of the second inner face **128** illustrated in FIG. 1, shown without the dried biological fluid spotting membrane **102**. The pocket **108** has a length and a height. The length of the pocket **108** is measured along a horizontal axis **130**, and is the distance between a first side wall **134** and a second side wall **136** of the pocket **108**. The height of the pocket **108** is measured along a vertical axis **132**, and is the distance between a top wall **138** and a bottom wall **140** of the pocket **108**. The length of the first window **112** may be less than the length of the pocket **108**, and the height of the first window **112** may be less than the height of the pocket **108**, such that the membrane **102** may be securely held between the top piece **104** and the bottom piece **106** when the top piece **104** is secured to the bottom piece **106** (i.e., when the male components **226a** - **226d** are detachably mated with the corresponding female components **126a** - **126d**).

[0038] FIG. 3B is a side cross-sectional elevation view of the bottom piece **106** illustrated in FIG. 3A. In some implementations, the first window **112** (FIGS. 1, 2A and 2B) is the only window of the holding device **100**, and the bottom face **340** serves as a solid backing for the membrane **102** and thus may serve as a disposable punching surface. In other implementations, as illustrated in FIGS. 3A-3B, the bottom face **340** may include a second window **312** formed therein. The second window **312** allows

a user to access the membrane **102** via the bottom face **340** of the holding device **100**. The second window **312** has a length and a height. The length of the second window **312** is measured along the horizontal axis **130**, and is the distance between a first side wall **320** and a second side wall **322** of the second window **312**. The height of the second window **312** is measured along the vertical axis **132**, and is the distance between a top wall **324** and a bottom wall **326** of the second window **312**. As with the first window **112**, the length of the second window **312** may be less than the length of the pocket **108**, and the height of the second window **312** may be less than the height of the pocket **108**. In some implementations, the length of the second window **312** may be substantially the same as the length of the first window **112**, and the height of the second window **312** may be substantially the same as the height of the first window **112**.

[0039] Returning to FIG. 1, the top piece **104** has a length and a height. The length of the top piece **104** is measured along the horizontal axis **114**, and is the distance between a first outer side wall **150** and a second outer side wall **152** of the top piece **104**. The height of the top piece **104** is measured along the vertical axis **120**, and is the distance between an outer top wall **154** and an outer bottom wall **156** of the top piece **104**. Similarly, the bottom piece **106** has a length and a height. The length of the bottom piece **106** is measured along the horizontal axis **130**, and is the distance between a first outer side wall **158** and a second outer side wall **160** of the bottom piece **106**. The height of the bottom piece **106** is measured along the vertical axis **132**, and is the distance between an outer top wall **162** and an outer bottom wall **164** of the bottom piece **106**. In some implementations, the length of the top piece **104** and the length of the bottom piece **106** may range from about 1 inch to about 6 inches, and the height of the top piece **104** and the height of the bottom piece **106** may range from about 1 inch to about 3 inches. In some implementations, the length and/or height of the top piece **104** may be less than the respective length and/or height of the bottom piece **106**.

[0040] The user of the holding device **100** may easily attach the top piece **104** to the bottom piece **106** by pressing the male components **226a** - **226d** into the corresponding female components **126a** - **126b**. The user of the holding device **100** may easily detach the top piece **104** from the bottom piece **106** by removing the male components **226a** - **226d** from the female components **126a** - **126b** (e.g., pulling the top piece **104** away from the bottom piece **106**). The membrane **102** may be positioned in the pocket **108**, and the top piece **104** may then be secured to the bottom piece **106**. One or more dried biological fluid spots may be formed on the membrane **102**. For example, a user (or an automated testing apparatus) may access the membrane **102** via the first window **112** (or, in some implementations, via the second window **312**), and apply a drop(s) of a biological fluid sample to the membrane to form a biological fluid spot.

The biological fluid spot may be allowed to dry over a period of time. A user may form a dried biological fluid spot on the membrane **102** without actually handling the membrane **102**, which may decrease the likelihood of contamination of the biological fluid sample. A user may extract a portion of the dried biological fluid spot (for example, by using a punch device, or any other suitable extraction apparatus) for assaying. A portion of the dried biological fluid spot may be extracted (e.g., punched) via the first window **112**, for example. The membrane **102** does not have to be handled by a user in order to extract a portion of the dried biological fluid spot. The user may detach the top piece **104** from the bottom piece **106**, and remove the membrane **102** from the pocket **108**. In some implementations, the top piece **104** and bottom piece **106** may be sterilized after the membrane **102** is removed. The user may position a second membrane within the pocket **108**. The user may secure the second membrane within the pocket **108** by detachably mating the male components **226a - 226d** and the corresponding female components **126a - 126d**. As may be seen from the present disclosure, the holding device **100** may be reused. The holding device **100** does not require the use of adhesives. Since the holding device **100** is made of injection molded plastic, the holding device **100** is a durable alternative to conventional cardboard holders. For example, the plastic holding device **100** may be less likely to bend or deform during shipping, handling, automated testing, etc.

[0041] FIG. 4 is an exploded view of another example of a holding device **400** for the dried biological fluid spotting membrane **102** according to an implementation disclosed herein. The holding device **400** includes a plastic body **402**. The body **402** may be composed of any suitable polymer such as described by example above, and may be formed by any suitable fabrication technique, such as injection molding. The plastic body **402** includes an inner face **436**, a bottom face (not shown) opposing the inner face **404** and a pocket **406** formed in the inner face **436**. The pocket **406** is configured for receiving the membrane **102**. The pocket **406** has a length and a height. The length of the pocket **406** is measured along a horizontal axis **408**, and is the distance between a first side wall **410** and a second side wall **412** of the pocket **406**. The height of the pocket **406** is measured along a vertical axis **414**, and is the distance between a top wall **416** and a bottom wall **418** of the pocket **406**. The holding device **400** includes a plastic laminate layer **420** that may be adhered to the inner face **436**. The plastic laminate layer **420** may be made of any suitable plastic material, and may be adhered to the inner face **436** by any suitable adhesive known to those skilled in the art. The laminate layer **420** includes a top face **404**. The top face **404** includes a first window **422** therein, which allows a user to access the membrane **102** when the laminate layer **420** is adhered to the inner face **436**. The first window **422** has a length and a height. The length of the first window **422** is measured along a horizontal axis **424**, and is the

distance between a first side wall **426** and a second side wall **428** of the first window **422**. The height of the first window **422** is measured along a vertical axis **430**, and is the distance between a top wall **432** and a bottom wall **434** of the first window **422**. The length of the first window **422** may be less than the length of the pocket **406**, and the height of the first window **422** may be less than the height of the pocket **406**, such that the membrane **102** may be securely held within the pocket **406** when the laminate layer **420** is adhered to the inner face **436**. In some implementations, the bottom face of the plastic body **402** may include a second window (not shown) therein, which allows a user to access the membrane **102** via the bottom face. The second window may be configured similarly to the second window **312** discussed above in conjunction with FIGS. 1- 3B.

[0042] FIG. 5 is a perspective view of another example of a holding device **500** for the dried biological fluid spotting membrane **102** according to the present invention. The holding device **500** may include a bottom face (not shown), a top face **502**, and a pocket **504** disposed between the bottom face and the top face **502**, where the pocket **504** includes the membrane **102** positioned therein. A bottom piece of the holding device **500** may include an inner face (not shown) and the bottom face. The inner face may include the pocket **504** formed therein. The pocket **504** has a length and a height. The length of the pocket **504** is measured along a horizontal axis **506**, and is the distance between a first side wall **508** and a second side wall **510** of the pocket **504**. The height of the pocket **504** is measured along a vertical axis **512**, and is the distance between a top wall **514** and a bottom wall **516** of the pocket **504**. The top face **502** includes a first window **518** therein, which allows a user to access the membrane **102** during dried blood spot testing, for example. The first window **518** has a length and a height. The length of the first window **518** is measured along the horizontal axis **506**, and is the distance between a first side wall **520** and a second side wall **522** of the first window **518**. The height of the first window **518** is measured along the vertical axis **512**, and is the distance between a top wall **524** and a bottom wall **526** of the first window **518**. The length of the first window **518** may be less than the length of the pocket **504**, and the height of the first window **518** may be less than the height of the pocket **504**, such that the membrane **102** may be more securely held within the pocket **504**. In some implementations, the bottom face may include a second window (not shown) therein, which allows a user to access the membrane **102** via the bottom face. The second window may be configured similarly to the second window **312** discussed above in conjunction with FIGS. 1- 3B.

[0043] The holding device **500** may be made according to the steps presented below. Unless expressly provided, the following steps are presented in no particular order. A bottom piece (not shown) may be injection molded. The membrane **102** may be positioned within the pocket **504**. The top face **502** may be injection molded (or oth-

erwise formed by a suitable fabrication technique) to the bottom piece (e.g., via overmolding, a process known by those skilled in the art).

[0044] It will be understood that various methods are intended to be within the scope of the present disclosure, including, but not limited to: methods for holding the dried biological fluid spotting membrane **102** during dried biological fluid spot testing; methods for assembling and disassembling the holding device **100, 400** or **500**; methods for preparing the dried biological fluid spotting membrane **102** for dried biological fluid spot testing; and methods for using the holding device **100, 400** or **500** in the context of dried biological fluid spot testing. In conjunction with holding and/or using the holding device **100, 400** or **500**, a window of the holding device **100, 400** or **500** may be utilized to access the membrane **102** for various purposes. For example, one or more drops of a biological fluid sample may be applied to the membrane **102** and allowed to dry (e.g., air dry) to create one or more dried biological fluid spots. As another example, a dried biological fluid spot or a portion thereof may be extracted from the membrane **102** via the window by any suitable means.

[0045] As one non-limiting example of extracting a dried biological fluid spot or portion thereof from the membrane **102**, a punch device (or punch tool) may be operated to punch out a dried biological fluid sample unit (i.e., a portion of the membrane **102** containing the dried biological fluid spot or a portion of the dried biological fluid spot) from the membrane **102**. For this purpose, the holding device **100, 400** or **500** may be placed or mounted on a suitable support surface, and the punch device may then be thrust through the window and through the membrane **102** where the target dried biological fluid spot is located. The punch device is typically cylindrical and thus the as-formed sample unit is typically disk-shaped. Once the sample unit has been formed it may be transported to an analytical device or any other desired destination. Depending on the design of the punch device, the as-formed sample unit may be captured in the punch device and transported therewith and/or the punch device may be utilized to perform certain sample preparation procedures such as, for example, solid phase extraction, sample clean-up, etc.

[0046] In some implementations, after forming the spot-containing sample unit, the sample unit may be exposed to a flow of one or more elution solvents (e.g., methanol, acetonitrile, ethanol, ethyl acetate, methyl tert-butyl ether, dichloromethane, chloroform, water, etc., with or without buffers or other additives) to create an analyte-inclusive liquid sample matrix. The analyte-inclusive liquid sample matrix may then be processed in any desired manner for separating, concentrating, purifying, and/or analyzing the analytes (i.e., subsequent analytical techniques) eluted from the sample unit. Examples of subsequent analytical techniques include, but are not limited to, protein precipitation, fraction collection, centrifugation, spectrophotometry, nuclear magnetic resonance (NMR) spectrometry, various types of SPE (e.g., normal-

phase, reversed-phase, ion-exchange, etc.), and various types of chromatography (e.g., preparative chromatography, liquid chromatography (LC), gas chromatography (GC), etc.) as well as hyphenated techniques entailing mass spectrometry (LC/MSⁿ, GC/MSⁿ, etc.). Other subsequent analytical techniques include the testing or processing of genetic material (i.e., "genetic testing") such as ribonucleic acid (RNA) or deoxyribonucleic acid (DNA). Examples of genetic testing include, but are not limited to, polymerase chain reaction (PCR), reverse transcriptase PCR (RT-PCR), ligase chain reaction (LCR), hybridization, genomic sequencing, labeling, assaying, etc. Hence, for example, in the case of sample units formed from dried blood spots, the eluents from these sample units may be tested for pharmaceutical compounds, other drug-related compounds, or other chemistries, or high molecular weight (HMW) molecules such as DNA, RNA, proteins or other polymers.

[0047] Some examples of punch devices and related devices that may be utilized in conjunction with the holding device **100, 400** or **500** include those disclosed in U.S. Patent Application Serial No. 12/916,834, titled DRIED BIOLOGICAL FLUID SPOT PUNCH DEVICE AND RELATED METHODS, filed November 1, 2010; and U.S. Patent Application Serial No. 12/917,138, titled APPARATUS FOR PUNCHING AND SOLID PHASE EXTRACTION OF DRIED BIOLOGICAL FLUID SPOT AND RELATED METHODS, filed November 1, 2010, both of which are incorporated herein by reference in their entireties.

[0048] As may be seen from the present disclosure, the holding devices **100, 400** and **500** described herein provide effective means for holding the membrane **102** during dried biological fluid spot testing, such as dried blood spot testing, including automated dried blood spot testing. In addition, the holding devices **100, 400** and **500** described herein provide effective means for holding the membrane **102** during shipping and handling. The holding devices **100, 400** and **500** may be held or manipulated in a manner that avoids having to contact the membrane **102** and the dried biological fluid spots contained thereon, thereby avoiding contamination of the dried biological fluid spots. In addition, the holding devices **100, 400** and **500** are effective in maintaining the form and/or shape of the membrane **102** during testing, thus facilitating reliable test results.

[0049] In general, terms such as "communicate" and "in communication with" (for example, a first component "communicates with" or "is in communication with" a second component) are used herein to indicate a structural, functional, mechanical, electrical, signal, optical, magnetic, electromagnetic, ionic or fluidic relationship between two or more components or elements. As such, the fact that one component is said to communicate with a second component is not intended to exclude the possibility that additional components may be present between, and/or operatively associated or engaged with, the first and second components.

[0050] It will be understood that various aspects or details of the invention may be changed without departing from the scope of the invention. Furthermore, the foregoing description is for the purpose of illustration only, and not for the purpose of limitation-the invention being defined by the claims. 5

[0051] The present invention relates to the following items:

1. A holding device for a dried biological fluid spotting membrane, comprising: 10

a plastic top face comprising a window formed therein, the window comprising a length and a height; 15
 a plastic bottom face; and
 a pocket disposed between the top face and the bottom face, the pocket comprising a length and a height, wherein the pocket is configured for receiving a dried biological fluid spotting membrane that is accessible through the window by a user during dried biological fluid spot testing, and at least one of the length and the height of the window is less than the length or the height of the pocket, respectively. 25

2. The holding device of item 1, wherein at least one of the top face and the bottom face is made of a plastic selected from the group consisting of polypropylene, polyethylene, polyolefin, polyamide, polyacrylate and a combination of two or more of the foregoing. 30

3. The holding device of item 1, further comprising the dried biological fluid spotting membrane positioned within the pocket. 35

4. The holding device of item 1, wherein the length of the window is less than the length of the pocket, and the height of the window is less than the height of the pocket. 40

5. The holding device of item 1, wherein the window of the top face is a first window and the bottom face comprises a second window formed therein, the second window comprising a length that is substantially the same as the length of the first window, and a height that is substantially the same as the height of the first window. 45

6. The holding device of item 1, further comprising a plastic laminate layer and a plastic body, wherein the laminate layer comprises the top face, the plastic body comprises the bottom face and an opposing inner face, the laminate layer is adhered to the inner face, the length of the window is less than the length of the pocket, and the height of the window is less than the height of the pocket. 50

7. The holding device of item 6, wherein the window of the top face is a first window, and the bottom face comprises a second window formed therein, the second window comprising a length that is substantially the same as the length of the first window, and a height that is substantially the same as the height of the first window.

8. The holding device of item 1, further comprising:

a plastic top piece comprising the top face and a first inner face opposing the top face, wherein the length of the window is less than the length of the pocket, and the height of the window is less than the height of the pocket;
 a plastic bottom piece comprising the bottom face and a second inner face opposing the bottom face, wherein one of the first inner face and the second inner face comprises a plurality of male components and the other of the first inner face and the second inner face comprises a plurality of female components, the female components being configured for detachably mating with the male components.

9. The holding device of item 8, wherein the pocket is formed in the second inner face.

10. The holding device of item 8, wherein the window of the top face is a first window, and the bottom face comprises a second window formed therein, the second window comprising a length that is substantially the same as the length of the first window, and a height that is substantially the same as the height of the first window.

11. A method for assembling the holding device of item 1, the method comprising:

positioning the dried biological fluid spotting membrane within the pocket; and
 securing the dried biological fluid spotting membrane within the pocket.

12. The method of item 11, wherein securing the dried biological fluid spotting membrane within the pocket comprises overmolding a top piece onto a bottom piece, the top piece comprising the top face, and the bottom piece comprising the pocket and the bottom face.

13. A method for assembling the holding device of item 6, the method comprising:

positioning the dried biological fluid spotting membrane within the pocket; and
 securing the dried biological fluid spotting membrane within the pocket by adhering the plastic

laminate layer to the inner face.

14. A method for assembling the holding device of item 8, the method comprising:

positioning the dried biological fluid spotting membrane within the pocket; and
securing the dried biological fluid spotting membrane within the pocket by detachably mating the female components with the male components.

15. A method for using the holding device of item 1, wherein the membrane is secured in the pocket, the method comprising forming a dried biological fluid spot on the membrane by accessing the membrane via the window, applying a drop of a biological fluid sample to the membrane to form a biological fluid spot, and allowing the biological fluid spot to dry.

16. The method of item 15, comprising accessing the dried biological fluid spot via the window and extracting at least a portion of the dried biological fluid spot formed on the membrane.

17. A method for using the holding device of item 8, wherein the membrane is secured in the pocket, the method comprising accessing the dried biological fluid spot via the window and extracting at least a portion of the dried biological fluid spot formed on the membrane.

18. The method of item 17, comprising removing the top piece from the bottom piece by detaching the male components from the female components, and removing the membrane from the pocket.

19. The method of item 18, comprising replacing the removed membrane with a second dried biological fluid spotting membrane by positioning the second membrane within the pocket, and securing the second membrane within the pocket by detachably mating the female components with the male components.

20. The method of item 17, comprising, before extracting, forming a dried biological fluid spot on the membrane by accessing the membrane via the window, applying a drop of a biological fluid sample to the membrane to form a biological fluid spot, and allowing the biological fluid spot to dry.

Claims

1. A holding device (100, 400, 500) for a dried biological fluid spotting membrane (102), comprising:

a plastic top face (110, 404, 502) comprising a window (112, 422, 518) formed therein, the window (112, 422, 518) comprising a length and a height;

a plastic bottom face (340); and

a pocket (108, 406, 504) disposed between the top face (110, 404, 502) and the bottom face (340), the pocket (108, 406, 504) comprising a length and a height, wherein the pocket (108, 406, 504) is configured for receiving a dried biological fluid spotting membrane (102) that is accessible through the window (112, 422, 518) by a user during dried biological fluid spot testing, and at least one of the length and the height of the window (112, 422, 518) is less than the length or the height of the pocket (108, 406, 504), respectively.

2. The holding device (100, 400, 500) of claim 1, wherein at least one of the top face (110, 404, 502) and the bottom face (340) is made of a plastic selected from the group consisting of polypropylene, polyethylene, polyolefin, polyamide, polyacrylate and a combination of two or more of the foregoing.

3. The holding device (100, 400, 500) of claim 1 or 2, further comprising the dried biological fluid spotting membrane (102) positioned within the pocket (108, 406, 504).

4. The holding device (100, 400, 500) of any one of claims 1 to 3, wherein the length of the window (112, 422, 518) is less than the length of the pocket (108, 406, 504), and the height of the window (112, 422, 518) is less than the height of the pocket (108, 406, 504).

5. The holding device (400) of any one of claims 1 to 4, further comprising a plastic laminate layer (420) and a plastic body (402), wherein the laminate layer (420) comprises the top face (404), the plastic body (402) comprises the bottom face and an opposing inner face (436), the laminate layer (420) is adhered to the inner face (436).

6. The holding device (100) of any one of claims 1 to 4, further comprising:

a plastic top piece (104) comprising the top face (110) and a first inner face (220) opposing the top face (110);

a plastic bottom piece (106) comprising the bottom face (340) and a second inner face (128) opposing the bottom face (340), wherein one of the first inner face (220) and the second inner face (128) comprises a plurality of male components (226) and the other of the first inner face (220) and the second inner face (128) comprises

- a plurality of female components (126), the female components (126) being configured for detachably mating with the male components (226).
7. The holding device (100) of claim 6, wherein the pocket (108) is formed in the second inner face (128).
 8. The holding device (100, 400, 500) of any one of claims 1 to 7, wherein the window (112, 422, 518) of the top face (110, 404, 502) is a first window (112, 422, 518) and the bottom face (340) comprises a second window (312) formed therein, the second window (312) comprising a length that is substantially the same as the length of the first window (112, 422, 518), and a height that is substantially the same as the height of the first window (112, 422, 518).
 9. A method for assembling the holding device (100, 400, 500) of any one of claims 1 to 8, the method comprising:
 - positioning the dried biological fluid spotting membrane (102) within the pocket (108, 406, 504); and
 - securing the dried biological fluid spotting membrane (102) within the pocket (108, 406, 504), preferably by adhering the plastic laminate layer (420) to the inner face (436) or by detachably mating the female components (126) with the male components (226).
 10. The method of claim 9, wherein securing the dried biological fluid spotting membrane (102) within the pocket (504) comprises overmolding a top piece onto a bottom piece, the top piece comprising the top face (502), and the bottom piece comprising the pocket (504) and the bottom face.
 11. A method for using the holding device (100, 400, 500) of any one of claims 1 to 8, wherein the membrane (102) is secured in the pocket (108, 406, 504), the method comprising forming a dried biological fluid spot on the membrane (102) by accessing the membrane (102) via the window (112, 422, 518), applying a drop of a biological fluid sample to the membrane (102) to form a biological fluid spot, and allowing the biological fluid spot to dry.
 12. The method of claim 11, comprising accessing the dried biological fluid spot via the window (112, 422, 518) and extracting at least a portion of the dried biological fluid spot formed on the membrane (102).
 13. A method for using the holding device (100) of any one of claims 6 to 8, wherein the membrane (102) is secured in the pocket (108), the method comprising accessing the dried biological fluid spot via the window (112) and extracting at least a portion of the dried biological fluid spot formed on the membrane (102).
 14. The method of claim 13, comprising removing the top piece (104) from the bottom piece (106) by detaching the male components (226) from the female components (126), and removing the membrane (102) from the pocket (108), and optionally further comprising replacing the removed membrane (102) with a second dried biological fluid spotting membrane by positioning the second membrane within the pocket (108), and securing the second membrane within the pocket (108) by detachably mating the female components (126) with the male components (226).
 15. The method of claim 13 or 14, comprising, before extracting, forming a dried biological fluid spot on the membrane (102) by accessing the membrane (102) via the window (112), applying a drop of a biological fluid sample to the membrane (102) to form a biological fluid spot, and allowing the biological fluid spot to dry.

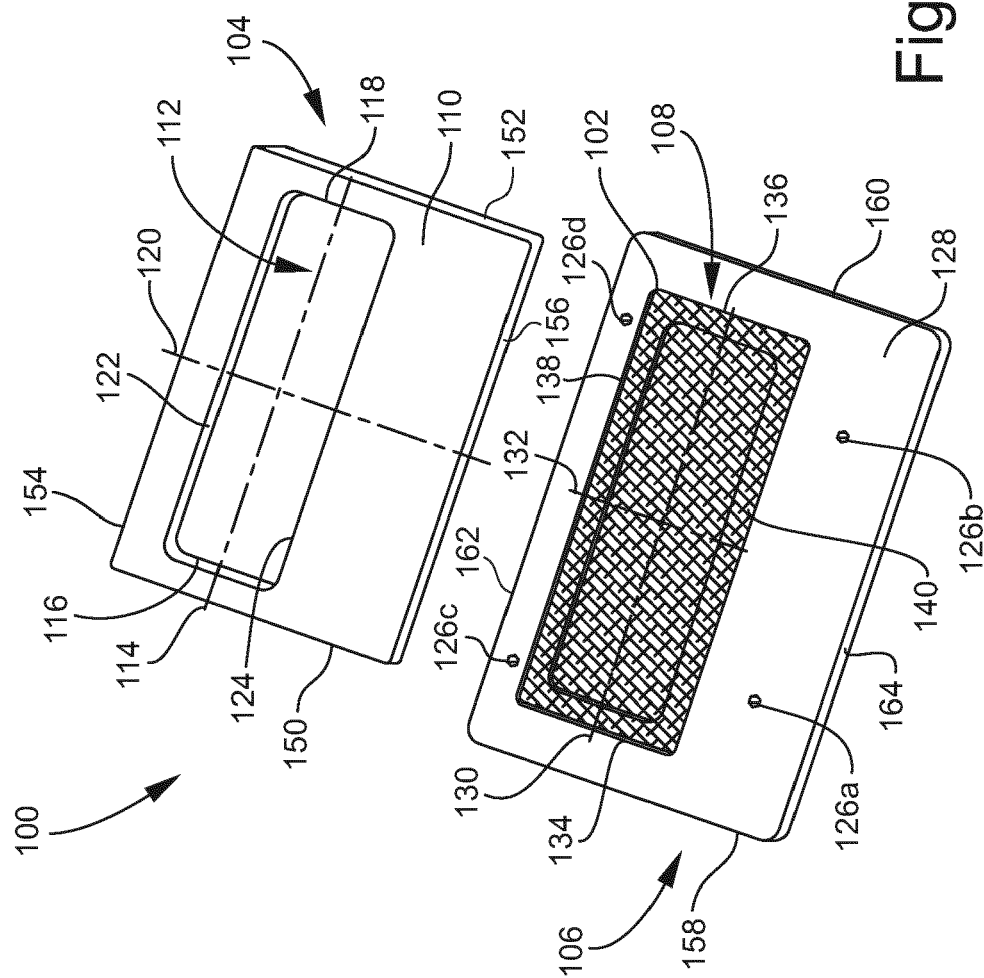


Fig. 1

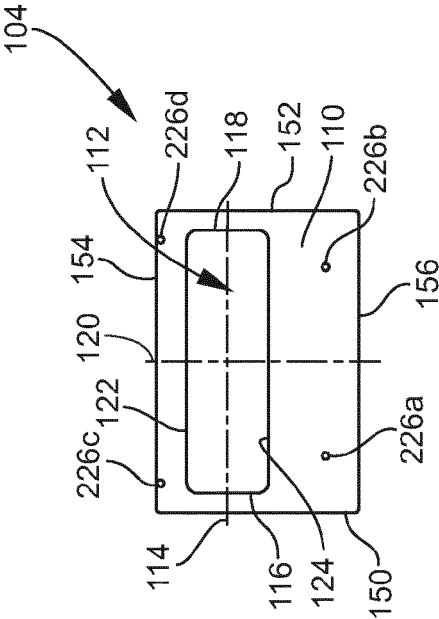


Fig. 2A

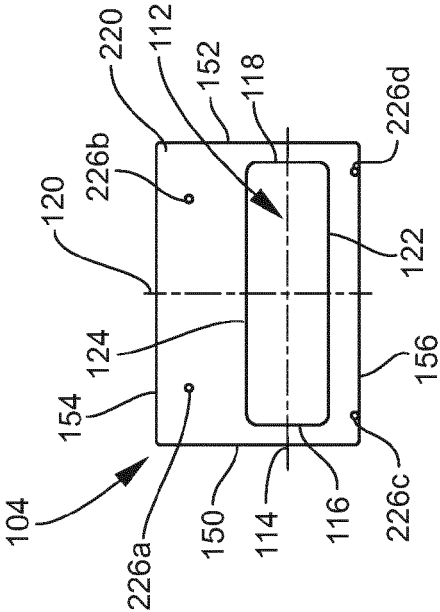


Fig. 2B

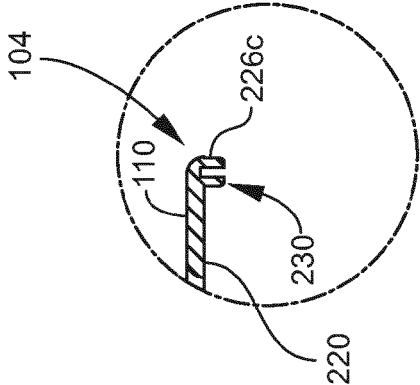


Fig. 2C

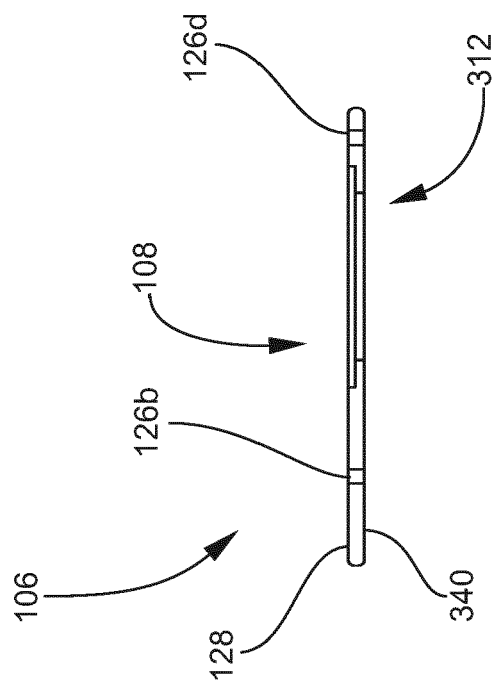
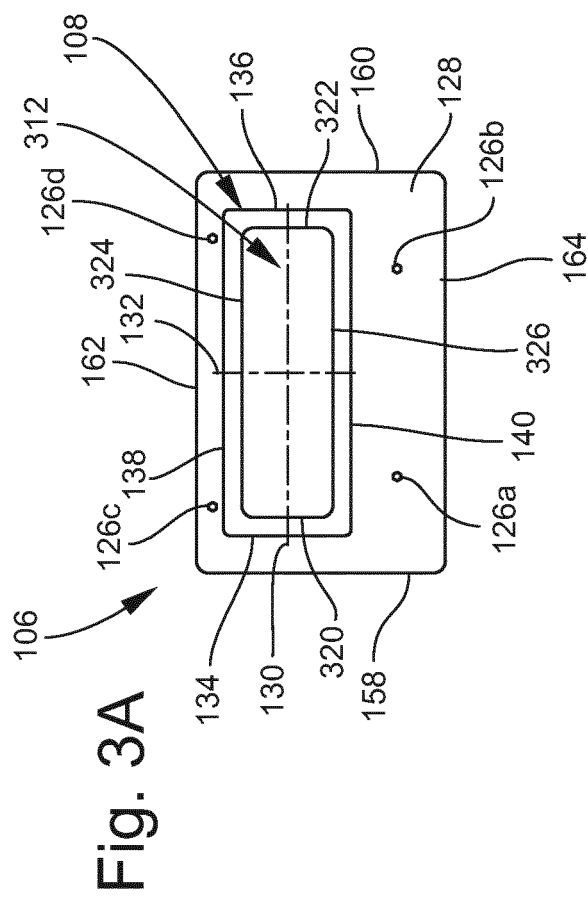


Fig. 3B

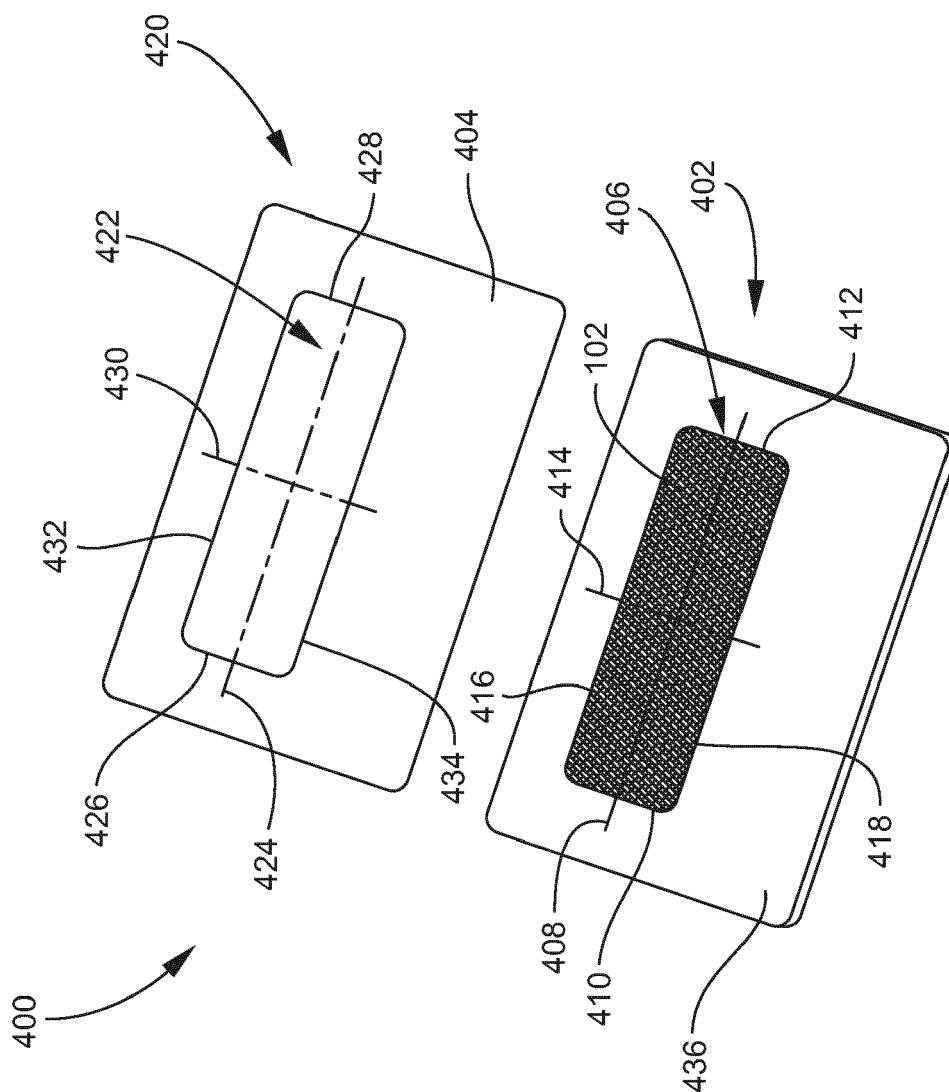


Fig. 4

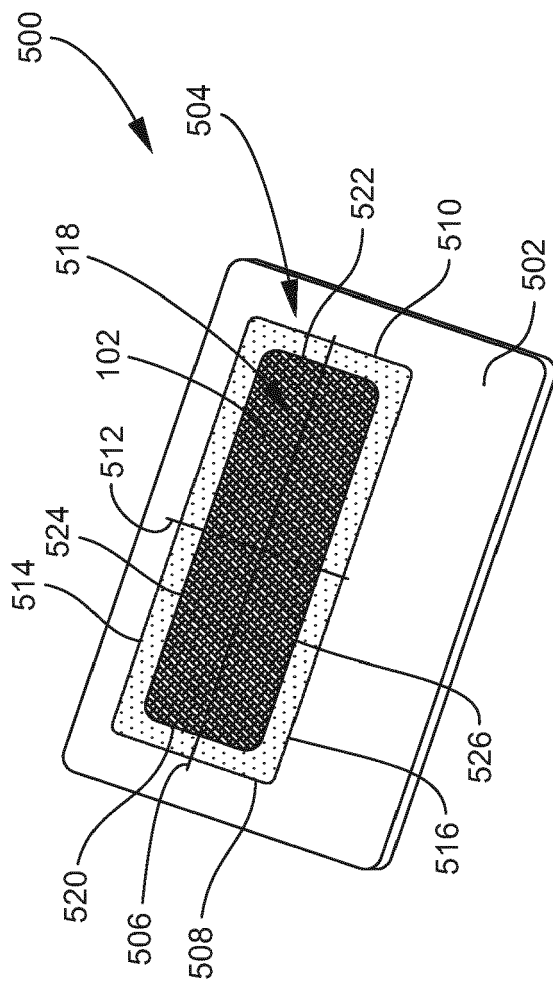


Fig. 5



EUROPEAN SEARCH REPORT

Application Number
EP 11 18 6685

DOCUMENTS CONSIDERED TO BE RELEVANT			
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (IPC)
X	US 2004/265187 A1 (DAVIN BRADLEY FERGUSON [US]) 30 December 2004 (2004-12-30) * paragraphs [0010], [0016], [0017], [0042], [0044], [0045], [0046]; figures 1D, 1E *	1,3-15	INV. B01L9/00
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A	WO 2005/121745 A1 (NIPPON SHEET GLASS CO LTD [JP]; FUJITA KOJI [JP]) 22 December 2005 (2005-12-22) * the whole document *	1-15	
The present search report has been drawn up for all claims			TECHNICAL FIELDS SEARCHED (IPC)
			B01L
Place of search		Date of completion of the search	Examiner
Munich		19 March 2012	Hoyal, Barnaby
CATEGORY OF CITED DOCUMENTS X : particularly relevant if taken alone Y : particularly relevant if combined with another document of the same category A : technological background O : non-written disclosure P : intermediate document T : theory or principle underlying the invention E : earlier patent document, but published on, or after the filing date D : document cited in the application L : document cited for other reasons & : member of the same patent family, corresponding document			

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**ANNEX TO THE EUROPEAN SEARCH REPORT
ON EUROPEAN PATENT APPLICATION NO.**

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19-03-2012

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