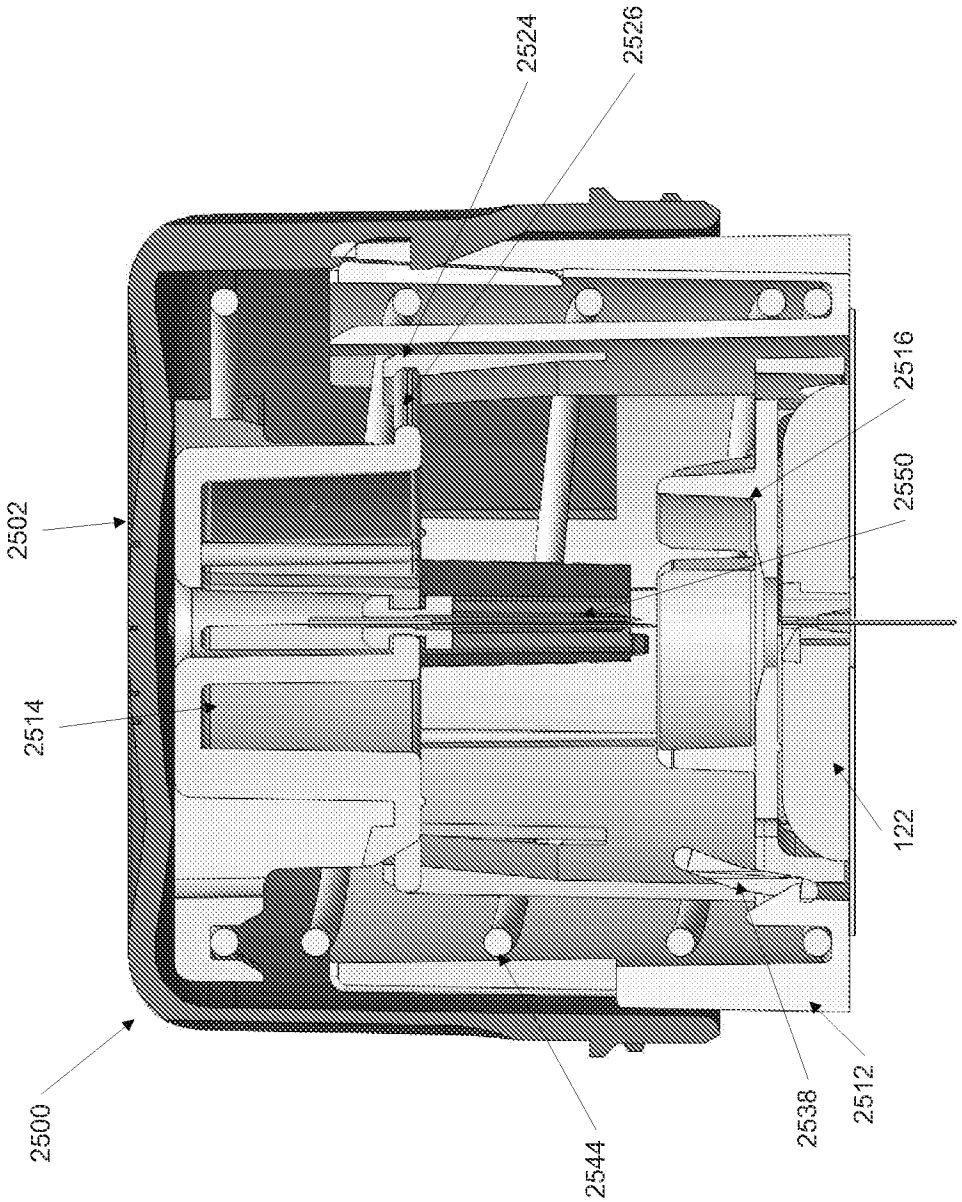


FIG. 73M

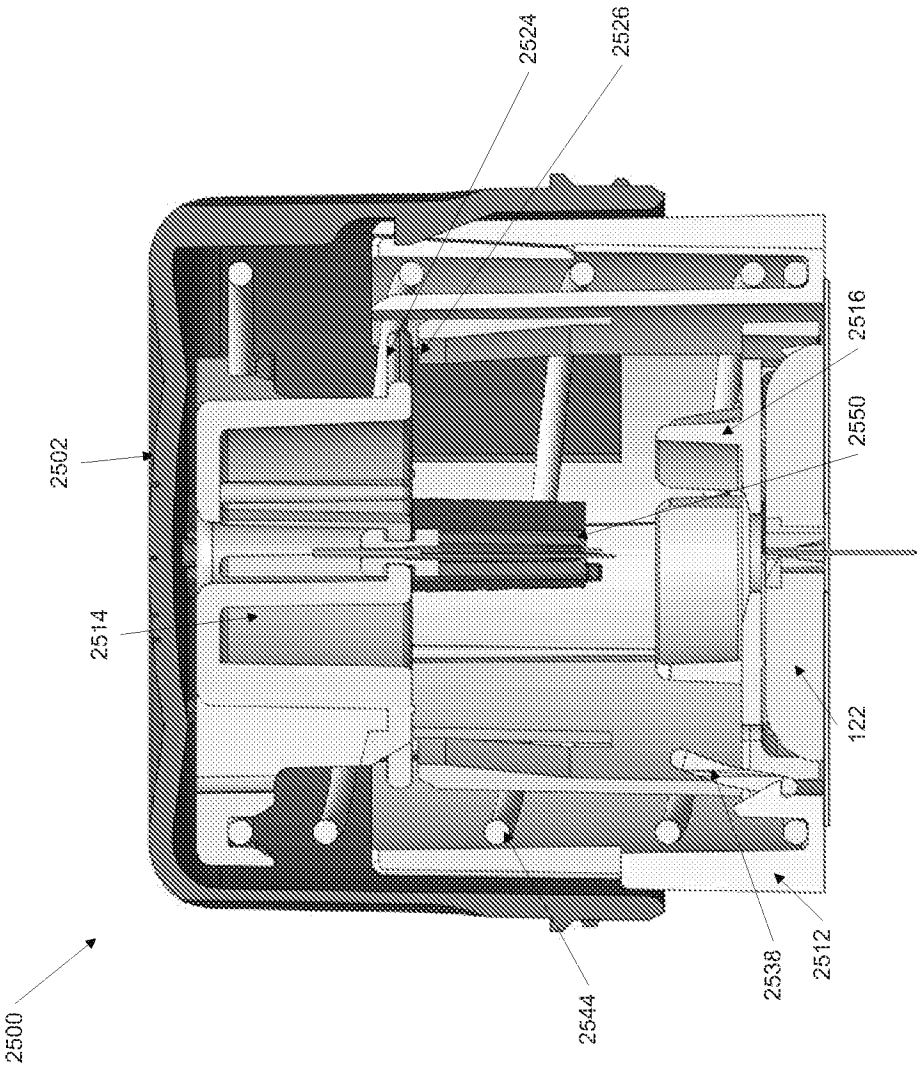


FIG. 73N

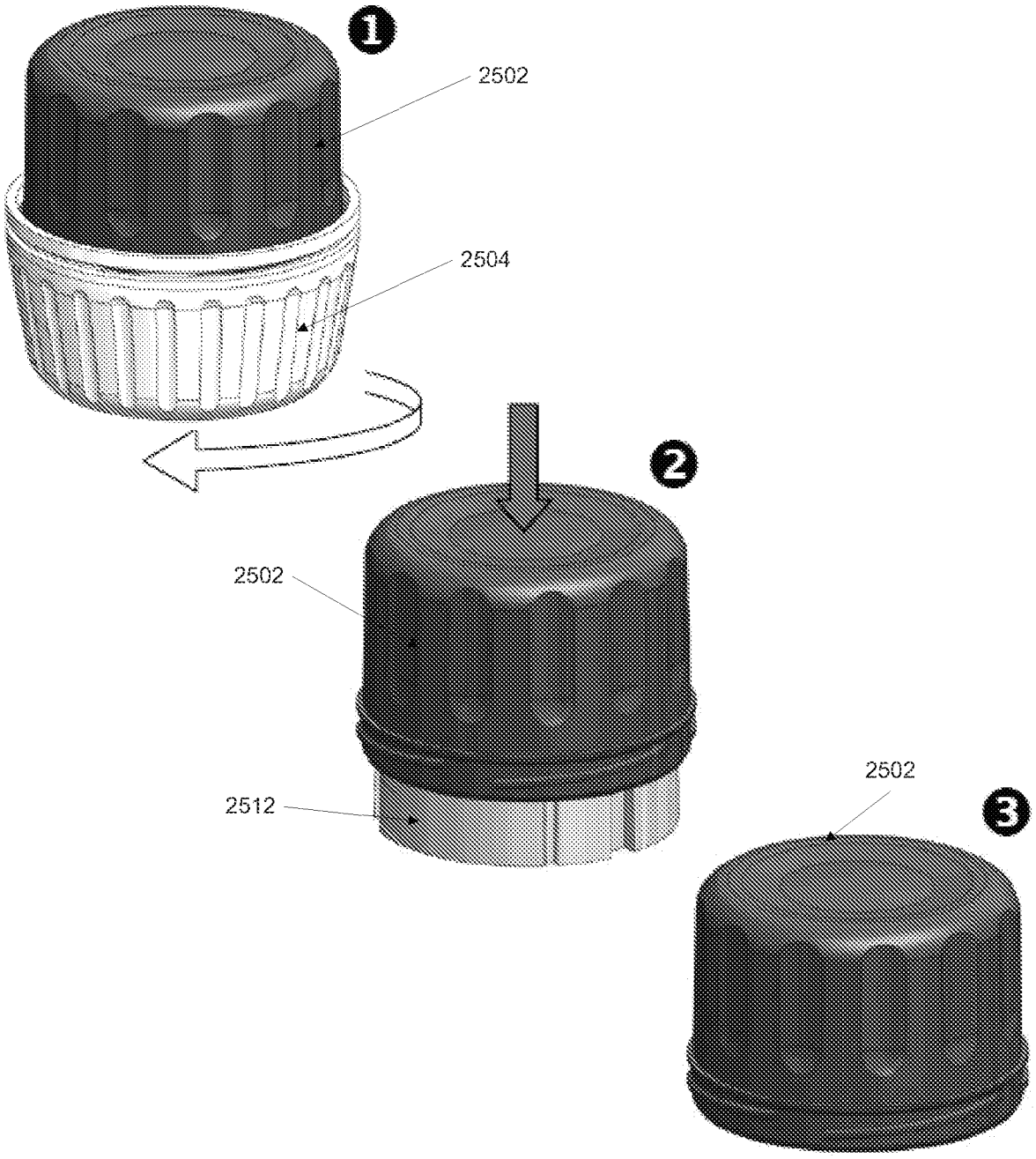


FIG. 73O

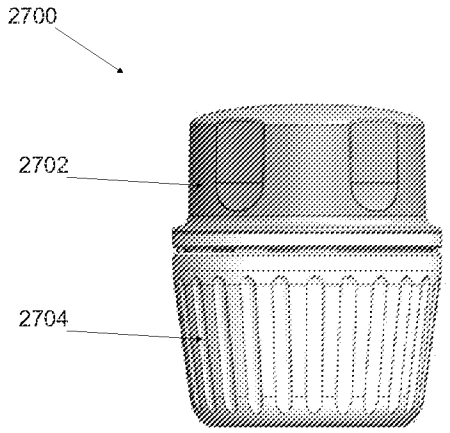


FIGURE 74

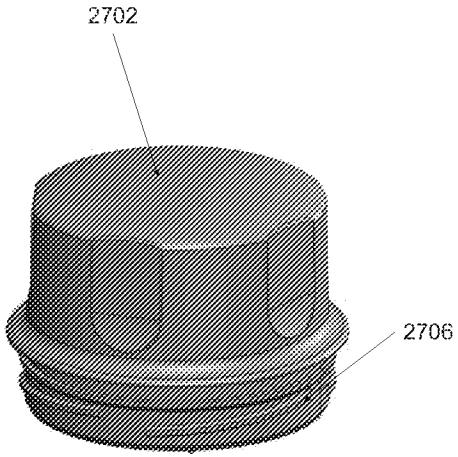


FIGURE 75

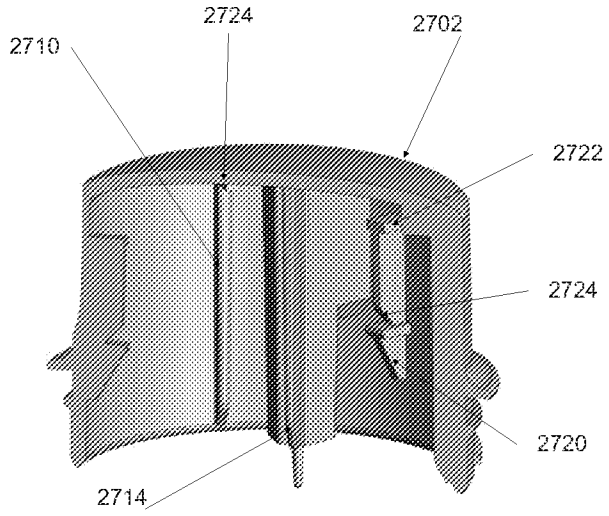


FIGURE 76

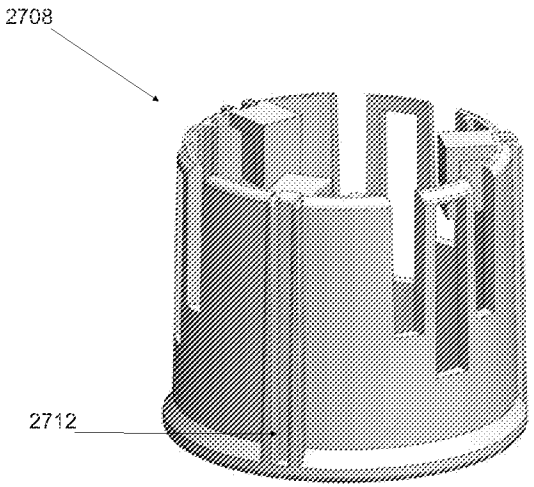


FIGURE 77

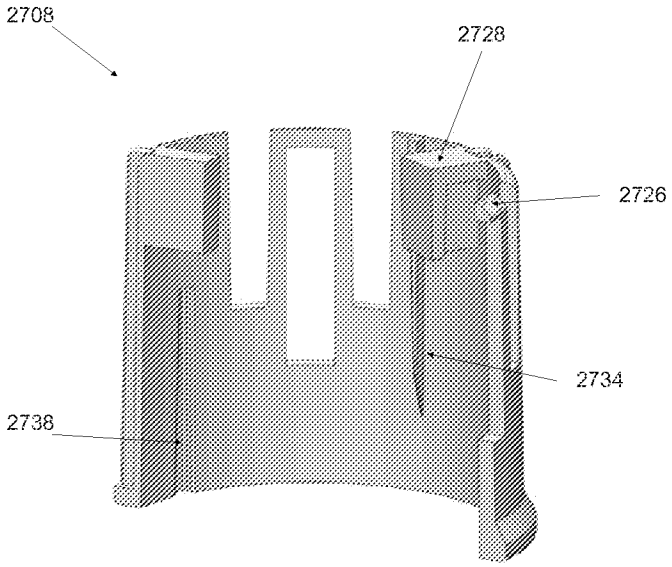


FIGURE 78

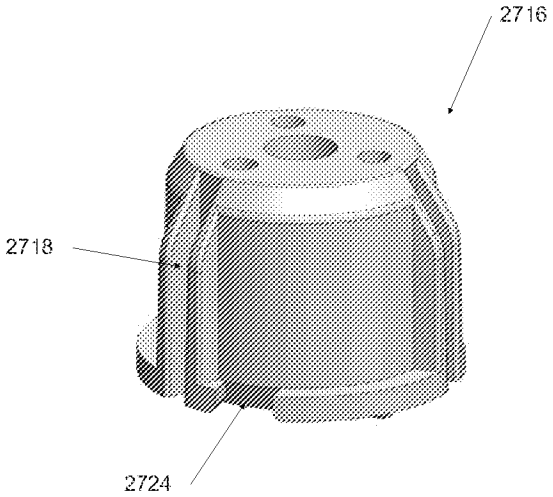


FIGURE 79

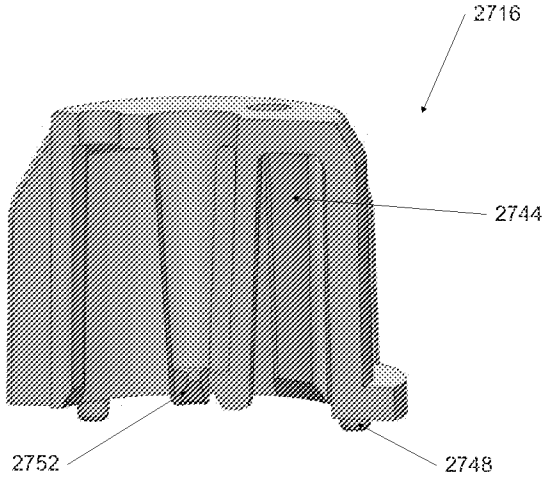


FIGURE 80

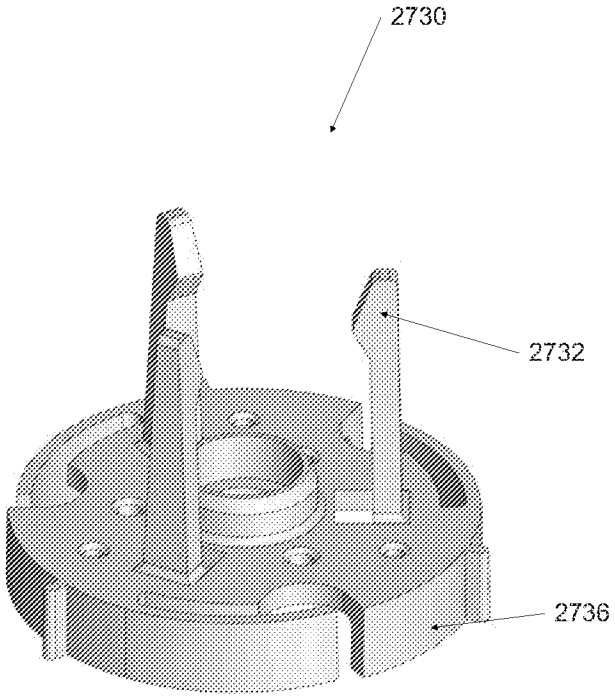


FIGURE 81

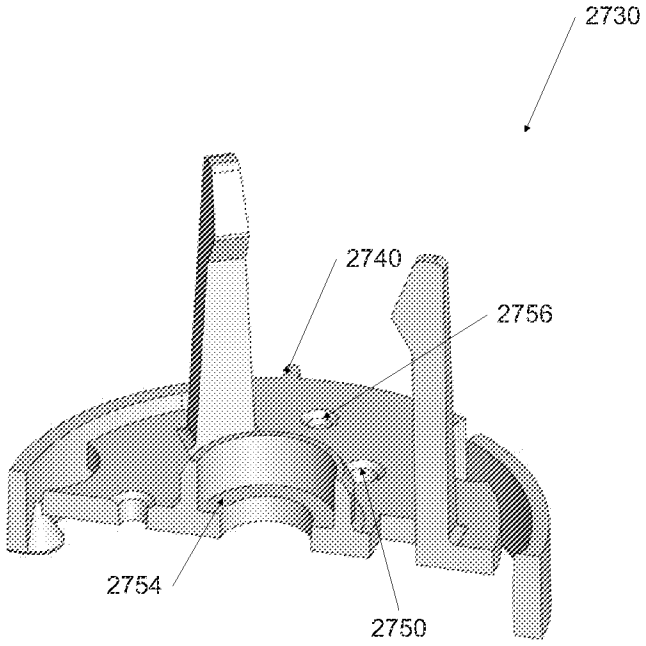


FIGURE 82

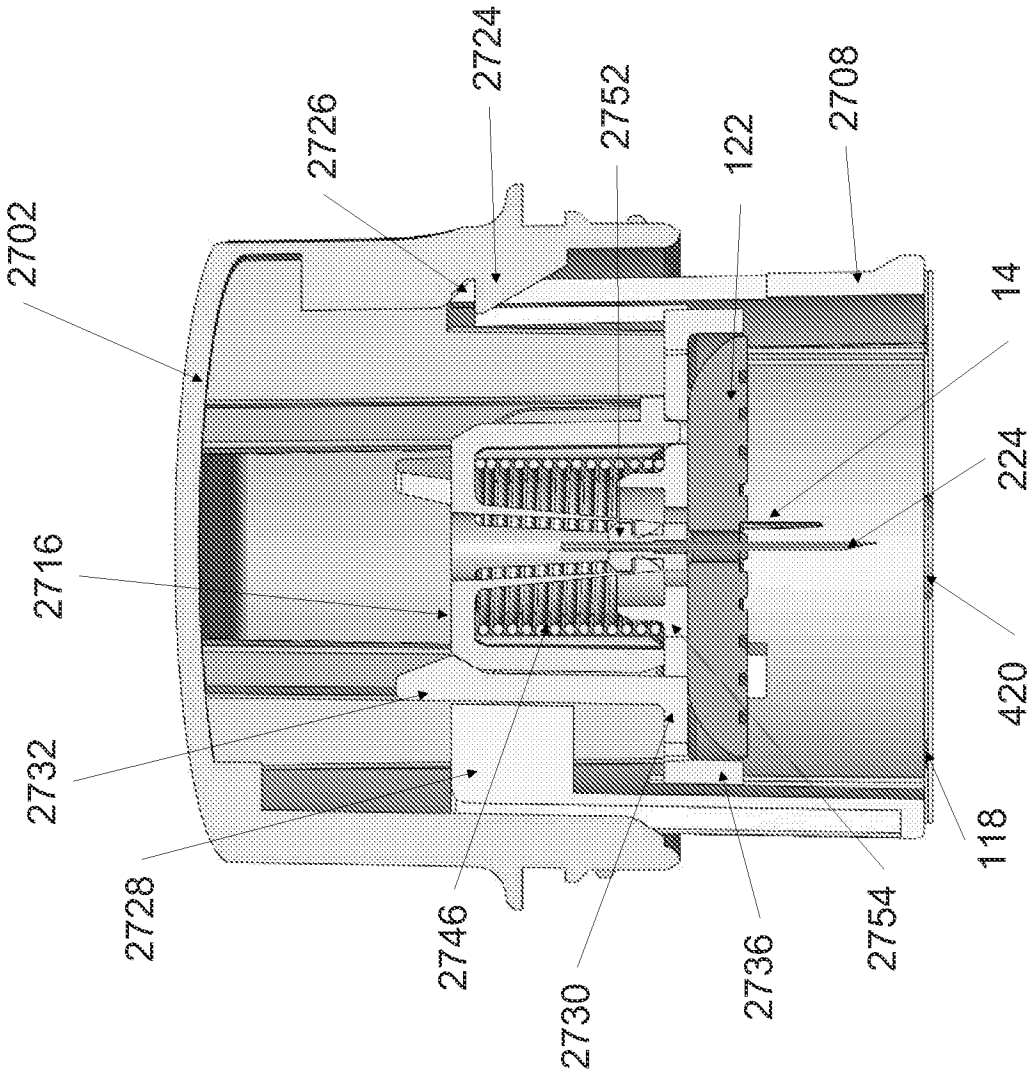

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FIGURE 83

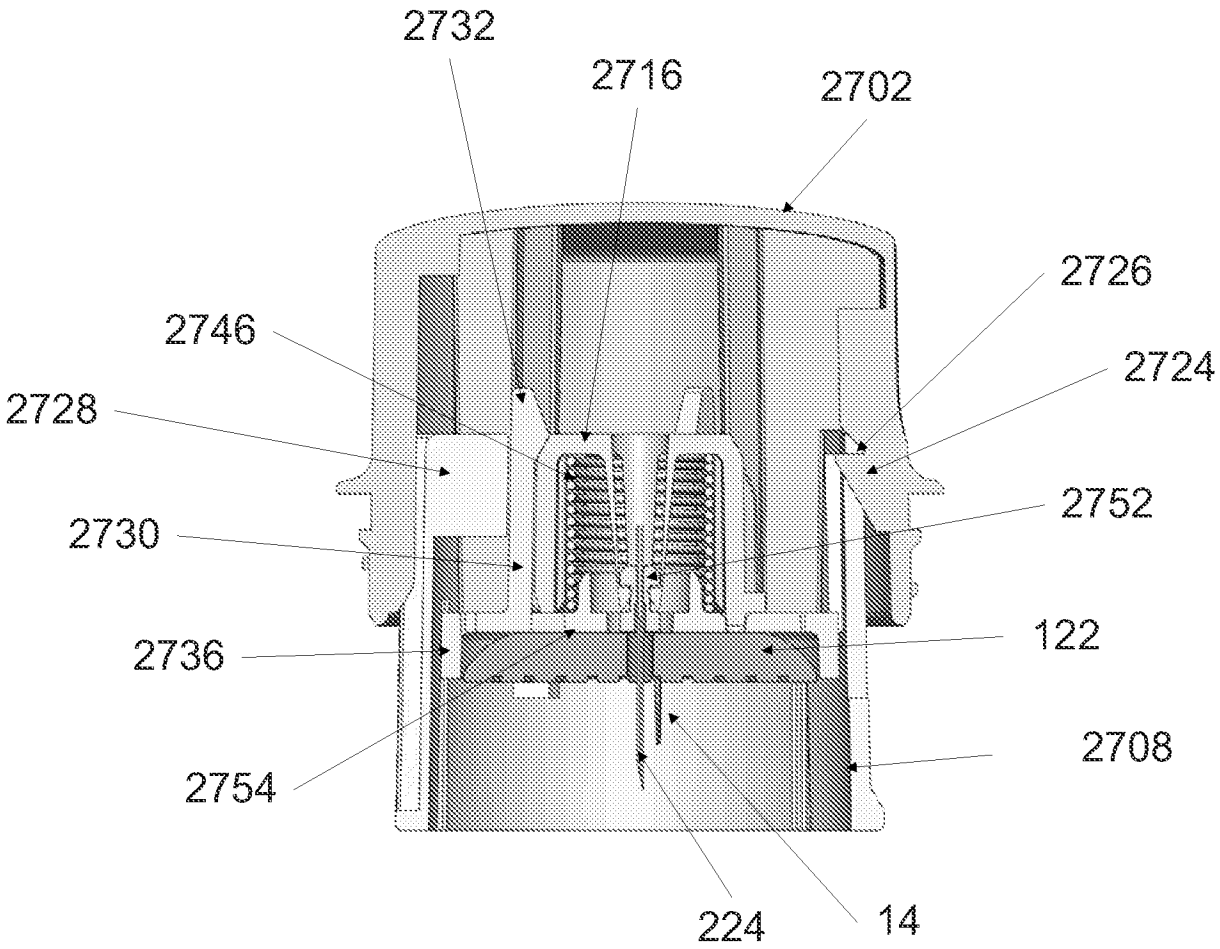

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FIGURE 84

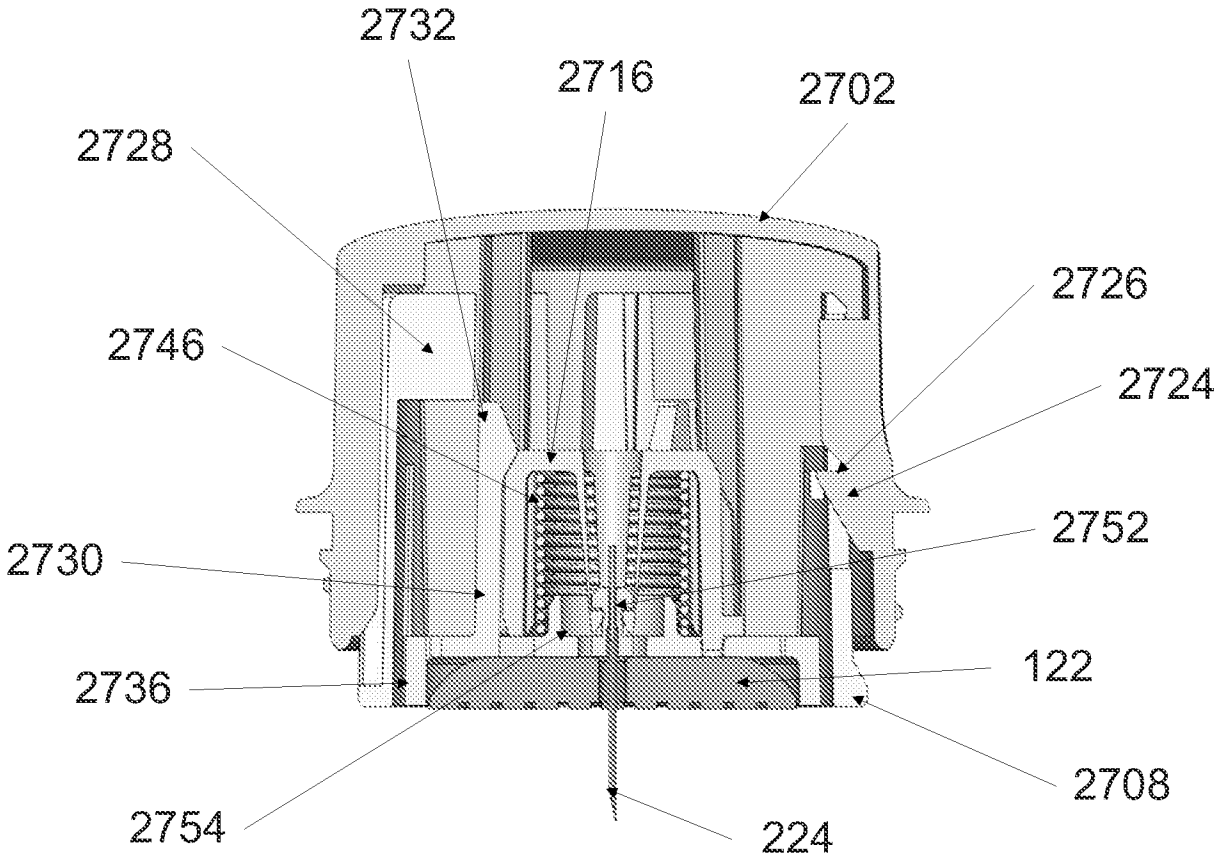

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FIGURE 85

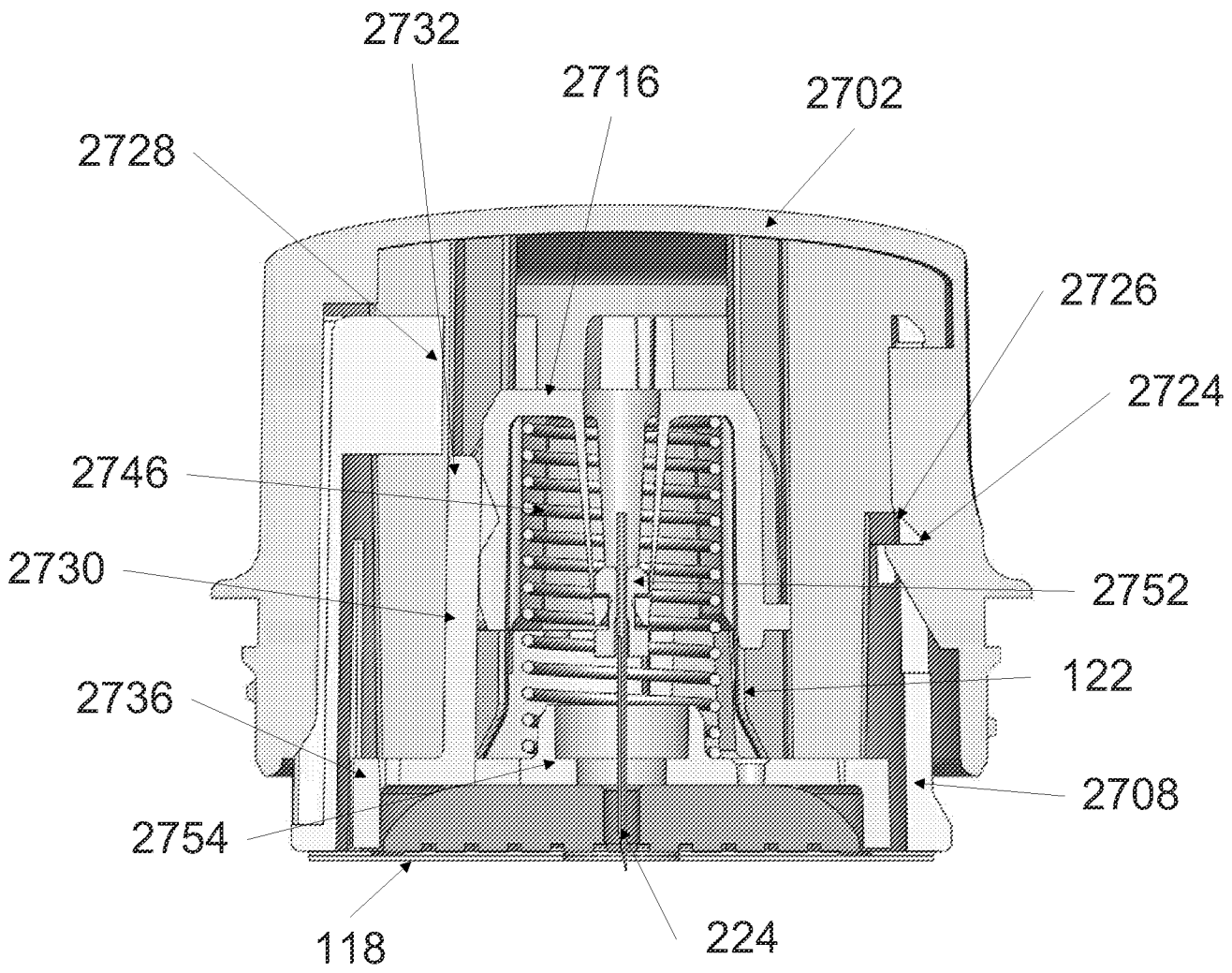

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FIGURE 86

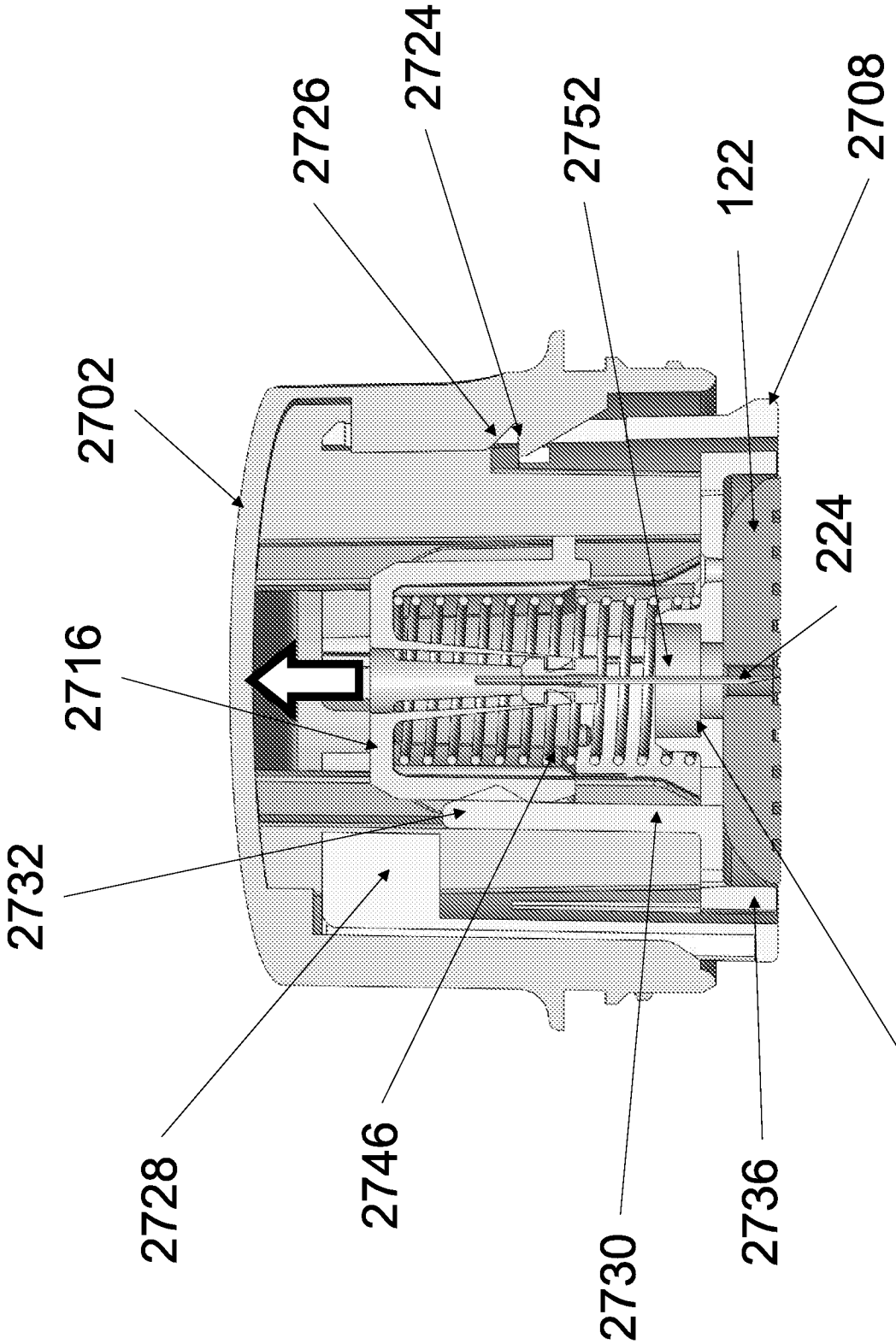

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FIGURE 87

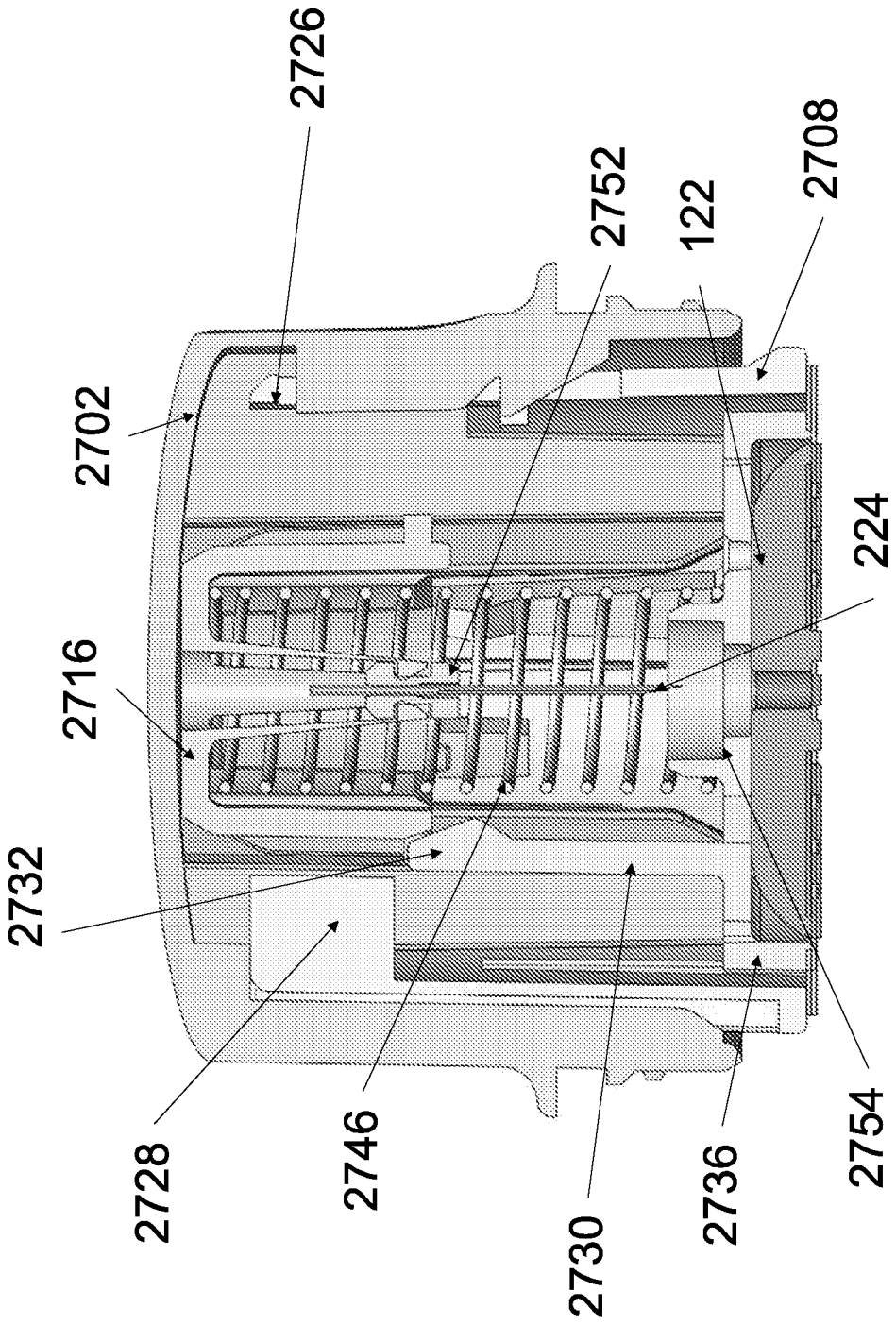

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FIGURE 88

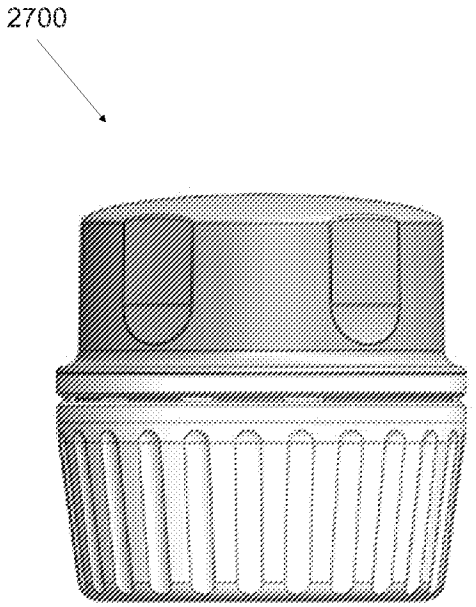


FIGURE 89

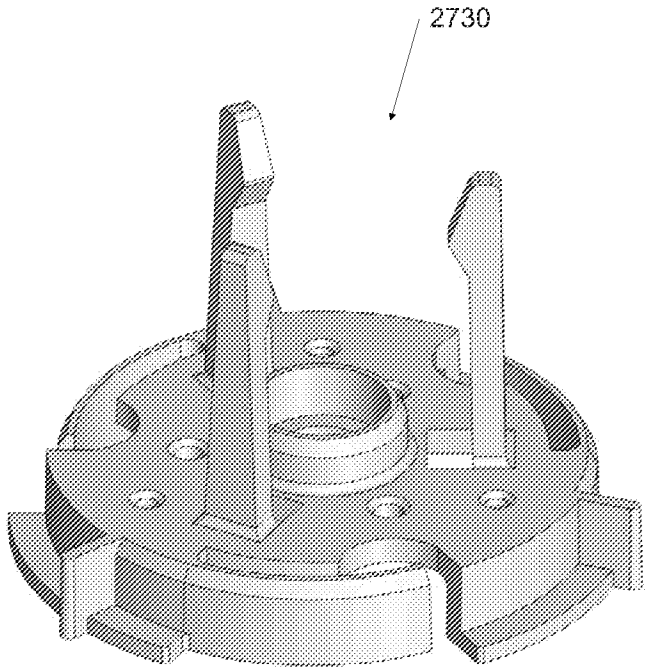


FIGURE 90

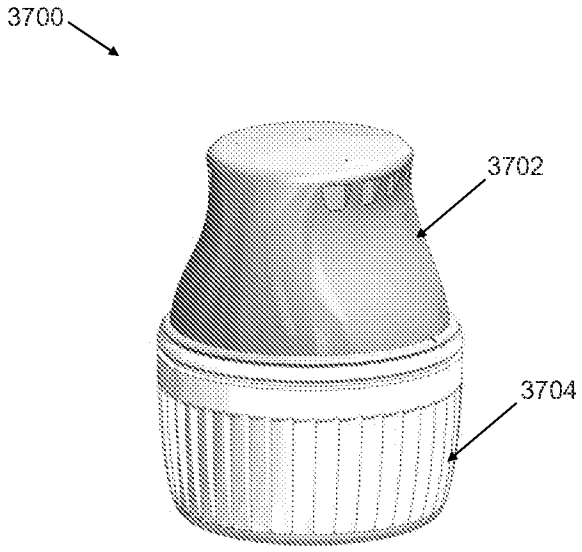


FIG. 91A

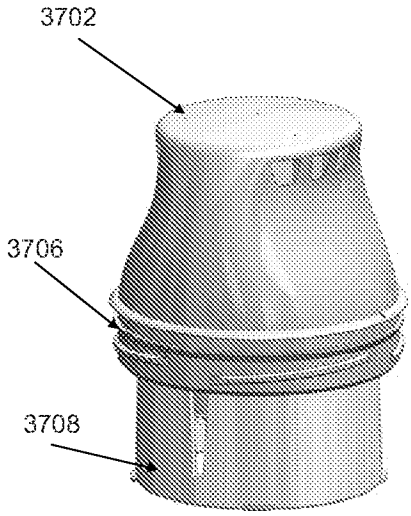


FIG. 91B

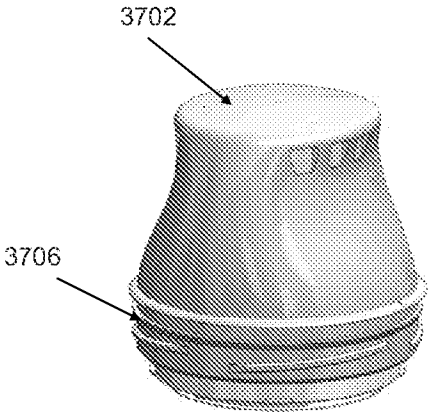


FIG. 91C

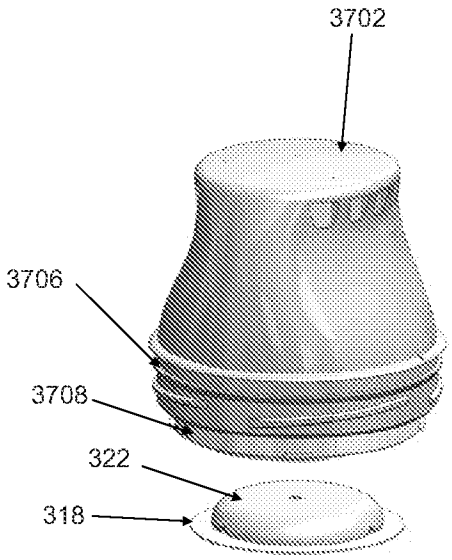


FIG. 91D

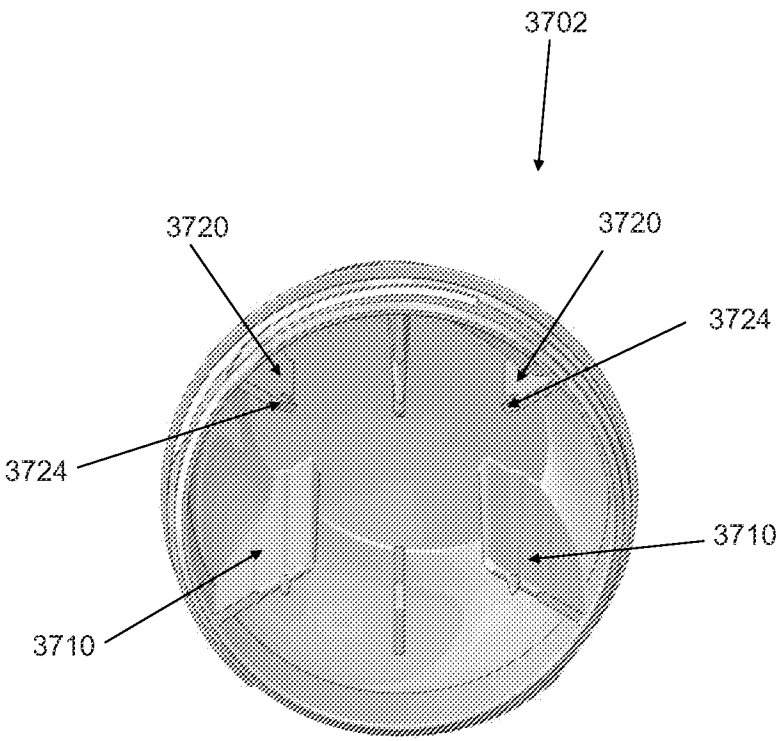


FIG. 92A

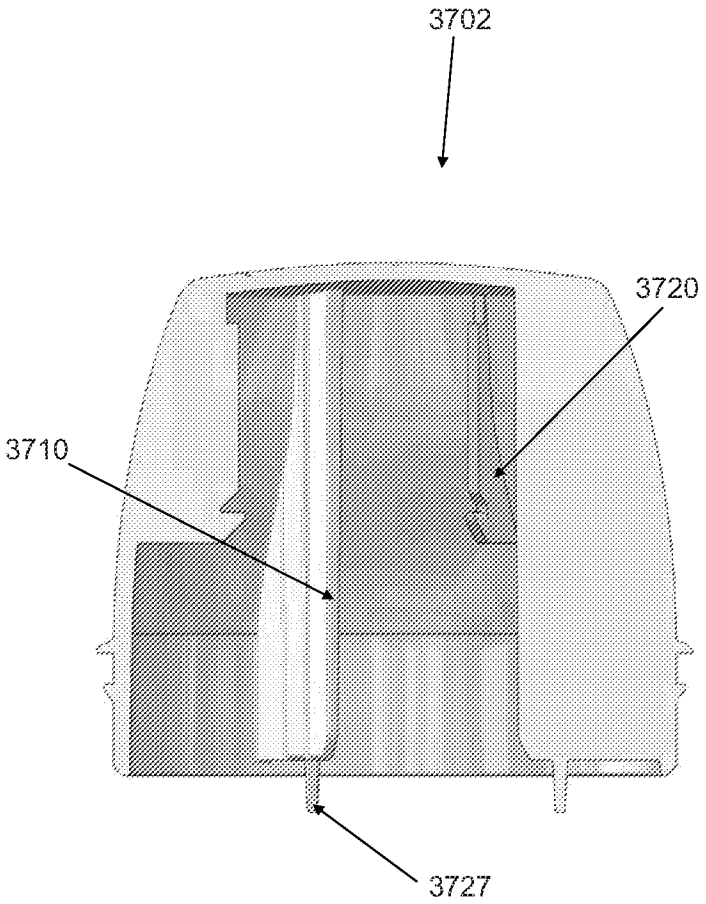


FIG. 92B

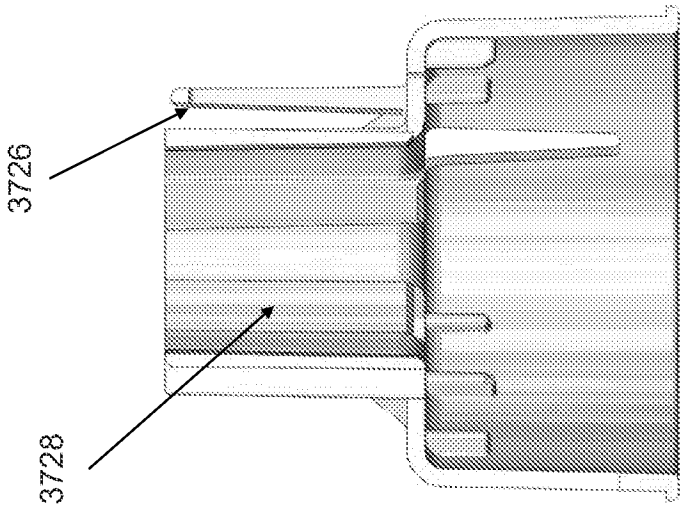


FIG. 93B

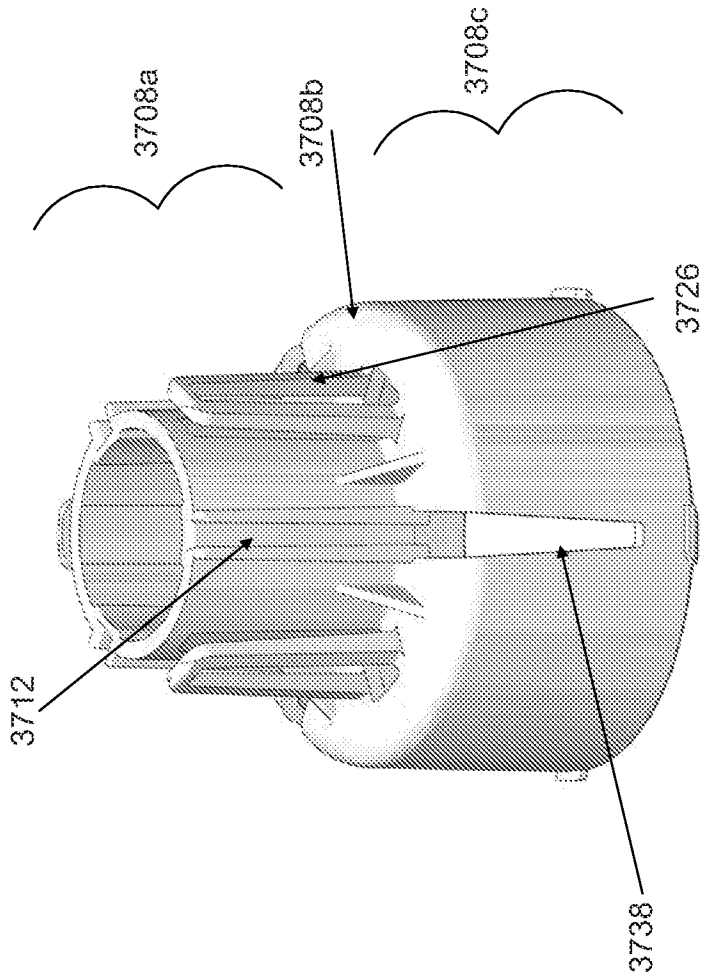


FIG. 93A

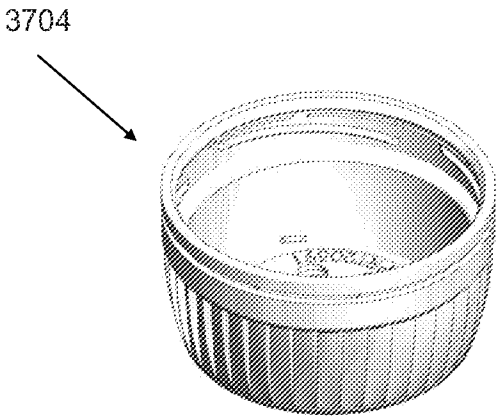


FIG. 94A

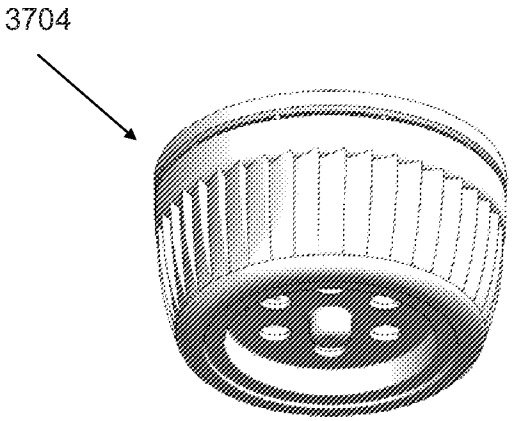


FIG. 94B

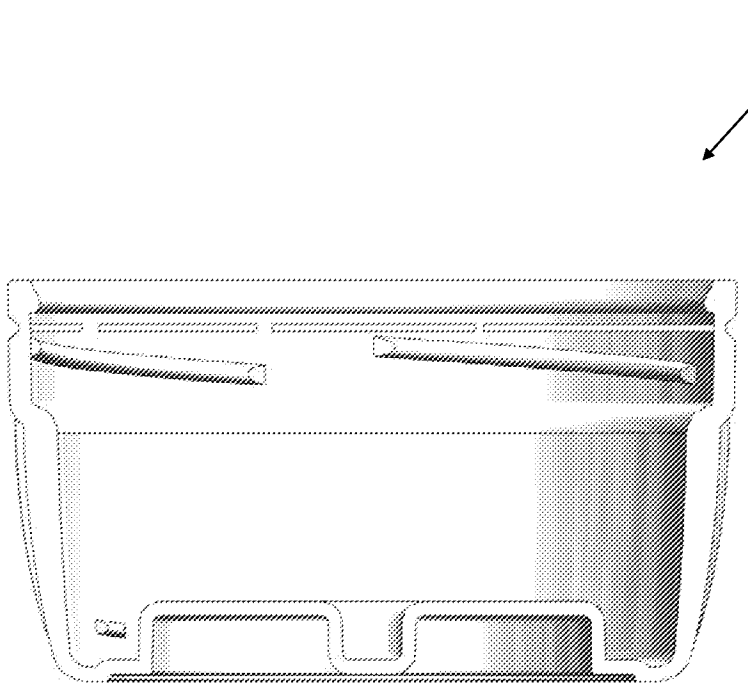


FIG. 94C

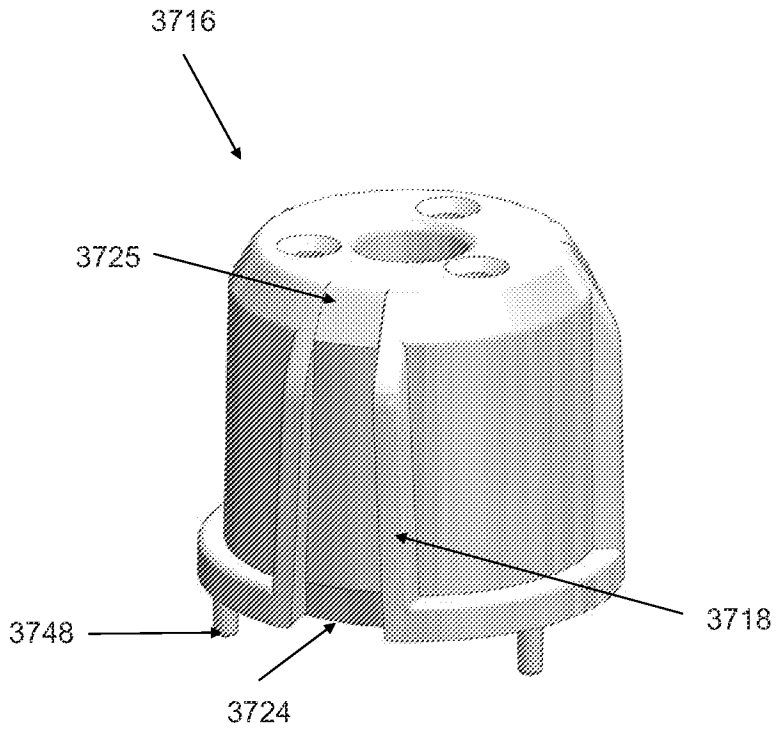


FIG. 95A

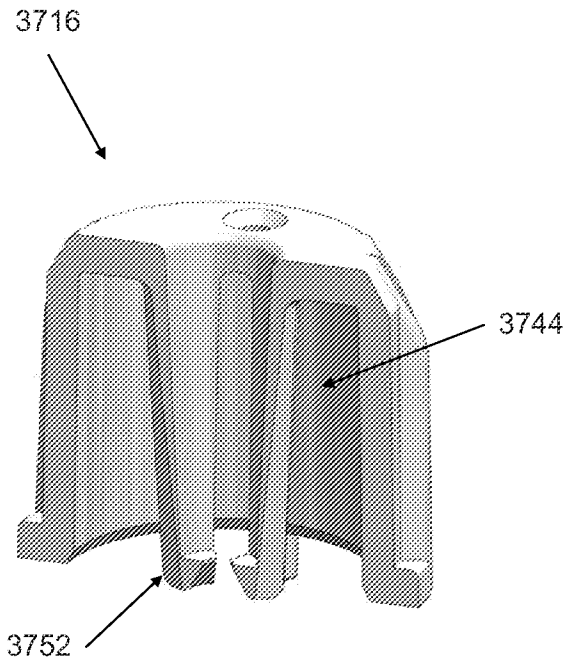


FIG. 95B

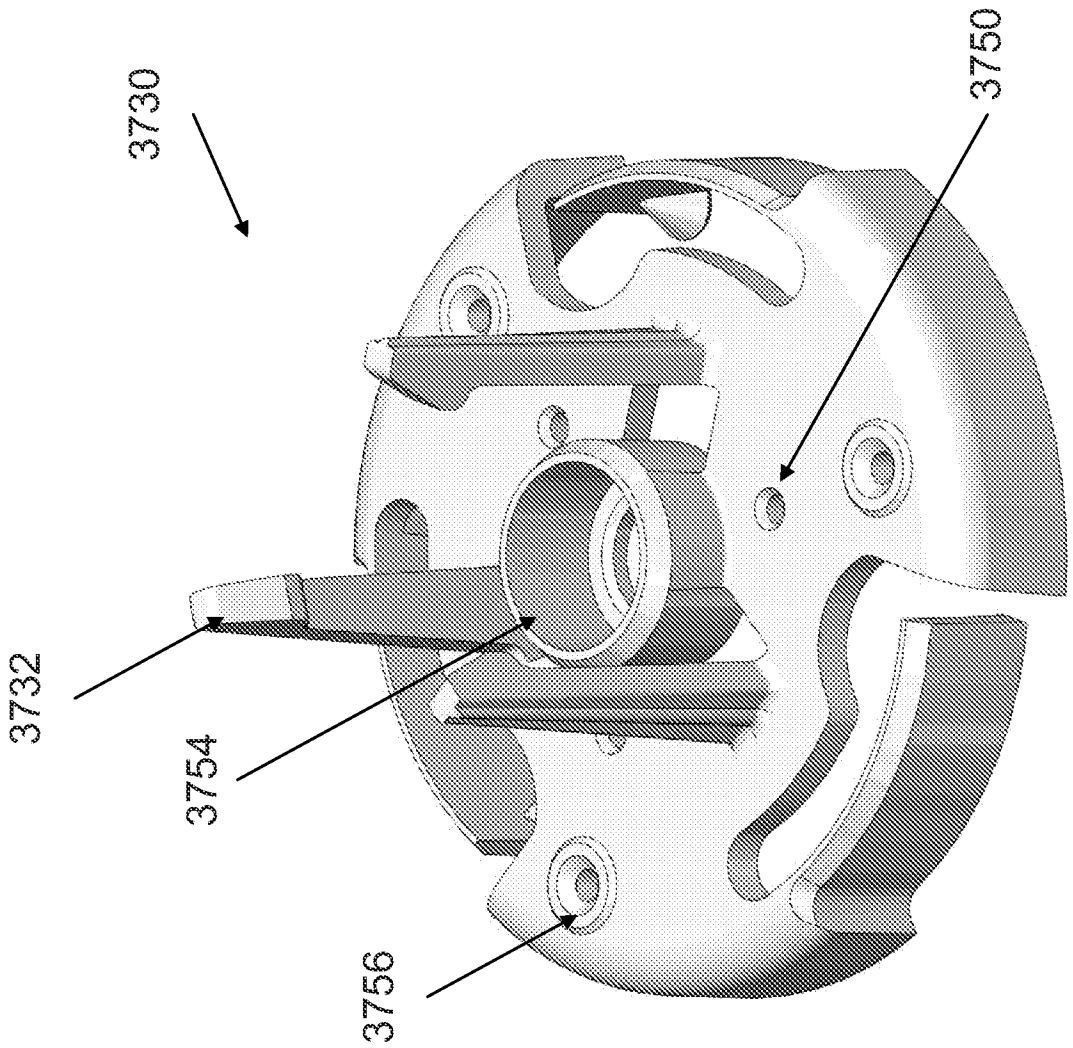


FIG. 96

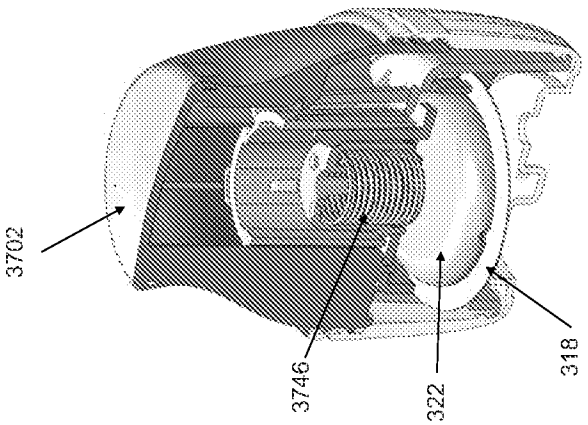


FIG. 97C

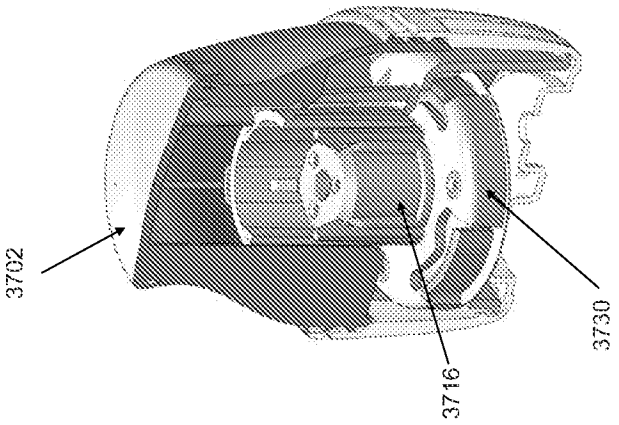


FIG. 97B

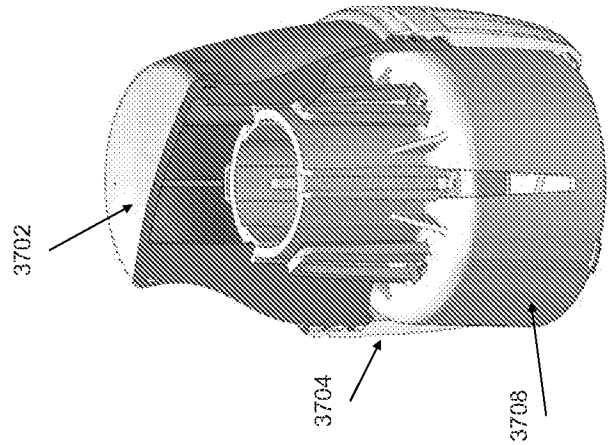


FIG. 97A

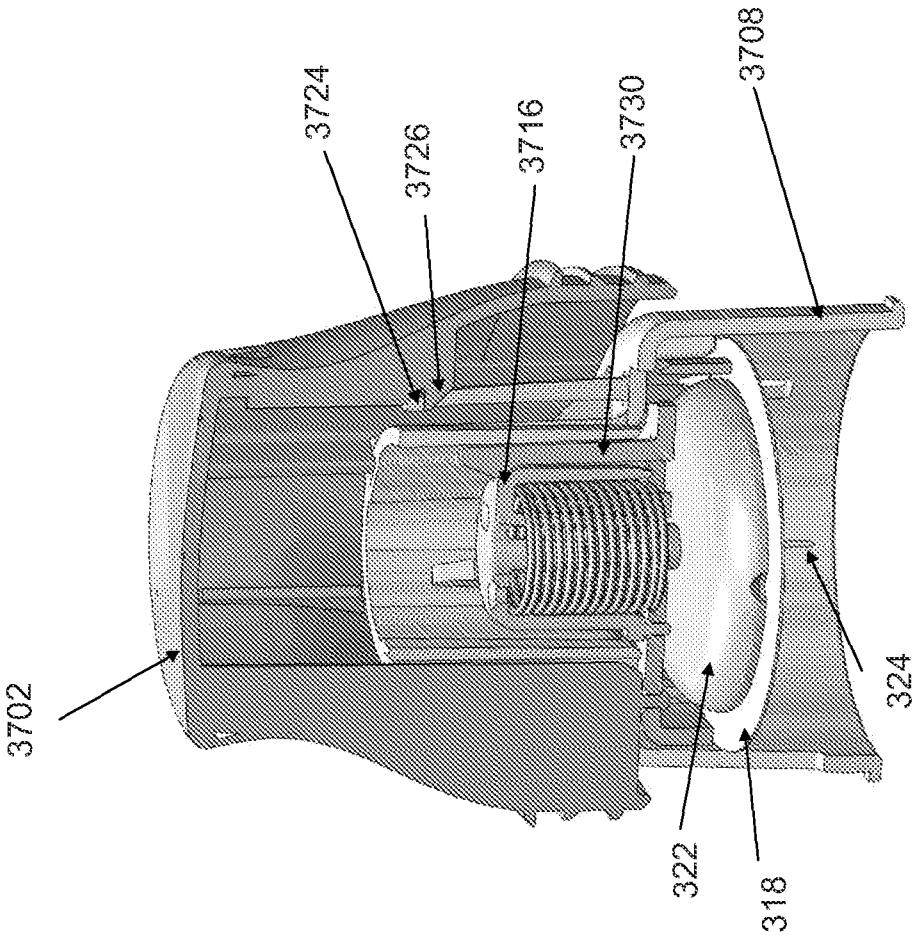


FIG. 98

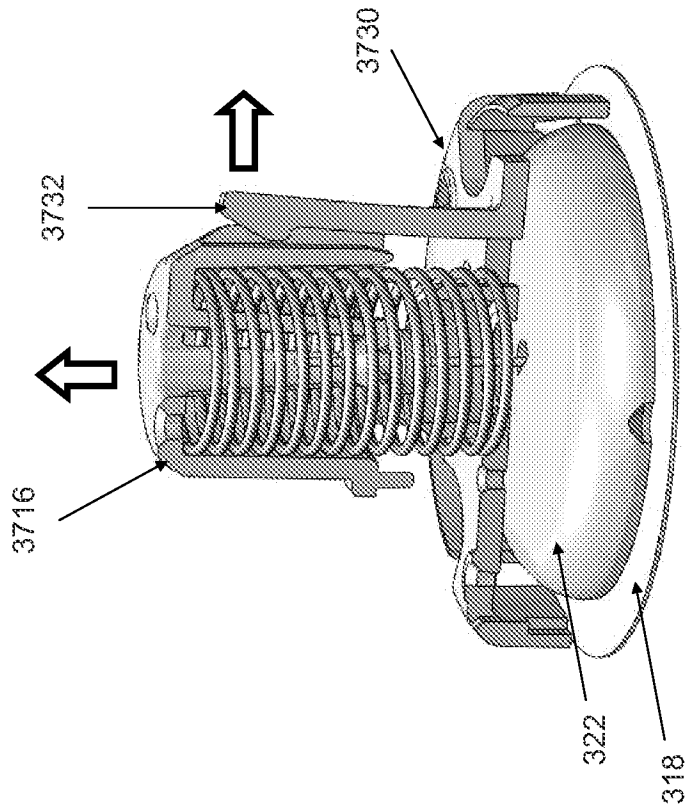


FIG. 99B

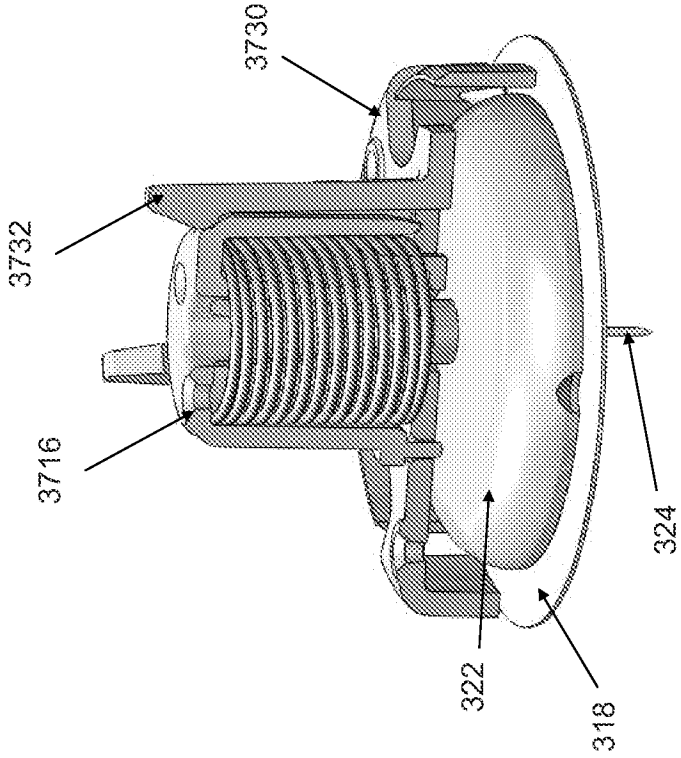


FIG. 99A

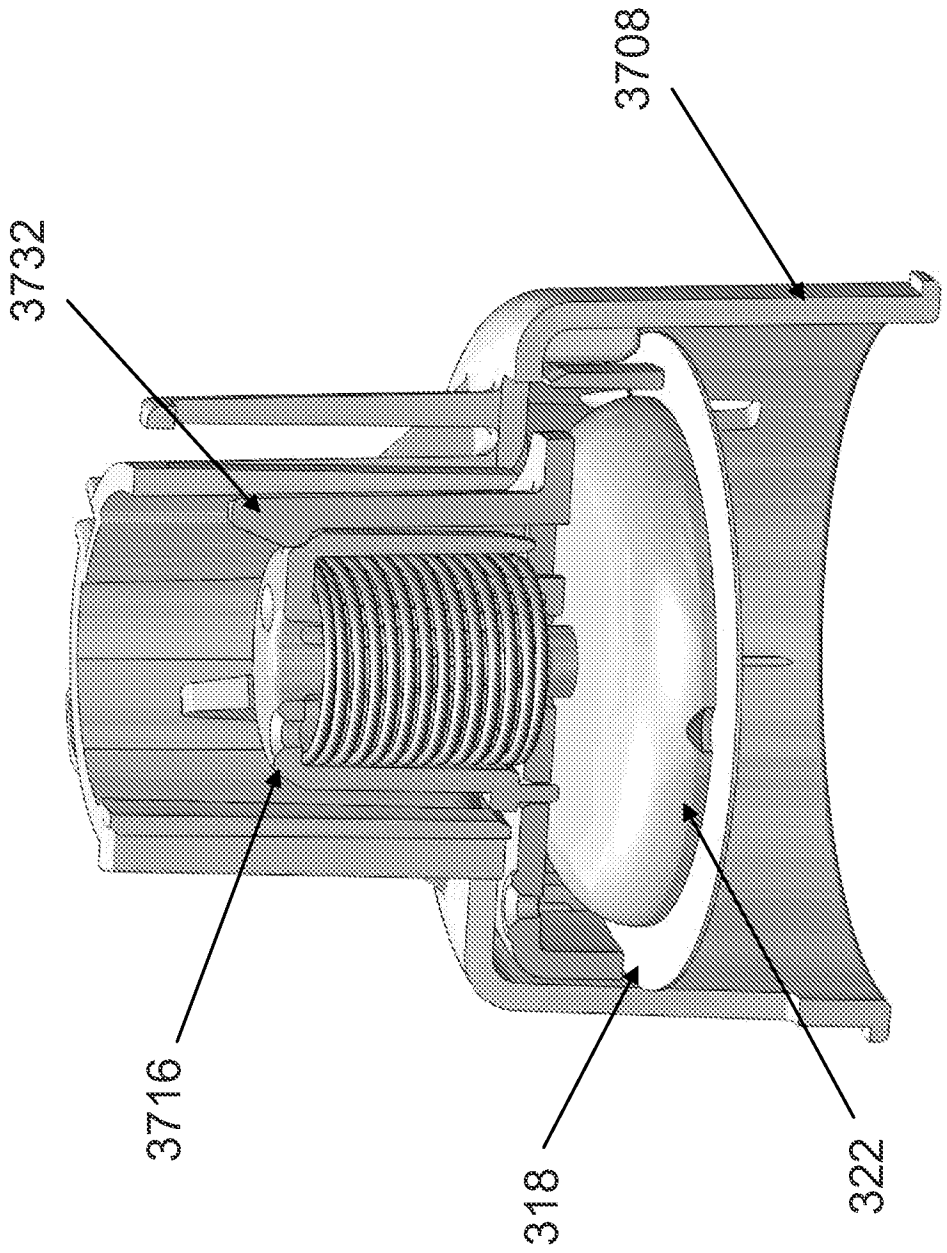


FIG. 100

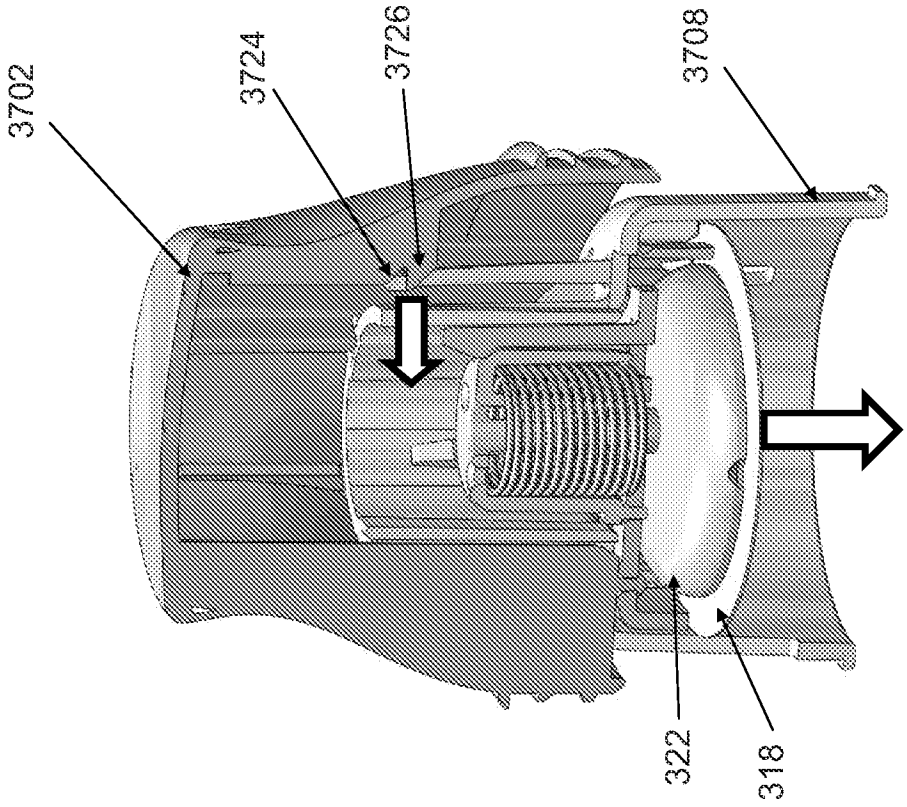


FIG. 101

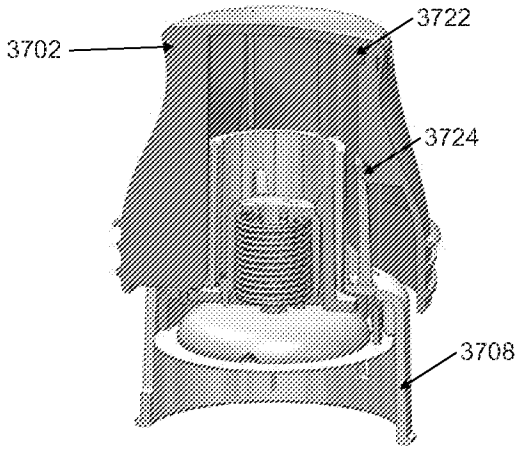


FIG. 102A

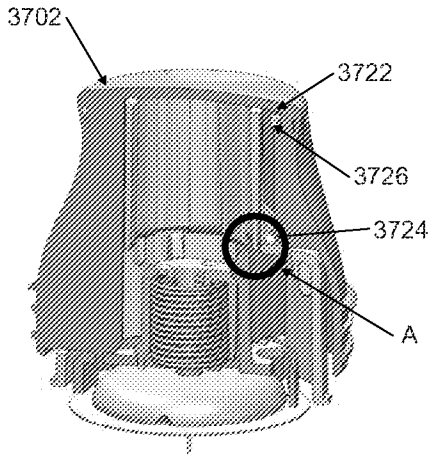


FIG. 102B

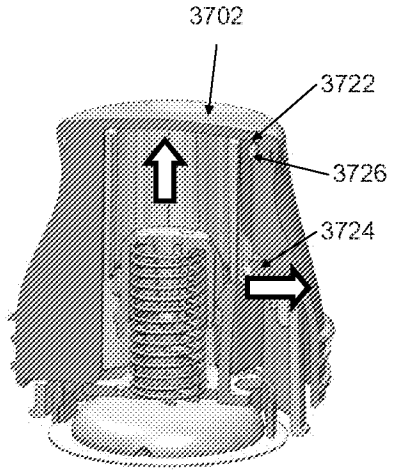


FIG. 102C

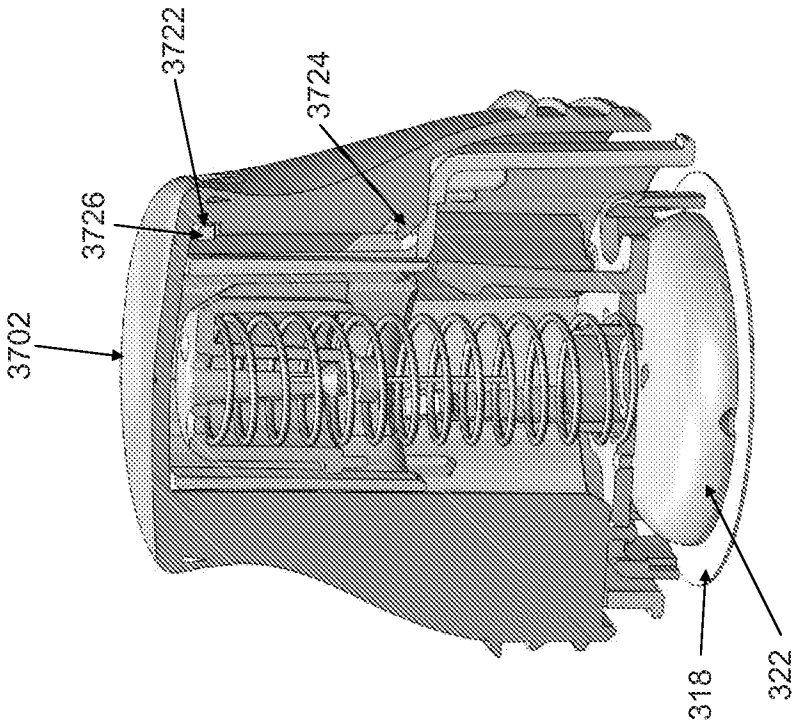


FIG. 103

Electronic Patent Application Fee Transmittal

Application Number:	
Filing Date:	
Title of Invention:	MEDICAL DEVICE INSERTERS AND PROCESSES OF INSERTING AND USING MEDICAL DEVICES
First Named Inventor/Applicant Name:	Manuel L. Donnay
Filer:	David W. Schalk
Attorney Docket Number:	031312-06899

Filed as Large Entity

Provisional Filing Fees

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Basic Filing:				
Provisional application filing	1005	1	220	220
Pages:				
Prov. Appl Size fee per 50 sheets >100	1085	2	270	540
Claims:				
Miscellaneous-Filing:				
Petition:				
Patent-Appeals-and-Interference:				
Post-Allowance-and-Post-Issuance:				

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Extension-of-Time:				
Miscellaneous:				
			Total in USD ($)	**760**

Electronic Acknowledgement Receipt

EFS ID:	8792732
Application Number:	61411262
International Application Number:	
Confirmation Number:	1235
Title of Invention:	MEDICAL DEVICE INSERTERS AND PROCESSES OF INSERTING AND USING MEDICAL DEVICES
First Named Inventor/Applicant Name:	Manuel L. Donnay
Customer Number:	90259
Filer:	David W. Schalk
Filer Authorized By:	
Attorney Docket Number:	031312-06899
Receipt Date:	08-NOV-2010
Filing Date:	
Time Stamp:	17:01:46
Application Type:	Provisional

Payment information:

Submitted with Payment	yes
Payment Type	Credit Card
Payment was successfully received in RAM	$760
RAM confirmation Number	4029
Deposit Account	
Authorized User	

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)

1	Provisional Cover Sheet (SB16)	ProvisionalSB.pdf	1060184 407e247cc9da985e02f2d9aebffa4b10540aaa25	no	3
Warnings:					
Information:					
2	Specification	application.pdf	326438 a2e9719b41f073c8c2fcd03eec5c031da498b5fa	no	110
Warnings:					
Information:					
3	Drawings-only black and white line drawings	drawings.pdf	12055652 c4f6ee71d892640fb4669b3cfde927e8f70f5bbd	no	102
Warnings:					
Information:					
4	Fee Worksheet (PTO-875)	fee-info.pdf	31596 298caafacb42f4dfb4cff9327a61351f709a4f92	no	2
Warnings:					
Information:					
		Total Files Size (in bytes):	13473870		

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New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

EXHIBIT 1

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United States Patent and Trademark Office
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APPLICATION NUMBER	FILING or 371(c) DATE	GRP ART UNIT	FIL FEE REC'D	ATTY.DOCKET.NO	TOT CLAIMS	IND CLAIMS
61/361,374	07/02/2010		490	031312-06499		

CONFIRMATION NO. 1217

90259
Hughes Hubbard and Reed LLP
One Battery Park Plaza
New York, NY 10004

FILING RECEIPT

OC000000042726492

Date Mailed: 07/27/2010

Receipt is acknowledged of this provisional patent application. It will not be examined for patentability and will become abandoned not later than twelve months after its filing date. Any correspondence concerning the application must include the following identification information: the U.S. APPLICATION NUMBER, FILING DATE, NAME OF APPLICANT, and TITLE OF INVENTION. Fees transmitted by check or draft are subject to collection. Please verify the accuracy of the data presented on this receipt. **If an error is noted on this Filing Receipt, please submit a written request for a Filing Receipt Correction. Please provide a copy of this Filing Receipt with the changes noted thereon. If you received a "Notice to File Missing Parts" for this application, please submit any corrections to this Filing Receipt with your reply to the Notice. When the USPTO processes the reply to the Notice, the USPTO will generate another Filing Receipt incorporating the requested corrections**

Applicant(s)

Manuel Donnay, Alameda, CA;
Peter G. Robinson, Alameda, CA;

Power of Attorney:
Walter Egbert III--37317

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Projected Publication Date: None, application is not eligible for pre-grant publication

Non-Publication Request: No

Early Publication Request: No

Title

Medical Device Inserters and Processes of Inserting and Using Medical Devices

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Electronic Acknowledgement Receipt

EFS ID:	7951653
Application Number:	61361374
International Application Number:	
Confirmation Number:	1217
Title of Invention:	Medical Device Inserters and Processes of Inserting and Using Medical Devices
First Named Inventor/Applicant Name:	Manuel Donnay
Customer Number:	90259
Filer:	Lisa A. Chiarini/Walter Egbert
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Attorney Docket Number:	031312-06499
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Payment was successfully received in RAM	$760
RAM confirmation Number	5401
Deposit Account	083264
Authorized User	ABRAMSON,RONALD

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Charge any Additional Fees required under 37 C.F.R. Section 1.16 (National application filing, search, and examination fees)

Charge any Additional Fees required under 37 C.F.R. Section 1.17 (Patent application and reexamination processing fees)

Doc Code: **TR.PROV**
Document Description: Provisional Cover Sheet (SB16)

PTO/SB/16 (04-07)
Approved for use through 06/30/2010 OMB 0651-0032
U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE
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Provisional Application for Patent Cover Sheet

This is a request for filing a PROVISIONAL APPLICATION FOR PATENT under 37 CFR 1.53(c)

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All Inventors Must Be Listed – Additional Inventor Information blocks may be generated within this form by selecting the **Add** button. — Add

Title of Invention	MEDICAL DEVICE INSERTERS AND PROCESSES OF INSERTING AND USING MEDICAL DEVICES
Attorney Docket Number (if applicable)	031312-06499

Correspondence Address

Direct all correspondence to (select one):

(•) The address corresponding to Customer Number	( ) Firm or Individual Name
Customer Number	90259

The invention was made by an agency of the United States Government or under a contract with an agency of the United States Government.

(•) No.

( ) Yes, the name of the U.S. Government agency and the Government contract number are:

PTO/SB/16 (04-07)
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Entity Status

Applicant claims small entity status under 37 CFR 1.27

◯ Yes, applicant qualifies for small entity status under 37 CFR 1.27

◉ No

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Signature	/Walter M. Egbert, III/			Date (YYYY-MM-DD)	2010-07-02
First Name	Walter M.	Last Name	Egbert III	Registration Number (If appropriate)	37317

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MEDICAL DEVICE INSERTERS AND PROCESSES OF INSERTING AND USING MEDICAL DEVICES

BACKGROUND OF THE INVENTION

[0001] Diabetes Mellitus is an incurable chronic disease in which the body does not produce or properly utilize insulin. Insulin is a hormone produced by the pancreas that regulates blood sugar (glucose). In particular, when blood sugar levels rise, *e.g.*, after a meal, insulin lowers the blood sugar levels by facilitating blood glucose to move from the blood into the body cells. Thus, when the pancreas does not produce sufficient insulin (a condition known as Type 1 Diabetes) or does not properly utilize insulin (a condition known as Type 2 Diabetes), the blood glucose remains in the blood, resulting in hyperglycemia or abnormally high blood sugar levels.

[0002] The fluctuations in blood glucose levels in people suffering from diabetes cause long-term, serious complications. Some of these complications include blindness, kidney failure, and nerve damage. Additionally, it is known that diabetes is a factor in accelerating cardiovascular diseases such as atherosclerosis (hardening of the arteries), leading to stroke, coronary heart disease, and other diseases. Accordingly, one important and universal strategy in managing diabetes is to control blood glucose levels.

[0003] One way to manage blood glucose levels is testing and monitoring blood glucose levels by using conventional *in vitro* techniques, such as drawing blood samples, applying the blood to a test strip, and determining the blood glucose level using colorimetric, electrochemical, or photometric test meters. Another more recent technique for monitoring blood glucose levels is by using an *in vivo* glucose-monitoring system, that continuously and/or automatically tests glucose, such as, for example, the FreeStyle Navigator® Continuous Glucose Monitoring

System, manufactured by Abbott Diabetes Care, Inc. Unlike conventional blood glucose meters, continuous analyte-monitoring systems employ a sensor at least a portion of which is positioned in a subject, which detects and monitors blood glucose levels. Prior to each use of a new sensor, the user self-inserts at least a portion of the sensor under his/her skin. An inserter assembly may be employed to insert the sensor in the body of the user. In this manner, an introducer sharp, while engaged to the sensor, pierces an opening into the skin of the user, releases the sensor, and is removed from the body of the user. Accordingly, there exists a need for an easy-to-use, simple, insertion assembly that is reliable, minimizes pain, and is easy to use.

SUMMARY

[0004] Sensors for detecting a physical parameter of a subject are disclosed herein. In some embodiments, a sensor is used to determine a level of analyte, such as, *e.g.*, glucose. Devices are disclosed for inserting a sensor into a subject, *e.g.*, at least partially beneath the skin of a subject. Sensor assemblies that include a medical device, such as a sensor and/or an infusion device, and a device to position at least a portion of the medical device are provided, as well as methods of positioning at least a portion of a medical device such as a sensor (*e.g.*, a glucose sensor) and/or an infusion device, and methods of using a positioned medical device, *e.g.*, methods for analyte testing are disclosed herein.

[0005] Sensor assembly embodiments include a housing adapted to adhere to the skin of a subject; an analyte sensor coupled or coupleable to the housing; and an insertion sharp having a longitudinal body including a longitudinal opening to receive at least a portion of the sensor. In some embodiments, the insertion sharp and analyte sensor may be retained in the sensor housing

using a resilient member, such as a spherical or ball-shaped member, press-fit into the sensor housing.

[0006] In certain embodiments, the sensor includes a body having a proximal section and a distal section, and the distal section may be longitudinally (or otherwise) aligned with the proximal section. Some sensor embodiments may include an intermediate section. An intermediate section, if present, may or may not be laterally displaced from at least the distal member, and a gap may be defined between the laterally displaced intermediate section and a portion of the distal section. A second gap may be defined in the sensor between the proximal section and the laterally displaced intermediate section. The proximal section of the sensor may have a substantially curved profile. A proximal section and a distal section of a given sensor may or may not be in axial alignment with respect to each other.

[0007] In some embodiments, the distal section of the sensor body is received in the longitudinally defined opening of the insertion sharp. A gap may be defined between the distal section and the laterally displaced intermediate section, which allows the distal section, in some embodiments a substantial portion – – including the entirety of the distal section – – to be received in the longitudinal opening of the insertion needle. The intermediate section and the proximal section may be proximate the distal section received in the insertion needle.

[0008] In some embodiments, the proximal section of the sensor may be disposed in a horizontal plane, and the distal section of the sensor body may be disposed in a vertical plane, at least during a sensing operation. In some embodiments, the sensor is configured for insertion in a soft tissue of a user. In some embodiments, the sensor is a glucose sensor.

[0009] Embodiments include sensor assemblies which include a sensor including a portion for operative contact with a fluid of the subject; a housing defining a distal surface adapted for attachment to the skin of a subject and housing a circuit coupled to sensor for performing a function with the sensor. In some embodiments, the sensor is integrated with the circuit within the housing to define an on-body device such as a single-unit on-body device. In some embodiments, a switch is provided at least partially disposed in the housing and having a member defining a first position which protrudes from the distal surface of the mount and a second position which is recessed in the mount, the member configured to activate the circuit when in the second position.

[0010] In some embodiments, the member is biased in the first position. The member may include an elongated member disposed in an opening in the mount. In some embodiments, the member is moved from the first position to the second position when the mount contacts the skin of the subject. In some embodiments, an adhesive layer is disposed on the skin of the subject, and wherein the member is moved from the first position to the second position when the mount contacts the adhesive layer.

[0011] In some embodiments, the switch activates the circuit upon the member reaching the second position. In some embodiments, the switch activates the circuit as long as the member is maintained in the second position. In some embodiments, the sensor is a glucose sensor.

[0012] In some embodiments, the circuit applies a potential to the sensor. In some embodiments, the circuit applies a current to the sensor.

[0013] Embodiments include apparatuses for inserting medical devices at least partially through the skin of a subject. An insertion apparatus may include a sheath defining a distal

surface for placement on the skin of the subject; a device support movable between a proximal and distal position, and adapted to support a medical device; a sharp support movable between a proximal position and a distal position, and adapted to support a sharp extending through a portion of the device support; a handle movable between a proximal position and distal position relative to the sheath and adapted to urge the device support and the sharp support from a proximal to a distal position. In some embodiments, the handle defines guides for slidable engagement with the sharp support and/or the device support. In some embodiments, a driver biases the handle towards the proximal position.

[0014] In some embodiments, the user attaches the inserter to the skin, pressing on the sheath to secure the device adhesively to the skin. The handle is pressed distally urging the device and sharp support into the skin and at the same time energizes the driver element. Once the handle is bottomed out and the medical device placed with respect to the skin, the user releases pressure on the handle. The driver element retracts the device and sharp support, while the device is left coupled to the skin (either mechanically or adhesively). The sharp is retracted from the skin, and the inserter device can be removed.

[0015] In variations of the above embodiment, the driver includes a compression member such as a compression spring. The handle is at least partially disposed within the sheath or is at least partially disposed surrounding the sheath. The sharp support may be permanently fixed to the handle. The device support may be permanently affixed to the handle.

[0016] In some embodiments, a stop portion for retaining the device support in the distal position is included. In some embodiments, the device support is coupled to the sharp support until the device support reaches a distal position.

[0017] In some embodiments, the device support is uncoupled from the sharp support when the device support reaches the distal position. In some embodiments, a retention member is provided to couple the sharp support to the sheath when the sharp support is disposed in the proximal position.

[0018] In some embodiments, the medical device is an analyte sensor. In some embodiments, the medical device is a glucose sensor. In some embodiments, the medical device is an infusion set.

[0019] In certain embodiments, apparatuses for inserting a medical device at least partially through the skin of a subject are provided which include a sheath defining a distal surface for placement on the skin of the subject; a handle movable between a proximal position and distal position; a device support for supporting the medical device and defining an aperture therethrough, the device support coupled to the handle; a sharp support for supporting a sharp extending through said aperture and coupled to the device support; and driver for biasing the sharp support towards the proximal position.

[0020] In some embodiments, the driver includes a compression spring. In some embodiments, the handle is at least partially disposed surrounding the sheath.

[0021] In some embodiments, a stop portion for retaining the device support in the distal position is included. In some embodiments, the device support is coupled to the handle until the device support reaches a distal position. In some embodiments, the device support is uncoupled from the sharp support when the device support reaches the distal position.

[0022] Embodiments of analyte sensors are provided which include a body having a proximal section and a distal section. The distal section may be longitudinally aligned with the proximal section. An intermediate section may be included between the proximal and distal sections, and in some embodiments the intermediate section is laterally displaced from at least the distal member. A gap may be defined between the laterally displaced intermediate section and a portion of the distal section.

[0023] In some embodiments, the proximal end is received within a needle seat to create an anchor region to allow the sensor body to slide into an opening defined in the insertion sharp but prevent the sensor body from inadvertently slipping out of the insertion needle. In some embodiments, a width of the distal section of the sensor body is sized to fit within the opening of the insertion sharp. In certain embodiments, the opening in the sharp has a diameter of about 20 to about 26 gauge, *e.g.*, 21 gauge to about 25 gauge, where in certain embodiments the sharp is 21 gauge or 23 gauge or 25 gauge. Such sharp may be used with a sensor having a width or diameter – – at least the portion that is carried by the sharp – – of about .20 mm to about .80 mm, *e.g.*, about .25 mm to about .60 mm, where in some embodiments the width or diameter of at least a portion of a sensor is .27 mm or .33 mm or .58 mm.

[0024] In some embodiments, the intermediate member includes a plane-altering portion. The plane-altering portion allows the proximal section of the sensor body to be in a plane different than the distal section of the sensor body. In some embodiments, the proximal section and the distal section are in planes substantially perpendicular to each other, *e.g.*, the area may define an angle of about 120° to about 60°, *e.g.*, about 90°.

[0025] In some embodiments, the proximal section has a curved portion.

[0026] In some embodiments, the sensor body includes conductive material disposed in or on a surface thereto to define one or more electrodes. The sensor body may include conductive material defining traces disposed in or on a surface of the sensor body. The traces are in communication with the one or more electrodes. The traces may be disposed in or on at least one surface of the proximal section of the sensor body. The one or more electrodes may be disposed on the distal section of the sensor body. At least one of the traces or electrodes may include a metal or carbon material such as gold, platinum, titanium, and carbon. At least one of the traces or electrodes may be formed by ablation of material. The ablation may include laser ablation. In some embodiments, the sensor is a wire.

[0027] In some embodiments, the sensor includes a sensing layer. The sensing layer may include an enzyme. The sensing layer may include an electron transfer agent. The electron transfer agent may be a redox mediator. In some embodiments, the electron transfer agent includes osmium transition metal complexes and one or more ligands. The electron transfer agent may be configured to transfer electrons directly between the analyte and the working electrode. The electron transfer agent may be configured to transfer electrons indirectly between the analyte and the working electrode.

[0028] In some embodiments, the sensing layer includes a redox polymer. The redox polymer may include osmium. The sensing layer may include a catalyst. The catalyst may include an enzyme. The catalyst may act as an electron transfer agent. In some embodiments, the enzyme includes glucose oxidase. In some embodiments, the enzyme includes glucose dehydrogenase.

[0029] In some embodiments, the sensing layer is configured such that the reaction of glucose in the presence of an enzyme forms hydrogen peroxide, and glucose level may be correlated to the level of hydrogen peroxide. In some embodiments, the sensor is a subcutaneous sensor.

[0030] These and other features, objects, and advantages of the disclosed subject matter will become apparent to those persons skilled in the art upon reading the detailed description as more fully described below.

BRIEF DESCRIPTION OF THE DRAWINGS

[0031] A detailed description of various aspects, features, and embodiments of the subject matter described herein is provided with reference to the accompanying drawings, which are briefly described below. The drawings are illustrative and are not necessarily drawn to scale, with some components and features being exaggerated for clarity. The drawings illustrate various aspects and features of the present subject matter and may illustrate one or more embodiment(s) or example(s) of the present subject matter in whole or in part.

[0032] **FIGURE 1** is a schematic view of the system in accordance with one embodiment of the disclosed subject matter;

[0033] **FIGURE 2** is a view, in partial cross section, of an electrochemical sensor in accordance with one embodiment of the disclosed subject matter;

[0034] **FIGURE 3** is a view, in partial cross-section, of an electrochemical sensor in accordance with another embodiment of the disclosed subject matter;

[0035] **FIGURE 4** is a view of the electrochemical sensor of FIGURE 3 in a folded configuration in accordance with the disclosed subject matter;

[0036] **FIGURE 5A** is a view of an electrochemical sensor in accordance with a further embodiment of the disclosed subject matter;

[0037] **FIGURE 5B** is a view of the electrochemical sensor of FIGURE 5 in a folded configuration in accordance with the disclosed subject matter;

[0038] **FIGURES 6A-6B** are views of an electrochemical sensor in accordance with a further embodiment of the disclosed subject matter;

[0039] **FIGURE 7** is a perspective view of an on-body unit in accordance with one embodiment of the disclosed subject matter;

[0040] **FIGURE 8** is a perspective view in partial cross-section of an on-body unit of FIGURE 7 in accordance with the disclosed subject matter;

[0041] **FIGURE 9** is a schematic view of the system in accordance with one embodiment of the disclosed subject matter;

[0042] **FIGURE 10** is a sectional, perspective view of another embodiment of an inserter in accordance with the disclosed subject matter;

[0043] **FIGURES 11-12** are perspective views of components of the inserter of FIGURE 10 in accordance with the disclosed subject matter;

[0044] **FIGURE 13** is a sectional, perspective view of a component of the inserter of FIGURE 10 in accordance with the disclosed subject matter;

[0045] **FIGURES 14-15** are perspective views of components of the inserter of FIGURE 10 in accordance with the disclosed subject matter;

[0046] **FIGURE 16** is a sectional view of the component of FIGURE 15 in accordance with the disclosed subject matter;

[0047] **FIGURES 17-18** are schematic views of a needle hub in accordance with one embodiment of the disclosed subject matter;

[0048] **FIGURE 19** is a distal end view of a sharp in accordance with one embodiment of the disclosed subject matter;

[0049] **FIGURE 20** is a side view of a sharp in accordance with one embodiment of the disclosed subject matter;

[0050] **FIGURE 21** is a side view of a sharp in accordance with one embodiment of the disclosed subject matter;

[0051] **FIGURE 21A** is a perspective view with parts separated of an inserter in accordance with one embodiment of the disclosed subject matter;

[0052] **FIGURE 21B** is a schematic view of an alternate embodiment for forming a sharp to be used in an inserter in accordance with one embodiment of the disclosed subject matter;

[0053] **FIGURE 22** is a perspective view of an inserter in accordance with one embodiment of the disclosed subject matter;

[0054] **FIGURE 23** is a perspective view with parts separated of an inserter in accordance with one embodiment of the disclosed subject matter;

[0055] **FIGURE 24** is an enlarged sectional view with parts separated of an inserter in accordance with one embodiment of the disclosed subject matter;

[0056] **FIGURES 24A-24C** depict an alternative method for retaining a sharp and sensor within the sensor housing;

[0057] **FIGURES 25-27** are perspective views of components of the inserter of FIGURE 10 in accordance with the disclosed subject matter;

[0058] **FIGURES 28-29** are sectional views of the inserter of FIGURE 10 in accordance with the disclosed subject matter;

[0059] **FIGURES 30-31** are sectional views of components of the inserter of FIGURE 10 in accordance with the disclosed subject matter;

[0060] **FIGURE 31A** is a sectional view of components of the inserter of FIGURE 10 shown separated from the on-body unit in accordance with the disclosed subject matter.

[0061] **FIGURES 32-33** illustrate, by schematic, a power supply switch mechanism including conductive plug of the on-body integrated sensor and sensor electronics assembly in accordance with embodiments of the disclosed subject matter;

[0062] **FIGURE 34** is a perspective view of an embodiment of an inserter in accordance with one embodiment of the disclosed subject matter;

[0063] **FIGURES 35-36** are perspective views of the inserter of FIGURE 34 in accordance with the disclosed subject matter;

[0064] **FIGURES 37-39** are sectional, perspective views of the inserter of FIGURE 34 in accordance with the disclosed subject matter;

[0065] **FIGURES 40-41** are perspective views of the inserter of FIGURE 34 in accordance with the disclosed subject matter;

[0066] **FIGURES 42-43** are perspective views of another embodiment of an inserter in accordance with the disclosed subject matter;

[0067] **FIGURES 44-49** are perspective views of components of the inserter of FIGURE 42 in accordance with the disclosed subject matter;

[0068] **FIGURE 50** is a sectional view of the inserter of FIGURE 42 in accordance with the disclosed subject matter;

[0069] **FIGURE 51** is a sectional, perspective view of the inserter of Figure 42 in accordance with the disclosed subject matter;

[0070] **FIGURE 52** is a perspective view of the inserter of FIGURE 42 in accordance with the disclosed subject matter;

[0071] **FIGURES 53-54** are sectional, perspective views of the inserter of FIGURE 42 in accordance with the disclosed subject matter;

[0072] **FIGURES 55-56** are perspective views of the inserter of FIGURE 42 in accordance with the disclosed subject matter;

[0073] **FIGURES 57-58** are perspective views of another embodiment of an inserter in accordance with the disclosed subject matter;

[0074] **FIGURES 59-63** are perspective views of components of the inserter of FIGURE 57 in accordance with the disclosed subject matter;

[0075] **FIGURE 64** is a sectional views of the inserter of FIGURE 57 in accordance with the disclosed subject matter;

[0076] **FIGURES 65-67** are sectional, perspective views of the inserter of Figure 57 in accordance with the disclosed subject matter;

[0077] **FIGURE 68** is a perspective view of another embodiment of an inserter In accordance with the disclosed subject matter;

[0078] **FIGURE 69** is a side view of the inserter of FIGURE 68 in accordance with the disclosed subject matter;

[0079] **FIGURES 70-71** are cross-sectional views of the inserter of FIGURE 68 in accordance with the disclosed subject matter;

[0080] **FIGURE 72** is a cross-sectional view of another inserter in accordance with the disclosed subject matter;

[0081] **FIGURE 72A** is an exploded perspective view of the inserter of FIGURE 72 in accordance with the disclosed subject matter;

[0082] **FIGURES 72B-I** are perspective views of the inserter of FIGURE 72 showing the assembly of various components in accordance with the disclosed subject matter;

[0083] **FIGURES 72J-N** are cross-sectional views of the inserter of FIGURE 72 in accordance with the disclosed subject matter;

[0084] **FIGURE 72O** illustrates a process for utilizing a sterilized versions of the inserter of FIGURE 72 in accordance with the disclosed subject matter;

[0085] **FIGURE 72P** illustrates an alternate process for utilizing a sterilized versions of the inserter of FIGURE 72 in accordance with the disclosed subject matter;

[0086] **FIGURE 73** is a perspective view of another inserter in accordance with the disclosed subject matter;

[0087] **FIGURE 73A** is a perspective view of a component of the inserter of FIGURE 73 in accordance with the disclosed subject matter;

[0088] **FIGURE 73B** is a cross-sectional view of a component of the inserter of FIGURE 73 in accordance with the disclosed subject matter;

[0089] **FIGURES 73C-G** are perspective views of a components of the inserter of FIGURE 73 in accordance with the disclosed subject matter;

[0090] **FIGURES 73H-N** are cross-sectional views of the inserter of FIGURE 73 in accordance with the disclosed subject matter;

[0091] **FIGURE 73O** illustrates a process for utilizing a sterilized versions of the inserter of FIGURE 72 in accordance with the disclosed subject matter;

[0092] **FIGURE 74** is a perspective view of another inserter in accordance with the disclosed subject matter;

[0093] **FIGURES 75-82** are additional views of the components of the inserter of FIGURE 74 in accordance with the disclosed subject matter;

[0094] **FIGURE 83-88** are cross-sectional views of the inserter of FIGURE 73 in accordance with the disclosed subject matter; and

[0095] **FIGURES 89-90** are views of an alternate embodiment of the inserter of FIGURE 73 in accordance with the disclosed subject matter.

DETAILED DESCRIPTION OF THE EMBODIMENTS

[0096] A detailed description of the disclosure is provided herein. It should be understood, in connection with the following description, that the subject matter is not limited to particular embodiments described, as the particular embodiments of the subject matter may, of course, vary. It is also to be understood that the terminology used herein is for the purpose of describing

particular embodiments only, and is not intended to be limiting, since the scope of the disclosed subject matter will be limited only by the appended claims.

[0097] Where a range of values is provided, it is understood that each intervening value between the upper and lower limit of that range, and any other stated or intervening value in that stated range, is encompassed within the disclosed subject matter. Every range stated is also intended to specifically disclose each and every "subrange" of the stated range. That is, each and every range smaller than the outside range specified by the outside upper and outside lower limits given for a range, whose upper and lower limits are within the range from said outside lower limit to said outside upper limit (unless the context clearly dictates otherwise), is also to be understood as encompassed within the disclosed subject matter, subject to any specifically excluded range or limit within the stated range. Where a range is stated by specifying one or both of an upper and lower limit, ranges excluding either or both of those stated limits, or including one or both of them, are also encompassed within the disclosed subject matter, regardless of whether or not words such as "from," "to," "through," or "including" are or are not used in describing the range.

[0098] Unless defined otherwise, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which this disclosed subject matter belongs. Although any methods and materials similar or equivalent to those described herein can also be used in the practice or testing of the present disclosed subject matter, this disclosure may specifically mention certain exemplary methods and materials.

[0099] All publications mentioned in this disclosure are, unless otherwise specified, incorporated by reference herein for all purposes, including without limitation to disclose and describe the methods and/or materials in connection with which the publications are cited.

[00100] The publications discussed herein are provided solely for their disclosure prior to the filing date of the present application. Nothing herein is to be construed as an admission that the present disclosed subject matter is not entitled to antedate such publication by virtue of prior invention. Further, the dates of publication provided may be different from the actual publication dates, which may need to be independently confirmed.

[00101] As used herein and in the appended claims, the singular forms "a," "an," and "the" include plural referents unless the context clearly dictates otherwise.

[00102] Nothing contained in the Abstract or the Summary should be understood as limiting the scope of the disclosure. The Abstract and the Summary are provided for bibliographic and convenience purposes and due to their formats and purposes should not be considered comprehensive.

[00103] As will be apparent to those of skill in the art upon reading this disclosure, each of the individual embodiments described and illustrated herein has discrete components and features which may be readily separated from or combined with the features of any of the other several embodiments without departing from the scope or spirit of the present disclosed subject matter. Any recited method can be carried out in the order of events recited, or in any other order which is logically possible. Reference to a singular item includes the possibility that there are plural of the same item present. When two or more items (for example, elements or processes) are referenced by an alternative "or," this indicates that either could be present separately or any

combination of them could be present together except where the presence of one necessarily excludes the other or others.

System Overview

[00104] Embodiments include analyte monitors that are provided in small, lightweight, battery-powered and electronically-controlled systems. Such systems may be configured to detect physical parameters of subjects, such as signals indicative of *in vivo* analyte levels using an electrochemical sensor, and collect such signals, with or without processing. The electrochemical sensors may employ any suitable measurement technique, *e.g.*, may detect current, may employ potentiometry, etc. Techniques may include, but are not limited to amperometry, coulometry, and voltammetry. In some embodiments, sensing systems may be optical, colorimetric, and the like. In some embodiments, the portion of the system that performs this initial processing may be configured to provide the raw or at least initially processed data to another unit for further collection and/or processing. Such provision of data may be effected, for example, by a wired connection, such as an electrical, or by a wireless connection, such as an IR or RF connection.

[00105] Certain embodiments of analyte-monitoring systems for *in vivo* measurement employ a sensor that measures analyte levels in interstitial fluids at least partially under the surface of the subject's skin. A sensor in such a system may operate as an electrochemical cell. Such a sensor may use any of a variety of electrode configurations, such as a three-electrode configuration (*e.g.,* with "working," "reference," and "counter" electrodes) driven by a controlled potential (potentiostat) analog circuit; a two-electrode system configuration (*e.g.,* with only working and counter electrodes or a working electrode and a counter/reference electrode), which may be self-

biasing and/or self-powered; and/or other configurations (see, *e.g.*, U.S. Patent Application Serial No. 12/393,921, the disclosure of which is incorporated by reference herein for all purposes). In some embodiments, the sensor may be positioned within a blood vessel.

[00106] In certain systems, the analyte sensor is in communication with a sensor control unit. As used in this disclosure, an on-body unit sometimes refers to such a combination of an analyte sensor with such a sensor control unit. The on-body unit may include a housing in which the sensor control unit electronics and at least a portion of the sensor are received.

[00107] Certain embodiments are modular. The on-body unit may be separately provided as a physically distinct assembly from a monitor unit, *e.g.*, which displays or otherwise indicates analyte levels to a user. The on-body unit may be configured to provide the analyte levels detected by the sensor and/or other information (such as temperature, sensor life, etc.) over a communication link to the monitor unit. The monitor unit, in some embodiments, may include, *e.g.*, a mobile telephone device, an in vitro glucose meter, a personal digital assistant, or other consumer electronics such as MP3 device, camera, radio, personal computer, etc., or other communication-enabled data-processing device.

[00108] The monitor unit may perform a variety of functions such as but not limited to data storage and/or processing and/or analysis and/or communication, etc., on the received analyte data to generate information pertaining to the monitored analyte levels and/or process the other information. The monitor unit may incorporate a display screen, which can be used, for example, to display measured analyte levels, and/or an audio component such as a speaker to audibly provide information to a user, and/or a vibration device to provide tactile feedback to a user. It is also useful for a user of an analyte-monitoring system to be able to see trend

indications (including the magnitude and direction of any ongoing trend, *e.g.*, the rate of change of an analyte or other parameter, and the amount of time a subject is above and/or below a threshold, such as a hypoglycemic and/or hyperglycemic threshold, etc.); such data may be displayed either numerically, or by a visual indicator such as an arrow that may vary in visual attributes, like size, shape, color, animation, or direction. The monitor unit may further be adapted to receive information from or about an *in vitro* anal yte test strip, which may be manually or automatically entered into the monitor unit. In some embodiments a monitor unit may incorporate an *in vitro* analyte test strip port and related electronics in order to be able to make discrete (*e.g.*, blood glucose) measurements using an *in vitro* test strip (see, *e.g.*, U.S. Patent No. 6,175,752, the disclosure of which is incorporated by reference herein for all purposes).

[00109] The modularity of these systems may vary where one or more components may be constructed to be single use and one or more may be constructed to be re-useable. In some embodiments the sensor is designed to be attachable and detachable from the sensor control unit (and the on-body unit may be reusable), *e.g.*, so that one or more of the components may be reused one or more times, while in other embodiments, the sensor and sensor control unit may be provided as an integrated, undetachable package, which may be designed to be disposable after use, *i.e.*, not re-used.

[00110] FIGURE 1 shows one embodiment of an analyte measurement system 10. In such a system, a data-processing unit or sensor control unit 12 may interact with an analyte sensor 14 to obtain signals representative of analyte levels. Sensor control unit 12 may further include communications circuitry with associated electronics (not shown). In some embodiments, the

sensor control unit 12 and at least a portion of a sensor are configured to be maintained "on the body" of the subject, in the substantially same position on the body of the subject, for a period of time that may include hours, days, weeks, or a month or more. Accordingly, the sensor control unit 12 and sensor 14 may be referred to collectively herein as an on-body unit 16. A monitor unit 18 may also be provided. In the embodiment shown, sensor control unit 12 and monitor unit 18 communicate *via* connection 20 (in this embodiment, a wireless radio frequency (RF) connection). Communication may occur, *e.g.*, *via* RF communication, infrared communication, Bluetooth communication, Zigbee communication, 802.1x communication, or WiFi communication, etc. In some embodiments, the communication may include a radio frequency of 433 MHz, 13.56 MHz, or the like. In some embodiments, communication between sensor control unit 12 and monitor unit 18 may include radio frequency identification (RFID) techniques, and may be active RFID or passive RFID, where in some embodiments passive RFID technology and the respective system components include the necessary components therefor. For example, in certain embodiments, the on-body unit 16 and the monitor unit 18 may be configured to communicate using RFID communication protocol, wherein the on-body unit 16 may be configured to communicate or provide analyte-related signals to the monitor unit 18 based on the presence or reception of at least one signal from the monitor unit 18. That is, in certain embodiments, the monitor unit 18 may be configured to provide or radiate RF power signals, and when the on-body unit 16 is positioned within the radiated or provided RF signal range radiated from the monitor unit 18, the on-body unit 16 in certain embodiments is configured to provide one or more signals associated with the monitored analyte level received from the analyte sensor 14 to the monitor unit 18. For example, in one embodiment, the monitor unit may include a backscatter RFID reader configured to transmit an RF field such that when

the on-body unit is within the transmitted RF field, an antenna is tuned and in turn provides a reflected or response signal (for example, a backscatter signal) to the monitor unit. The reflected or response signal may include sampled analyte level data from the analyte sensor. Additional exemplary details for various embodiments can be found in, *e.g.*, U.S. Patent Application Serial No. 12/698,124 filed February 1, 2010, the disclosure of which is incorporated by reference herein for all purposes.

[00111] In some embodiments, a secondary monitor unit 22 may be provided. A data-processing terminal 24 may also be included, *e.g.*, for providing further processing or review of analyte data. In some embodiments, the secondary monitor unit 22 may include similar components and/or functionalities as the monitor unit 18, or alternatively, include more or less functionalities or components compared to the monitor unit 18 to, for example, analyze, process, store, and/or communicate data from the analyte sensor 14 and/or monitor unit 18.

[00112] In some embodiments, system 10 may be a continuous analyte monitor (*e.g.*, a continuous glucose-monitoring system or CGM), and accordingly operate in a mode in which the communications *via* connection 20 has sufficient range to support a flow of data from on-body unit 16 to monitor unit 18. In some embodiments, the data flow in a CGM system is automatically provided by the on-body unit 16 to the monitor unit 18. For example, no user intervention may be required for the on-body unit 16 to send the data to the monitor unit 18, *e.g.*, it may be continually and/or automatically broadcasted. In some embodiments, the on-body unit 16 provides signal relating to analyte level to the monitor unit 18 automatically and periodically. For example, one or more signals may be provided, *e.g.*, automatically sent, on a schedule, *e.g.*, once every 250ms, once a second, once a minute, etc. That is, in certain embodiments, the on-

body unit 16 may be configured and/or programmed to communicate or transmit the data acquired from the analyte sensor 14 based on a predetermined schedule, and continue to broadcast or transmit signals related to the real time monitored analyte levels based on the predetermined schedule. In such embodiments, the monitor unit 18 may be configured to receive and/or anticipate and acquire the transmitted signals from the on-body unit 16 based on the predetermined schedule, for example, for further processing, such as display, storing, analysis, and/or further data communication.

[00113] In some embodiments, one or more signals may be provided to the monitor unit 18 upon the occurrence of, or impending occurrence of, an event, *e.g.*, a hyperglycemic event or a hypoglycemic event, etc. In some embodiments, the one or more signals may be provided to the monitor unit 18 on an adaptive schedule. For example, the schedule for automatically communicating the one or more signals may be adjusted by machine learning techniques (*e.g.*, supervised learning techniques, unsupervised learning techniques, data mining, etc.) according to parameters received by the sensor control unit 12 and/or monitor unit 18, such as, *e.g.*, analyte values and trends, activity levels, meal times, etc.). In some embodiments, sensor control unit 12 may further include local memory in which it may record "logged data" or buffered data collected over a period of time and provide some or all of the accumulated data to monitor unit 18 from time-to-time. Or, a separate data-logging unit may be provided to acquire periodically provided data from sensor control unit 12. Data transmission in a CGM system may be one-way communication, *e.g.*, the on-body unit 16 provides data to the monitor unit 18 without receiving signals from the monitor unit 18 In some embodiments, two-way communication is provided between the on-body unit 16 and the monitor unit 18, using, for example, one or more transceivers or other bi-directional communication components. Such two-way communication

may be achieved in certain embodiments independently. That is, in certain embodiments, certain data communication from the on-body unit 16 may be independent of the data received from the monitor unit 18. In other embodiments, certain data communication from the on-body unit 16 may in response or responsive to the data, signal, request, or one or more commands received from the monitor unit 18.

[00114] In some embodiments, one or more signals may be provided to the monitor unit 18 from the on-body unit on user demand. According to such embodiments, the monitor unit 18 requests data from the on-body unit 16. Accordingly, embodiments include systems in which data is transferred from the on-body unit to the monitor unit only when the monitor unit invokes data from the on-body unit.

[00115] The data transfer request may be provided in several ways. For example, in some embodiments, one or both of the on-body unit 16 and monitor unit 18 may include a mechanical switch activatable by a user or activated upon some other action or event, the activation of which initiates the transfer of signal from the on-body unit 16 to the monitor unit 18. A mechanical switch may be provided which is activatable by the user to cause power to be turned on to the on-body system, *e.g.*, to electronic components that control the sensor.

[00116] In some embodiments, the monitor unit 18 is placed in close proximity (*e.g.*, within a range of about one to about ten inches or less in certain embodiments) with the communications electronics of the on-body unit to cause initiation of data transfer from the on-body unit to the monitor unit, either over a wired connection, or wirelessly by various means, including, for example, various RF-carried encodings and protocols and IR links.

[00117] In some embodiments, a signal relating to analyte level is instantaneously generated by the analyte sensor 14 upon receipt of the request, and provided to the monitor unit 18 as requested.

[00118] In other embodiments, a signal relating to analyte level is obtained according to a schedule, *e.g.*, once every 250ms, once a second, once a minute, etc., and at least temporarily stored. Upon receipt of the data transfer request at the on-body unit 16 from the monitor unit 18, analyte-related information is provided to the monitor unit 18 from the on-body unit 16. In some cases, analyte-related information provided to the monitor unit 18 is or at least includes the most recent analyte signal(s).

[00119] In further embodiments, additional data is provided to the monitor unit 18 on demand. For example, analyte trend data may be provided. Such trend data may include two or more analyte data points to indicate that analyte levels are rising, falling, or stable. Analyte trend data may include data from longer periods of time, such as, *e.g.*, several minutes, several hours, several days, or several weeks.

[00120] Further details regarding on-demand systems are disclosed in U.S. Patent Publication Nos. 2009/0018425 A1, published January 15, 2009; 2009/0054749 A1, published February 26, 2009; 2009/0257911 A1, published October 15, 2009, 2009/0281406 A1, published November 12, 2009; 2009/0294277 A1, published December 3, 2009; 2008/0058625 A1, published March 6, 2008; 2008/0064937 A1, published March 13, 2008; 2008/0071157 A1, published March 20, 2008; 2008/0071158 A1, published March 20, 2008; 2008/0179187 A1, published July 31, 2008; 2008/0319295 A1, published December 25, 2008;2008/0319296 A1, published December 25, 2008; 2007/0149873 A1, published June 28, 2007;2007/0149875 A1, published June 28, 2007;

2009/0321277 A1, published December 31, 2009; 2010/0030052 A1, published February 4, 2010; and pending U.S. Patent Application Nos. 12/211,014, filed September 15, 2008; 12/242,780, filed September 30, 2008; 12/393,921, filed February 27, 2009; 12/495,709, filed June 30, 2009; 12/495,712, filed June 30, 2009; 12/495,730, filed June 30, 2009; 12/544,061, filed August 19, 2009; 12/625,185, filed November 24, 2009; 12/625,208, filed November 24, 2009; 12/625,524, filed November 24, 2009; 12/625,525, filed November 24, 2009; 12/625,528, filed November 24, 2009; 12/624,767, filed November 24, 2009; 12/628,177, filed November 30, 2009; 12/628,198, filed November 30, 2009; 12/628,201, filed November 30, 2009; 12/628,203, filed November 30, 2009; 12/628,210, filed November 30, 2009; 12/698,129, filed February 1, 2010; 12/698,124, filed February 1, 2010; 12/714,439, filed February 26, 2010; 61/163,006, filed March 24, 2009; 61/227,967, filed July 23, 2009; 61/238,159, filed August 29, 2009; 61/238,483, filed August 31, 2009; 61/238,494, filed August 31, 2009; 61/238,581, filed August 31, 2009; 61/247,508, filed September 30, 2009; 61/247,514, filed September 30, 2009; 61/247,516, filed September 30, 2009; 61/247,519, filed September 30, 2009; 61/249,535, filed October 7, 2009; 61/256,925, filed October 30, 2009; 61/291,326, filed December 31, 2009; 61/299,924, filed January 29, 2010; 61/297,625, filed January 22, 2010; 61/297,615, filed January 22, 2010, each of which is incorporated by reference herein for all purposes.

The Sensor

[00121] The analyte sensor 14 of the analyte measurement system 10 may be used to monitor levels of a wide variety of analytes. Analytes that may be monitored include, for example, acetylcholine, amylase, bilirubin, cholesterol, chorionic gonadotropin, creatine kinase (*e.g.*, CK-MB), creatine, DNA, fructosamine, glucose, glutamine, growth hormones, hormones, ketones,

lactate, peroxide, prostate-specific antigen, prothrombin, RNA, thyroid-stimulating hormone, and troponin. The concentration of drugs, such as, for example, antibiotics (*e.g.*, gentamicin, vancomycin, and the like), digitoxin, digoxin, drugs of abuse, theophylline, and warfarin, may also be monitored. One or more analyte may be monitored by a given sensor.

[00122] In one embodiment of the present disclosure, sensor 14 is physically positioned in or on the body of a user whose analyte level is being monitored. Sensor 14 may be configured to continuously sample the analyte level of the user and convert the sampled analyte level, *e.g.*, glucose concentration into a corresponding data signal, *e.g.*, a current or voltage, for input into sensor control unit electronics. Alternatively, sensor 14 may be configured to sample analyte levels on demand. The sensor control unit electronics may amplify, filter, average, and/or otherwise process signal provided by the sensor.

[00123] The sensor may take on a number of forms. For example, the sensor may include a flexible or rigid substrate. In some embodiments, the sensor may be a wire. In some embodiments, the sensor may include two or three or more electrodes.

[00124] An embodiment of the sensor 14 is illustrated in FIGURE 2. The shape(s) described herein are exemplary only. Other sensor shapes are contemplated. In some embodiments, sensor 14 includes a substrate which is a dielectric, *e.g.*, a polymer or plastic material, such as polyester or polyamide. In this embodiment, the sensor is constructed so that a portion is positionable beneath skin and a portion is above skin. Accordingly, sensor 14 includes an insertion or internal portion 30 and an external or electrical contact portion 32. The contact portion 32 typically includes several conductive contacts 36, 38, and 40 (herein shown as three contacts) for connection to other electronics, *e.g.*, at the sensor control unit 12. The contacts provided in this

embodiment are for a working electrode, a reference electrode, and a counter electrode. In some embodiments, two or more working electrodes are provided. The operative portions of these electrodes, that is, working electrode, reference electrode, and counter electrode (not individually shown), are provided at the insertion portion, *e.g.*, at the distal end of insertion portion 30, *e.g.*, portion 34. In some embodiments, one or more electrodes may be external to the body, *e.g.*, an external counter electrode. The contact and operative portions of the electrodes are connected by circuit traces 42, 44, and 46 running on the surface of the substrate. In some embodiments, the traces are provided in channels, or may be embedded within the substrate, or may traverse different sides of the substrate. The conductive contacts, conductive traces, and electrodes are fabricated from conductive material, such as platinum, palladium, gold, carbon, or the like. More than one material may be used for a given sensor. Further details of sensors are described, *e.g.*, in U.S. Patent Nos. 6,175,572 and 6,103,033, which are incorporated by reference herein for all purposes.

[00125] Sensor 14 may include a proximal retention portion 48. In some embodiments, the insertion portion 30 and the proximal retention portion 48 are substantially longitudinally aligned. The insertion portion 30 and the proximal retention portion 48 are sized and configured to be positioned with a sharp for installation into the skin of a subject, as described herein. In use, the sensor 14 may be configured to bend (*e.g.*, along the line B) and therefore be positioned in two substantially perpendicular, intersecting planes.

[00126] As illustrated in FIGURE 3, sensor 14' is substantially identical to sensor 14, with many of the differences illustrated in FIGURE 3 and noted herein. Sensor 14'' further includes additional features useful for connecting to, *e.g.*, mounting to or in or on, a housing associated

with the sensor control unit 12. For example, sensor 14' includes a laterally displaced portion (or sensor tab) 50' and a connector portion, shown in this embodiments as a longitudinal displaced portion 52' which provides a path for electrical connections, *e.g.*, the conductive traces, between the proximal and distal portions of the sensor. Sensor 14' is further provided with a notch or cut-out 54' between the proximal retention portion 48' and the longitudinal displaced portion 52'. Such configuration facilitates the sensor 14' to bend (*e.g.*, along the line indicated by line B) and therefore be positioned in two substantially perpendicular, intersecting planes, as illustrated in FIGURE 4. As will be described below, the sensor tab 50' can be encased in the portion of the body of the sensor control unit 12 to aid in securing and positioning the sensor 14'. Proximal retention portion 48' maintains its longitudinal alignment with insertion portion 30 for positioning within an insertion sharp.

[00127] FIGURES 5A and 5B illustrate a further embodiment of a sensor 14" in accordance with the disclosure. Sensor 14" is substantially identical to sensor 14 and 14', with certain exemplary differences illustrated in FIGURE 4 and noted herein. For example, sensor 14" includes a contact portion 32' which defines a fan-like configuration having a curved edge. The contact portion 32" typically includes several conductive contacts 36", 38", and 40" (herein shown as three contacts) for connection to other electronics, *e.g.*, at the sensor control unit 12. The contacts provided in this embodiment are for a working electrode, a reference electrode, and a counter electrode. In some embodiments, two or more working electrodes are provided. The operative portions of these electrodes, that is, working electrode, reference electrode, and counter electrode (not individually shown), are provided at the insertion portion, *e.g.*, at the distal end of insertion portion 30", *e.g.*, portion 34". The contact and operative portions of the electrodes are connected by circuit traces 42", 44", and 46" running on the surface of substrate, provided in

channels, embedded within the substrate, or traversing different sides of the substrate, substantially as described in connection with FIGURES 2 and 3. Sensor 14" defines a sensor flag indentation 56 " which also serves to assist in retaining the sensor 14" in a vertical orientation, as will be described below, and provides a discrete location for mating with a feature of the sensor control unit 12, *e.g.*, the bottom surface of a printed circuit board. Sensor 14" is likewise capable of bending along axis B, as illustrated in FIGURE 5B. In any of the embodiments of the sensor described herein, the distance between insertion portion 30 to retention portion 48 may be, *e.g.*, about 5 mm, or about 10 mm, or about 15 mm, or about 20 mm.

[00128] FIGURE 6A illustrates a further embodiment of a sensor 14"' in accordance with the disclosure. Sensor 14"' is substantially identical to sensor 14, 14' and 14", with certain exemplary differences illustrated in FIGURE 6A and noted herein. For example, sensor 14"' includes a contact portion 32"'. The contact portion 32"' typically includes several conductive contacts 36"', 38"', and 40"' (herein shown as three contacts) for connection to other electronics, *e.g.*, at the sensor control unit 12. The contacts provided in this embodiment are for a working electrode, a reference electrode, and a counter electrode. In some embodiments, two or more working electrodes are provided. The operative portions of these electrodes, that is, working electrode, reference electrode, and counter electrode (not individually shown), are provided at the insertion portion, *e.g.*, at the distal end of insertion portion 30"', *e.g.*, portion 34"'. As shown, contact portion 32"', proximal retention portion 48"'and the distal portion 30"' of sensor 14"' are linearly aligned with respect to one another. The contact and operative portions of the electrodes may be connected by circuit traces running on the surface of the substrate. In some embodiments, the circuit traces may be embedded within the substrate, or traversing different

sides of the substrate. Sensor 14''' is likewise capable of bending along axis B, as illustrated in FIGURE 6B. In FIGURE 6B, contacts 36''', 38''', and 40''' are not visible, because they are located on the underside of contact portion 32''' and thus not shown in this view. It is understood that sensor 14''' may be positioned such that when the sensor is placed in contact with surrounding circuitry the contacts are downwardly positioned to engage circuitry below the contact portion 32''' or, in some embodiments, the contacts are upwardly directed to engage circuitry positioned above the contact portion 32'''. In any of the embodiments of the sensor described herein, the distance between insertion portion 30 to retention portion 48 may be, *e.g.*, about 5 mm, or about 10 mm, or about 15 mm, or about 20 mm.

[00129] Embodiments of analyte sensors have been described herein to operate electrochemically, through an arrangement of electrodes having chemical sensing layers applied thereto, by generating an electrical current proportional to the volume of a redox reaction of the analyte (and indicative of analyte concentration), catalyzed by an analyte-specific oxidizing enzyme. Embodiments exist in which the number of electrodes provided to bring about and detect the level of these reactions is two, three, or a greater number. However, other types of sensors may be employed as described herein.

[00130] A portion of sensor 14 (which collectively refers to sensors 14', 14', and 14''' herein) may be situated above the surface of the skin, with a distal portion 30 penetrating through the skin and into the subcutaneous space in contact with the user's biofluid, such as interstitial fluid. Further details regarding the electrochemistry of sensor 14 is provided in U.S. Patent Nos. 5,264,104; 5,356,786; 5,262,035; 5,320,725; and 6,990,366, each of which is incorporated by reference herein for all purposes.

[00131] In some embodiments, the sensor is implantable into a subject's body for a usage period (*e.g.*, a minute or more, at least one day or more, about one to about 30 days or even longer, about three to about ten days, about three to about seven days, or in some embodiments, longer periods of up to several weeks) to contact and monitor an analyte present in a biological fluid. In this regard, the sensor can be disposed in a subject at a variety of sites (*e.g.*, abdomen, upper arm, thigh, etc.), including intramuscularly, transcutaneously, intravascularly, or in a body cavity.

[00132] In some embodiments, sensor 14 is employed by insertion and/or implantation into a user's body for some usage period. In such embodiments, the substrate may be formed from a relatively flexible material.

[00133] While the embodiments illustrated in FIGURES 2-6 have three electrodes, other embodiments can include a fewer or greater number of electrodes. For example, a two-electrode sensor can be utilized. The sensor 14 may be externally-powered and allow a current to pass proportional to the amount of analyte present. Alternatively, the sensor 14 itself may act as a current source in some embodiments. In some two-electrode embodiments, the sensor may be self-biasing and there may be no need for a reference electrode. An exemplary self-powered, two-electrode sensor is described in U.S. Patent Application Serial No. 12/393,921, filed February 26, 2009, and entitled "Self-Powered Analyte Sensor," which is hereby incorporated by reference herein for all purposes. The level of current provided by a self-powered sensor may be low, for example, on the order of nanoamperes, in certain embodiments.

On Body Unit

[00134] An exemplary configuration for a sensor 14 (and sensors 14' 14", and 14"') and sensor control unit 12 (*e.g.,* collectively, on-body unit 16) is illustrated in FIGURES 7-8. Sensor control unit 12, including its associated electronics 80, are housed in housing 122. Sensor housing 122 may be provided with a substantially circular configuration, or other shape. Sensor housing 122 has a reduced height (*i.e.*, "Z"-dimension) to provide a low profile when sitting on the skin of the subject. In some embodiments, the height is about 3 mm to about 25 mm, *e.g.*, may be about 4 mm, about 5 mm, about 10 mm, or about 15 mm. In certain embodiments, the sensor housing 122 may have a variable height such that it may have at least one portion that has a height that differs from at least one other portion. For example, electronics 80 may include one or more of, *e.g.*, an analog interface for connecting to the sensor 14, a processor, which may include, *e.g.*, an ASIC 91, antenna 94, power supply 82 to power the sensor and/or communications components, and capacitors 93. In some embodiments, power supply 82 provides a current or voltage to the analyte sensor only. In some embodiments, power supply 82 also powers a communications circuit for providing signal to the monitor unit 18. Power supply 82 may be used to charge capacitors 93 for such periodic signal communication. A serial communication section may be provided. A temperature sensor, such as a thermistor that detects skin temperature, sensor temperature, and/or ambient temperature may be included to provide compensation to the analyte signal. An RF communication circuit is provided to communicate with the monitor unit 18. (See, FIGURES 1 or 9.) A data storage unit may be provided to store analyte data over a period of time, which in some embodiments may be a short term of time, *e.g.,* several hours or minutes, or over a longer term, *e.g.*, several days or weeks. Additional optional electronics include a serial communication section, a leakage detection circuit, or user input, *e.g.,*

a switch to activate/deactivate some or all functions of the device. Many of the components may be combined together and/or their function provided by common components. Furthermore, certain components may be eliminated entirely. For example, a power supply may be omitted if power is provided by inductive coupling.

[00135] In some embodiments, a portion of sensor 14 is disposed on or within housing 122, *e.g.*, in a bent configuration, as illustrated in certain embodiments herein, *e.g.*, in FIGURES 4, 6, and 6B. In some embodiments, a portion of the contact portion of the sensor may be located on an outer surface of the sensor housing 122. The contact portion 32 of sensor 14 may be oriented in a substantially horizontal configuration (*e.g.*, substantially parallel to the skin surface to which it is attached), and secured to a printed circuit board of the sensor control unit 12. The insertion portion 30 of the sensor 14 may extend in a substantially downwardly vertical orientation for placement in the skin of the subject. In some embodiments, the insertion portion 30 is provided with a substantially sharpened and/or pointed configuration to facilitate piercing of the skin. See, *e.g.*, U.S. Patent Application Serial No. 61/238,159 filed August 29, 2009, which is incorporated by reference herein for all purposes. It is understood that sensor 14 may be disposed in other configurations, *e.g.*, in an entirely substantially vertical configuration, etc. As a further example, the insertion portion 30 may be disposed at an oblique angle, *e.g.*, between about 0° and about 90° with respect to the skin surface.

[00136] Adhesive pad 118 is illustrated in FIGURE 8 to attach sensor housing 122 to the skin of the subject. In some embodiments, adhesive pad 118 is used instead of a separate mount. Adhesive pad 118 may include adhesive on both distal (upper) and proximal (lower) surfaces, such that adhesive pad is attached or attachable to both sensor housing 122 and the skin of the

subject. In some embodiments, adhesive pad 118 may be first attached to the skin of the subject with the adhesive on the distal surface thereof. Subsequently, the housing 122 is adhered to the proximal surface of the adhesive pad 118. In other embodiments, proximal surface of adhesive pad 118 is first attached to sensor housing 122, and subsequently, the distal surface of adhesive pad 118 is then attached to the skin of the subject.

[00137] As illustrated in FIGURE 9, the on-body unit 16 communicates with the monitor unit 18. Such communication may be one-way communication, *e.g.*, from the on-body unit 16 to the monitor unit 18. In some embodiments, the communication may be two-way, *e.g.*, both from the on-body unit 16 to the monitor unit 18 and from the monitor unit 18 to the on-body unit 16. Communication between the on-body unit 16 and monitor unit 18 may be achieved using one or more radio frequency communication protocols, inductive coupling, magnetic coupling, direct wired connection, infrared data communication protocol, and the like as described herein.

Insertion Assembly

[00138] Insertion assemblies are provided, which are used to install a medical device to the subject. In some embodiments, an insertion assembly includes an inserter and the medical device itself. The inserter can be configured to insert various medical devices into the subject, such as for example, an analyte sensor, an infusion set, or a cannula. In some embodiments, the inserter can be configured to install a combination of such devices, *e.g.*, a combined sensor/infusion set, etc., at the same or different times or locations. For example, in certain embodiments a given inserter can be configured to install a first device and a second device at different times. In this regard, the inserter can be reusable. For example, an inserter may be modifiable to be used with more than one medical device, to include more than one type of

medical device, *e.g.*, by attaching an adapter and/or removing detaching a portion of an inserter. The inserter can install the medical device in, under, or through the skin of the subject, or place the medical device on the surface of the skin. The medical device can include features or structures, *e.g.*, barbs, tabs, adhesive, etc., to maintain the device in position with respect to the skin after insertion. The inserter device may also be used as a lancet, *e.g.*, to pierce the skin without inserting or installing a medical device.

[00139] In some embodiments, an insertion assembly includes an inserter, a medical device, such as an analyte sensor, and a mount for supporting the medical device at least partially in or on the skin of the subject. In some embodiments, the mount is a support structure, plate and/or member which is attached, adhered, or otherwise secured to the skin of the subject. The mount may be inserted simultaneously with the medical device by the inserter. In other embodiments, the mount is installed after or before installation of the medical device. A mount may be applied by the inserter or separately. The mount may include features or structures (*e.g.*, adhesive, guides, barbs, tabs, etc.) to maintain the sensor in position with respect to the skin after insertion and/or maintain the sensor in relative position with respect to the sensor control unit. In some embodiments, an adhesive pad or strip is used to secure the medical device, *e.g.*, the sensor and/or the sensor control unit, and no mount is used.

[00140] In some embodiments, an insertion assembly includes an inserter, an analyte sensor, a mount, and a power supply. The mount and power supply may be inserted simultaneously with the analyte sensor by the inserter. In other embodiments, the mount and battery are installed after or before installation of the analyte sensor. In such case the mount and/or power supply may be applied by the inserter or separately. The power supply may be used to provide a current

or a potential to the sensor and/or to provide power for communication of one or more signals to the monitor unit.

[00141] In some embodiments, an insertion assembly includes an inserter, a medical device such as an analyte sensor, a mount, and a sensor control unit. The mount and sensor control unit may be deployed and/or installed simultaneously with the analyte sensor by the inserter. In other embodiments, the mount and sensor control unit are installed after or before installation of the analyte sensor. For example, the mount and the analyte sensor may be installed by the inserter, and the sensor control unit may be subsequently installed. In other embodiments, the mount is installed, followed by insertion of the analyte sensor by the inserter, and further followed by installation of the sensor control unit. In other embodiments, the mount and sensor control unit are installed first, and the analyte sensor is subsequently installed.

[00142] In some embodiments, electronics of the sensor control unit provide a voltage or current to the analyte sensor. In some embodiments, the electronics processes signals provided by the analyte sensor. In further embodiments, the electronics may include communication functionality for providing signal relating to signal provided by the analyte sensor to a further component, such as, *e.g.*, a monitor unit, a computer, or other component. In some embodiments, communications circuitry, such as RFID antenna or communications circuitry, is provided. The power supply may be used to power some or all of these functions. In some embodiments, power is provided from the monitor unit, *e.g.*, via inductive coupling.

[00143] An inserter can include a plurality of different components. For example, an inserter may include one or more components for advancing a sharp towards the skin of the subject. The sensor and sensor control unit and/or mounting structure may be supported by a support

structure, such as a carriage. A driver may be provided for advancing the sharp and/or the analyte sensor/support structure. In some embodiments, the actuator is directly or indirectly coupled to the sharp and/or support structure, such that manual force and speed applied by the user to the actuator is transferred to the sharp and/or support structure. In some embodiments, the applied force drives the sharp and/or support structure between a retracted position and an advanced position. In some embodiments, the sensor and sensor control unit and/or mounting structure is maintained in a retracted position prior to installation by contacting projections extending inwardly from a sheath. In accordance with this embodiment, the sensor and sensor control unit and/or mounting structure are temporarily maintained operatively between the support structure and the projections disposed on the interior wall of the sheath.

[00144] An inserter can also include one or more components for retracting the sharp, while allowing the analyte sensor and optional mount and/or electronics to remain on the subject. The components for retracting the sharp can include a retractor. It is understood that the retractor and the actuator may be the same structure or include some common components. In some embodiments, the retractor is directly or indirectly coupled to the sharp such that the manual force applied by the user is transferred from the retractor to the sharp to retract the sharp from the skin. In other embodiments, a drive assembly may be provided to retract the sharp. For example, the drive assembly may include a spring, motor, hydraulic piston, etc., to retract the sharp away from the skin of the subject. The drive assembly may also include a linear drive component.

[00145] In some embodiments, the retractor withdraws the sharp upon actuation by the user. In such cases, the user actuates the retractor when it is desired to withdraw the sharp. For

example, the retractor may include a release switch. Upon activation of the release switch, the drive assembly, *e.g.*, the spring or other driver, retracts the sharp from the skin. In other embodiments, the retractor and the actuator include common components. After activating the actuator to advance the sharp and the analyte sensor, the user releases the actuator, which allows the drive assembly to withdraw the sharp from the skin.

[00146] In some embodiments, the retractor withdraws the sharp without further user interaction after actuation of insertion. For example, the inserter may include features or components which automatically retract the sharp upon advancement of the sharp and support structure by a predetermined amount. Inserter devices, in which no further action by the user is required to initiate withdrawal of the sharp after insertion, are referred to herein as having "automatic" withdrawal of the sharp.

Inserter Devices

[00147] An inserter 100 in accordance with an exemplary embodiment is illustrated in FIGURE 10. In some embodiments, inserter 100 has a maximum diameter of about 30mm to about 60 mm, *e.g.*, about 40 mm, about 43 mm, about 43.5 mm, about 50.5 mm, about 54.5 mm, etc. In some embodiments, inserter 100 has a maximum height of about 40 mm to about 80 mm, *e.g.*, about 44 mm, about 46 mm, about 50 mm, about 53 mm, about 67 mm, about 71 mm, etc. In some embodiments, inserter 100 has a volume of about 35 cm^3 to about 110 cm^3, *e.g.*, about 40 cm^3, about 41 cm^3, about 50 cm^3, about 60 cm^3, about 61 cm^3, about 62 cm^3, about 69 cm^3, about 70 cm^3, about 79 cm^3, about 90 cm^3, about 106 cm^3, etc. Inserter 100 includes a handle 102 and a removable distal cap 104. The cap 104 may maintain a sterile, contaminant-free environment for the medical device and sharp housed therein. As illustrated in FIGURES 10-13,

distal cap 104 is detachably secured to handle 102, *e.g.*, by use of one or more mating members, *e.g.*, threads 110 and 111, or hooks, tape, magnets, adhesive, friction-fit, snap-fit, and the like. Inserter 100 includes a base 142 which defines a distal surface 112, which may be a substantially planar surface as shown in this embodiment, for placement on the skin S of a subject, and in other embodiments may be a curved or inclined surface, *e.g.*, a concave or convex surface. Inserter 100 may be utilized to advance a medical device into the skin of the subject, *e.g.*, an analyte sensor, and infusion set, etc., as described herein. In some embodiments, handle 102 is advanced relative to base 142 in order to advance the medical device into the skin of the patient, as will be described in greater detail herein.

[00148] The components of inserter 100 are illustrated in FIGURES 11-27. As illustrated in FIGURE 11, handle 102 includes a contact surface 114 for contact by a user to depress to advance the sensor housing 122 (as illustrated in FIGURE 10) and sensor 14 towards the skin of the subject. Threads 110 are provided on handle 102 (as illustrated in FIGURE 11) for attachment to cap 104 *via* threads 111 (as illustrated in FIGURES 12-13). Cap 104 can include a receptacle, such as an upwardly extending sleeve 125 to assist holding sensor housing 122 fixed in position. The distal portion of cap 104 includes a recess 115 for retaining a desiccant 190 therein. In some embodiments, a silica gel or molecular sieves may be used. Such material can be in granular form (pellets) or pressed into tablets, or otherwise. In some embodiments, silica gel tablets are used. Embodiments may include desiccant and/or packaging as described in U.S. Patent Application Serial No. 12/714,439, which is incorporated by reference herein for all purposes.

[00149] Cap 104 may be provided with one or more apertures 117, which allows for passage of air to the desiccant 190 to remove moisture from the interior of the inserter 100. Cap 104 may include a stop such as an annular ridge 113, which engages the distal edge portion 116 of handle 102. In some embodiments, a stop such as annular ridge 113 prevents distal movement of handle 102 (as well as sensor housing 122) when cap 104 is attached to handle 102.

[00150] Base 142, as illustrated in FIGURES 10 and 14, includes a distal sheath portion 192, which shields sharp 124 and sensor housing 122 prior to deployment and a distal rim 112 having a substantially planar surface configuration to rest on the subject's skin S. Base 142 also includes side walls 191, which along with inner rail 128 defines a recess for retraction spring 146. Base 142 provides a spring retention portion 148, as illustrated in FIGURE 29.

[00151] Support member or shuttle 134, as illustrated in FIGURES 15-16, supports needle hub 136, from which sharp 124 extends longitudinally within the inserter 100. In some embodiments, the sharp is supported at an oblique angle, *e.g.*, between and including about 0° (parallel to the skin) and about 90° (normal to the skin) with respect to the skin surface. Needle hub 136 can be secured to shuttle 134 *via* interlocking snaps or tabs, an O-ring configuration, adhesive, insert-molding, or other techniques known in the art. Alternatively, needle hub 136 may be integrally molded with shuttle 134. In some embodiments, sharp 124 is a solid needle. In some embodiments, sharp 124 is provided with a substantially cylindrical configuration defining an interior bore, *e.g.*, a rigid cylindrical member or a hypodermic-style needle.

[00152] Needle hub 136 is further illustrated in FIGURES 17-18. Needle hub 136 supports sharp 124, having a sharpened distal portion 160. In some embodiments, as discussed herein, a longitudinal wall opening or gap 162 is provided in at least a portion of the wall of the sharp 124.

The length N of the gap 162 is selected to be commensurate with the length of the insertion portion 30 through to the proximal retention portion 48 of the sensor, and in certain embodiments may be about 3 mm to about 50 mm, *e.g.*, about 5 mm, or about 10 mm, or about 15 mm, or about 20 mm. The length L of the sharp 124 may be about 3 mm to about 50 mm, *e.g.*, 5mm or more, or about 10 mm, or about 20 mm, or about 30 mm, or about 50 mm, and is selected based upon the length of the insertion portion 30 of a sensor and the desired depth of the insertion portion 30 of the sensor 14. In some embodiments, the distance or spacing between the two edges of the gap is about 0.2mm to about 0.5mm, *e.g.*, about 0.22mm, about 0.25mm, etc.

[00153] The distal portion 160 of sharp 124 is illustrated in greater detail in FIGURES 19-21. As illustrated in FIGURE 19, sharp 124 has a substantially "C"- or "U"-shaped profile in this embodiment, but may have other configurations, *e.g.*, substantially "V"-shaped. A longitudinal gap 162 is provided in the wall of the sharp 124. FIGURE 20 illustrates distal portion 160 is provided with an angled tip. In some embodiments, the angled tip may be provided with a first angled tip portion 164 and a second steep-angled tip portion 166. The exemplary configuration, which includes multiple edges and faces, provides a sharp point to reduce penetration force, trauma, and bleeding for the subject. The distal section of the sensor body has a width sized to fit within the notch 162 of the insertion sharp 124 having a diameter less than about 20 to about 26 gauge, *e.g.*, 21 gauge to about 25 gauge, where in certain embodiments the sharp is 21 gauge or 23 gauge or 25 gauge. Such sharp may be used with a sensor having a width or diameter - - at least the portion that is carried by the sharp - - of about .20 mm to about .80 mm, *e.g.*, about .25 mm to about .60 mm, where in some embodiments the width or diameter of at least a portion of a sensor is .27 mm or .33 mm or .58 mm. In some embodiments, sharp 124 is fabricated from a sheet of metal and folded into a substantially "V" or "U" or "C" configuration in cross-section.

Various technologies can be used to manufacture a folded sheet of metal to form sharp 124. For example, etched-sheet metal technology can be used to form the sharp 124. In this manner, the sharp can be formed having a very sharp edge so that penetration through the skin during insertion is less painful. In other embodiments, a progressive die technology may be utilized to form a complex sheet-metal shape that has a sharp edge as depicted in FIGURE 21A. In some embodiments, the sharp 124 can be molded with a plastic cap so that the sharp can be handled during the inserter assembly process. Further, the die cut sharp may be molded with plastic to reinforce the "V," "U," or "C" shaped sheet metal configuration. In other embodiments, a laser-cut sharp can be formed. In this manner, the laser can be used to form the wall opening or gap 162 and first-angled tip portion 164 and a second, steep-angled tip portion 166.

[00154] In another embodiment, sharp 224 may be formed from a standard hypodermic needle utilizing the method depicted in FIGURE 21B. First, the hypodermic needle (having a circular cross-section) is cut to the desired length for sharp 224. Next, the hypodermic needle is compressed so that its cross-section is permanently deformed from a circular shape to an oval shape. The tip of the hypodermic needle is then ground to a bevel to produce a sharp point to reduce the required penetration force, as previously discussed. Finally, the top section of the needle is removed by appropriate techniques (e.g., grinding, electropolish, etc.). The resulting sharp 224 has a "U"-shaped configuration and provides ample space for the insertion of sensor 14. In some embodiments, the tip-grinding step and the compression step may be carried out in reversed order.

[00155] Due to the compression step, a user may initially start with a larger diameter hypodermic needle so that the finished sharp 224 will have similar dimensions to the previously described sharps.

[00156] FIGURES 22-23 illustrate the position of sensor housing 122 with respect to the needle hub 136 and sharp 124. The sensor housing 122 can be configured to hold at least a portion of sensor 14 and sensor control unit 12. As illustrated in FIGURE 22, the sharp 124 extends through an aperture 168 in the sensor housing 122. Thus, in some embodiments, the sharp 124 is uncoupled to sensor housing 122. The distal portion of sensor 14 is positioned with the sharp 124. As further illustrated in FIGURE 23, electronics 80 of the sensor control unit 12 (*e.g.*, a printed circuit board containing electronics components of the on-body unit 16) and sensor hub 123 are positioned within sensor housing 122. Sensor 14 may include a positioning structure, or slit 127 which receives a positioning member, such as tab 129 of sensor hub 123. A power supply 82, such as a battery, *e.g.*, a single use disposable battery, or rechargeable battery, is provided. The power supply 82 is used to provide potential or current to the sensor in some embodiments. In embodiments where a passive communications protocol such as passive RFID is used, no power supply is provided for the communications. Such power is provided by the monitor unit 18. In some embodiments where the sensor control unit is used to transmit one or more signals, one or more power supplies may be used to provide power for such communications circuitry. In some embodiments, the active operational life of the battery may exceed the active operational life of the sensor 14.

[00157] FIGURE 24 illustrates in cross-section the orientation of the sensor housing 122 with respect to the sharp 124 of inserter 100. As discussed herein, sensor 14 is disposed in a

substantially bent configuration in some embodiments, such that a portion of the sensor, *e.g.*, the insertion portion 30 and the proximal retention portion 48, are substantially vertical (*e.g.*, substantially aligned with the longitudinal axis of the inserter 100 and substantially perpendicular to the skin surface) and the contact portion 32 (shown in profile) is oriented in a substantially horizontal configuration, and in electrical contact with the data-processing unit electronics, such as circuit 80. The sensor tab 50 can be encased in the plastic of the sensor housing 122 (*e.g.*, "overmolded") and secured in place. The notch 56 provides further stability to the sensor 14, *e.g.*, by allowing the sensor tab 50 to be encased by the material of the sensor housing 122, and further provides a means for vertically orienting the sensor 14 during mounting, *e.g.*, by allowing vertical positioning of the notch 56 with respect to a vertical landmark of the sensor housing 122.

[00158] The sensor 14, mounted with the sensor housing 122, can be disposed within a recess of the carriage 130 such as a concave recess in the carriage 130. Alternatively, the sensor 14, mounted with the sensor housing 122 can be disposed between the support structure and one or more projections extending from the wall of the sheath. In yet another alternative, the sensor 14 mounted with the sensor housing 122 can be held in position by a releasable friction fit coupling to the sharp 124. In this manner, the carriage need not have a recess within which the sensor mounted with the sensor housing is disposed. In the initial configuration of the inserter 100 (see, *e.g.*, FIGURE 22) the sharp 124 extends through a longitudinal aperture 168 formed in a carriage 130. In some embodiments, the aperture 168 is appropriately sized, such that neither the sharp 124 nor needle hub 136 is in contact with the carriage 130. Accordingly, the needle hub 136 (and sharp 124) on the one hand, and the carriage 130 and the sensor housing 122, on the other hand, move simultaneously but independently from one another. In other embodiments, a friction fit may be provided between the aperture and the sharp.

[00159] The insertion portion 30 and proximal retention portion 48 of the sensor 14 are disposed within a longitudinal bore 162 within the sharp 124 (See, *e.g.*, FIGURE 19). The proximal retention portion 48 is disposed within the longitudinal bore of the sharp 124 and provides additional stability to the mounting of the sensor 14 within the sharp 124. The longitudinal wall gap or opening 162 of sharp 124 is aligned with the sensor 14, such that the tab 50 and the contact portion 32 extend laterally outward from the sharp 124.

[00160] In some embodiments, a resilient member 70 may be included to provide frictional contact with the sharp 124 and/or the sensor 14. Such frictional contact provides additional stability between the sensor housing 122 and sharp 124, as depicted in FIGURES 24A-24C. In some embodiments, resilient member 70 may be formed as a spherical, ovoid, cylindrical, cube-shaped member, etc. Resilient member 70 may be formed from any elastomeric material, e.g., molded plastic components, rubber, nitrile, viton, urethane, etc.

[00161] In some embodiments, resilient member 70 is press-fit into a recess, such as an eccentric bore 72 located in sensor housing 122 (FIGURE 24C). When sharp 124 is inserted within an aperture in the sensor housing 122, the resilient member 70 exerts a pressure on sharp 124 and sensor 14 to hold them firmly in groove 74. In some embodiments, groove 74 is a V-shape. Alternatively, groove 74 may be U-shaped depending on the configuration of sensor 14 and sharp 124. In some embodiments, resilient member 70 is provided with a flattened or recessed surface which abuts sharp 124.

[00162] With continued reference to FIGURES 15 and 16, shuttle 134 includes wings 182 and resilient distally extending fingers 184. Inner rail 128 is illustrated in FIGURE 25. As illustrated in FIGURE 26, shuttle 134 is sized and configured for longitudinal movement within inner rail

128. Wings 182 of shuttle 134 are configured for longitudinal movement within axial notches 188 of inner rail 128. When fingers 184 of shuttle 134 are disposed in their normally biased outward position, fingers 184 engage the lower surface 194 of inner rail 128. In the configuration illustrated in FIGURE 26, shuttle 134 is locked with respect to inner rail 128. As will be discussed herein, fingers 184 may be biased radially inward to allow upward movement of shuttle 134 relative to inner rail 128.

[00163] As illustrated in FIGURE 10, inner rail 128 includes an upper surface 186 for engagement with handle 102. In some embodiments, surface 186 is adhered or otherwise fixed to handle 102.

[00164] The relationship of inner rail 128, shuttle 134 and base 142 is illustrated in FIGURE 27. In an initial configuration, inner rail 128 and shuttle 134 are in a locked relationship by engagement of wings 182 and fingers 184. Inner rail 128 and shuttle 134 are axially movable within base 142. Spring 146, which is secured between spring retention portion 148 of base 142 and wings 182 of shuttle 134 biases the inner rail 128 and shuttle 134 in a proximal (upward) direction.

[00165] Inserter 100 is illustrated in section in FIGURES 28-29 prior to use in a sensor predeployment position. Cap 104 is attached to the distal portion of inserter 100, *e.g.*, *via* inter-engagement of threads 110 and 111.

[00166] As illustrated in FIGURE 28, the inserter 100 includes an initial configuration in which the handle 102 is disposed in a proximal position with respect to the base 142. In such configuration, the sharp 124 is disposed in a configuration spaced apart from an aperture of the adhesive layer 118.

[00167] As illustrated in FIGURE 30, inner rail 128 includes a carriage 130. In a sensor insertion position, the handle 102 is depressed downward (arrow D) against the bias of spring 146, the inner rail 128 moves downwardly with the carriage 130 and the sensor housing 122. Shuttle 134 supports needle hub 136, from which sharp 124 extends longitudinally within the inserter 100. Initially, shuttle 134 is coupled to inner rail 128 *via* inter-engagement of fingers 184 of shuttle 134 with distal surface 194 of inner rail 128, and both shuttle 134 and inner rail 128 move distally together as a unit.

[00168] As the sharp 124 is urged distally towards the subject's skin (FIGURE 30), it carries the sensor insertion portion 30 of sensor 14 into the subcutaneous portion of the subject's skin S and into contact with the interstitial fluid. As carriage 130 reaches a distal position, the distal surface of the sensor housing 122 engages the upper surface of adhesive pad 118, thereby becoming adhered to the skin surface S of the subject.

[00169] In some embodiments, components are provided which allow the shuttle to be disengaged from the handle 102. For example, flanges 170 on base 142 engage fingers 184 of shuttle 134. Fingers 184 are pivoted or bend inwards by contact with flanges 170 (as indicated by arrows F).

[00170] As illustrated in FIGURE 31, such pivoting of fingers 184 causes fingers 184 to become disengaged from distal edge 194 of inner rail 128. Shuttle 134 is thereby disengaged from inner rail 128. Disengagement of the shuttle 134 from the inner rail 128 permits the spring 146 decompress and to expand, thereby advancing the shuttle 134 to a proximal or retracted position, and withdrawing the sharp 124 from the sensor housing 122, withdrawing from its position around sensor 14, and receding from skin S of the subject, while leaving the sensor 14 in

the skin and the on body unit 16 attached to the skin surface by adhesive pad 118. Once the sharp has been withdrawn from the subject, it is no longer accessible from the distal portion of the inserter 100, which prevents accidental needle sticks. When the carriage 130 reaches the distal position in which flanges 170 engage fingers 184 of needle shuttle 134, needle shuttle 134 withdraws sharp 124 automatically without further input from the user.

[00171] As illustrated in FIGURE 31A, the inserter 100 may be removed from the skin S of the subject, leaving the on-body unit 16 installed on the subject, e.g., lower surface of housing 122 adhered to the skin S via adhesive pad 118 and sensor 14 at least partially inserted in the skin and in contact with the interstitial fluid.

[00172] Prior to activation of the on-body unit 16 which includes the integrated sensor 14 and sensor control unit 12 for use, there may be a period of time from the manufacturing that the assembly 16 may be in a "sleep" or "idle" mode. With a power supply such as a battery integrated within the assembly, for reasons including cost optimization and prolonging shelf life, some embodiments of the present disclosure include optional systems that are activated merely by positioning the sensor 14 and on-body unit 16 on a skin surface as described above, *i.e.*, no additional action may be required of the user other than applying a force to sensor housing 122. As such, insertion of the sensor 14 and/or mounting of the sensor housing 122 causes activation of the electronics 80. In certain embodiments, activation switch configurations are included which may be configured to be triggered, for example, by the insertion device activation, thereby turning on the integrated sensor and sensor electronics assembly into an active mode.

[00173] As illustrated in FIGURE 29, inserter 100 may be provided with a switch 185, which provides automatic activation of the electronics 80 of the sensor control unit 12. In some

embodiments, the switch 185 is a longitudinally slidable member or plunger extending distally from or otherwise disposed on the distal surface of the sensor housing 122. When the sensor housing is advanced proximally, it engages the adhesive pad 118, or alternatively the skin surface of the subject. Upon such engagement, the switch 185 is moved axially (proximally) with respect to the housing 122. When the sensor housing 122 is in approximation with the adhesive pad 118 and/or the skin of the subject, the plunger switch 185 is in the proximal position (not shown). Such axial movement may be used to activate the sensor electronics 80. In some embodiments, a switch 185 is spring biased. Accordingly, as long as the sensor housing 122 is maintained in a fixed relationship with the adhesive pad 118 against the bias, electronic activation is maintained in such embodiments. If the sensor housing 122 is removed from the adhesive or the skin, the switch 185 moves with the bias, and the electronics are deactivated. In other embodiments, the switch 185 provides a one-time activation of the electronics. In such cases, once the electronics are activated, the sensor housing 122 is not required to remain in contact with the adhesive or the skin in order to maintain activation.

[00174] As illustrated in FIGURES 32-33, embodiments of a power supply switch mechanism include conductive plugs of the on-body unit 16 in accordance with the present disclosure. FIGURES 32-33 illustrate enlarged sectional views of sensor housing 122. As shown, the sensor electronics assembly circuit board 860 may be provided with a physical gap 858 that breaks the electrical circuit between the power supply (*e.g.*, battery) and the other circuitry of the sensor electronics assembly.

[00175] In one embodiment, when the predetermined force is applied on the insertion device 100 as discussed above, a conductive portion 852 provided within the housing 122 of the sensor

electronics may be moved in a direction as shown by arrow 854 such that electrical contact is established in the physical gap 858 on the circuit board, by for example, the conductive portion 852 coming into physical contact with the conductive portions of the circuit board 860. In this manner, in one embodiment, the electrical path from the power supply and the remaining circuitry on the circuit board of the sensor electronics is completed, thereby powering the sensor electronics.

[00176] By way of another example, referring to FIGURE 33, the conductive portions 860 of the circuit board are provided on the board itself, and the conductive plug 856, for example, when pushed into the cavity 858, establishes electrical contact between the conductive portions 860 of the circuit board.

[00177] In one embodiment, as discussed above, the actuation of the insertion device 100 to position the sensor 14 and sensor electronics assembly triggers the switch mechanism shown in FIGURES 32-33 by also moving the conductive portion 852 or the conductive plug 856 in the direction complimentary to the direction of the introducer movement, and thereby switching on the sensor electronics. Within the scope of the present disclosure, the activation of the sensor electronics by moving the conductive portion 852 or the conductive plug 856 may include a separate procedure, where, after positioning the sensor and the sensor electronics assembly on the skin surface, a predetermined force is applied on the housing of the integrated sensor 14 and sensor electronics assembly such that the desired movement of the conductive portion 852 or the conductive plug 856 may be achieved. Further embodiments of the insertion devices are described in U.S. Patent Application Serial Nos. 61/149,639, filed February 3, 2009, and No. 12/698,129, filed February 1, 2010, which are incorporated by reference herein in their entirety.

[00178] An inserter 200 in accordance with another exemplary embodiment is illustrated in FIGURE 34. In some embodiments, inserter 200 has a maximum diameter, of about 30mm to about 60 mm, *e.g.*, about 40 mm, about 43 mm, about 43.5 mm, about 50.5 mm, about 54.5 mm, etc. In some embodiments, inserter 200 has a maximum height of about 40 mm to about 80 mm, *e.g.*, about 44 mm, about 46 mm, about 50 mm, about 53 mm, about 67 mm, about 71 mm, etc. In some embodiments, inserter 200 has a volume of about 35 cm^3 to about 110 cm^3, *e.g.*, about 40 cm^3, about 41 cm^3, about 50 cm^3, about 60 cm^3, about 61 cm^3, about 62 cm^3, about 69 cm^3, about 70 cm^3, about 79 cm^3, about 90 cm^3, about 106 cm^3, etc.

[00179] With reference to FIGURE 34, inserter 200 includes a housing 202 and a removable distal cap 204 for maintaining a sterile environment for the medical device and sharp housed therein. Housing 202 and distal cap 204 may be fabricated from any suitable materials such as metal, plastic, etc. In some embodiments cap 204 may be fabricated from a polymer or plastic material. Also provided is a removable proximal cover 206, which, among other things, prevents accidental deployment of the inserter 200. In some embodiments, proximal cover 206 is a sheet of material such as a foil sheet or the like secured to the upper surface of housing 202 using an adhesive, and may include a tab 208 to assist removal of the cover 206. Proximal cover 206 may also be a plastic sheet or member that forms a seal with housing 202. In some embodiments, proximal cover 206 may include a pull tab or a perforated section for easy removal.

[00180] As illustrated in FIGURE 35, proximal cover 206 and distal cap 204 are shown removed from inserter 200. Distal cap 204 is secured to housing 202, *e.g.*, by use of threads 210. In some embodiments, distal cap 204 is secured by a friction fit, snap fit, a bayonet mount, an adhesive, etc. Housing 202 includes a distal surface 212 for placement on the skin of a subject.

Inserter 200 includes an actuator 214 to advance a medical device into the skin of the subject. In some embodiments, actuator 214 is disposed within an opening 216 in housing 202 and can be longitudinally moveable within housing 202.

[00181] The distal portion of inserter 200 is illustrated in FIGURE 36. In some embodiments, an adhesive pad 218, having adhesive material 218 on both faces, is provided across the distal portion 212 of the housing 202. A central aperture 220 may be provided in adhesive pad 218. As will be described in greater detail herein, inserter 200 supports a medical device, such an analyte sensor housing 122 (not shown) and a sharp 224. In some embodiments, sensor housing 122, includes an analyte sensor 14 and a sensor control unit 12. During insertion, sharp 224 passes through aperture 220 and into the skin of the subject carrying at least the sensor with it.

[00182] FIGURE 37 illustrates inserter 200 in cross-section, in an initial configuration prior to use, after removal of the distal cap 204. Actuator 214 may be cylindrical in shape (or other shape as appropriate) and, including an upper contact surface 226, capable of being depressed by a user and/or a mechanism, as described herein. Actuator 214 may further include side walls 228 extending downwardly from upper surface 226, and which engage or otherwise contact the upper surface of carriage 230. Carriage 230 provides a support for holding the medical device, such as sensor housing 122 of on-body unit 16, prior to and during installation. In some embodiments, carriage 230 includes a distal portion 232, which may be configured to form a substantially concave recess 232a as shown in this embodiment, for supporting the medical device therein. In some embodiments, the sensor housing 122 is supported within the recess 232a of carriage 230 in a snap-fit or other relationship. In some embodiments, carriage 230 does not include a recess.

In such embodiments, carriage may include one or more projections which contact and/or advance the sensor housing 122.

[00183] In FIGURE 38 the longitudinal axis L of the inserter 200 is illustrated. Extending distally from the upper surface 226 of actuator 214 and substantially parallel to the longitudinal axis is a support member 234, which may have an elongated configuration. Support member 234 supports needle hub 236, from which sharp 224 extends longitudinally within the inserter 200. In some embodiments, the sharp 224 is supported at an oblique angle, *e.g.*, between and including about 0° and 90° with respect to the skin surface. Needle hub 236 can be secured to support member 234 via an interlocking O-ring configuration, adhesive, or other techniques known in the art. Support member 234 can be omitted and needle hub 236 can be secured to the actuator 214 directly in some embodiments.

[00184] In some embodiments, sharp 224 is a solid needle. In some embodiments, sharp 224 is provided with a substantially cylindrical configuration defining an interior bore, *e.g.*, a rigid cylindrical member or a hypodermic-style needle. Sharp 224 may also be provided with an elongated longitudinal opening or gap in the wall of the sharp 224 (see, sharp 224 in FIGURES 22-24). In some embodiments, sharp 224 is fabricated from a sheet of metal, and folded into a substantially "V" or "U" or "C" configuration in cross-section to define the longitudinal recess.

[00185] The sensor 14, mounted with the sensor housing 122, is carried by the carriage, *e.g.*, disposed within the concave recess 232a in the carriage 230, as described hereinabove (see, *e.g.*, FIGURES 22-24). In the initial configuration of the inserter 200 (see, *e.g.*, FIGURE 37), the sharp 224 extends through a longitudinal aperture 268 formed in the carriage 230. In some embodiments, the aperture 268 is appropriately sized, such that neither the sharp 224 nor needle

hub 236 is in contact with the carriage 230. In other words, in some embodiments a clearance may be provided between the surfaces of the carriage and the sharp and needle hub. In some cases, sharp 224 is capable of substantial lateral movement or "play" with respect to aperture 268. Accordingly, the needle hub 236 (and sharp 224) on the one hand, and the carriage 230 and the sensor housing 122, on the other hand, can move simultaneously but independently from one another.

[00186] Referring back to FIGURE 23, the insertion portion 30 and proximal retention portion 48 of the sensor 14 are disposed within a longitudinal bore of the sharp 224. The proximal retention portion 48 is disposed within the longitudinal bore of the sharp 224 and provides additional stability to the disposition of the sensor 14 within longitudinal bore of the sharp 224. The longitudinal wall gap of sharp 224 is aligned with the sensor 14, such that the tab 50 and the contact portion 32 extend laterally outward from the sharp 224.

[00187] With continued reference to FIGURE 37, an optional sheath 242 is positioned within housing 202, having an annular configuration and including a circumferential recess 244 in which a retraction spring 246 is positioned. The distal portion of spring 246 contacts a spring retention portion 248 in sheath 242. The proximal portion of spring 246 contacts one or more tabs 250 extending laterally outwardly from actuator 214. In the initial configuration, the spring 246 may be in a semi-compressed state, *i.e.*, not fully compressed, nor fully extended. It is understood that sheath 242 may be omitted from inserter 200, and a recess, such as recess 244, provided within housing 202. Similarly, recess 244 may be omitted entirely, and spring 246 or other actuator may be disposed between stops in housing 202.

[00188] Depression of the actuator 214 causes distal longitudinal movement of the carriage 230 and sharp 224, from a proximal position to a distal position. During such downward, distal movement, spring 246 is further compressed between spring retention portion 248 and flanges 250.

[00189] As illustrated in FIGURE 38, depression of the actuator 214 advances the inserter 200 from an initial configuration to a deployed configuration. Depression of the contact surface 226 moves the actuator side walls 228 and the tabs 250 downwardly distally against the bias of spring 246. Contact of the side wall 228 of the actuator 214 with the upper surface of the carriage 230 during depression of the actuator 214 imposes a downward force and consequential distal movement of the carriage 230. As the sharp 224 is urged distally, it carries the sensor insertion portion 30 into the subcutaneous portion of the subject's skin S.

[00190] As illustrated in FIGURE 37, flanges 270 are disposed in the inner wall of sheath 242. When carriage 230 reaches a distal position, as shown in FIGURE 38, the flanges 270 engage the proximal (upper) surface of the carriage 230, and thereby inhibit proximal movement of the carriage 230 (see also FIGURE 41). The distal (lower) surface of the sensor housing 122 engages the upper surface of adhesive pad 218, thereby becoming adhered to the skin surface S of the subject. As the flanges 270 engage the carriage 230, the flanges 270 also engage fingers 274 disposed on the proximal face of the carriage 230. Fingers 274 are pivoted inwards by flanges 270. Such pivoting of fingers 274 causes fingers 274 to become disengaged from retention tab 250 on actuator 214. Spring 246 is thereby permitted to decompress and expand, and thereby provide an upward force on actuator 214. If the user or some apparatus provides no downward force, or minimal downward force to overcome the bias of spring 246, the actuator

214, along with needle hub 236 and sharp 224 move proximally, withdrawing the sharp 224 from the skin S of the subject.

[00191] As shown in FIGURES 39 and 40, the actuator 214 and coupled sharp 224 is permitted to advance to a more proximal position than at the initial configuration illustrated in FIGURES 35 and 37. Thus the sharp 224 retracts from a distal position to a proximal position after installation of the on-body unit and insertion of at least a portion of the sensor. As illustrated in FIGURE 41, the carriage 230 is maintained in a distal position, but the sharp 224 has been withdrawn from the subject and is no longer accessible from the distal portion of the inserter 200, which prevents accidental needle sticks.

[00192] A further embodiment of an inserter is illustrated in FIGURES 42-56 and designated inserter 300. In some embodiments, inserter 300 has a maximum diameter of about 30mm to about 60 mm, *e.g.*, about 40 mm, about 43 mm, about 43.5 mm, about 50.5 mm, about 54.5 mm, etc. In some embodiments, inserter 300 has a maximum height of about 40 mm to about 80 mm, *e.g.*, about 44 mm, about 46 mm, about 50 mm, about 53 mm, about 67 mm, about 71 mm, etc. In some embodiments, inserter 300 has a volume of about 35 cm^3 to about 110 cm^3, *e.g.*, about 40 cm^3, about 41 cm^3, about 50 cm^3, about 60 cm^3, about 61 cm^3, about 62 cm^3, about 69 cm^3, about 70 cm^3, about 79 cm^3, about 90 cm^3, about 106 cm^3, etc.

[00193] As illustrated in FIGURE 42-43, inserter 300 includes, *e.g.*, a handle 302, a sheath 342, and a removable distal cap 304 for maintaining a sterile environment for the medical device and sharp housed therein. FIGURE 43 illustrates that distal cap 304 is removed from handle 302. Distal cap 304 is secured to handle 302 by one of a number of securement means, *e.g.*, by use of threads 310. Sheath 342 defines a distal surface 312 for placement on the skin of a

subject. Inserter 300 may be utilized to advance a medical device into the skin of the subject. In some embodiments, handle 302 is advanced relative to sheath 342 in order to advance the medical device into the skin of the patient.

[00194] The components of inserter 300 are illustrated in FIGURES 44-49. As illustrated in FIGURE 44, handle 302 may include threads 310 for attachment of cap 304 via threads 311 (as illustrated in FIGURE 46). It is understood that other securement techniques, such as a snap-fit or friction-fit may be used to secure cap 304. Cap 304 may include a receptacle 325 for positioning of the sharp 324. Sheath 342, as illustrated in FIGURE 45, includes longitudinal notches 382.

[00195] Projections 386 on carriage 330, as illustrated in FIGURE 47, are configured to engage sheath to secure carriage 330 within the inserter 300, thereby preventing release of the carriage from the inserter. Notches 384 allow for the free travel of projections 386. The bottom of the notches acts as the retention portion that prevents the carriage 330 from falling out of the inserter 300. Projections 375 engage with the triangular latch features 370 of the sheath 342 as illustrated in FIGURES 51 and 53.

[00196] Carriage 330 also is provided with fingers 374 which engage a shoulder wall 376 of handle 302 (as illustrated in FIGURE 51), as will be described in greater detail herein.

[00197] Inserter 300 also includes a spring retention component 348, as illustrated in FIGURE 48. Spring retention component 348 defines an upper surface 349, which engages spring 346 (as illustrated in FIGURE 51). Spring retention component 348 also includes locking towers 351, which engage flanges 328 of needle carrier 334 to prevent accidental deployment of the sharp 324 after use of the inserter 300 is completed.

[00198] Inserter 300 is illustrated in cross-section in FIGURE 50 prior to use. Cap 304 is attached to the distal portion of inserter 300, via securement means, such as inter-engagement of threads 310 and 311. Cap 304 includes a desiccant tablet 390; a seal, such as a foil seal 392; and a Tyvek® layer 394, which allows breathability between the desiccant tablet 390 and the interior of the inserter 300.

[00199] As illustrated in FIGURE 51, the inserter 300 includes an initial configuration in which the handle 302 is disposed in a proximal position with respect to the sheath 342. In such configuration, the sharp 324 is disposed in a configuration spaced apart from the aperture 320 of the adhesive layer 318. The distal portion of inserter 300 is illustrated in FIGURE 52.

[00200] With continued reference to FIGURE 51, the longitudinal axis L of the inserter 300 is illustrated. Extending distally from the upper surface of handle 302 is an inner wall portion 326 and intermediate wall portion 374. Support member 334 extends from wall portion 326 and supports needle hub 336, from which sharp 324 extends longitudinally within the inserter 300. In some embodiments, the sharp is supported at an oblique angle, *e.g.*, between 0° and 90° with respect to the skin surface.

[00201] Sheath 342 is positioned within handle 302, having an annular configuration in which a retraction spring 346 is positioned. The distal portion of spring 346 contacts a surface 349 of spring retention component 348. The proximal portion of spring 346 contacts the inner surface 350 of handle 302. In the initial configuration, the spring 346 is in an extended or semi-extended configuration.

[00202] FIGURE 53 illustrates inserter 300 in cross-section, during insertion. Depression of handle 302 with respect to sheath 342 against the bias of spring 346 causes distal longitudinal

movement of the carriage 330 and sharp 324, from a proximal position towards a distal position. During such downward, distal movement, spring 346 is compressed between surface 349 of spring retention component 348 and surface 350 of handle 302. As the sharp 324 is urged distally, it carries the sensor insertion portion 30 of sensor 14 into the subcutaneous portion of the subject's skin S.

[00203] As carriage 330 reaches a distal position, the distal surface of the sensor housing 122 engages the upper surface of adhesive pad 318, thereby becoming adhered to the skin surface S of the subject. Also, flange 370 engages fingers 374 disposed on the carriage 330. Fingers 374 are pivoted outwards by flanges 370 in direction T. Such pivoting of fingers 374 causes fingers 374 to become disengaged from slots 376 in intermediate housing walls 374. Carriage 330 is thereby disengaged from handle 302 and needle carrier 334.

[00204] As illustrated in FIGURE 54, handle 302, along with needle hub 336 and sharp 324 are permitted to move proximally, while the sheath 342 and sensor housing 122 remain adjacent to the skin of the subject. If the user or some apparatus provides no downward force, or minimal downward force to the handle 302 to overcome the bias of spring 346, spring 346 is permitted to expand, thereby withdrawing the sharp 324 from the skin S of the subject.

[00205] Upon reaching the proximal position, flanges 328 on needle carrier 334 engage locking towers 351 of needle floor component 348. The inter-engagement of flanges 328 and locking towers 351 prevents inadvertent deployment of sharp 324 after installation of the medical device.

[00206] As shown in FIGURES 55 and 56, the carriage 330 is maintained in a distal position, but the sharp 324 has been withdrawn from the subject and is no longer accessible from the distal portion of the inserter 300, which prevents accidental needle sticks.

[00207] A further embodiment of an inserter is illustrated in FIGURES 57-67, and designated inserter 400. In some embodiments, inserter 400 has a maximum diameter of about 30mm to about 60 mm, *e.g.*, about 40 mm, about 43 mm, about 43.5 mm, about 50.5 mm, about 54.5 mm, etc. In some embodiments, inserter 400 has a maximum height of about 40 mm to about 80 mm, *e.g.*, about 44 mm, about 46 mm, about 50 mm, about 53 mm, about 67 mm, about 71 mm, etc. In some embodiments, inserter 400 has a volume of about 35 cm^3 to about 110 cm^3, *e.g.*, about 40 cm^3, about 41 cm^3, about 50 cm^3, about 60 cm^3, about 61 cm^3, about 62 cm^3, about 69 cm^3, about 70 cm^3, about 79 cm^3, about 90 cm^3, about 106 cm^3, etc.

[00208] Inserter 400 generally includes, *e.g.*, a handle 402, sheath 442, and a removable distal cap 404 for maintaining a sterile environment for the medical device and sharp housed therein. As illustrated in FIGURE 58, distal cap 404 is shown removed from handle 402. Distal cap 404 is detachably secured to handle 402, *e.g.*, by use of threads 410. Sheath 442 includes a distal surface 412 for placement on the skin of a subject. Inserter 400 may be utilized to advance a medical device into the skin of the subject. In some embodiments, handle 402 is advanced relative to sheath 442 in order to advance the medical device distally and into the skin of the patient.

[00209] The components of inserter 400 are illustrated in FIGURES 59-63. As illustrated in FIGURE 59, handle 402 includes threads 410 for attachment of cap 404 via threads 411 (as illustrated in FIGURE 61). Cap 404 may include a receptacle 425 for positioning of the sharp

424. Sheath 442, as illustrated in FIGURE 60, includes longitudinal notches 482. Projections 486 on carriage 430, as illustrated in FIGURE 62, are configured to engage sheath 442 to secure carriage 430 within inserter 400, thereby preventing release of the carriage from the inserter. Sheath 442 also includes notches 484 which receive projection 475 of carriage 430. Notches 484 allow for the free travel of projections 486. The bottom of the notches acts as the retention portion that prevents the carriage 430 from falling out of the inserter 400. Projections 475 engage with the latch features 470 of the sheath 442 as illustrated in FIGURES 66 and 67. Carriage 430 also is provided with fingers 474 which engages a shoulder wall 476 of needle carrier 436, as illustrated in FIGURES 65-66, and as will be described in greater detail herein.

[00210] Sheath 442 also includes a spring retention portion 448, provided at the distal end of circumferential notch 496, as illustrated in FIGURES 60, 64 and 65. Needle carrier 434, as illustrated in FIGURE 63, includes wings 450, which provide an upper engagement surface for spring 446. Wings 450 also include recesses 451 including a shoulder 476 for engagement with fingers 474 of carriage 430.

[00211] Inserter 400 is illustrated in cross-section in FIGURE 64 in a state prior to use and prior to removal of cap 404, which is shown attached to the distal portion of handle 402, via inter-engagement of threads 410 and 411. Cap 404 includes a desiccant tablet 490, a seal such as a foil seal 492, and a Tyvek® layer 494, which allows breathability between the desiccant tablet 490 and the interior of the inserter 400.

[00212] As illustrated in FIGURE 65, the inserter 400 is shown in an initial configuration in which handle 402 is disposed in a proximal position with respect to the sheath 442. In such configuration, the sharp 424 is disposed in a configuration spaced apart from the aperture 420 of

the adhesive layer 418. The longitudinal axis L of the inserter 400 is illustrated. Extending distally from the upper surface of handle 402 is inner wall 475. The distal end portions of wall 475 provide a downward force on the carriage 430 upon depression of the handle 402 by a user. Alternatively, instead of handle having a distally extending inner wall, the carriage can include one or more upwardly extending walls or projections (not shown). The one or more upwardly extending inner walls or projections can have a length sufficient to either contact the upper surface of 402 or, alternatively, contact corresponding downwardly extending inner walls of the handle 402. In this manner, depression of handle 402 by a user provides a downward force on the one or more upwardly extending walls or projections of the carriage to advance the carriage (and on-body unit) distally to an installation and insertion position. In one embodiment a downwardly extending wall of the handle 402 and a corresponding upwardly extending wall of the carriage are aligned such that depression of the handle 402 by a user allows the upwardly extending wall and the downwardly extending wall to make direct contact, thereby permitting the carriage 430 and on-body unit to advance distally. In such embodiment, the downwardly extending inner wall of the handle has a distal end that is disposed proximally of the proximal most end of sheath 442.

[00213] Needle carrier 434 can be axially moveable within handle 402. Needle carrier 434 supports needle hub 436, from which sharp 424 extends longitudinally within inserter 400. In some embodiments, sharp 424 is supported at an oblique angle, *e.g.*, between and including about 0° and 90° with respect to the skin surface. Initially, needle carrier 434 is coupled to carriage 430 via inter-engagement of fingers 474 of carriage 430 with shoulder 476 of needle carrier 434. Spring 446 is disposed between spring retention portion 448 of sheath 442 and wings 450 (FIGURE 63) of needle carrier 434. Initially, spring 446 is in an expanded or semi-

expanded state while handle 402 is disposed proximally from sheath 442. In another exemplary embodiment, needle carrier 434 can be secured to handle 402, for example, secured to downwardly extending inner wall 475. In this manner, needle carrier and carriage 430 are longitudinally moveable with respect to sheath 442. In this regard, needle carrier 434 includes one or more apertures to receive one or more downwardly extending inner walls 475 of handle 402. In some embodiments, neither the needle carrier 434 nor the carriage 430 are in slidable contact with sheath 442, *e.g.*, spaced apart from sheath 442, during longitudinal movement of the needle carrier 434 and/or carriage 430.

[00214] FIGURE 66 illustrates inserter 400 in cross-section, during insertion. Depression of handle 402 with respect to sheath 442, against the bias of spring 446, causes distal longitudinal movement of the carriage 430 and needle carrier 434, from a proximal position towards a distal position. During such downward proximal movement, spring 446 is compressed between spring retention portion 448 and wings 450 (FIGURE 63) of needle carrier 434. As the sharp 424 is urged distally, it carries the sensor insertion portion 30 of sensor 14 (FIGURE 23) into the subcutaneous portion of the subject's skin S.

[00215] As carriage 430 reaches a distal position, the distal surface of the sensor housing 122 engages the upper surface of adhesive pad 418, thereby becoming adhered to the skin surface S of the subject. Flange 470 engages fingers 474 disposed on the carriage 430. Fingers 474 are pivoted outwards by flanges 470 in direction T. Such pivoting of fingers 474 causes fingers 474 to become disengaged from shoulder 476 of needle carrier 434. Needle carrier 434 is thereby disengaged from carriage 430.

[00216] As illustrated in FIGURE 67, disengagement of the needle carrier 434 from the carriage 430 permits the spring 446 to expand, thereby advancing the needle carrier 434 to a proximal position and withdrawing the sharp 424 from the skin S of the subject while leaving the sensor 14 in the skin. Once the sharp 424 has been withdrawn from the subject, it is no longer accessible from the distal portion of the inserter 400 and unable to make contact by accident with the subject's skin because it is positioned at a proximal position within the carrier handle 402.

[00217] A further embodiment of an inserter is illustrated in FIGURES 68-71 and designated inserter 500. In some embodiments, inserter 500 has a maximum diameter of about 30 mm to about 60 mm, *e.g.*, about 40 mm, about 43 mm, about 43.5 mm, about 50.5 mm, about 54.5 mm, etc. In some embodiments, inserter 500 has a maximum height of about 40 mm to about 80 mm, *e.g.*, about 44 mm, about 46 mm, about 50 mm, about 53 mm, about 67 mm, about 71 mm, etc. In some embodiments, inserter 500 has a volume of about 35 cm^3 to about 110 cm^3, *e.g.*, about 40 cm^3, about 41 cm^3, about 50 cm^3, about 60 cm^3, about 61 cm^3, about 62 cm^3, about 69 cm^3, about 70 cm^3, about 79 cm^3, about 90 cm^3, about 106 cm^3, etc.

[00218] Inserter 500 includes, *e.g.*, a bellows portion 502, a sheath 542, and a removable distal cap 504 for maintaining a sterile environment for the medical device and sharp housed therein. As illustrated in FIGURE 69, distal cap 504 is shown removed from sheath 542. Sheath 542 defines a distal surface 512 for placement on the skin of a subject. Inserter 500 may be utilized to advance a medical device into the skin of the subject. In some embodiments, bellows portion 502 is compressed in order to advance the medical device into the skin of the subject. Bellows portion 502 includes a series of concentric folds, including raised portions 516 and folded portions 518.

[00219] Inserter 500 is illustrated in cross-section in FIGURE 70 prior to use and prior to removal of cap 504, which is attached to sheath 542 via inter-engagement of threads 510 on sheath and threads 511 on cap 504. Cap 504 includes a desiccant tablet 590. Cap 504 may further include a receptacle for maintaining the position of the sharp 524 within the sheath 542 prior to use.

[00220] As illustrated in FIGURE 70, the inserter 500 includes an initial configuration in which the bellows portion 502 is disposed in a relaxed, extended position. In such configuration, the sharp 524 is disposed in a position spaced apart from the aperture 520 of the adhesive layer 518. The proximal end portion of the housing includes a button or actuator portion 514. Extending distally from the actuator portion 514 are side walls 528 and needle hub 536. Downward force on the actuator portion 514 causes a downward force on the needle hub 536 and on the carriage 530 (through coupling to side walls 528). Carriage 530 includes a recess 532 for reception of the sensor housing 122 therein. Sharp 524 extends longitudinally from needle hub 536 within the inserter 500. In some embodiments, the sharp is supported at an oblique angle, *e.g.*, between including about 0° and 90° with respect to the skin surface.

[00221] FIGURE 71 illustrates inserter 500 in cross-section, during insertion. Depression of bellows portion 502 with respect to sheath 542 against the bias of spring 546 causes distal longitudinal movement of the carriage 530 and sharp 524 from a proximal position toward a distal position. During such downward, proximal movement, spring 546 is compressed between an upper (proximal) portion adjacent to actuator 514 and a lower (distal) portion adjacent to sheath 542. As the sharp 524 is urged distally, it carries the sensor insertion portion 30 of sensor 14 (FIGURE 23) into the subcutaneous portion of the subject's skin S.

[00222] By removing downward force on the actuator portion 514, the bias of spring 546 provides an upward (proximal) force, which permits sharp 524 to withdraw from the skin S of the subject. Once the sharp 524 has been withdrawn from the subject, it is no longer accessible from the distal portion of the inserter 500, and unable to make contact by accident with the subject's skin.

[00223] An inserter 2400 in accordance with another exemplary embodiment is illustrated in FIGURE 72. In some embodiments, inserter 2400 has a maximum diameter, of about 30mm to about 60 mm, *e.g.*, about 40 mm, about 43 mm, about 43.5 mm, about 50.5 mm, about 54.5 mm, etc. In some embodiments, inserter 2400 has a maximum height of about 40 mm to about 80 mm, *e.g.*, about 44 mm, about 46 mm, about 50 mm, about 53 mm, about 67 mm, about 71 mm, etc. In some embodiments, inserter 2400 has a volume of about 35 cm^3 to about 110 cm^3, *e.g.*, about 40 cm^3, about 41 cm^3, about 50 cm^3, about 60 cm^3, about 61 cm^3, about 62 cm^3, about 69 cm^3, about 70 cm^3, about 79 cm^3, about 90 cm^3, about 106 cm^3, etc.

[00224] With reference to FIGURE 72, inserter 2400 includes a housing 2402 and a removable distal cap 2412 for maintaining a sterile environment for the medical device and sharp housed therein. Housing 2402 and distal cap 2412 may be fabricated from any suitable materials such as metal, plastic, etc. In some embodiments, cap 2412 may be fabricated from a polymer or plastic material.

[00225] An exploded view of the components of inserter 2400 is illustrated in FIGURE 72A. As shown, inserter 2400 generally comprises plunger 2405, spring 2406, housing 2402, sharp 2404, sensor housing 122, sharp holder 2408, adhesive patch 218, and cap 2412 when fully assembled.

[00226] A more detailed view of sharp holder 2408 is shown in FIGURE 72B. Needle holder 2408 retains sharp 2404 in a fixed position with respect to itself within inserter 2400, thereby allowing it to safely penetrate a subject's skin during later use.

[00227] To assemble inserter 2400, sharp 2404 is inserted through an opening in sensor housing 122 as shown in FIGURE 72C. Needle holder 2408 prevents sharp 2404 from being fully inserted through sensor housing 122. In some embodiments, sensor housing 122 includes an analyte sensor 14 and a sensor control unit 12.

[00228] Next, plunger 2405, spring 2406, and housing 2402 are assembled as shown in FIGURES 72D-72F. Plunger 2405 contains a spring retention member which is inserted through the center of spring 2406. Lip 2414 of plunger 2405 engages inner wall 2416 of housing 2402 when assembled (FIGURE 72). This causes spring 2406 to be contained between lip 2418 of housing member 2402 and the bottom surface 2424 of plunger 2405. The resulting sub-assembly of inserter 2400 shown in allows plunger 2405 to move between a proximal position, with spring 2406 fully extended, and a distal position, wherein bottom surface 2424 engages wall 2426 of housing 2402.

[00229] The sensor housing assembly shown in FIGURE 72C is then inserted into the inserter sub-assembly shown in FIGURES 72D-72F. As shown in FIGURE 72F, sensor housing 122 is inserted into housing 2402 with the tip of sharp 2404 pointing away from plunger 2405. The resulting assembly is depicted in FIGURE 72G. As shown in FIGURE 72, grooves on sharp holder 2408 engage tabs 2422 on plunger 2405.

[00230] Finally, adhesive patch 218 is placed over the opening of housing 2402 and cap 2412 is friction fit over housing 2402 as shown in FIGURE 72H. The fully assembled inserter 2400 is

depicted in FIGURE 72I. In some embodiments, adhesive pad 218 has an adhesive material on both faces. A central aperture 220 may be provided in adhesive pad 218 to allow sharp 2404 to be deployed into the skin of a subject. During insertion, sharp 2404 passes through aperture 220 and into the skin of the subject carrying at least the sensor with it.

[00231] FIGURE 72J illustrates inserter 2400 in cross-section, in an initial configuration prior to use, after removal of the distal cap 2412. As shown, sharp 2404 extends longitudinally within the inserter 2400. In some embodiments, sharp 2404 is supported at an oblique angle, *e.g.*, between and including about 0° and 90° with respect to the skin surface.

[00232] In some embodiments, sharp 2404 is a solid needle. In some embodiments, sharp 2404 is provided with a substantially cylindrical configuration defining an interior bore, *e.g.*, a rigid cylindrical member or a hypodermic-style needle. Sharp 2404 may also be provided with an elongated longitudinal opening or gap in the wall of the sharp 2404. In some embodiments, sharp 2404 is a fabricated from a sheet of metal, and folded into a substantially "V" or "U" or "C" configuration in cross-section to define the longitudinal recess.

[00233] Depression of plunger 2405 causes distal longitudinal movement of sensor housing 122 and sharp 2404, from a proximal position to a distal position. During such downward, distal movement, spring 246 is further compressed between lip 2418 and bottom surface 2424. Lip 2414 is pushed outward by sensor housing 122 and the friction between sensor housing 122 and lip 2414 of the housing hold the sensor housing 122 up against plunger 2405.

[00234] As illustrated in FIGURE 72K, depression of plunger 2405 advances the inserter 2400 from an initial configuration to a deployed configuration. Contact of plunger 2405 and sharp holder 2408 during depression of plunger 2405 imposes a downward force and

consequential distal movement of sharp 2405.the carriage 230. As the sharp 2404 is urged distally, it carries the sensor insertion portion 30 into the subcutaneous portion of the subject's skin S.

[00235] When plunger 2505 reaches a distal position, as shown in FIGURE 72L, bottom surface 2424 engages wall 2426 and prevents further downward movement. The distal (lower) surface of sensor housing 122 engages the upper surface of adhesive pad 218, thereby becoming adhered to the skin surface S of the subject.

[00236] As the subject or some apparatus removes force from pusher 2405, spring 2406 urges pusher 2405 toward its proximal position as shown in FIGURE 72M, leaving sensor housing 122 adhered to the skin surface S of the subject. Tabs 2424 provide additional force on sensor housing 122 to assist holding it to adhesive patch 218 while the sharp 2404 is withdrawn through sensor housing 122. Eventually, the upward force exerted by spring 2406 returns inserter 2400 to its initial configuration as illustrated in FIGURE 72N.

[00237] In some embodiments, inserter 2400 may be distributed in a sterilized package 2480 as depicted in FIGURE 72O. To use inserter 2400 in this configuration, a user would first clean the insertion site on the skin with alcohol. The subject would then remove inserter 2400 from sterilized package 2480 as shown in step 1. Next a subject would place the inserter on the insertion site and push down on inserter 2400 until sensor housing 122 is adhered to the subject's skin as shown in steps 2-3. Finally, the subject would remove inserter 2400 from the insertion site and dispose of the inserter.

[00238] In another embodiment, the sterilized inserter 2500 shown in FIGURE 72O may be utilized with driver apparatus 3900 (FIGURES 93-93H) as shown in FIGURE 72P. In this

manner, insertion of sensor housing unit is semi-automated which may deliver a more consistent user experience and reduce the risk of user error. Additionally, because inserter 2500 is already sterilized, utilizing the method depicted in FIGURE 72P also reduces the risk of possible infection.

[00239] A further embodiment of an inserter is illustrated in FIGURES 73-73N, and designated inserter 2500. In some embodiments, inserter 2500 has a maximum diameter of about 30mm to about 60 mm, *e.g.*, about 40 mm, about 43 mm, about 43.5 mm, about 50.25 mm, about 52 mm, etc. In some embodiments, inserter 2500 has a maximum height of about 40 mm to about 80 mm, *e.g.*, about 44 mm, about 46 mm, about 50.25 mm, about 53 mm, about 67 mm, about 71 mm, etc. In some embodiments, inserter 2500 has a volume of about 35 cm^3 to about 110 cm^3, *e.g.*, about 40 cm^3, about 41 cm^3, about 50 cm^3, about 60 cm^3, about 61 cm^3, about 62 cm^3, about 69 cm^3, about 70 cm^3, about 79 cm^3, about 90 cm^3, about 106 cm^3, etc.

[00240] Inserter 2500 generally includes, *e.g.*, a handle 2502, sheath 2512, and a removable distal cap 2504 for maintaining a sterile environment for the medical device and sharp housed therein (FIGURE 73). As illustrated in FIGURES 73A-73B, handle 2502 is shown removed from distal cap 2504. Distal cap 2504 is detachably secured to handle 2502, *e.g.*, by use of threads 2506. It is understood that cap may be secured using snap-fit or press-fit configuration. Inserter 2500 may be utilized to advance a medical device into the skin of the subject. In some embodiments, handle 2502 is advanced relative to sheath 2512 in order to advance the medical device distally and into the skin of the patient.

[00241] Handle 2502 further includes needle carrier guides 2508 which allow the needle carrier 2514 to slidingly move relative to distal cap 2504. Detent 2507 prevents sheath 2512

from moving towards a "firing position" until a minimum force is applied. Location feature 2510 allows for the proper positioning of distal cap 2508 and carriage 2516 when engaged.

[00242] Further components of inserter 2500 are illustrated in FIGURES 73C-73G. Sheath 2512, as illustrated in FIGURES 73C, may include longitudinal notches 2518 which snap into detents 2507. Retention members, such as ribs 2520, pinch spring arms 2522 located on carriage 2516 to prevent sensor housing 122 from falling out of inserter 2500 when sheath 2512 is in the extended position. Ribs 2520 do not extend to the bottom of sheath 2512, thus allowing carriage 2516 to release sensor housing 122 when it has traveled to the bottom of sheath 2512 during insertion. Interfering structure, such as locking beam 2524, prevents inserter 2500 from being used again once needle carrier 2514 passes the locking beam (FIGURE 73N). Specifically, locking feature 2526 of needle carrier 2514 engages with locking beam 2524 to prevent further use of inserter 2500.

[00243] Needle carrier 2514 is illustrated in greater detail in FIGURES 73D-73E. In some embodiments, needle carrier 2514 includes guides, such as rail guides 2528, which interface with rail guides 2508, thereby allowing needle carrier 2514 to slidingly move relative to handle 2502. Notches 2527 are provided in sheath 2512 which has a larger dimension than the wings 2550 of needle carrier 2514, such that the needle carrier 2514 does not contact sheath 2512 during longitudinal movement of needle carrier 2514. Needle carrier 2514 also comprises detents/notches 2530 which interface with the upper edge of the spring when inserter 2500 is fully assembled (see FIGURES 73H-73N). In some embodiments, needle carrier 2514 comprises an attachment feature 2532 capable of accommodating a custom needle hub or

attachment. Rails 2524, located on the inner perimeter of needle carrier 2514, slidingly engage with slots 2536 located on carriage 2516.

[00244] Carriage 2516 is illustrated in greater detail in FIGURES 73F-73G. As shown, carriage 2516 may comprise latches 2538 which connect it to needle carrier 2514 by locking with latches 2540. Spring hook 2542 allows for support for retaining sensor housing 122 when the inserter has not been fired and allows for release of sensor housing 122 when it has been attached to the skin of the user.

[00245] Inserter 2500 is illustrated in cross-section in FIGURE 73H in a state prior to use in which handle 2502 is disposed in a proximal position with respect to the sheath 2512. In such configuration, the sharp 2550 is disposed in a configuration spaced apart from the aperture 420 of the adhesive layer (not shown). The longitudinal axis L of the inserter 2500 is illustrated. The upper surface of spring 2544 is retained in inserter 2500 by detents/notches 2530 located on needle carrier 2514. The bottom surface of spring 2544 is retained by spring floor 2545 located on sheath 2512. Initially, spring 2544 is in an expanded or semi-expanded state while handle 2502 is disposed proximally from sheath 2512.

[00246] Extending distally from the upper surface of handle 2502 is inner wall 2552. In some embodiments, the distal end portions of wall 2508 provide a downward force on carriage 2516 upon depression of handle 2502 by a user. Alternatively, instead of handle 2502 having a distally extending inner wall 2508carriage 2516 can include one or more upwardly extending walls or projections (not shown). The one or more upwardly extending inner walls or projections can have a length sufficient to either contact the upper surface of handle 2502 or, alternatively, contact corresponding downwardly extending inner walls of handle 2502. In this manner,

depression of handle 2502 by a user provides a downward force on the one or more upwardly extending walls or projections of carriage 2516 to advance carriage 2516 (and sensor housing 122) distally to an installation and insertion position. In such embodiment, the downwardly extending inner wall of the handle has a distal end that is disposed proximally of the proximal most end of sheath 2512.

[00247] Sharp 2550 extends longitudinally from needle carrier 2514 within inserter 2500. In some embodiments, sharp 2550 is supported at an oblique angle, *e.g.*, between and including about 0° and 90° with respect to the skin surface.

[00248] FIGURE 73I illustrates inserter 2500 in cross-section after a user applies an initial downward force to button 2502. In some embodiments, a predetermined minimum force must be used so that longitudinal notches 2518 advance past detent 2507.

[00249] After detent 2507 has been overcome, further depression of handle 2502 with respect to sheath 2512, against the bias of spring 2544, causes distal longitudinal movement of the carriage 2516 and needle carrier 2514, from a proximal position towards a distal position as shown in FIGURE 73J. During such downward proximal movement, spring 2544 is compressed between detents/notches 2530 and retention tab 2546. As sharp 2550 is further urged distally, it carries the sensor insertion portion 30 of sensor 14 (FIGURE 23) into the subcutaneous portion of the subject's skin S.

[00250] As carriage 2516 reaches a distal position as shown in FIGURE 73J, the distal surface of the sensor housing 122 engages the upper surface of adhesive pad (not shown), thereby becoming adhered to the skin surface S of the subject. Latch 2538 engages the upper surface of retention tab 2546 as shown in FIGURES 73K. As a result, the top portion of latch 2538 is

pivoted outward in direction T. Such pivoting of latch 2538 causes needle carrier to become disengaged from carriage 2516.

[00251] As illustrated in FIGURE 73L, disengagement of the needle carrier 2514 from the carriage 2516 permits spring 2544 to expand, thereby advancing the needle carrier 2514 to a proximal position and withdrawing the sharp 2550 from the skin S of the subject while leaving the sensor housing 122 attached to the skin. As the sharp is withdrawn (FIGURE 73M), locking feature 2526 advances past locking beam 2524 because of the upward force exerted on needle carrier 2514 by spring 2544.

[00252] Referring now to FIGURE 73N, once the sharp 2550 has been withdrawn from the subject, button 2500 cannot be pressed again because any downward movement will be blocked by the interaction of locking beam 2524 and locking feature 2526.

[00253] In some embodiments, inserter 2500 may come in a sterilized package which is capable of a one-time use as shown in FIGURE 73O. To use inserter 2500 in this manner, a user would first sterilize the insertion site on the skin with alcohol. The subject would then twist off cap 2504 as shown in step 1. Next a subject would place the inserter on the sterilized insertion site and push down on inserter 2500 until sensor housing 122 is adhered to the subject's skin as shown in steps 2-3. Finally, the subject would remove inserter 2500 from the insertion site and dispose of the inserter. In this manner, the inserter 2500 itself serves as its own sterilized packaging.

[00254] A further embodiment of an inserter is illustrated in FIGURES 74-90, and designated inserter. In some embodiments, inserter 2700 has a maximum diameter of about 30mm to about 60 mm, *e.g.*, about 40 mm, about 43 mm, about 43.5 mm, about 46 mm, about 50 mm, etc. In

some embodiments, inserter 2700 has a maximum height of about 40 mm to about 80 mm, *e.g.*, about 44 mm, about 46 mm, about 49.5 mm, about 55 mm, about 67 mm, about 71 mm, etc. In some embodiments, inserter 2700 has a volume of about 35 cm^3 to about 110 cm^3, *e.g.*, about 40 cm^3, about 41 cm^3, about 50 cm^3, about 60 cm^3, about 61 cm^3, about 62 cm^3, about 69 cm^3, about 70 cm^3, about 79 cm^3, about 90 cm^3, about 106 cm^3, etc.

[00255] Inserter 2700 generally includes, *e.g.*, a housing 2702 (FIGURES 75-76), sheath 2708 (FIGURES 77-78), and a removable distal cap 2704 for maintaining a sterile environment for the medical device and sharp housed therein (FIGURE 74). As illustrated in FIGURES 75-76, housing 2702 is shown removed from distal cap 2704. Distal cap 2704 is detachably secured to housing 2702, *e.g.*, by use of threads 2706. It is understood that cap may be secured using snap-fit or press-fit configuration. Inserter 2700 may be utilized to advance a medical device into the skin of the subject. Sheath 2708 generally a cavity or open space, within which sharp carrier 2716 and medical device carrier 2730 are moveable. In some embodiments, housing 2702 is advanced relative to sheath 2708 in order to advance the medical device distally and into the skin of the patient.

[00256] Housing 2702 includes sheath guide rail 2710 which interfaces with rail guides 2712 located on sheath 2708 (FIGURE 77), thereby allowing housing 2702 to slidingly move relative to sheath 2708. Housing 2702 may further includes sharp carrier guide rail 2714 which interfaces with rail guides 2718 located on sharp carrier 2716 (FIGURE 70). Sheath 2708, sharp carrier 2716, and housing 2702 may alternatively move relative to one another without the use of guide rails.

[00257] Ledge 2720 and/or ledge 2722 are provided on an interior portion of housing 2702. Ledge 2720 engages sheath 2708 to hold sheath 2708 in a pre-use position prior to insertion of the medical device. Ledge 2722 engages sheath 2708 to secure sheath 2708 in a post-use position after insertion of the medical device. Housing 2702 further includes detent 2724 which prevents housing 2702 from moving relative to sheath 2708 until a minimum force has been applied, e.g., distally by user to housing 2702. In some embodiments, housing 2702 includes insertion hard stop 2724. The sheath 2708 is secured to the housing 2702 via snap 2726. Snap 2726 snaps into the housing detent 2724 (In some embodiments, it is pinched between ledge 2720 and detent 2724, thus controlling its height relative to the housing 2702). The needle carrier 2716 is located and secured to the medical device carrier 2730 (located via interaction of locating features 2748 and 2750 and secured via interaction of carrier arms 2732 and angled top surface of 2716). The insertion hard stop 2724 is a controlled surface onto which the top of sheath surface 2728 will engage at the end of the insertion stroke to prevent further relative movement in some embodiments.

[00258] Further components of inserter 2700 are illustrated in FIGURES 77-82. Sheath 2708 is a generally cylindrical component. As illustrated in FIGURES 77-78, sheath 2708 may include attachment snaps 2726 which are biased into detent 2724 of housing 2702 to create a minimum force that must be overcome in order to advance sharp 224 into the subject's skin and install the sensor housing 122. In some embodiments, the force to be overcome can be about 0.5 lbf to about 5 lbf., e.g., about 1lbf, about 2 lbf, about 3 lbf, about 4 lbf, etc. Support wall 2728 prevents carrier arms 2732 on carrier 2730 from bending outwardly, clear of sharp carrier 2716. Ribs 2734 pinch carrier arms 2732 on carrier 2730, thus preventing sensor housing 122 from falling out of inserter 2700 when sheath 2708 is in the extended position. Ribs 2734 are not

present at the bottom of sheath 2708, thus allowing room for spring arms 2736 on carrier 2730 to release sensor housing 122 when carrier 2730 has traveled to the bottom of sheath 2708. Slot 2738, located on sheath 2708, interfaces with locating feature 2740 on carrier 2730, thus orienting carrier 2730 to sheath 2708 during assembly.

[00259] Referring next to FIGURES 79-80, depicted is sharp carrier 2716 in a perspective and cross-sectional view, respectively. Sharp carrier 2716 contains notches 2724 which allow clearance for the passage of carrier arms 2732 located on medical device carrier 2730. Guidance walls 2744 securely hold spring 2746 in place (FIGURE 83). Locating features 2748, e.g., bosses or tabs, align with locating features 2750, e.g., recesses or apertures, on carrier 2730. Snap features 2752 secure sharp 224 securely within inserter 2700. It is contemplated that sharp 224 may be secured to sharp carrier 2716 by other techniques, e.g., friction fit, adhesive, welding, etc.

[00260] Medical device carrier 2730 is depicted in more detail in FIGURES 81-82. As shown, carrier 2730 contains spring locating ring 2754 which receives one end of spring 2746. In some embodiments, spring 2746 surrounds spring locating ring 2754. In some embodiments, the inner area remains clear to leave room for the deflection of sharp carrier feature snaps 2752 that deflect out when the sharp is inserted. Carrier 2730 further comprises locating features 2756 which interface with locating features on housing 2702.

[00261] Inserter 2700 is illustrated in cross-section in FIGURE 83 in a state prior to use in which housing 2702 is disposed in a proximal position with respect to the sheath 2708. In such orientation, sharp 224 is disposed in a configuration spaced apart from the aperture 420 of the adhesive layer 118. The upper surface of spring 2746 is retained in inserter 2700 by sharp carrier

2716. The bottom surface of spring 2746 is retained by spring location ring 2754. Initially, spring 2746 is in a compressed or semi-compressed state while housing 2702 is disposed proximally from sheath 2708.

[00262] Sharp 224 extends longitudinally from sharp carrier 2716 within inserter 2700. In some embodiments, sharp 224 is supported at an oblique angle, *e.g.*, between and including about 0° and 90° with respect to the skin surface.

[00263] FIGURE 84 illustrates inserter 2700 in cross-section after a user applies an initial downward force to housing 2702. In some embodiments, a predetermined minimum force must be used so that attachment snaps 2726 advance past detent 2724.

[00264] After detent 2724 has been overcome, e.g., snap 2726 is radially displaced, further depression of housing 2702 with respect to sheath 2708 causes distal longitudinal movement of the carrier 2730 and sharp carrier 2716, from a proximal position towards a distal position as shown in FIGURE 85. As sharp 224 is further urged distally, it carries the sensor insertion portion 30 of sensor 14 (FIGURE 23) into the subcutaneous portion of the subject's skin S.

[00265] As carrier 2716 reaches a distal position, the distal surface of the sensor housing 122 engages the upper surface of adhesive pad 118, thereby becoming adhered to the skin surface S of the subject. Concurrently, carrier arms 2732 are advanced distally and clear the support wall 2728. This allows carrier arms 2732 to deflect radially outwardly. When carrier arms 2732 deflect outwardly, shoulder portions of carrier arms 2732 are no longer in an interference relationship with the sharp carrier 2716. Thus spring 2746 is permitted to expand as shown in FIGURE 87, thereby advancing the sharp carrier 2716 to a proximal position and withdrawing the sharp 224 from the skin S of the subject while leaving the sensor housing 122 attached to the

skin. Handle 2702 is maintained in the distal position. Sheath snap 2726 of the sheath 2708 have now moved up to lock over feature 2722 of the housing 2702. Now the housing 2702 and the sheath 2708 can no longer move longitudinally with respect to each other.

[00266] In some embodiments, the changing interaction of sheath snap 2726 with the housing detent/ledges 2720, 2724, and 2722 determine whether the sheath 2708 is locked. When snap 2726 is in the pre-fire position, ledge 2720 prevents sheath 2708 from being pulled out of the housing 2702. In this position, detent 2724 may also impede the movement of pushing the sheath 2708 into the housing 2702. When the detent is overcome by a at least at minimum force, the sheath 2704 moves longitudinally with respect to the housing 2702 until the snap 2726 snaps over housing ledge 2722. At this point, ledge 2722 prevents the sheath 2708 from being pulled out of the housing again, but from a new position (this position may be referred to as the used/post-fire position). Sharp carrier snap 2752 function is to hold onto the sharp/needle. in some embodiments, the sharp/needle carrier 2716 is held in the post-fire position relative to the housing 2702 by, e.g., an interference between the rails of the housing 2714 and the guide rails of the sharp carrier 2718 (this interference is only present once the sharp carrier is fully retracted) and/or by medical device carrier projections 2732 interfering with the bottom/floor of the sharp carrier (See, e.g., FIG. 88).In another embodiment of inserter 2700, adhesive pad 118 may be attached directly to sensor housing 122. This necessitates a different shape of inserter 2700 as depicted in FIGURE 89. Additionally, carrier 2630 is slightly wider to accommodate adhesive pad 118 attached to sensor housing 122 (FIGURE 90).

[00267] It is understood that the subject matter described herein is not limited to particular embodiments described, as such may, of course, vary. It is also understood that the terminology

used herein is for the purpose of describing particular embodiments only, and is not intended to be limiting, since the scope of the present subject matter is limited only by the appended claims.

[00268] Additional detailed description of embodiments of the disclosed subject matter is provided in but not limited to: U.S. Patent No. 7,381,184; U.S. Patent No. 7,299,082; U.S. Patent No. 7,167,818; U.S. Patent No. 7,041,468; U.S. Patent No. 6,942,518; U.S. Patent No. 6,893,545; U.S. Patent No. 6,881,551; U.S. Patent No. 6,773,671; U.S. Patent No. 6,764,581; U.S. Patent No. 6,749,740; U.S. Patent No. 6,746,582; U.S. Patent No. 6,736,957; U.S. Patent No. 6,730,200; U.S. Patent No. 6,676,816; U.S. Patent No. 6,618,934; U.S. Patent No. 6,616,819; U.S. Patent No. 6,600,997; U.S. Patent No. 6,592,745; U.S. Patent No. 6,591,125; U.S. Patent No. 6,560,471; U.S. Patent No. 6,540,891; U.S. Patent No. 6,514,718; U.S. Patent No. 6,514,460; U.S. Patent No. 6,503,381; U.S. Patent No. 6,461,496; U.S. Patent No. 6,377,894; U.S. Patent No. 6,338,790; U.S. Patent No. 6,299,757; U.S. Patent No. 6,284,478; U.S. Patent No. 6,270,455; U.S. Patent No. 6,175,752; U.S. Patent No. 6,161,095; U.S. Patent No. 6,144,837; U.S. Patent No. 6,143,164; U.S. Patent No. 6,134,461;U.S. Patent No. 6,121,009; U.S. Patent No. 6,120,676; U.S. Patent No. 6,071,391; U.S. Patent No. 5,918,603; U.S. Patent No. 5,899,855; U.S. Patent No. 5,822,715; U.S. Patent No. 5,820,551; U.S. Patent No. 5,628,890; U.S. Patent No. 5,601,435; U.S. Patent No. 5,593,852; U.S. Patent No. 5,509,410; U.S. Patent No. 5,320,715; U.S. Patent No. 5,264,014; U.S. Patent No. 5,262,305; U.S. Patent No. 5,262,035; U.S. Patent No. 4,711,245; U.S. Patent No. 4,545,382; U.S. Patent Publication No. 2004/0186365, published September 23, 2004; U.S. Patent Application No. 61/238,646, filed August 31, 2009; U.S. Patent Application No. 12/698,129, filed February 1, 2010; U.S. Patent Application No. 61/317,243, filed March 24, 2010; U.S. Patent Application No. 61/345,562, filed May 17, 2010; and International Application No. PCT/US10/22860, filed

February 22, 2010, the disclosures of each of which is incorporated by reference herein for all purposes.

CLAIMS

WHAT IS CLAIMED IS:

1. An apparatus for inserting a medical device into the skin of a subject, which comprises:

a sheath defining a distal surface for placement on the skin of the subject;

a device support movable between a proximal and distal position, and adapted to support the medical device;

a sharp support movable between a proximal and a distal position, and adapted to support a sharp extending through a portion of said device support;

a handle movable between a proximal position and a distal position relative to the sheath and adapted to urge the device support and the sharp support from a proximal to a distal position to insert the sharp into the skin of the subject; and

a driver for advancing the sharp support towards the proximal position when the sharp support reaches the distal position.

2. The apparatus of claim 1, wherein the driver comprises a compression spring.

3. The apparatus of claim 2, wherein the handle is maintained in a distal position when the sharp support is advanced to the proximal position.

4. The apparatus of claim 1, wherein the handle is at least partially disposed surrounding the sheath.

5. The apparatus of claim 1, wherein the medical device is an analyte sensor.

6. The apparatus of claim 1, wherein the medical device is a glucose sensor.

7. The apparatus of claim 1, wherein the medical device is an infusion set.

8. The apparatus of claim 1, wherein at least one of the handle and the sheath comprises a detent.

9. The apparatus of claim 8 wherein the detent is configured such that advancing the handle distally further requires application of a minimum force to overcome the detent to allow distal movement of the handle relative to the detent.

10. A method for using a medical device comprising:

providing an apparatus comprising a sheath defining a distal surface, a device support adapted to support the medical device and movable between a proximal and distal position, a sharp support adapted to support a sharp extending through a portion of said device support and movable between a proximal and a distal position, a handle movable between a proximal position and a distal position relative to the sheath, and a driver for advancing the sharp support towards the proximal position when the sharp support reaches the distal position;

disposing the distal surface of the sheath on the skin of the subject; and

advancing the handle distally, thereby urging the device support and the sharp support from a proximal to a distal position to insert the sharp into the skin of the subject; and releasing the driver to advance the sharp support towards the proximal position when the sharp support reaches the distal position.

11. The method of claim 10 further comprising providing a detent on at least one of the handle and the sheath.

12. The method of claim 11, wherein the advancing the handle distally further comprises applying a minimum force to overcome the detent to allow distal movement of the handle relative to the detent.

ABSTRACT

An apparatus for insertion of a medical device in the skin of a subject is provided, as well as methods of inserting medical devices.

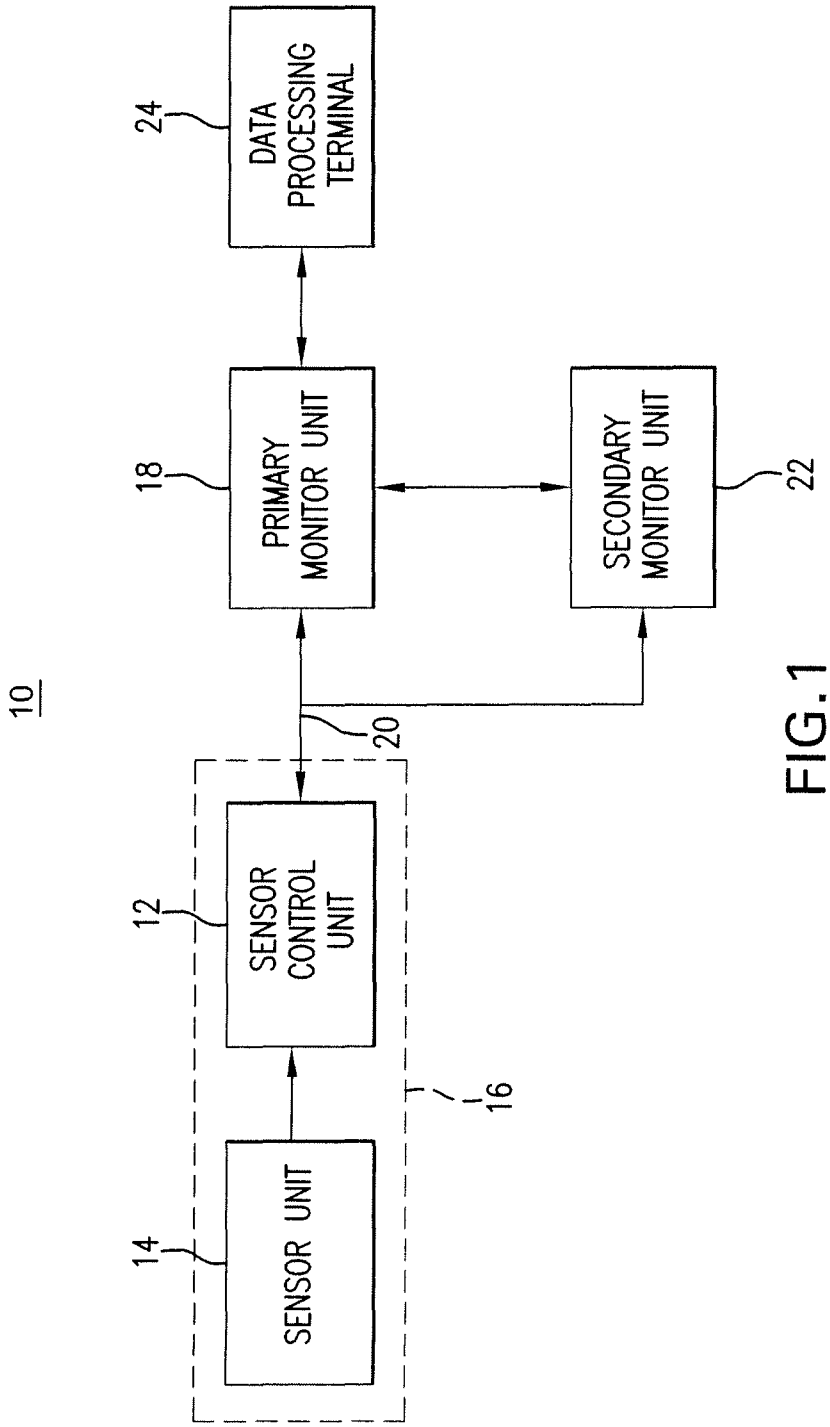

10
SENSOR UNIT
14
SENSOR CONTROL UNIT
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16
20
PRIMARY MONITOR UNIT
18
SECONDARY MONITOR UNIT
22
DATA PROCESSING TERMINAL
24

FIG. 1

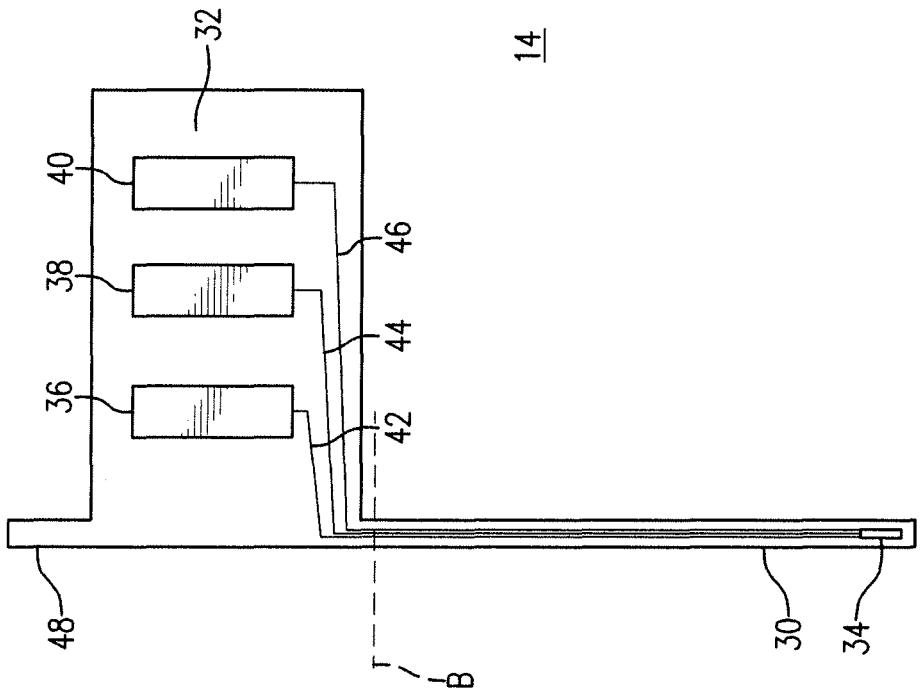


FIG.2

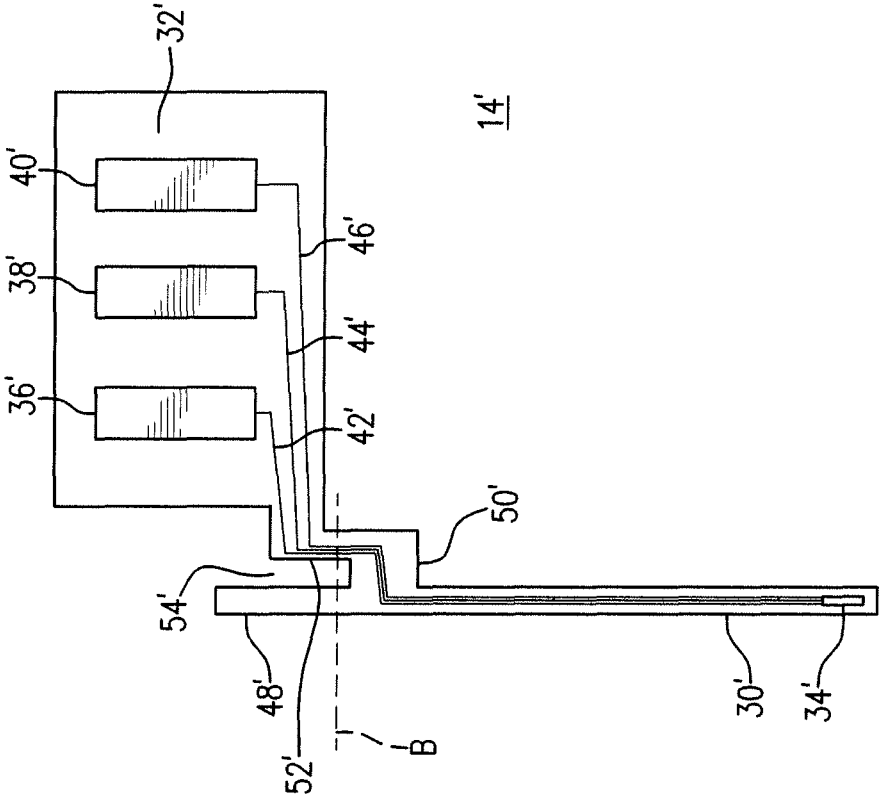


FIG.3

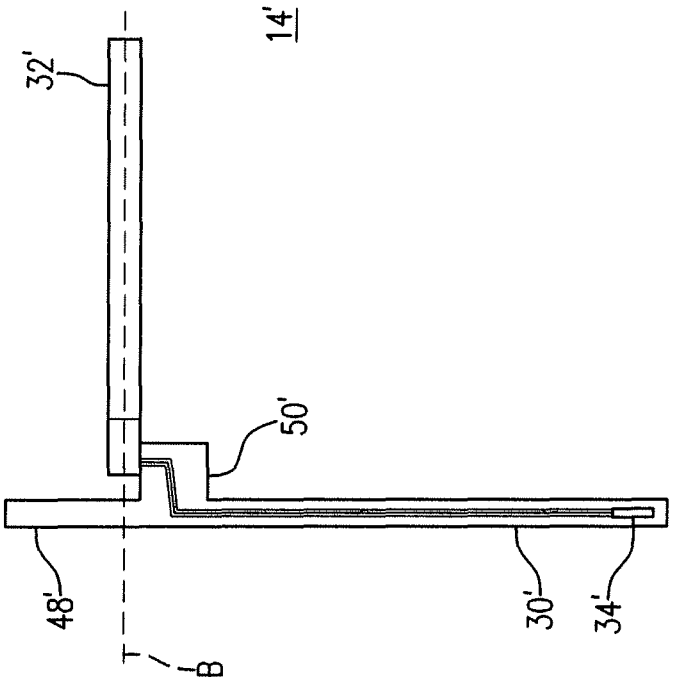


FIG.4

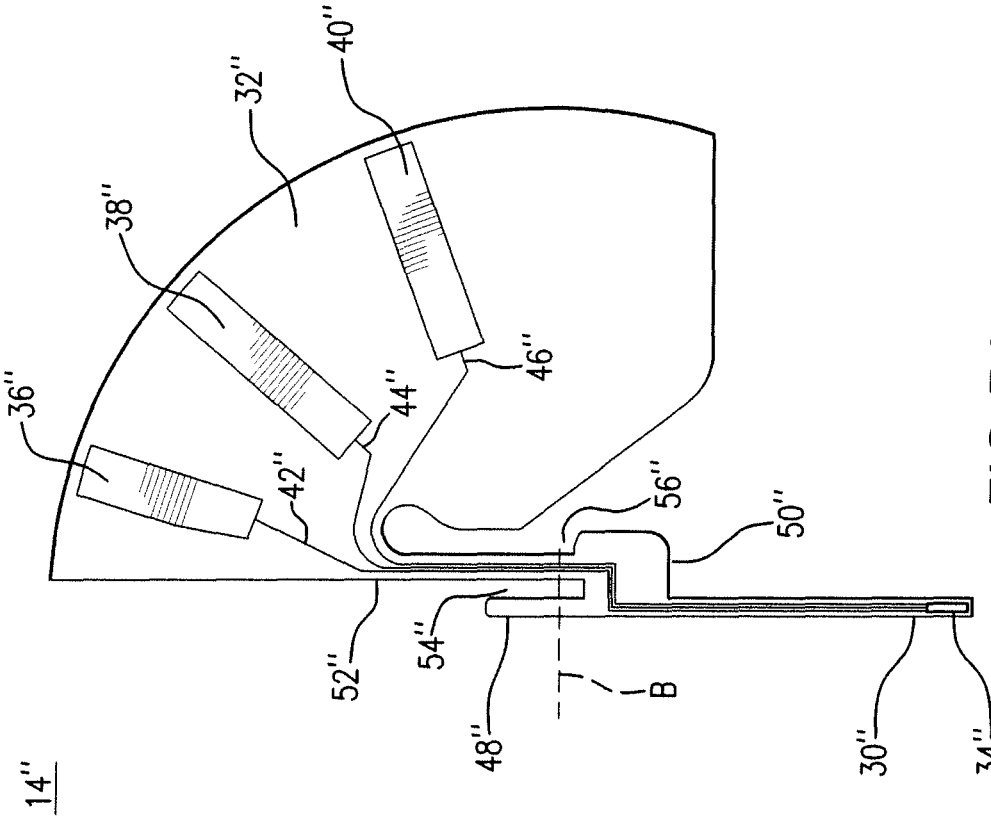


FIG.5A

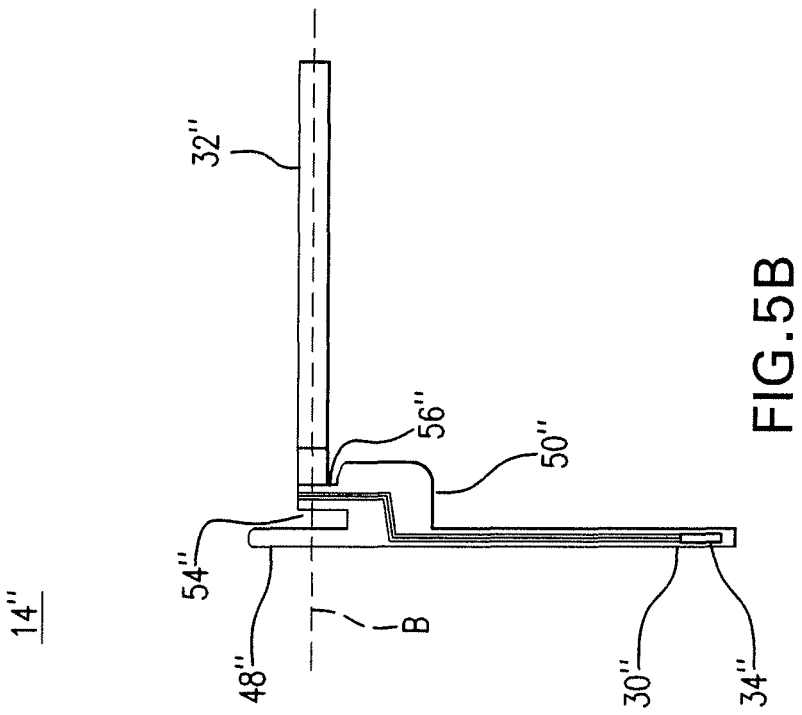


FIG.5B

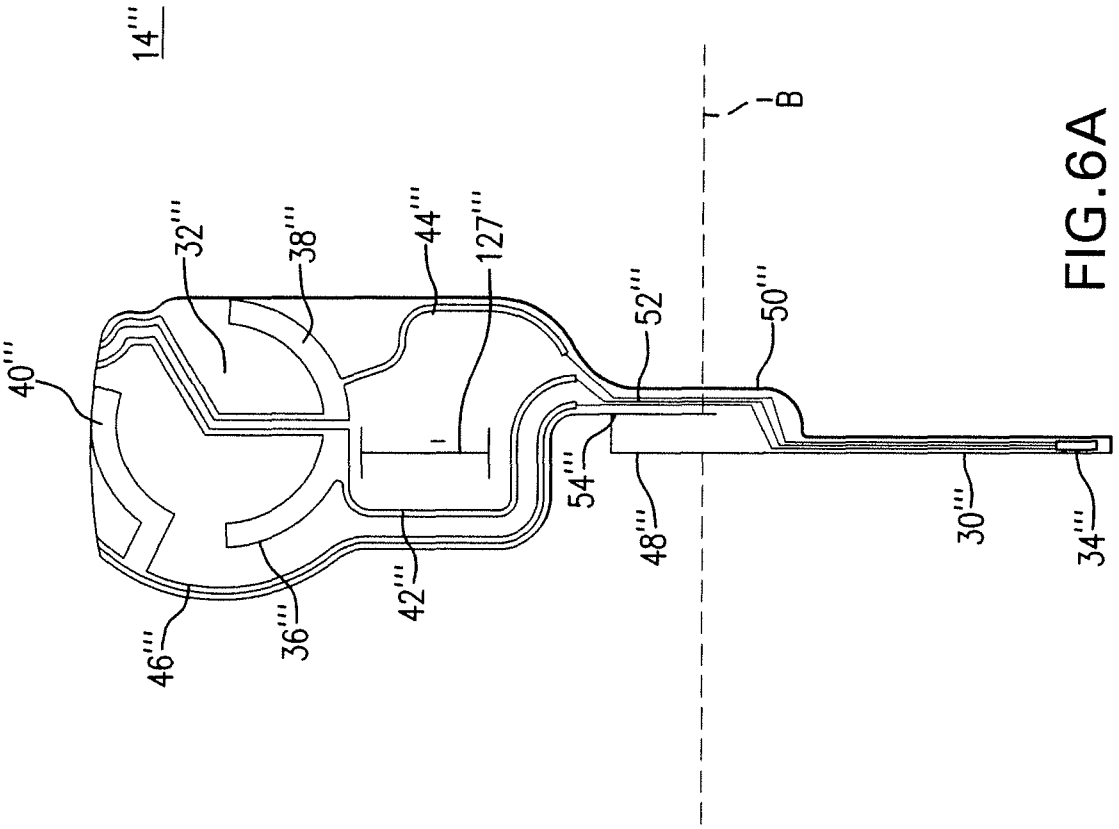


FIG.6A

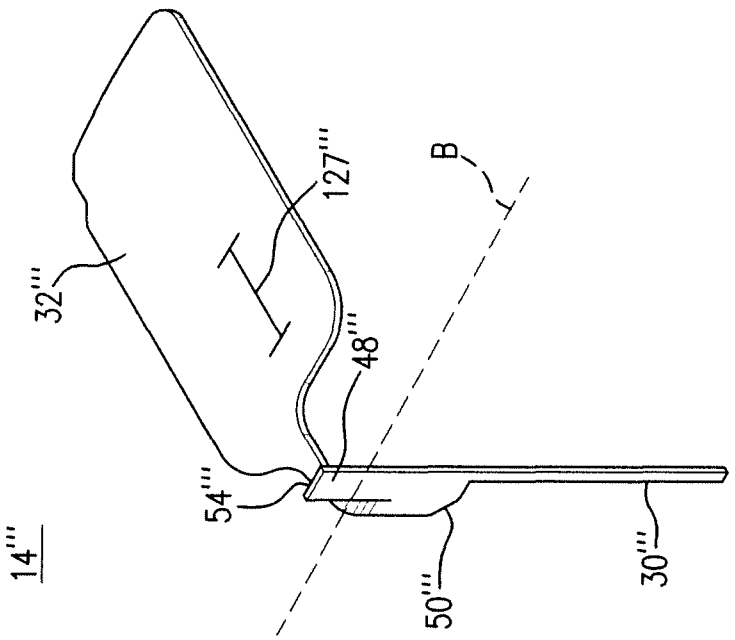


FIG.6B

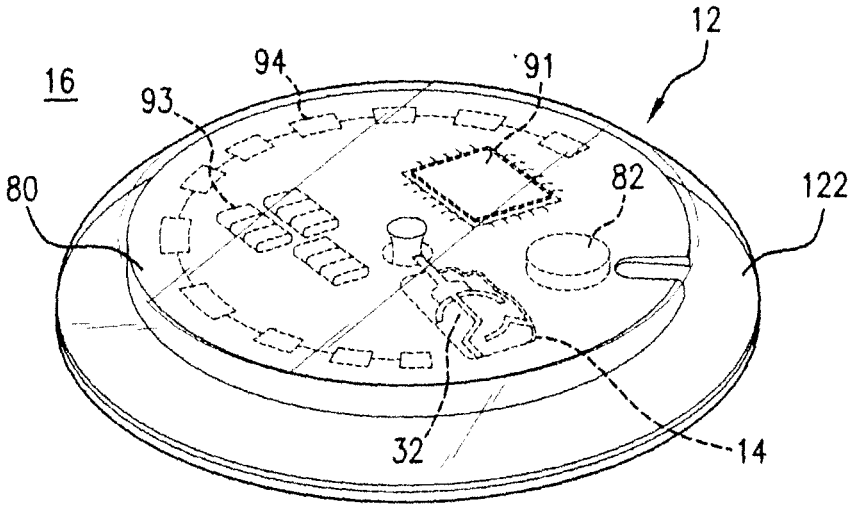


FIG.7

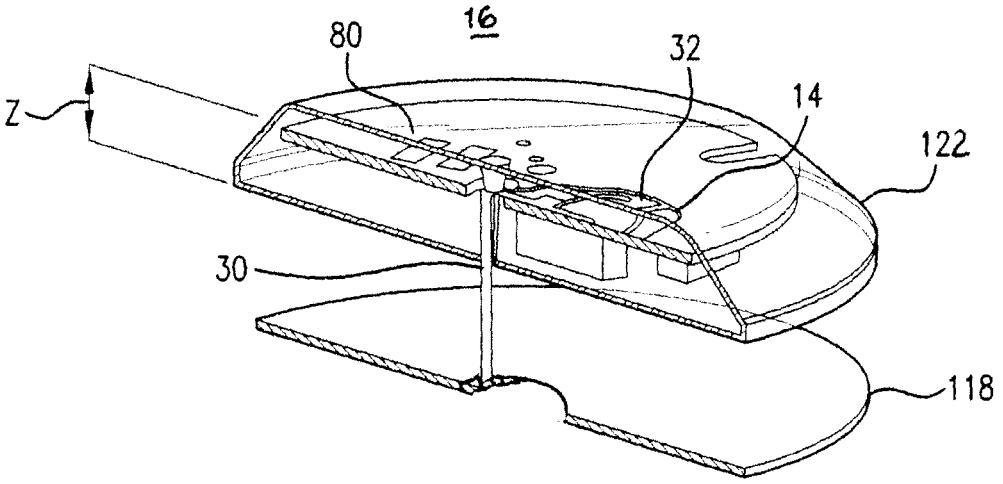


FIG.8

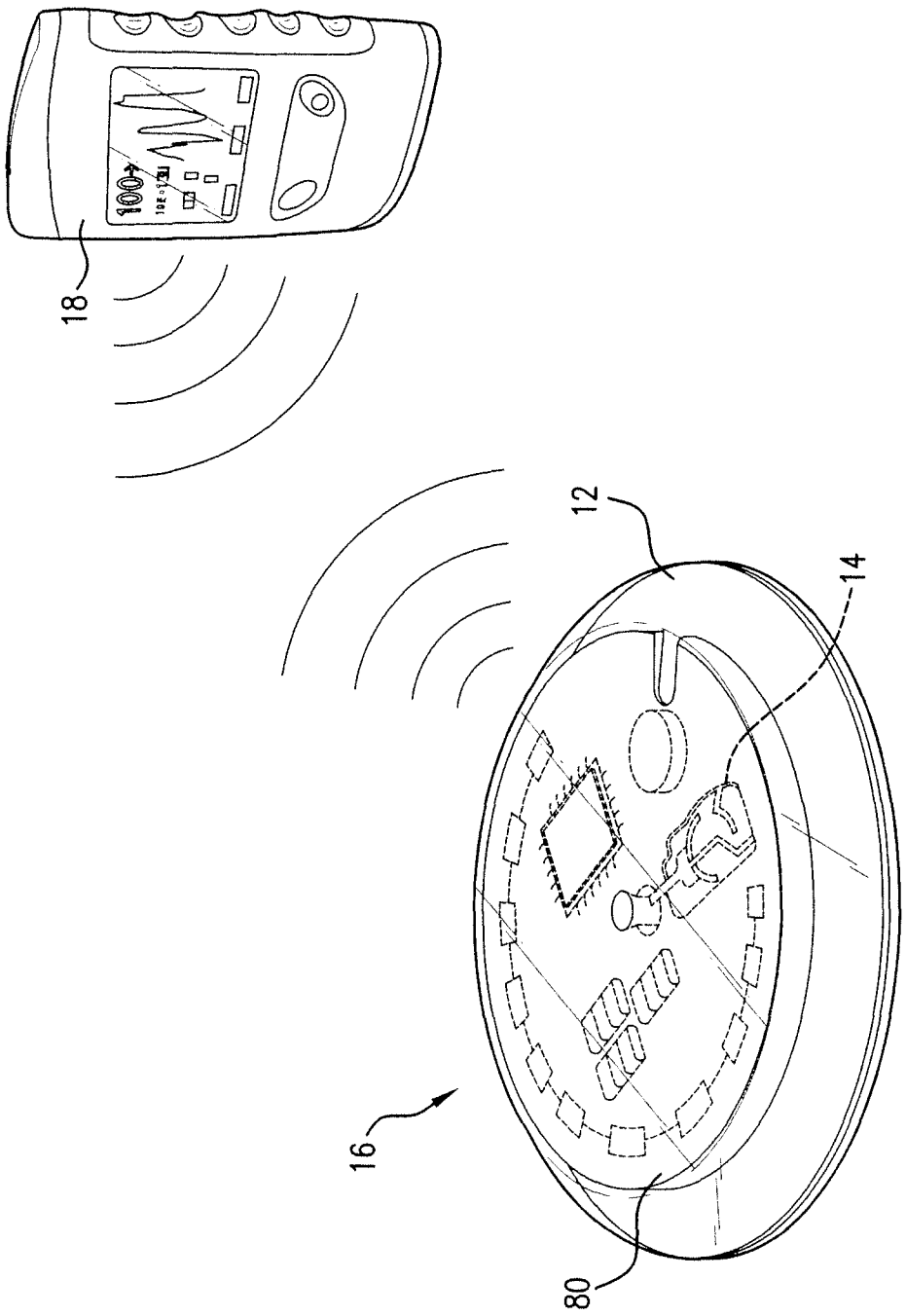


FIG.9

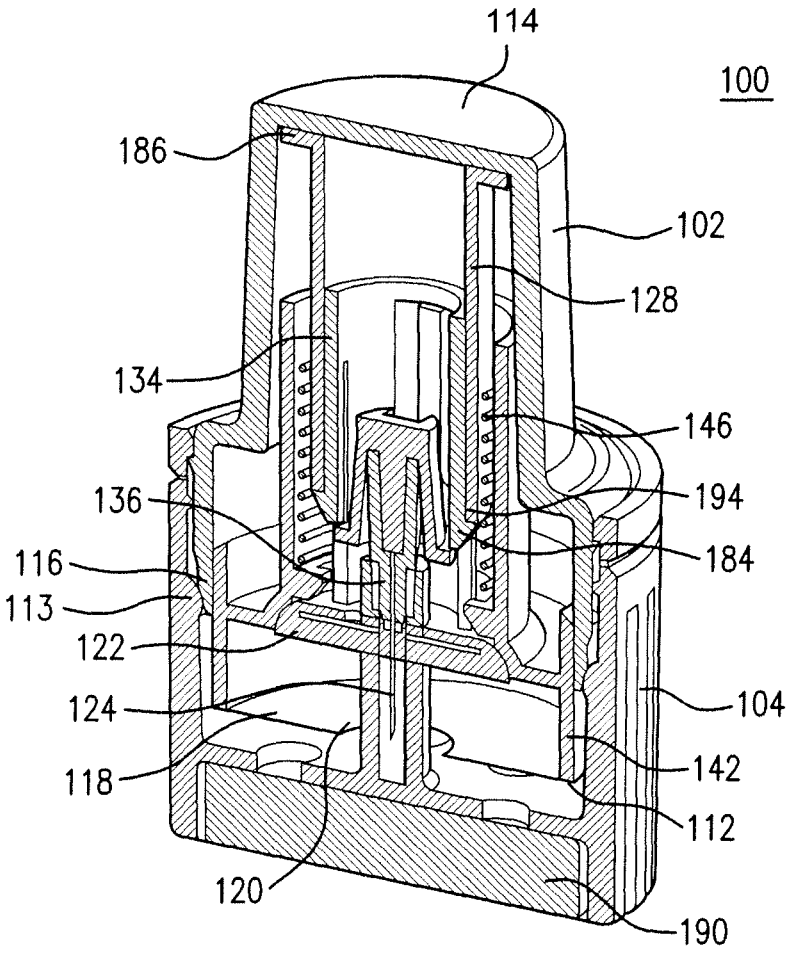

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FIG.10

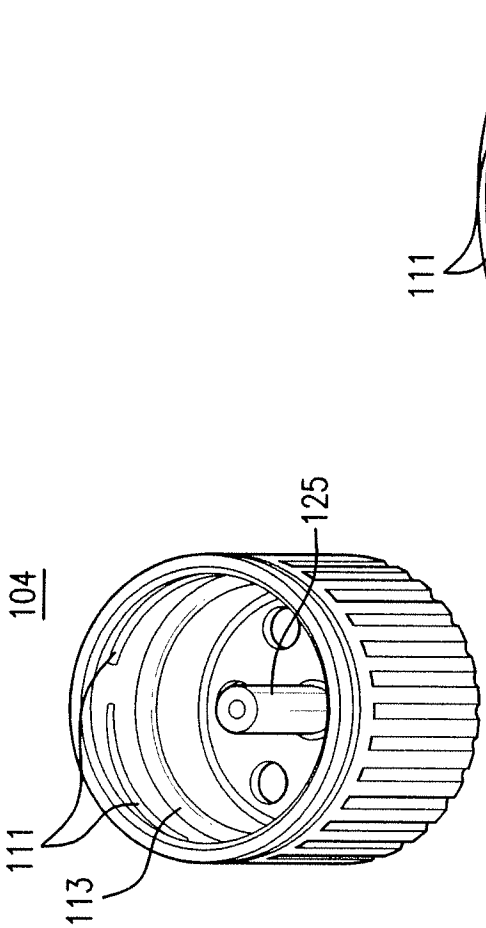


FIG.12

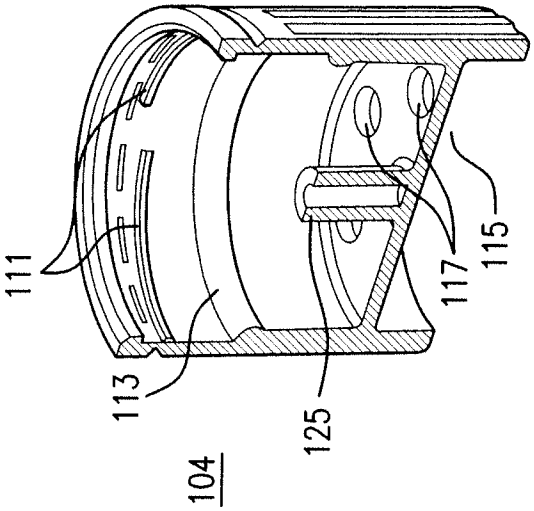


FIG.13

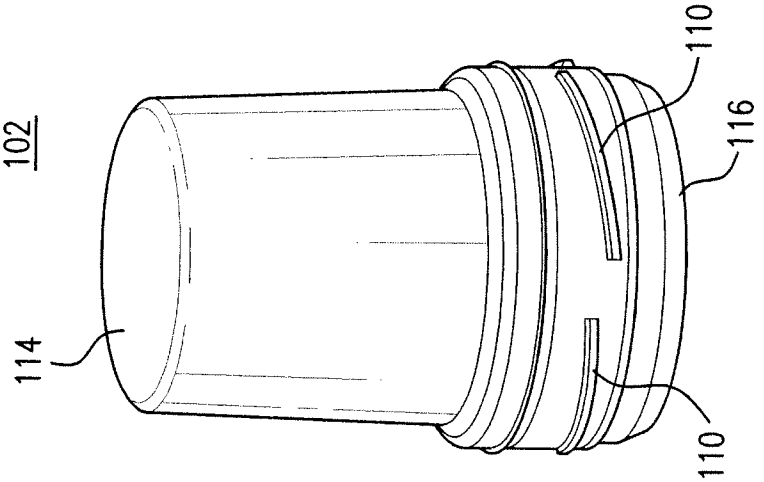


FIG.11

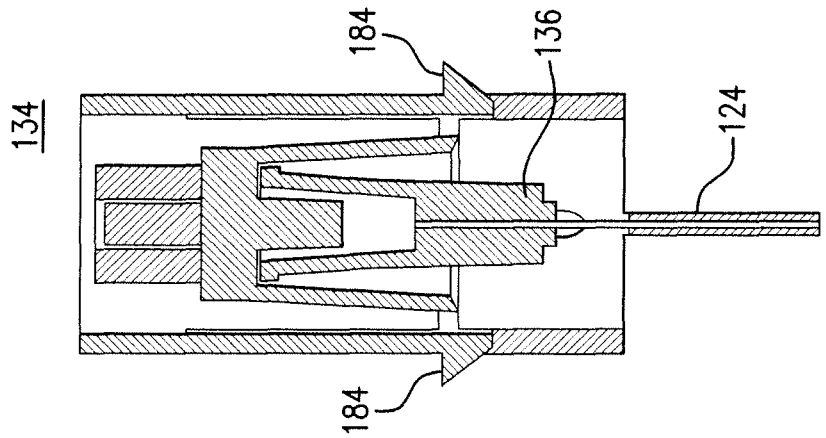


FIG.16

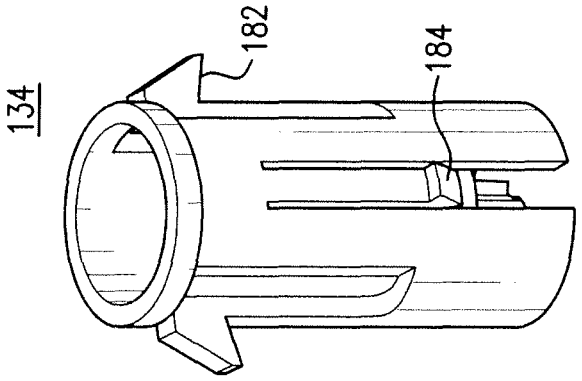


FIG.15

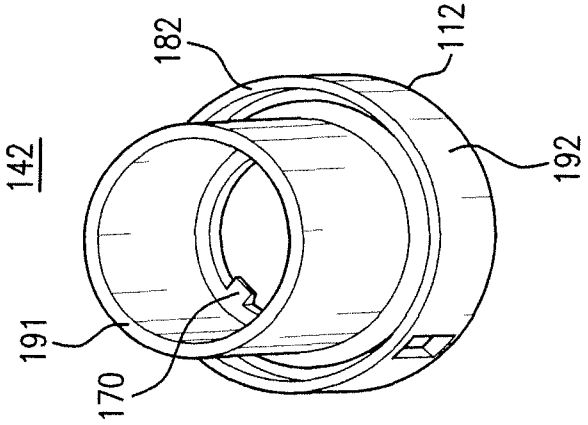


FIG.14

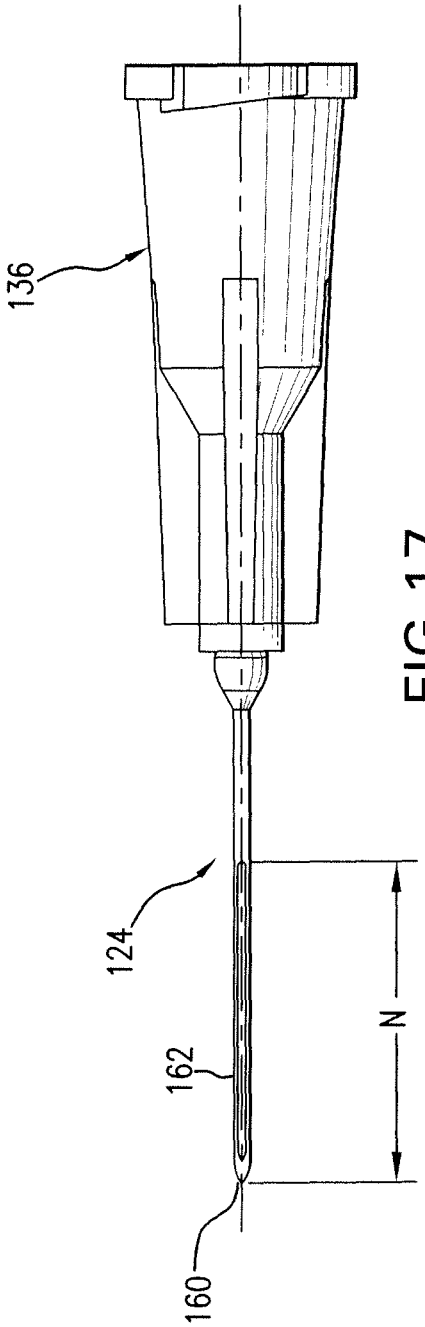


FIG. 17

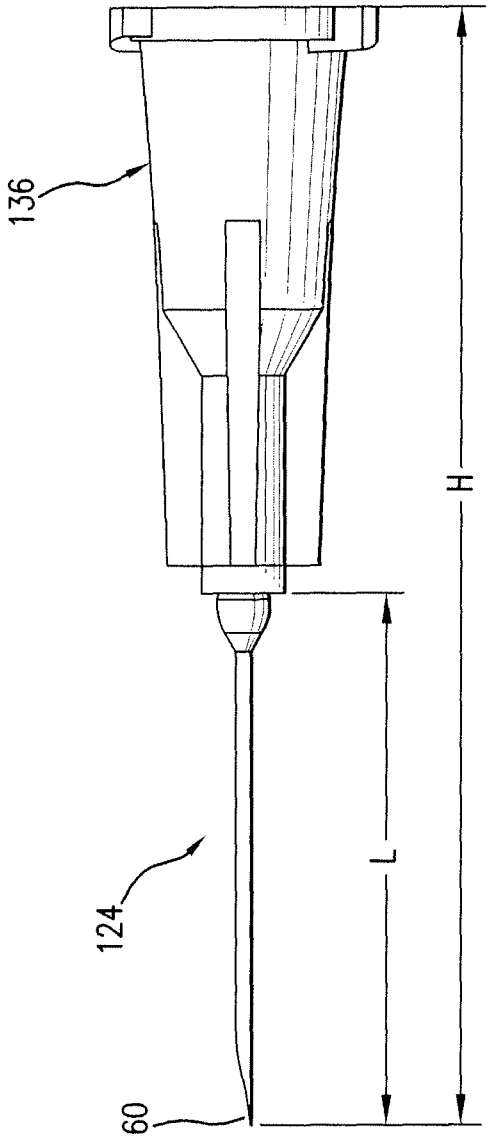


FIG. 18

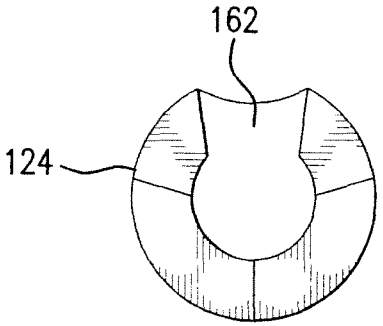


FIG.19

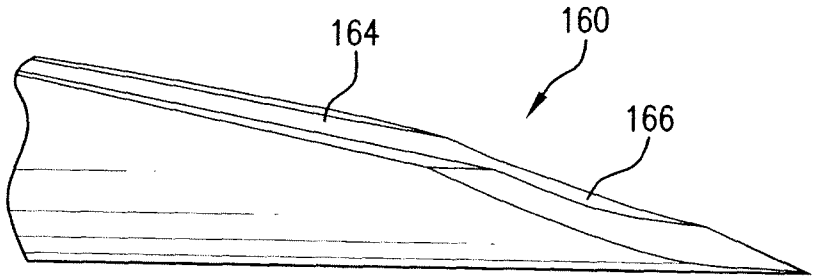


FIG.20

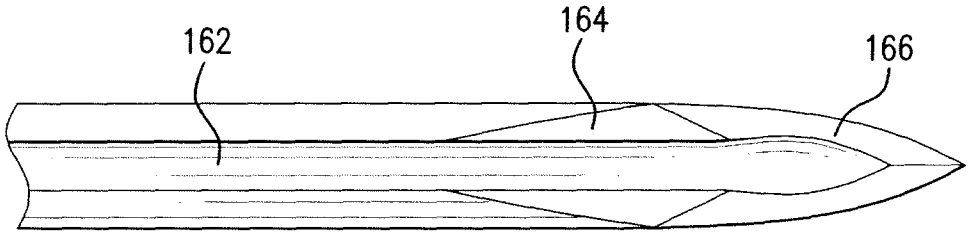


FIG.21

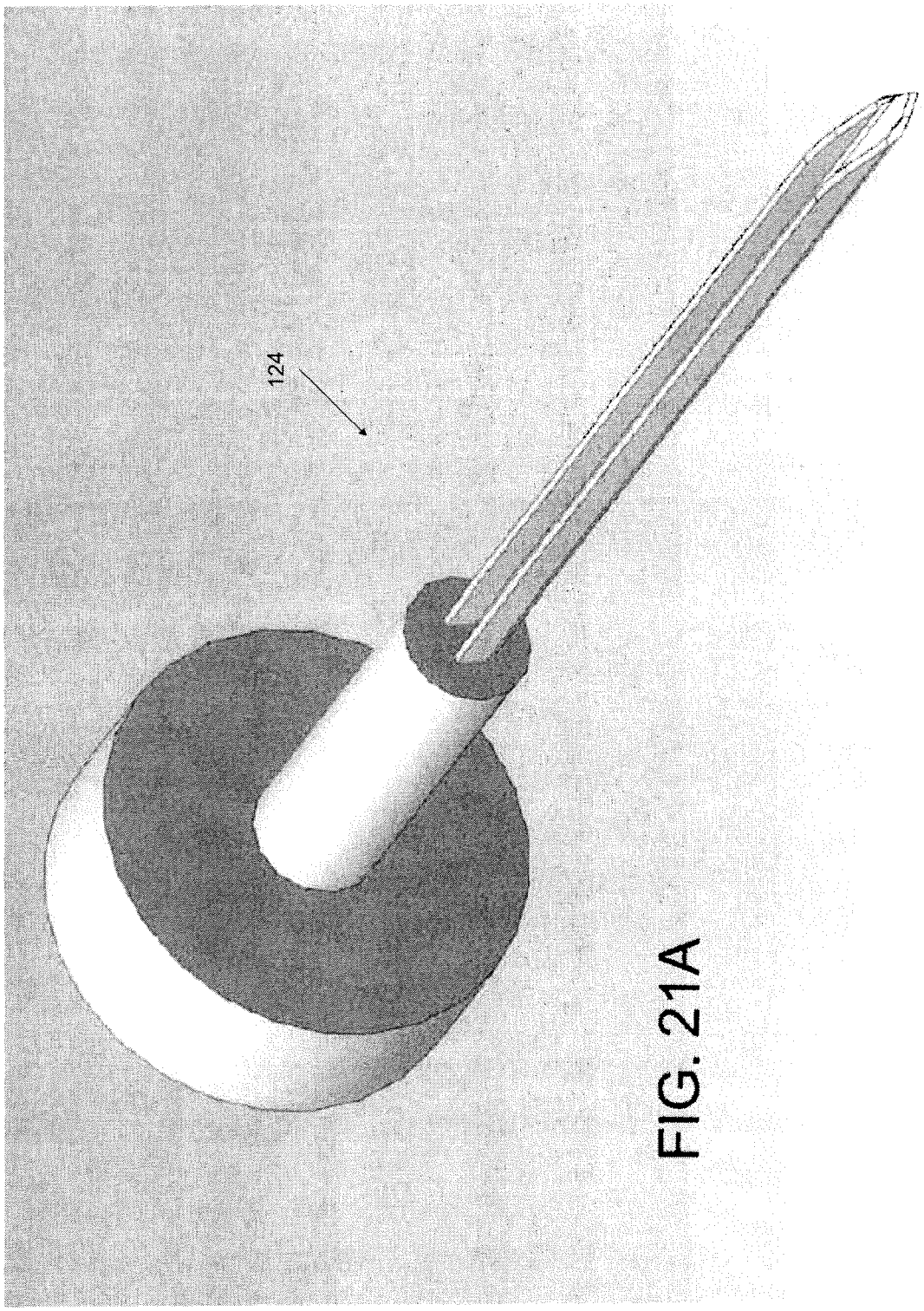


FIG. 21A

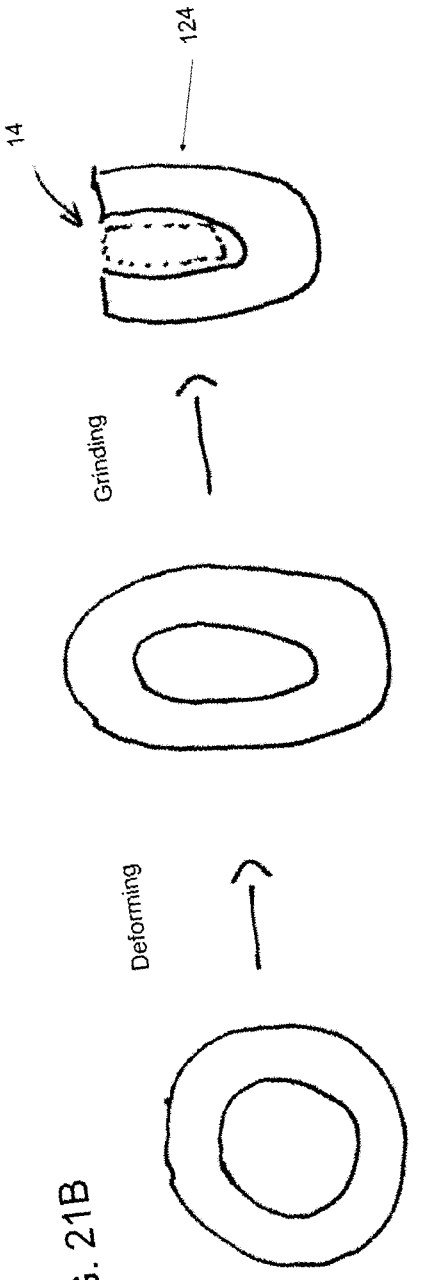


FIG. 21B

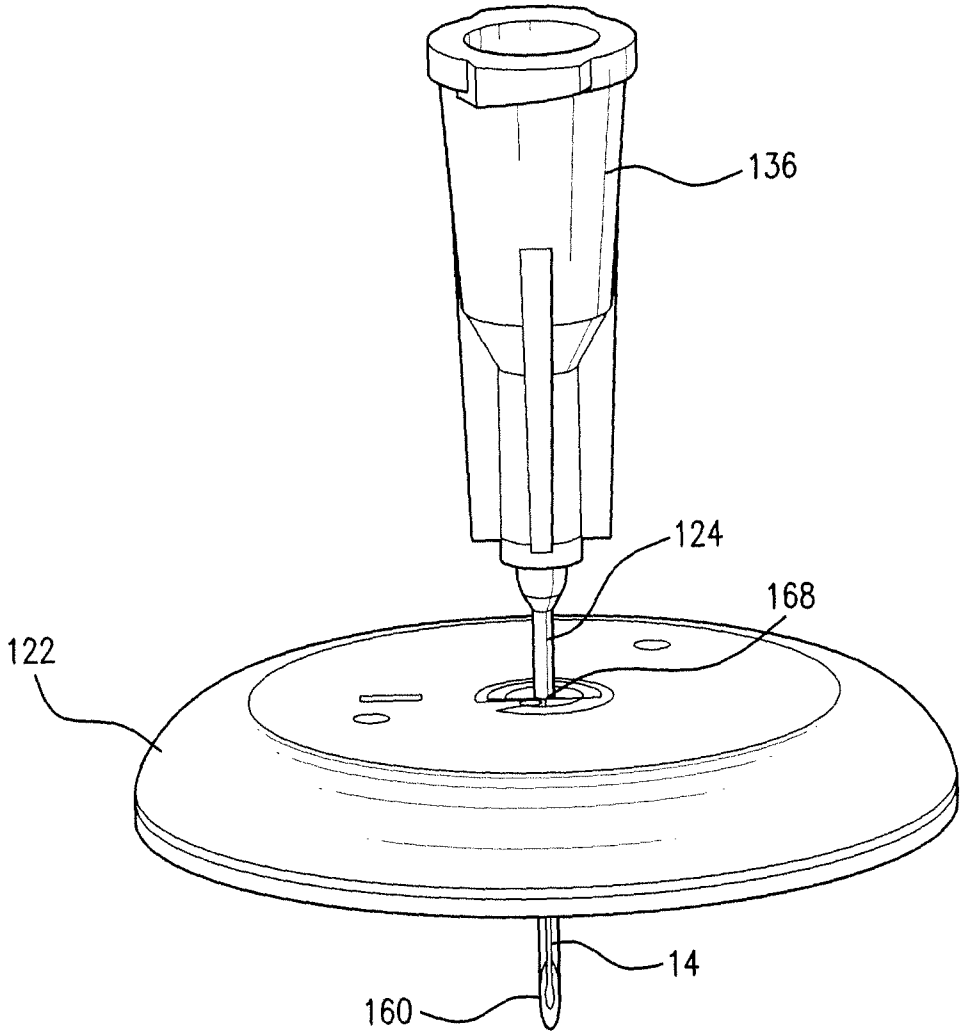


FIG.22

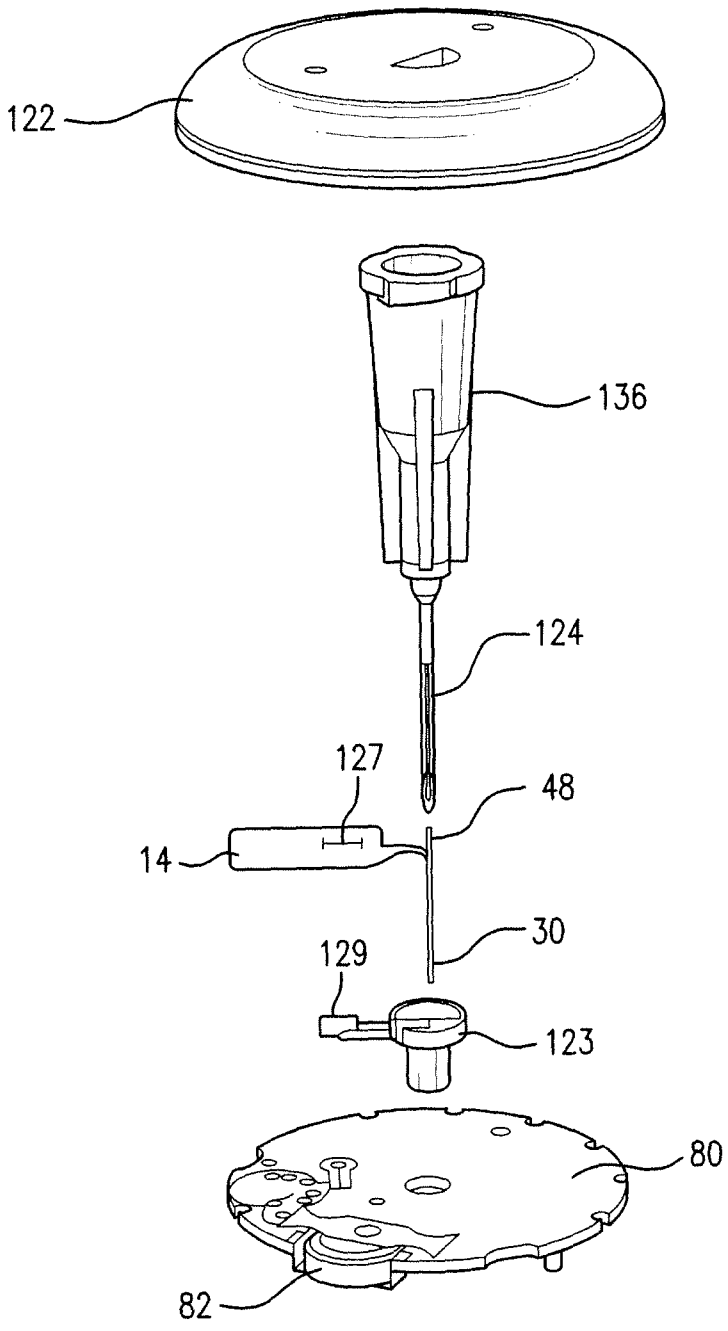


FIG.23

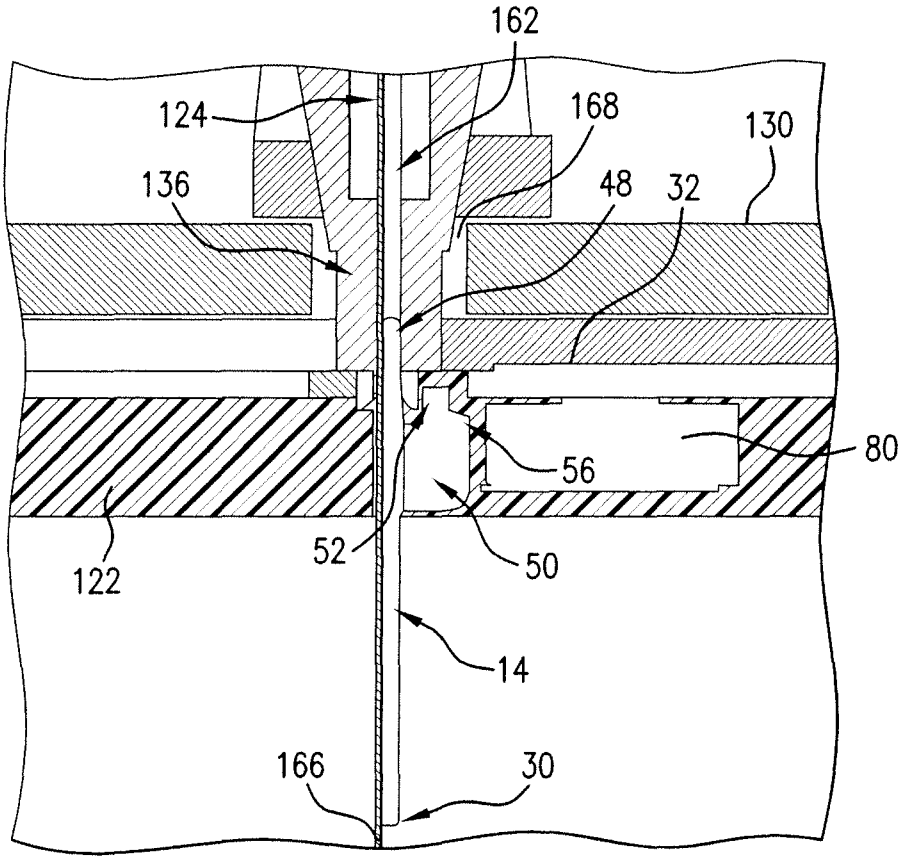


FIG.24

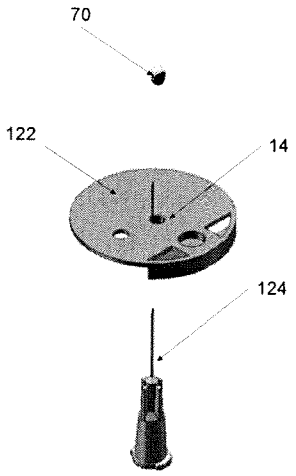


FIGURE 24A

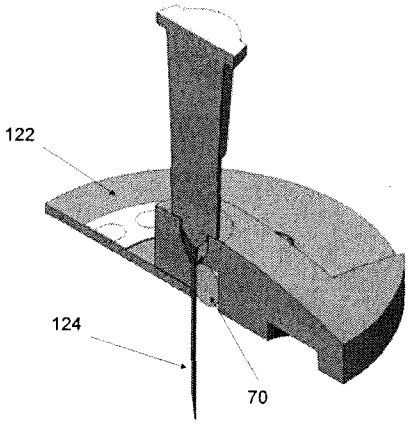


FIGURE 24B

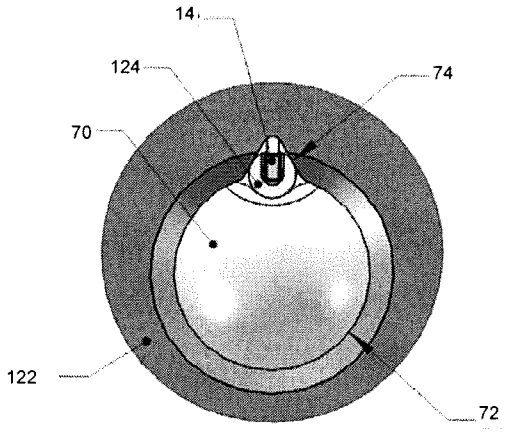


FIGURE 24C

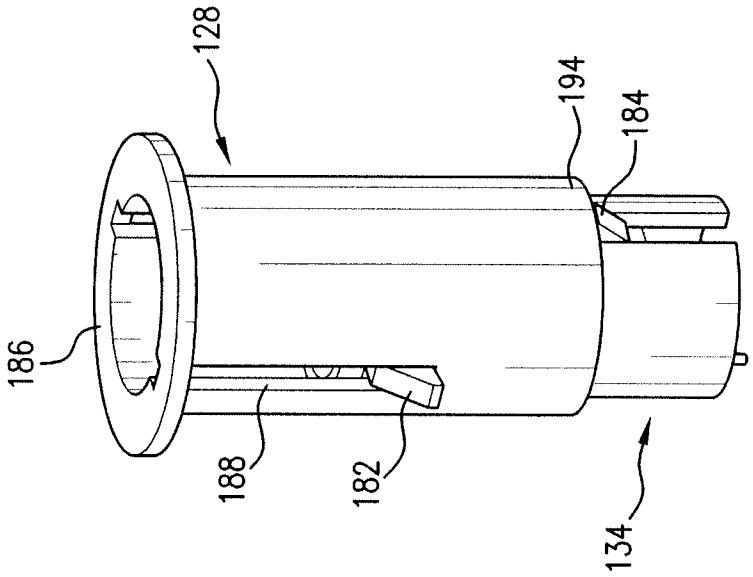


FIG.26

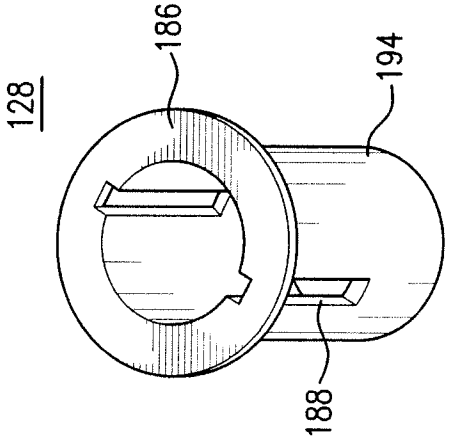


FIG.25

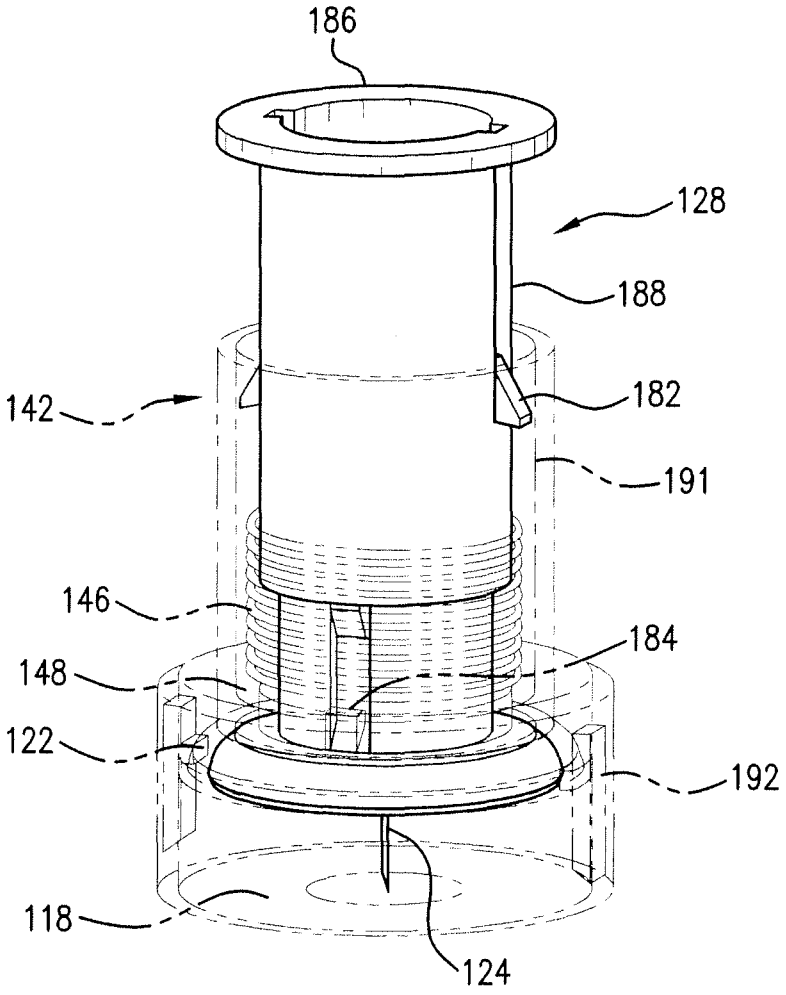


FIG.27

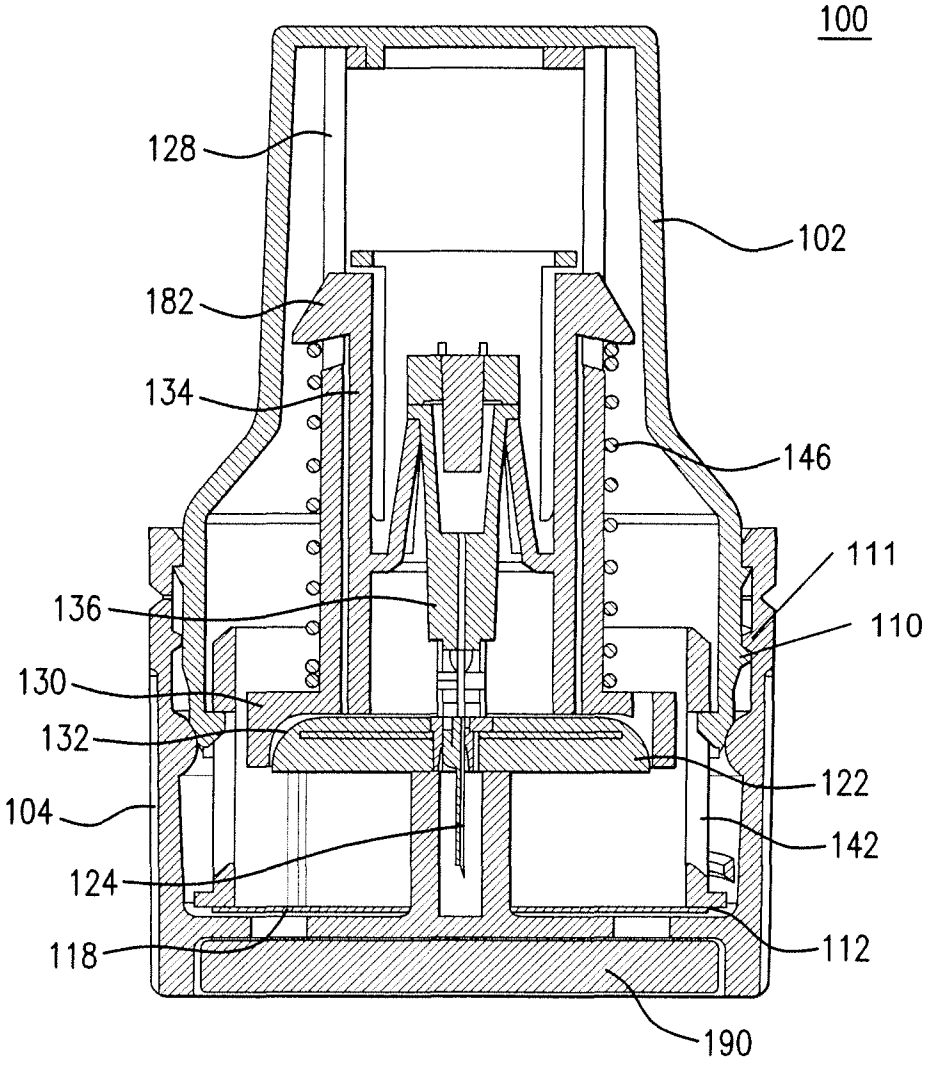

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FIG.28

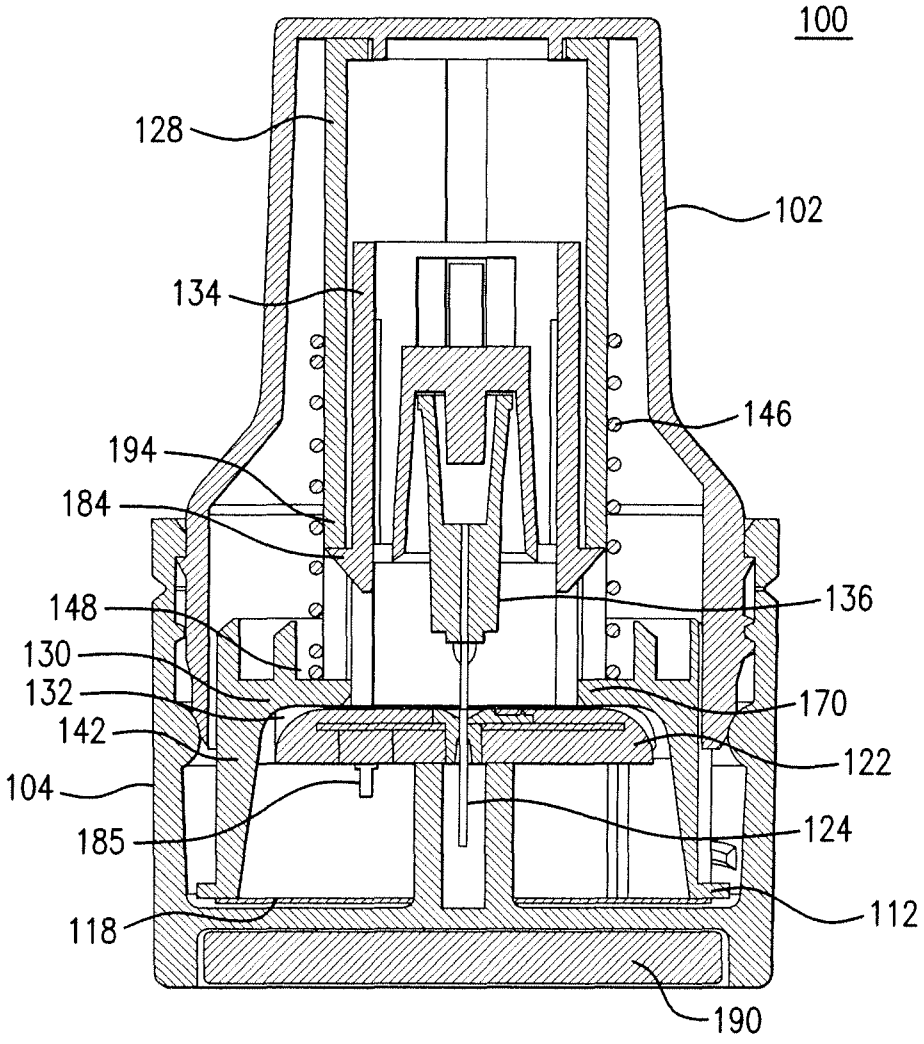

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FIG.29

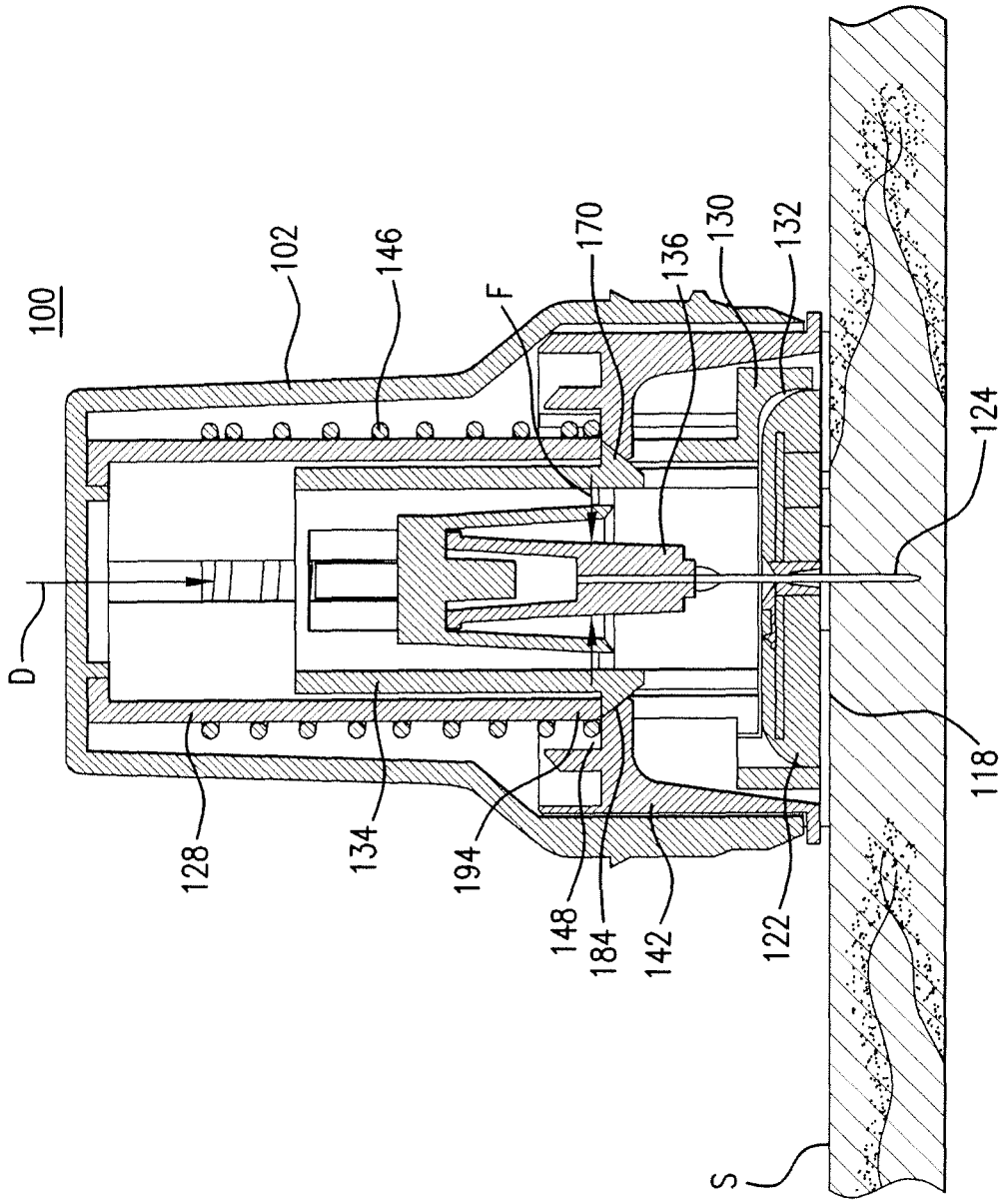

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FIG.30

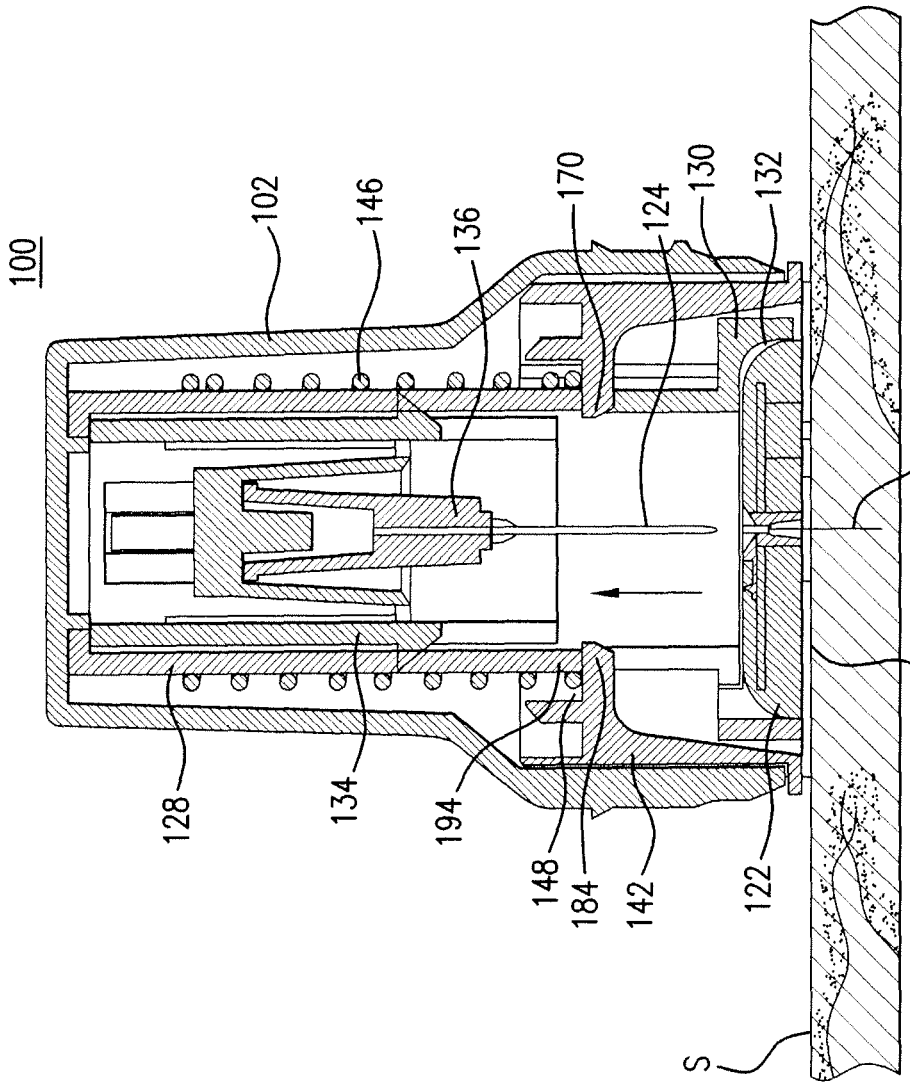

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FIG.31

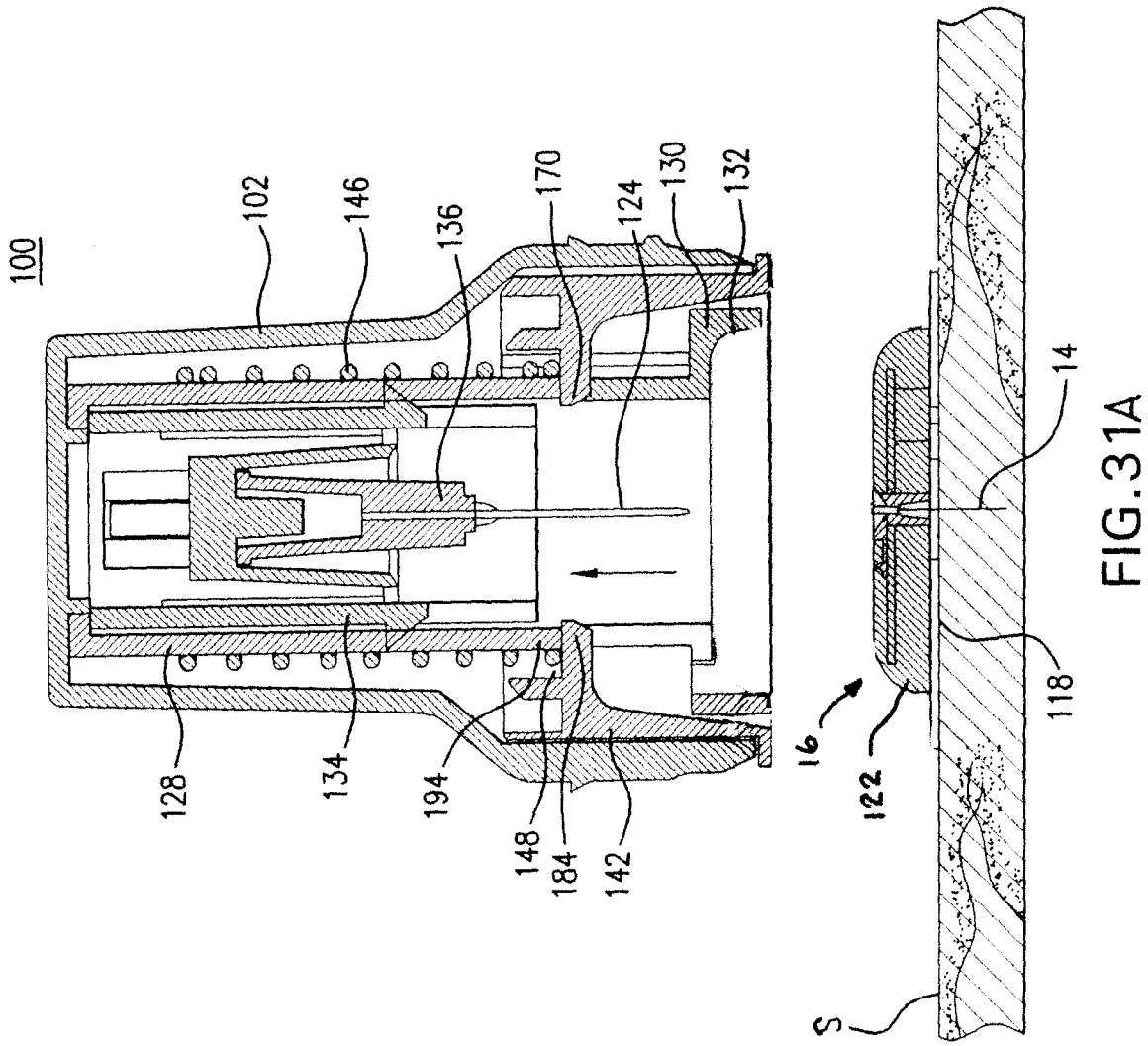

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FIG.31A

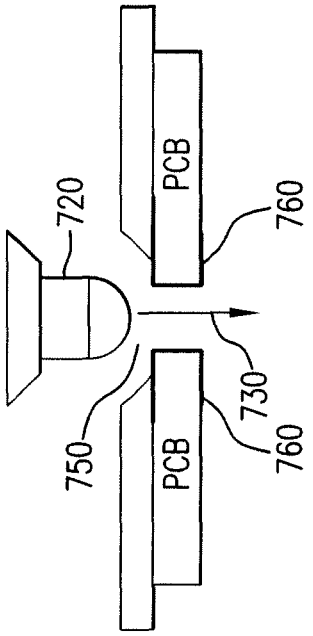


FIG.32

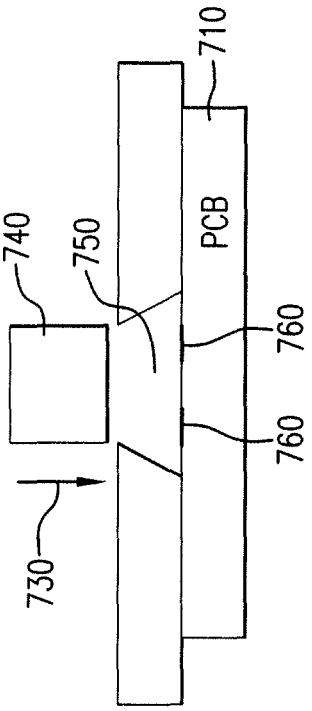


FIG.33

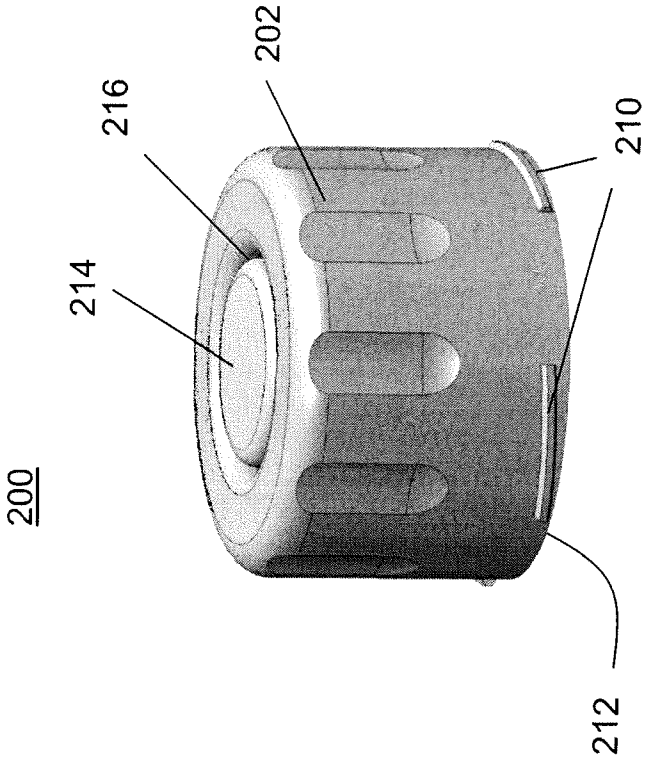


FIGURE 35

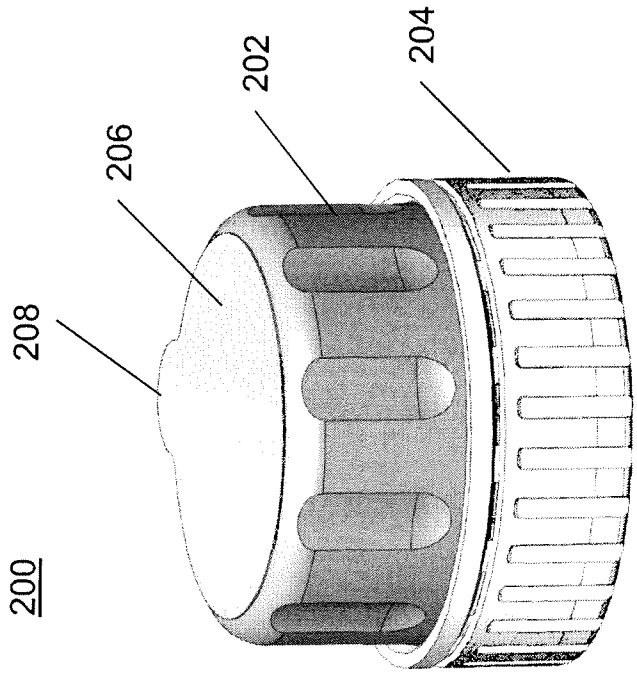


FIGURE 34

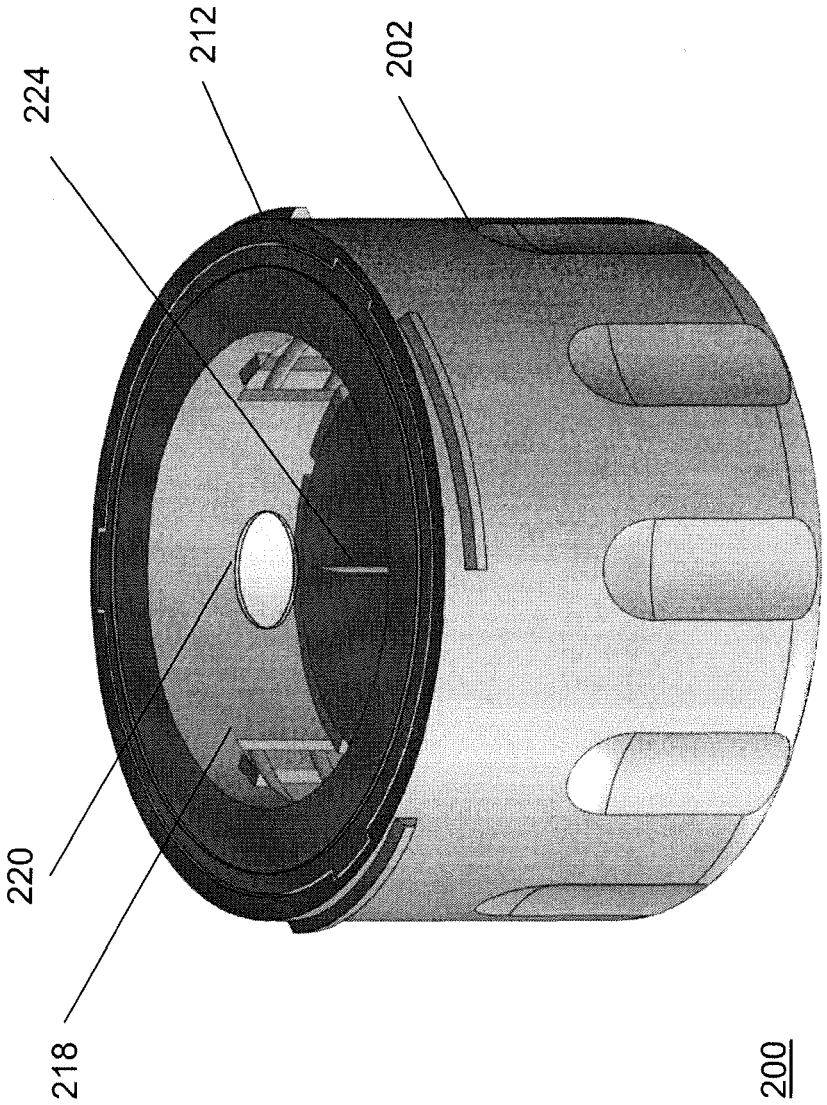


FIGURE 36

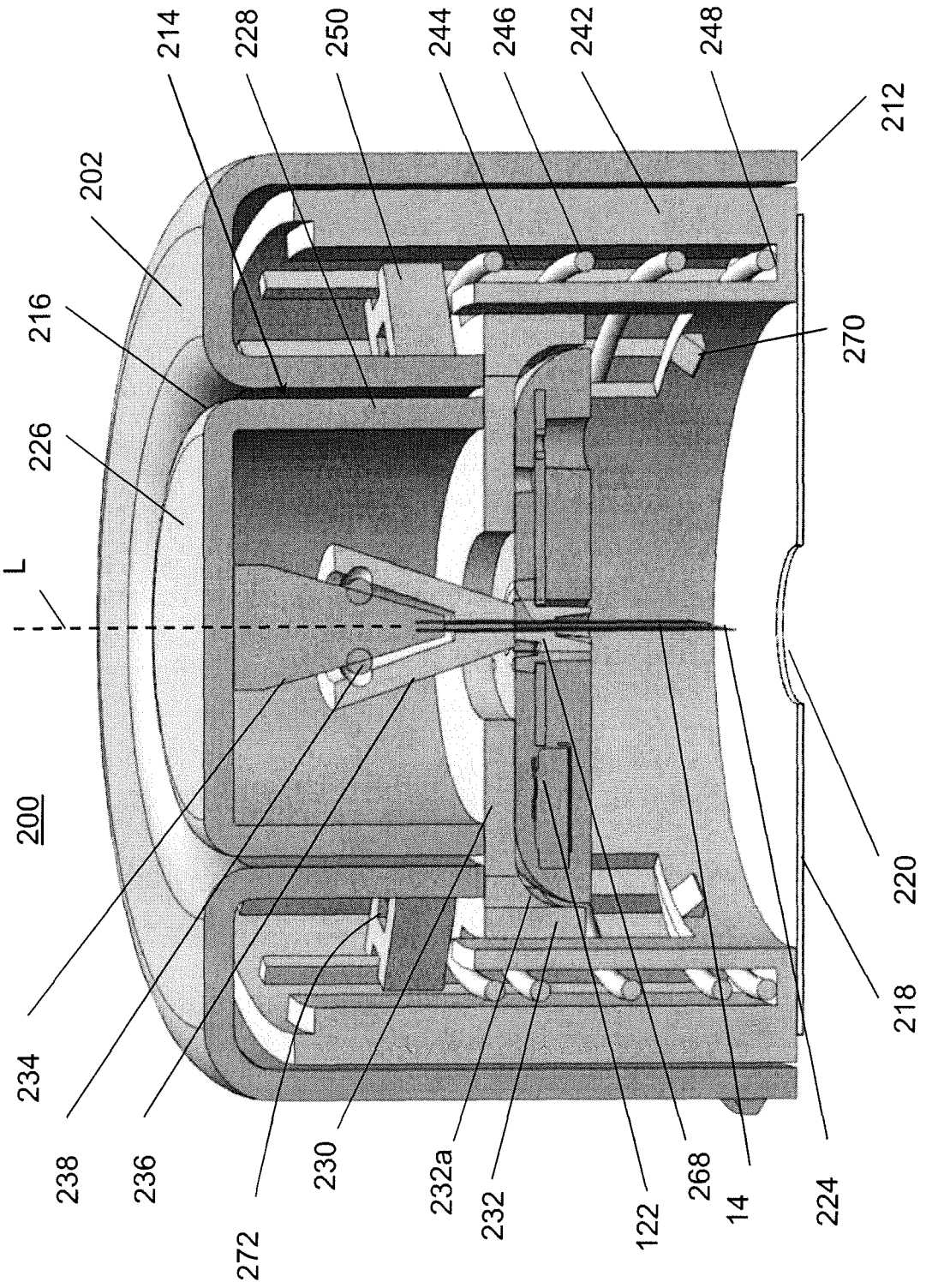

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FIGURE 37

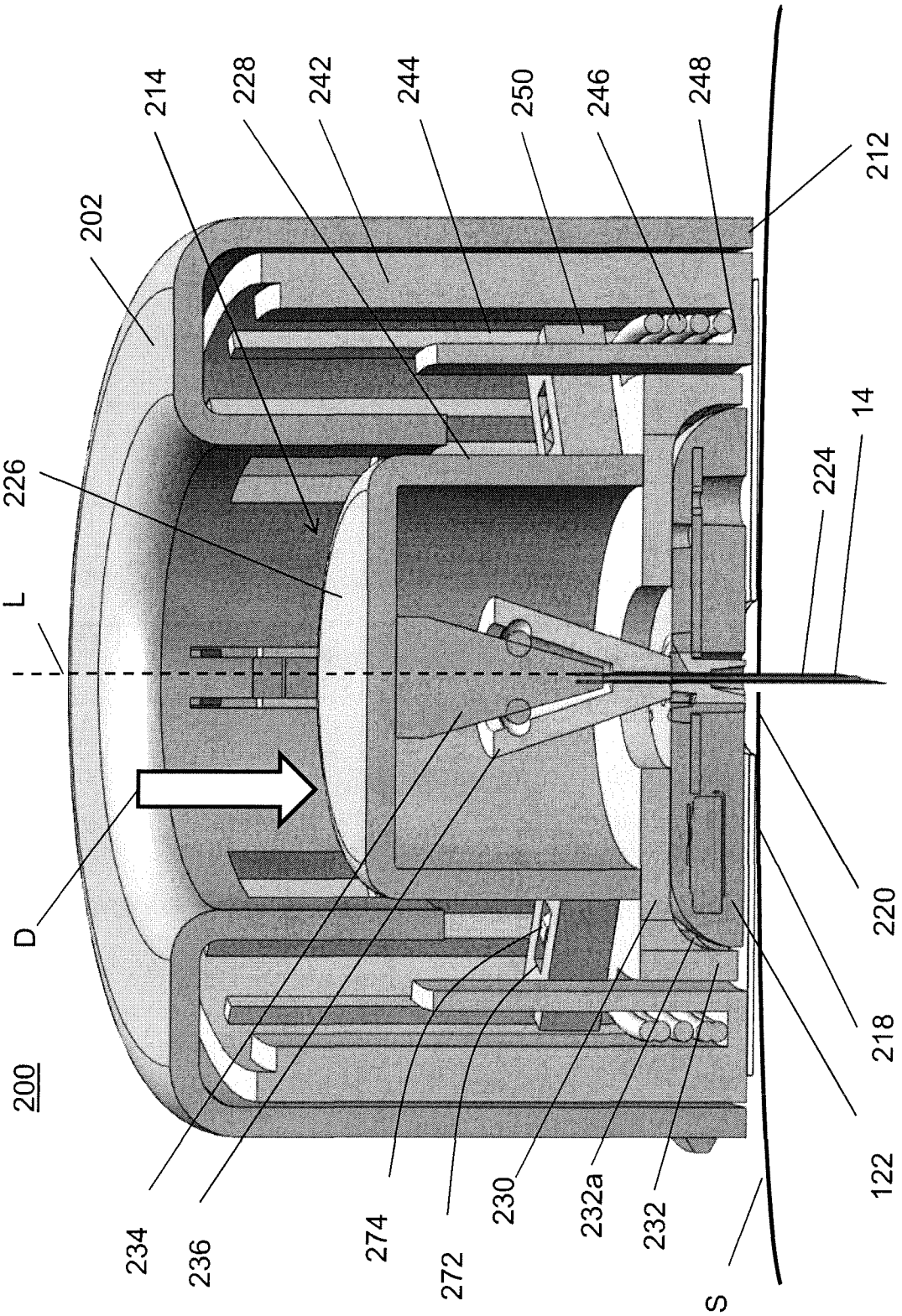

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FIGURE 38

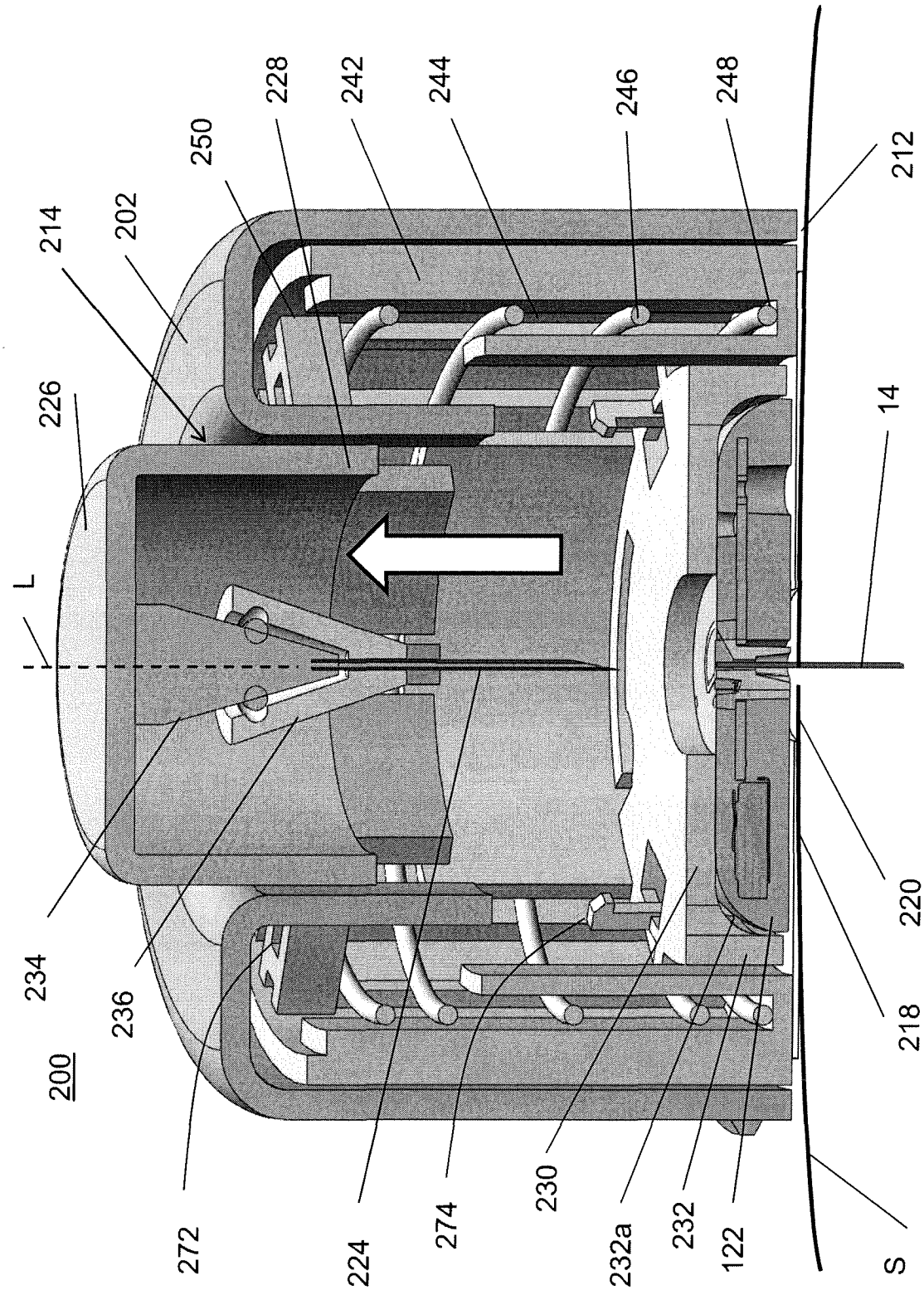

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FIGURE 39

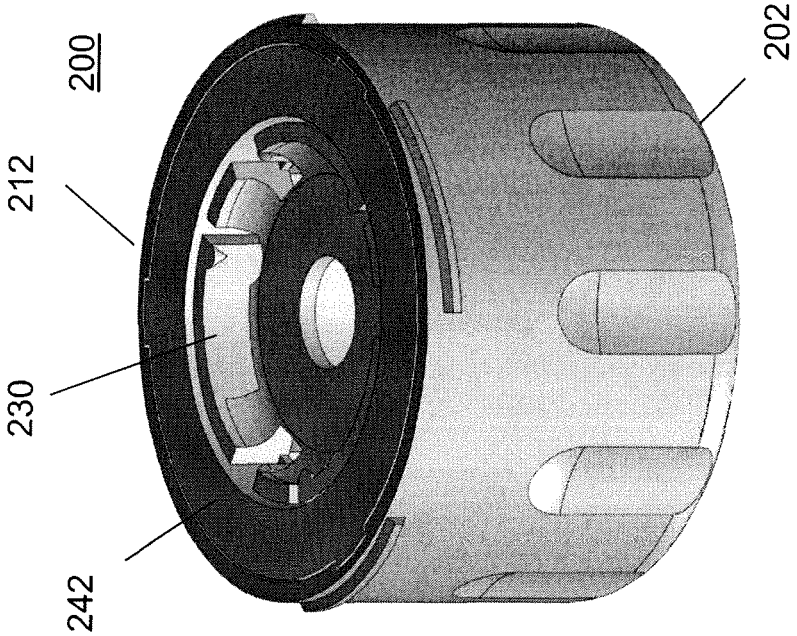


FIGURE 41

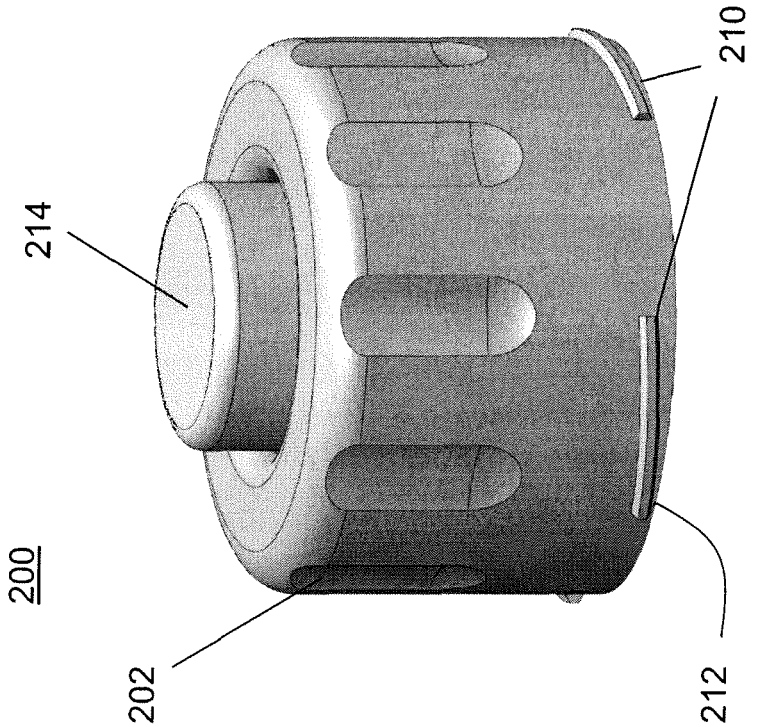


FIGURE 40

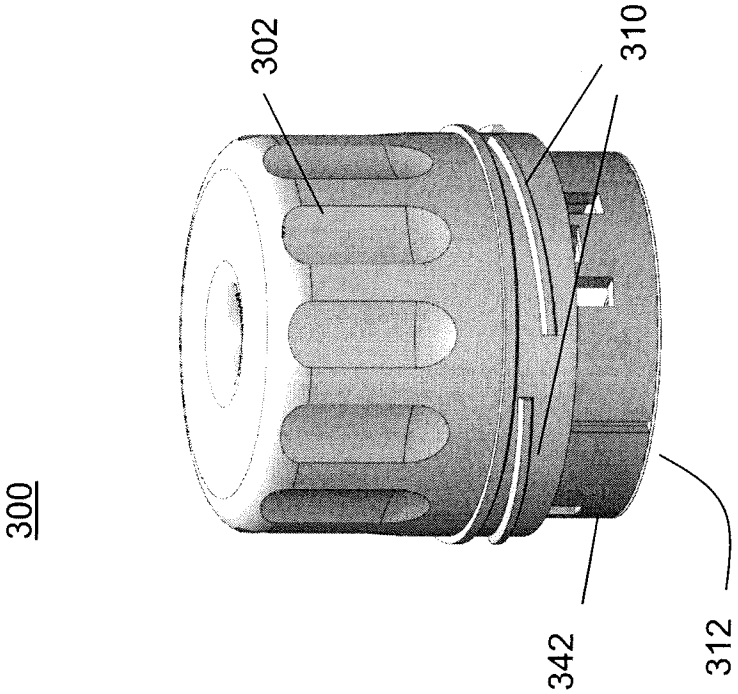


FIGURE 43

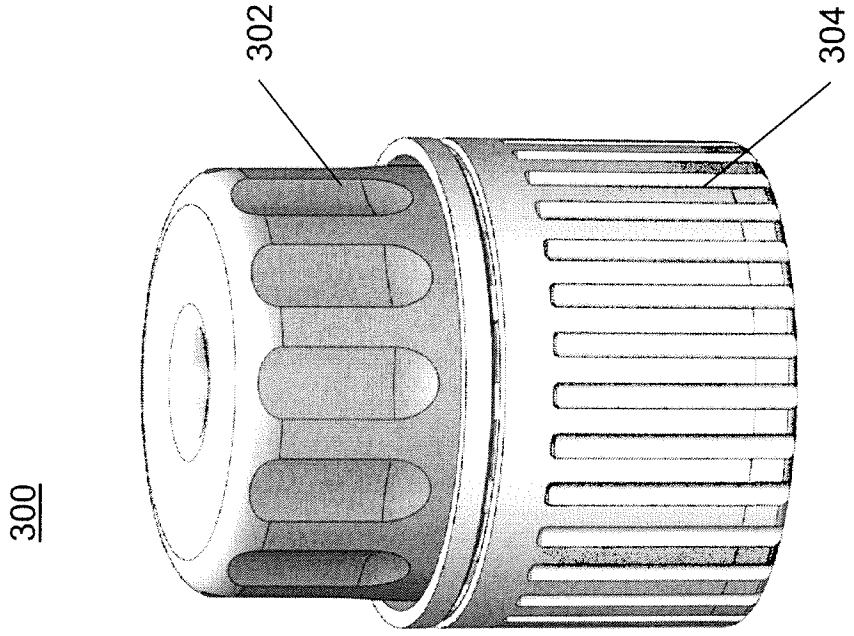


FIGURE 42

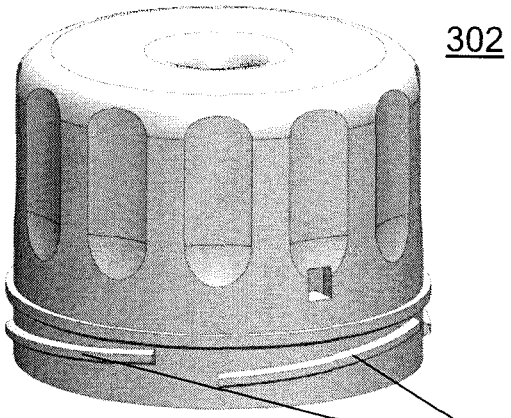


FIGURE 44

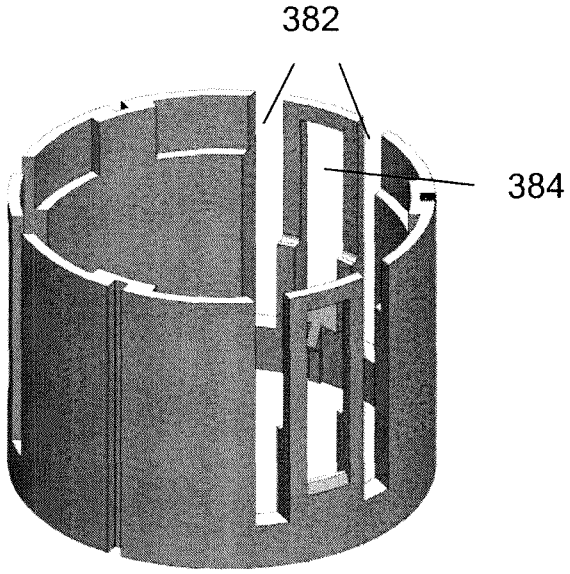


FIGURE 45

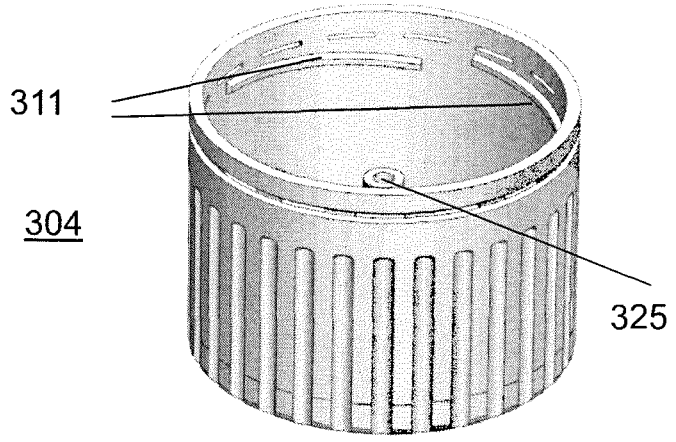


FIGURE 46

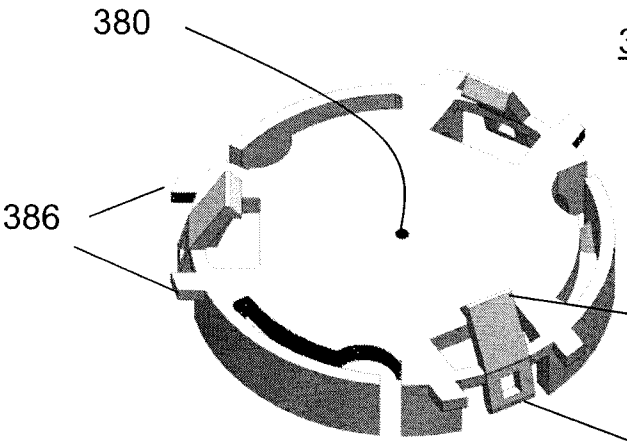


FIGURE 47

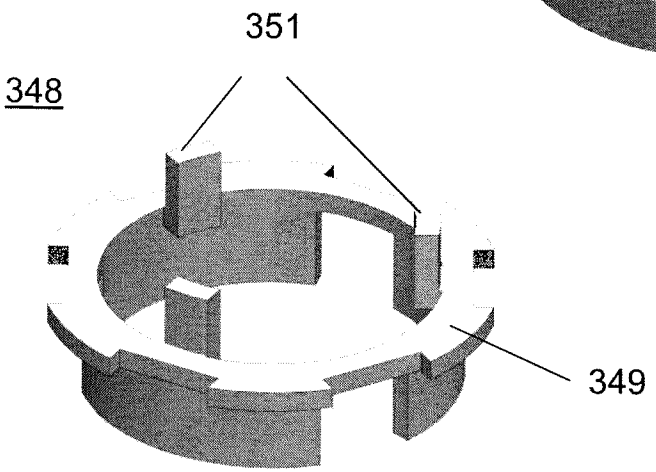


FIGURE 48

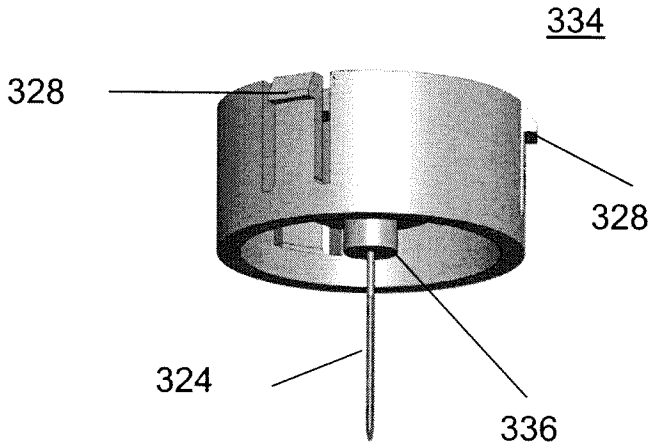


FIGURE 49

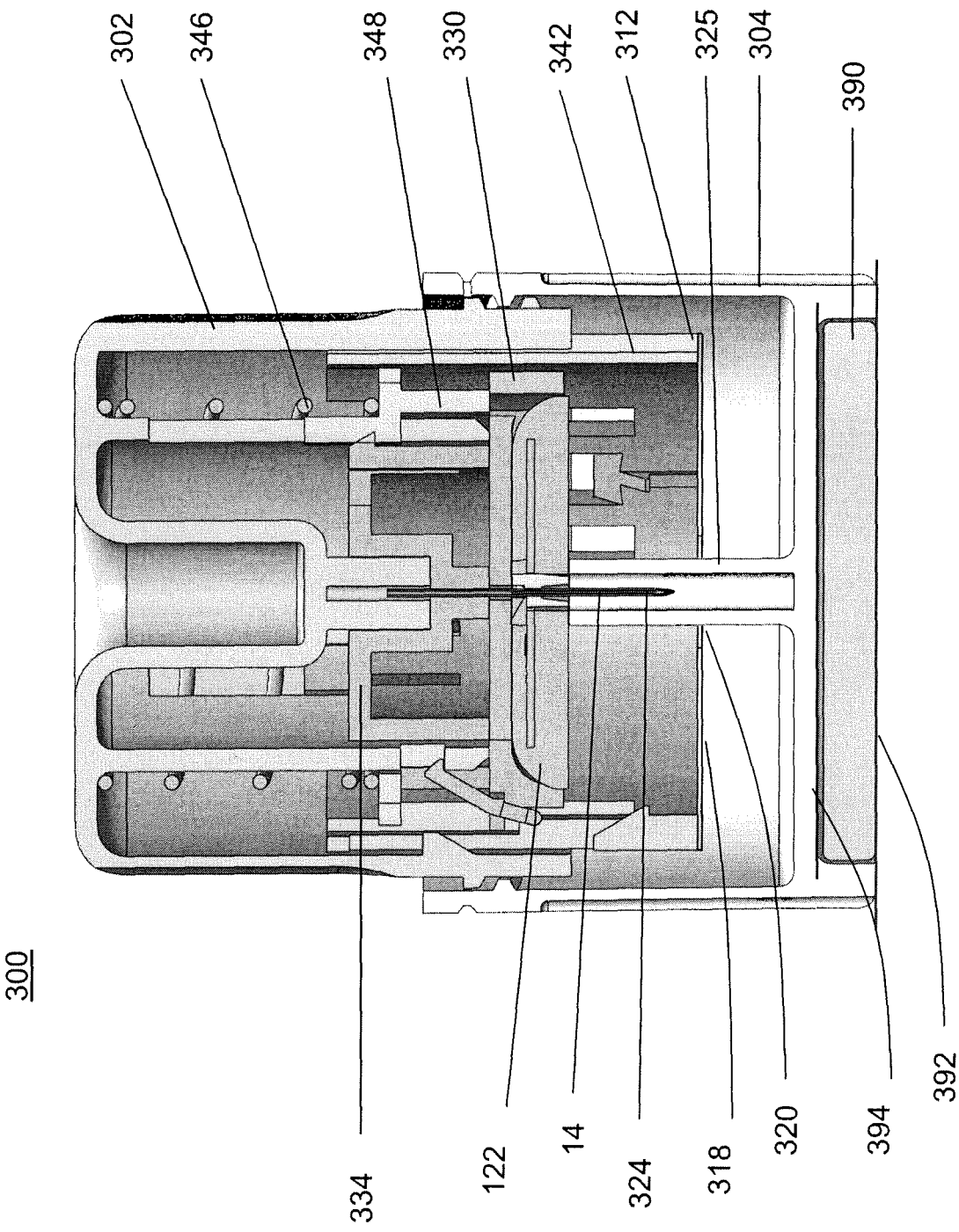

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FIGURE 50

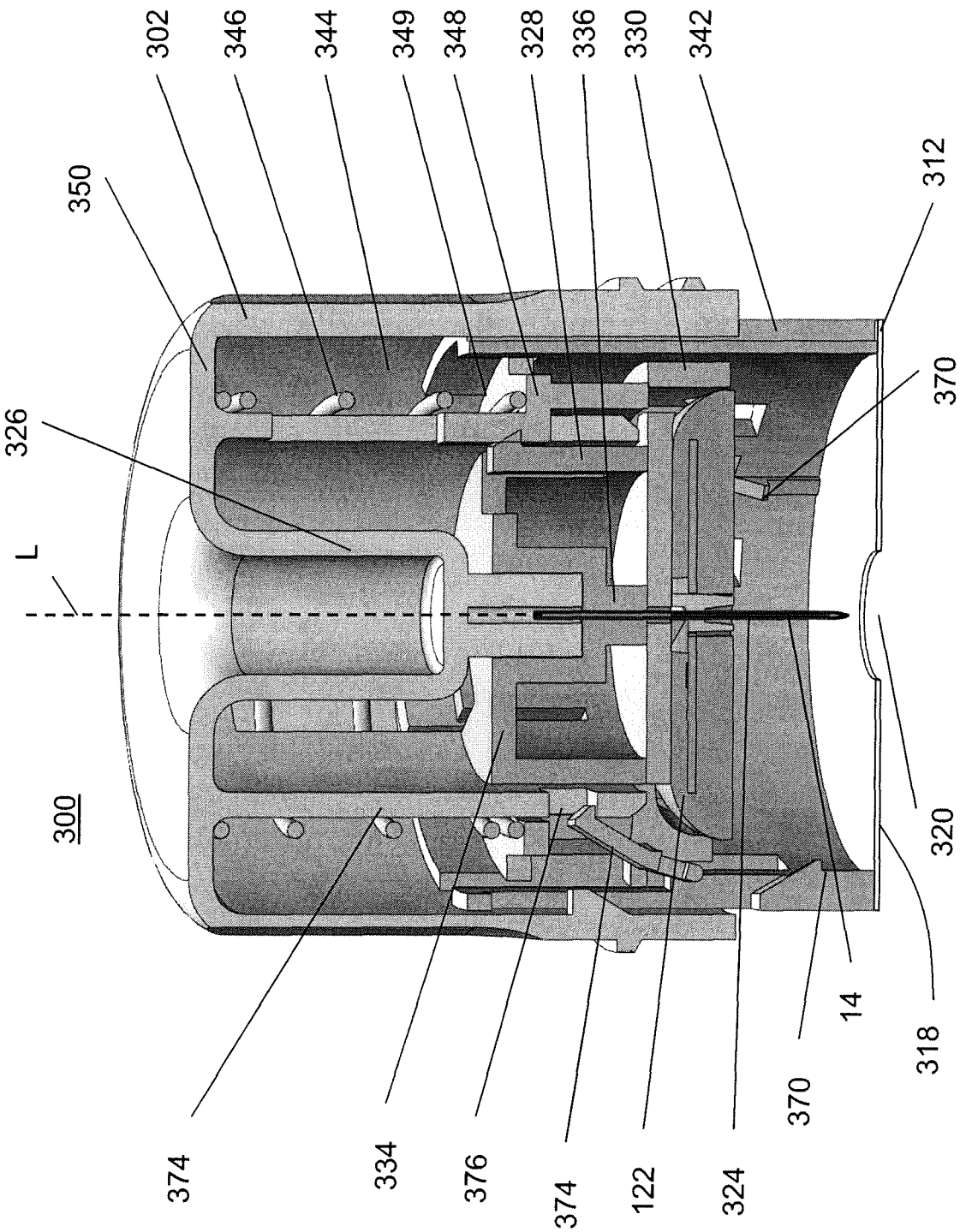

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FIGURE 51

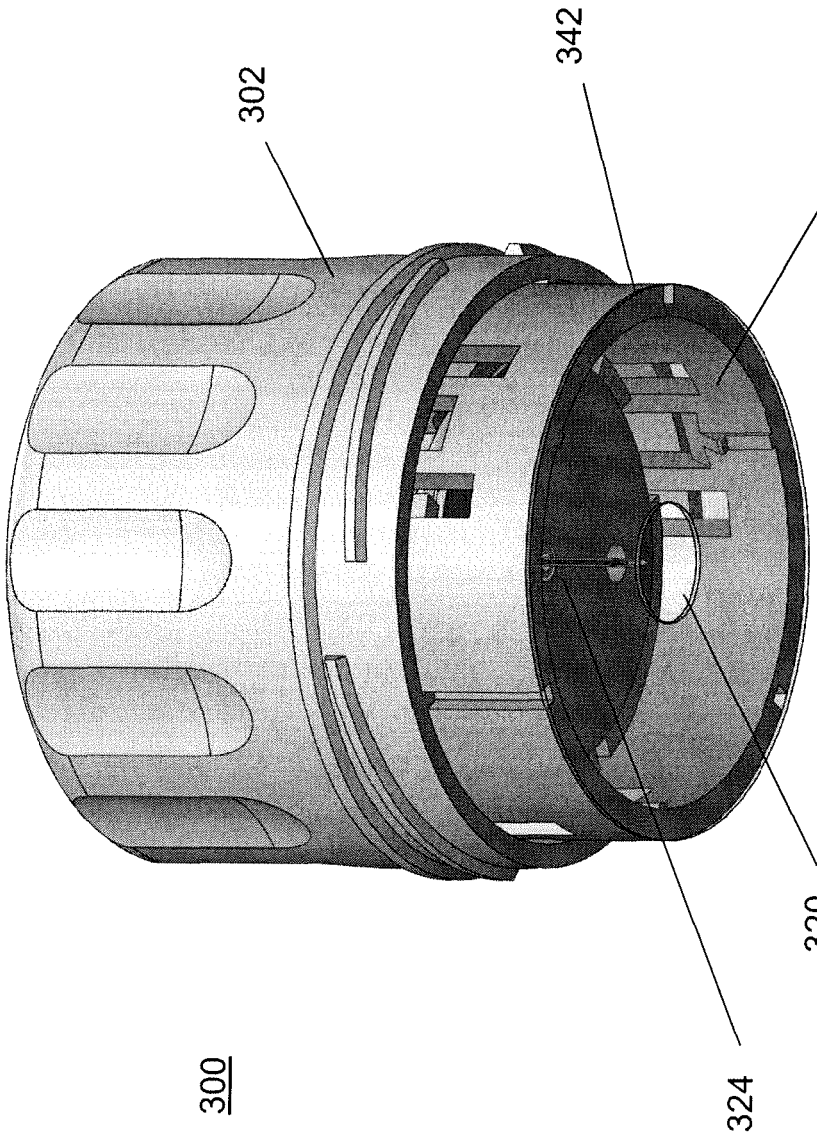


FIGURE 52

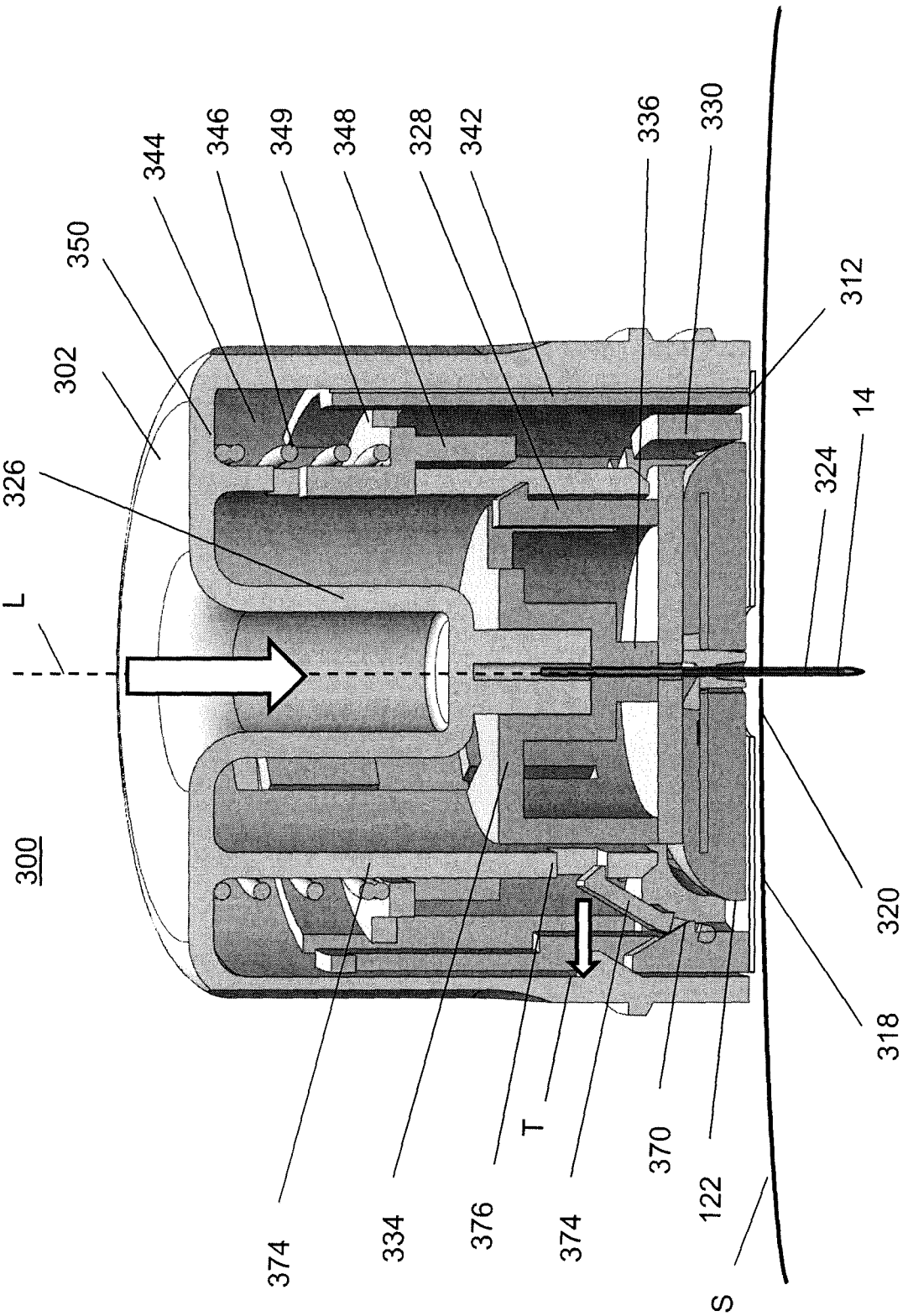

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FIGURE 53

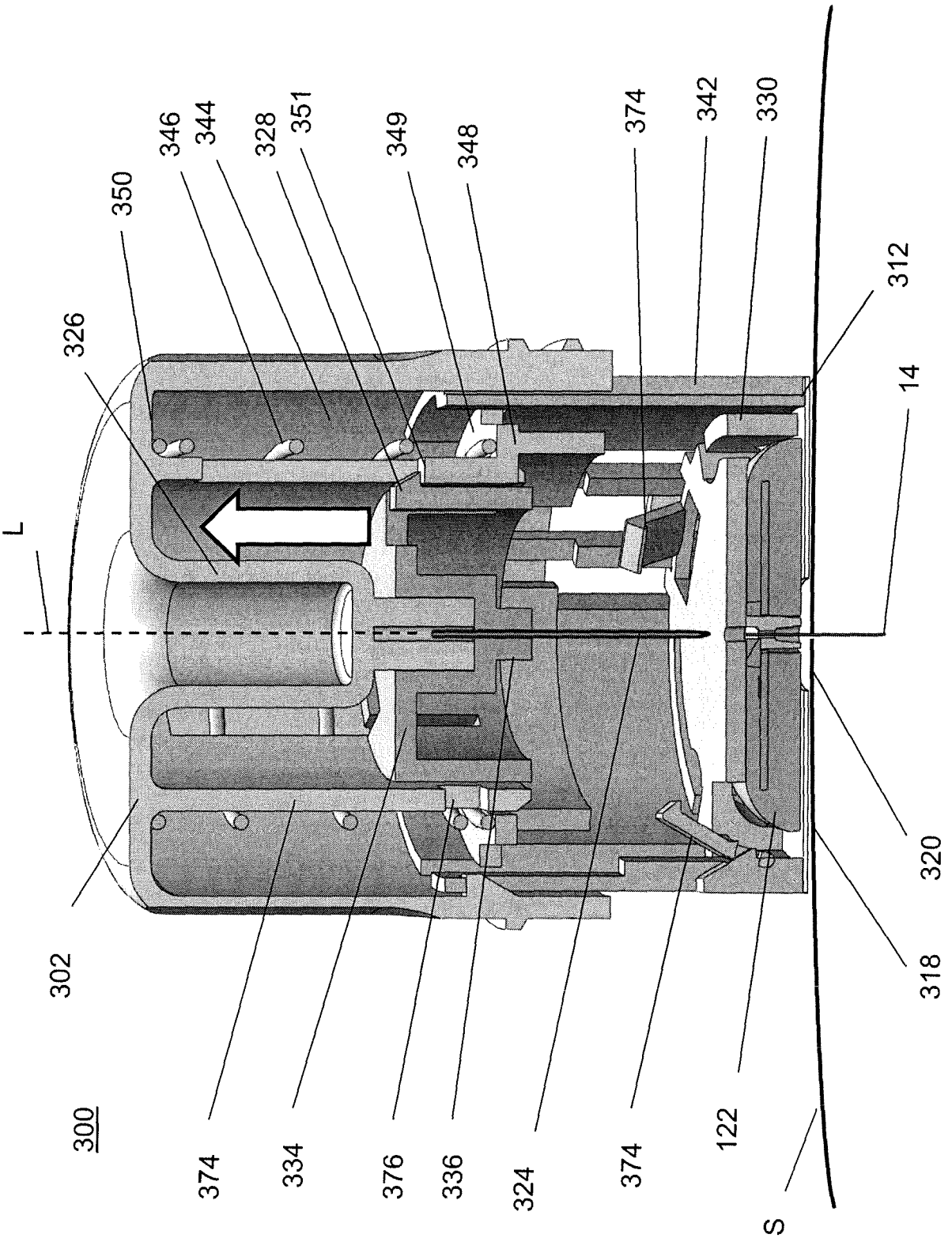

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FIGURE 54

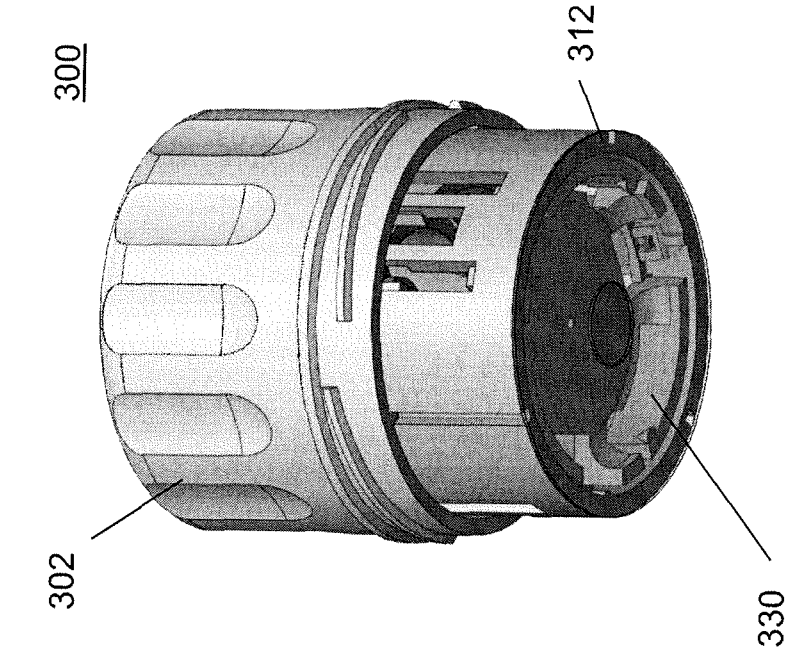


FIGURE 56

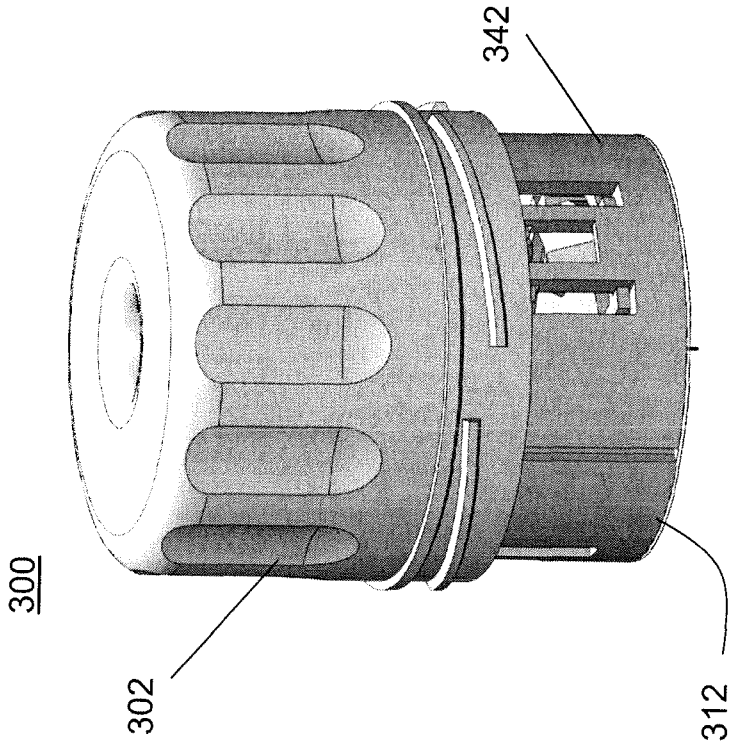


FIGURE 55

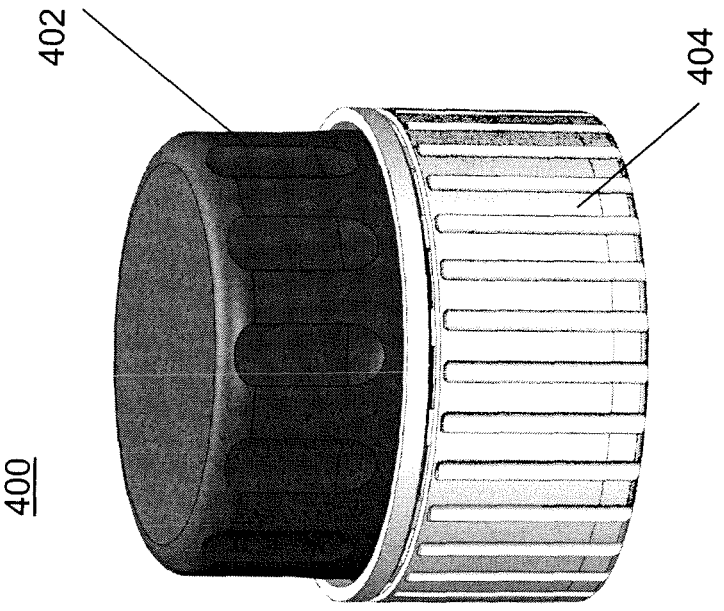


FIGURE 57

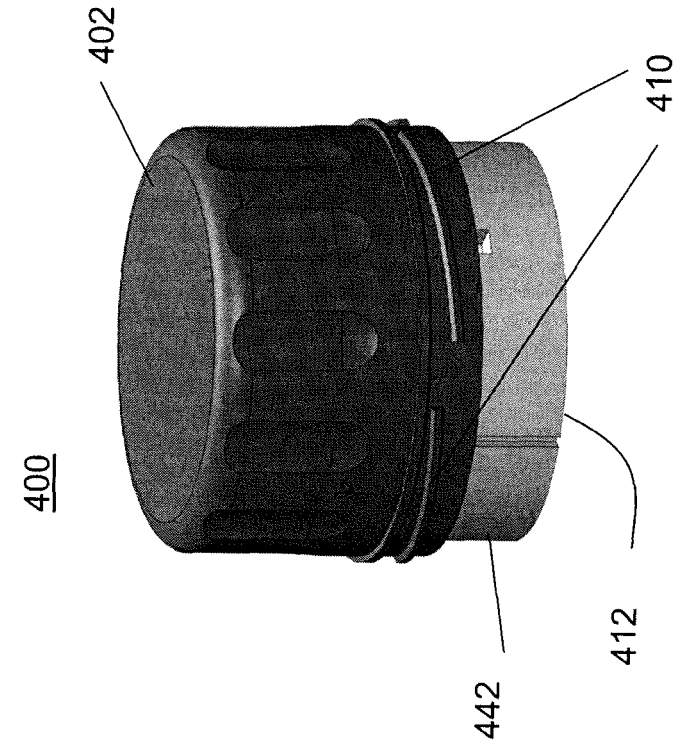


FIGURE 58

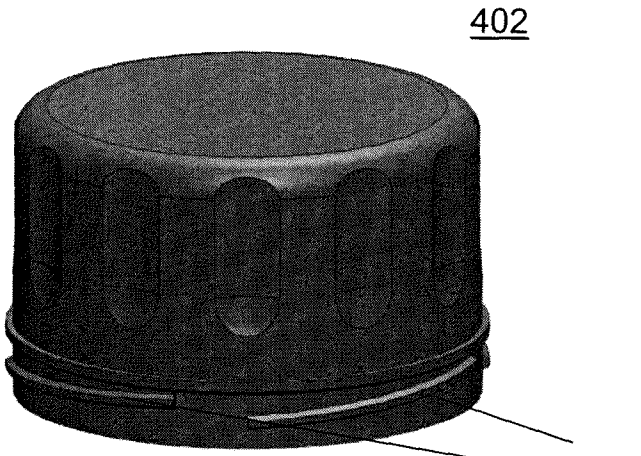


FIGURE 59

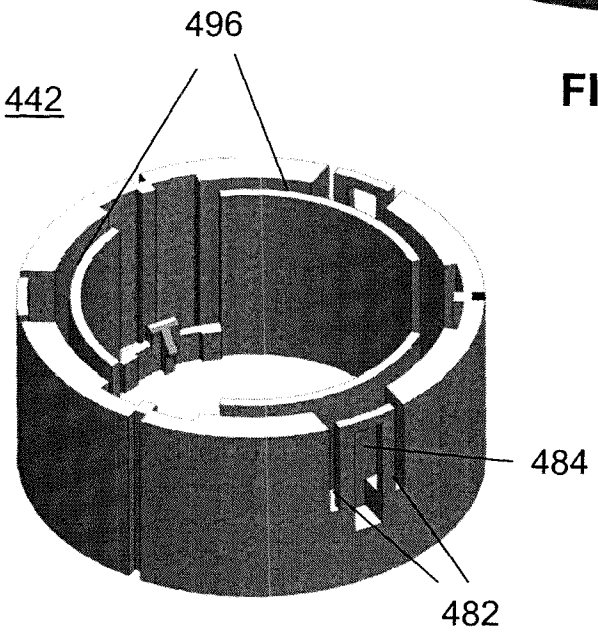


FIGURE 60

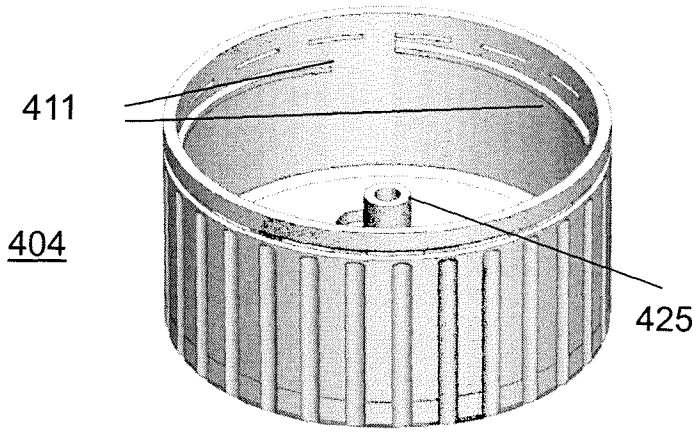


FIGURE 61

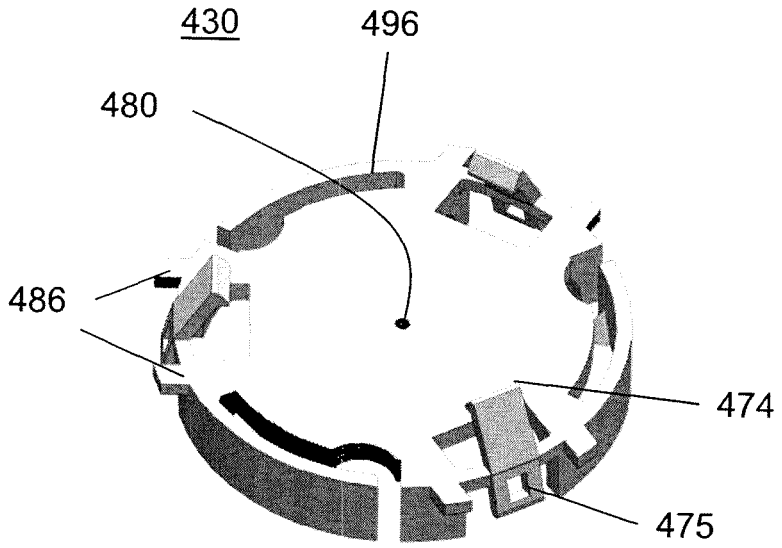


FIGURE 62

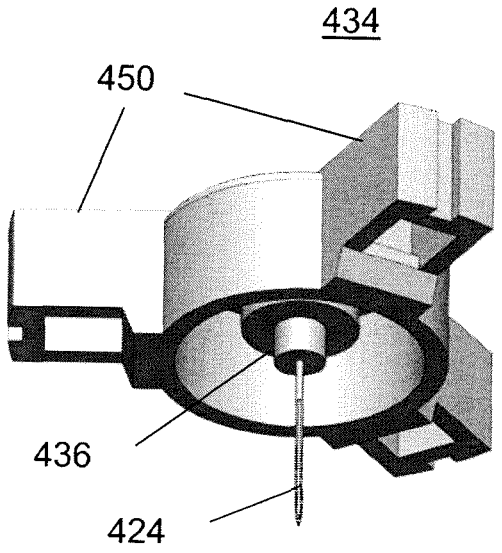


FIGURE 63

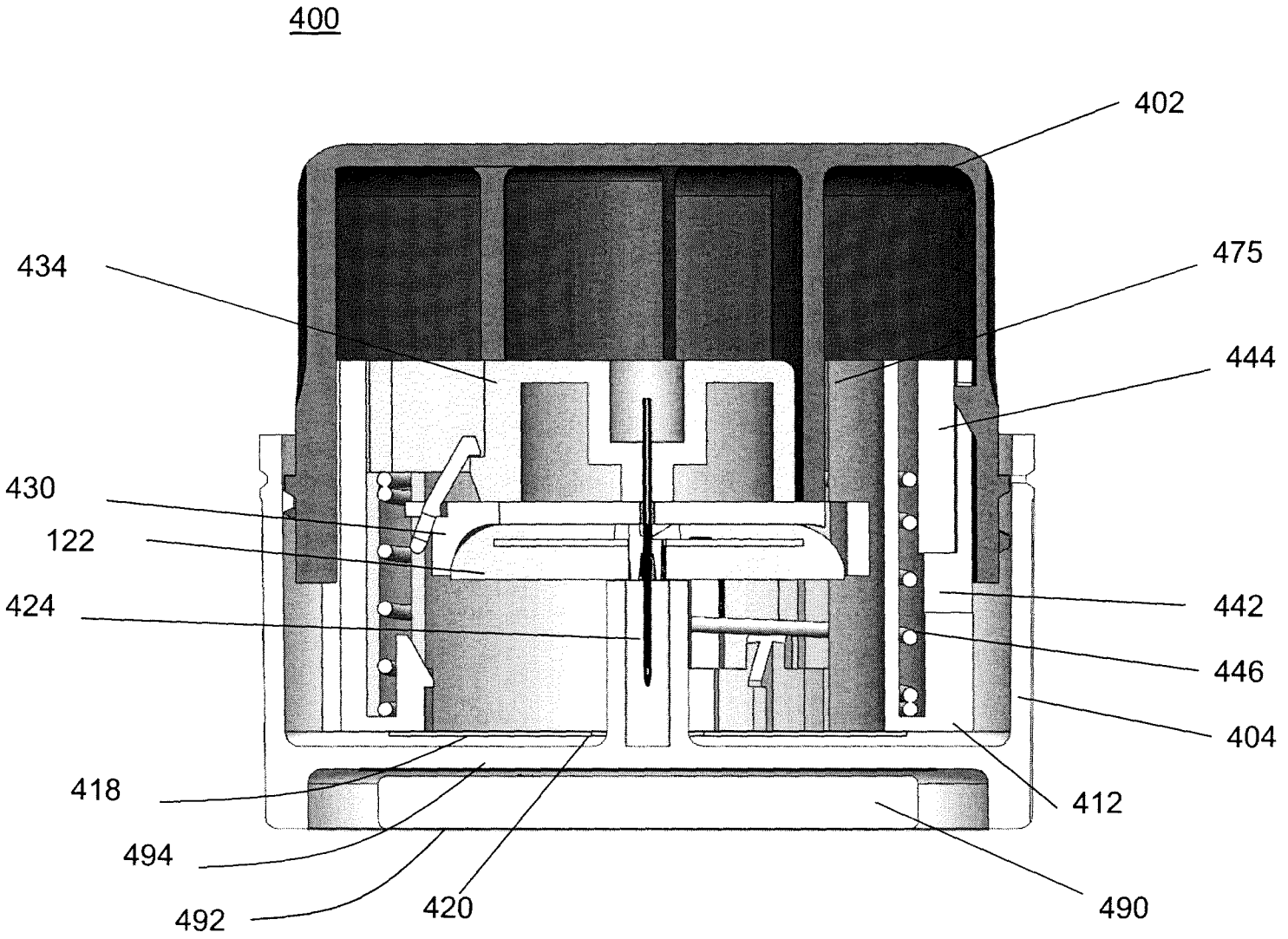

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FIGURE 64

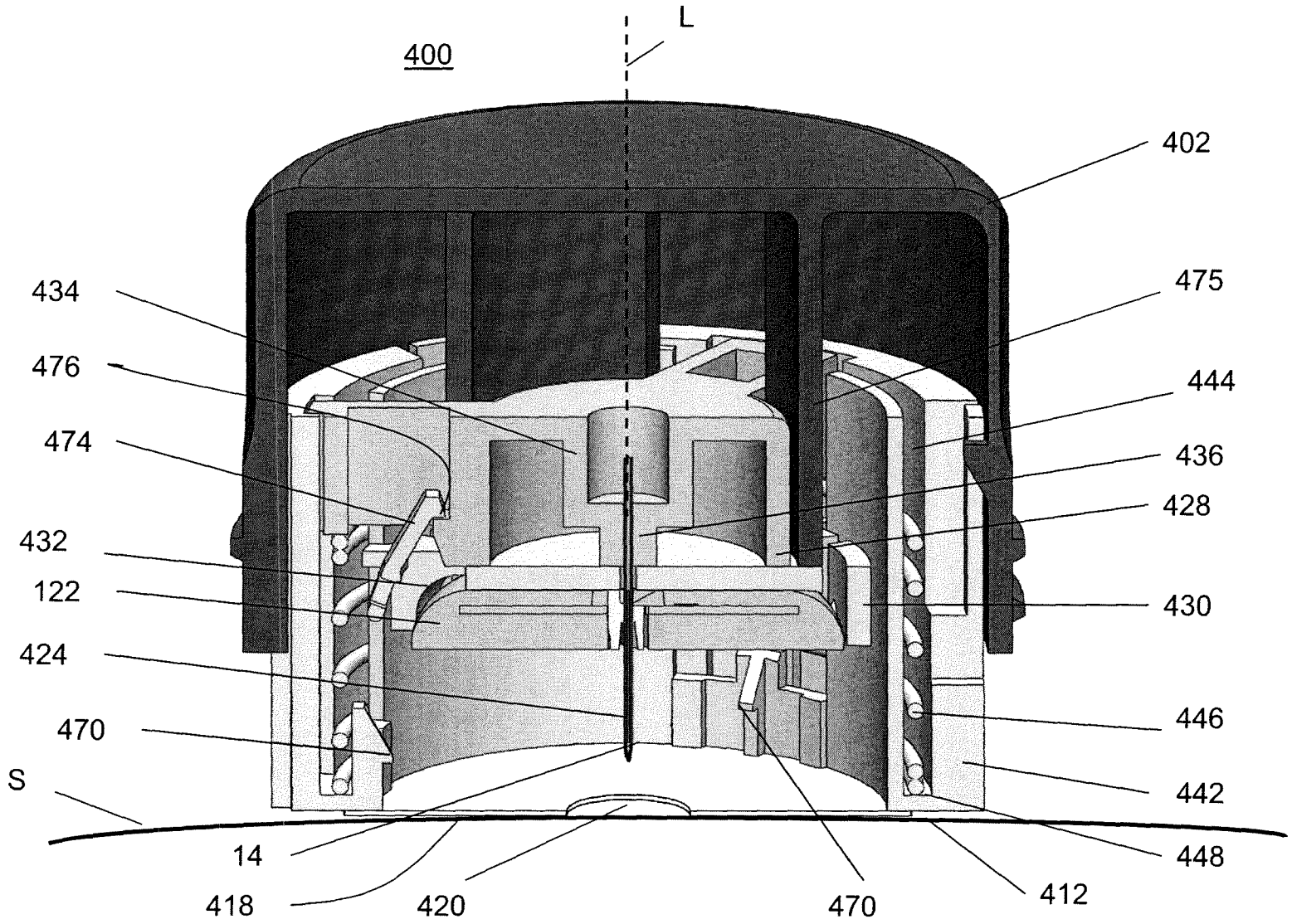

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FIGURE 65

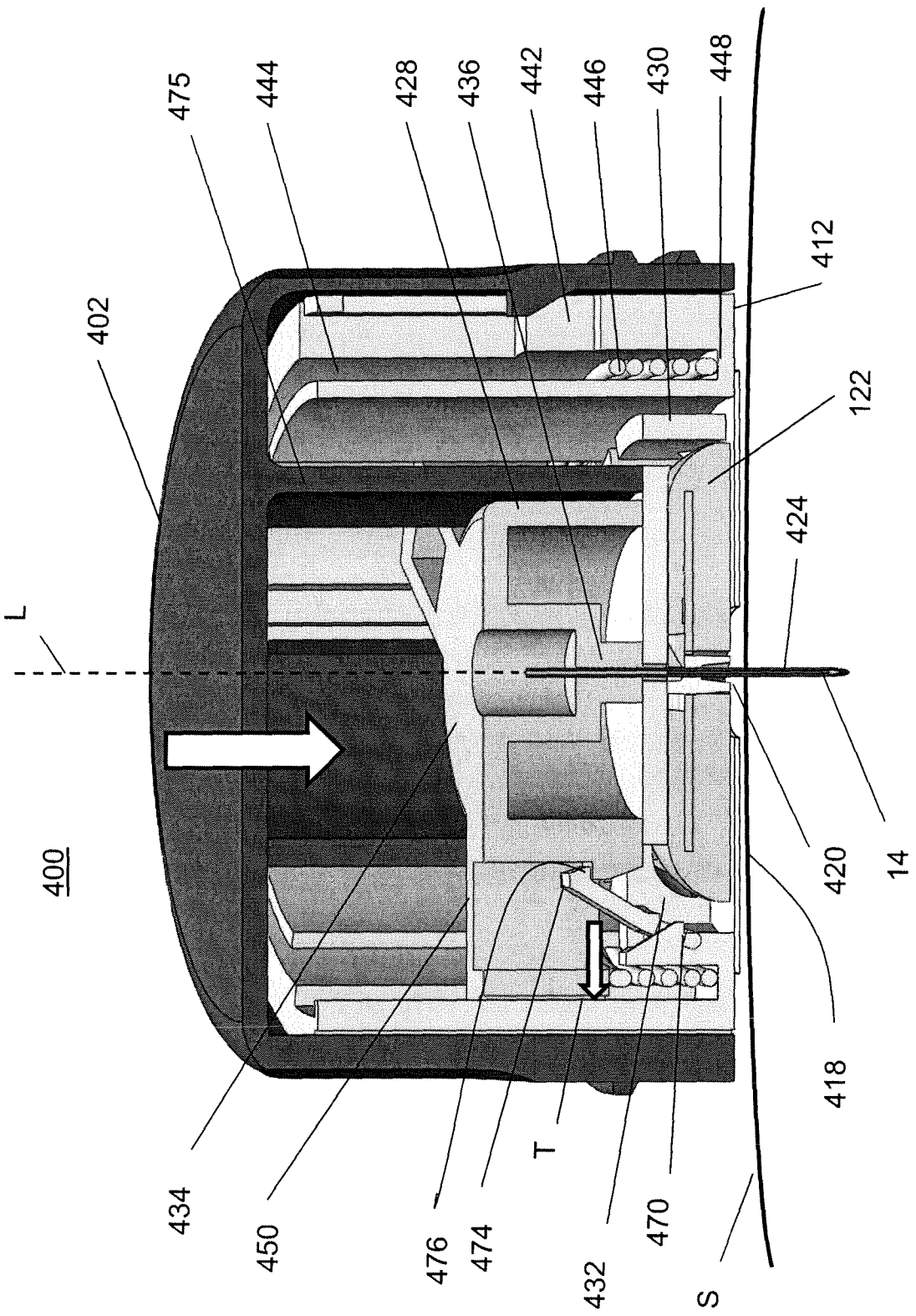

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FIGURE 66

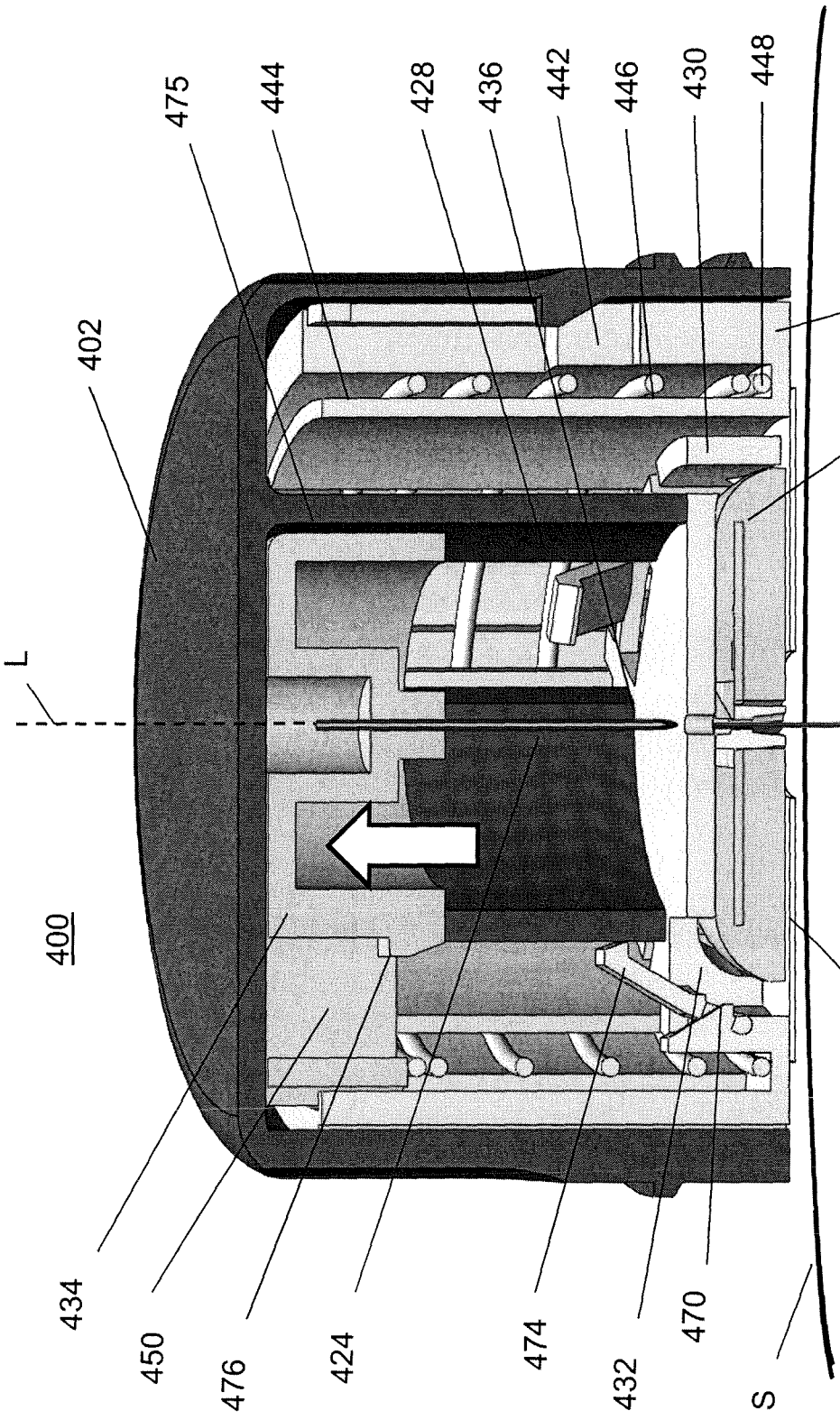

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FIGURE 67

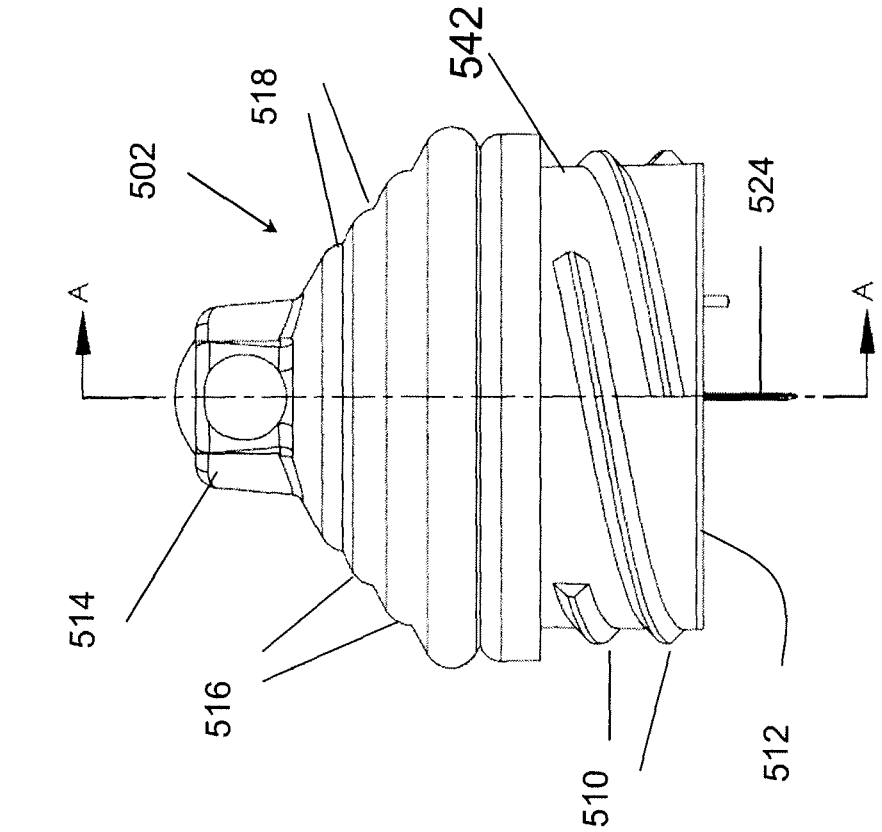


FIGURE 69

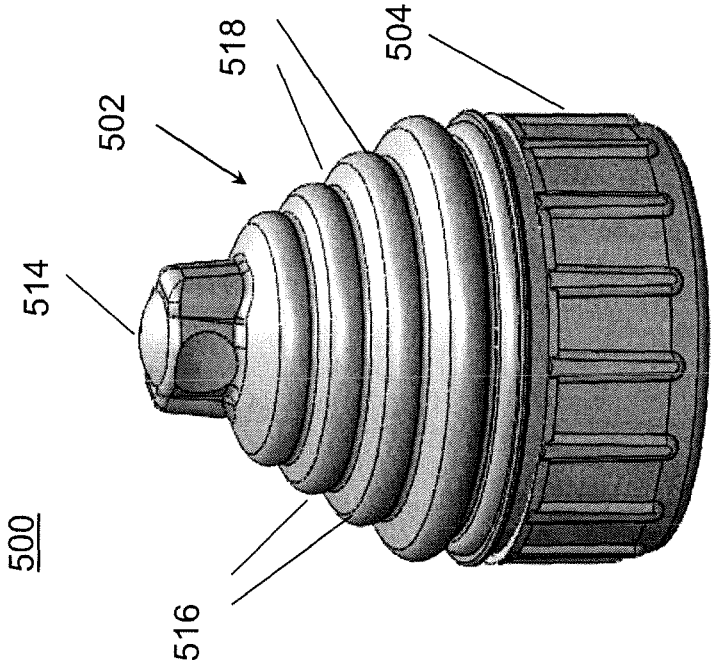


FIGURE 68

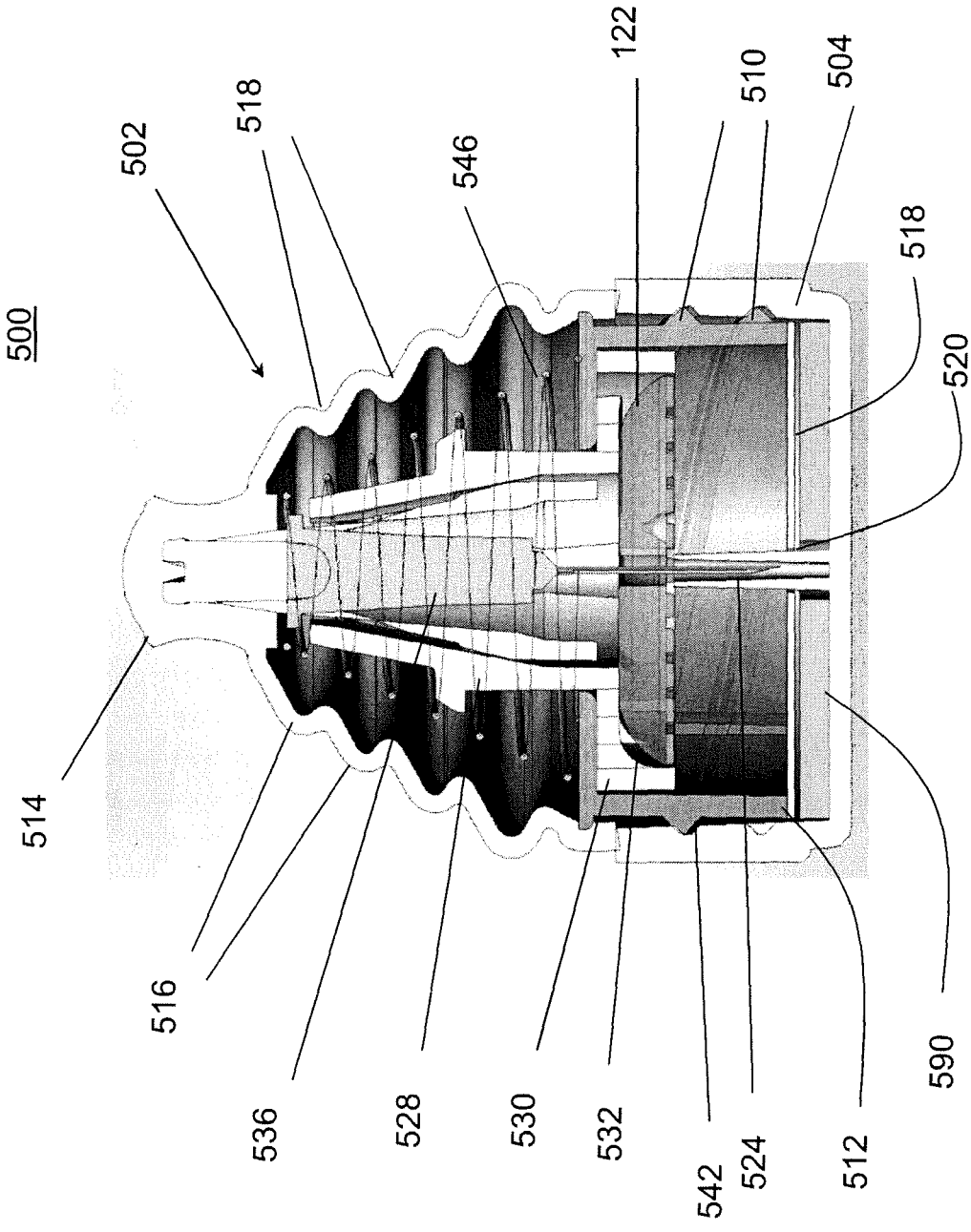

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FIGURE 70

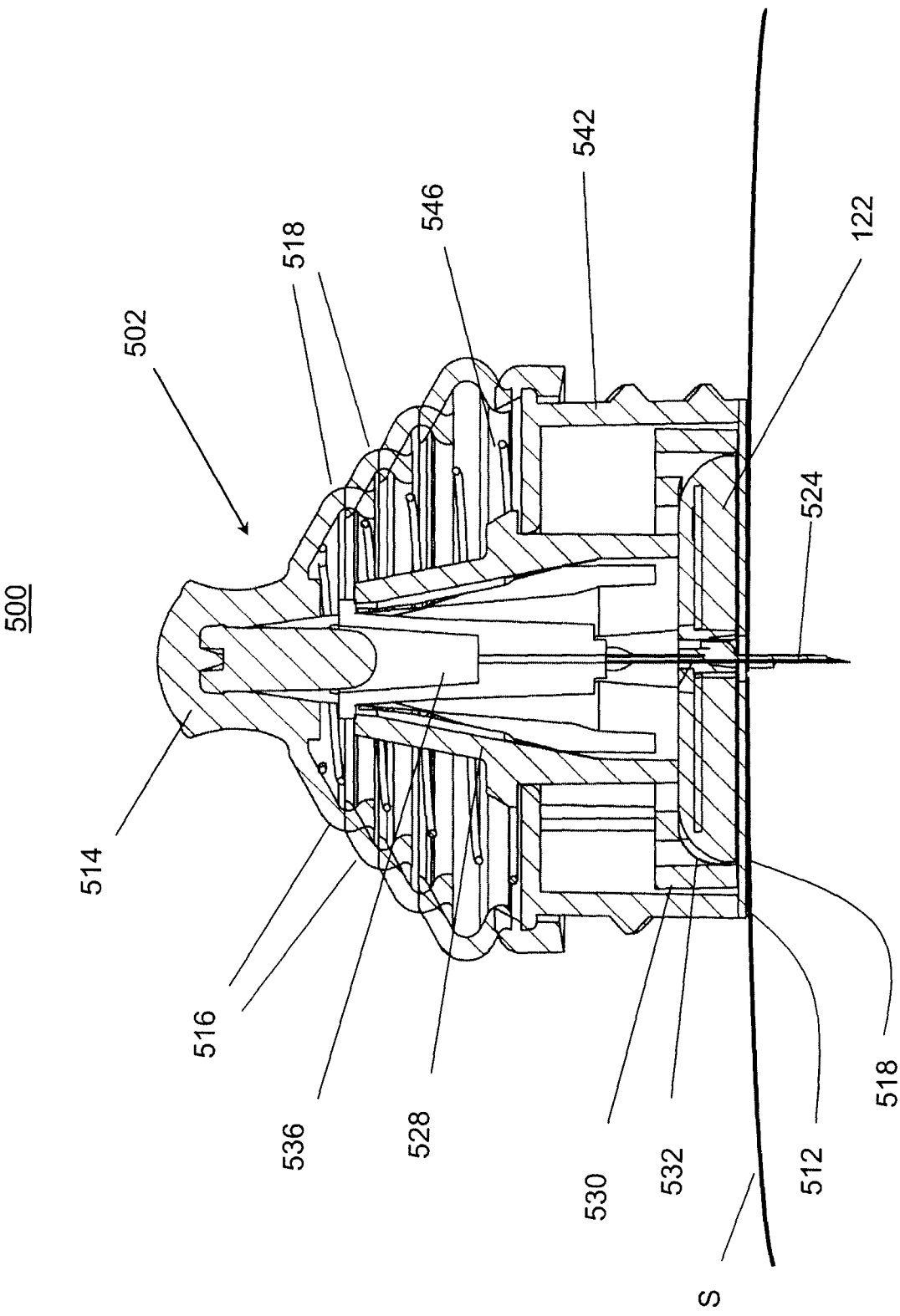


FIGURE 71

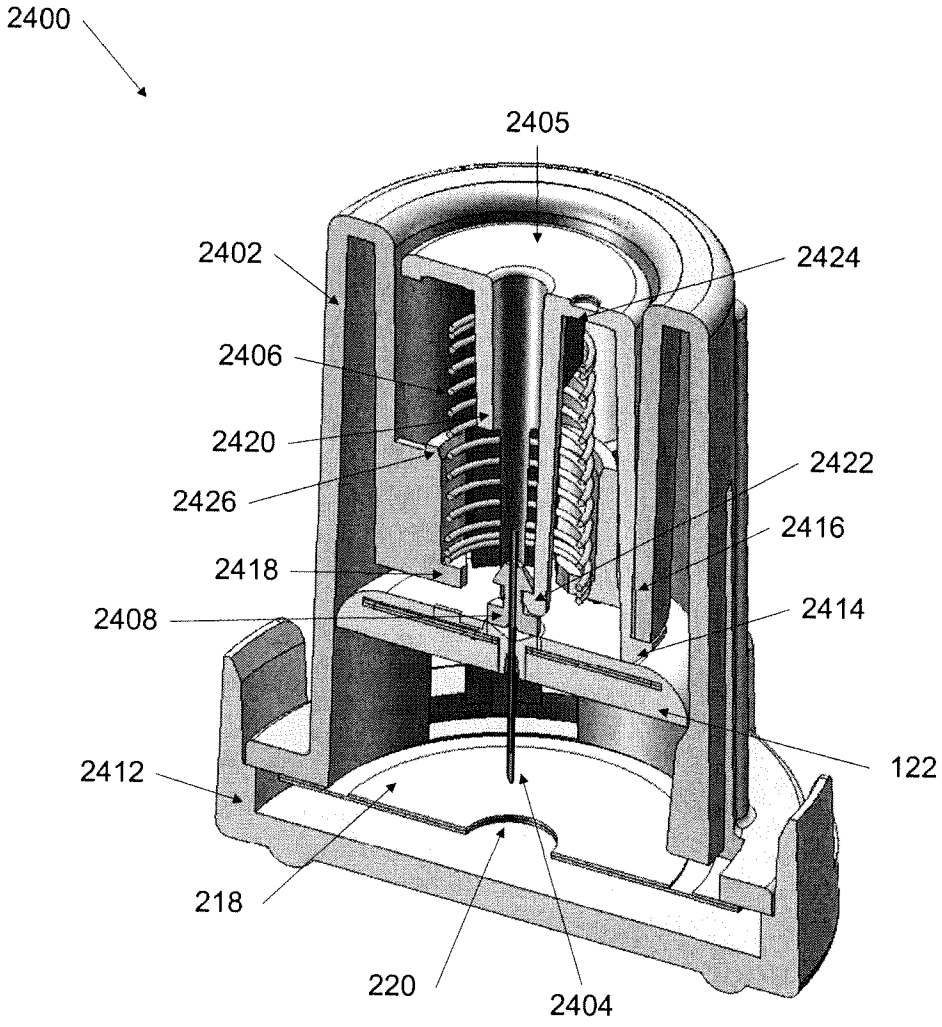

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FIG. 72

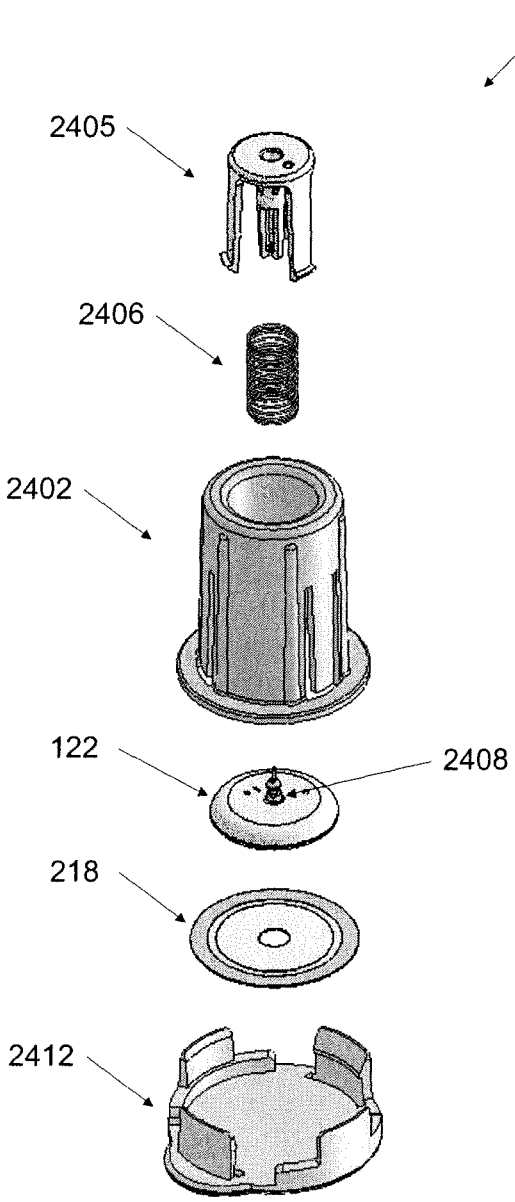


FIG. 72A

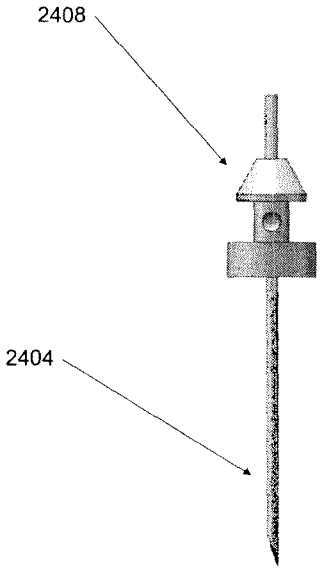


FIG. 72B

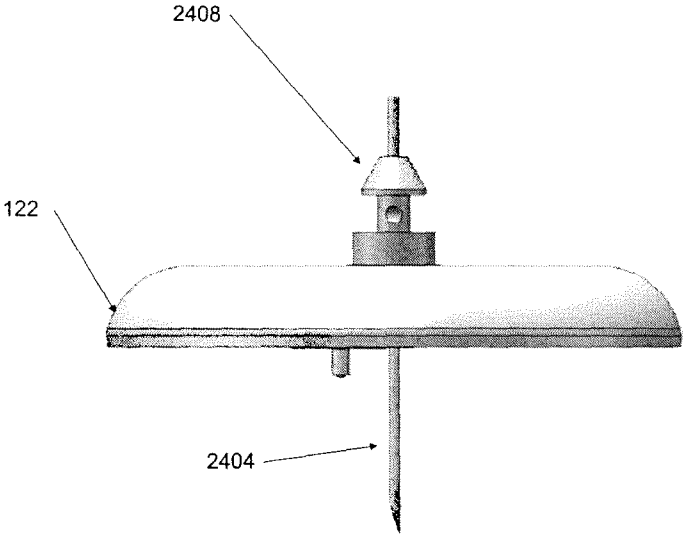


FIG. 72C

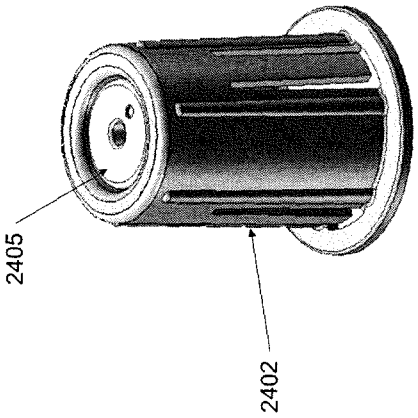


FIG. 72E

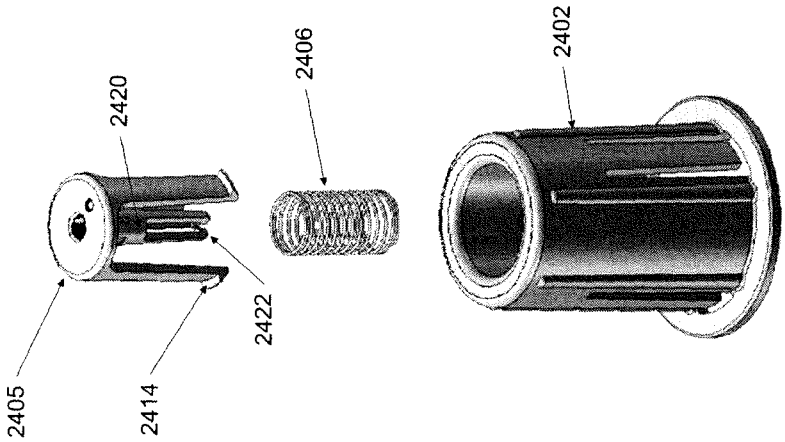


FIG. 72D

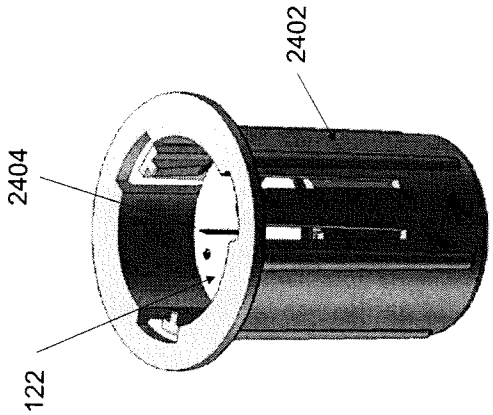


FIG. 72G

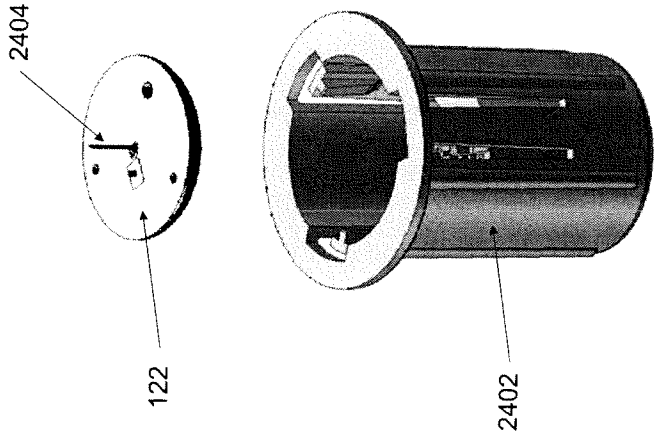


FIG. 72F

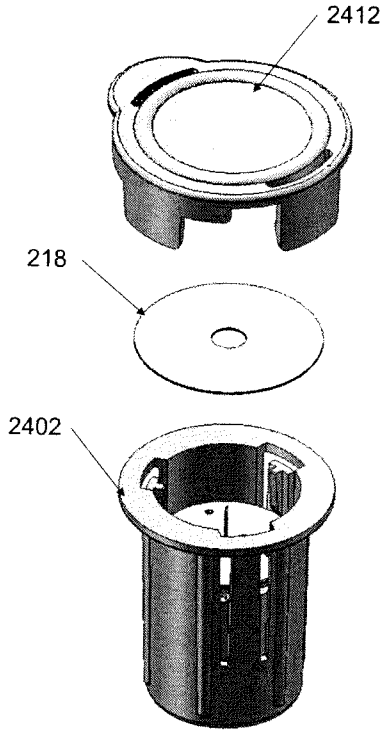


FIG. 72H

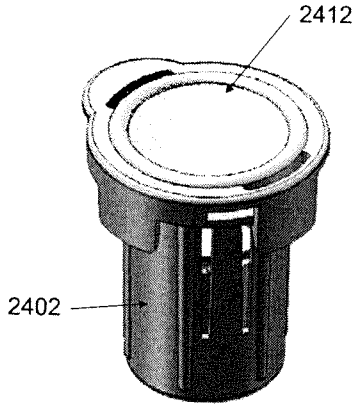


FIG. 72I

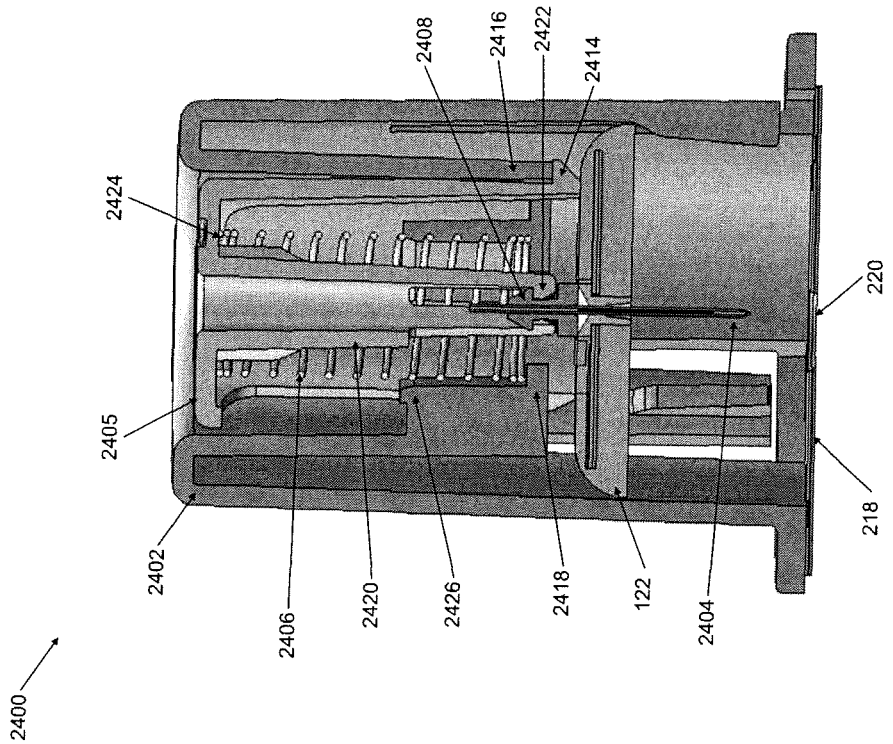

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FIG. 72J

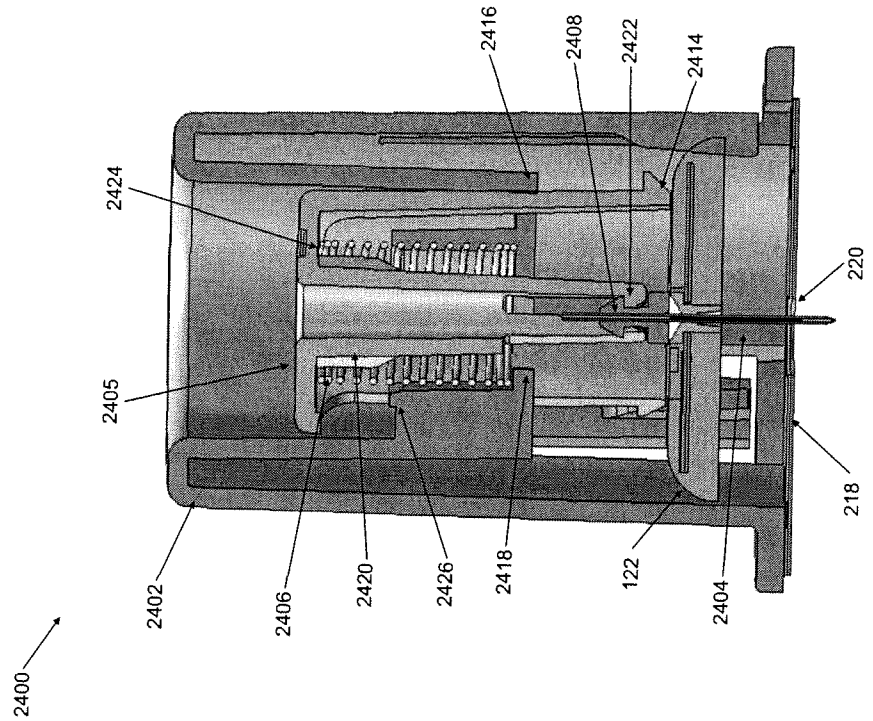

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FIG. 72K

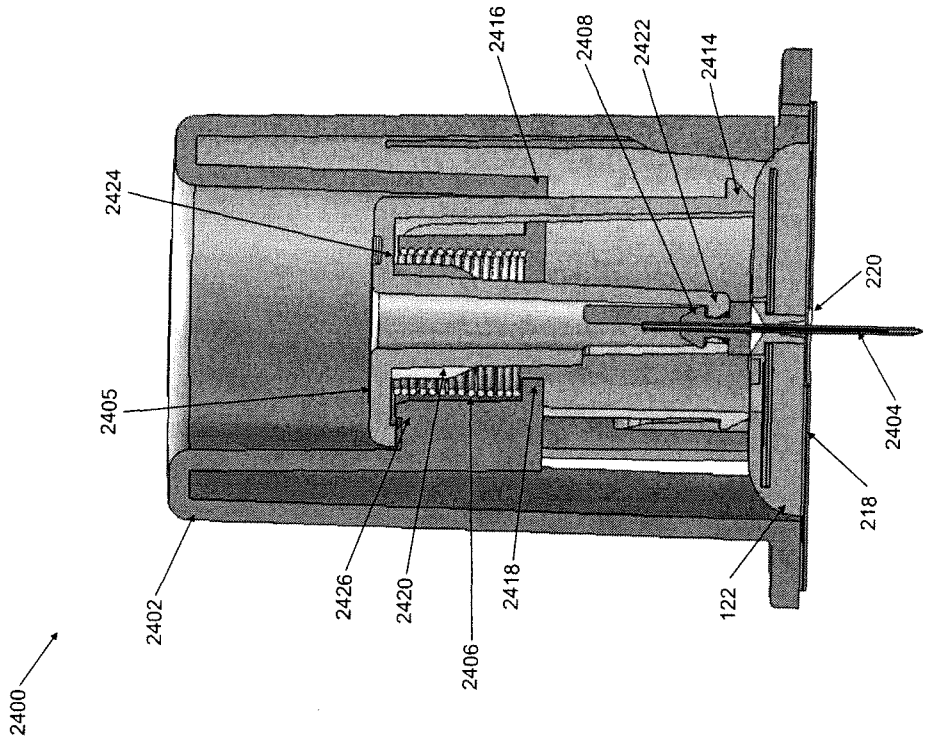

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FIG. 72L

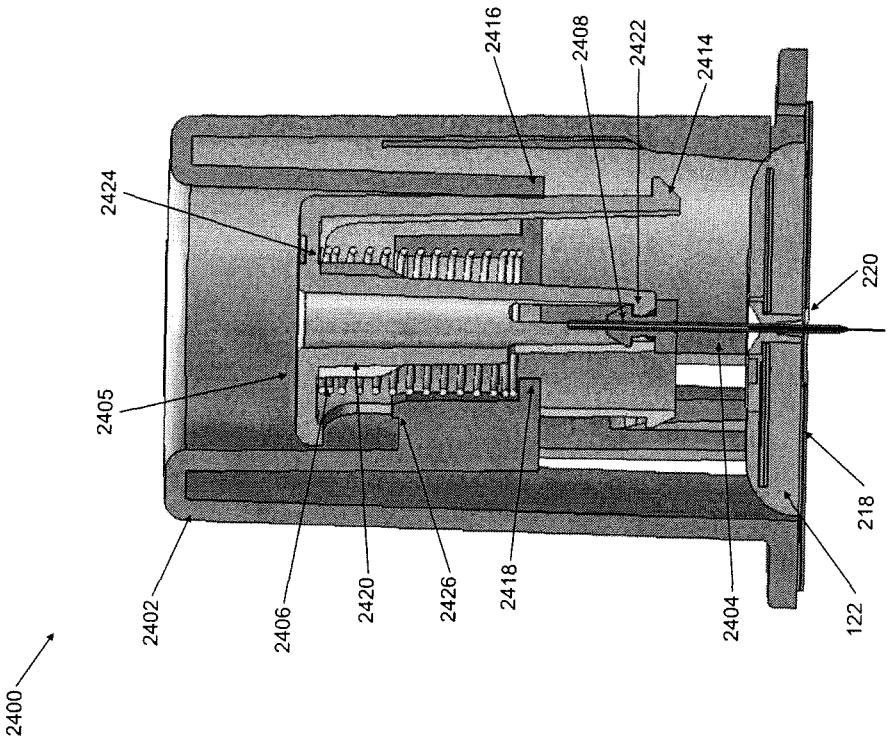

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FIG. 72M

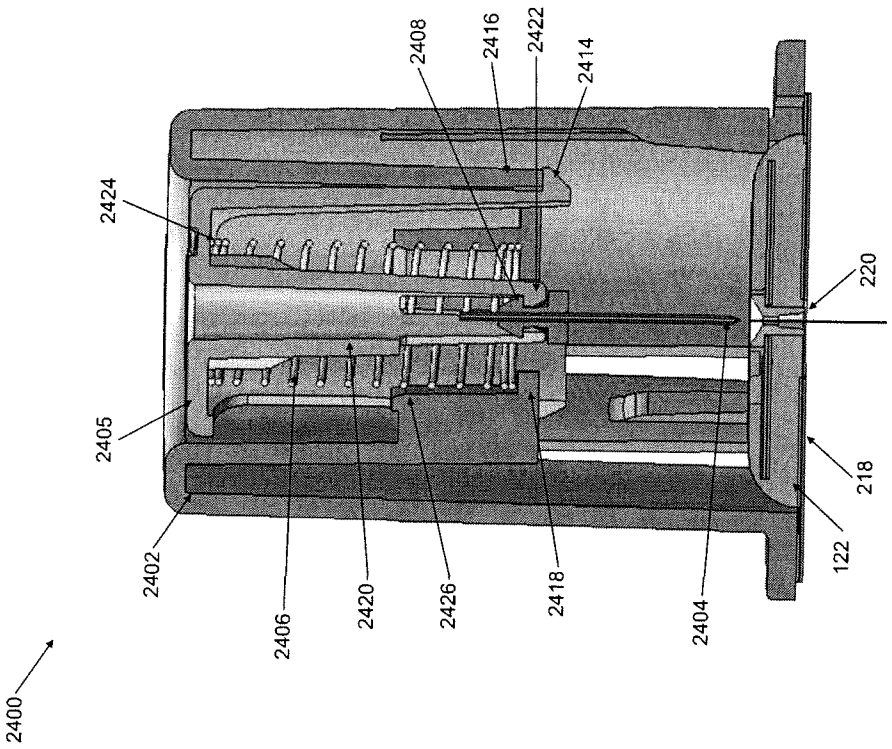

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FIG. 72N

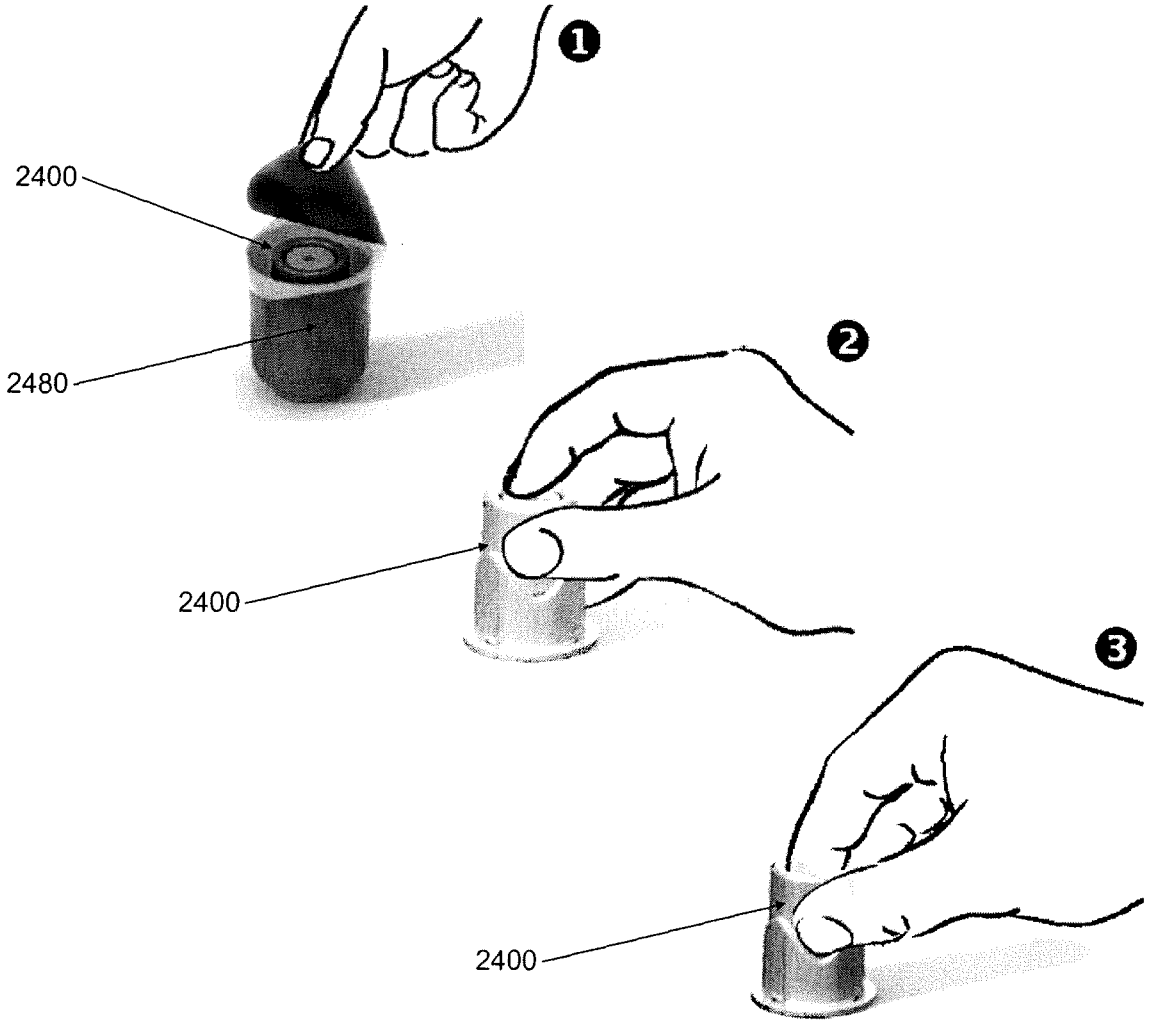


FIG. 72O

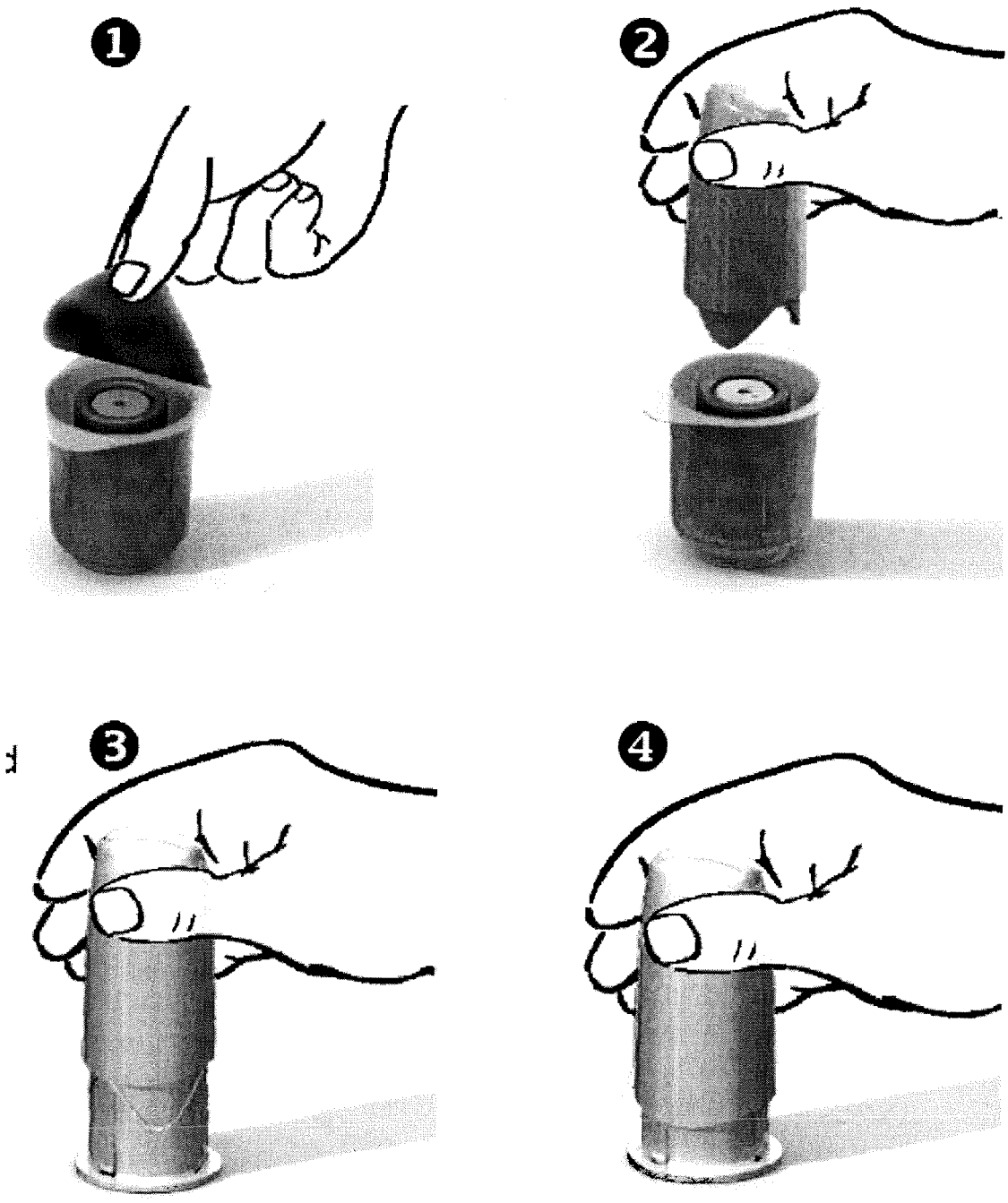


FIG. 72P

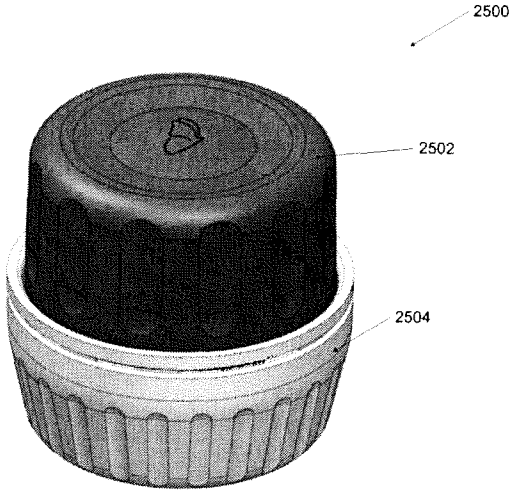


FIG. 73

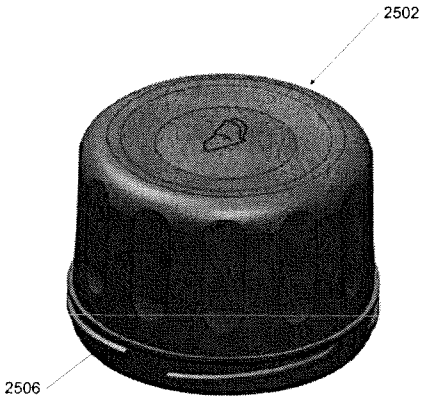


FIG. 73A

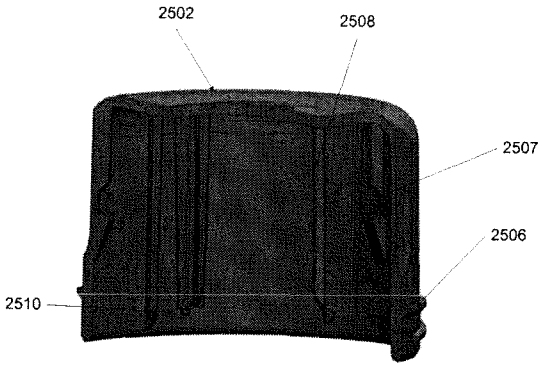


FIG. 73B

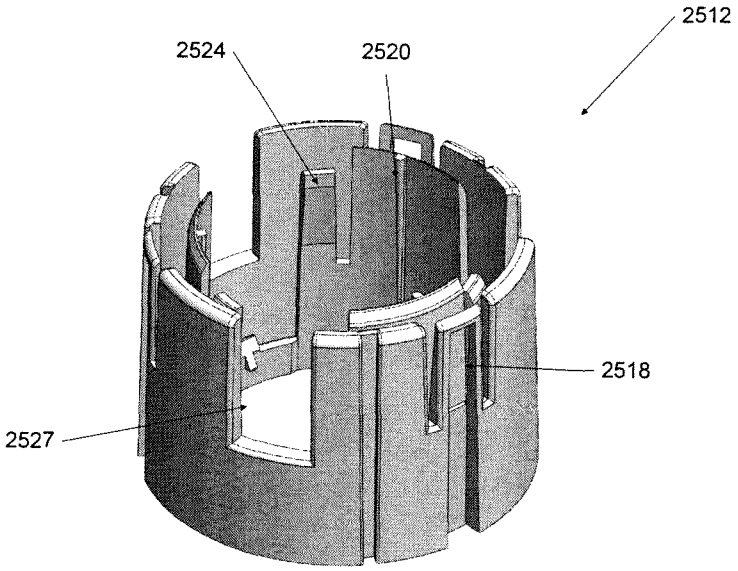


FIG. 73C

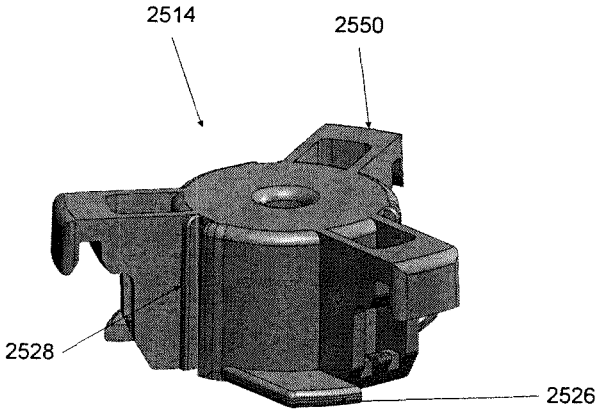


FIG. 73D

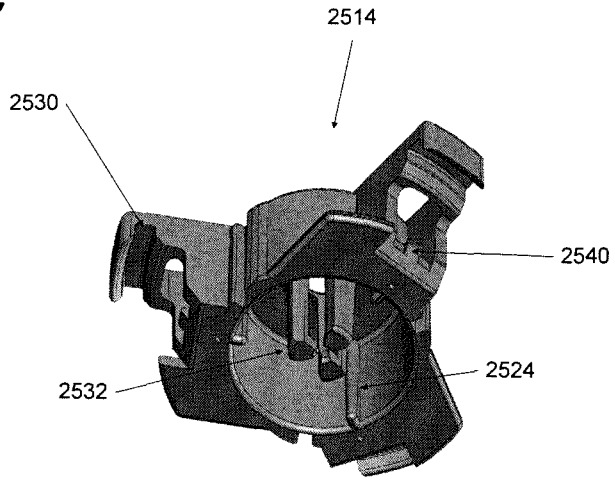


FIG. 73E

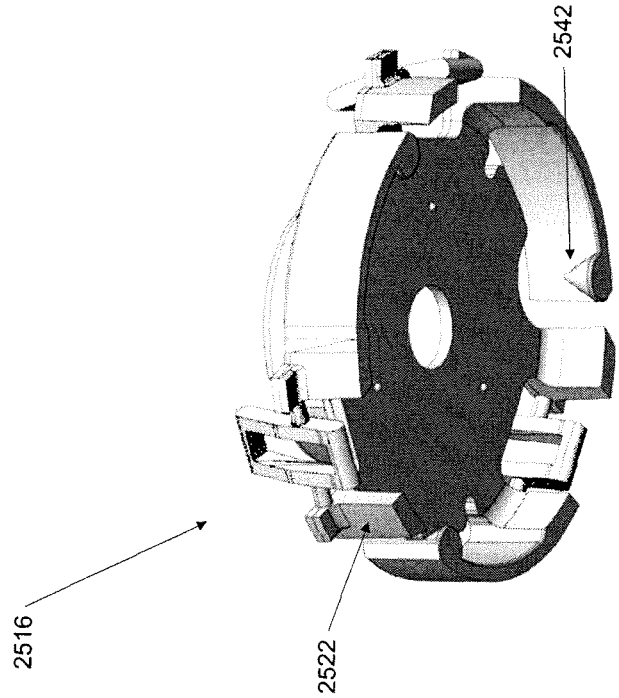


FIG. 73G

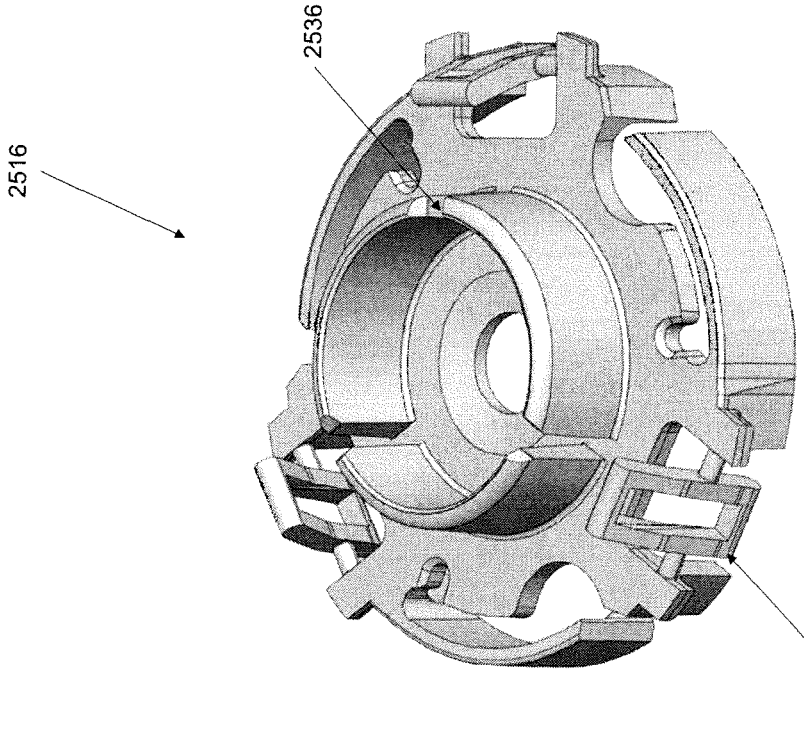


FIG. 73F

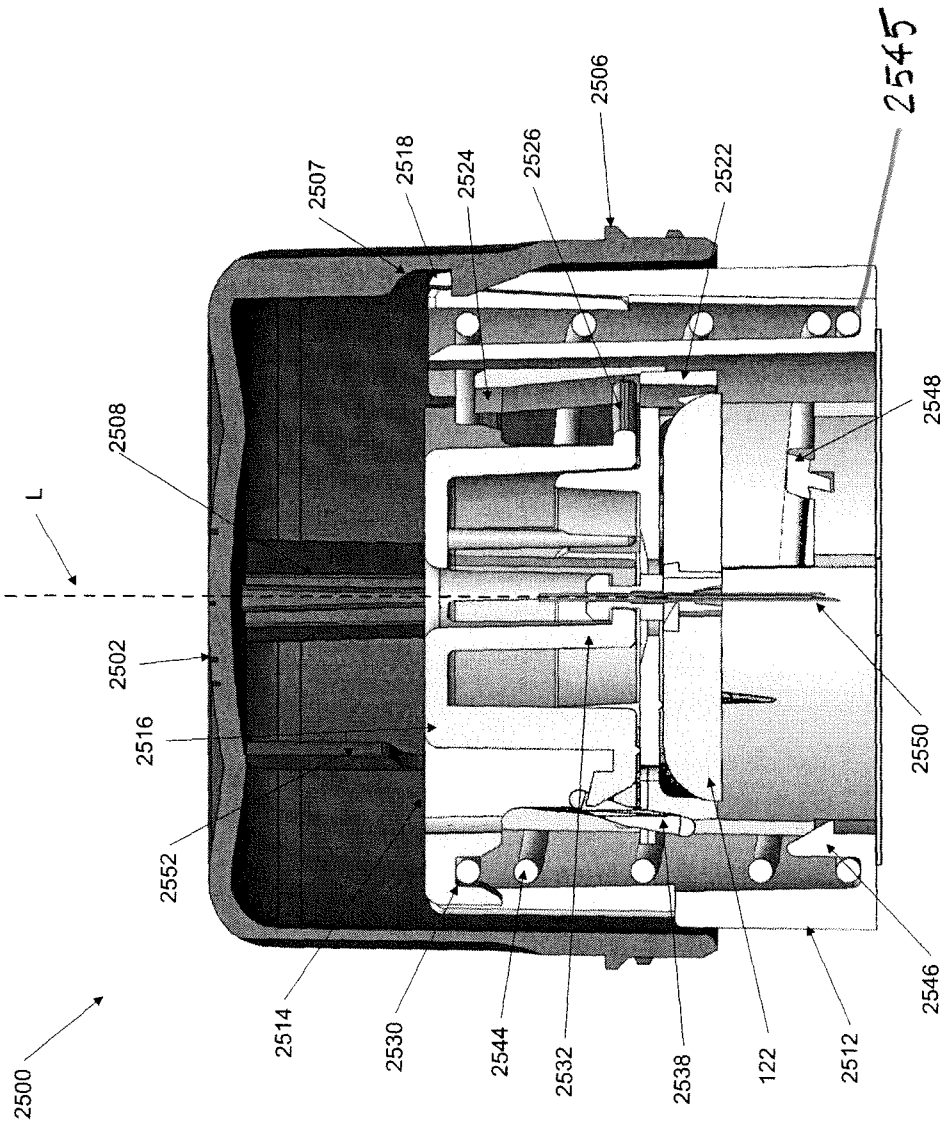

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FIG. 73H

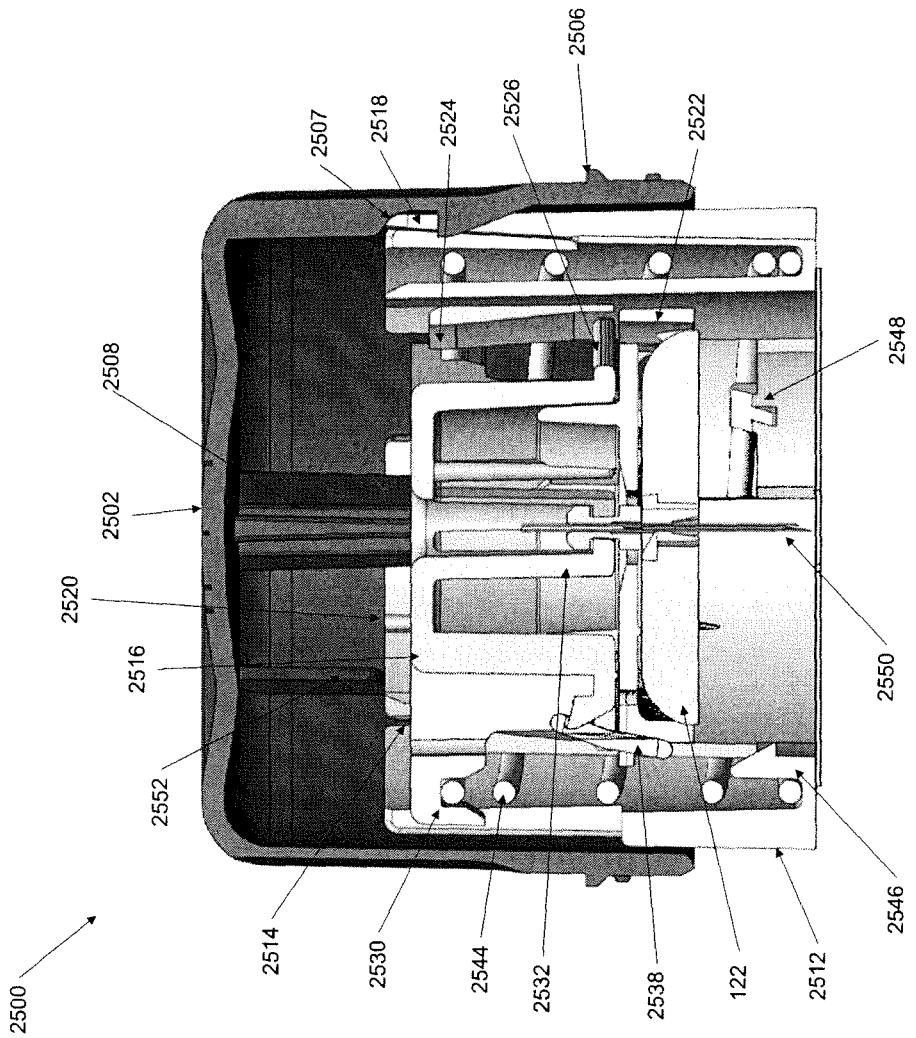

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FIG. 73I

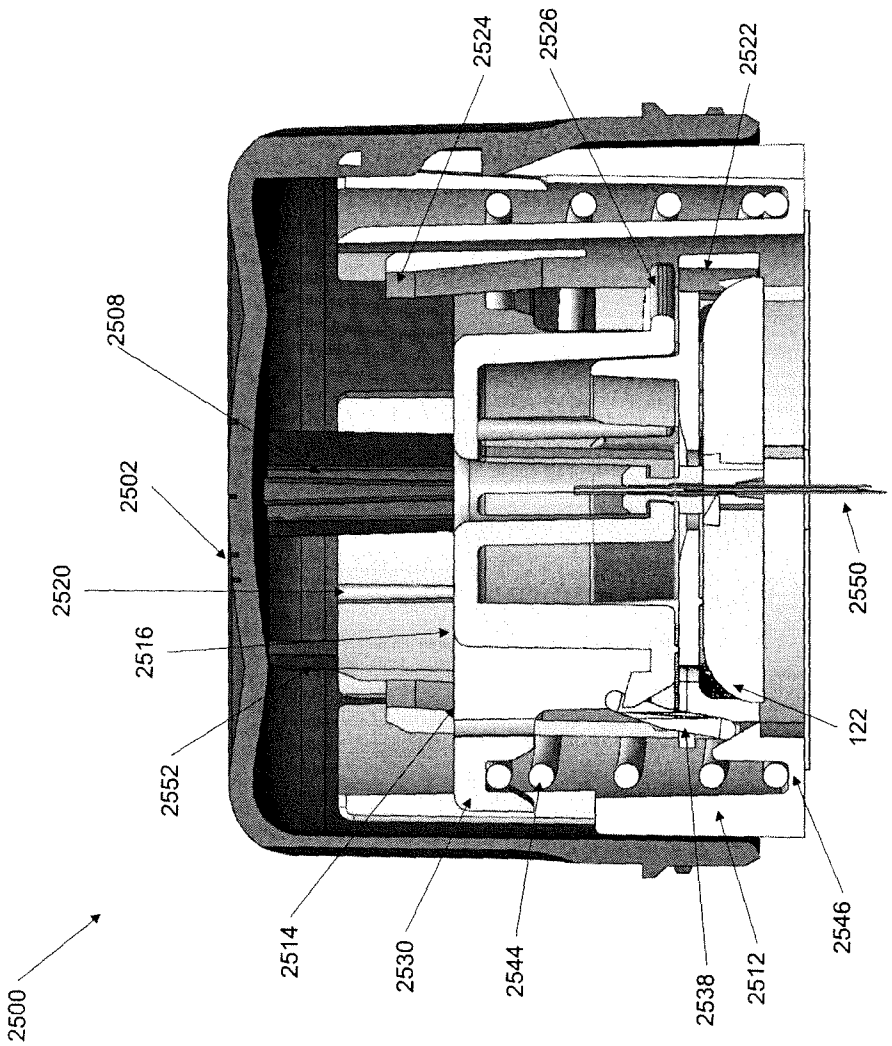

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FIG. 73J

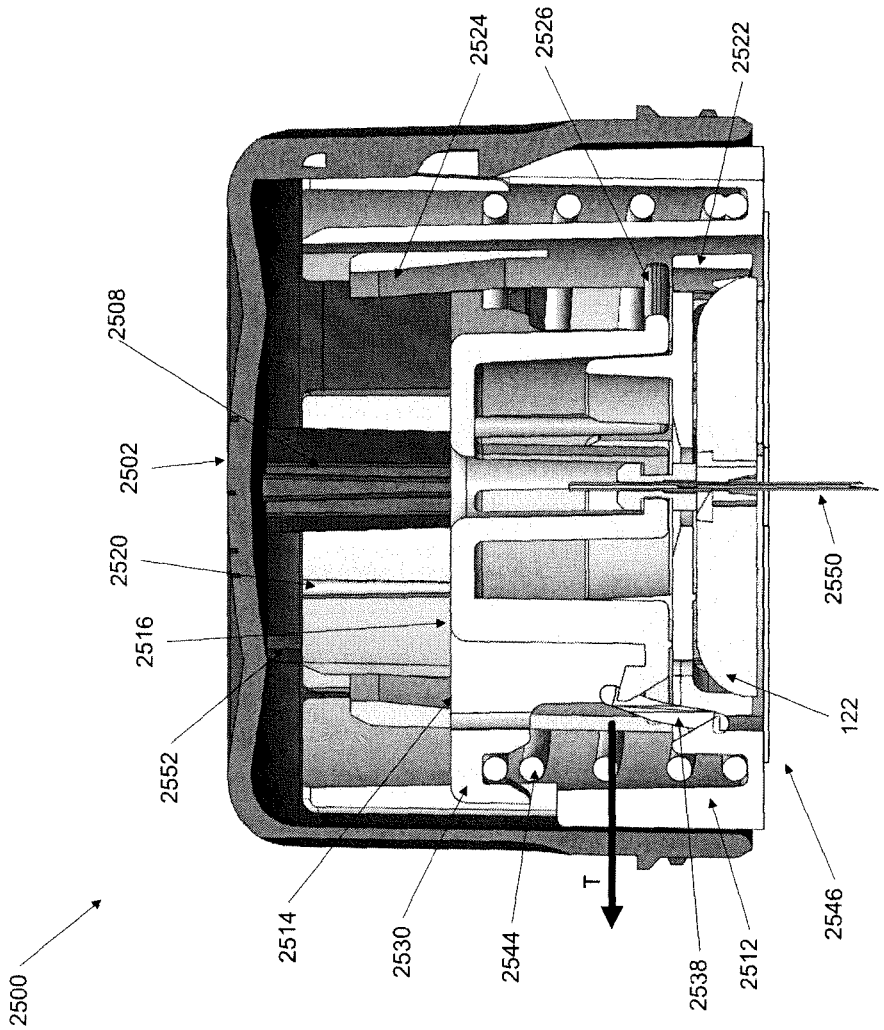

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FIG. 73K

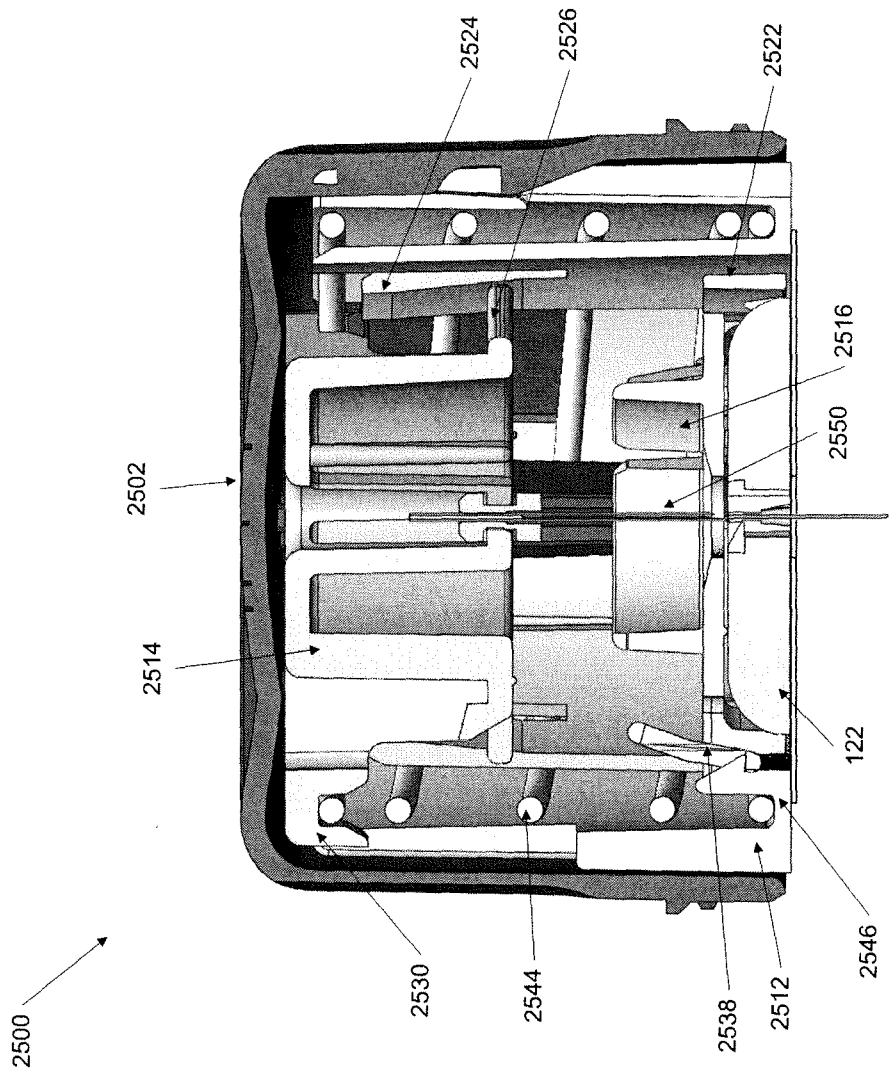

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FIG. 73L

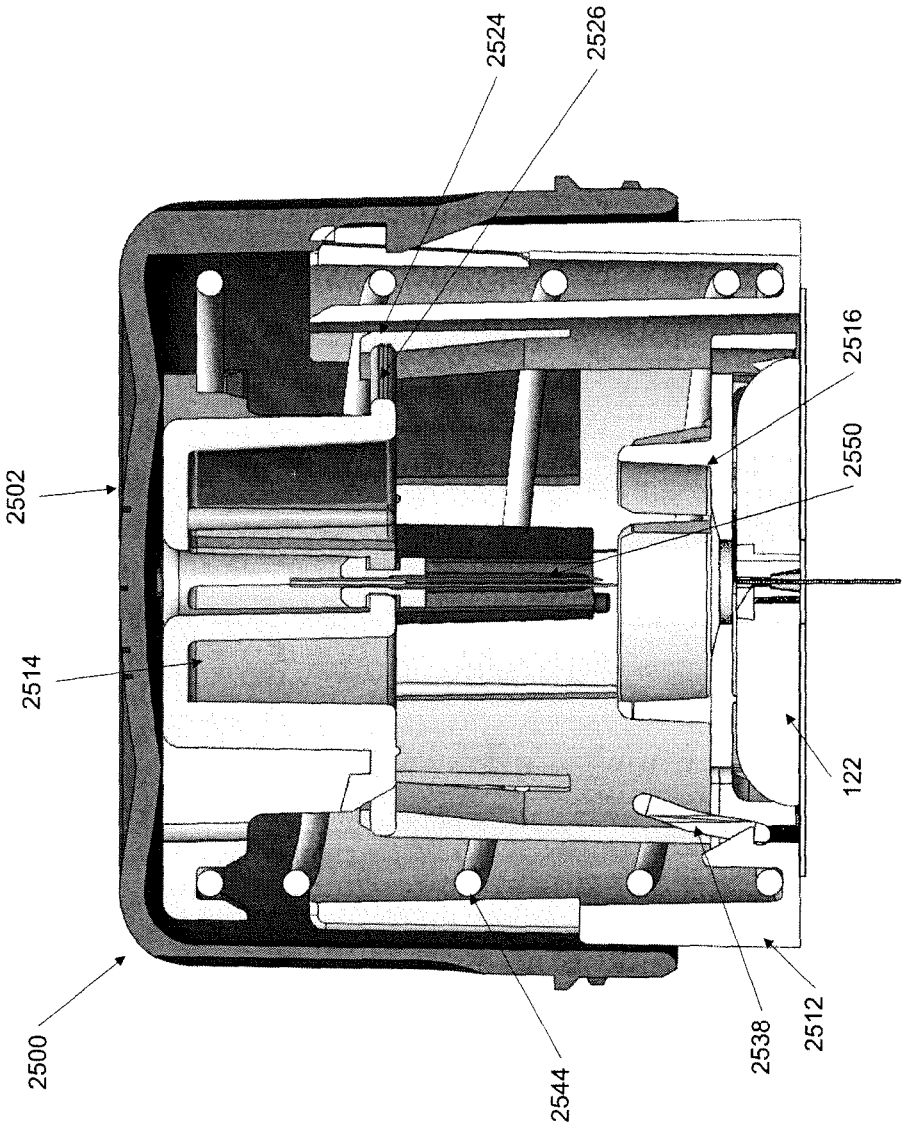


FIG. 73M

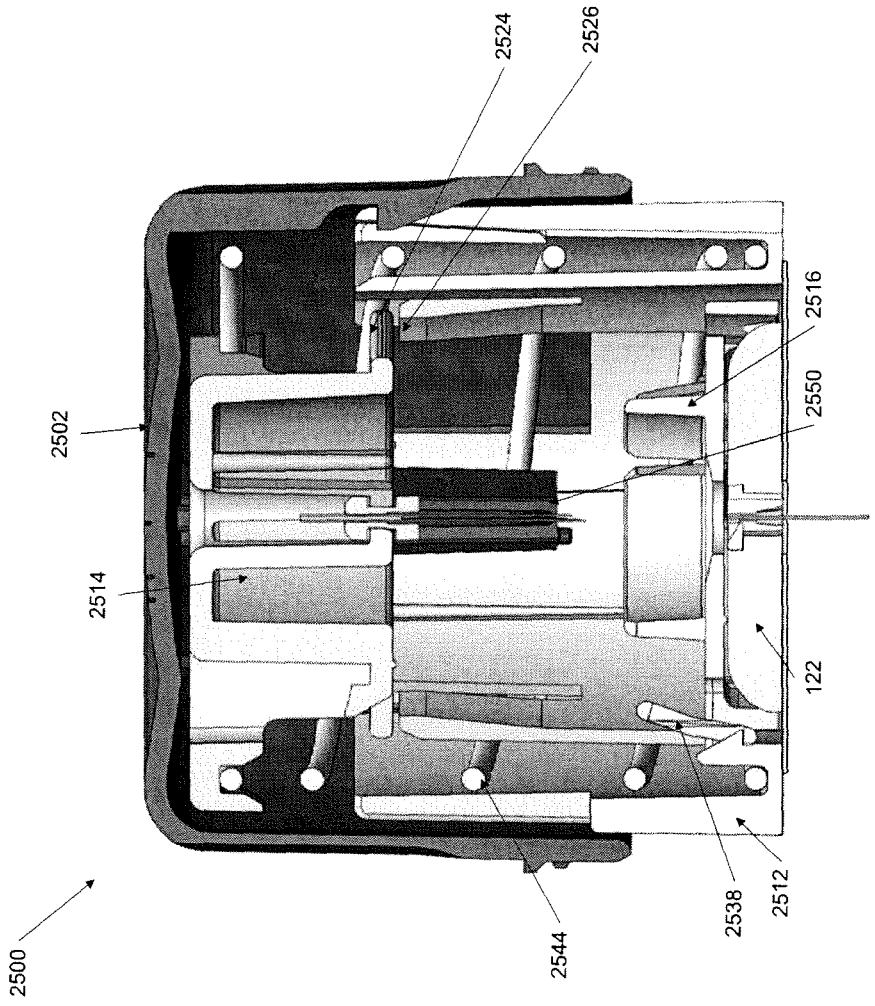


FIG. 73N

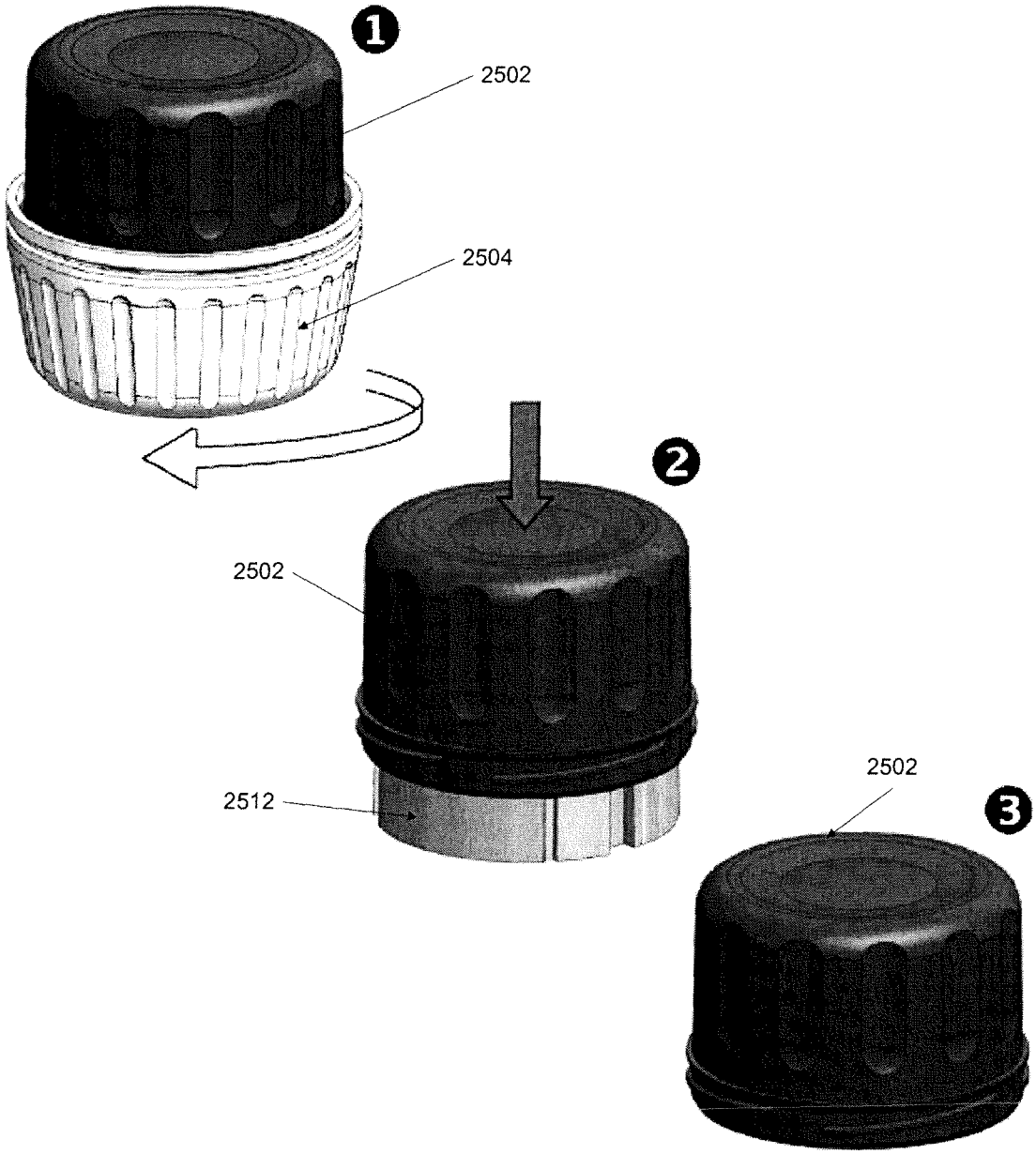


FIG. 73O

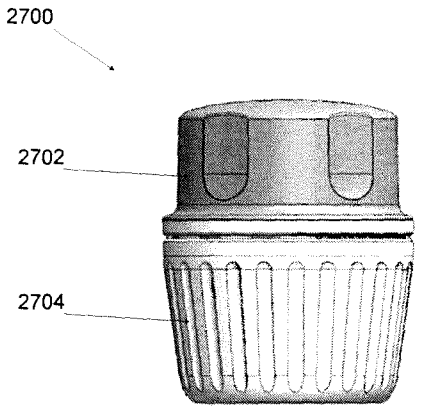


FIGURE 74

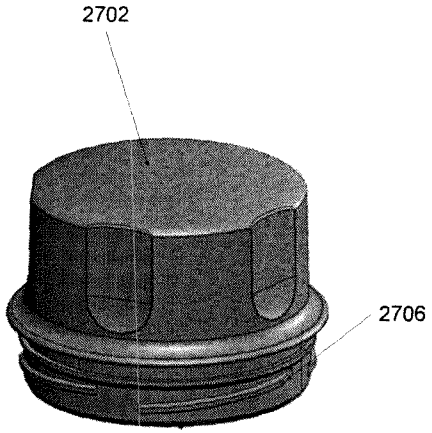


FIGURE 75

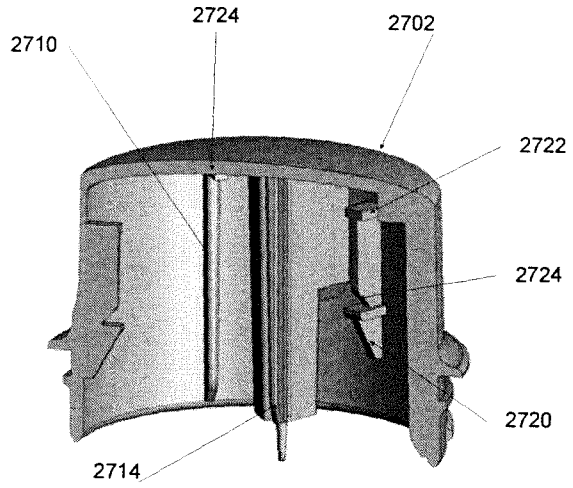


FIGURE 76

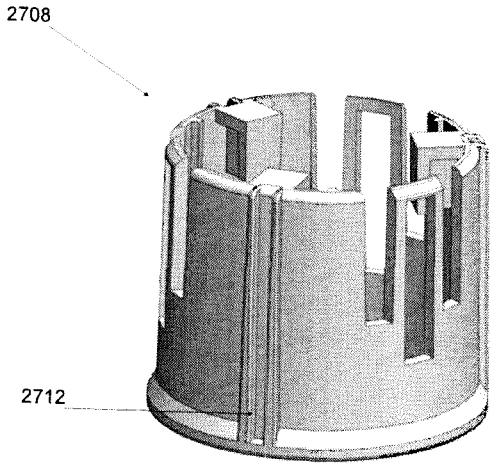


FIGURE 77

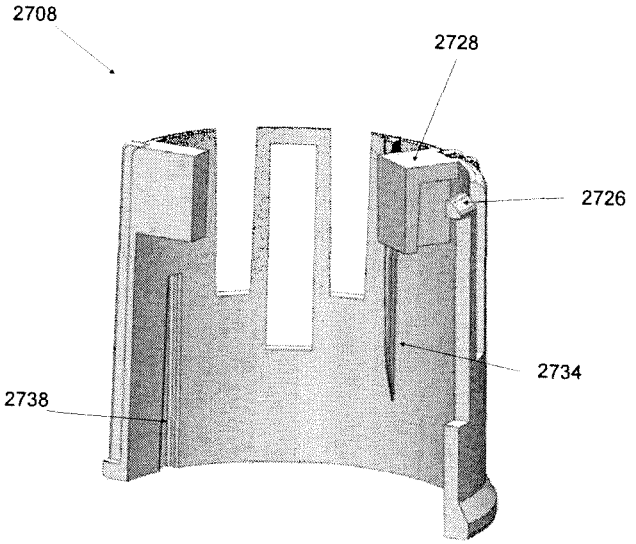


FIGURE 78

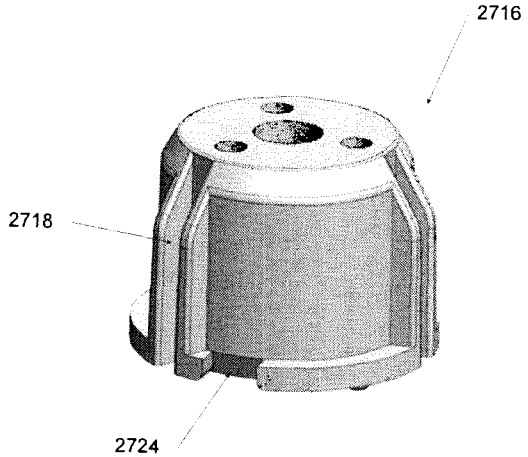


FIGURE 79

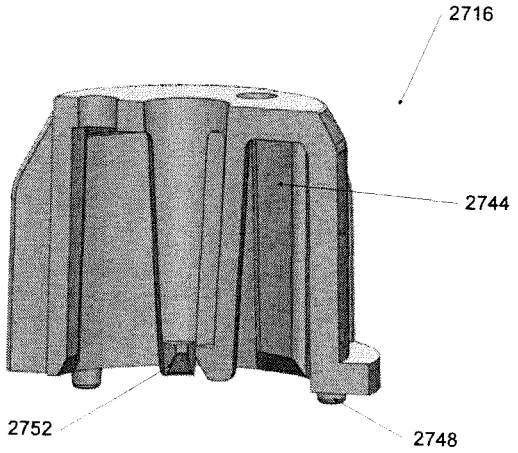


FIGURE 80

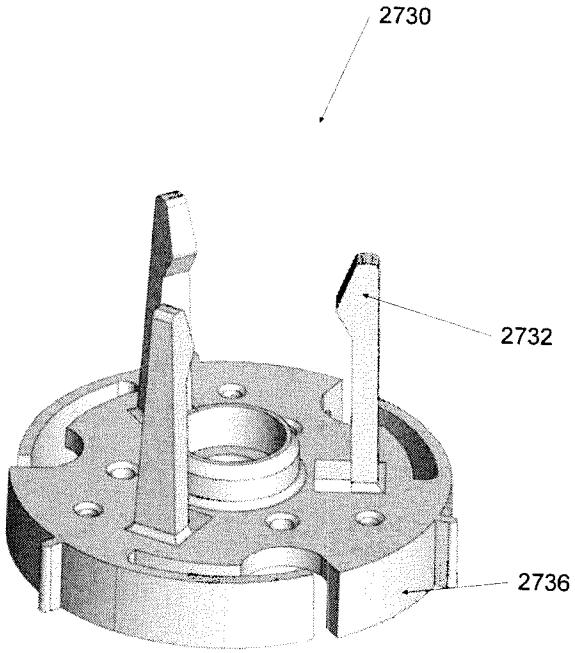


FIGURE 81

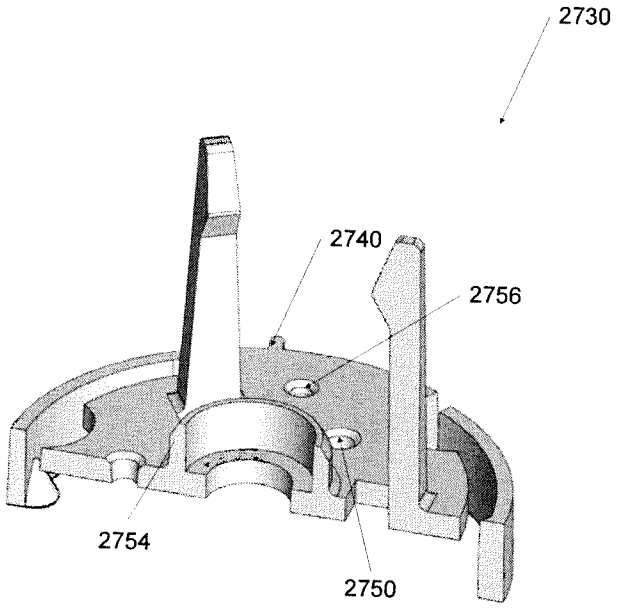


FIGURE 82

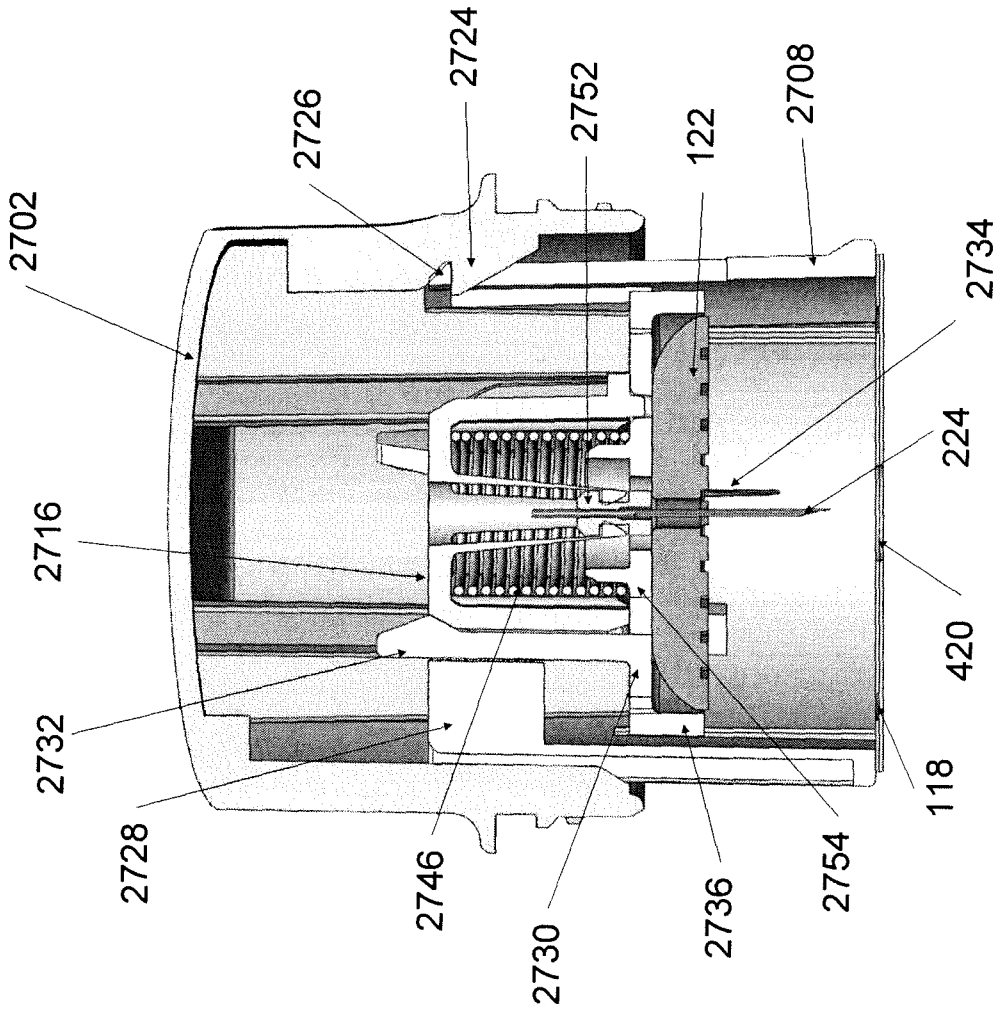

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FIGURE 83

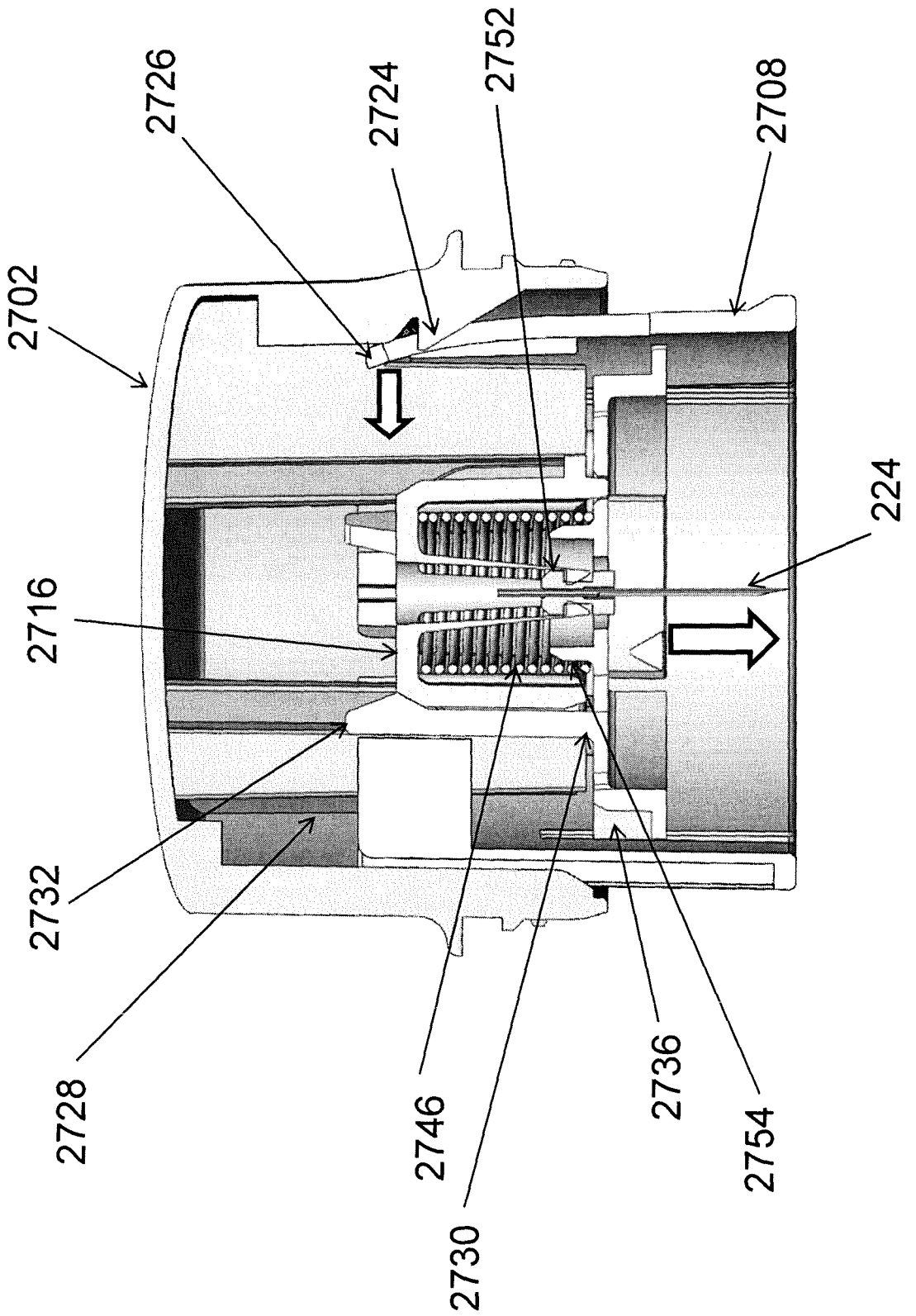

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FIGURE 83A

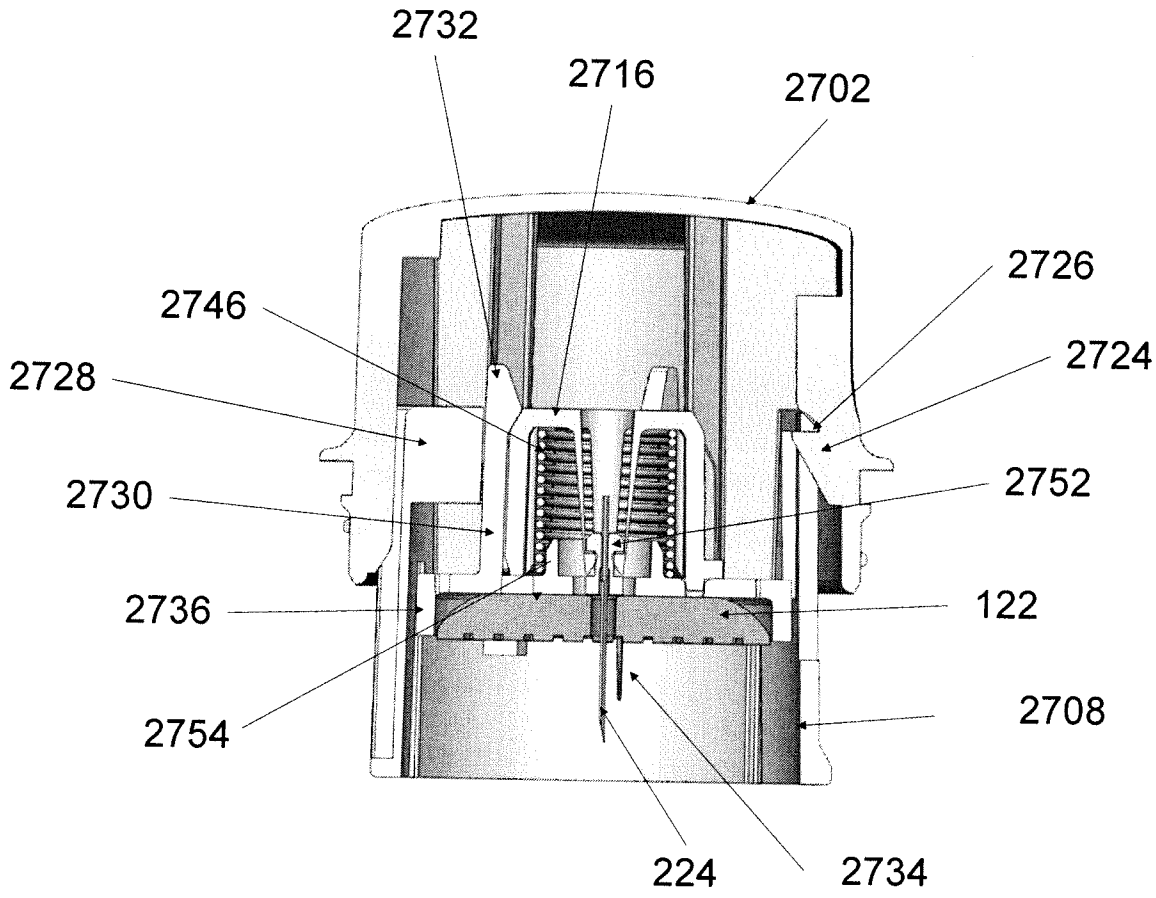

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FIGURE 84

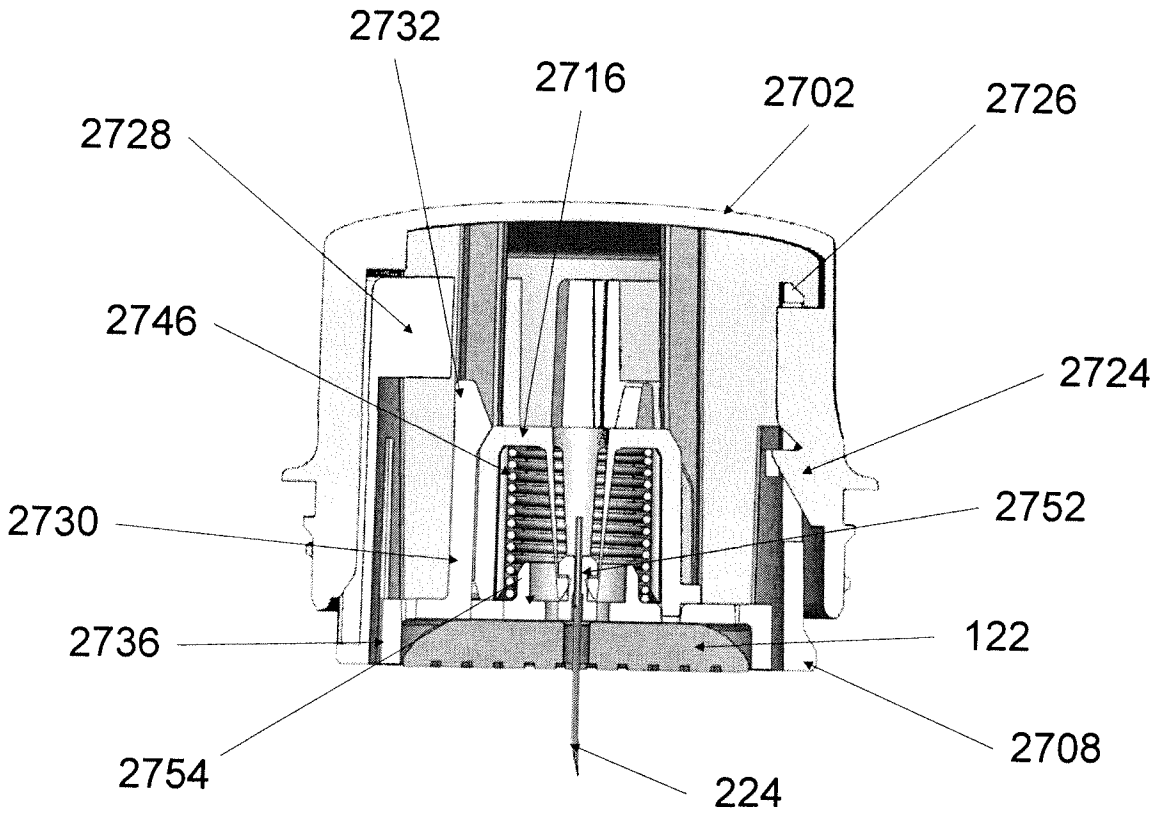

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FIGURE 85

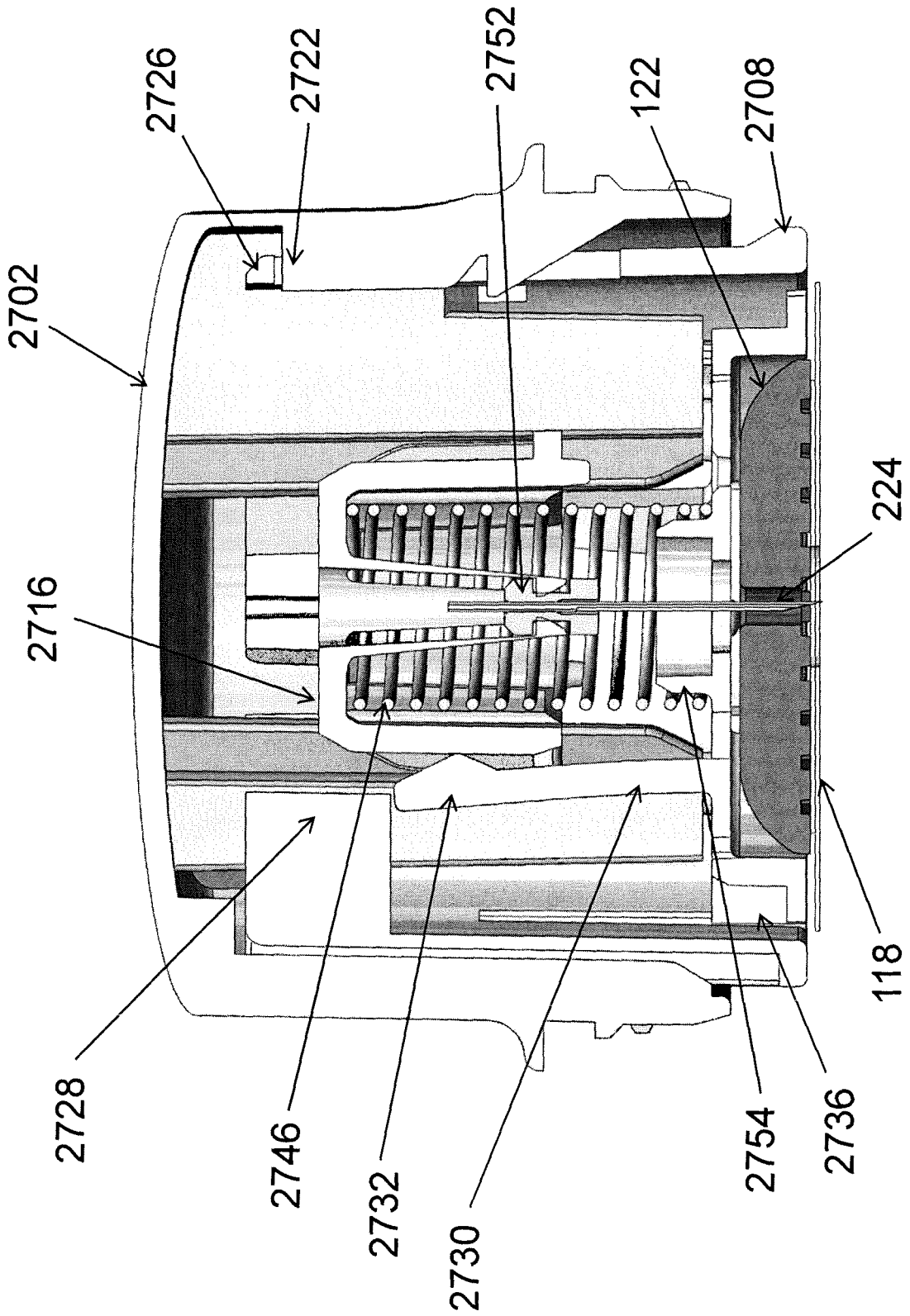

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FIGURE 86

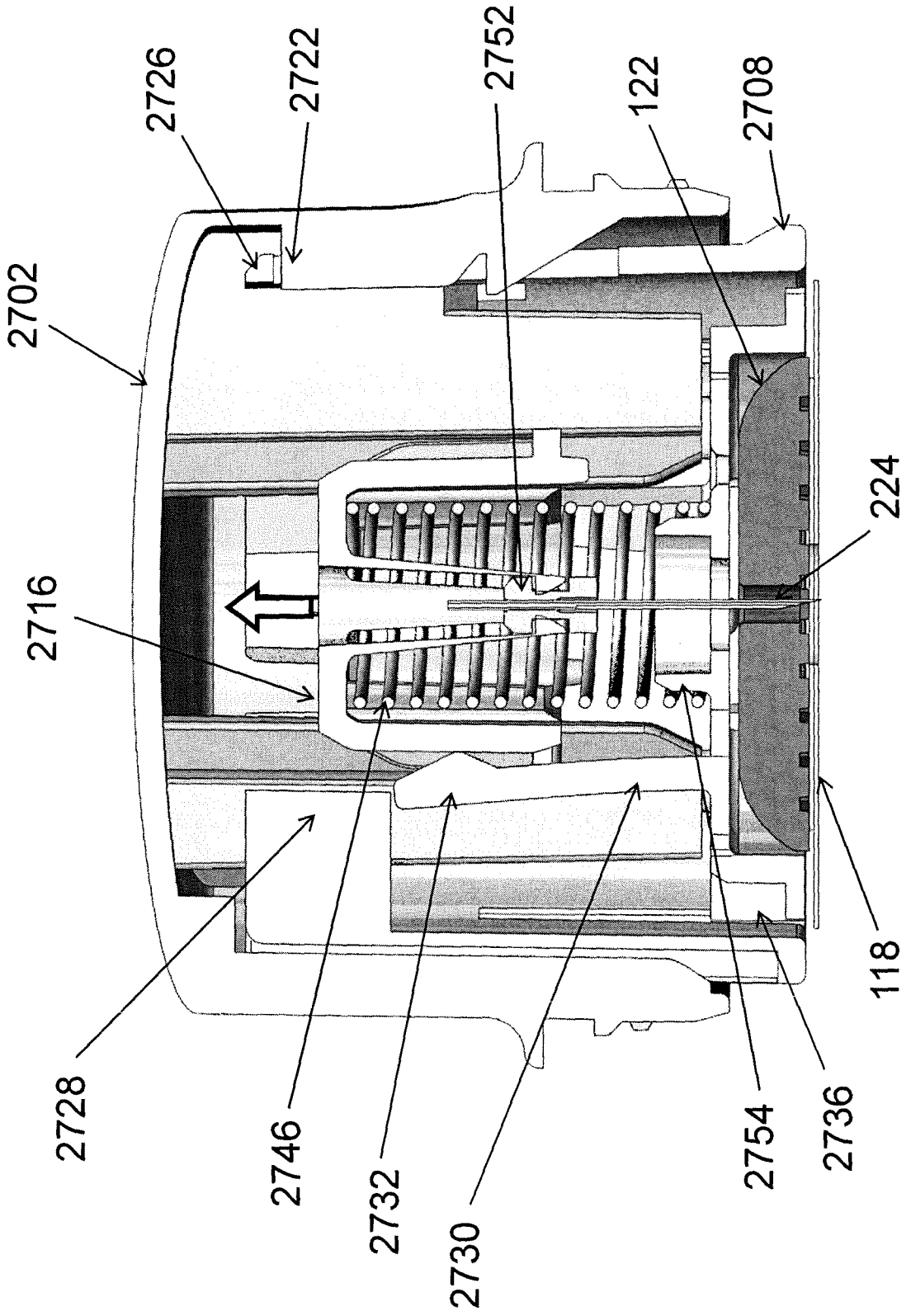

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FIGURE 87

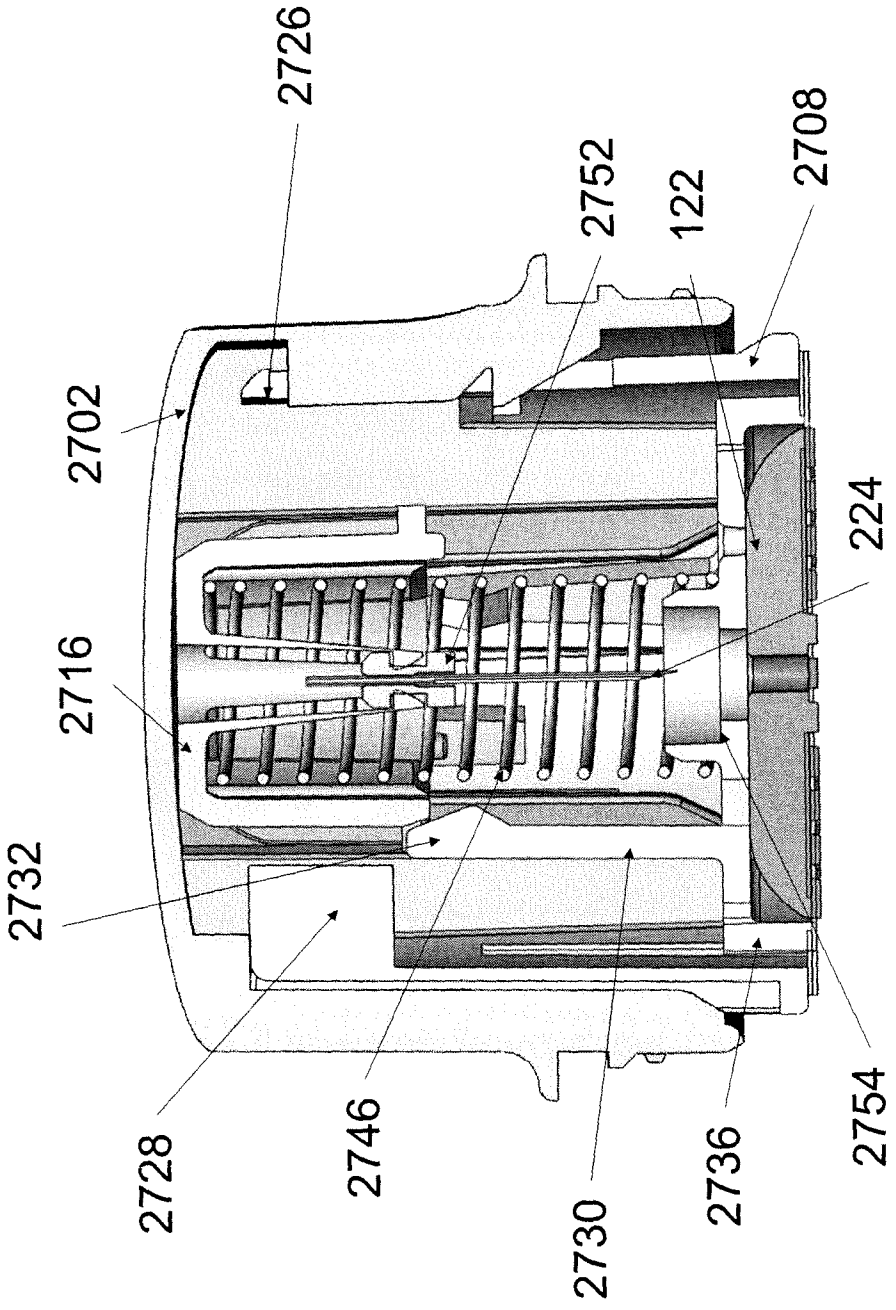

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FIGURE 88

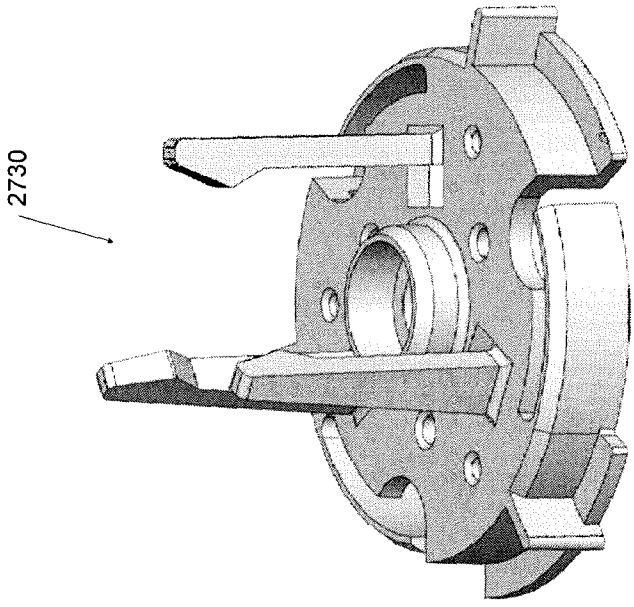


FIGURE 90

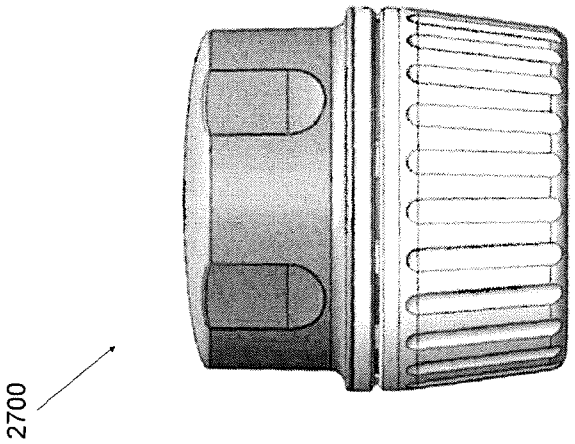


FIGURE 89

Electronic Patent Application Fee Transmittal

Application Number:	
Filing Date:	
Title of Invention:	Medical Device Inserters and Processes of Inserting and Using Medical Devices
First Named Inventor/Applicant Name:	Manuel Donnay
Filer:	Lisa A. Chiarini/Walter Egbert
Attorney Docket Number:	031312-06499

Filed as Large Entity

Provisional Filing Fees

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Basic Filing:				
Provisional application filing	1005	1	220	220
Pages:				
Prov. Appl Size fee per 50 sheets >100	1085	2	270	540
Claims:				
Miscellaneous-Filing:				
Petition:				
Patent-Appeals-and-Interference:				
Post-Allowance-and-Post-Issuance:				

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Extension-of-Time:				
Miscellaneous:				
			Total in USD ($)	**760**

Electronic Acknowledgement Receipt

EFS ID:	7951653
Application Number:	61361374
International Application Number:	
Confirmation Number:	1217
Title of Invention:	Medical Device Inserters and Processes of Inserting and Using Medical Devices
First Named Inventor/Applicant Name:	Manuel Donnay
Customer Number:	90259
Filer:	Lisa A. Chiarini/Walter Egbert
Filer Authorized By:	Lisa A. Chiarini
Attorney Docket Number:	031312-06499
Receipt Date:	02-JUL-2010
Filing Date:	
Time Stamp:	22:43:02
Application Type:	Provisional

Payment information:

Submitted with Payment	yes
Payment Type	Credit Card
Payment was successfully received in RAM	$760
RAM confirmation Number	5401
Deposit Account	083264
Authorized User	ABRAMSON,RONALD

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File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1		10544USL1.pdf	16820191 05a8f5981c1bc3bf21fc60234a9a1da02cf12ff8	yes	178

	Multipart Description/PDF files in .zip description		
	Document Description	**Start**	**End**
	Provisional Cover Sheet (SB16)	1	2
	Specification	3	89
	Drawings-only black and white line drawings	90	178

Warnings:

Information:

2	Fee Worksheet (PTO-875)	fee-info.pdf	31247 be541956d3a366c3f6db8455220f9b01fd7a16e2	no	2

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New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

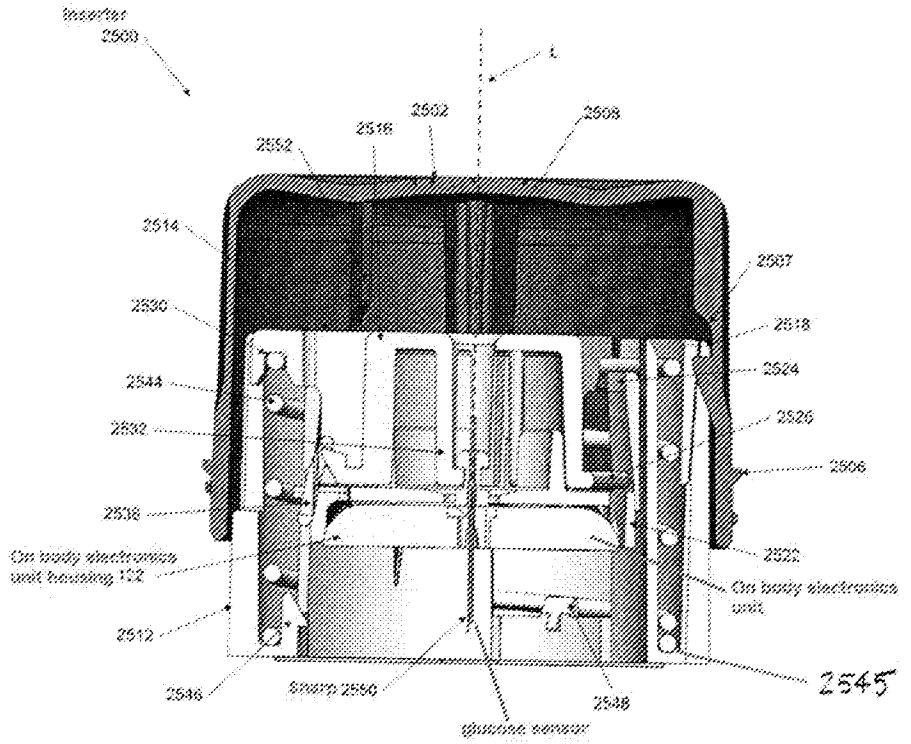
National Stage of an International Application under 35 U.S.C. 371

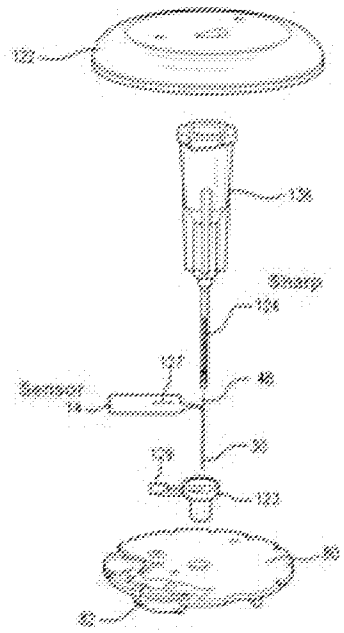
If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

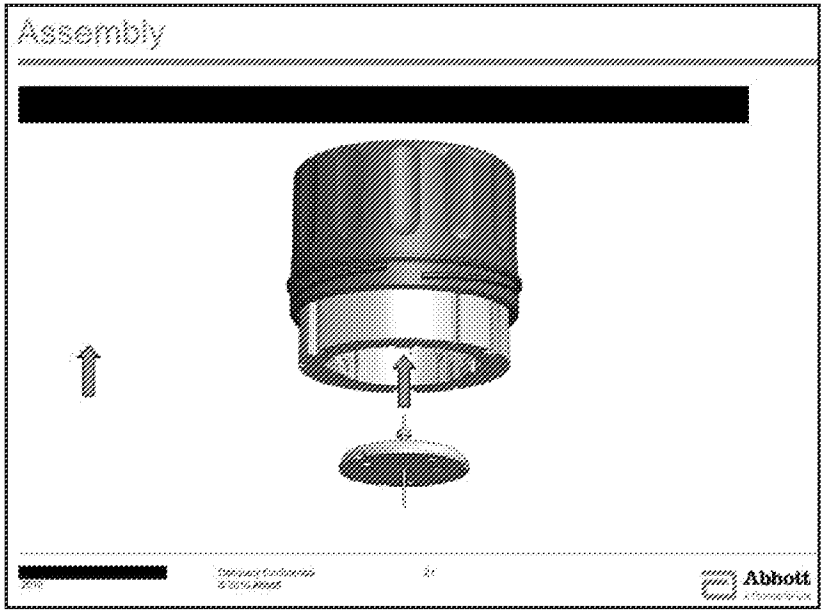
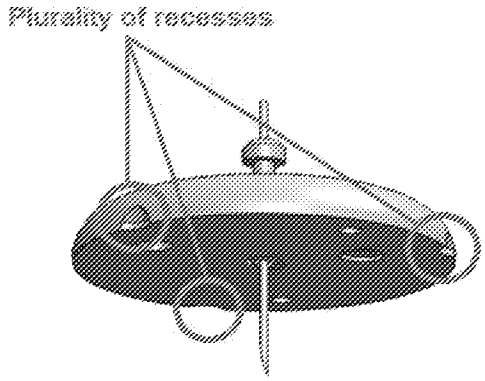
New International Application Filed with the USPTO as a Receiving Office

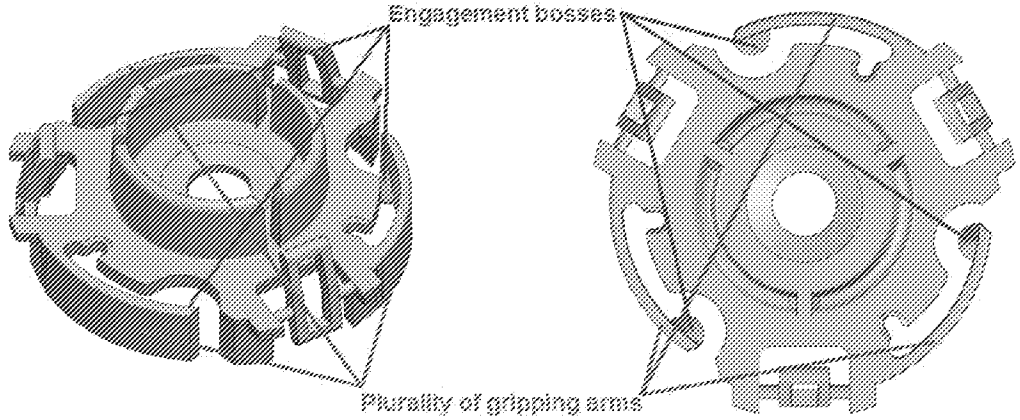
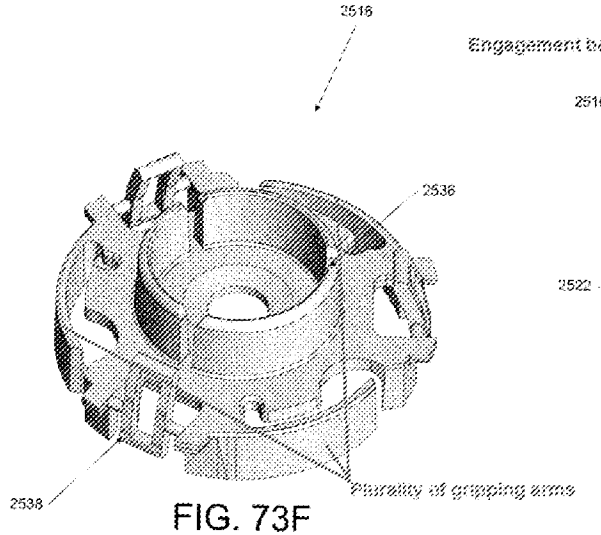
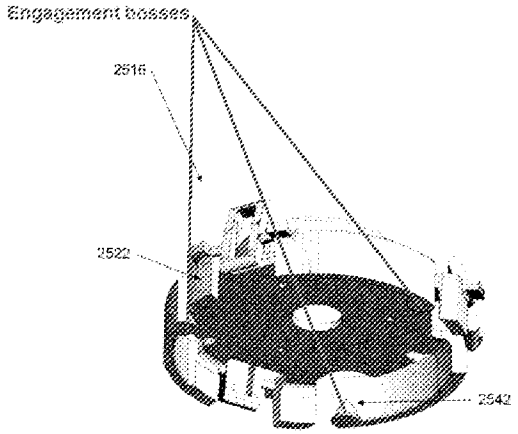
If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

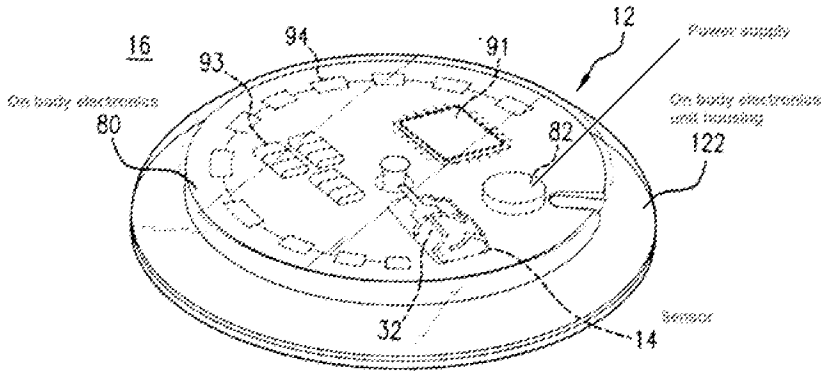
APPENDIX A

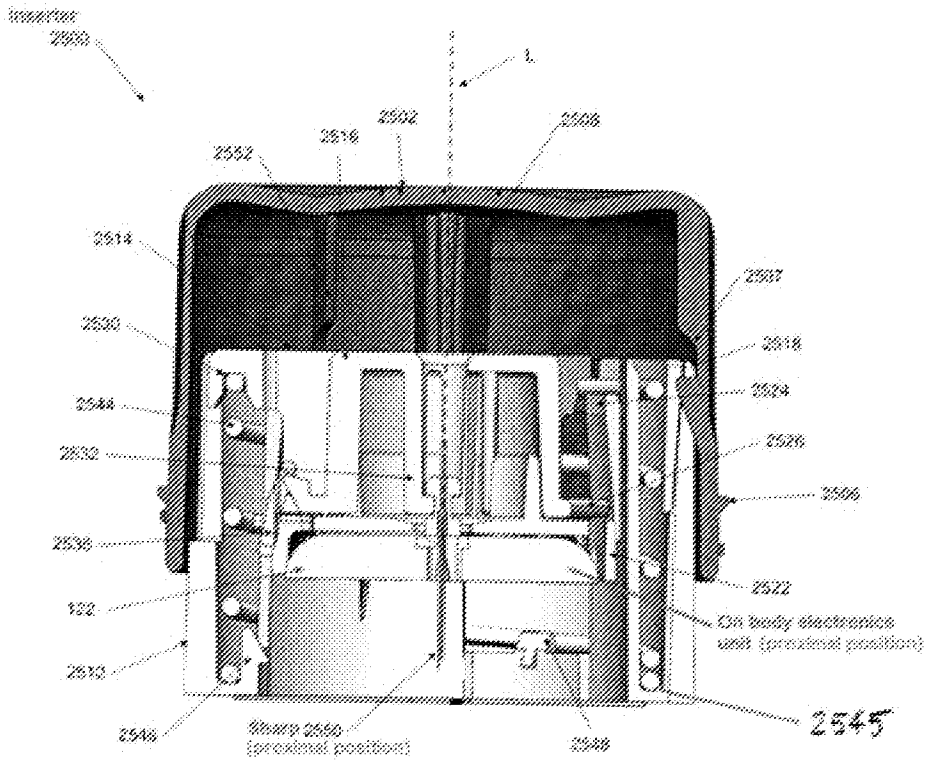
Claim No.	Pending Claim of '110 Application	Example Citation(s)
26A	A glucose monitoring assembly, the assembly comprising: **(1) an inserter comprising** **a sharp** configured to insert a portion of a glucose sensor into a subject; and (2) **an on body electronics unit, comprising**: **an on body electronics unit housing** comprising a plurality of recesses disposed on a periphery of the on body electronics unit housing, wherein the plurality of recesses comprises a first recess in a spaced relation to a second recess, and wherein the plurality of recesses is detachably engaged with the inserter; **the glucose sensor**; and on body electronics coupled with the glucose sensor, wherein the on body electronics is disposed within the on body electronics unit housing, and wherein the on body electronicsincludes a processor, memory, a power supply, and wireless communication circuitry configured to wirelessly communicate data indicative of a glucose level, wherein the inserter is configured to advance the on body electronics unit and the sharp from a proximal position entirely within the inserter to a distal position, and wherein the inserter is further configured to retract the sharp from the distal position to a retracted position entirely within the inserter.	**Exhibit 1**, U.S. Provisional Appl. No. 61/361,374 ("the '374 Provisional"), filed July 2, 2010, at Figs. 73-73O; *see, e.g.*, Fig. 73H (with labels added):  FIG. 73H *See also, e.g.*, **Exhibit 1** at: • Para. [00122] ("Sensor 14 may be configured to continuously sample the analyte of the user and convert the sampled analyte level, *e.g.*, a glucose concentration into a corresponding data signal . . . .")

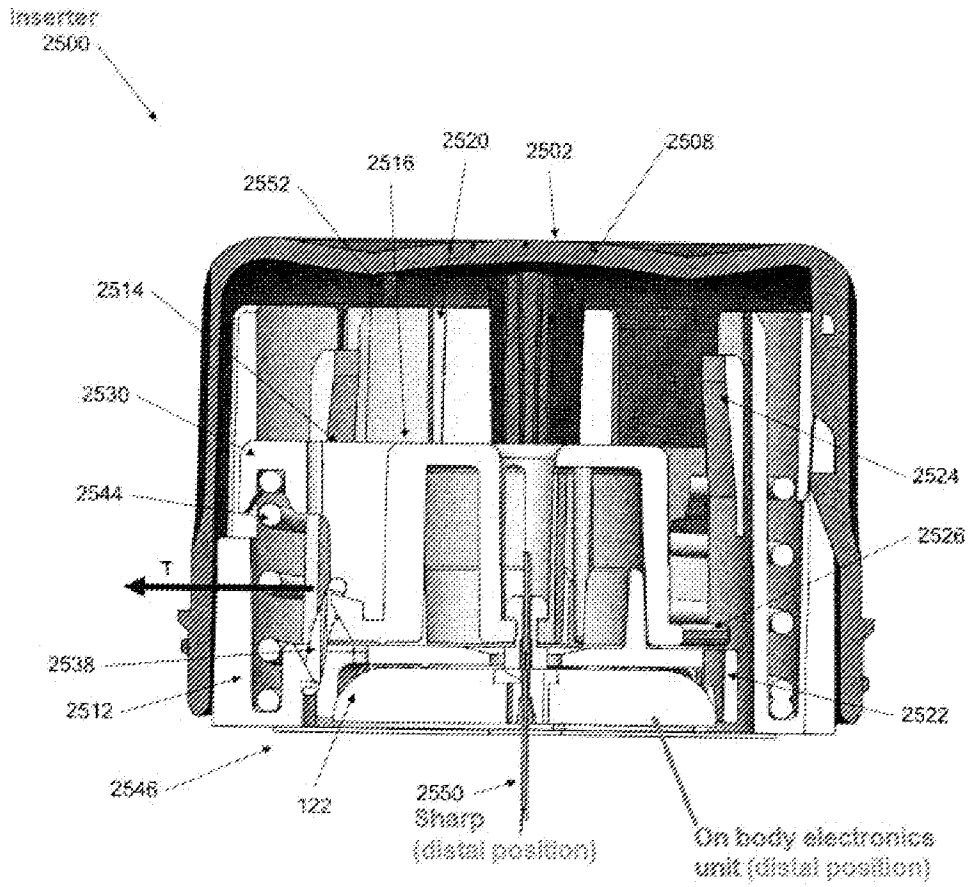
Claim No.	Pending Claim of '110 Application	Example Citation(s)
26B	A glucose monitoring assembly, the assembly comprising: (1) an inserter comprising **a sharp configured to insert a portion of a glucose sensor into a subject**; and (2) an on body electronics unit, comprising: an on body electronics unit housing comprising a plurality of recesses disposed on a periphery of the on body electronics unit housing, wherein the plurality of recesses comprises a first recess in a spaced relation to a second recess, and wherein the plurality of recesses is detachably engaged with the inserter; the glucose sensor; and on body electronics coupled with the glucose sensor, wherein the on body electronics is disposed within the on body electronics unit housing, and wherein the on body electronicsincludes a processor, memory, a power supply, and wireless communication circuitry configured to wirelessly communicate data indicative of a glucose level, wherein the inserter is configured to advance the on body electronics unit and the sharp from a proximal position entirely within the inserter to a distal position, and wherein the inserter is further configured to retract the sharp from the distal position to a retracted position entirely within the inserter.	**Exhibit 1** at: • Para. [00125] ("Sensor 14 may include a proximal retention portion 48. . . . The insertion portion 30 and the proximal retention portion 48 are sized and configured to be positioned with a sharp for installation into the skin of a subject[.]"). • Para. [00130] ("A portion of sensor 14 . . . may be situated above the surface of the skin, with a distal portion 30 penetrating through the skin and into the subcutaneous space in contact with the user's biofluid, such as interstitial fluid."). • Para. [00143] ("[A]n inserter may include one or more components for advancing a sharp towards the skin of the subject."). • Para. [00249] ("As sharp 2550 is further urged distally, it carries the sensor insertion portion 30 of sensor 14 (FIGURE 23) into the subcutaneous portion of the subject's skin S."). • Fig. 23 (with labels added):  FIG. 23

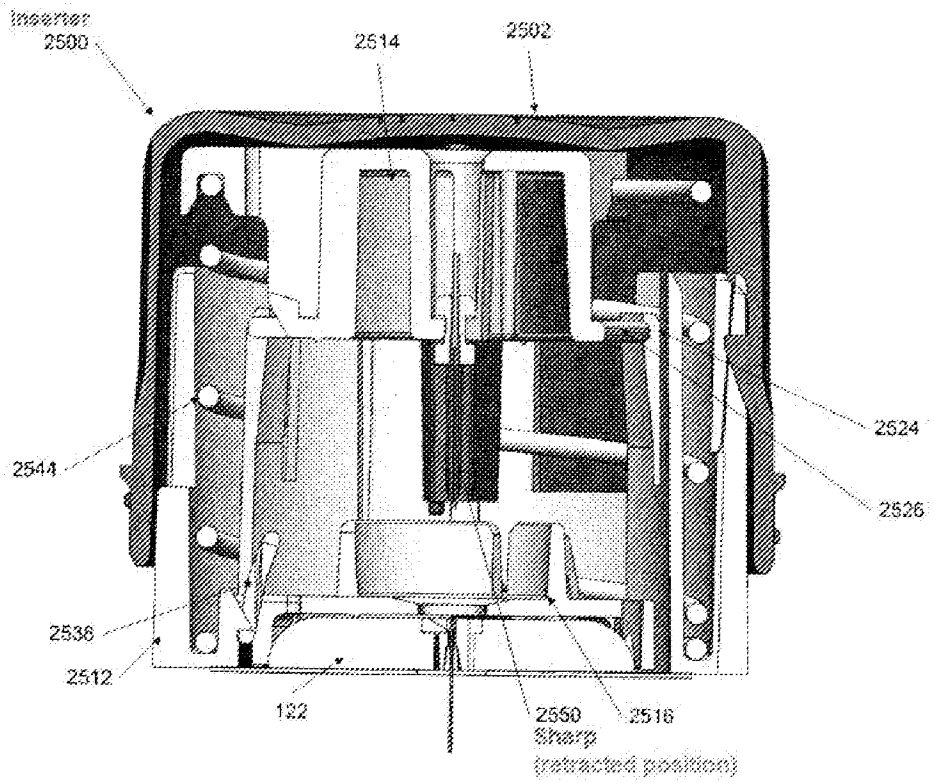
Claim No.	Pending Claim of '110 Application	Example Citation(s)
26C	A glucose monitoring assembly, the assembly comprising: (1) an inserter comprising a sharp configured to insert a portion of a glucose sensor into a subject; and (2) an on body electronics unit, comprising: **an on body electronics unit housing comprising a plurality of recesses disposed on a periphery of the on body electronics unit housing, wherein the plurality of recesses comprises a first recess in a spaced relation to a second recess, and wherein the plurality of recesses is detachably engaged with the inserter;** the glucose sensor; and on body electronics coupled with the glucose sensor, wherein the on body electronics is disposed within the on body electronics unit housing, and wherein the on body electronics includes a processor, memory, a power supply, and wireless communication circuitry configured to wirelessly communicate data indicative of a glucose level, wherein the inserter is configured to advance the on body electronics unit and the sharp from a proximal position entirely within the inserter to a distal position, and wherein the inserter is further configured to retract the sharp from the distal position to a retracted position entirely within the inserter.	**Exhibit 2**, *Mechanical Inserter, April 27, 2010* [*by*]: *Manuel Donnay* [PowerPoint] at 21 (depicting a plurality of recesses disposed on a periphery of the on body electronics unit housing, wherein the plurality of recesses comprises a first recess in a spaced relation to a second recess).  

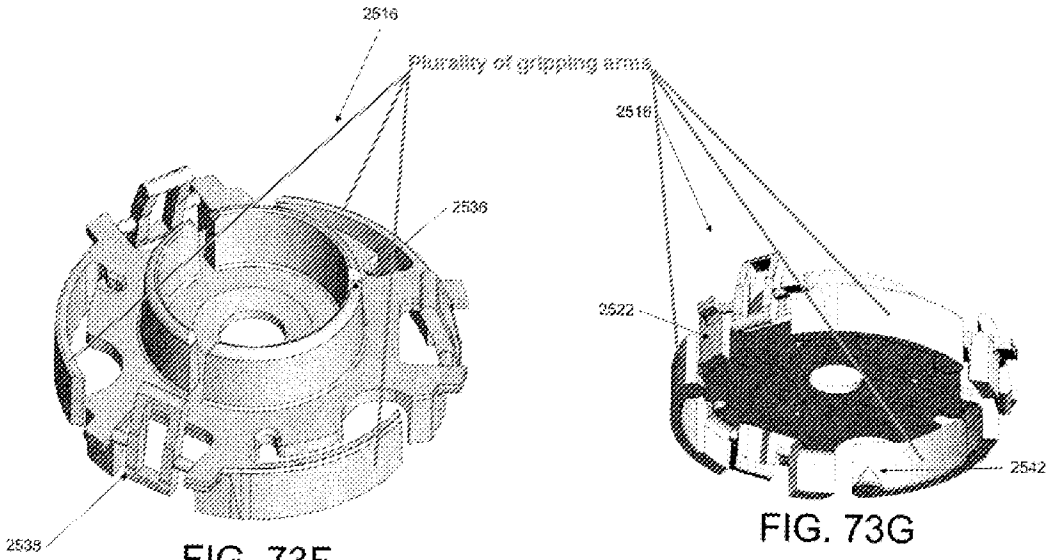
Claim No.	Pending Claim of '110 Application	Example Citation(s)
		See **Exhibit 2** at 10-11 (showing parts of inserter, e.g., plurality of gripping arms with engagement bosses, with which the plurality of recesses is detachably engaged).  *See also* **Exhibit 1** at Figs. 73F-G (showing same).  FIG. 73F  FIG. 73G

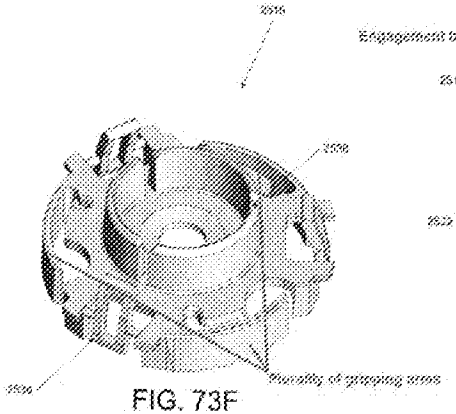
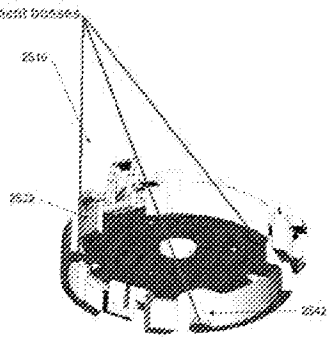
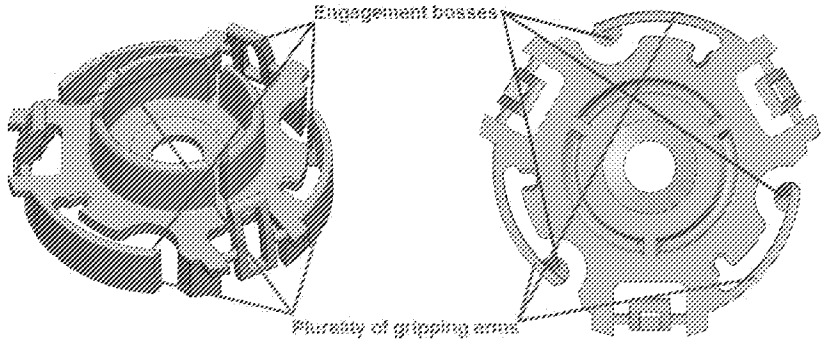
Claim No.	Pending Claim of '110 Application	Example Citation(s)
26D	A glucose monitoring assembly, the assembly comprising: (1) an inserter comprising a sharp configured to insert a portion of a glucose sensor into a subject; and (2) an on body electronics unit, comprising: an on body electronics unit housing comprising a plurality of recesses disposed on a periphery of the on body electronics unit housing, wherein the plurality of recesses comprises a first recess in a spaced relation to a second recess, and wherein the plurality of recesses is detachably engaged with the inserter; the glucose sensor; and **on body electronics coupled with the glucose sensor, wherein the on body electronics is disposed within the on body electronics unit housing, and wherein the on body electronics includes a processor, memory, a power supply, and wireless communication circuitry configured to wirelessly communicate data indicative of a glucose level,** wherein the inserter is configured to advance the on body electronics unit and the sharp from a proximal position entirely within the inserter to a distal position, and wherein the inserter is further configured to retract the sharp from the distal position to a retracted position entirely within the inserter.	**Exhibit 1** at: • Para. [00134] ("Sensor control unit 12, including its associated electronics 80, are housed in housing 122. . . . [E]lectronics 80 may include one or more of, *e.g.*, an analog interface for connecting to the sensor 14, a processor, which may include, *e.g.*, an ASIC 91, antenna 94, power supply 82 to power the sensor and/or communications components[.]"). • Para. [00110] ("Communication may occur, *e.g.*, via RF communication, infrared communication, Bluetooth communciaiton, Zigbee communication, 802.1x communication, or WiFi communication, etc."). • Para. [00110] ("[W]hen the on-body unit 16 is positioned within the radiated or provided RF signal range radiated from the monitor unit 18, the on-body unit 16 in certain embodiments is configured to provide one or more signals associated with the monitored analyte level received from the analyte sensor 14 to the monitor unit 18."). • Para. [00113] ("[S]ensor control unit 12 may further include local memory[.]"). • Para. [00142] ("In some embodiments, communications circuitry, such as RFID antenna or communications circuitry, is provided."). • Para. [00156] ("The sensor housing 122 can be configured to hold at least a portion of sensor 14 and sensor control unit 12. . . . [E]lectronics 80 of the sensor control unit 12 . . . are positioned within sensor housing 122."). • *See also* Fig. 7 (with labels added):  FIG. 7

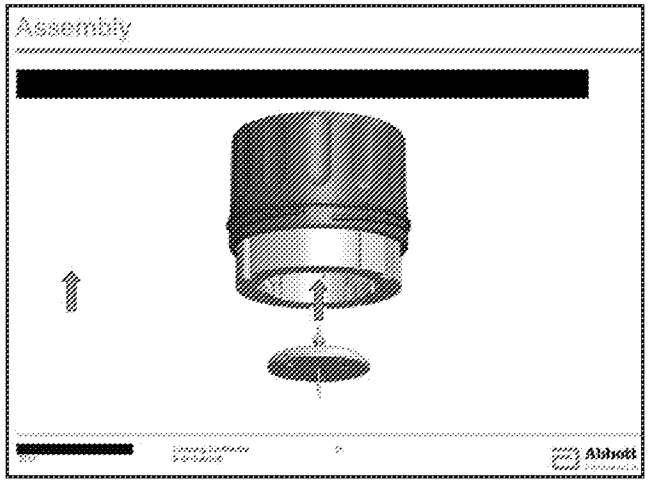
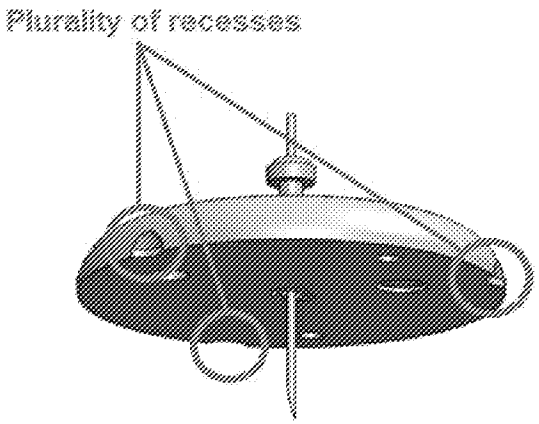
Claim No.	Pending Claim of '110 Application	Example Citation(s)
26E	A glucose monitoring assembly, the assembly comprising: (1) an inserter comprising a sharp configured to insert a portion of a glucose sensor into a subject; and (2) an on body electronics unit, comprising: an on body electronics unit housing comprising a plurality of recesses disposed on a periphery of the on body electronics unit housing, wherein the plurality of recesses comprises a first recess in a spaced relation to a second recess, and wherein the plurality of recesses is detachably engaged with the inserter; the glucose sensor; and on body electronics coupled with the glucose sensor, wherein the on body electronics is disposed within the on body electronics unit housing, and wherein the on body electronicsincludes a processor, memory, a power supply, and wireless communication circuitry configured to wirelessly communicate data indicative of a glucose level, **wherein the inserter is configured to advance the on body electronics unit and the sharp from a proximal position entirely within the inserter** to a distal position, and wherein the inserter is further configured to retract the sharp from the distal position to a retracted position entirely within the inserter.	**Exhibit 1** at Fig. 73H (with labels added):  FIG. 73H

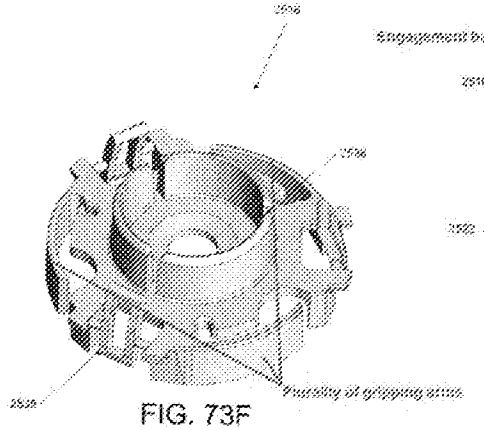
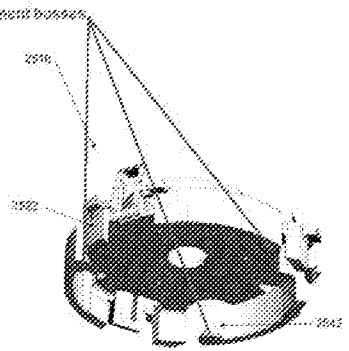
Claim No.	Pending Claim of '110 Application	Example Citation(s)
26F	A glucose monitoring assembly, the assembly comprising: (1) an inserter comprising a sharp configured to insert a portion of a glucose sensor into a subject; and (2) an on body electronics unit, comprising: an on body electronics unit housing comprising a plurality of recesses disposed on a periphery of the on body electronics unit housing, wherein the plurality of recesses comprises a first recess in a spaced relation to a second recess, and wherein the plurality of recesses is detachably engaged with the inserter; the glucose sensor; and on body electronics coupled with the glucose sensor, wherein the on body electronics is disposed within the on body electronics unit housing, and wherein the on body electronicsincludes a processor, memory, a power supply, and wireless communication circuitry configured to wirelessly communicate data indicative of a glucose level, **wherein the inserter is configured to advance the on body electronics unit and the sharp** from a proximal position entirely within the inserter **to a distal position**, and wherein the inserter is further configured to retract the sharp from the distal position to a retracted position entirely within the inserter.	**Exhibit 1** at Fig. 73K (with labels added):  FIG. 73K

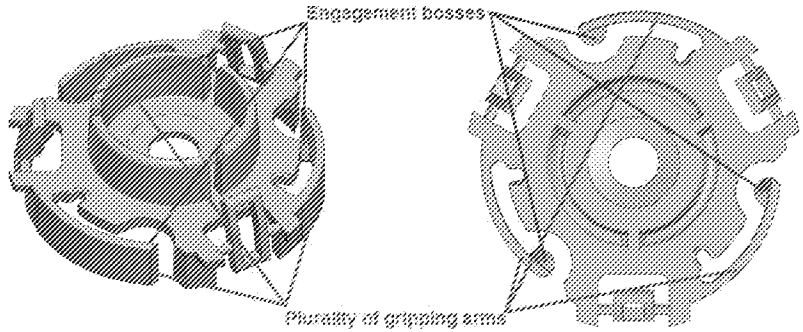
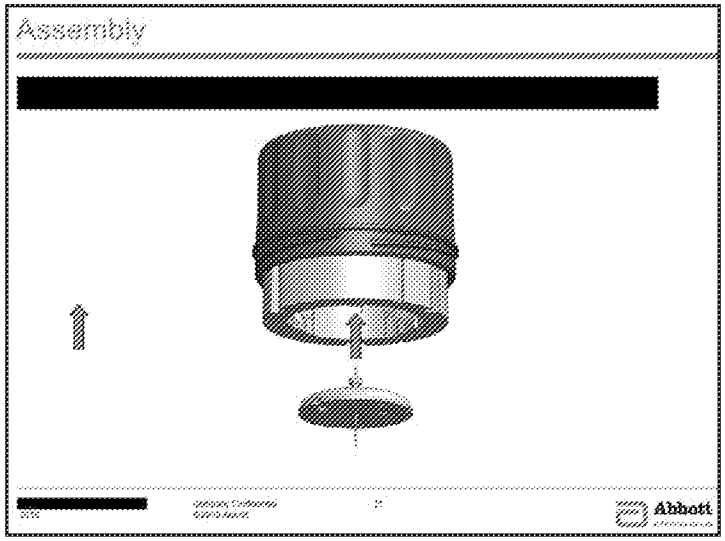
Claim No.	Pending Claim of '110 Application	Example Citation(s)
26G	A glucose monitoring assembly, the assembly comprising: (1) an inserter comprising a sharp configured to insert a portion of a glucose sensor into a subject; and (2) an on body electronics unit, comprising: an on body electronics unit housing comprising a plurality of recesses disposed on a periphery of the on body electronics unit housing, wherein the plurality of recesses comprises a first recess in a spaced relation to a second recess, and wherein the plurality of recesses is detachably engaged with the inserter; the glucose sensor; and on body electronics coupled with the glucose sensor, wherein the on body electronics is disposed within the on body electronics unit housing, and wherein the on body electronicsincludes a processor, memory, a power supply, and wireless communication circuitry configured to wirelessly communicate data indicative of a glucose level, wherein the inserter is configured to advance the on body electronics unit and the sharp from a proximal position entirely within the inserter to a distal position, and **wherein the inserter is further configured to retract the sharp from the distal position to a retracted position entirely within the inserter**.	**Exhibit 1** at Fig. 73M (with label added):  FIG. 73M

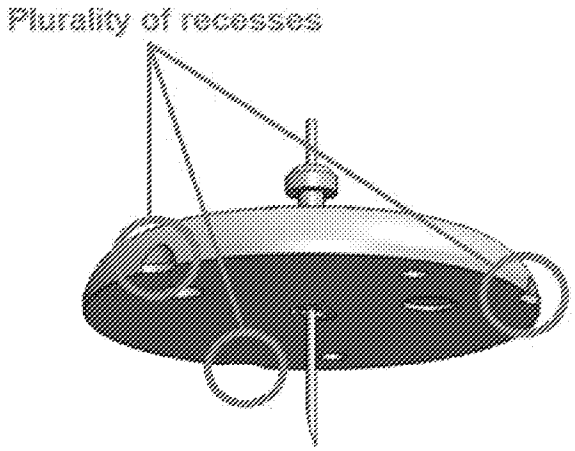
Claim No.	Pending Claim of '110 Application	Example Citation(s)
27	The glucose monitoring assembly of claim 26, wherein the inserter further comprises a plurality of gripping arms.	**Exhibit 1** at: • Para. [00242] ("Retention members, such as ribs 2520, pinch spring arms 2522 located on carriage 2516 to prevent sensor housing from falling out of inserter 2500 when sheath 2512 is in the extended position."). • Figs. 73F-G (with labels added):  FIG. 73F FIG. 73G

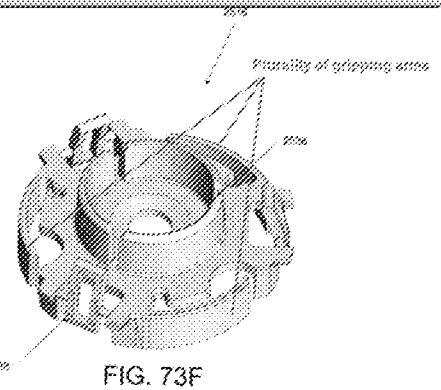
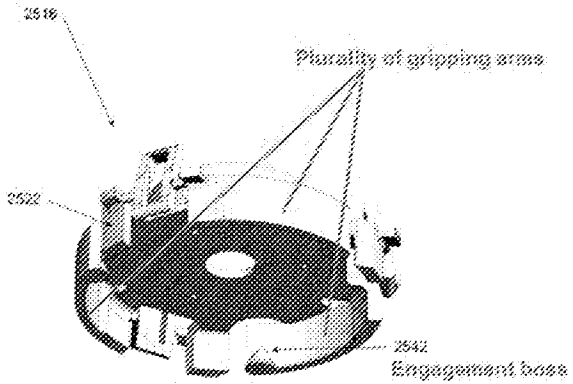
Claim No.	Pending Claim of '110 Application	Example Citation(s)
28A	The glucose monitoring assembly of claim 27, **wherein each gripping arm of plurality of gripping arms is configured to be engaged with a corresponding recess of the plurality of recesses of the on body electronics unit housing when the on body electronics unit is in the proximal position**, and wherein each gripping arm of the plurality of gripping arms is further configured to be disengaged from the corresponding recess of the plurality of recesses when the on body electronics unit is in the distal position.	**Exhibit 1** at: • Para. [00242] ("Retention members, such as ribs 2520, pinch spring arms 2522 located on carriage 2516 to prevent sensor housing 122 from falling out of inserter 2500 when sheath 2512 is in the extended position.") • Para. [00244] ("Spring hook 2542 allows for support for retaining sensor housing when the inserter has not been fired and allows for release of sensor housing 122 when it has been attached to the skin of the user."). • Figs. 73F-G (showing plurality of gripping arms each of which is configured to engage with a corresponding recess of the on body electroncis unit housing)  FIG. 73F  FIG. 73G *See also* **Exhibit 2** at 10-11 (showing same). 

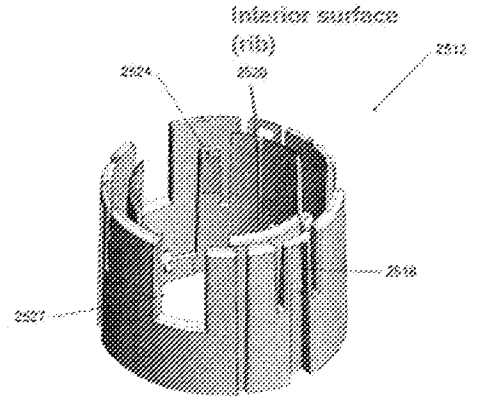
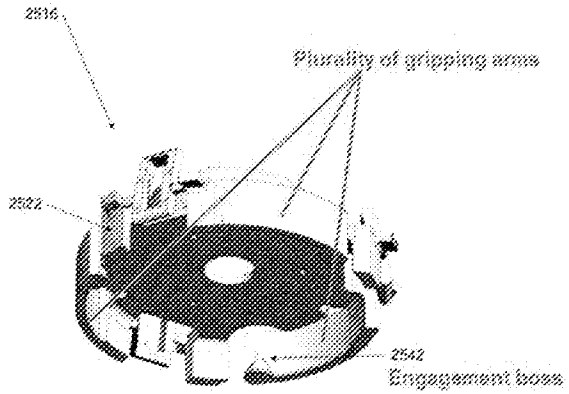
Claim No.	Pending Claim of '110 Application	Example Citation(s)
		See also **Exhibit 2** at 21:  

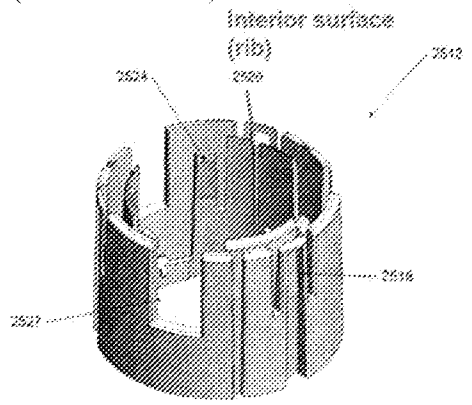
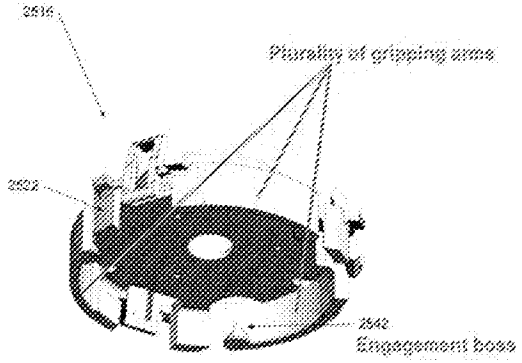
Claim No.	Pending Claim of '110 Application	Example Citation(s)
28B	The glucose monitoring assembly of claim 27, wherein each gripping arm of plurality of gripping arms is configured to be engaged with a corresponding recess of the plurality of recesses of the on body electronics unit housing when the on body electronics unit is in the proximal position, and **wherein each gripping arm of the plurality of gripping arms is further configured to be disengaged from the corresponding recess of the plurality of recesses when the on body electronics unit is in the distal position**.	**Exhibit 1** at: • Para. [00242] ("Retention members, such as ribs 2520, pinch spring arms 2522 located on carriage 2516 to prevent sensor housing 122 from falling out of inserter 2500 when sheath 2512 is in the extended position."). • Para. [00244] ("Spring hook 2542 allows for support for retaining sensor housing when the inserter has not been fired and allows for release of sensor housing 122 when it has been attached to the skin of the user."). • Figs. 73F-G (showing plurality of gripping arms each of which is configured to engage with a corresponding recess of the on body electroncis unit housing).  FIG. 73F  FIG. 73G *See also* **Exhibit 2** at 10-11 (showing same).

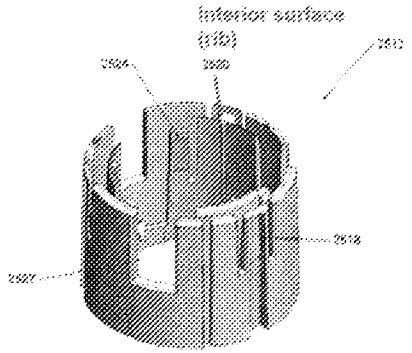
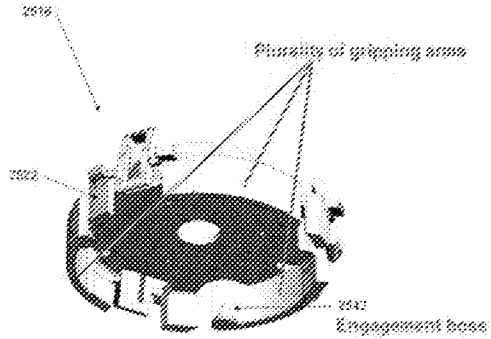
Claim No.	Pending Claim of '110 Application	Example Citation(s)
		 *See also* **Exhibit 2** at 21: 

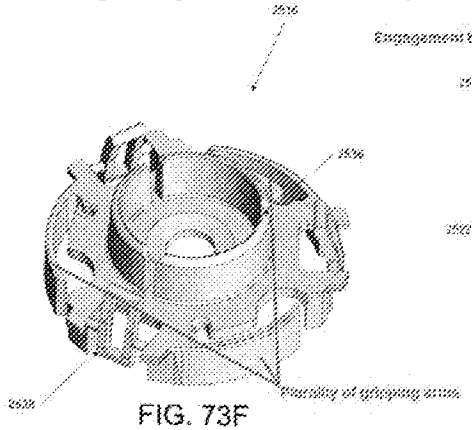
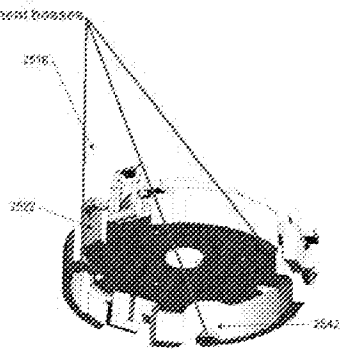
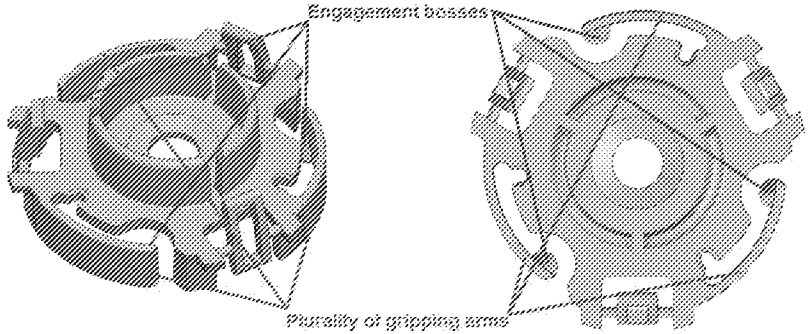
Claim No.	Pending Claim of '110 Application	Example Citation(s)
		
29	The glucose monitoring assembly of claim 27, wherein each gripping arm of the plurality of gripping arms is biased in a radially outward direction.	**Exhibit 1** at: • Para. [00242] ("Retention members, such as ribs 2520, pinch *spring arms 2522* located on carriage 2516 to prevent sensor housing 122 from falling out of inserter 2500 when sheath 2512 is in the extended position. Ribs 2520 do not extend to the bottom of sheath 2512, thus allowing carriage 2516 to release sensor housing 122 when it has traveled to the bottom of sheath 2512 during insertion.") (italics added). • Figs. 73F-G (with labels added) (disclosing each gripping arm of the plurality of gripping arms biased in a radially outward direction):

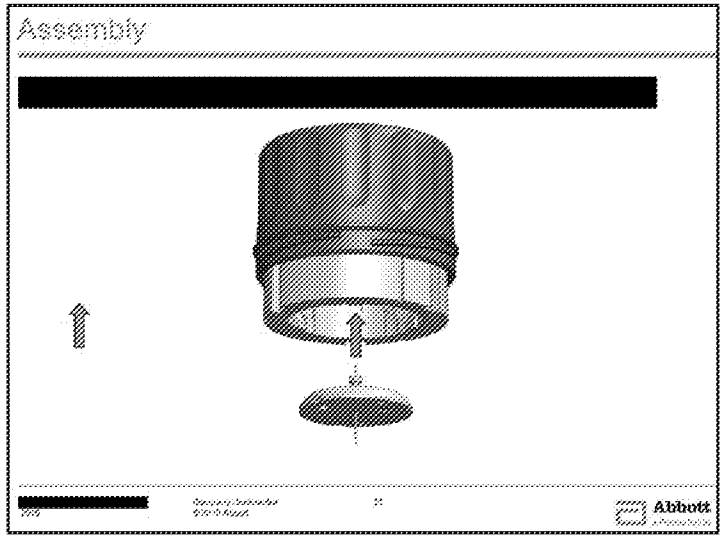
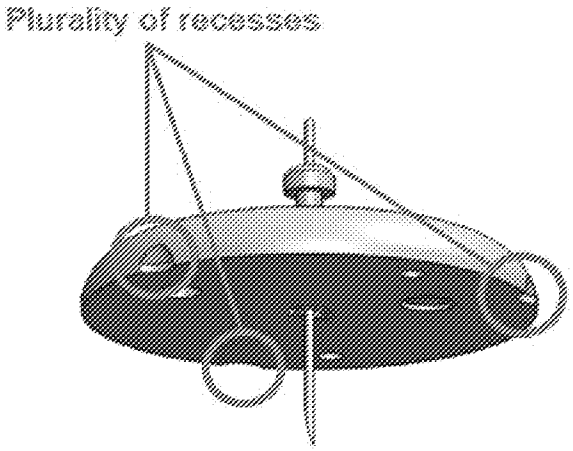
Claim No.	Pending Claim of '110 Application	Example Citation(s)
		 FIG. 73F  FIG. 73G

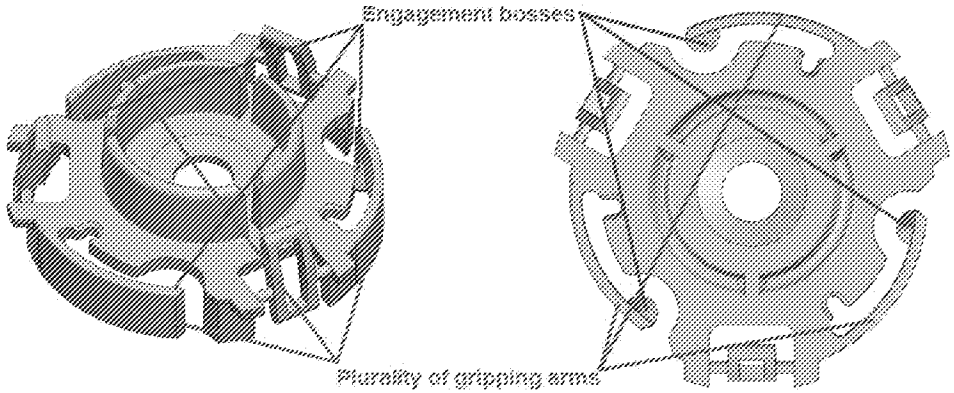
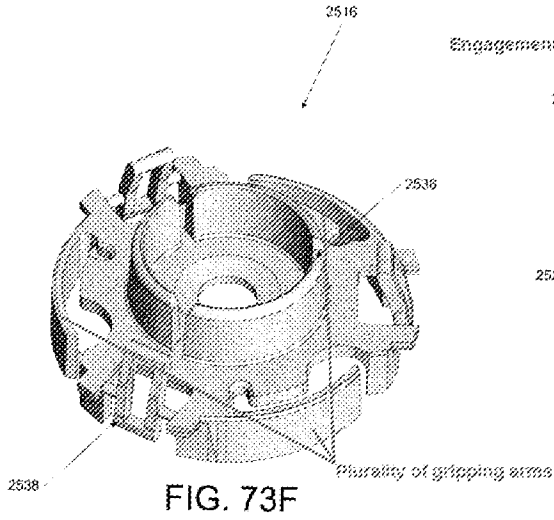
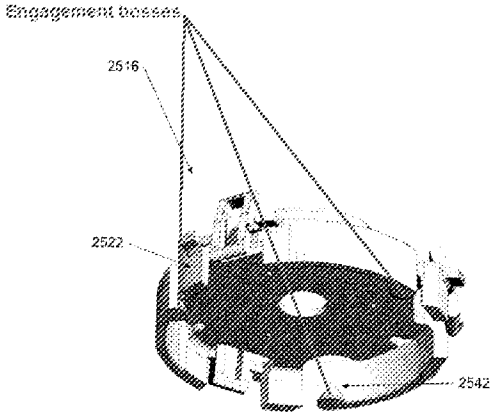
Claim No.	Pending Claim of '110 Application	Example Citation(s)
30	The glucose monitoring assembly of claim 32, wherein the corresponding gripping arm of the plurality of gripping arms is configured to deflect in a radially outward direction when the each interior surface of the plurality of interior surfaces is not in contact with the corresponding gripping arm of the plurality of gripping arms.	**Exhibit 1** at: • Para. [00242] ("Retention members, such as ribs 2520, pinch spring arms 2522 located on carriage 2516 to prevent sensor housing 122 from falling out of inserter 2500 when sheath 2512 is in the extended position. Ribs 2520 do not extend to the bottom of sheath 2512, thus allowing carriage 2516 to release sensor housing 122 when it has traveled to the bottom of sheath 2512 during insertion.") • Figs. 73C and 73G (with labels added):  FIG. 73C  FIG. 73G

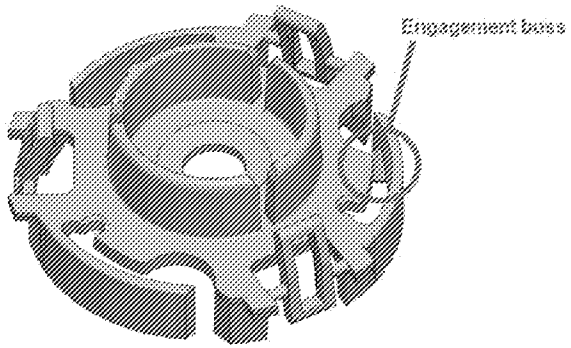
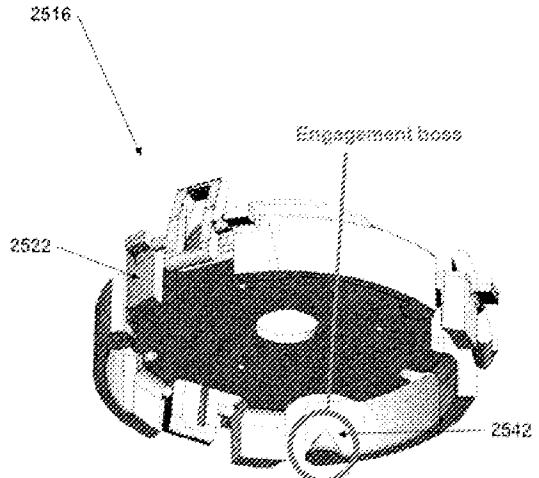
Claim No.	Pending Claim of '110 Application	Example Citation(s)
31	The glucose monitoring assembly of claim 27, wherein the inserter further comprises a plurality of interior surfaces, wherein each interior surface of the plurality of interior surfaces is configured to hold a corresponding gripping arm of the plurality of gripping arms against a corresponding recess of the plurality of recesses of the on body electronics unit housing when the on body electronics unit is in the proximal position.	**Exhibit 1** at: • Para. [00242] ("Retention members, such as ribs 2520, pinch spring arms 2522 located on carriage 2516 to prevent sensor housing 122 from falling out of inserter 2500 when sheath 2512 is in the extended position.") • Para. [00244] ("Spring hook 2542 allows for support for retaining sensor housing when the inserter has not been fired and allows for release of sensor housing 122 when it has been attached to the skin of the user."). • Figs. 73C and 73G (with labels added):  FIG. 73C  FIG. 73G

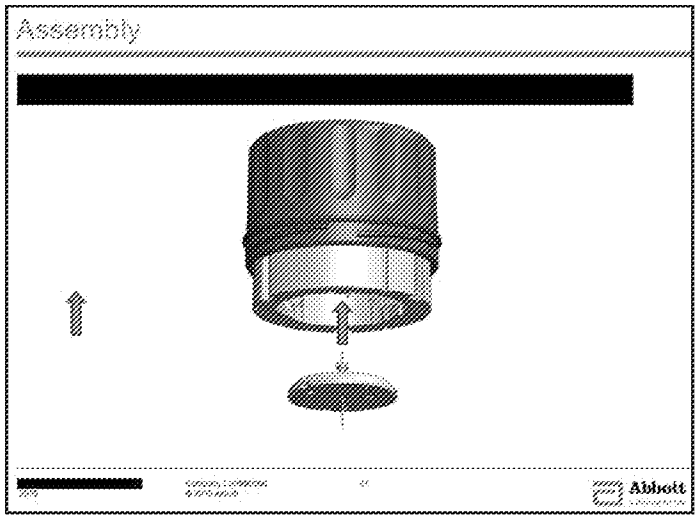
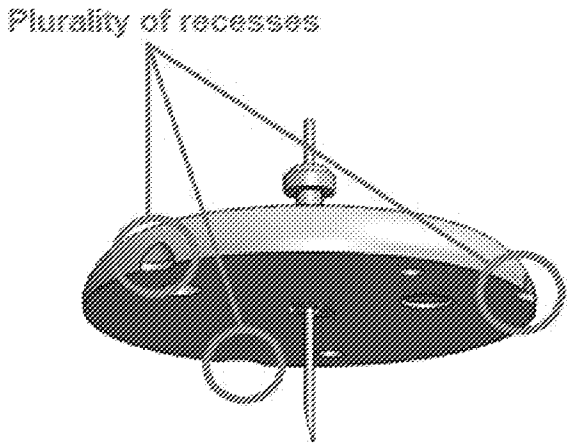
Claim No.	Pending Claim of '110 Application	Example Citation(s)
32	The glucose monitoring assembly of claim 31, wherein the inserter is further configured such that the each interior surface of the plurality interior surfaces is not in contact with the on body electronics unit is in the distal position.	**Exhibit 1** at: • Para. [00242] ("Retention members, such as ribs 2520, pinch spring arms 2522 located on carriage 2516 to prevent sensor housing 122 from falling out of inserter 2500 when sheath 2512 is in the extended position. Ribs 2520 do not extend to the bottom of sheath 2512, thus allowing carriage 2516 to release sensor housing 122 when it has traveled to the bottom of sheath 2512 during insertion.") • Para. [00244] ("Spring hook 2542 allows for support for retaining sensor housing when the inserter has not been fired and allows for release of sensor housing 122 when it has been attached to the skin of the user."). • Figs. 73C and 73G (with labels added):  FIG. 73C  FIG. 73G

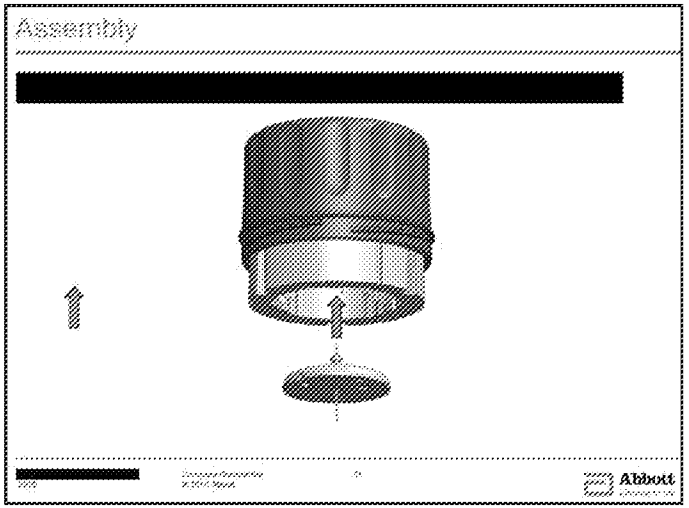
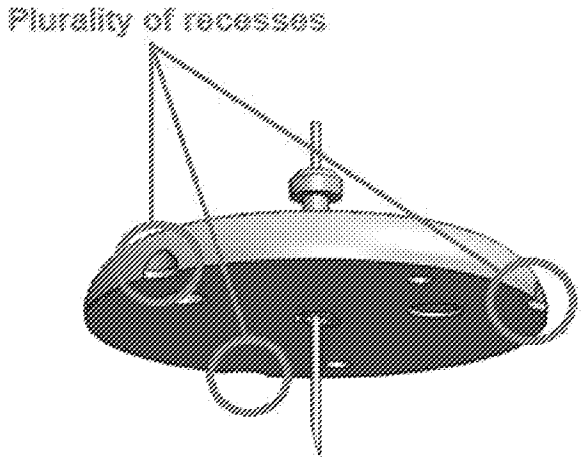
Claim No.	Pending Claim of '110 Application	Example Citation(s)
33	The glucose monitoring assembly of claim 27, wherein each gripping arm of the plurality of gripping arms comprises an engagement boss configured to engage with a corresponding recess of the plurality of recesses on the on body electronics unit housing when the on body electronics unit is in the proximal position.	**Exhibit 1** at: • Para. [00242] ("Retention members, such as ribs 2520, pinch spring arms 2522 located on carriage 2516 to prevent sensor housing 122 from falling out of inserter 2500 when sheath 2512 is in the extended position."). • Para. [00244] ("Spring hook 2542 allows for support for retaining sensor housing when the inserter has not been fired and allows for release of sensor housing 122 when it has been attached to the skin of the user."). • Figs. 73F-G (showing plurality of gripping arms each of which is configured to engage with a corresponding recess of the on body electroncis unit housing).  FIG. 73F  FIG. 73G *See also* **Exhibit 2** at 10-11 (showing same). 

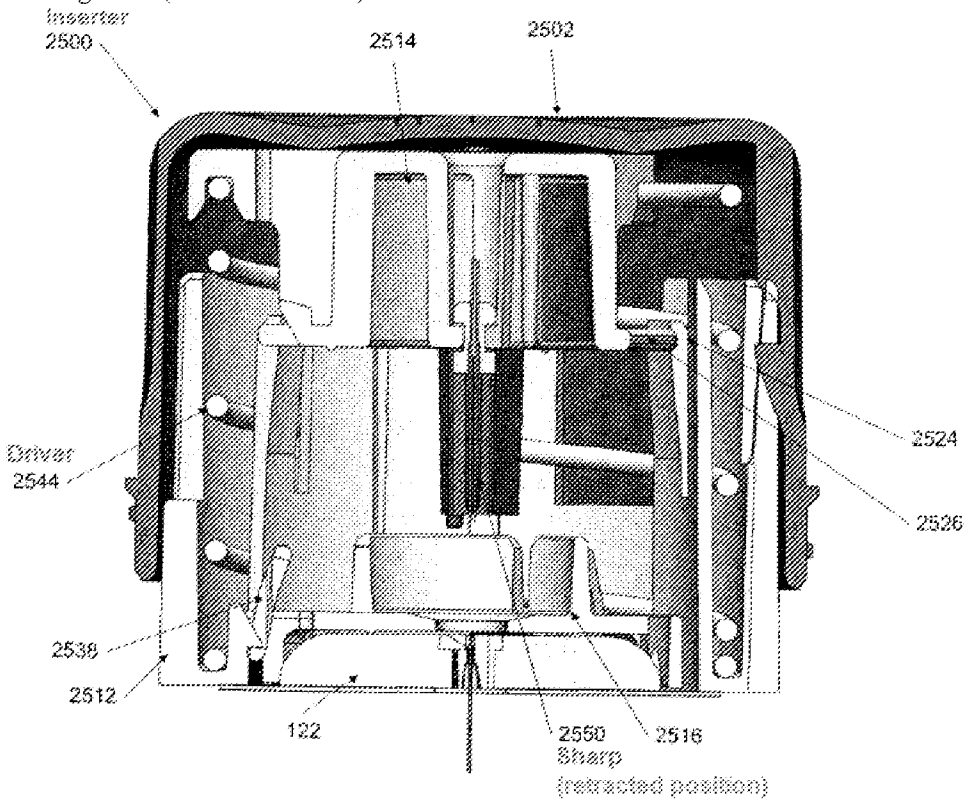
Claim No.	Pending Claim of '110 Application	Example Citation(s)
		See also **Exhibit 2** at 21:  

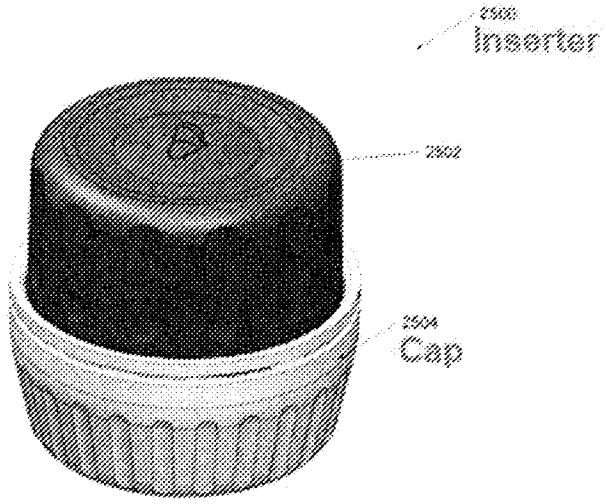
Claim No.	Pending Claim of '110 Application	Example Citation(s)
34	The glucose monitoring assembly of claim 33, wherein the engagement boss is disposed on a tip portion of the gripping arm.	*See* **Exhibit 2** at 10-11 (showing engagement bosses disposed on the tip portions of the gripping arms).  *See also* **Exhibit 1** at Figs. 73F-G (showing same).  FIG. 73F  FIG. 73G

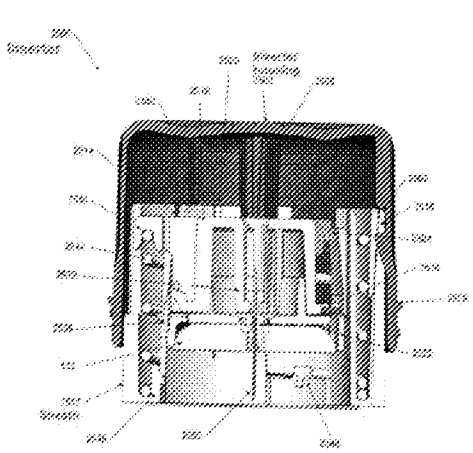
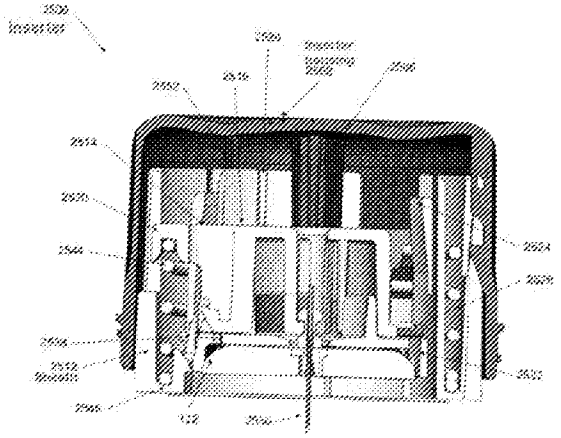
Claim No.	Pending Claim of '110 Application	Example Citation(s)
35	The glucose monitoring assembly of claim 33, wherein the engagement boss comprises a conical shape.	*See* **Exhibit 2** at 11 (showing engagement bosses comprising a conical shape).  *See also* **Exhibit 1** at Fig. 73G (showing same).  FIG. 73G

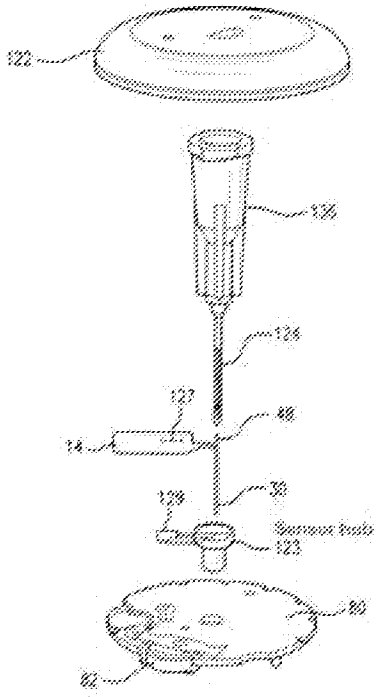
Claim No.	Pending Claim of '110 Application	Example Citation(s)
36	The glucose monitoring assembly of claim 26, wherein each recess of the plurality of recesses comprises a concave portion.	**Exhibit 2** at 21 (showing each recess of the plurality of recesses comprising a concave portion):  

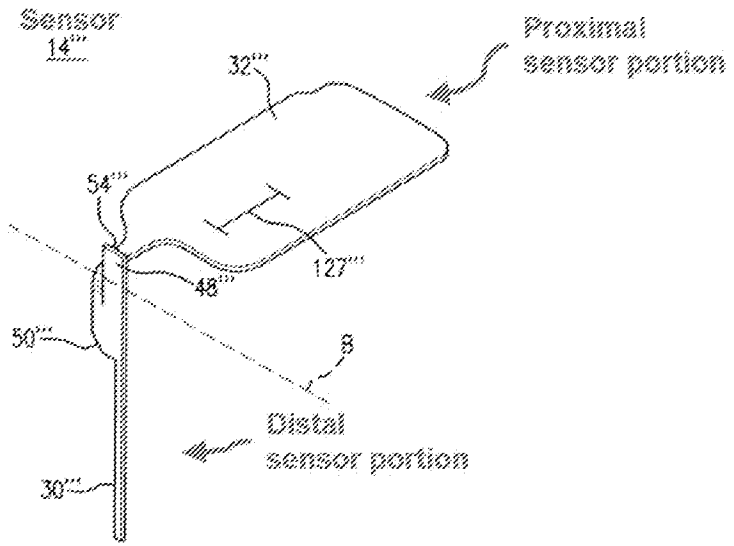
Claim No.	Pending Claim of '110 Application	Example Citation(s)
37	The glucose monitoring assembly of claim 26, wherein each recess of the plurality of recesses is disposed on a side wall of the on body electronics unit housing.	**Exhibit 2** at 21 (showing each recess of the plurality of recesses is disposed on a side wall of the on body electronics unit housing):  

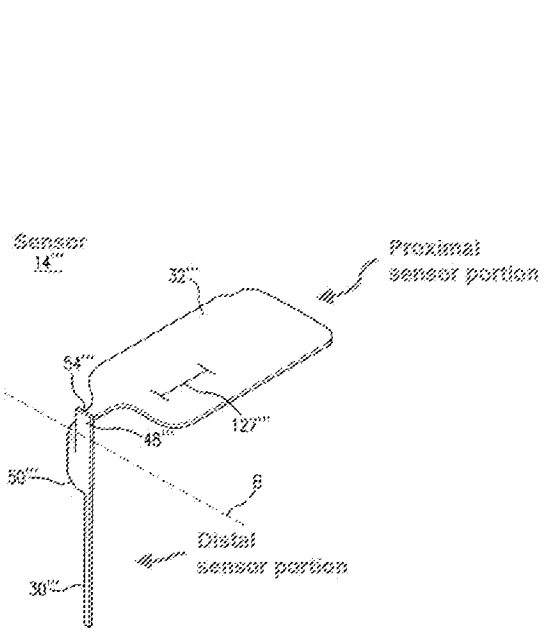
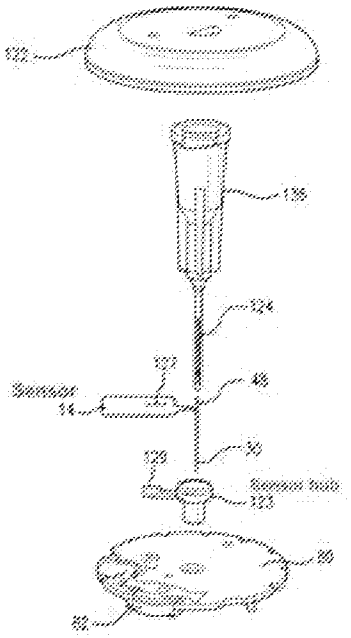
Claim No.	Pending Claim of '110 Application	Example Citation(s)
38	The glucose monitoring assembly of claim 26, wherein the inserter further comprises a driver disposed in the inserter, wherein the driver is configured to apply a force that retracts the sharp after the sharp reaches the distal position.	**Exhibit 1** at: • Para. [00251] ("[D]isengagement of the needle carrier 2514 from the carriage 2516 permits spring 2544 to expand, thereby advancing the needle carrier 2514 to a proximal position and withdrawing the sharp 2550 from the skin S of the subject while leaving the sensor housing 122 attached to the skin."). • Fig. 73M (with labels added):  FIG. 73M

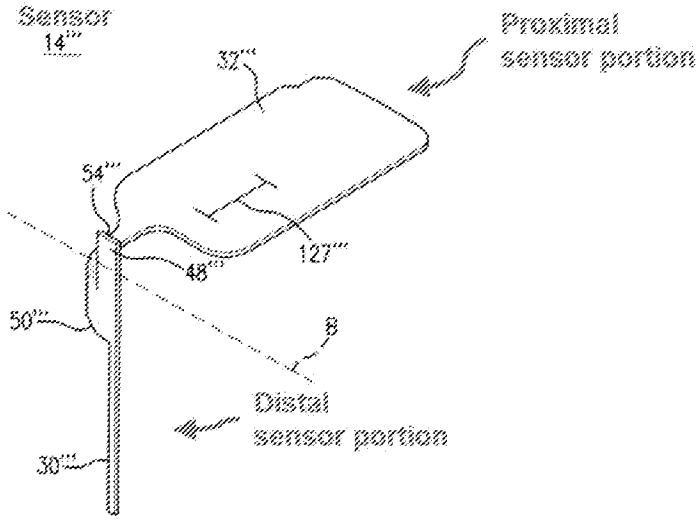
Claim No.	Pending Claim of '110 Application	Example Citation(s)
39	The glucose monitoring assembly of claim 26, further comprising a cap removably attached to a distal portion of the inserter.	**Exhibit 1** at: • Para. [00240] ("Inserter 2500 generally includes . . . a removable distal cap 2504[.]"); *see also, e.g.*, paras. [00147]-[00149] (disclosing a cap removably attached to a distal portion of the inserter). • Fig. 73 (with labels added):  FIG. 73

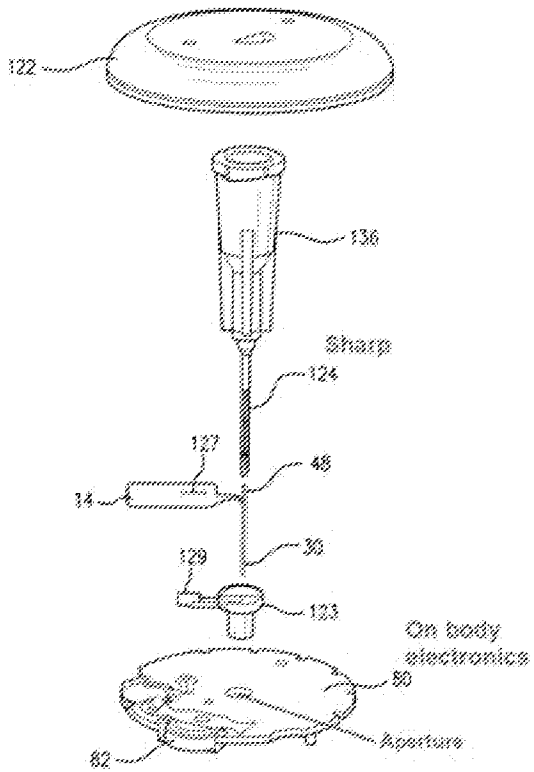
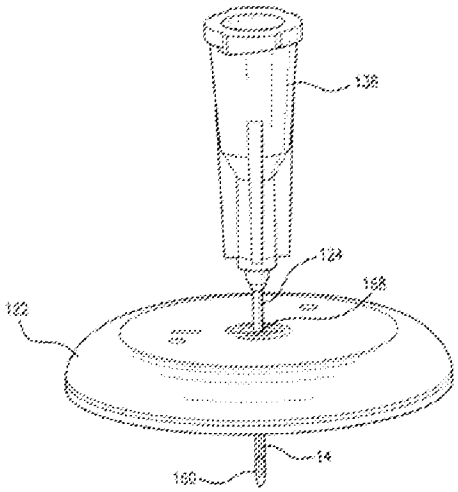
Claim No.	Pending Claim of '110 Application	Example Citation(s)
43	The glucose monitoring assembly of claim 26, wherein the inserter further comprises an inserter housing and a sheath, and wherein the inserter is configured to move in a downward direction towards the skin surface relative to the sheath in response to an application of force on the inserter, and wherein the sheath is configured to remain stationary relative to the skin surface in response to the application of force on the inserter housing.	**Exhibit 1** at: • Para. [00240] ("Inserter 2500 generally includes, e.g., a handle . . . handle 2502 is advanced relative to sheath 2512 in order to advance the medical device distally and into the skin of the patient."). • Figs. 73I and 73J (with labels added):  FIG. 73I  FIG. 73J

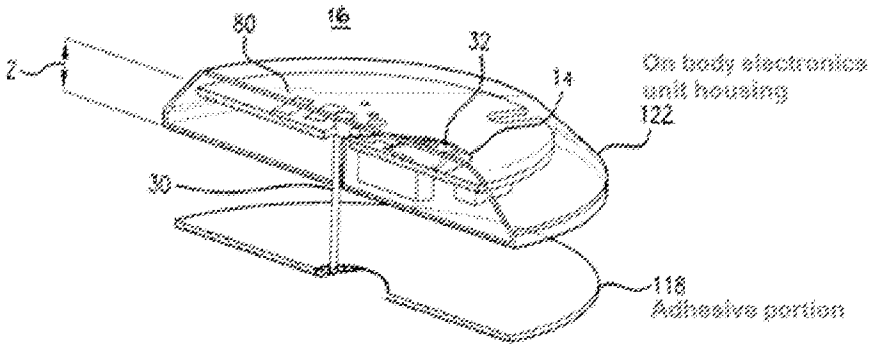
Claim No.	Pending Claim of '110 Application	Example Citation(s)
45A	The glucose monitoring assembly of claim 26, **wherein the on body electronics unit further comprises a sensor hub**, wherein the glucose sensor comprises a distal sensor portion and a proximal sensor portion, wherein the distal sensor portion is configured to sense the glucose level of the subject, wherein the proximal sensor portion is engaged with the sensor hub, and wherein the distal sensor portion is substantially orthogonal to the proximal sensor portion.	**Exhibit 1** at: • Para. [00156] ("As further illustrated in FIGURE 23, electronics 80 of the sensor control unit 12 . . . and sensor hub 123 are positioned within sensor housing 122."). • Fig. 23 (with label added):  FIG.23

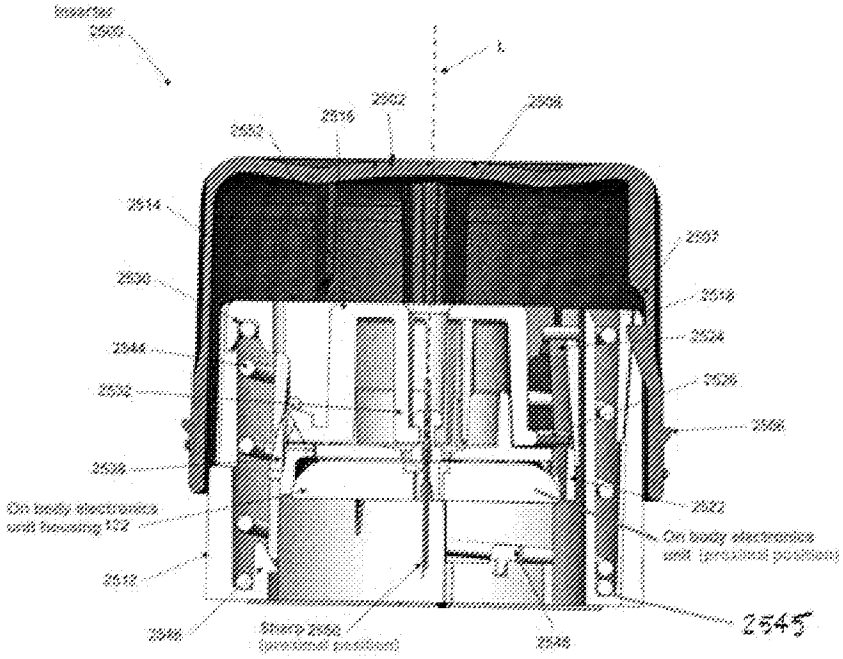
Claim No.	Pending Claim of '110 Application	Example Citation(s)
45B	The glucose monitoring assembly of claim 26, wherein the on body electronics unit further comprises a sensor hub, **wherein the glucose sensor comprises a distal sensor portion and a proximal sensor portion,** wherein the distal sensor portion is configured to sense the glucose level of the subject, wherein the proximal sensor portion is engaged with the sensor hub, and **wherein the distal sensor portion is substantially orthogonal to the proximal sensor portion.**	**Exhibit 1** at: • Para. [0006] ("[T]he sensor includes a body having a proximal section and a distal section . . . ."). • Para. [0008] ("[T]he proximal section of the sensor may be disposed in a horizontal plane, and the distal section of the sensory body may be disposed in a vertical plane."); *see also* para. [0024] ("[T]he proximal section and the distal section are in planes substantially perpendicular to each other, e.g., the area may define an angle of . . . about 90°."); and *see also* para. [00125] ("In use, the sensor 14 may be configured to bend (e.g., along the line B) and therefore be positioned in two substantially perpendicular, intersecting planes."). • Fig. 6B (with labels added):  FIG.6B

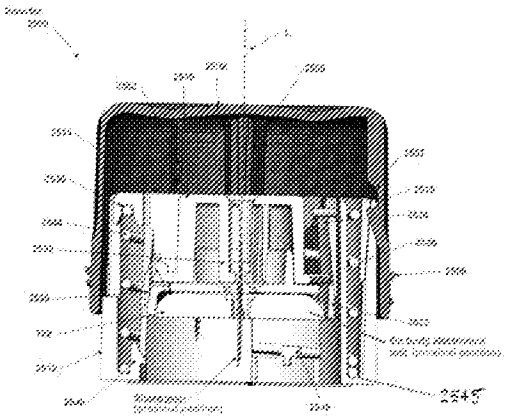
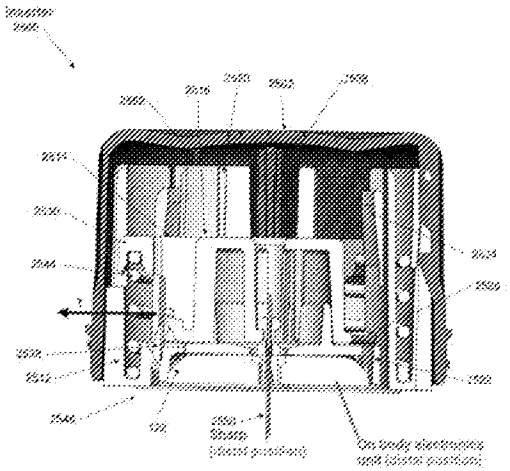
Claim No.	Pending Claim of '110 Application	Example Citation(s)
45C	The glucose monitoring assembly of claim 26, wherein the on body electronics unit further comprises a sensor hub, wherein the glucose sensor comprises a distal sensor portion and a proximal sensor portion, wherein the distal sensor portion is configured to sense the glucose level of the subject, **wherein the proximal sensor portion is engaged with the sensor hub**, and wherein the distal sensor portion is substantially orthogonal to the proximal sensor portion.	**Exhibit 1** at: • Para [00156] ("Sensor 14 may include a positioning structure, or slit 127 which receives a positioning member, such as tab 129 of sensor hub 123."). • Figs. 6B & 23 (with labels added):  FIG.6B  FIG.23

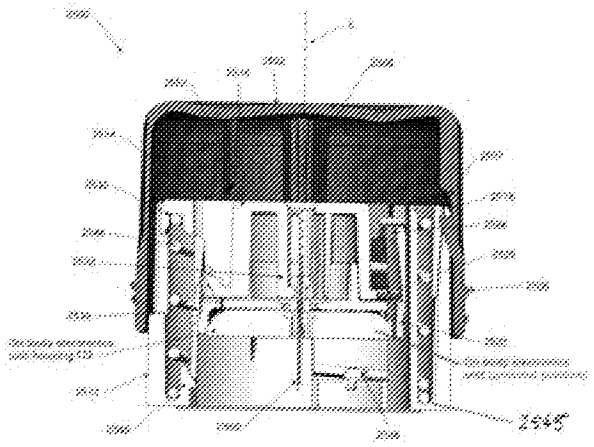
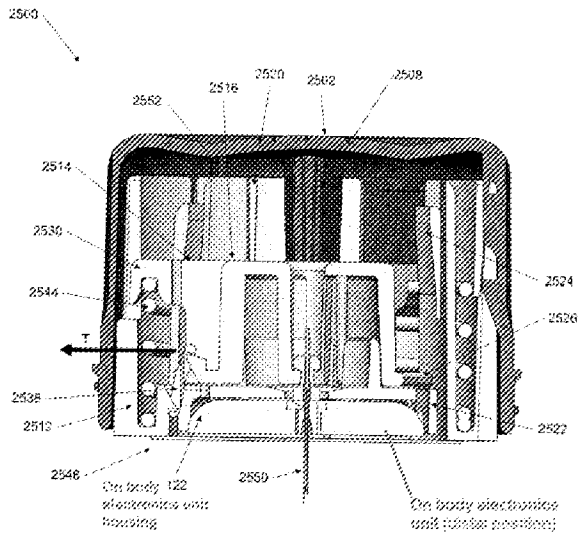
Claim No.	Pending Claim of '110 Application	Example Citation(s)
45D	The glucose monitoring assembly of claim 26, wherein the on body electronics unit further comprises a sensor hub, wherein the glucose sensor comprises a distal sensor portion and a proximal sensor portion, **wherein the distal sensor portion is configured to sense the glucose level of the subject,** wherein the proximal sensor portion is engaged with the sensor hub, and wherein the distal sensor portion is substantially orthogonal to the proximal sensor portion.	**Exhibit 1** at: • Para. [00130] ("A portion of the sensor 14 . . . may be situated above the surface of the skin, with a distal portion 30 penetrating through the skin and into the subcutaneous space in contact with the user's biofluid, such as interstitial fluid."). • Para. [00131] ("[T]he sensor is implantable into a subject's body for a usage period . . . to contact and monitor an analyte present in a biological fluid."). • Fig. 6B (with labels added):  FIG.6B

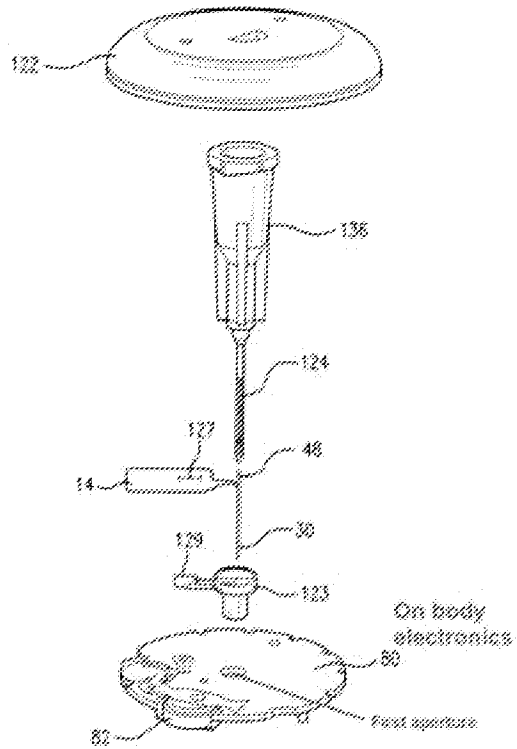
Claim No.	Pending Claim of '110 Application	Example Citation(s)
46	The glucose monitoring assembly of claim 26, wherein the on body electronics comprises an aperture, and wherein the sharp extends through the aperture of the on body electronics.	**Exhibit 1 at** Fig. 23 (with labels added).  FIG.23  FIG.22
47	The glucose monitoring assembly of claim 26, wherein the inserter further comprises a distal end configured to be placed on a skin surface of the subject before advancement of the on body electronics unit and the sharp.	*See claim 26 above.* *See also, e.g.*, Para. [00253] ("[A] user would first sterilize the insertion site on the skin with alcohol. The subject would then twist off cap 2504 as shown in step 1. Next a subject would place the inserter on the sterilized insertion site . . . .").

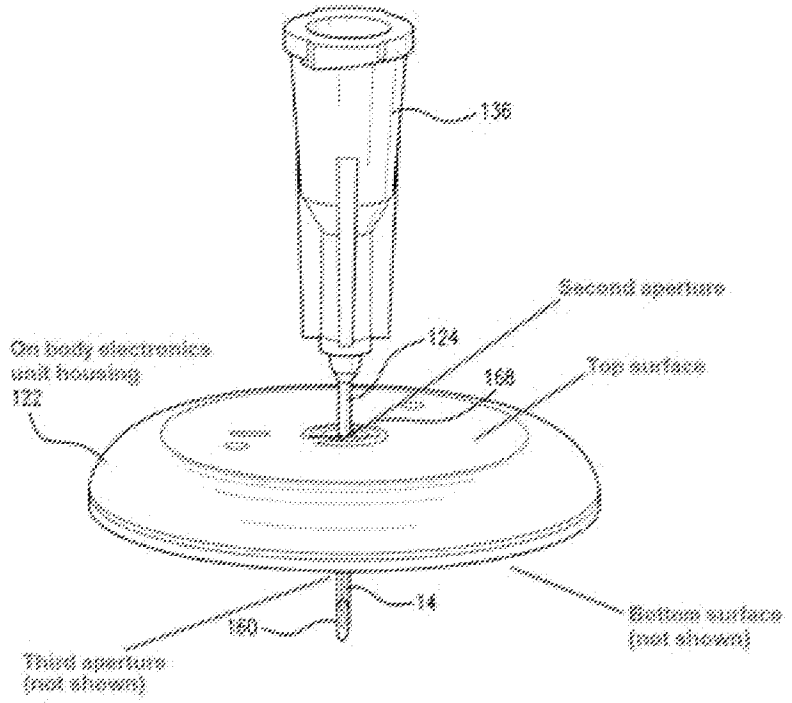
Claim No.	Pending Claim of '110 Application	Example Citation(s)
48	The glucose monitoring assembly of claim 26, wherein at least a portion of the on body electronics is in a low power state when the on body electronics unit is in the proximal position.	**Exhibit 1** at: • Para. [00172] ("Prior to activation of the on-body unit 16 which includes the integrated sensor 14 and sensor control unit 12 for use, there may be a period of time from the manufacturing that the assembly 16 may be in a 'sleep' or 'idle' mode."). • Para. [00172] ("With a power supply such as a battery integrated within the assembly . . . some embodiments of the present disclosure include optional systems that are activated merely by positioning the sensor 14 and on-body unit 16 on a skin surface[.]").
49	The glucose monitoring assembly of claim 26, further comprising an adhesive portion configured to secure the on body electronics unit housing to a skin surface of the subject.	**Exhibit 1** at: • Para. [00136] ("Adhesive pad 118 is illustrated in FIGURE 8 to attach sensor housing 122 to the skin of the subject."). • Para. [00250] ("As carriage 2516 reaches a distal position as shown in FIGURE 73J, the distal surface of the sensor housing 122 engages the upper surface of adhesive pad (not shown), thereby becoming adhered to the skin surface S of the subject."). • Fig. 8 (with labels added):  FIG.8
50	The glucose monitoring assembly of claim 26, wherein at least a portion of the on body electronics is in a no power state when the on body electronics unit is in the proximal position.	*See claim 48 above.*

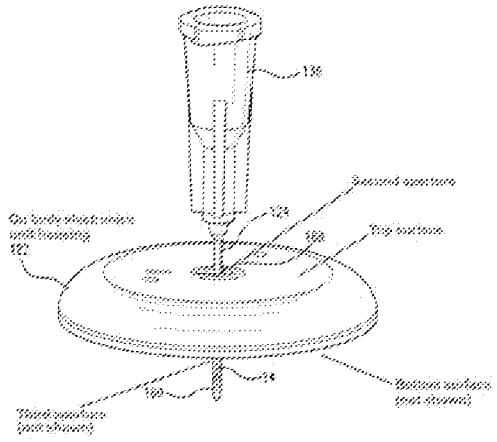
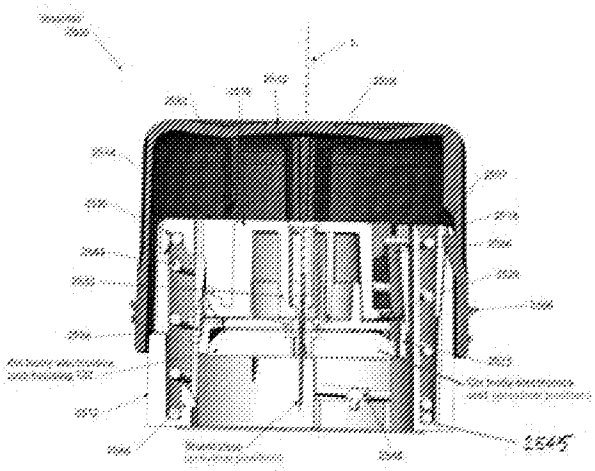
Claim No.	Pending Claim of '110 Application	Example Citation(s)
51	The glucose monitoring assembly of claim 26, wherein at least a portion of the on body electronics is in an inactive mode when the on body electronics unit is in the proximal position.	*See claim 48 above.*
52	The glucose monitoring assembly of claim 47, wherein the distal end of the inserter defines a plane, and wherein a bottom surface of the on body electronics unit housing is parallel to the plane when the on body electronics unit and the sharp are in the proximal position.	**Exhibit 1** at Fig. 73H (with labels added):  FIG. 73H

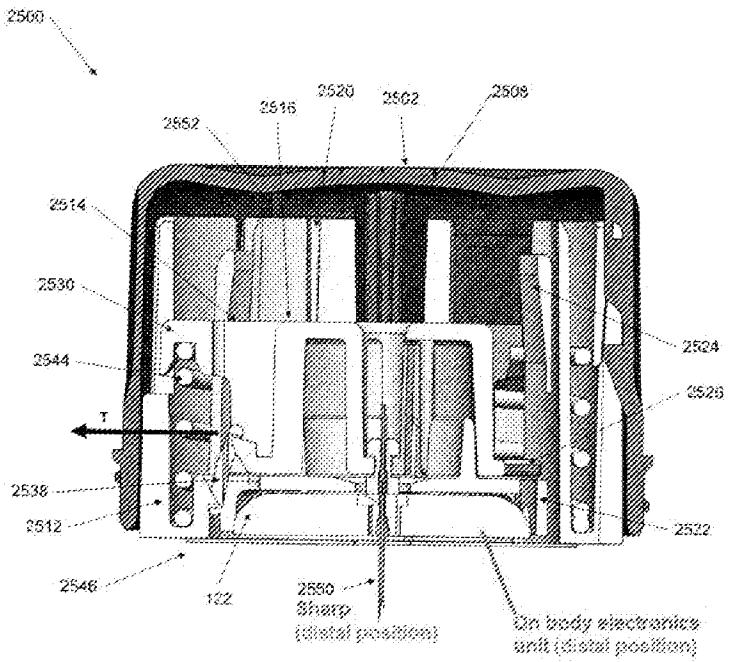
Claim No.	Pending Claim of '110 Application	Example Citation(s)
53	The glucose monitoring assembly of claim 26, wherein the on body electronics unit and the sharp are configured to advance in a linear direction when advancing from the proximal position within the inserter to the distal position.	**Exhibit 1** at Figs. 73H and 73K (with labels added):  FIG. 73H  FIG. 73K

Claim No.	Pending Claim of '110 Application	Example Citation(s)
54	The glucose monitoring assembly of claim 26, wherein a distance between the on body electronics unit housing when the on body electronics unit is in the proximal position and the on body electronics unit housing when the on body electronics unit is in the distal position is greater than a maximum height of the on body electronics unit housing.	**Exhibit 1** at Figs. 73H and 73K (with labels added):  FIG. 73H 

Claim No.	Pending Claim of '110 Application	Example Citation(s)
55A	The glucose monitoring assembly of claim 46, **wherein the aperture of the on body electronics is a first aperture**, wherein the on body electronics unit housing further comprises a top surface and a bottom surface, wherein the top surface comprises a second aperture, wherein the bottom surface comprises a third aperture, and wherein the sharp extends through the first aperture, the second aperture, and the third aperture when the on body electronics unit is in the proximal position.	**Exhibit 1** at Fig. 23 (with labels added).  FIG. 23

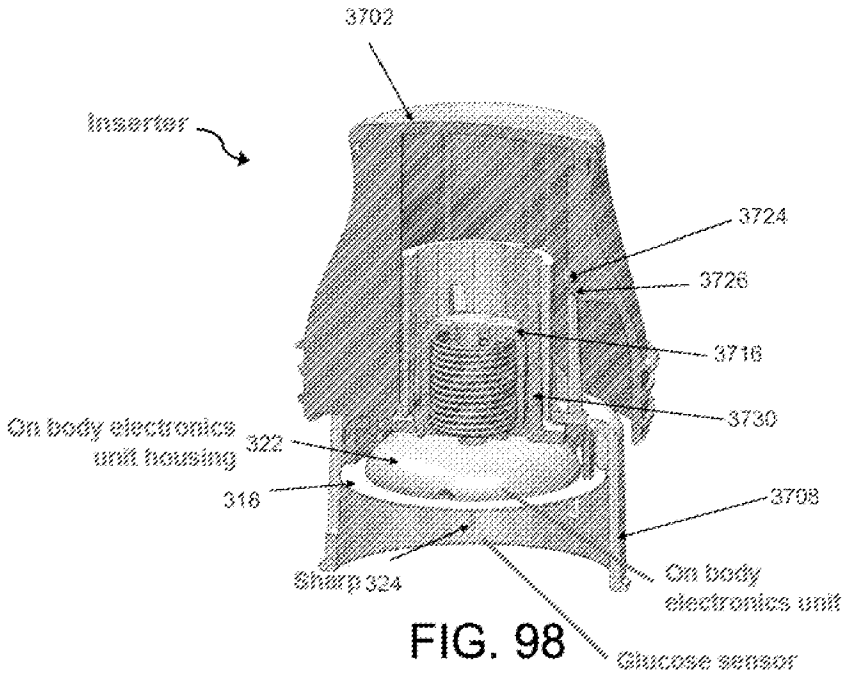
Claim No.	Pending Claim of '110 Application	Example Citation(s)
55B	The glucose monitoring assembly of claim 46, wherein the aperture of the on body electronics is a first aperture, **wherein the on body electronics unit housing further comprises a top surface and a bottom surface, wherein the top surface comprises a second aperture, wherein the bottom surface comprises a third aperture**, and wherein the sharp extends through the first aperture, the second aperture, and the third aperture when the on body electronics unit is in the proximal position.	**Exhibit 1** at Fig. 22 (with labels added).  FIG.22

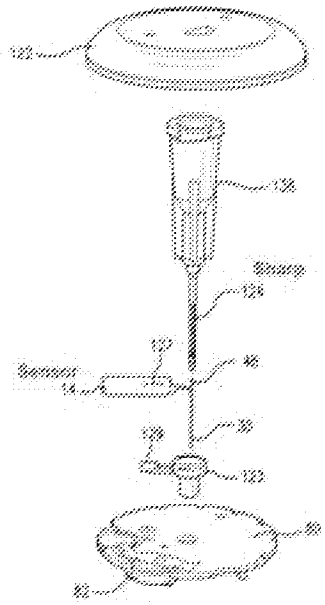
Claim No.	Pending Claim of '110 Application	Example Citation(s)
55C	The glucose monitoring assembly of claim 46, wherein the aperture of the on body electronics is a first aperture, wherein the on body electronics unit housing further comprises a top surface and a bottom surface, wherein the top surface comprises a second aperture, wherein the bottom surface comprises a third aperture, **and wherein the sharp extends through the first aperture, the second aperture, and the third aperture when the on body electronics unit is in the proximal position**.	**Exhibit 1** at Figs. 22 and 73H (with labels added).  FIG. 22  FIG. 73H

Claim No.	Pending Claim of '110 Application	Example Citation(s)
56	The glucose monitoring assembly of claim 26, wherein the sharp is further configured to pierce a skin surface of the subject at an angle substantially perpendicular to the skin surface of the subject.	**Exhibit 1** at: • [00247] ("[S]harp 2550 is supported at an oblique angle, e.g., between and including about 0° and 90° with respect to the skin surface."). • Fig. 73K (with labels added):  FIG. 73K • *See also, e.g.*, [00157] ("[T]he [sensor] insertion portion 30 [disposed in the sharp is] substantially vertical (e.g., substantially aligned with the longitudinal axis of the inserter 100 and substantially perpendicular to the skin surface) . . . .")

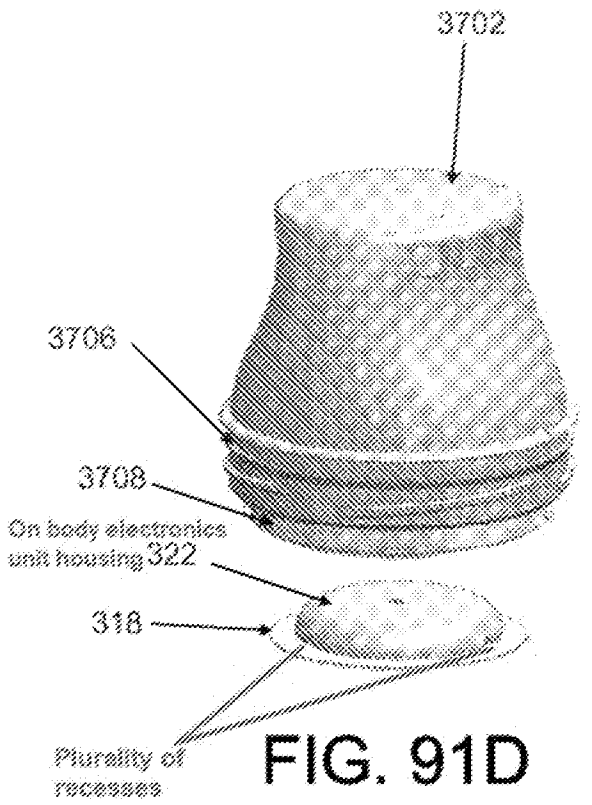
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APPENDIX B

Claim No.	Pending Claim of '110 Application	Example Citation(s)
26A	A glucose monitoring assembly, the assembly comprising: **(1) an inserter comprising** **a sharp** configured to insert a portion of a glucose sensor into a subject; and (2) **an on body electronics unit, comprising**: **an on body electronics unit housing** comprising a plurality of recesses disposed on a periphery of the on body electronics unit housing, wherein the plurality of recesses comprises a first recess in a spaced relation to a second recess, and wherein the plurality of recesses is detachably engaged with the inserter; **the glucose sensor**; and on body electronics coupled with the glucose sensor, wherein the on body electronics is disposed within the on body electronics unit housing, and wherein the on body electronicsincludes a processor, memory, a power supply, and wireless communication circuitry configured to wirelessly communicate data indicative of a glucose level, wherein the inserter is configured to advance the on body electronics unit and the sharp from a proximal position entirely within the inserter to a distal position, and wherein the inserter is further configured to retract the sharp from the distal position to a retracted position entirely within the inserter.	**Exhibit 8**, U.S. Provisional Appl. No. 61/411,262 ("the '262 Application"), filed November 8, 2010, at Figs. 91A-103; *see, e.g.*, Fig. 98 (with labels added):  FIG. 98 *See also, e.g.*, **Exhibit 8** at: • Para. [00149] ("Sensor 14 may be configured to continuously sample the analyte of the user and convert the sampled analyte level, e.g., a glucose concentration into a corresponding data signal[.]").

Claim No.	Pending Claim of '110 Application	Example Citation(s)
26B	A glucose monitoring assembly, the assembly comprising: (1) an inserter comprising **a sharp configured to insert a portion of a glucose sensor into a subject**; and (2) an on body electronics unit, comprising: an on body electronics unit housing comprising a plurality of recesses disposed on a periphery of the on body electronics unit housing, wherein the plurality of recesses comprises a first recess in a spaced relation to a second recess, and wherein the plurality of recesses is detachably engaged with the inserter; the glucose sensor; and on body electronics coupled with the glucose sensor, wherein the on body electronics is disposed within the on body electronics unit housing, and wherein the on body electronicsincludes a processor, memory, a power supply, and wireless communication circuitry configured to wirelessly communicate data indicative of a glucose level, wherein the inserter is configured to advance the on body electronics unit and the sharp from a proximal position entirely within the inserter to a distal position, and wherein the inserter is further configured to retract the sharp from the distal position to a retracted position entirely within the inserter.	**Exhibit 8** at: • Para. [00152] ("Sensor 14 may include a proximal retention portion 48. . . . The insertion portion 30 and the proximal retention portion 48 are sized and configured to be positioned with a sharp for installation into the skin of a subject[.]"). • Para. [00157] ("A portion of sensor 14 . . . may be situated above the surface of the skin, with a distal portion 30 penetrating through the skin and into the subcutaneous space in contact with the user's biofluid, such as interstitial fluid."). • Para. [00170] ("[A]n inserter may include one or more components for advancing a sharp towards the skin of the subject."). • Para. [00306] ("As sharp 324 is further urged distally, it carries the sensor insertion portion 30 of sensor 14 (FIGURE 23) into the subcutaneous portion of the subject's skin S."). • Fig. 23 (with labels added):  FIG.23

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Claim No.	Pending Claim of '110 Application	Example Citation(s)
26C	A glucose monitoring assembly, the assembly comprising: (1) an inserter comprising a sharp configured to insert a portion of a glucose sensor into a subject; and (2) an on body electronics unit, comprising: **an on body electronics unit housing comprising a plurality of recesses disposed on a periphery of the on body electronics unit housing, wherein the plurality of recesses comprises a first recess in a spaced relation to a second recess, and wherein the plurality of recesses is detachably engaged with the inserter;** the glucose sensor; and on body electronics coupled with the glucose sensor, wherein the on body electronics is disposed within the on body electronics unit housing, and wherein the on body electronics includes a processor, memory, a power supply, and wireless communication circuitry configured to wirelessly communicate data indicative of a glucose level, wherein the inserter is configured to advance the on body electronics unit and the sharp from a proximal position entirely within the inserter to a distal position, and wherein the inserter is further configured to retract the sharp from the distal position to a retracted position entirely within the inserter.	**Exhibit 8** at Fig. 91D (with labels added) (depicting a plurality of recesses disposed on a periphery of the on body electronics unit housing, wherein the plurality of recesses comprises a first recess in a spaced relation to a second recess).  FIG. 91D

Claim No.	Pending Claim of '110 Application	Example Citation(s)
		Exhibit 8 at Figs. 96, 97B, and 97C (showing parts of inserter, e.g., plurality of gripping arms with engagement bosses, with which the plurality of recesses is detachably engaged).

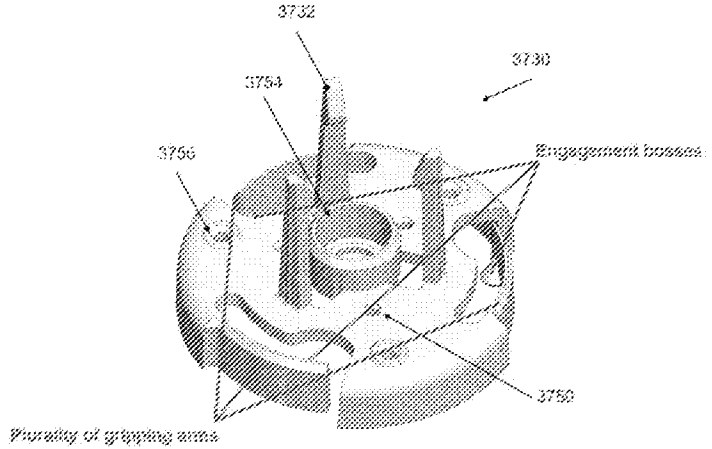


FIG. 96

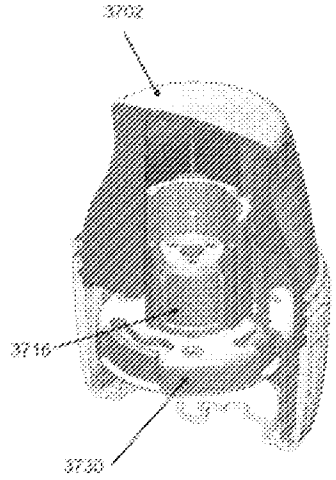


FIG. 97B

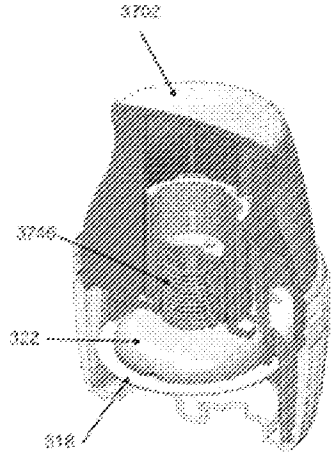
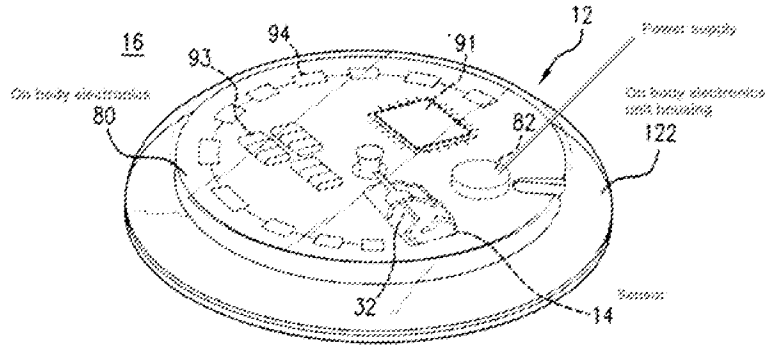
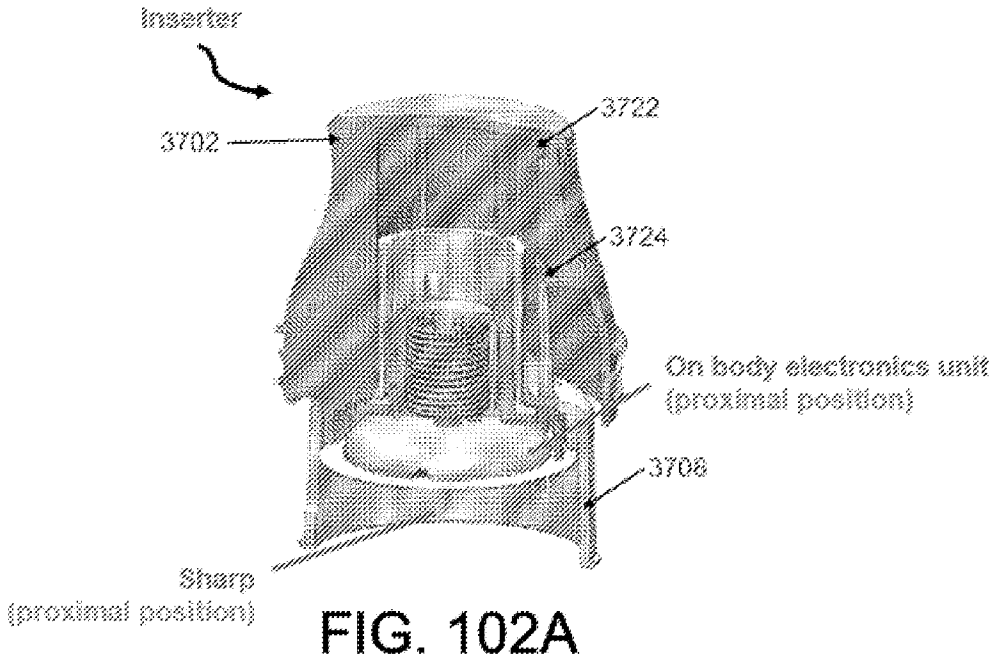
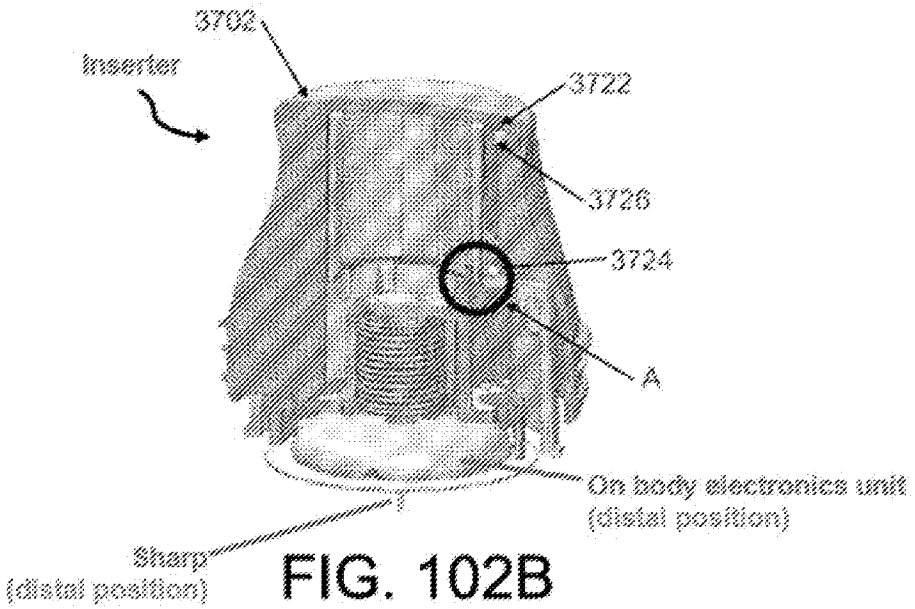


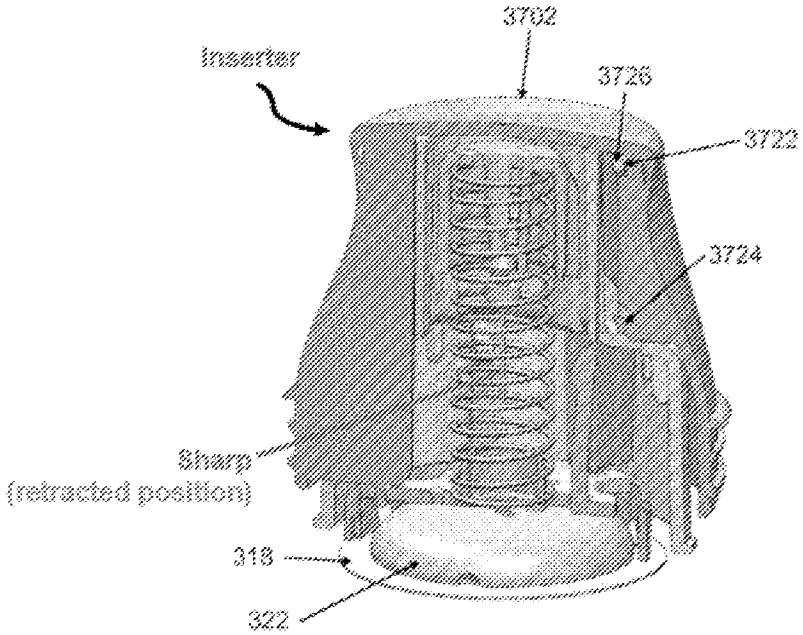
FIG. 97C

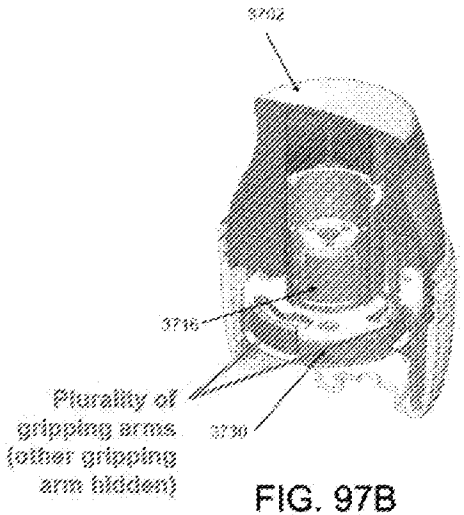
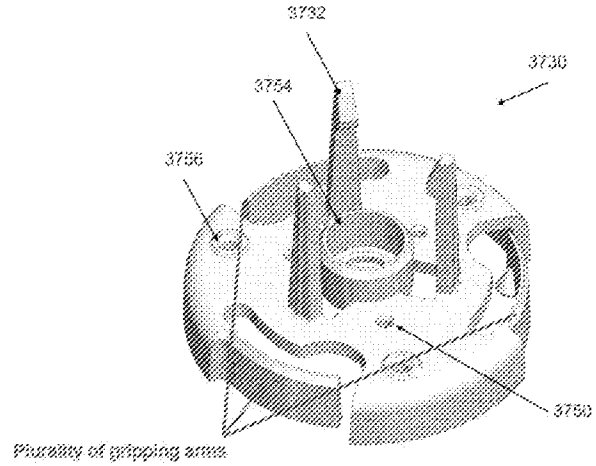
Claim No.	Pending Claim of '110 Application	Example Citation(s)
26D	A glucose monitoring assembly, the assembly comprising: (1) an inserter comprising a sharp configured to insert a portion of a glucose sensor into a subject; and (2) an on body electronics unit, comprising: an on body electronics unit housing comprising a plurality of recesses disposed on a periphery of the on body electronics unit housing, wherein the plurality of recesses comprises a first recess in a spaced relation to a second recess, and wherein the plurality of recesses is detachably engaged with the inserter; the glucose sensor; and **on body electronics coupled with the glucose sensor, wherein the on body electronics is disposed within the on body electronics unit housing, and wherein the on body electronics includes a processor, memory, a power supply, and wireless communication circuitry configured to wirelessly communicate data indicative of a glucose level,** wherein the inserter is configured to advance the on body electronics unit and the sharp from a proximal position entirely within the inserter to a distal position, and wherein the inserter is further configured to retract the sharp from the distal position to a retracted position entirely within the inserter.	**Exhibit 8** at: • Para. [00161] ("Sensor control unit 12, including its associated electronics 80, are housed in housing 122. . . . [E]lectronics 80 may include one or more of, *e.g.*, an analog interface for connecting to the sensor 14, a processor, which may include, *e.g.*, an ASIC 91, antenna 94, power supply 82 to power the sensor and/or communications components[.]"). • Para. [00112] ("Communication may occur, *e.g.*, *via* RF communication, infrared communication, Bluetooth communciaiton, Zigbee communication, 802.1x communication, or WiFi communication, etc."). • Para. [00112] ("[W]hen the on-body unit 16 is positioned within the radiated or provided RF signal range radiated from the monitor unit 18, the on-body unit 16 in certain embodiments is configured to provide one or more signals associated with the monitored analyte level received from the analyte sensor 14 to the monitor unit 18."). • Para. [00115] ("[S]ensor control unit 12 may further include local memory[.]"). • Para. [00169] ("In some embodiments, communications circuitry, such as RFID antenna or communications circuitry, is provided."). • Para. [00183] ("The sensor housing 122 can be configured to hold at least a portion of sensor 14 and sensor control unit 12. . . . [E]lectronics 80 of the sensor control unit 12 . . . are positioned within sensor housing 122."). • *See also* Fig. 7 (with labels added):  FIG. 7

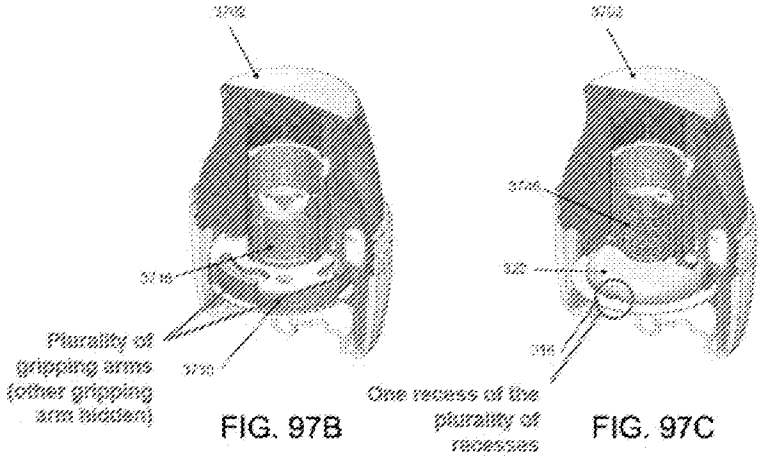
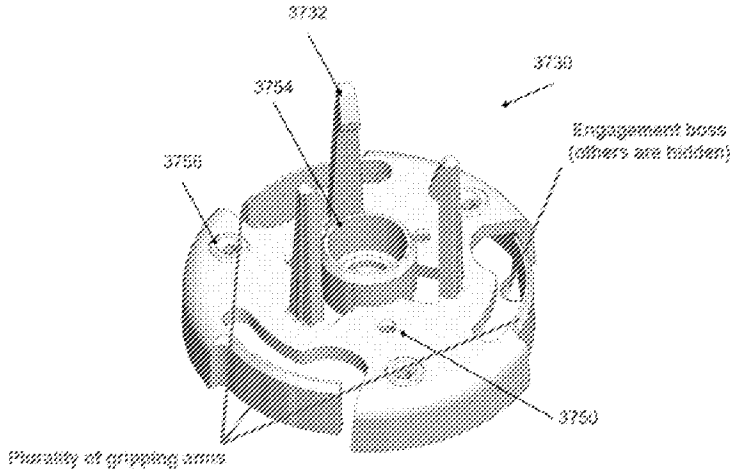
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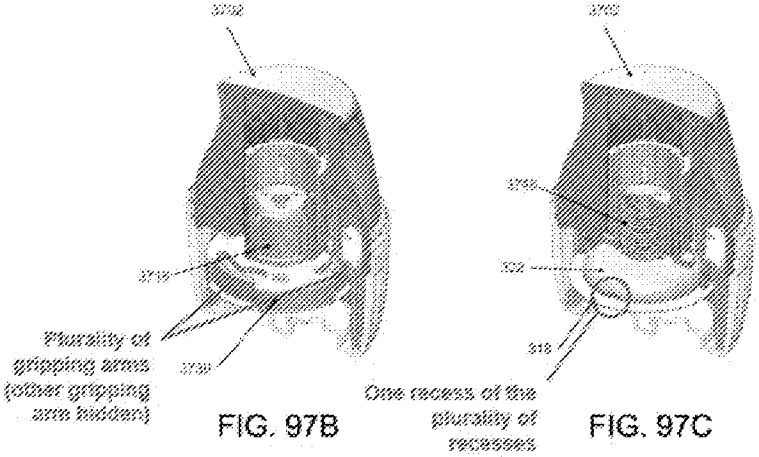
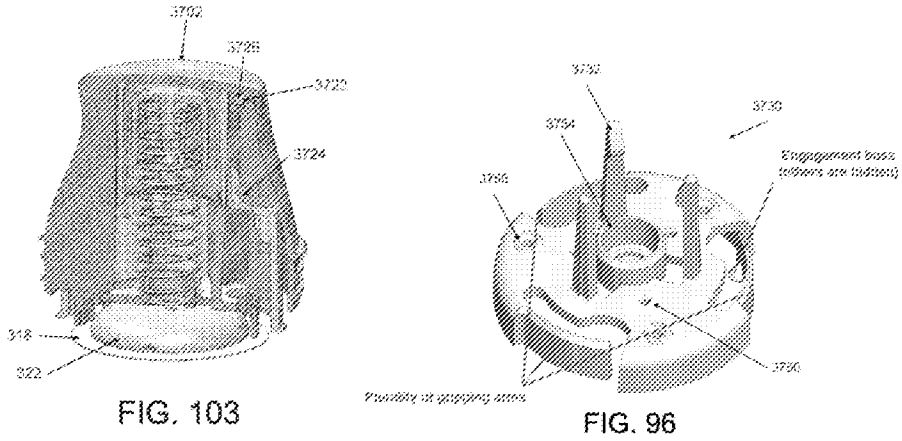
Claim No.	Pending Claim of '110 Application	Example Citation(s)
26E	A glucose monitoring assembly, the assembly comprising: (1) an inserter comprising a sharp configured to insert a portion of a glucose sensor into a subject; and (2) an on body electronics unit, comprising: an on body electronics unit housing comprising a plurality of recesses disposed on a periphery of the on body electronics unit housing, wherein the plurality of recesses comprises a first recess in a spaced relation to a second recess, and wherein the plurality of recesses is detachably engaged with the inserter; the glucose sensor; and on body electronics coupled with the glucose sensor, wherein the on body electronics is disposed within the on body electronics unit housing, and wherein the on body electronicsincludes a processor, memory, a power supply, and wireless communication circuitry configured to wirelessly communicate data indicative of a glucose level, **wherein the inserter is configured to advance the on body electronics unit and the sharp from a proximal position entirely within the inserter** to a distal position, and wherein the inserter is further configured to retract the sharp from the distal position to a retracted position entirely within the inserter.	**Exhibit 8** at Fig. 102A (with labels added):  FIG. 102A

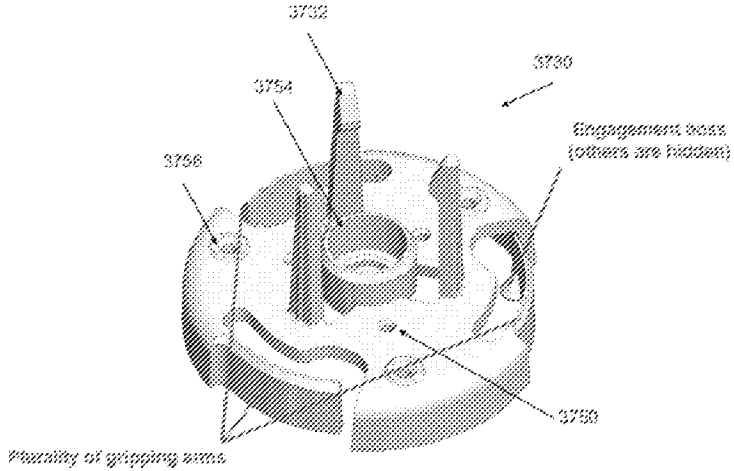
Claim No.	Pending Claim of '110 Application	Example Citation(s)
26F	A glucose monitoring assembly, the assembly comprising: (1) an inserter comprising a sharp configured to insert a portion of a glucose sensor into a subject; and (2) an on body electronics unit, comprising: an on body electronics unit housing comprising a plurality of recesses disposed on a periphery of the on body electronics unit housing, wherein the plurality of recesses comprises a first recess in a spaced relation to a second recess, and wherein the plurality of recesses is detachably engaged with the inserter; the glucose sensor; and on body electronics coupled with the glucose sensor, wherein the on body electronics is disposed within the on body electronics unit housing, and wherein the on body electronicsincludes a processor, memory, a power supply, and wireless communication circuitry configured to wirelessly communicate data indicative of a glucose level, **wherein the inserter is configured to advance the on body electronics unit and the sharp** from a proximal position entirely within the inserter **to a distal position**, and wherein the inserter is further configured to retract the sharp from the distal position to a retracted position entirely within the inserter.	**Exhibit 8** at Fig. 102B (with labels added):  FIG. 102B

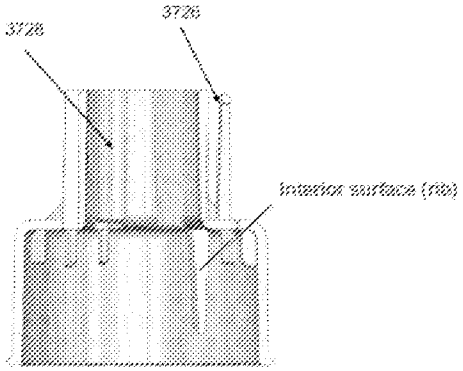
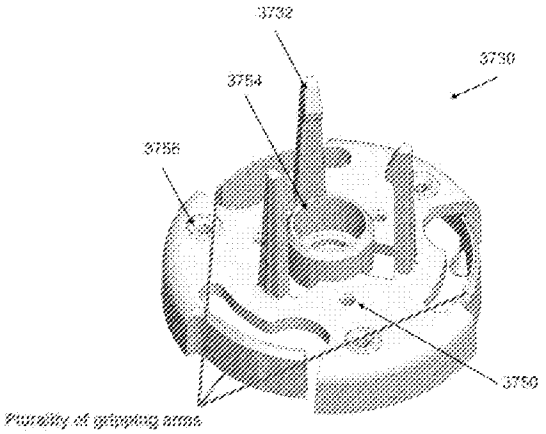
Claim No.	Pending Claim of '110 Application	Example Citation(s)
26G	A glucose monitoring assembly, the assembly comprising: (1) an inserter comprising a sharp configured to insert a portion of a glucose sensor into a subject; and (2) an on body electronics unit, comprising: an on body electronics unit housing comprising a plurality of recesses disposed on a periphery of the on body electronics unit housing, wherein the plurality of recesses comprises a first recess in a spaced relation to a second recess, and wherein the plurality of recesses is detachably engaged with the inserter; the glucose sensor; and on body electronics coupled with the glucose sensor, wherein the on body electronics is disposed within the on body electronics unit housing, and wherein the on body electronicsincludes a processor, memory, a power supply, and wireless communication circuitry configured to wirelessly communicate data indicative of a glucose level, wherein the inserter is configured to advance the on body electronics unit and the sharp from a proximal position entirely within the inserter to a distal position, and **wherein the inserter is further configured to retract the sharp from the distal position to a retracted position entirely within the inserter**.	**Exhibit 8** at Fig. 103 (with label added):  FIG. 103

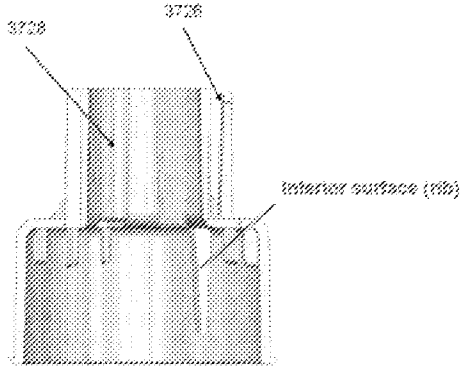
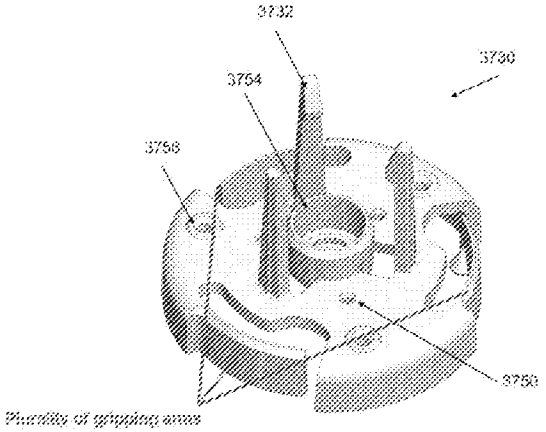
Claim No.	Pending Claim of '110 Application	Example Citation(s)
27	The glucose monitoring assembly of claim 26, wherein the inserter further comprises a plurality of gripping arms.	**Exhibit 8 at** Figs. 96 and 97B (with labels added):  FIG. 97B  FIG. 96 *See also, e.g.*, **Exhibit 8** at Para. [00301].

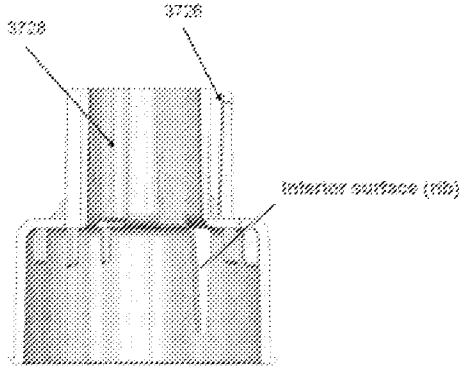
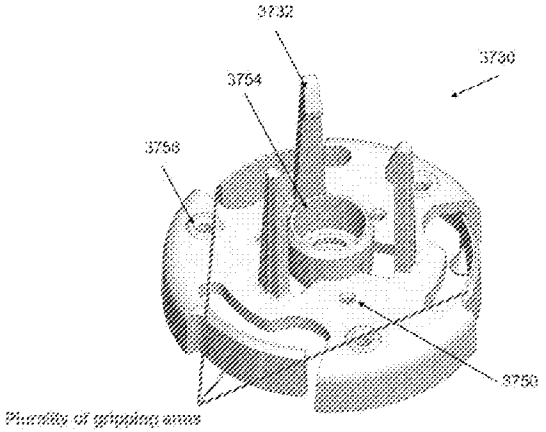
Claim No.	Pending Claim of '110 Application	Example Citation(s)
28A	The glucose monitoring assembly of claim 27, **wherein each gripping arm of plurality of gripping arms is configured to be engaged with a corresponding recess of the plurality of recesses of the on body electronics unit housing when the on body electronics unit is in the proximal position**, and wherein each gripping arm of the plurality of gripping arms is further configured to be disengaged from the corresponding recess of the plurality of recesses when the on body electronics unit is in the distal position.	**Exhibit 8** at Figs. 96, 97B, and 97C (with labels added) (depicting each gripping arm of a plurality of gripping arms configured to engage with a corresponding recess of the plurality of recesses on the on body electronics unit housing; Fig. 96 depicts one of the engagement bosses that engages with a corresponding recess).  FIG. 97B FIG. 97C  FIG. 96 *See also, e.g.*, **Exhibit 8** at Para. [00301].

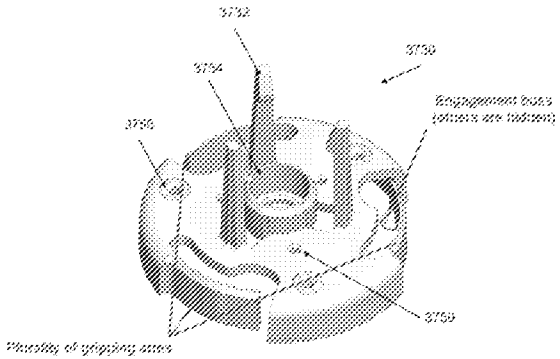
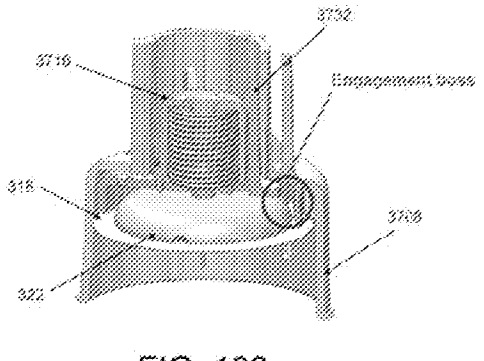
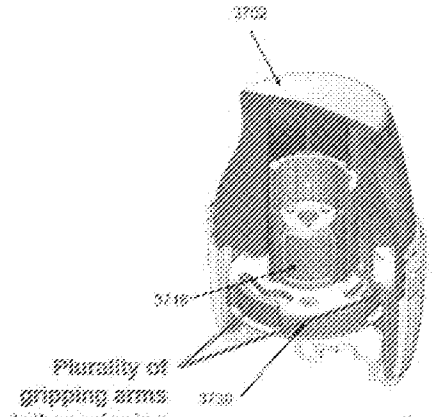
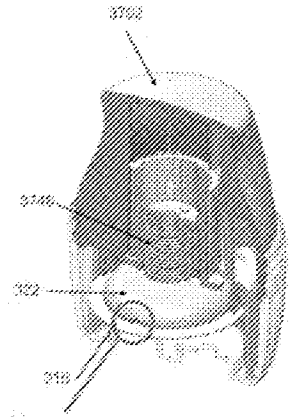
Claim No.	Pending Claim of '110 Application	Example Citation(s)
28B	The glucose monitoring assembly of claim 27, wherein each gripping arm of plurality of gripping arms is configured to be engaged with a corresponding recess of the plurality of recesses of the on body electronics unit housing when the on body electronics unit is in the proximal position, and **wherein each gripping arm of the plurality of gripping arms is further configured to be disengaged from the corresponding recess of the plurality of recesses when the on body electronics unit is in the distal position**.	**Exhibit 8** at Figs. 96, 97B, 97C, and 103 (with labels added) (depicting each gripping arm of a plurality of gripping arms configured to disengage from a corresponding recess of the plurality of recesses on the on body electronics unit housing).  FIG. 97B FIG. 97C  FIG. 103 FIG. 96 *See also, e.g.*, **Exhibit 8** at Para. [00301].

Claim No.	Pending Claim of '110 Application	Example Citation(s)
29	The glucose monitoring assembly of claim 27, wherein each gripping arm of the plurality of gripping arms is biased in a radially outward direction.	**Exhibit 8** at Fig. 96 (with label added) (showing each gripping arm of the plurality of gripping arms biased in a radially outward direction).  FIG. 96 *See also, e.g.*, **Exhibit 8** at Para. [00301]; *see also id.* at Para. [00269] and Figs. 73F-G.

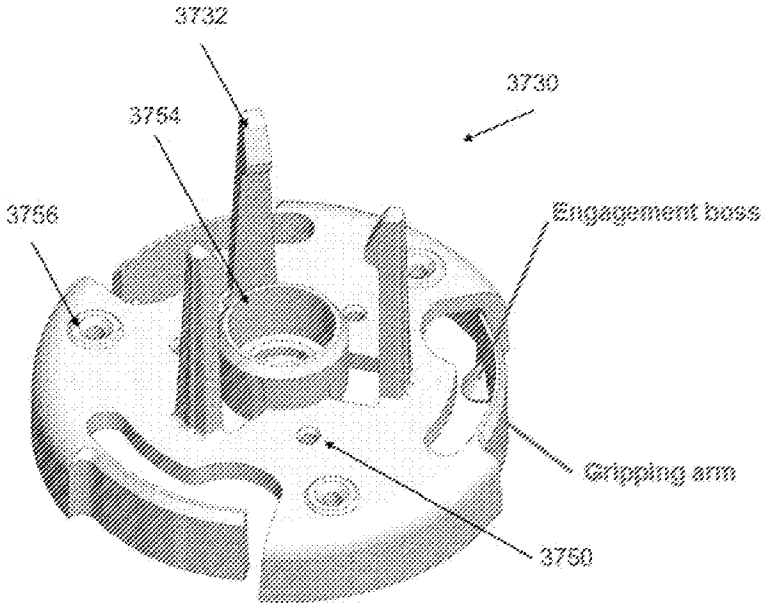
Claim No.	Pending Claim of '110 Application	Example Citation(s)
30	The glucose monitoring assembly of claim 32, wherein the corresponding gripping arm of the plurality of gripping arms is configured to deflect in a radially outward direction when the each interior surface of the plurality of interior surfaces is not in contact with the corresponding gripping arm of the plurality of gripping arms.	**Exhibit 8** at: • Para. [00301] ("The medical device carrier 37[3]0 further includes snaps 3542 which loosely hold the sensor housing unit 322 in place. Ribs on the interior surface of the distal portion 3708c of the sheath hold these snaps securely in place while the sheath is fully extended. When the medical device carrier 37[3]0 advances along the sheath to reach the proximal position during use, the snaps [3]542 are no longer supported by the sheath and the force of the adhesive skin patch 318 overcomes the retention force of the snaps 3542.") • Figs. 93B and 96 (with labels added):  FIG. 93B  FIG. 96 *See also, e.g.*, **Exhibit 8** at Para. [00269] and Figs. 73C, 73G.

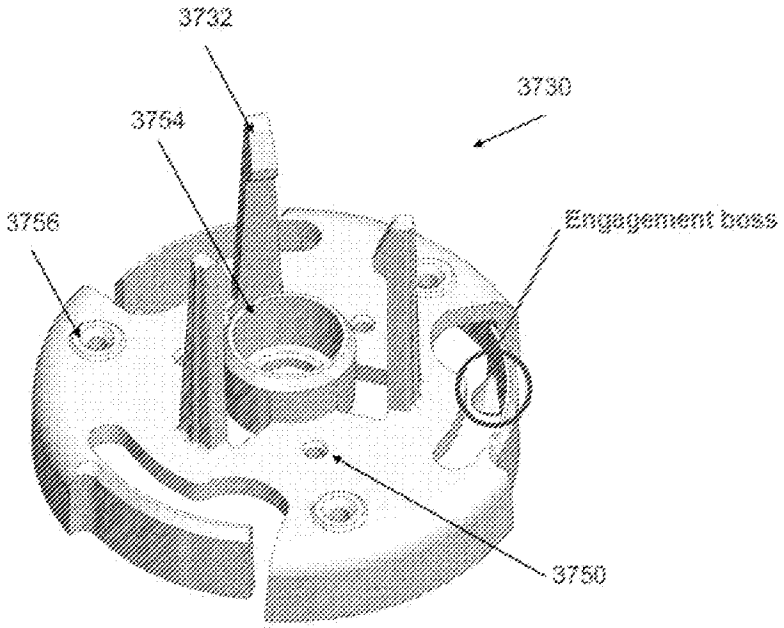
Claim No.	Pending Claim of '110 Application	Example Citation(s)
31	The glucose monitoring assembly of claim 27, wherein the inserter further comprises a plurality of interior surfaces, wherein each interior surface of the plurality of interior surfaces is configured to hold a corresponding gripping arm of the plurality of gripping arms against a corresponding recess of the plurality of recesses of the on body electronics unit housing when the on body electronics unit is in the proximal position.	**Exhibit 8** at: • Para. [00301] ("The medical device carrier 37[3]0 further includes snaps 3542 which loosely hold the sensor housing unit 322 in place. Ribs on the interior surface of the distal portion 3708c of the sheath hold these snaps securely in place while the sheath is fully extended. When the medical device carrier 37[3]0 advances along the sheath to reach the proximal position during use, the snaps [3]542 are no longer supported by the sheath and the force of the adhesive skin patch 318 overcomes the retention force of the snaps 3542.") • Figs. 93B and 96 (with labels added):  FIG. 93B  FIG. 96 *See also, e.g.*, **Exhibit 8** at Paras. [00269], [00271], and Figs. 73C, 73G.

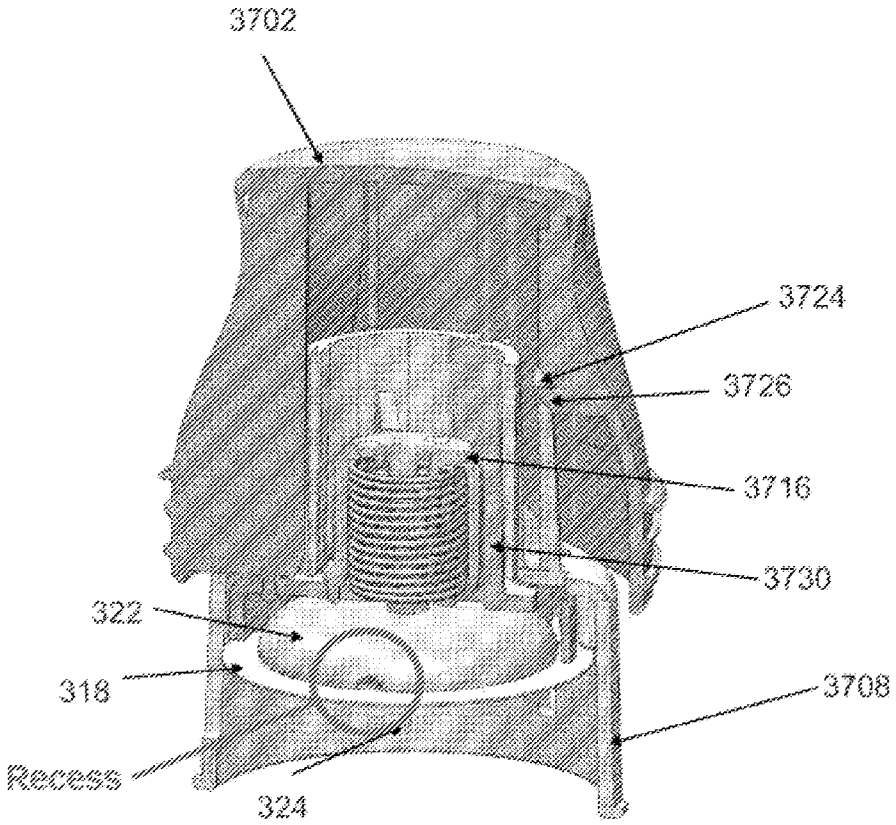
Claim No.	Pending Claim of '110 Application	Example Citation(s)
32	The glucose monitoring assembly of claim 31, wherein the inserter is further configured such that the each interior surface of the plurality interior surfaces is not in contact with the on body electronics unit is in the distal position.	**Exhibit 8** at: • Para. [00301] ("The medical device carrier 37[3]0 further includes snaps 3542 which loosely hold the sensor housing unit 322 in place. Ribs on the interior surface of the distal portion 3708c of the sheath hold these snaps securely in place while the sheath is fully extended. When the medical device carrier 37[3]0 advances along the sheath to reach the proximal position during use, the snaps [3]542 are no longer supported by the sheath and the force of the adhesive skin patch 318 overcomes the retention force of the snaps 3542.") • Figs. 93B and 96 (with labels added):  FIG. 93B  FIG. 96 *See also, e.g.*, **Exhibit 8** at Paras. [00269], [00271], and Figs. 73C, 73G.

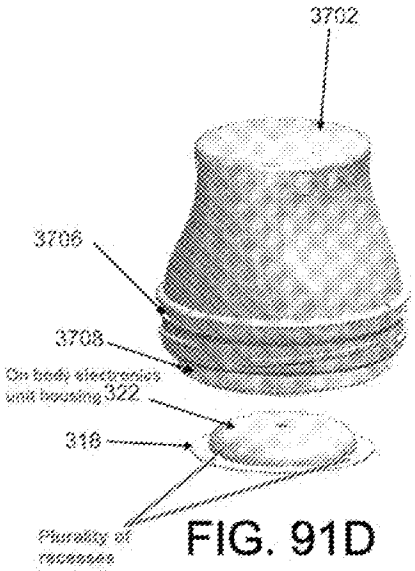
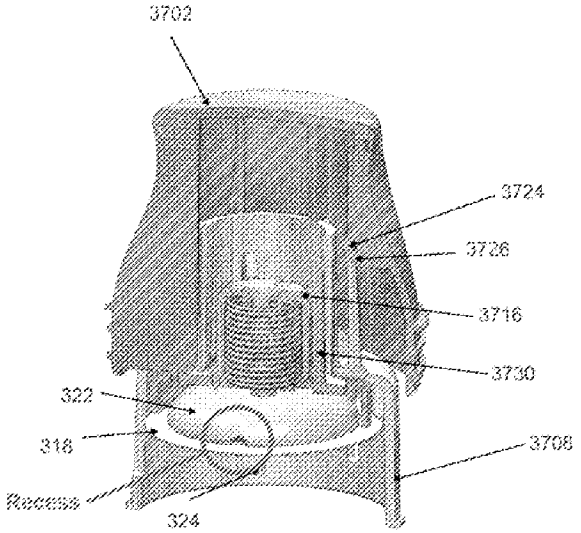
Claim No.	Pending Claim of '110 Application	Example Citation(s)
33	The glucose monitoring assembly of claim 27, wherein each gripping arm of the plurality of gripping arms comprises an engagement boss configured to engage with a corresponding recess of the plurality of recesses on the on body electronics unit housing when the on body electronics unit is in the proximal position.	**Exhibit 8** at Figs. 96, 97B, 97C, and 100 (with labels added) (showing a plurality of gripping arms, each with an engagement boss configured to engage with a corresponding recess of the plurality of recesses).  FIG. 96  FIG. 100  FIG. 97B  FIG. 97C *See also, e.g.,* **Exhibit 8** at Paras. [00269], [00271], and Figs. 73F-G.

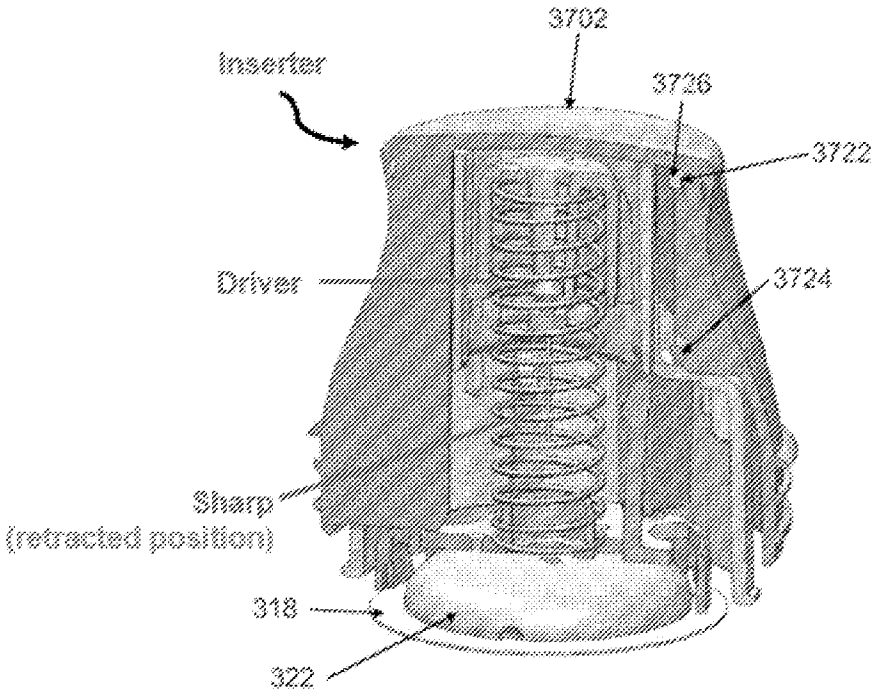
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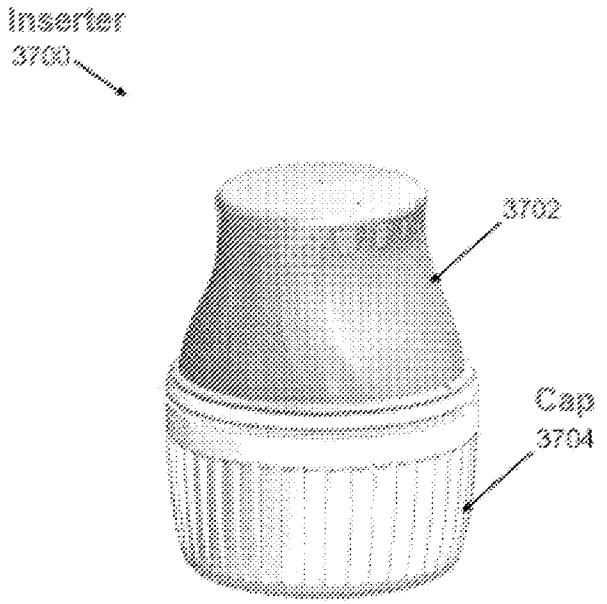
Claim No.	Pending Claim of '110 Application	Example Citation(s)
34	The glucose monitoring assembly of claim 33, wherein the engagement boss is disposed on a tip portion of the gripping arm.	**Exhibit 8** at Fig. 96 (with labels added) (showing an engagement boss disposed on a tip portion of a gripping arm).  FIG. 96

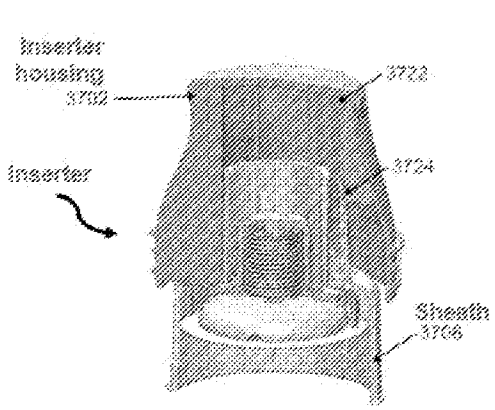
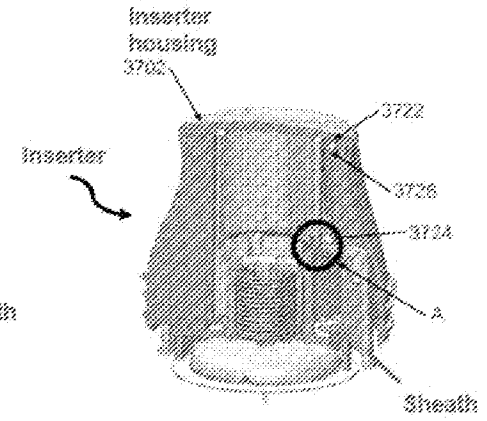
Claim No.	Pending Claim of '110 Application	Example Citation(s)
35	The glucose monitoring assembly of claim 33, wherein the engagement boss comprises a conical shape.	**Exhibit 8** at Fig. 96 (with label added) (showing an engagement boss comprising a conical shape).  FIG. 96

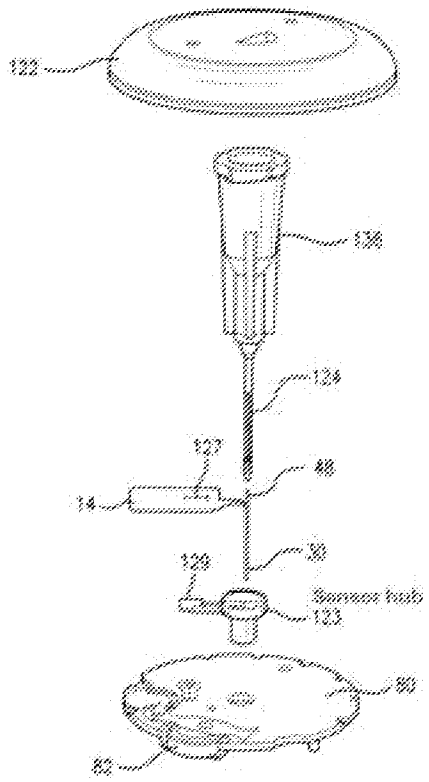
Claim No.	Pending Claim of '110 Application	Example Citation(s)
36	The glucose monitoring assembly of claim 26, wherein each recess of the plurality of recesses comprises a concave portion.	**Exhibit 8** at Fig. 98 (with label added) (showing recess comprising a concave portion).  FIG. 98

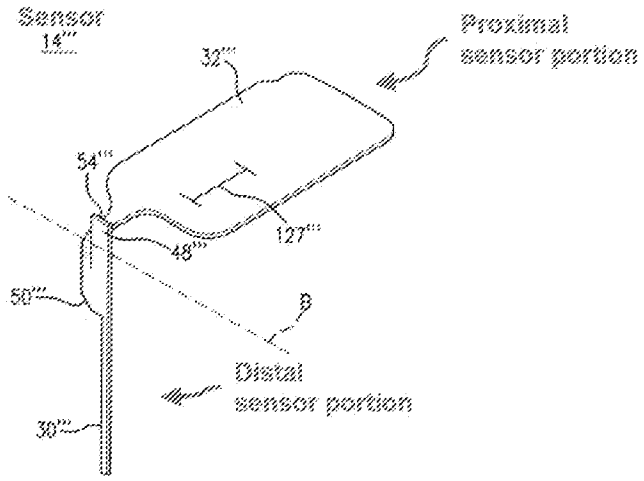
Claim No.	Pending Claim of '110 Application	Example Citation(s)
37	The glucose monitoring assembly of claim 26, wherein each recess of the plurality of recesses is disposed on a side wall of the on body electronics unit housing.	**Exhibit 8** at Figs. 91D and 98 (with labels added) (showing each recess of the plurality of recesses being disposed on a side wall of the on body electronics unit housing).  FIG. 91D  FIG. 98

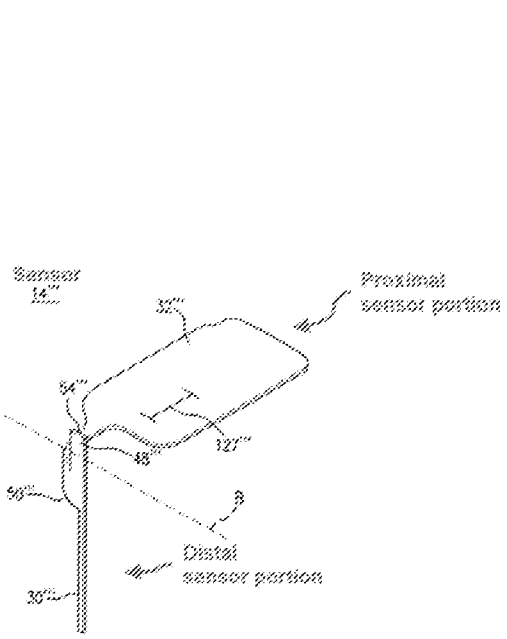
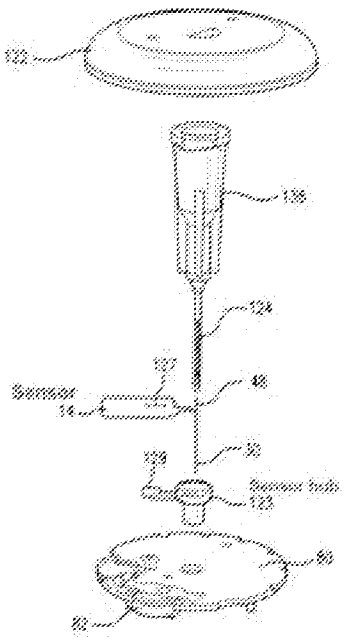
Claim No.	Pending Claim of '110 Application	Example Citation(s)
38	The glucose monitoring assembly of claim 26, wherein the inserter further comprises a driver disposed in the inserter, wherein the driver is configured to apply a force that retracts the sharp after the sharp reaches the distal position.	**Exhibit 8** at: • Para. [00307] ("[S]pring 3746 is permitted to expand . . . thereby retracting the sharp carrier 3716 to a proximal position and withdrawing the sharp 324 from the skin S of the subject while leaving the sensor housing 322 attached to the skin."). • Fig. 103 (with labels added):  FIG. 103

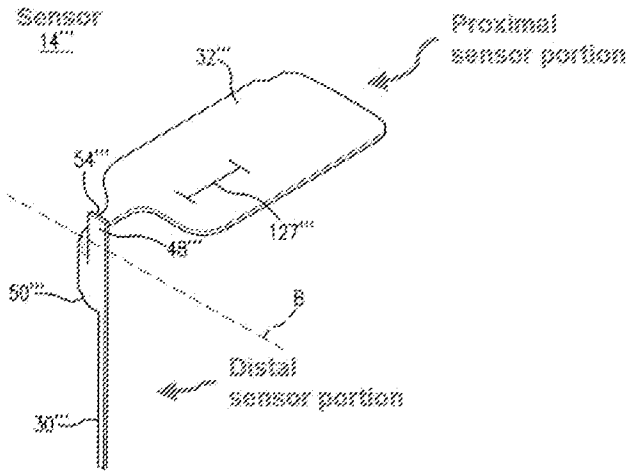
Claim No.	Pending Claim of '110 Application	Example Citation(s)
39	The glucose monitoring assembly of claim 26, further comprising a cap removably attached to a distal portion of the inserter.	**Exhibit 8** at: • Para. [00295] ("Inserter 3700 generally includes, *e.g.*, a housing 3702 (FIGURES 91-92B), sheath 3708 (FIGURE 93A-B), and a removable distal cap 3704 (FIGURE 94A-C) for maintaining a sterile environment for the medical device and sharp housed therein."). • Fig. 91A (with labels added):  FIG. 91A

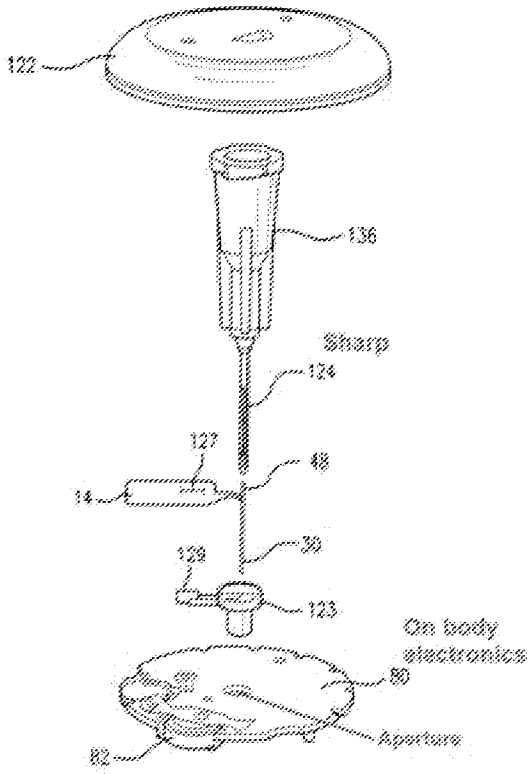
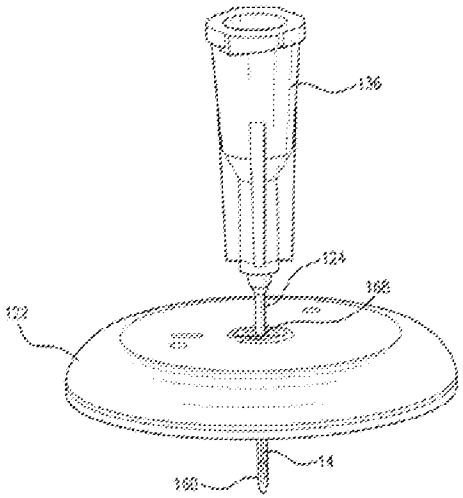
Claim No.	Pending Claim of '110 Application	Example Citation(s)
43	The glucose monitoring assembly of claim 26, wherein the inserter further comprises an inserter housing and a sheath, and wherein the inserter is configured to move in a downward direction towards the skin surface relative to the sheath in response to an application of force on the inserter, and wherein the sheath is configured to remain stationary relative to the skin surface in response to the application of force on the inserter housing.	**Exhibit 8** at: • Para. [00296] ("Housing 3702 includes sheath guide rail 3710 which interfaces with rail guides 3712 located on sheath 3708, thereby allowing housing 3702 to slidingly move relative to sheath 3708."). • Figs. 102A and 102B (with labels added):  FIG. 102A  FIG. 102B

Claim No.	Pending Claim of '110 Application	Example Citation(s)
45A	The glucose monitoring assembly of claim 26, **wherein the on body electronics unit further comprises a sensor hub**, wherein the glucose sensor comprises a distal sensor portion and a proximal sensor portion, wherein the distal sensor portion is configured to sense the glucose level of the subject, wherein the proximal sensor portion is engaged with the sensor hub, and wherein the distal sensor portion is substantially orthogonal to the proximal sensor portion.	**Exhibit 8** at: • Para. [00183] ("As further illustrated in FIGURE 23, electronics 80 of the sensor control unit 12 . . . and sensor hub 123 are positioned within sensor housing 122."). • Fig. 23 (with label added):  FIG. 23

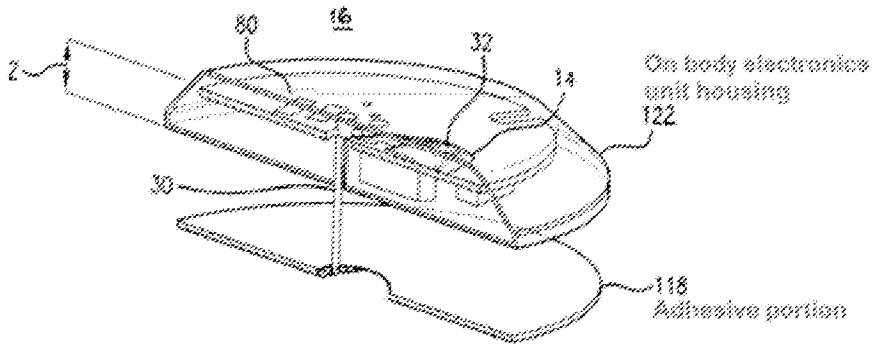
Claim No.	Pending Claim of '110 Application	Example Citation(s)
45B	The glucose monitoring assembly of claim 26, wherein the on body electronics unit further comprises a sensor hub, **wherein the glucose sensor comprises a distal sensor portion and a proximal sensor portion,** wherein the distal sensor portion is configured to sense the glucose level of the subject, wherein the proximal sensor portion is engaged with the sensor hub, and **wherein the distal sensor portion is substantially orthogonal to the proximal sensor portion.**	**Exhibit 8** at: • Para. [0006] ("[T]he sensor includes a body having a proximal section and a distal section . . . ."). • Para. [0008] ("[T]he proximal section of the sensor may be disposed in a horizontal plane, and the distal section of the sensory body may be disposed in a vertical plane."); *see also* para. [0024] ("[T]he proximal section and the distal section are in planes substantially perpendicular to each other, e.g., the area may define an angle of . . . about 90°."); and *see also* para. [00152] ("In use, the sensor 14 may be configured to bend (*e.g.*, along the line B) and therefore be positioned in two substantially perpendicular, intersecting planes."). • Fig. 6B (with labels added):  FIG.6B

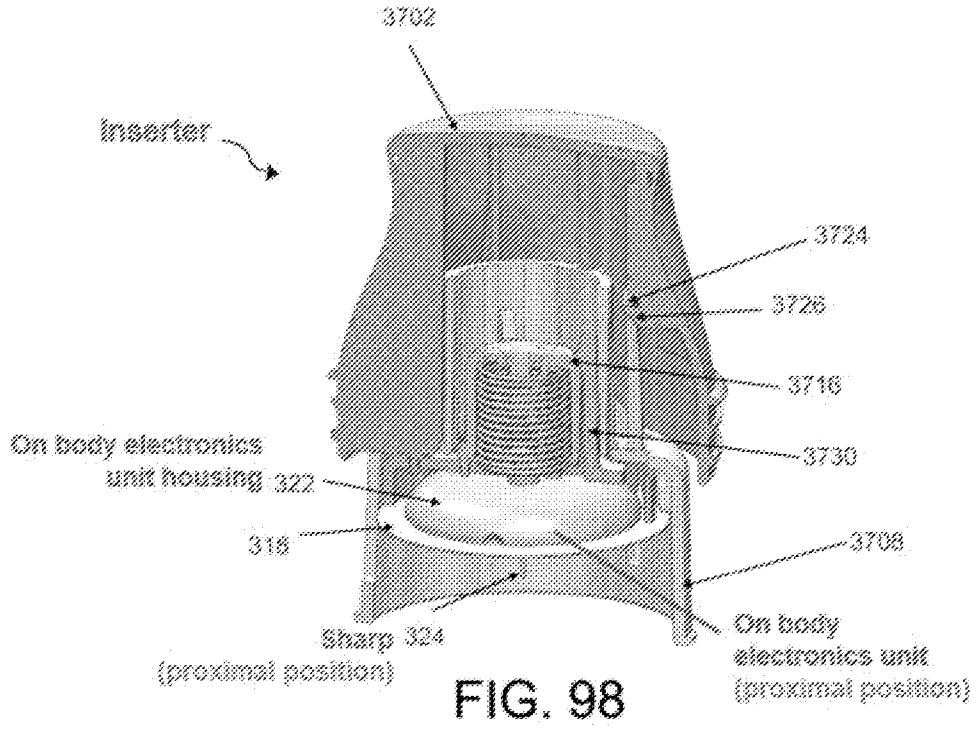
Claim No.	Pending Claim of '110 Application	Example Citation(s)
45C	The glucose monitoring assembly of claim 26, wherein the on body electronics unit further comprises a sensor hub, wherein the glucose sensor comprises a distal sensor portion and a proximal sensor portion, wherein the distal sensor portion is configured to sense the glucose level of the subject, **wherein the proximal sensor portion is engaged with the sensor hub**, and wherein the distal sensor portion is substantially orthogonal to the proximal sensor portion.	**Exhibit 8** at: • Para [00183] ("Sensor 14 may include a positioning structure, or slit 127 which receives a positioning member, such as tab 129 of sensor hub 123."). • Figs. 6B & 23 (with labels added):  FIG.6B  FIG.23

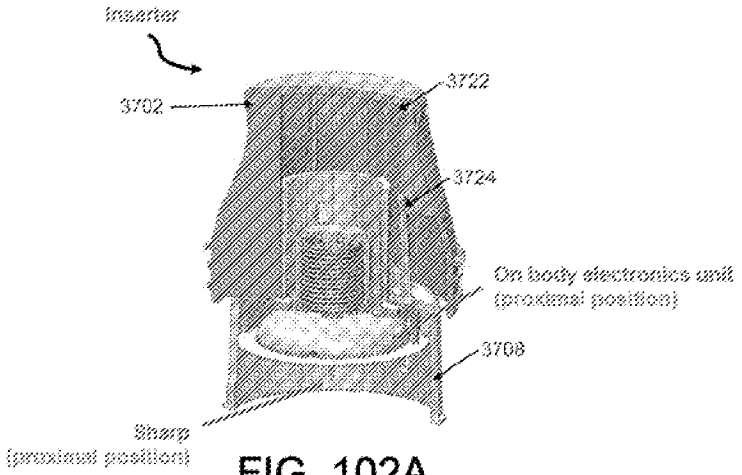
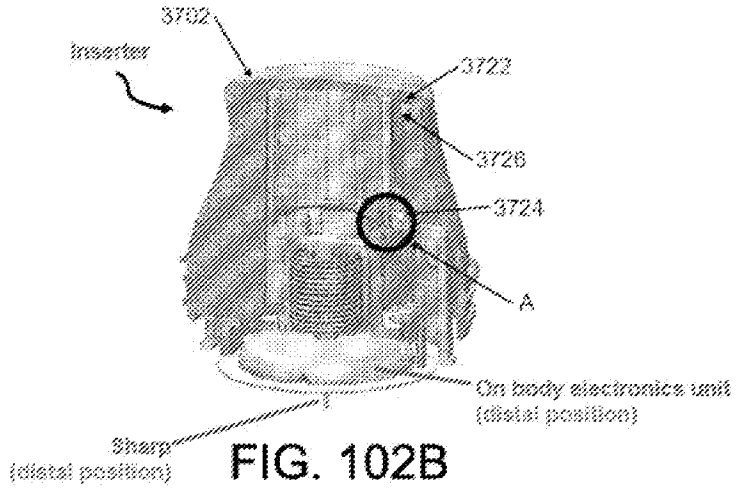
Claim No.	Pending Claim of '110 Application	Example Citation(s)
45D	The glucose monitoring assembly of claim 26, wherein the on body electronics unit further comprises a sensor hub, wherein the glucose sensor comprises a distal sensor portion and a proximal sensor portion, **wherein the distal sensor portion is configured to sense the glucose level of the subject,** wherein the proximal sensor portion is engaged with the sensor hub, and wherein the distal sensor portion is substantially orthogonal to the proximal sensor portion.	**Exhibit 8** at: • Para. [00157] ("A portion of the sensor 14 . . . may be situated above the surface of the skin, with a distal portion 30 penetrating through the skin and into the subcutaneous space in contact with the user's biofluid, such as interstitial fluid."). • Para. [00158] ("[T]he sensor is implantable into a subject's body for a usage period . . . to contact and monitor an analyte present in a biological fluid."). • Fig. 6B (with labels added):  FIG.6B

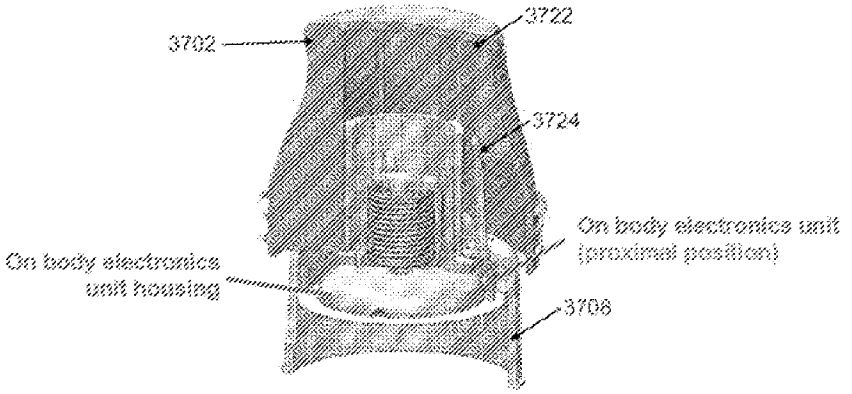
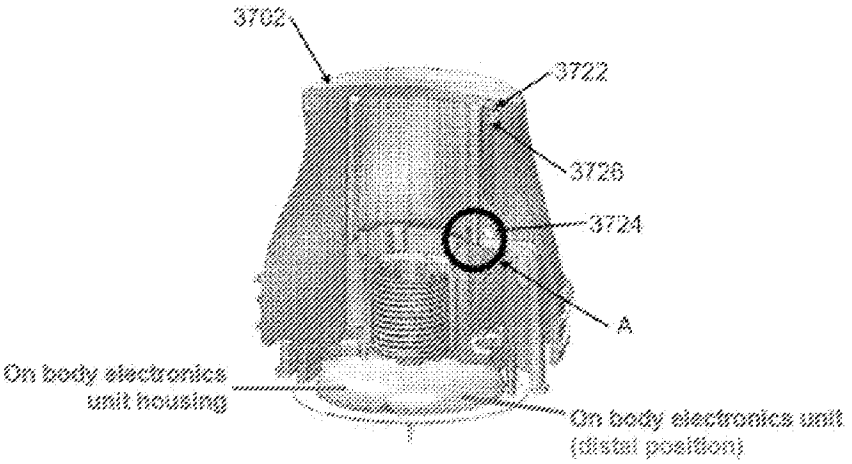
Claim No.	Pending Claim of '110 Application	Example Citation(s)
46	The glucose monitoring assembly of claim 26, wherein the on body electronics comprises an aperture, and wherein the sharp extends through the aperture of the on body electronics.	**Exhibit 8** at Figs. 22 and 23 (with labels added):  FIG.23  FIG.22
47	The glucose monitoring assembly of claim 26, wherein the inserter further comprises a distal end configured to be placed on a skin surface of the subject before advancement of the on body electronics unit and the sharp.	*See claim 26 above.* *See also, e.g.*, **Exhibit 8** at Figs. 91B, 102A-C, and Paras. [00295]-[00296], [00280].

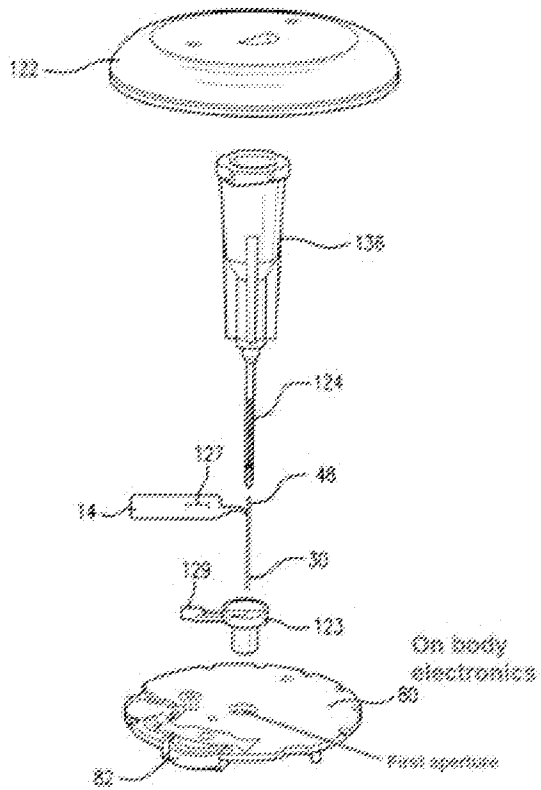
Page 1042 of 2126

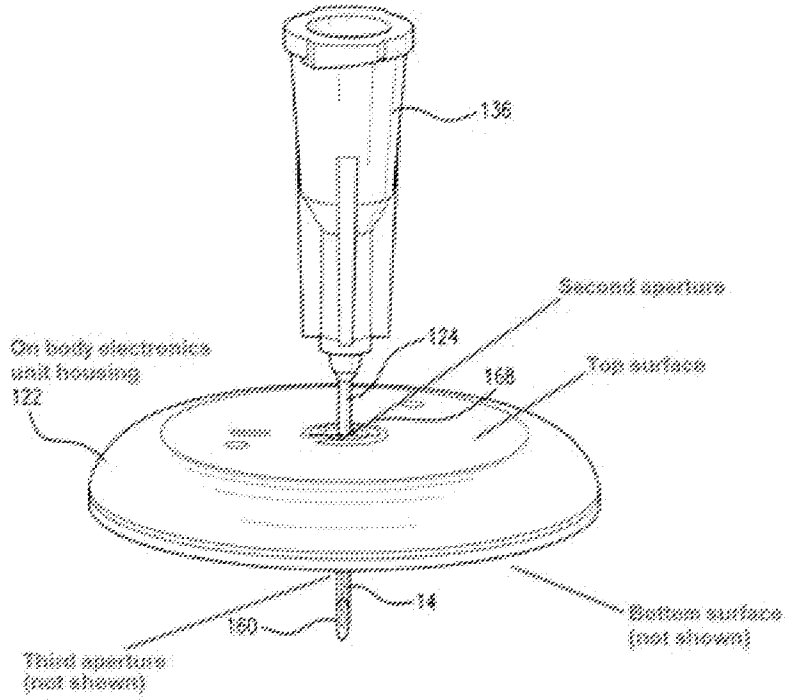
Claim No.	Pending Claim of '110 Application	Example Citation(s)
48	The glucose monitoring assembly of claim 26, wherein at least a portion of the on body electronics is in a low power state when the on body electronics unit is in the proximal position.	**Exhibit 8** at: • Para. [00199] ("Prior to activation of the on-body unit 16 which includes the integrated sensor 14 and sensor control unit 12 for use, there may be a period of time from the manufacturing that the assembly 16 may be in a 'sleep' or 'idle' mode."). • Para. [00199] ("With a power supply such as a battery integrated within the assembly . . . some embodiments of the present disclosure include optional systems that are activated merely by positioning the sensor 14 and on-body unit 16 on a skin surface[.]").
49	The glucose monitoring assembly of claim 26, further comprising an adhesive portion configured to secure the on body electronics unit housing to a skin surface of the subject.	**Exhibit 8** at: • Para. [00163] ("Adhesive pad 118 is illustrated in FIGURE 8 to attach sensor housing 122 to the skin of the subject."). • Para. [00307] ("As carriage 3716 reaches a distal position, the distal surface of the sensor housing 122 engages the upper surface of adhesive pad 318, thereby becoming adhered to the skin surface S of the subject."). • Fig. 8 (with labels added):  FIG.8
50	The glucose monitoring assembly of claim 26, wherein at least a portion of the on body electronics is in a no power state when the on body electronics unit is in the proximal position.	*See claim 48 above.*

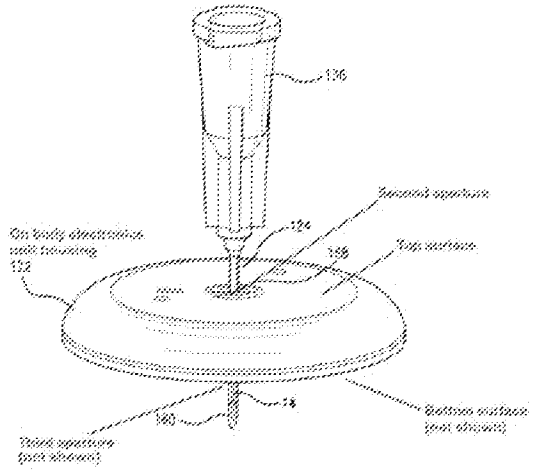
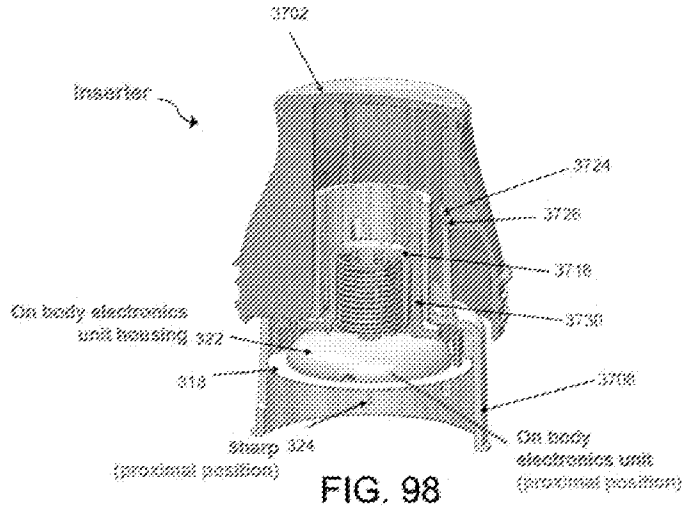
Claim No.	Pending Claim of '110 Application	Example Citation(s)
51	The glucose monitoring assembly of claim 26, wherein at least a portion of the on body electronics is in an inactive mode when the on body electronics unit is in the proximal position.	*See claim 48 above.*
52	The glucose monitoring assembly of claim 47, wherein the distal end of the inserter defines a plane, and wherein a bottom surface of the on body electronics unit housing is parallel to the plane when the on body electronics unit and the sharp are in the proximal position.	**Exhibit 8** at Fig. 98 (with labels added):  FIG. 98

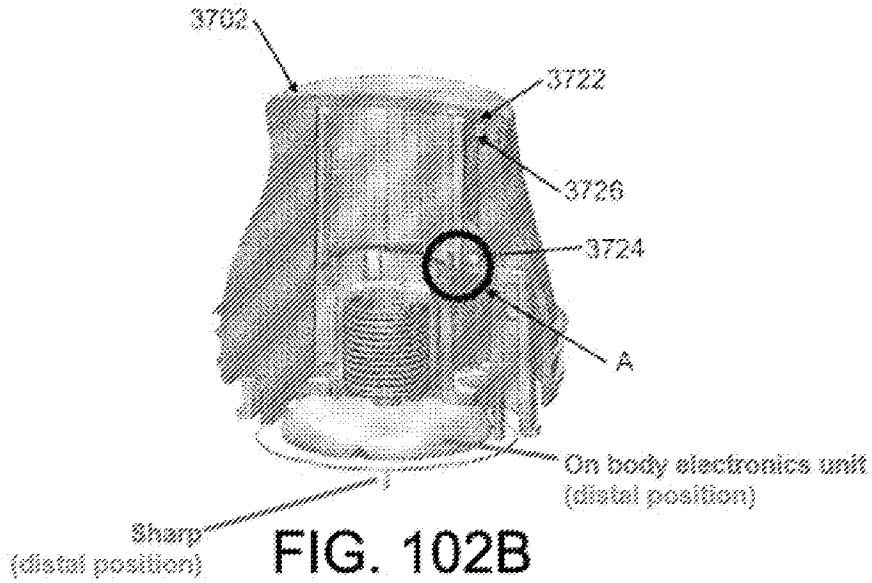
Claim No.	Pending Claim of '110 Application	Example Citation(s)
53	The glucose monitoring assembly of claim 26, wherein the on body electronics unit and the sharp are configured to advance in a linear direction when advancing from the proximal position within the inserter to the distal position.	**Exhibit 8** at Figs. 102A and 102B (with labels added):  FIG. 102A  FIG. 102B

Claim No.	Pending Claim of '110 Application	Example Citation(s)
54	The glucose monitoring assembly of claim 26, wherein a distance between the on body electronics unit housing when the on body electronics unit is in the proximal position and the on body electronics unit housing when the on body electronics unit is in the distal position is greater than a maximum height of the on body electronics unit housing.	**Exhibit 8** at Figs. 102A and 102B (with labels added):  FIG. 102A  FIG. 102B

Claim No.	Pending Claim of '110 Application	Example Citation(s)
55A	The glucose monitoring assembly of claim 46, **wherein the aperture of the on body electronics is a first aperture**, wherein the on body electronics unit housing further comprises a top surface and a bottom surface, wherein the top surface comprises a second aperture, wherein the bottom surface comprises a third aperture, and wherein the sharp extends through the first aperture, the second aperture, and the third aperture when the on body electronics unit is in the proximal position.	**Exhibit 8** at Fig. 23 (with labels added):  FIG.23

Claim No.	Pending Claim of '110 Application	Example Citation(s)
55B	The glucose monitoring assembly of claim 46, wherein the aperture of the on body electronics is a first aperture, **wherein the on body electronics unit housing further comprises a top surface and a bottom surface, wherein the top surface comprises a second aperture, wherein the bottom surface comprises a third aperture**, and wherein the sharp extends through the first aperture, the second aperture, and the third aperture when the on body electronics unit is in the proximal position.	**Exhibit 8** at Fig. 22 (with labels added):  FIG.22

Claim No.	Pending Claim of '110 Application	Example Citation(s)
55C	The glucose monitoring assembly of claim 46, wherein the aperture of the on body electronics is a first aperture, wherein the on body electronics unit housing further comprises a top surface and a bottom surface, wherein the top surface comprises a second aperture, wherein the bottom surface comprises a third aperture, **and wherein the sharp extends through the first aperture, the second aperture, and the third aperture when the on body electronics unit is in the proximal position**.	**Exhibit 8** at Figs. 22 and 102A (with labels added):  FIG. 22  FIG. 98

Claim No.	Pending Claim of '110 Application	Example Citation(s)
56	The glucose monitoring assembly of claim 26, wherein the sharp is further configured to pierce a skin surface of the subject at an angle substantially perpendicular to the skin surface of the subject.	**Exhibit 8 at** Fig. 102B (with labels added):  FIG. 102B • *See also, e.g.*, [00184] ("[T]he [sensor] insertion portion 30 [disposed in the sharp is] substantially vertical (e.g., substantially aligned with the longitudinal axis of the inserter 100 and substantially perpendicular to the skin surface) . . . .")

Docket No.: A0130.0107.01C8
(PATENT)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of:
Manuel Luis Donnay et al.

Application No.: 17/019,110 | Confirmation No.: 1087

Filed: September 11, 2020 | Art Unit: 3791

For: MEDICAL DEVICE INSERTERS AND PROCESSES OF INSERTING AND USING MEDICAL DEVICES | Examiner: Huong Q. Nguyen

INFORMATION DISCLOSURE STATEMENT (IDS)

EFS Web
Commissioner for Patents

Dear Sir:

Pursuant to 37 CFR 1.56, 1.97 and 1.98, the attention of the Patent and Trademark Office is hereby directed to the references listed on the attached PTO/SB/08. It is respectfully requested that the information be expressly considered during the prosecution of this application, and that the references be made of record therein and appear among the "References Cited" on any patent to issue therefrom.

Timing of Filing of the Information Disclosure Statement:

☒ This IDS is being filed before the First Office Action.

☐ This IDS is being filed after the issuance of the First Office Action but before the issuance of a Final Office Action.

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Certifications:

If checked, the undersigned makes the following statement(s):

☐ Statement under 37 CFR § 1.97(e):

☐ Each item of information contained in this information disclosure statement was first cited in a communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of this information disclosure statement; or

☐ No item of information contained in this information disclosure statement was cited in a communication from a foreign patent office in a counterpart foreign application, and, to the knowledge of the undersigned after making reasonable inquiry, no item of information contained in this information disclosure statement was known to any individual designated in § 1.56(c) more than three months prior to the filing of the information disclosure statement.

☐ Statement Under 37 C.F.R. § 1.704(d):

Each item of information contained in this information disclosure statement was cited a counterpart application less than thirty days prior to the filing of this information disclosure statement.

Fee Required by 37 C.F.R. § 1.97(c)(2) or 1.97(d)(2):

☐ If checked, the fee of $260.00 set forth in 37 C.F.R. §1.17(p).

Copies of Information:

In accordance with 37 C.F.R. §1.98(a), the following are enclosed:

☒ A legible copy of each document (or relevant portion thereof) cited in the attached PTO/SB/08, except for U.S. patent and U.S. published applications.

☒ With respect to any information which is not in English, a concise explanation of the relevance, as it is presently understood by the individual designated in § 1.56(c) most

knowledgeable about the content of the information, is attached. This concise explanation is provided by way of:

☒ A translation of the relevant portions of the non-English language information;

☐ A statement explaining the relevant portions of the non-English language information;

☐ A copy [and where not in the English language, a translation] of at least the relevant portion(s) of the communication from _____in which the information was cited; or

☐ This information is contained in the specification of the present application.

☐ In accordance with 37 C.F.R. 1.98(d), copies of the cited documents are not enclosed as they were provided in application Serial No. _____, filed _____, which the present application relies upon for an earlier effective filing date under 35 U.S.C. 120.

Materiality:

Whether or not the information and references disclosed in this Information Disclosure Statement is "material" pursuant to 37 CFR 1.56, this submission is not intended to constitute an admission that any patent, publication or other information referred to therein is "prior art" for this invention unless specifically designated as such.

In accordance with 37 CFR 1.97(g), the filing of this Information Disclosure Statement shall not be construed to mean that a search has been made or that no other material information as defined in 37 CFR 1.56(a) exists.

It is submitted that the Information Disclosure Statement is in compliance with 37 CFR 1.98 and the Examiner is respectfully requested to consider the listed references.

Dated: November 19, 2021

Respectfully submitted,

Electronic signature: /Glen Liu/
Glen Liu
Registration No.: 75,058
ONE LLP
4000 MacArthur Boulevard
East Tower, Suite 500
(949) 432-9993
Attorney for Applicants

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT

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Sheet	1	of	4

Complete if Known	
Application Number	17/019,110
Filing Date	September 11, 2020
First Named Inventor	Manuel Luis Donnay
Art Unit	3791
Examiner Name	Huong Q. Nguyen
Attorney Docket Number	A0130.0107.01C8

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Sheet 2 of 4

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Application Number	17/019,110
Filing Date	September 11, 2020
First Named Inventor	Manuel Luis Donnay
Art Unit	3791
Examiner Name	Huong Q. Nguyen
Attorney Docket Number	A0130.0107.01C8

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Examiner Signature		Date Considered	

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT				Application Number	17/019,110
				Filing Date	September 11, 2020
				First Named Inventor	Manuel Luis Donnay
				Art Unit	3791
(use as many sheets as necessary)				Examiner Name	Huong Q. Nguyen
Sheet	3	of	4	Attorney Docket Number	A0130.0107.01C8

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OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS

Examiner Initials'	Cite No.[1]	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T[2]
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				First Named Inventor	Manuel Luis Donnay
				Art Unit	3791
(use as many sheets as necessary)				Examiner Name	Huong Q. Nguyen
Sheet	4	of	4	Attorney Docket Number	A0130.0107.01C8

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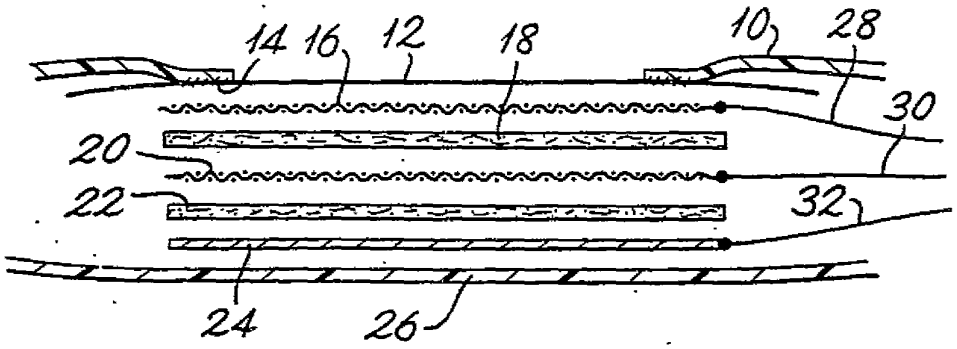
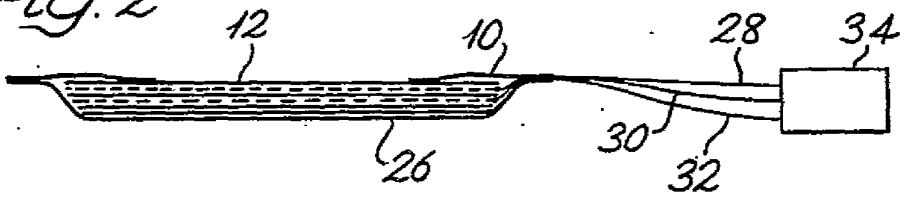


Fig. 1

Fig. 2



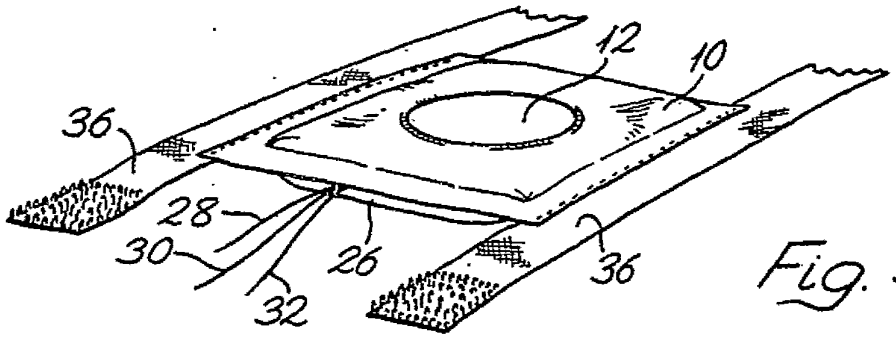


Fig. 3

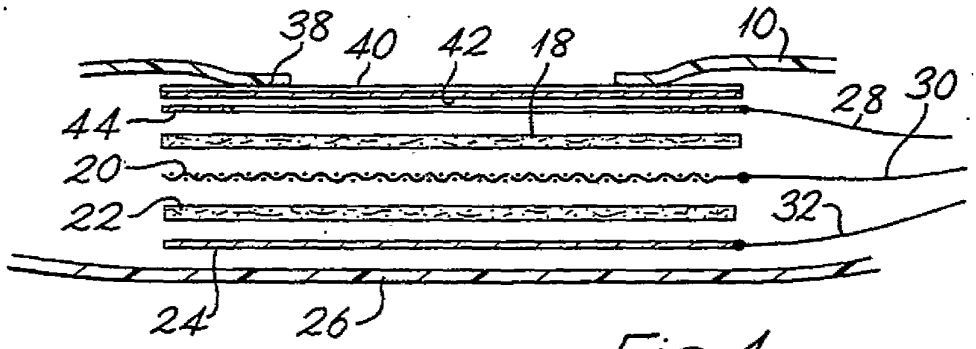


Fig. 4

TRANSCUTANEOUS GAS SENSOR

When a measurement is required of the concentration of a gas in a body tissue, it is preferable if the method of measurement is non-invasive. When the concentration of a gas is low, it may be difficult to make a reliable measurement by such a method.

One example of a non-invasive measurement is that in which oxygen in arterial blood is measured transcutaneously by placing a gas sensor housed in a rigid container on a patient's body over an artery. A disadvantage of the method is that the skin must be heated to about 40°C to increase its permeability to oxygen, with the attendant risk of burning unless the sensor is frequently moved to different locations. Consequently the sensor cannot be left in position for long periods for use in a gas monitoring mode. Moreover, adequate sealing between the sensor and the skin is not ensured.

According to the invention, a transcutaneous gas sensor comprises a series of essentially flat, flexible components, the components being in order:-

a first fluid-impermeable film of high polymeric material, at least an area of which is permeable to the gas to be sensed;

a working electrode;

a first porous insulating layer;

a reference electrode;

a second porous insulating layer;

a counter electrode; and

a second fluid-impermeable film of high polymeric material;

the three electrodes and the two insulating layers being of approximately the same area, the first and second films being of larger area than the other components and being sealed together at their edges in a liquid-tight manner so as to retain an electrolyte, and there being also provided a connection to each electrode which extends outside the first and second films through a liquid-tight seal.

The working electrode may be a platinum electrode, either in the form of a gauze, or in the form of a metallised membrane of hi ʰ polymeric material, the membrane then constituting the gas-permeable area of the first film.

The reference electrode may be a gauze of silver, having an anodization coating of silver chloride.

The counter electrode may be a lead/lead dioxide electrode, formed electrochemically in situ by providing a sheet or gauze of lead, and causing the conditions in the sensor to be such that lead is oxidised in the electrolyte.

The gas permeable area of the first film may comprise a piece of relatively thin film sealed at its edges to cover an aperture in a relatively thick, gas-impermeable film, which in turn is sealed to the second film. The relatively thin film may be the membrane layer of a metallised membrane electrode.

The invention will now be described by way of example with reference to the accompanying drawings in which:-

Figure 1 illustrates in exploded form the layers in a first embodiment of a transcutaneous gas sensor;

Figure 2 is a section through the sensor in its operating form;

Figure 3 is a view of the sensor; and

Figure 4 illustrates in exploded form the layers in a second embodiment of a transcutaneous gas sensor.

In Figure 1, a first sheet 10 of polyethylene 0.5 to 1.0 millimetres thick has a circular aperture which is closed by a sheet 12 of 6 to 12 microns thick polyethylene film; the sheets are heat sealed together around the aperture, as indicated at reference 14. Below the polyethylene film 12 is a platinum gauze 16, a filter paper 18, a silver/silver chloride gauze 20, a filter paper 22, a lead/lead oxide sheet or gauze 24

and a second sheet 26 of polyethylene 0.5 to 1.0 millimetres thick. The polyethylene sheets are of larger areas than the metal and filter paper layers, and are heat sealed together at their outer edges to give a sandwich construction of sensor as illustrated in Figure 2. Just before the final length of heat seal is made, the sensor is filled with an electrolyte, then fully sealed. Wire contacts 28, 30, 32 to respectively the working, reference and counter electrodes extend through the heat seal and are connected to a potentiostatic electrical circuit 34.

A suitable electrolyte is a conductive gel, such as "Neptic" (Registered Trade Mark) electrode gel, which contains sodium chloride and glycerol, and is used for electrocardiograph or electroencephalograph electrodes. Alternatively, a gel made up with sodium sulphate may be used.

In use, the potentiostatic circuit 34 applies a voltage (which may be variable) to the lead/lead oxide counter electrode 24 such that the platinum working electrode 16 is held at a fixed potential with respect to the silver/silver chloride reference electrode 20 which is constant and at which any hydrogen gas permeating through the permeable membrane 12 is oxidised. There is a corresponding reduction reaction at the counter electrode and the current generated by the electrochemical reaction is measured as the potential drop across a current measuring resistor in series with the counter electrode. The electrochemical cell is operated in the diffusion limited mode i.e. the rate of reaction is limited by the diffusion or mass transport of the reacting gas passing through the polyethylene film 12; the current generated is proportional to the concentration (partial pressure) of reactive gas in the gas sample. The current is measured by the circuit 34.

When the cell is constructed, a sheet or gauze of freshly

scraped lead is placed at the counter electrode position, and is oxidised in situ when the sensor is complete and filled with electrolyte. The membrane 12 is exposed to an oxygen-containing gas, such as air, and the connections 28, 32 of the working electrode and counter electrode to the circuit 34 are reversed. The circuit is arranged to apply to the working electrode a potential (about - 400 to-600 millivolts) with respect to the reference electrode 20 such that the lead sheet or gauze is oxidised. A layer of lead dioxide forms on the surface of the lead to give a lead/lead dioxide electrode. For use as a hydrogen sensor, the two connections are then reversed to their original positions and a potential of +200 to +300 millivolts with respect to the reference electrode is applied.

The layer of lead dioxide formed in this way is ordered, with regular close packing, and adheres to the lead very strongly; the electrode is therefore insensitive to vibration. Further, only one allotrope of three possible oxides is formed giving further stability in contrast with a mixed allotrope lead dioxide which has varying electrical properties.

The thickness of the lead dioxide layer increases with time in accordance with Faraday's and Coulomb's laws and since lead dioxide is reduced in the sensing mode of the cell, the life of the counter electrode can be predicted. It is a great advantage that the counter electrode can be regenerated after use by reversal of the two electrode connections as before. As an example, if the hydrogen sensor is to measure very low concentrations of hydrogen, such as a few parts per million, then a lead/lead dioxide counter electrode having a life of 12 months can be prepared by running the cell in the reverse mode for 8 hours.

The fully-prepared sensor is moderately flexible, and even when flexed the components retain essentially the same geometric

relationship. As a consequence the electrochemical kinetic equilibria are undisturbed by minor flexing. The flexibility allows the sensor to be applied to a curved surface, such as a human limb, and an air-tight seal between the skin and the gas permeable film can be made. The sensor is very sensitive and the skin does not need to be heated to allow measurement of hydrogen concentration to be made, even if it is as low as 1 or 2 parts per million. The sensor can be left in place to allow continuous gas monitoring over extended periods.

An external construction suitable for application to a human limb is illustrated in Figure 3. Two edges of the square sensor are attached to strips 36 of "Velcro" (Registered Trade Mark). The sensor is placed in position with membrane 12 on the skin over a vein or artery in a limb, and the strips 36 are wrapped round to overlap and hold the sensor securely in position without discomfort.

In a modification (not illustrated) a rubber washer is placed between the human limb and the outer part of the area of the device which contacts it. Use of such a washer minimises noise generation due to movement of the patient.

A modified construction is shown in Figure 4. Items identical to those in Figure 1 are given the same reference numerals. The aperture in the first sheet 10 is attached by a heat seal 38 to the membrane layer 40 of a metallised membrane electrode, which comprises a 6 to 25 micron sheet of polycarbonate or polyethylene on to which a layer 42 of platinum has been deposited. The metal layer 42 is in contact with a platinum ring 44 to which the working electrode connection 28 is attached. The other parts of the cell are identical to those in Figure 1. It is an advantage of the use of a metallized membrane electrode that the response time of the cell is reduced in comparison with a cell having a gas-permeable layer and a separate platinum gauze working electrode.

By choice of suitable materials for the permeable film, the electrodes and the electrolyte, gases other than hydrogen can be sensed. However, it is an advantage of the use of a dilute sodium chloride as in the example above that if the membrane punctures when in contact with a patient, the released liquid is not harmful.

CLAIMS

1. A transcutaneous gas sensor comprises a series of essentially flat, flexible components, the components being in order:-

a first fluid-impermeable film of high polymeric material, at least an area of which is permeable to the gas to be sensed;

a working electrode;

a first porous insulating layer;

a reference electrode;

a seond porous insulating layer;

a counter electrode; and

a second fluid-impermeable film of high polymeric material;

the three electrodes and the two insulating layers being of approximately the same area, the first and second films being of larger area than the other components and being sealed together at their edges in a liquid-tight manner so as to retain an electrolyte, and there being also provided a connection to each electrode which extends outside the first and second films through a liquid-tight seal.

2. A sensor according to Claim 1 in which the working electrode is a platinum gauze.

3. A sensor according to Claim 1 in which the working electrode is a metallised membrane of high polymeric material, the membrane also constituting the gas-permeable area of the first film.

4. A sensor according to any preceding claim in which the reference electrode is a silver gauze having an anodisation coating of silver chloride.

5. A sensor according to any preceding claim in which the counter electrode is a lead/lead dioxide electrode formed electrochemically in situ by providing a sheet or gauze of lead, and causing the lead to be oxidised in the electrolyte.

6. A sensor according to any preceding claim in which the gas permeable area of the first film comprises an area of

relatively thin film sealed at its edges to cover an aperture in a relatively thick, gas-impermeable film.

7. A sensor according to any preceding claim containing an electrolyte which is an electrically conductive gel.

8. A transcutaneous gas sensor substantially as hereinbefore described with reference either to Figure 1, 2 and 3 or to Figure 4 of the accompanying drawings.

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DESCRIPTION JP2004214014A

10 Electrical connector

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14 The present invention describes electricity used for connecting a glass substrate and a circuit board of a liquid crystal display, connecting circuit boards to each other, or electrically connecting a semiconductor package and an inspection device. It is about the connector. Conventional Technology An electric connector is used for conductive connection of an electronic device. As an electric connector of this type, although not shown, a conductive rubber layer and an insulating rubber layer containing carbon black powder are used. Alternately laminated zebra type (see Patent Document 1), zebra type in which conductive rubber layers filled with a large amount of metal particles and insulating rubber layers are alternately laminated (see Patent Document 2), in the insulating rubber layer An heterogeneous conductive type or the like in which a plurality of conductive thin wires are incorporated and arranged is known (see Patent Document 3). Japanese Patent Application Laid-Open No. 6-168754 [Patent Document 2] Japanese Patent Application Laid-Open No. 2000-357547 [Patent Document 3] Japanese Patent Application Laid-Open No. 6-688923 [0004]] Since the conventional electric connector is configured as described above, there are the following problems. First, in the case of the zebra type electric connector disclosed in Patent Document 1, since the volume resistivity of the conductive rubber layer is high, there is no variation like a color liquid crystal module or a liquid crystal module having 16 or more gradations of black and white. For connections that require resistivity, for connections that want to minimize the variation in connection resistance between terminals of electrical joints, and for connections with circuit boards that require high current values, such as plasma display modules. When a current of 100 mA or more is passed, there is a problem that the electric connector generates heat and causes an unnecessary temperature rise. Further, in the case of the zebra type electric connector disclosed in Patent Document 2, although the volume resistivity of the conductive member is low, the hardness is high, so that the conductive

connection is made unless a high compressive load is applied at the time of the conductive connection. Cannot be expected to stabilize. Further, when a high compressive load is applied, the electric joint made of a circuit board, an electronic component, or the like may be damaged. Further, when the conductive rubber layer and the insulating rubber layer are alternately laminated and molded, the metal particles do not come into contact with each other unless high pressure is applied to the molding, so that the original low volume resistivity cannot be obtained and the processing is performed. There is a problem that there are restrictions on conditions and processing equipment. Further, in the case of the anisotropic conductive type electric connector disclosed in Patent Document 3, since the conductive thin wire is likely to buckle due to the compressive force at the time of conductive connection, it is absolutely used for an inspection device that is used repeatedly. There is a problem that it cannot be done.

Further, in order to make all the conductive thin wires completely conductively connected, it is necessary to compress the entire electric connector with a high pressure, which increases the burden on the terminals of the semiconductor package and the inspection device. Further, since the connection end surface of each conductive thin wire cannot be said to be a uniform flat surface, point contact is likely to occur, and a connection failure is likely to occur. Furthermore, in order to reduce the contact resistance, it is necessary to plate the conductive thin wire and its connection end face with gold, which causes a problem that the manufacturing cost increases. The present invention has been made in view of the above, and is expected to stabilize the conduction connection without causing an unnecessary temperature rise, is less likely to damage the electrical connector, and is restricted by processing conditions, processing equipment, and the like. It is an object of the present invention to provide an inexpensive electric connector capable of suppressing connection failure without causing the occurrence of the above. [Means for Solving the Problems] In the present invention, in order to achieve the above problems, opposing electrical joints are electrically connected, and a plurality of conductive layers and insulating layers are arranged side by side. Each conductive layer is provided as a conductive member containing 200 to 500 parts by mass of chain powder in 100 parts by mass of an insulating elastomer resin. It is preferable that the chain powder of the conductive member is a metal powder having a diameter of 10 to 200 nm which is connected to form a substantially chain shape. Here, the electrical joints within the scope of the claims include at least a glass substrate of a liquid crystal display, a module for a plasma display, a circuit board, various semiconductor packages, electronic components, acoustic components, inspection devices, and the like. The conductive layer and the insulating layer can be formed in a sheet shape or a block shape. Further, the metal powder of the chain powder may be granular or plate-shaped. BEST MODE FOR CARRYING OUT THE INVENTION Hereinafter, a preferred embodiment of the present invention will be described with reference to the drawings. As shown in FIGS. 1 and 2, the electric connector in the present embodiment has a plurality of conductive layers 1. And the insulating layer 2 are arranged alternately in a horizontal row, and each conductive layer 1 is placed in 100 parts by mass of the insulating elastomer resin, and 200 to 500 parts by mass of the chain powder 4 is placed in the vertical thickness direction, which is the conductive

connection direction. The conductive member contained therein, and the chain powder 4 of the conductive member was formed into a metal powder 5 having a substantially chain shape and having a diameter of 10 to 200 nm, and was sandwiched between a pair of opposing electric joints (not shown). Conductive connection is made by pressure welding in the state. Each conductive layer 1 is formed in a rectangular sheet, is in close contact with the adjacent insulating layer 2, is pressure-welded and conductively connected, and is 40 ° to 80 ° Hs, preferably 40 ° to 60 ° Hs. It is said to be the hardness of.

87 This is because, if the hardness of the conductive layer 1 is within the relevant range, a large number of metal powders 5 exhibit a substantially chain shape, so that even if the compression ratio is as small as 2 to 10% at the time of conduction connection, uniform and stable conduction is achieved. This is because the connection becomes possible. As the insulating elastomer resin 3 which is the base material of the conductive layer 1, an elastic material which is stable in shape, is not significantly deformed by its own weight, or is not plastically deformed after curing is used. Specifically, each copolymer rubber such as natural rubber, butadiene / styrene, acrylonitrile / butadiene, acrylonitrile / butadiene / styrene, ethylene / propylene, ethylene / propylene / butadiene, chloropyrene rubber, silicone rubber, butadiene rubber, isoprene. In addition to synthetic rubbers such as rubber, chlorosulfonated polyethylene rubber, polysulfide rubber, butyl rubber, fluororubber, urethane rubber, and polyisobutylene rubber, thermoplastic elastomers such as polyester elastomer, plasticized vinyl chloride resin, vinyl acetate resin, etc. Examples thereof include vinyl chloride / vinyl acetate copolymer resin. Among these, silicone rubber, which has excellent aging characteristics, electrical insulation, heat resistance, compression set, workability, and high frequency characteristics, has a low dielectric constant, and is stable in price, is the most suitable. Silicone rubbers include polysiloxanes such as dimethyl, methylphenyl, and methylvinyl, halogenated polysiloxanes that have been given appropriate rheological properties by blending a filler such as silica, or metal salts. Examples thereof include vulcanized or cured halogenated polysiloxanes. The chain powder 4 includes a large number of metal powders 5 having a size of 10 to 200 nm, and the large number of metal powders 5 are connected to form a substantially chain shape. The chain powder 4 is blended in an amount of 200 to 500 parts by mass, preferably 250 to 300 parts by mass. This is because if it is less than 200 parts by mass, a predetermined connection resistance (100 mΩ) cannot be obtained. On the contrary, if it exceeds 500 parts by mass, the elastic property cannot be ensured. Further, each metal powder 5 is made into a granular or plate shape by using nickel, tin, palladium, a silver alloy, an iron alloy powder or the like. The material of the metal powder 5 is not particularly limited due to the property that the metal becomes magnetic due to miniaturization, but nickel is optimal from the viewpoint of processing and cost. Gold plating or silver plating is selectively applied to the metal powder 5 from the viewpoint of stabilizing and lowering the resistance at the time of conduction connection.

118 The reason why the metal powder 5 has a size of 10 to 200 nm is that the metal powder 5 functions as an ultrafine powder, in other words, when it is nanosized, it functions as a magnet and is connected in a substantially chain shape without applying a magnetic field. .. Further, if the metal powder 5 is less than 10 nm, chain forming becomes difficult and lumps

are likely to be formed. On the contrary, if it exceeds 200 nm, the magnet function deteriorates and it tends to be agglomerated. Each insulating layer 2 is formed on a rectangular sheet having the same size as the conductive layer 1 by using a predetermined insulating elastomer resin 3, and is in close contact with the adjacent conductive layer 1. The insulating elastomer resin 3 of the insulating layer 2 may be different from the insulating elastomer resin 3 of the conductive layer 1, but is preferably the same. This is based on the reason that if the same material is used, the adhesion with the conductive layer 1 can be strengthened and integration can be easily achieved. When manufacturing such a zebra type electric connector, first, the insulating layer 2 is molded by a calendar, and a large number of chain powders 4 are oriented in a certain direction on the molded insulating layer 2. The conductive layers 1 may be laminated, and these operations may be repeated thereafter. As an example, first, the insulating elastomer resin 3 is formed into a thin film (for example, 25 to 100 μm) on a polyethylene terephthalate film by a calendar and heat-cured to form an insulating layer 2. Further, about 200 to 500 parts by mass of a large number of chain powders 4 are blended with the insulating elastomer resin 3, and about 10 to 10 of the conductive layer 1 are oriented in the same direction with an extruder. It is extruded to a thickness of 20 times, gradually thinned with a roll, transferred or topping on the insulating layer 2 to form a conductive layer (for example, 25 to 100 μm) 1, and then a film is formed from the obtained sheet. Is peeled off to form a laminated sheet. Next, the above operation is repeated to form a large number of laminated sheets, and these are laminated in the same order to form a block body, and this block body is vulcanized. After the block body is vulcanized in this way, it is sliced in a direction crossing the laminated surface to form a sheet in which a plurality of conductive layers 1 and insulating layers 2 are alternately arranged, and this sheet is secondarily vulcanized. The electric connector of FIG. 1 can be manufactured by cutting the conductive layer 1 and the insulating layer 2 with a predetermined width. The electric connector manufactured in this way is interposed and sandwiched between the circuit board which is an electric junction and the semiconductor package, and the upper semiconductor package is pressed down toward the lower circuit board, so that the plurality of conductive layers 1 are formed. These circuit boards and the semiconductor package are electrically connected.

152 According to the above configuration, since the conductive chain powder 4 connected in a chain is oriented in the conduction connection direction, each chain powder 4 functions as a conductor, and a small content is good and low. Since the resistance can be obtained and the chain powder 4 is connected in a chain, it is possible to suppress and prevent the change in the resistance value, and the temperature does not rise unnecessarily. Further, since the chain powder 4 is fixed in the conductive layer 1 and the resistance value is stable without separating each chain powder 4 at the time of compression connection, it is possible to greatly suppress the variation in the resistance of the conductive layer 1. Further, as compared with the case of filling only powder, a low connection resistance having an appropriate resistance value (for example, about 1/4 to 1/6) can be obtained even if the content is small (for example, about 1/2 to 1/3). Therefore, it is possible to greatly reduce the manufacturing cost. Further, if each chain powder 4 is plated with gold or silver, the

contact resistance can be further reduced. Further, even if the content is small, the elastic characteristics of the conductive layer 1 are not impaired at all. Explaining this point in detail, the metal particles contained in the conductive layer 1 in the conventional electric connector are generally silver particles of about 10 to 100 μm, and when the connection resistance is 100 mΩ or less, they are insulated as a binder. It was necessary to fill as much as 500 to 800 parts by mass with respect to 100 parts by mass of the sex silicone rubber. Therefore, the elastic characteristics of the conductive layer 1 could not be properly secured. On the other hand, according to the present embodiment, since the chain powder 4 is blended in an amount of 200 to 500 parts by mass, preferably 250 to 300 parts by mass, the connection resistance can be set to 15 to 25 mΩ or less. The elastic properties of the conductive layer 1 are not impaired at all. Further, since it can be compressed with a low load, it is possible to greatly improve the reduction of the compression set of the silicone rubber due to the high filling. Further, since it is possible to obtain an electric connector (conductive layer 15 μm and insulating layer 15 μm) having an ultra-low pitch, for example, a 30 μm pitch, which could not be manufactured in the past, an ultra-low pitch circuit board or a liquid crystal module can also be connected. be able to. Furthermore, as the size and thickness of the electric connector are reduced, the height of the electric connector can be lowered, so that stable resistance can be expected even at a height of 1 mm, which was not possible in the past. Next, FIG. 3 shows a second embodiment of the present invention. In this case, the insulating layers 1 and the insulating layer 2 are provided with insulating properties on both left and right sides of the plurality of conductive layers 1 and the insulating layer 2 arranged in a row. The support layers 10 are adhered to each other.

186 The thickness and material of each support layer 10 may be the same as or different from that of the insulating layer 2. Since the other parts are the same as those in the above embodiment, the description thereof will be omitted. In this embodiment as well, the same effects as those in the above embodiment can be expected, and when the compressive load between the plurality of conductive layers 1 and the insulating layer 2 is high, for example, the rubber hardness is as low as 40 ° Hs or less. It is clear that the compression load of the entire electric connector can be expected to be reduced by using the support layer 10 made of the insulating rubber and the foamed rubber. Further, at the time of conductive connection of this electric connector, since the metal powder 5 in the conductive layer 1 is a chain powder 4 in which the metal powder 5 is connected in a chain shape, the volume resistivity is really small, and a stable resistance value that is not affected by the compressibility is obtained. be able to. Further, since the load applied to the glass substrate and the circuit board at the time of connection is small, secondary problems do not occur. [Effect of the Invention] As described above, according to the present invention, stabilization of the conduction connection can be expected without causing an unnecessary temperature rise, there is little risk of damage to the electrical joint, and processing conditions and processing equipment. There is an effect that there are no restrictions on such things. In addition, poor connection can be suppressed, and even circuit connections that require a high current value from a minute current can be used in a sufficiently stable state. Further, since the compressibility at the time of connection can be lowered and the load can be made

low, for example, when used at the time of inspection of a semiconductor package or the like, it is possible to prevent deformation of the semiconductor package terminal and internal destruction of the chip. Further, by reducing the load applied to a circuit board made of, for example, a glass substrate, it becomes possible to contribute to the miniaturization and weight reduction of inspection equipment and electronic equipment. Further, an electric connector having a lower pitch and an electric connector having a lower height can be obtained, and the content of the chain powder can be reduced, so that the cost of the conductive member can be reduced. .. Further, since it can be manufactured with existing equipment, productivity can be improved and manufacturing cost can be expected to be reduced. BRIEF DESCRIPTION OF THE DRAWINGS FIG. 1 is a perspective explanatory view showing an embodiment of an electric connector according to the present invention. FIG. 2 is a schematic cross-sectional explanatory view showing an embodiment of an electric connector according to the present invention. FIG. 3 is a perspective explanatory view showing a second embodiment of the electric connector according to the present invention. [Explanation of Codes] 1 Conductive layer 2 Insulating layer 3 Insulating elastomer resin 4 Chain powder 5 Metal powder 6 Support layer

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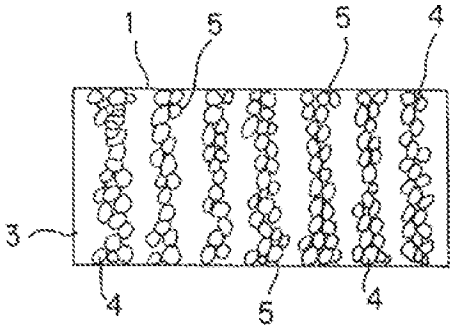
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(54)【発明の名称】電気コネクタ

(57)【要約】
【課題】無用な温度上昇を招くことなく導通接続の安定化が期待でき、電気接合物の破損のおそれが少なく、加工条件や加工設備等に制約が生じることがなく、しかも、接続不良を抑制できる安価な電気コネクタを提供する。
【解決手段】複数の導電層１と絶縁層とを交互に横一列に並べ備え、各導電層１を、絶縁性エラストマー樹脂１００質量部に、２００～５００質量部の鎖状粉末４を上下厚さ方向に含有した導電部材とする。そして、鎖状粉末４を、略鎖状をなす１０～２００ｎｍの金属粉末５とする。
【選択図】　図２



【特許請求の範囲】
【請求項１】
対向する電気接合物を電気的に接続する電気コネクタであって、
複数の導電層と絶縁層とを並べ設け、各導電層を、絶縁性エラストマー樹脂１００質量部に、２００～５００質量部の鎖状粉末を含有した導電部材としたことを特徴とする電気コネクタ。
【請求項２】
導電部材の鎖状粉末を、連なって略鎖状をなす１０～２００ｎｍの金属粉末とした請求項１記載の電気コネクタ。
【発明の詳細な説明】
【０００１】
【発明の属する技術分野】
本発明は、液晶表示体のガラス基板と回路基板との接続、回路基板同士の接続、あるいは半導体パッケージと検査装置との電気的な接続等に用いられる電気コネクタに関するものである。
【０００２】
【従来の技術】
電子機器の導通接続には電気コネクタが使用されるが、この種の電気コネクタとしては、図示しないが、カーボンブラック粉末を含有する導電ゴム層と絶縁ゴム層とが交互に積層されたゼブラタイプ（特許文献１参照）、多量の金属粒子の充填された導電ゴム層と絶縁ゴム層とが交互に積層されたゼブラタイプ（特許文献２参照）、絶縁ゴム層中に複数本の導電細線が内蔵して配列された異方導電タイプ等が知られている（特許文献３参照）。
【０００３】
【特許文献１】
特開平６－１６８７５４号公報
【特許文献２】
特開２０００－３５７５４７号公報
【特許文献３】
特開平６－６８９２３号公報
【０００４】
【発明が解決しようとする課題】
従来の電気コネクタは、以上のように構成されているので、以下のような問題がある。先ず、特許文献１に開示されているゼブラタイプの電気コネクタの場合には、導電ゴム層の体積抵抗率が高いので、カラー液晶モジュール、白黒１６階調以上の液晶モジュールのようなバラツキのない低抵抗を必要とする接続、電気接合物の端子間における接続抵抗のバラツキを可能な限り小さくしたい場合の接続、さらにはプラズマディスプレイ用モジュール等の高電流値を必要とする回路基板との接続において、電流を１００ｍＡ以上流すと、電気コネクタが発熱して無用な温度上昇を招くという問題がある。
【０００５】
また、特許文献２に開示されているゼブラタイプの電気コネクタの場合には、導電部材の体積抵抗率が低いものの、硬度が高いので、導通接続時に高圧縮荷重を加えないと導通接続の安定化が期待できない。また、高圧縮荷重を作用させると、回路基板や電子部品等からなる電気接合物が破損するおそれがある。また、導電ゴム層と絶縁ゴム層とを交互多重に積層して成形するときには、高圧力を加えて成形しないと、金属粒子同士が接触しないので、本来の低い体積抵抗率が得られず、加工条件や加工設備等に制約が生じるという問題がある。
【０００６】
また、特許文献３に開示されている異方導電タイプの電気コネクタの場合には、導通接続時の圧縮力で導電細線が座屈しやすいので、繰り返し使用する検査装置には到底使用することができないという問題がある。また、全ての導電細線を完全に導通接続するには、電

気コネクタ全体を高圧力で圧縮する必要があるので、半導体パッケージの端子や検査装置の負担が増大することとなる。さらに、各導電細線の接続端面が均一な平坦面とはいえないので、点接触となりやすく、接続不良を招きやすい。さらにまた、接触抵抗を小さくするためには、導電細線やその接続端面を金メッキする必要があるので、製造コストが嵩むという問題がある。

【０００７】

本発明は、上記に鑑みなされたもので、無用な温度上昇を招くことなく導通接続の安定化が期待でき、電気接合物の破損のおそれが少なく、加工条件や加工設備等に制約の生じることがなく、しかも、接続不良を抑制することのできる安価な電気コネクタを提供することを目的としている。

【０００８】

【課題を解決するための手段】

本発明においては、上記課題を達成するため、対向する電気接合物を電気的に接続するものであって、

複数の導電層と絶縁層とを並べ設け、各導電層を、絶縁性エラストマー樹脂１００質量部に、２００～５００質量部の鎖状粉末を含有した導電部材としたことを特徴としている。なお、導電部材の鎖状粉末を、連なって略鎖状をなす１０～２００ｎｍの金属粉末とすることが好ましい。

【０００９】

ここで特許請求の範囲における電気接合物には、少なくとも液晶表示体のガラス基板、プラズマディスプレイ用モジュール、回路基板、各種の半導体パッケージや電子部品、音響部品、検査装置等が含まれる。導電層と絶縁層とは、シート形、あるいはブロック形に形成することができる。また、鎖状粉末の金属粉末は、粒状又は板状等とすることができる。

【００１０】

【発明の実施の形態】

以下、図面を参照して本発明の好ましい実施形態を説明すると、本実施形態における電気コネクタは、図１や図２に示すように、複数の導電層１と絶縁層２とを交互に横一列に並べ備え、各導電層１を、絶縁性エラストマー樹脂１００質量部に、２００～５００質量部の鎖状粉末４を導通接続方向である上下厚さ方向に含有した導電部材とするとともに、この導電部材の鎖状粉末４を、略鎖状をなす１０～２００ｎｍの金属粉末５とし、相対向する一対の電気接合物間（図示せず）に挟持された状態で圧接されることにより導通接続するようにしている。

【００１１】

各導電層１は、矩形のシートに形成されて隣接する絶縁層２に密着し、圧接して導通接続される観点から、４０°～８０°Ｈｓ、好ましくは４０°～６０°Ｈｓの硬度とされる。これは、導電層１の硬度を係る範囲とすれば、多数の金属粉末５が略鎖状を呈する関係上、導通接続時に圧縮率が２～１０％ときわめて小さい値でも、均一に安定した導通接続が可能になるからである。

【００１２】

導電層１の母材である絶縁性エラストマー樹脂３としては、形状的に安定し、自重で著しく変形したり、硬化後に塑性変形しない弾性材料が使用される。具体的には、天然ゴム、ブタジエン・スチレン、アクリロニトリル・ブタジエン、アクリロニトリル・ブタジエン・スチレン、エチレン・プロピレン、エチレン・プロピレン・ブタジエン等の各共重合体ゴム、クロロピレンゴム、シリコーンゴム、ブタジエンゴム、イソプレンゴム、クロロスルホン化ポリエチレンゴム、ポリサルファイドゴム、ブチルゴム、フッ素ゴム、ウレタンゴム、ポリイソブチレンゴム等の合成ゴム類の他、ポリエステルエラストマー等の熱可塑性エラストマー、可塑化塩化ビニル系樹脂、酢酸ビニル系樹脂、塩化ビニル・酢酸ビニル共重合体樹脂等があげられる。これらの中でも、時効特性、電気絶縁性、耐熱性、圧縮永久歪み、加工性、高周波特性に優れ、誘電率の小さく価格の安定なシリコーンゴムが最適

である。

【００１３】

シリコーンゴム類としては、ジメチル、メチルフェニル、メチルビニル等の各ポリシロキサン類、シリカのような充填剤を配合して適当なレオロジー特性が付与されたハロゲン化ポリシロキサン類、あるいは金属塩類でバルカナイズ若しくは硬化されたハロゲン化ポリシロキサン類があげられる。

【００１４】

鎖状粉末４は、１０～２００ｎｍの大きさを有する多数の金属粉末５を備え、この多数の金属粉末５が連なって略鎖形を形成する。この鎖状粉末４は、２００～５００質量部、好ましくは、２５０～３００質量部配合される。これは、２００質量部未満の場合には、所定の接続抵抗（１００ｍΩ）を得ることができないからである。逆に、５００質量部を超える場合、弾性特性を確保することができないからである。また、各金属粉末５は、ニッケル、錫、パラジウム、銀合金、鉄合金粉末等を用いて粒状あるいは板状とされる。金属粉末５の材料は、微細化により金属が磁性を帯びる特性上、特に限定されるものではないが、加工やコストの観点からニッケルが最適である。

【００１５】

金属粉末５には、導通接続時の抵抗を安定させて低くする観点から、金メッキや銀メッキが選択的に施される。金属粉末５が１０～２００ｎｍの大きさなのは、金属粉末５が極微細粉末、換言すれば、ナノサイズ化されると磁石として機能し、磁界を作用させなくても略鎖形に連なるからである。また、金属粉末５を１０ｎｍ未満とすると、鎖状成形が困難化して塊になりやすいからである。逆に、２００ｎｍを超えると、磁石機能が劣化し、塊になりやすいという理由に基づく。

【００１６】

各絶縁層２は、所定の絶縁性エラストマー樹脂３を用いて導電層１と同じ大きさの矩形のシートに形成され、隣接する導電層１に密着する。この絶縁層２の絶縁性エラストマー樹脂３は、導電層１の絶縁性エラストマー樹脂３と相違しても良いが、同一であるのが好ましい。これは、同一の材料とすれば、導電層１との密着を強化して一体化を容易に図ることができるという理由に基づく。

【００１７】

このようなゼブラタイプの電気コネクタを製造する場合には、先ず、絶縁層２をカレンダーにより成形し、この成形した絶縁層２上に、多数の鎖状粉末４が一定方向に配向された導電層１を積層し、以下、これらの作業を繰り返せば良い。一例をあげると、先ず、ポリエチレンテレフタレート製のフィルム上に絶縁性エラストマー樹脂３をカレンダーにより薄い膜状に製膜（例えば、２５～１００μｍ）し、加熱硬化させて絶縁層２を形成する。

【００１８】

また、絶縁性エラストマー樹脂３に多数の鎖状粉末４を約２００～５００質量部配合し、押出機で多数の鎖状粉末４を同一方向に配向させながら導電層１の約１０～２０倍の厚さに押し出すとともに、ロールで徐々に薄くし、先の絶縁層２上に転写又はトッピングして導電層（例えば、２５～１００μｍ）１を形成し、その後、得られたシートからフィルムを剥離して積層シートを形成する。

【００１９】

次いで、上記作業を繰り返して多数の積層シートを形成し、これらを同じ順序で積層してブロック体とし、このブロック体を加硫処理する。こうしてブロック体を加硫処理したら、これを積層面を横切る方向にスライスして複数の導電層１と絶縁層２とが交互に配列されたシートを形成し、このシートを二次加硫して導電層１と絶縁層２とを横切る所定の幅で裁断すれば、図１の電気コネクタを製造することができる。

こうして製造された電気コネクタは、電気接合物である回路基板と半導体パッケージとの間に介在挟持され、上方の半導体パッケージが下方の回路基板方向に圧下押圧されることにより、複数の導電層１がこれら回路基板と半導体パッケージとを導通接続する。

【００２０】

上記構成によれば、導通接続方向に、鎖状に連なる導電性の鎖状粉末４が配向されるので、各鎖状粉末４が導電体として機能し、少ない含有量で良好な低抵抗を得ることができるとともに、鎖状粉末４が鎖状に連なることから、抵抗値の変化をも抑制防止することができ、かつ無用な温度上昇を招くこともない。また、導電層１内に鎖状粉末４が固着し、圧縮接続時に各鎖状粉末４が分離することなく抵抗値が安定するので、導電層１の抵抗のバラツキを大いに抑制することができる。また、粉末のみを充填する場合に比べ、含有量が少なくても（例えば、１／２～１／３程度）適切な抵抗値（例えば、１／４～１／６程度の低い接続抵抗が得られる）が得られるので、製造コストを大いに抑制することが可能になる。

【００２１】

また、各鎖状粉末４に金メッキや銀メッキを施せば、接触抵抗をさらに低下させることが可能になる。また、少ない含有量でも導電層１の弾性特性を何ら損なうことがない。

この点を詳しく説明すると、従来の電気コネクタにおける導電層１に含有される金属粒子は約１０～１００μｍ程度の銀粒子が一般的であり、接続抵抗を１００ｍΩ以下にする場合には、バインダーとして絶縁性シリコーンゴム１００質量部に対して５００～８００質量部程度と多く充填する必要があった。このため、導電層１の弾性特性を適切に確保することができなかった。

【００２２】

これに対し、本実施形態によれば、鎖状粉末４を２００～５００質量部、好ましくは、２５０～３００質量部配合するので、接続抵抗を１５～２５ｍΩ以下とすることができ、導電層１の弾性特性を何ら損なうことがない。また、低荷重で圧縮することができるので、高充填によるシリコーンゴムの圧縮永久歪みの低下を大いに改善することができる。さらに、従来では製造不可能であった超低ピッチ、例えば３０μｍピッチ等の電気コネクタ（導電層１５μｍと絶縁層１５μｍ）を得ることができるので、超低ピッチの回路基板や液晶モジュールをも接続することができる。さらにまた、小型薄型化に伴い、電気コネクタの高さをも低くすることができるので、従来では不可能だった１ｍｍの高さにおいても、安定した抵抗の獲得が期待できる。

【００２３】

次に、図３は本発明の第２の実施形態を示すもので、この場合には、一列に並んだ複数の導電層１と絶縁層２との左右両側面に、絶縁性のサポート層１０をそれぞれ接着するようにしている。

各サポート層１０の厚さや材質は、絶縁層２と同一でもよいし、異なるものでも良い。その他の部分については、上記実施形態と同様であるので説明を省略する。

【００２４】

本実施形態においても上記実施形態と同様の作用効果が期待でき、しかも、複数の導電層１と絶縁層２との圧縮荷重が高い場合に、例えばゴム硬度４０°Ｈｓ以下の低硬度の絶縁ゴム、発泡ゴムからなるサポート層１０を使用すれば、電気コネクタ全体の圧縮荷重の低減が期待できるのは明らかである。また、この電気コネクタの導通接続の際、導電層１内の金属粉末５が鎖状に連なる鎖状粉末４であるので、体積抵抗率が実に小さく、圧縮率に影響されない安定した抵抗値を得ることができる。さらに、接続時にガラス基板や回路基板に与える負荷が少ないので、二次的な不具合を起こすこともない。

【００２５】

【発明の効果】

以上のように本発明によれば、無用な温度上昇を招くことなく導通接続の安定化が期待でき、電気接合物の破損のおそれが少なく、加工条件や加工設備等に制約の生じることがないという効果がある。また、接続不良を抑制することができ、微小電流から高い電流値を必要とする回路接続でも、十分安定した状態で使用することができる。

【００２６】

また、接続時の圧縮率を低く、低荷重にすることができるので、例えば半導体パッケージ等の検査時に用いれば、半導体パッケージ端子の変形、チップの内部破壊の防止を図るこ

とができる。また、例えばガラス基板等からなる回路基板に与える負荷の低減により、検査機器、電子機器の小型化、軽量化に資することが可能になる。また、より低ピッチの電気コネクタや高さの低い電気コネクタをも得ることができるし、鎖状粉末の含有量を減少させることができるので、導電部材のコスト低減を実現することが可能になる。さらに、既存の設備で製造することができるので、生産性を向上させることができ、製造コストの低減が期待できる。

【図面の簡単な説明】

【図１】本発明に係る電気コネクタの実施形態を示す斜視説明図である。

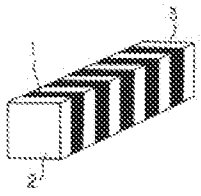
【図２】本発明に係る電気コネクタの実施形態を示す模式断面説明図である。

【図３】本発明に係る電気コネクタの第２の実施形態を示す斜視説明図である。

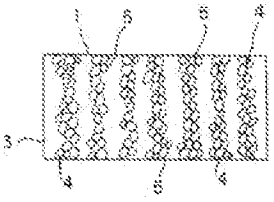
【符号の説明】

1 導電層
2 絶縁層
3 絶縁性エラストマー樹脂
4 鎖状粉末
5 金属粉末
6 サポート層

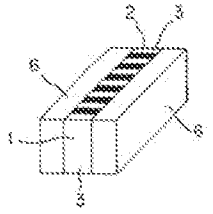
【図１】



【図２】



【図３】



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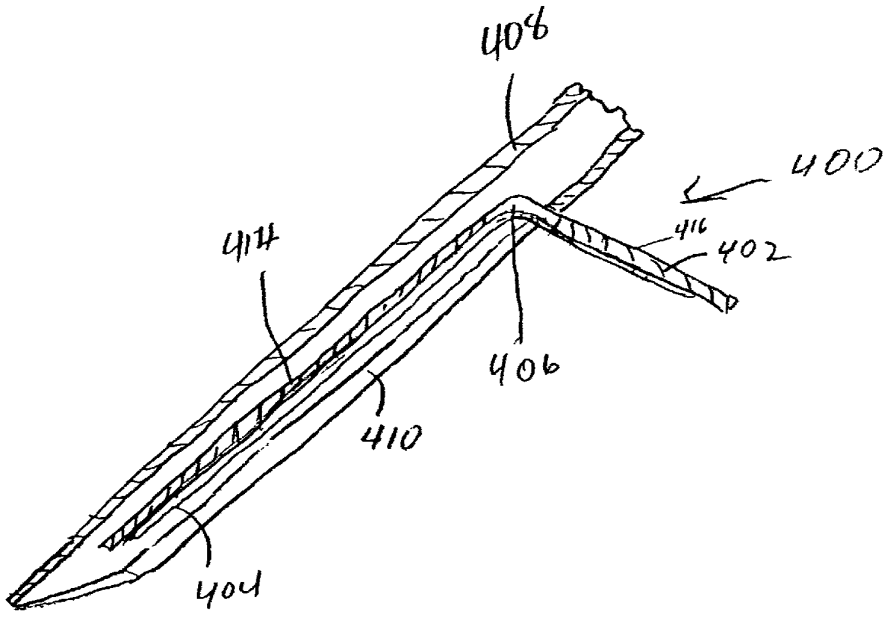
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[Continued on next page]

(54) Title: IMPROVED ANALYTE SENSOR AND METHOD OF MAKING THE SAME



(57) Abstract: A sensor and method of making the same for implantation in a body that includes a substrate with notches cut in the substrate to form a necked down region in the substrate; and at least one sensor electrode formed from one or more conductive layers. Preferably, the thickness of the substrate ranges from approximately 25 μ to 350 μ, but the thickness of the substrate can range from 5 μ to 750 μ. The sensor may be incorporated in to a sensor assembly includes a slotted needle having a slot. The notches creating the necked down region allow the substrate to slide into the slotted needle, which has the slot narrow enough to permit passage of the necked down region. However, a non-necked down region of the substrate is prevented from pulling out of the slotted needle through the slot. The slot of the slotted needle may also permit the necked down region of the substrate to slide down the slot.

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For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

Title:

IMPROVED ANALYTE SENSOR AND METHOD OF MAKING THE SAME

Related Applications:

This application is a continuation of U.S. Patent Application Serial No. 09/502,444, filed February 11, 2000, which is a continuation of U.S. Patent Application Serial No. 09/502.204 filed February 10, 2000, both of which are specifically incorporated by reference.

Field of the Invention

The present invention relates to methods for producing sensors that include flexible substrates and one or more sensor electrodes, and in particular embodiments to sensor sets including such sensors.

Background of the Invention

Methods for producing sensors, particularly sensors useful in sensor sets for the determination of a body characteristic such as blood glucose levels, are known. Examples of such sensors, sensor sets and methods for production thereof are described, e.g., in commonly assigned U.S. Patent No. 5,390,691; No. 5,391,250; No. 5,482,473; No. 5,299,571; No. 5,586,553; and No. 5,568,806, each of which is incorporated in its entirety herein by reference.

Certain known methods, such as that described in U.S. Patent No. 5,391, 250, form the sensor electrodes by an etching process. Etching processes are often multi-step procedures that can be time-consuming and expensive. Accordingly, a need exists for a simplified process for producing sensors.

Alternative methods described in PCT/US99/03781, published September 10, 1999 and based on U.S Patent Application Serial No. 09/034,422, form sensor electrodes by, for example, first forming a channel in a substrate, which can be a continuous web, and then depositing conductive material in the channel to form the electrode.

A need also exists for an improved process that enables continuous formation of sensors.

Summary of the Preferred Embodiments

It is an object of an embodiment of the present invention to provide an improved sensor and method of making the same, which obviates for practical purposes, the above mentioned limitations.

According to an embodiment of the invention, a sensor and a method of making the same for implantation in a body includes a substrate with notches cut in the substrate to form a necked down region in the substrate; and at least one sensor electrode formed from one or more conductive layers. In preferred embodiments, the thickness of the substrate ranges from approximately 25μ to 350μ, but the thickness of the substrate can range from 5μ to 750μ. In particular embodiments, a sensor assembly includes the sensor and a slotted needle having a slot. The notches creating the necked down region allow the substrate to slide into the slotted needle, which that has the slot narrow enough to permit passage of the necked down region. However, a non-necked down region of the substrate is prevented from pulling out of the slotted needle through the slot. In other embodiments, the slot of the slotted needle permits the necked down region of the substrate to slide down the slot.

In further embodiments, a width of the substrate in the non-necked down portion is sized to fit within a slotted needle having a diameter smaller than 21 gauge, 22 gauge, 23 gauge, 24 gauge or the like. In additional embodiments, at least one of the at least one sensor electrode is formed on a first surface of the substrate. In alternative embodiments, all of the at least one sensor electrode are only formed on the first surface. In other alternative embodiments, at least another one of the at least one sensor electrodes is formed on a second surface of the substrate. In still other alternative embodiments, a third one of the at least one sensor electrode is a reference electrode configured to contact a skin surface.

In yet another embodiment, sensors are formed as a part of sensor set that includes a sensor, mounting base and insertion needle. The mounting base adapted for mounting onto a patient's skin. The insertion needle is carried by the

mounting base to protrude from the mounting base and has at least a portion of the sensor nested within the insertion needle. The insertion needle defines a longitudinally extending slot along one side to permit sliding withdrawal of the insertion needle from the mounting base and the nested portion of the sensor. The slot is also configured to accept the necked down region of the substrate.

In accordance with one aspect of the present invention, there is provided a method of making a sensor that includes the steps of providing a pre-formed self-supporting flexible substrate; sputter-depositing a metal layer on the substrate; etching the sputter-deposited metal layers to form a sensor electrode having a proximal segment and a distal segment; plating a metal layer on the sensor electrode; and separating the sensor electrode and at least a portion of the substrate underlying the sensor electrode from the remainder of the substrate. Preferably, the substrate is comprised of a polymeric material, such as a polyimide, and in more particular embodiments, the substrate is supplied in the form of a continuous web.

In particular embodiments, a plurality of metal layers are sequentially sputter-deposited, and the plated layer is formed on the uppermost sputter-deposited layer of the sensor electrode. Preferably, the sputter-deposited metal layers are comprised of different metals, such as layers of chromium and copper.

According to another preferred embodiment, prior to the sputter-deposition step a layer of a material that promotes adhesion between the sputter-deposited metal layer and the substrate is deposited on the substrate. In other embodiments, during the plating step, a layer of copper or a layer of gold is plated on the sensor electrode. Alternatively, a plurality of layers are sequentially plated on the sensor electrode.

In other embodiments, prior to the separation step, the sensor electrode is provided with a coating, such as a coating of a polymeric material, and/or a biocompatible polymeric material. Preferably, the coating is subsequently removed from the proximal segment and the distal segment of the sensor electrode. In further embodiments, the coating is removed from the distal segment of the sensor electrode and the distal segment is subsequently provided with an electrode chemistry. In other embodiments, the sensor electrode is

provided with a membrane after the distal segment is provided with the electrode chemistry.

According to a particular embodiments, a plurality of sprocket holes are formed in the substrate adjacent to the sensor electrode. Also, in preferred embodiments, the step of removing the sensor is carried out using a laser.

In preferred embodiments, the substrate has an upper surface and a lower surface. The sensor electrode is formed on the upper surface, and after the etching step a bead is formed on at least one of the lower surface and the sensor electrode. The bead is formed, according to one particular embodiment, below and in alignment with the sensor electrode. According to another particular embodiment, a first bead is formed on the lower surface of the substrate and a second bead is formed on the sensor electrode. Preferably, the bead is formed using a liquid polymer, and is formed using a molding process.

In accordance with another embodiment of the present invention, a method of making a sensor includes the steps of providing a pre-formed self-supporting flexible substrate; sequentially sputter-depositing a plurality of metal layers on the substrate, the plurality of layers including an uppermost layer; plating a metal layer on the uppermost sputter-deposited metal layer; etching the plated and sputter-deposited metal layers to form a sensor electrode having a proximal segment and a distal segment; sequentially plating first and second metal layers on the sensor electrode; coating the sensor electrode with a polymeric material; forming at least one opening in the coating; and separating the sensor electrode and at least a portion of the substrate underlying the sensor electrode from the remainder of the substrate.

In preferred embodiments, layers of chromium and copper are sequentially sputter-deposited. Preferably, at least one layer of copper is plated on the sputtered layer(s) prior to etching, and layers of copper and gold are sequentially plated after the etching step.

In accordance with an additional embodiment of the present invention, a method of making a sensor includes the steps of providing a pre-formed self-supporting flexible substrate; sputter-depositing at least one metal layer on the substrate; etching the at least one metal layer to form a sensor electrode having a

proximal segment and a distal segment; and separating the sensor electrode and at least a portion of the substrate underlying the sensor electrode from the remainder of the substrate.

In accordance with still another embodiment of the present invention, a method of making a sensor includes the steps of providing a substrate having an upper surface and a lower surface; sputter-depositing at least one metal layer on at least one surface of the substrate; etching the at least one metal layer to form a sensor electrode having first and second edges, a proximal segment and a distal segment; forming a bead on at least one of the upper surface and the lower surface of the substrate; and separating the sensor electrode and the portion of the substrate underlying the sensor electrode from the remainder of the substrate.

In preferred embodiments, the sensor electrode is formed on one of the upper and lower surfaces of the substrate and the bead is formed on the other surface of the substrate. In a further embodiments, the bead is formed on the substrate beneath the sensor electrode.

According to particular embodiments, the bead is formed by forming a perforation in the substrate adjacent to the first and second edges of the sensor electrode; securing the lower surface of the substrate to a mold, the mold having a channel that extends beneath the sensor electrode; flowing a liquid polymer over the upper surface of the substrate and through the perforations into the channel until the polymer beads on the upper surface of the substrate and covers at least a portion of the sensor electrode; curing the liquid polymer; and removing the substrate from the mold. In further embodiments, the perforations on each side of the sensor electrode include at least one perforation gap. The liquid polymer that flows over the sensor electrode does not cover the portion of the sensor electrode between the perforation gaps. The perforations on each side of the sensor electrode may include a plurality of perforation gaps. In still other embodiments, each perforation has a perforation gap adjacent to at least one of the proximal and distal segments of the sensor electrode. In a preferred embodiment, the distal segment is provided with an electrode chemistry.

According to yet another embodiment of the present invention, a method of making a sensor includes the steps of: providing a substrate having an upper

surface and a lower surface; forming at least one channel in at least one of the upper and lower surfaces of the substrate; disposing a conductive material in the at least one channel to form at least one electrode; and forming a bead on at least one of the upper and lower surfaces of the substrate to produce a sensor.

According to a further embodiment of the present invention, a method of making a sensor includes the steps of: providing a substrate having an upper surface and a lower surface; disposing a conductive material on at least one of the upper and lower surfaces of the substrate by non-impact printing to form at least one electrode; and forming a bead on at least one of the upper and lower surfaces of the substrate to produce a sensor.

According to yet a further embodiment of the present invention, a method of making a sensor includes the steps of: providing a substrate having an upper surface and a lower surface; providing a film or sheet comprising a conductive material; transferring the conductive material from the film or sheet to the substrate to form at least one electrode; and forming a bead on at least one of the upper and lower surfaces of the substrate to produce a sensor.

According to still a further embodiment of the present invention, a method of making a sensor includes the steps of: providing a substrate having an upper surface and a lower surface; depositing at least one layer of a metal on the upper surface of the flexible substrate; etching the at least one metal layer to form a sensor electrode having first and second edges, a proximal segment and a distal segment; forming a perforation in the substrate adjacent to the first and second edges of the sensor electrode; securing the lower surface of the substrate to a mold, the mold having a channel that extends below the metal layer; flowing a liquid polymer over the upper surface of the substrate and through the perforations into the channel until the polymer covers the upper surface of the substrate and at least a portion of the sensor electrode; curing the liquid polymer; removing the substrate from the mold; and removing the sensor electrode, the cured polymer and the portion of the substrate between the first and second perforations by separating the substrate adjacent to the perforations.

According to another embodiment of the present invention, a method of making a sensor includes the steps of: providing a substrate; forming a bead on a

surface of the substrate; forming a sensor electrode on the substrate; and separating the bead, the sensor electrode and at least a portion of the substrate between the bead and the sensor electrode from the remainder of the substrate.

According to yet another embodiment of the present invention, a method of making a sensor includes the steps of: providing a substrate; forming a sensor electrode on a surface of the substrate; forming a bead on the substrate; and separating the bead, the sensor electrode and at least a portion of the substrate between the bead and the sensor electrode from the remainder of the substrate.

In accordance with further embodiments of the present invention, sensors produced according to the foregoing methods are also provided. In accordance with other embodiments of the present invention, sensor sets that include sensors, as described herein, together with appropriate mounting bases and insertion needles are provided. In additional embodiments, the sensor sets include cannula in which portions of the sensor are disposed and which in turn are at least partially disposed within the insertion needles. In other embodiments, the sensor includes a bead, which is at least partially nested within the insertion needle, obviating the need for a cannula.

Other objects, features and advantages of the present invention will become apparent to those skilled in the art from the following detailed description. It is to be understood, however, that the detailed description and specific examples, while indicating preferred embodiments of the present invention, are given by way of illustration and not limitation. Many changes and modifications within the scope of the present invention may be made without departing from the spirit thereof, and the invention includes all such modifications.

Brief Description of the Drawings

A detailed description of embodiments of the invention will be made with reference to the accompanying drawings, wherein like numerals designate corresponding parts in the several figures.

FIGS. 1-4 illustrate an embodiment of a first method according to the invention in which a substrate, illustrated as a flexible tape supplied from a reel,

is provided with at least one metal layer deposited on its upper surface, an optional plating of one or more metal layers, followed by an etching step to form one or more sensor electrodes, and an optional plating of one or more additional layers, after which the metal layer(s) and the underlying portion of the substrate are subsequently separated from the remainder of the substrate;

FIG. 1 is an illustration of a reel and tape used to provide a substrate for use in the methods in accordance with embodiments of the present invention;

FIG. 2a is a cross-sectional view of the substrate as viewed along the line 2-2 in FIG. 1 with the inclusion of a sputter deposited layer.

FIG. 2b is a cross-sectional view of the substrate with multiple sputter deposited layers;

FIG. 2c is a cross-sectional view of the substrate with multiple sputter deposited and plated layers;

FIG. 2d is a cross-sectional view of the sensor electrode after it has been etched back and the substrate after it has been formed with sprocket holes;

FIG. 2e is a cross-sectional view of a sensor electrode after additional layers have been plated onto the sensor electrode;

FIG. 3a is a cross-sectional view of the substrate and sensor electrode after being covered by a polymer coating;

FIG. 3b is a cross-sectional view of the substrate and sensor electrode after the polymer coating has been etched back;

FIG. 4 is a cross-sectional view of the sensor after being separated from the remainder of the substrate;

FIG. 5 is a perspective view illustrating a sensor set that includes a sensor formed according to the invention;

FIG. 6 is an enlarged longitudinal vertical section taken generally on the line 6-6 of FIG. 5;

FIG. 7 is an enlarged longitudinal sectional of a slotted insertion needle used in the insertion set of FIGS. 5 and 6;

FIG. 8 is an enlarged transverse section taken generally on the line 8-8 of FIG. 7;

FIG. 9 is an enlarged transverse section taken generally on the line 9-9 of FIGS. 7;

FIG. 10 is an enlarged fragmented sectional view corresponding generally with the encircled region 10 of FIG. 6;

FIG. 11 is an enlarged transverse section taken generally on the line 11-11 of FIG. 6;

FIGS. 12a-b are transverse sections of alternative embodiments of a sensor produced according to the invention that include tubular (FIG. 12a) or solid (FIG. 12b) beads;

FIG. 13 is a transverse section illustrating the engagement of the sensor of FIG. 12a and a slotted insertion needle;

FIG. 14 is a transverse section illustrating another alternative embodiment of a sensor of the invention including beads on each side of the sensor, and the engagement of the sensor with a slotted insertion needle;

FIGS. 15-21 illustrate another alternative embodiment of a method according to the invention, wherein

FIGS. 15a-b are side sectional views illustrating deposition of a metal layer (FIG. 15a) or metal layers (FIG. 15b) on a flexible substrate,

FIG. 16 is a transverse section illustrating formation of perforations on either side of the metal layer of FIG. 15a,

FIG. 17 is a transverse section showing the position of the substrate of FIG. 16 in relation to a mold having defined therein a channel;

FIGS. 18a-b illustrate provision of a liquid polymer through the perforations formed in the substrate into the mold channel (FIG. 18a) and its beading over the upper surface of the substrate and the metal layer (FIG. 18b);

FIG. 19 is a transverse section illustrating the curing of the liquid polymer;

FIG. 20 is a side section illustrating disengagement of the mold from the substrate and the cured polymer;

FIG. 21 is a transverse section along the lines 21-21 of FIG. 20 showing separation of the completed sensor from the remainder of the substrate;

FIG. 22 is a sectional view of an alternative embodiment of the inventive method in which a sensor membrane is provided after the liquid polymer is supplied;

FIGS. 23-25 illustrate alternative methods for producing sensors, after which beads are provided in accordance with the methods described herein, in which

FIGS. 23a-b illustrate a first alternative method in which channels are formed in a substrate and subsequently filled with a conductive material to form the sensor electrodes,

FIG. 24 illustrate a second alternative method in which sensor electrodes are formed electrographically using a conductive toner, and

FIGS. 25a-b illustrate a third alternative method in which sensors are formed by a printing process;

FIG. 26 is a top plan view of a sensor in accordance with another embodiment of the present invention;

FIG. 27 is a side plan view of the sensor shown in FIG. 26; and

FIG. 28 is a partial cross-sectional view of the sensor of FIG. 26 inside of an insertion needle.

Fig. 29 is a top plan view of another sensor similar to the embodiment of the sensor shown in Fig. 26.

Figs. 30(a) and (b) are plan views of an alternative embodiment of the sensor shown in Figs. 26-29.

Figs. 31(a) and (b) are plan views of another alternative embodiment of the sensor shown in Figs. 26-29.

Detailed Description of the Preferred Embodiments

As shown in the drawings for purposes of illustration, the invention is embodied in an improved sensor and method of manufacturing the sensor. In preferred embodiments of the present invention, the sensor is a glucose sensor that utilizes glucose oxidase. However, alternative embodiments may use other materials, such as optical, fluorescence or electrical materials to sense the glucose levels, or may uses other materials to sense the presence of different analytes,

such as, including but not limited to, HIV, viruses, medication levels, cholesterol, hormones, fluids or the like. Preferred embodiments are for use with humans. However, it will be recognized that further embodiments of the invention may be used in animals, laboratory tests, agriculture related testing, or the like.

According to embodiments of the inventive method, sensors are produced by deposition of a metal layer or layers followed by etching production methods. Subsequent layers are then added by electroplating. The metal layer(s) can be deposited on either a non-self supporting substrate, or in a preferred embodiment on a self-supporting substrate such as a polyimide tape. Thus, sensors can be produced cleanly and at high density on the substrate according to the inventive method; and in further embodiments, the sensors can be produced on one or both sides of the substrate.

Referring now to FIGS. 1-4, a substrate 10 is provided in accordance with a first embodiment of the inventive method. In preferred embodiments, substrate 10 is a flexible, self-supporting substrate in the form of a continuous tape 12 supplied from a reel 14. The continuous tape 12 is preferably formed from a polymeric material such as a polyimide. However, other flexible, self-supporting materials can be used. The thickness of tape 12 is preferably about 10μ to 125μ. However, in alternative embodiments, thinner or thicker films from 5μ to 500μ may be used. In particular embodiments, sprocket holes 15 (see Fig. 2c) are formed in the substrate adjacent the outer edge of the tape 12 to facilitate manufacturing of the sensors through automated processes. For instance, the tape 12 is fed through stages that perform various steps of the methods described in this application. Sensor electrodes 20 can be formed on the tape 12 using techniques described in "3M Specifications and Design Guidelines, Microflex circuits for IC Interconnect Solutions," pages 1-32 (the entire document), 1997 (3M Electronic Products Division, Austin TX), "3M Offers More Solutions for the Semiconductor Industry" the entire document, 1997 (3M Electronic Products Division, Austin TX), and "Microflex Solutions from 3M", the entire document, 1996 (3M Electronic Products Division, Austin TX), all of which are publicly available from 3M and are specifically incorporated herein by reference.

Alternatively, substrate 10 can be formed by a casting process, for example by spin-coating a layer of a liquid polyimide or other polymeric material onto a temporary glass carrier and then cured. Such substrates can be self-supporting or non-self supporting. The sensor electrodes 20 can be formed on the substrate 10 using techniques described in "Micron Wide Conductors and Spaces on ... PZT, Alumina, Glass and Flexible Materials" 1 page, no date (Metrigraphics, Wilmington, MA), "Flexibel circuits at Extreme Density, 8 unnumbered pages of various dates (Metrigraphics, Wilmington, MA), and "Metrigraphics Ion Beam Etching Capability", 1 page, no date (Metrigraphics, Wilmington, MA), and all of which are publicly available and are specifically incorporated herein by reference.

Substrate 10 has an upper surface 16 and a lower surface 18. The substrate 10 is preferably cleaned, and subsequently at least one metal layer 20a is formed on the upper surface 16 of the substrate 10 by a deposition process (see FIG. 2a). A particularly preferred process is sputter deposition, or sputtering. Sputtering can be carried out using commercially available sputtering reactors using an RF (radio frequency). Magnetron sputtering can also be carried out; magnetron sputtering uses a magnetic field to concentrate electrons near the target surface to increase the deposition rate. Other known deposition processes, such as chemical vapor deposition (CVD) methods, can also be employed. The thickness of the deposited layer preferably ranges from about 0.05μ to about 300.0μ, more preferably about 0.5μ to about 25.0μ. When multiple layers are deposited, the total thickness of the layers preferably has a thickness within the foregoing ranges.

One or more metal layers can be deposited on the substrate 10 according to the inventive method. For example, two layers 20a and 20b of different metals can be deposited (see FIG. 2b). Exemplary metals include, but without limitation, elemental metals such as chromium, gold, copper, aluminum, nickel, tantalum and titanium, alloys such as Inconel and Nichrome, and mixtures thereof. The term "metal layer" is also intended to encompass layers that include one or more non-metallic elements in a mixture or chemical combination with one or more metallic elements, and thus also encompasses materials such as oxides, for

example alumina. Reactive as well as non-reactive layers can be formed; reactive materials, such as tantalum oxide, chromium oxide, etc., are also intended to be encompassed by the term "metal layer." Specific combinations of metal layers that are useful according to the invention include chromium and copper; copper and gold; and chromium, gold and chromium; copper, nickel and gold; and chromium, copper, nickel and gold.

In particular embodiments, chromium forms the first sputtered metal layer. Chromium provides an additional benefit in promoting adhesion between certain polymeric materials, such as polyimides, and other metals. Other metal layers, such as nickel or the like, that promote adhesion can also be employed if desired.

As shown in FIG 2d, in particular embodiments, subsequent to the sputter deposition step but prior to an etching step, one or more metal layers 20c can be plated on the upper surface of the sputter deposited metal layer (or the uppermost sputter deposited layer if more than one such layer is prepared). Such layers, in preferred embodiments, are comprised of copper. However, in alternative embodiments, other metals, such as nickel, chromium, gold, or the like, may be plated onto the layers used to form the sensor electrodes.

After the sputter deposition of the metal layer(s), and/or one or more layers are applied by plating, an etching process is carried out in order to form the sensor electrode 20 (see FIG. 2d). Any conventional etching process can be employed. For example, the etching processes described above and in U.S. Patent No. 5,391,250 issued February 21, 1995 to Cheney, II et al. and entitled "Method of Fabricating Thin Film Sensors", which is incorporated herein in its entirety by reference, may be used to form one or more sensor electrodes. In alternative embodiments, the one or more metal layers applied by plating prior to etching may be omitted and just the sputtered layers are etched. Preferred embodiments form the sprocket holes 15 by etching at the same time that metal etching process is carried out. Alternative embodiments may form the sprocket holes 15 before or after the etching of the metal layer(s). Sprocket holes 15 may be formed by other methods, such as water knife, laser ablation, punching, cutting, or the like.

In further embodiments, subsequent to the etching step one or more additional metal layers 23a, 23b can be plated on the sensor electrode(s) 20' (see Fig. 2e). The optional additional plating step is advantageous in providing a protective coating over the sputter-deposited metal layers, including the sides thereof. In particular embodiments, layers of copper; copper and gold; or copper, nickel and gold are plated after the etching step. In preferred embodiments, gold is plated over the sensor electrodes 20' as the final layer 23b to seal in all of the other layers.

As shown in FIG. 3a, in a preferred embodiment, prior to separation from the remainder of the substrate, the sensor can be provided with a polymeric coating 26, preferably formed from a non-toxic, biocompatible polymer. For instance, the polymer coating 26 provides an insulative and/or protective coating that covers the substrate 10 and the sensor electrodes 20. Exemplary useful polymers include, without limitation, polyimide, biocompatible soldermasks, epoxy acrylate copolymers, or the like. In preferred embodiments, the polymers are photo-imaginable to permit portions of the polymers to be removed for exposure of contacts, electrodes for application of sensor chemistry, or the like. Portions of the coating polymer are masked to form a pattern, which is them exposed and developed to remove the portions of the polymer coating 26 for further processing of the sensor 8. In alternative embodiments, the coating polymer may be removed by other methods, such as by laser ablation, chemical milling, or the like. Use of a secondary photo resist can be employed to target specific sites for removal. As shown in FIG. 3b, the coating polymer 26 is etched (ablated, milled, or the like) back to expose windows (or openings) 28 to expose the contact pads to permit connection with a monitoring device (discussed below) and to form windows (or openings) 28 over the sensor electrodes 20 to allow sensor chemistry materials to be applied to the exposed sensor electrodes 20 to complete the manufacture of the sensors 8.

In further embodiments, the exposed areas that form windows (or openings 28) are plated with additional layers of metal. This saves money and can reduce the thickness of the sensor electrodes, except where the thickness or layer is required. Plating after forming the windows (or openings) 28 also allows

the plating to fill in any potential leaks around the windows (or openings) 28 caused by gaps between the polymer layer and the sensor electrodes. Additionally, if the final metal layer is plated after the last etching and coating step, the surface of the final metal layer is in its best condition for application of enzymes and membranes. Thus, doing a final plating step increase reliability and predictability of sensor performance. In preferred embodiments, the final metal layer is gold. However, in alternative embodiments, other final metal layers, such as platinum, iridium, chromium, copper or the like may be used.

After completion of the etching and optional plating steps and any polymer coating steps, the sensor 8, including a portion of the substrate underlying the metal layer(s) 23n forming the sensor electrode 20 and any polymer coating 26, is removed from the remainder of the substrate (see FIG. 4). In a preferred embodiment, the sensor is removed from the remainder portions 22 of the substrate 10 by cutting along lines 24, for example using a laser. Other known cutting devices, such as blades, ultrasonic, water knifes, or the like, can also be used.

Sensors formed according to the inventive method are usefully employed in a variety of known sensor sets. Exemplary sensor sets are illustrated in FIGS. 5-11, generally similar to those described herein, not including a bead, into a sensor set generally similar to that described in U.S. Patent No. 5,586,533, to Halili et al., and entitled "Transcutaneous Sensor Insertion Set", and U.S. Patent No. 5,954,643 issued September 21, 1999 to Van Antwerp et al. and entitled "Insertion Set for a Transcutaneous Sensor", which are incorporated herein in its entirety by reference. In an embodiment illustrated in FIGS. 5-10, a sensor set referred to generally by the reference numeral 110 is provided for transcutaneous placement of a flexible sensor 112 (see FIG. 6) at a selected site within the body of a patient. The insertion set 110 includes a rigid hollow slotted insertion needle 114 for quick and easy placement at a desired placement site (e.g., transcutaneous, intraperitoneal, peritoneal, etc.) of a cannula 115 with a distal segment 116 of the sensor 112 therein. The distal segment 116 has at least one sensor electrode 118 (three are illustrated, which generally correspond to the sensor electrode 20 described above), formed by deposition as described above,

exposed to patient fluid through a window 119 in the cannula 115. The insertion needle 114 is then withdrawable to leave the cannula 115 with the sensor distal segment 116 and the sensor electrodes 118 in place at the selected site.

The sensor set 110 is particularly designed for facilitating accurate placement of a flexible thin film electrochemical sensor of the type used for monitoring specific blood parameters representative of patient condition. The sensor set 110 is designed to place the sensor at a selected site within the body of a patient, in a manner minimizing patient discomfort and trauma. In one preferred application, the sensor 112 may be designed to monitor blood glucose levels, and may be used in conjunction with automated or semiautomated medication infusion pumps of the external or implantable type as described in U.S. Pat. Nos. 4,562,751; 4,678,408; 4,685,903 or 4,573,994, to deliver insulin to a diabetic patient.

The flexible electrochemical sensor 112 is constructed according to the methods described herein. The sensor electrodes 118 (shown in exaggerated form in the drawings) are exposed for direct contact with patient interstitial fluid, or the like, when the sensor is transcutaneously placed. The distal segment 116 is joined to a proximal segment 120, (see FIG. 6) the end of which terminates in suitable conductive contact pads or the like. As is known in the art, and illustrated schematically in FIG. 6, the proximal segment 120 and the contact pads are adapted for electrical connection to a suitable monitor 122 for monitoring patient condition in response to signals derived from the sensor electrodes 118 in manners known to those skilled in the art.

According to the embodiment of FIGS. 5 and 6, the sensor 112 is carried by a mounting base 126 adapted for placement onto the skin of a patient. An exemplary mounting base 126 comprises an enlarged and generally rectangular pad having an underside surface coated with a suitable pressure sensitive adhesive layer, with a peel-off paper strip 128 normally provided to cover and protect the adhesive layer, until the insertion set 110 is ready for use. As shown in FIGS. 5 and 6, the mounting base comprises upper and lower layers 130 and 132, with the proximal segment 120 of the sensor 112 sandwiched between the layers 130 and 132. The proximal sensor segment 120 has a forwardmost end

joined to the distal segment 116 which is folded angularly to extend downwardly through a slot 134 formed in the lower base layer 132.

The insertion needle 114 is adapted for slide-fit reception through a needle port 136 formed in the upper base layer 130 and further through the lower slot 134 in the lower base layer 132. As shown, the insertion needle 114 has a sharpened tip 138 and an open slot 140 which extends longitudinally from the tip 138 at the underside of the needle to a position at least within the slot 134 in the lower base layer 132. Above the mounting base 126, the insertion needle 114 can have a full round cross sectional shape and is desirably closed at a rear end. In a more specific preferred embodiment, the slotted needle 114 has a part-circular cross sectional shape, with an arcuate dimension or span greater than 180°, such as an arcuate dimension of about 210°. This leaves a longitudinal slot in the needle with an arcuate dimension of about 150°.

The cannula 115 illustrated in FIGS. 10 and 11 comprises a first portion 144 of part circular cross section fitted within the insertion needle 114 to extend downwardly from the mounting base 126. This cannula 115 is preferably constructed from a suitable medical grade plastic or elastomer, such as polytetrafluoroethylene, silicone, etc., to define an open lumen 142 in a second portion for receiving, protecting and guidably supporting the distal segment 116 of the sensor 112. The cannula 115 has one end fitted into the slot 134 formed in the lower layer 132 of the mounting base 126, wherein the cannula 115 is desirably secured to the mounting base by a suitable adhesive or other selected attachment methods. From the mounting base 126, the cannula extends angularly downwardly with the first portion 144 nested within the insertion needle 114, terminating slightly before the needle tip 138. Importantly, at least one window 119 is formed in the lumen 142 near the distal end, in general alignment with the sensor electrodes 118, to permit direct electrode exposure to patient body fluid when the sensor is transcutaneously placed.

According to the preferred embodiment illustrated FIG. 11, the second portion 142 of the cannula 115 has a part-circular cross sectional shape which cooperates with the part-circular shape of the insertion needle 114 to define a substantially full-circle geometry for facilitated insertion through the patient's

skin. The first portion 144 of the cannula 115 has a smaller cross sectional profile than the second portion 142, for sliding nested reception into the needle 114. The needle 114 and first cannula portion 144 are thus mechanically interlocked to prevent lateral dislocation of the cannula 115 from the insertion needle, while permitting longitudinal sliding motion of the needle over the cannula first portion 144. The distal or free end of the cannula second portion 142 is appropriately cut or otherwise set at an oblique angle, as viewed in FIG. 6, to form a continuation of the angle-cut tip 138 of the insertion needle.

In use, the sensor set 110 permits quick and easy placement of the sensor distal segment 116 at a selected site within the body of the patient. More specifically, the peel-off strip 128 (FIG. 5) is removed from the mounting base 126, at which time the mounting base 126 can be pressed onto and seated upon the patient's skin. The set may be inserted by hand or inserted with an insertion tool, such as disclosed in U.S. Patent Application Serial No. 09/215,356 (PCT No. US98/26978) filed December 18, 1998, and entitled "Insertion Device for an Insertion Set and Method of Using the Same", which is incorporated herein by reference. During this step, the insertion needle 114 pierces the patient's skin and carries the protective cannula 115 with the sensor distal segment 116 therein to the appropriate transcutaneous placement site. During insertion, the cannula 115 provides a stable support and guide structure to carry the sensor to the desired insertion site.

When the sensor 112 is placed at the insertion site, with the mounting base 126 seated upon the patient's skin, the insertion needle 114 can be slidably withdrawn from the patient. During this withdrawal step, the insertion needle 114 slides over the first portion 144 of the protective cannula 115, leaving the sensor distal segment 116 with electrodes 118 at the selected insertion site. These electrodes 118 are directly exposed to patient body fluid via the window 119. The sensor proximal segment 120 is appropriately coupled to the monitor 132, so that the sensor 112 can then be used over a prolonged period of time for taking chemistry readings, such as blood glucose readings in a diabetic patient. If desired, the first portion 144 of the cannula 115 can be hollow as shown to form a second lumen available to deliver medication and/or sensor calibration fluid to

the vicinity of the electrodes 118, or alternately to withdraw patient fluid such as blood for analysis.

Sensors produced as described above can also beneficially be included in sensor sets such as those described in PCT Application Serial No. WO 98/56293, to applicant MiniMed Inc., published December 17, 1998, which corresponds to copending, commonly assigned U.S. Patent Application Serial No. 08/871,831, filed June 9, 1997, entitled "Insertion Set for a Transcutaneous Sensor", now U.S. Patent No. 5,954,643, and in copending, commonly assigned U.S. Patent Application Serial No. 09/161,128, to Mastrototaro et al., filed September 25, 1998, now U.S. Patent No. 5,951,521, the disclosures of each of which are incorporated in their entireties herein by reference.

In an alternative method according to the invention, illustrated in FIGS. 12-14, one or more beads are provided to the sensor. The beads facilitate engagement of the sensors directly with a slotted insertion needle without the need for a cannula. Use of beads on each side of the substrate that is used to form the sensor, can also enable production of sensors having sensor electrodes on each side of the substrate.

As shown in FIGS. 12a-b, a bead, which can be hollow (see FIG. 12a, bead (or tube) 150) or solid (FIG. 12b, bead 152), is formed on the lower surface 18 of the substrate 10. The bead can be formed on the surface of the substrate by a variety of means, such as by securing a cylindrical element to the surface, by molding, laminating, or the like. The bead can be provided either before or after the sensor is removed from the remainder of the substrate 10. Once formed, the bead directly engages a slotted insertion needle 114 (FIG. 13) of a sensor set as described herein.

In FIG. 14, an alternative embodiment of a sensor includes beads, preferably solid beads 152, formed on both the upper surface 16 and the lower surface 18 of the substrate 10. This embodiment is useful in preparing sensors having sensor electrodes 20 on each side of the substrate. Such two-sided sensors can be used, for example, to detect two different body conditions, such as blood glucose level and the presence of an antibody, simultaneously, when appropriate

electrode chemistries are provided; or the same body condition, such as glucose levels, by providing a cross-check using two different sensor readings.

Another alternative method according to the invention is illustrated in Figures 15-21. In FIG. 15a, at least one metal layer 220a is deposited on the upper surface 212 of the substrate 210 and formed into a sensor electrode as described above. Two or more metal layers can be deposited to form the sensor electrode, as illustrated in Figure 15b, in which first and second metal layers 220a, 220b are sequentially deposited on upper surface 212 of substrate 210. Also, although formation of one sensor electrode is illustrated for the sake of clarity, two or more sensor electrodes 220 can be formed on the same substrate by deposition of appropriate metal layers at different sites on the substrate. And multiple sensors may be formed on the substrate at the same time. The method of forming the sensor electrode 220 may be carried out as described for the sensor electrode 20 above and as shown in FIGS. 1-4.

After formation of the sensor electrodes 220 on the upper surface 212 of substrate 210, substrate 210 is perforated on either side of the metal layer(s) (see FIG. 16). Perforations 230 can be formed by any desired means, for example by laser cutting, etching, the use of a blade or other appropriate tool, or the like. The perforations preferably are sized to permit flow of a fluid, in particular a liquid polymer, through the perforations. In alternative embodiments, the perforations may be formed at the same time the sprocket holes on the tape 12 (as described above) are formed. Preferred embodiments use chemical etching to form the perforations.

Once the perforations 230 are formed, the lower surface 214 of substrate 210 is secured to a mold 232. The mold 232 may be attached while the substrate 210 is still a part of the tape 12, or after the substrate 210 has been cut from the tape 12. In addition, cut sections of the tape 12 may include one or more sensors. The mold may also be applied to substrates formed as sheets rather than tapes 12, as described above.

Mold 232, as shown in FIG. 17, has defined in its upper surface adjacent to the lower surface 214 of substrate 210 a channel 234, which preferably extends below the metal layer(s). Next, a liquid polymer 240 is flowed through the

perforations 230 and into the channel 234 in mold 232. The liquid polymer is preferably a biocompatible polymer, such as polyurethane, polycarbonate, silicone, acrylic or other thermoplastics. In preferred embodiments, the polymer flow is continued until the liquid polymer fills the mold and overflow to form a bead on the upper surface 212 of substrate 210 and the upper surface of the metal layer(s). This upper bead can also provide an upper protective coating to the sensor. See FIGS. 18a-b.

The liquid polymer 240 is then cured, for example by exposure to a source 245 of actinic radiation, heat or the like (see FIG. 19) to form bead 242 on the lower surface 214 of substrate 210 and coating 244 on the upper surface 212 and over the metal layer(s). After completion of the curing step, mold 232 is removed from contact with the substrate 210, for example by sliding the mold laterally away from the substrate in the direction defined by channel 234 (see FIG. 20). Finally, the finished sensor, including the metal layer(s), the cured polymer and the portion of the substrate therebetween and between the first and second perforations, is removed from the remainder of the substrate by separating the substrate adjacent the perforations. As shown in FIG. 21, the sensor 260 is separated from the remainder 262 of the substrate along separation lines 254, 256, which are formed, for example, by cutting using a laser, etching, a blade or another appropriate tool, or the like.

The liquid polymer 240 can be flowed over the entire surface of the metal layer(s) if desired. Preferably, however, one or more portions of the metal layers remain exposed. In this preferred alternative, the perforations 230 are formed such that they include one or more perforation gaps, that is, segments that include no perforations. The surface of the metal layer(s) extending between these perforation gaps remains uncovered by the liquid polymer, which does not bead over such areas.

As shown in FIG. 20, perforation gaps 246, 248 adjoining the perforations 230 allow proximal segment 250 and distal segment 252 of the sensor electrodes 220 to remain exposed without the liquid polymer 240 beading up over these segments. Proximal segment 250 can, as discussed above, terminate in a

conductive contact pad, while the distal segment 252 can include a portion that is provided with an appropriate electrode chemistry.

In an alternative embodiment, additional protective layers or membranes can be provided to the upper surface of the substrate and the metal layer(s). In Figure 22, a sensor membrane 264 is placed above the metal layer and adhered to the liquid polymer prior to, or after, curing to improve biocompatibility of the sensor.

Sensors including beads can also be prepared by methods other than those set forth above. For example, sensors can be prepared by any of the methods set forth in U.S. Patent App. No. 09/034,433, to Say et al., corresponding to PCT Application No. PCT/US99/03781, published September 10, 1999 under International Publication No. WO 99/45375 and incorporated herein in its entirety by reference, and provided with beads according to the methods set forth herein.

In one such method, one or more channels 312 are formed in the substrate 310, for example by an embossing process using an embossing die or roller (see FIG. 23a). Other methods for forming the channels, such as the use of a laser, or photolithography and etching of the substrate can also be employed if desired.

Once the channels 312 have been formed, a conductive material 314 is placed, flowed, applied, filled, flooded or otherwise disposed within the channels 312 to form the sensor electrodes 316 (FIG. 23b). The conductive material can be applied as a precursor conductive material having a liquid form. An exemplary precursor conductive material is a carbon-based ink that can be flooded in liquid form into the channels 312. Other conductive inks or pastes that include carbon or metal, such as gold, copper or silver, can also be used. Other techniques for applying the conductive material or precursor conductive material, including spraying, coating, flooding, applying with a saturated roller, pumping, as well as impact and non-impact printing methods such as electrostatic or magnetographic methods.

According to a second embodiment, a non-impact process is used to form the sensor electrodes 324. Exemplary non-impact processes include electrophotography and magnetography, in which an image of the conductive traces is electrically or magnetically formed on a drum 320. The image attracts a

toner material 322 to the drum. The toner 322 material is subsequently transferred to the substrate 310, for example by rolling, followed preferably by a curing step to adhere the toner material to the substrate. See FIG. 24. Other useful non-impact processes include ink jet printing and piezo jet printing, in which an image is formed by ejection of a conductive material, such as a conductive ink, onto the substrate. Still other useful non-impact processes include the use of photosensitive resins to form a layer on the substrate in which channels are defined, followed by filling the channels with conductive material to form the sensor electrodes.

According to a third embodiment, a film of conductive material 332 is formed, for example, as a continuous sheet or as a coating layer deposited on a carrier film 330. The film is brought, for example, between a print head 334 and the substrate 310. A pattern of sensor electrodes 336 is formed on the substrate 310 using the print head. The conductive material is transferred by pressure and/or heat to the substrate 310. See FIGS. 25a-b. Channels can be formed in the substrate as a result of the printing process, or alternatively the conductive material can be deposited on the substrate substantially without the formation of depressions or channels.

Once the sensor electrodes have been formed, a bead 342 can be provided in accordance with the methods described above.

FIGS. 26-29 illustrate a sensor 400 formed in accordance with another embodiment of the present invention. The sensor 400 includes a substrate 402 and at least one sensor electrode 404 formed from one or more conductive layers. In particular embodiments, the layers are formed from metal. However, alternative embodiments may utilize semiconductors, conductive polymers, DNA, RNA, molecular wires, or the like. The substrate 402 and the sensor 404 are formed and process by methods similar to those described above in the other embodiments. However, in this embodiment, the substrate 402 is formed from a thicker film (from a reel or as a sheet) so that no bead is required. The thickness of the substrate ranges from approximately 25μ to 350μ. In further embodiments, thicker films may be used up to 750μ or thinner films down to 5μ may be used, with the thickness being determined by the strength of the substrate 402 material,

the substrate material's resistance to tearing, the flexibility of the substrate material, or the like. For instance, if the substrate is contained within a slotted needle (or supporting structure) during insertion, a comparable normal or thinner thickness to the other embodiments described above may be used.

The sensor 400 is formed to obviate the need for a sensor set housing that remains attached to the body or the use of an additional bead, as described above in FIGS. 5-25b. To achieve this capability, the substrate 402 is formed (or cut) to include one or more notches 406. The notches 406 create a necked down region in the sensor 400 that allows the sensor 400 to slide into a slotted needle 408 that has a slot 410 that is narrow enough to permit passage of the necked down region 412 of the sensor 400, but prevent the non-necked down region 414 of the sensor 400 from pulling out of the slotted needle 408 through the slot 410. The slot 410 does permit the necked down region 412 of the sensor 400 to slide down the slot 410.

To insert the sensor, a sensor 400 is placed inside a slotted needle 408 by sliding the necked down region 412 into the slot 410 of the slotted needle 408 so that the non-necked down region 414 is slid up and into the interior of the slotted needle 408, while a connection region 416 remains outside of the slotted needle. The slotted needle 408, including the sensor 400, is inserted into a body (not shown). The sensor 400 is held against the body by the connection region 416 and the slotted needle 408 is then pulled out of the body (alternatively, the sensor may be included in a sensor set that holds the needle and the sensor). As the slotted needle 408 is pulled from the body, the necked down region 412 slides down the slot 410 of the slotted needle 410 and remains implanted in the body. Thus, in this embodiment, a sensor set and bead are not required, and the substrate 402 is of sufficient strength to remain in the body without any other support structures. In particular embodiments, the sensor may fit within a 21 gauge to a 27 gauge slotted needle for easy insertion into the skin.

In an alternative of these embodiments, to provide for the manufacture of a narrower sensor in width, with the aim to further minimize the size of the needle used to surround the sensor during insertion, several different approaches to sensor electrode layouts may be used. In one embodiment, two electrodes 502

and 504 are formed on one side 506 of the sensor 500 and a single electrode 508 is formed on the other side 510 (see Figs. 30(a) and 30(b)). This allows the size of the electrodes to be maintained with a consummate reduction in width. In further alternative embodiments, one electrode 552 is formed on one side 554 of the sensor 550 and another single electrode 556 is formed on the back 558 of the sensor 550 (see Figs. 31(a) and 31(b)). A third electrode 560, if needed, such as a ground (or reference) electrode is formed before the necked down region of the sensor to form an electrode that rests on (or is in contact with) the top of the skin (see Fig. 31(a). This substantially reduces the width of the sensor permitting small gauge needles to be used. For instance slotted needles of 22 gauge to 28 gauge may be used.

While the description above refers to particular embodiments of the present invention, it will be understood that many modifications may be made without departing from the spirit thereof. In particular, it is to be understood that the exemplary embodiments set forth herein, whether referred to as preferred embodiments or otherwise, are in no way to be taken as limiting the scope of the present invention. The accompanying claims are intended to cover such modifications as would fall within the true scope and spirit of the present invention.

The presently disclosed embodiments are therefore to be considered in all respects as illustrative and not restrictive, the scope of the invention being indicated solely and exclusively by the appended claims, rather than the foregoing description, and all changes which come within the meaning and range of equivalency of the claims are therefore intended to be embraced therein.

WHAT IS CLAIMED IS:

1. A sensor for implantation in a body, the sensor comprising:

a substrate with notches cut in the substrate to form a necked down region in the substrate; and

at least one sensor electrode formed from one or more conductive layers.

2. A sensor in accordance with claim 1, wherein the thickness of the substrate ranges from approximately 25μ to 350μ.

3. A sensor in accordance with claim 1, wherein the thickness of the substrate ranges from 5μ to 750μ.

4. A sensor assembly in accordance with claim 1; further including:

a slotted needle having a slot; and

wherein the notches creating the necked down region that allows the substrate to slide into the slotted needle that has the slot narrow enough to permit passage of the necked down region, but prevents a non-necked down region of the substrate from pulling out of the slotted needle through the slot.

5. A sensor assembly in accordance with claim 4, wherein slot of the slotted needle permits the necked down region of the substrate to slide down the slot.

6. A sensor in accordance with claim 1, wherein a width of the substrate in the non-necked down portion is sized to fit within a slotted needle having a diameter smaller than 21 gauge.

7. A sensor in accordance with claim 6, wherein a width of the substrate in the non-necked down portion is sized to fit within a slotted needle having a diameter smaller than 22 gauge.

8. A sensor in accordance with claim 7, wherein a width of the substrate in the non-necked down portion is sized to fit within a slotted needle having a diameter smaller than 23 gauge.

9. A sensor in accordance with claim 8, wherein a width of the substrate in the non-necked down portion is sized to fit within a slotted needle having a diameter smaller than 24 gauge.

10. A sensor in accordance with claim 1, wherein at least one of the at least one sensor electrode is formed on a first surface of the substrate.

11. A sensor in accordance with claim 10, wherein all of the at least one sensor electrode are only formed on the first surface.

12. A sensor in accordance with claim 10, wherein at least another one of the at least one sensor electrodes is formed on a second surface of the substrate.

13. A sensor in accordance with claim 12, wherein a third one of the at least one sensor electrode is a reference electrode configured to contact a skin surface.

14. A method of making a sensor comprising the steps of:

i) providing a preformed self-supporting flexible substrate;

ii) sputter-depositing at least one metal layer on the substrate;

iii) etching the at least one metal layer to form a sensor electrode having a proximal segment and a distal segment;

iv) plating a metal layer on the sensor electrode; and

v) separating the sensor electrode and at least a portion of the substrate underlying the sensor electrode from the remainder of the substrate.

15. The method of claim 14, wherein the substrate is comprised of a polymeric material.

16. The method of claim 15, wherein the polymeric material is a polyimide.

17. The method of claim 14, wherein in step i) the substrate is a continuous web.

18. The method of claim 14, wherein in step ii) a plurality of metal layers are sequentially sputter-deposited, and in step iv) the plated layer is formed on the uppermost sputter-deposited layer.

19. The method of claim 18, wherein the plurality of metal layers are comprised of at least two different metal layers.

20. The method of claim 19, wherein the plurality of metal layers are layers of chromium and copper that are sequentially sputter-deposited.

21. The method of claim 14, wherein prior to step ii) a layer of a material that promotes adhesion between the sputter-deposited metal layer and the substrate is deposited on the substrate.

22. The method of claim 14, wherein in step iv) a layer of copper is plated on the sensor electrode.

23. The method of claim 14, wherein in step iv) a plurality of layers are sequentially plated on the sensor electrode.

24. The method of claim 14, wherein in step iv) a layer of gold is plated on the sensor electrode.

25. The method of claim 14, wherein in step iv) layers of copper and gold are sequentially plated on the sensor electrode.

26. The method of claim 14, wherein before step v) the sensor electrode is provided with a coating.

27. The method of claim 26, wherein the coating comprises a polymeric material.

28. The method of claim 27, wherein the polymeric material is biocompatible.

29. The method of claim 27, wherein the polymeric material is selected from the group consisting of acrylates, polyimide, soldermasks, and epoxy acrylate copolymers.

30. The method of claim 26, wherein the coating is subsequently removed from at least one of the proximal segment and the distal segment of the sensor electrode.

31. The method of claim 30, wherein the coating is removed from both the proximal segment and the distal segment of the sensor electrode.

32. The method of claim 30, wherein the coating is removed from the distal segment of the sensor electrode and the distal segment is subsequently provided with an electrode chemistry.

33. The method of claim 32, wherein the sensor electrode is provided with a membrane after the distal segment thereof is provided with the electrode chemistry.

34. The method of claim 26, wherein a plurality of sprocket holes are formed in the substrate adjacent to the sensor electrode.

35. The method of claim 14, wherein the substrate has an upper surface on which the sensor electrode is formed and a lower surface, and wherein after step iv) a bead is formed on at least one of the lower surface and the sensor electrode.

36. The method of claim 35, wherein the bead is formed below and in alignment with the sensor electrode.

37. The method of claim 35, wherein a first bead is formed on the lower surface of the substrate and a second bead is formed on the sensor electrode.

38. The method of claim 35, wherein the bead is formed using a liquid polymer.

39. The method of claim 35, wherein the bead is formed by a molding process.

40. The method of claim 14, wherein step v) is carried out using a laser.

41. The method according to claim 14, wherein in step ii) a plurality of metal layers is sequentially sputter-deposited on the substrate, the plurality of layers including an uppermost layer, and a metal layer is plated on the uppermost sputter-deposited metal layer; wherein in step iii) the plated and sputter-deposited metal layers are etched to form the sensor electrode having the proximal segment and the distal segment; and wherein in step iv) sequentially plating first and second metal layers on the sensor electrode; and

further comprising between the steps iv) and v) the steps of:

a) coating the sensor electrode with a polymeric material; and

b) forming at least one opening in the coating.

42. The method of claim 41, wherein in step ii) layers of chromium and copper are sequentially sputter-deposited.

43. The method of claim 41, wherein in step ii) a layer of copper is plated.

44. The method of claim 41, wherein in step iv) layers of copper and gold are sequentially plated.

45. The method of claim 41, wherein in step vi) the polymeric material is a polyimide.

46. The method according to claim 14, wherein in step i) the substrate is provided having an upper surface and a lower surface, wherein in step ii) at least one metal layer is sputter-deposited on at least one surface of the substrate, wherein in step iii) the at least one metal layer is etched to form the sensor electrode to have first and second edges, and

further comprising a step z) forming a bead on at least one of the upper surface and the lower surface of the substrate.

47. The method of claim 46, wherein the substrate is comprised of a polymeric material.

48. The method of claim 47, wherein the polymeric material is a polyimide.

49. The method of claim 46, wherein in step i) the substrate is provided in the form of a tape supplied from a reel.

50. The method of claim 46, wherein in step i) the substrate is formed by a casting process.

51. The method of claim 46, wherein in step ii) a plurality of metal layers are sequentially deposited on the substrate.

52. The method of claim 51, wherein layers of chromium and copper are sequentially deposited on the substrate.

53. The method of claim 46, wherein in step z) the sensor electrode is formed on one of the upper and lower surfaces of the substrate and the bead is formed on the other surface of the substrate.

54. The method of claim 53, wherein in step z) the bead is formed on the substrate beneath the sensor electrode.

55. The method of claim 54, wherein in step z) the bead is formed by

a) forming a perforation in the substrate adjacent to the first and second edges of the sensor electrode;

b) securing the lower surface of the substrate to a mold, the mold having defined therein a channel that extends beneath the sensor electrode;

c) flowing a liquid polymer over the upper surface of the substrate and through the perforations therein into the channel until the polymer beads on the upper surface of the substrate and covers at least a portion of the sensor electrode;

d) curing the liquid polymer; and

e) removing the substrate from the mold.

56. The method of claim 55, wherein in step z-a) the perforations on each side of the sensor electrode include at least one perforation gap, so that the liquid polymer that flows over the sensor electrode does not cover the portion of the sensor electrode between the perforation gaps.

57. The method of claim 56, wherein the perforations on each side of the sensor electrode include a plurality of perforation gaps.

58. The method of claim 57, wherein each perforation has a perforation gap adjacent to at least one of the proximal and distal segments of the sensor electrode.

59. The method of claim 58, wherein each perforation has a perforation gap adjacent to both the proximal segment and the distal segment of the sensor electrode.

60. The method of claim 59, wherein the distal segment is provided with an electrode chemistry.

61. The method of claim 46, wherein a first bead is formed on one surface of the substrate, a second bead is formed on the other surface of the substrate, and the sensor electrode is formed adjacent to at least one of the beads.

62. The method of claim 46, wherein at least one sensor electrode is formed on each surface of the substrate and a bead is formed on each surface of the substrate adjacent to the sensor electrode.

63. The method of claim 46, wherein after step iii) at least one additional metal layer is formed on the sensor electrode.

64. The method of claim 46, wherein after step iii) a layer of gold is electroplated on the sensor electrode.

65. The method of claim 46, wherein the step z) includes:

a) forming a perforation in the substrate adjacent the first and second edges of the sensor electrode;

b) securing the lower surface of the substrate to a mold, the mold having a channel that extends below the metal layer;

c) flowing a liquid polymer over the upper surface of the substrate and through the perforations therein into the channel until the polymer covers the upper surface of the substrate and at least a portion of the sensor electrode;

d) curing the liquid polymer; and

e) removing the substrate from the mold; and

wherein step ix) includes removing the sensor electrode, the cured polymer and the portion of the substrate between the first and second perforations by separating the substrate adjacent to the perforations.

66. The method of claim 65, wherein after step iii) at least one additional metal layer is formed on the sensor electrode.

67. The method of claim 66, wherein after step iii) a layer of gold is electroplated on the sensor electrode.

68. The method of claim 66, wherein after step viii) the distal segment of the sensor electrode is provided with the electrode chemistry.

69. A method of making a sensor comprising the steps of:

i) providing a substrate;

ii) forming at least one sensor electrode on the substrate;

iii) forming a bead on the substrate; and

iv) separating the bead, the sensor electrode and at least a portion of the substrate between the bead and the sensor electrode from the remainder of the substrate.

70. The method of claim 69, wherein in step i) the substrate is provided having an upper surface and a lower surface, wherein in step ii) at least one channel is formed in at least one of the upper and lower surfaces of the substrate, and a conductive material is disposed in the at least one channel to form the at least one sensor electrode, and wherein in step iii) a bead is formed on at least one of the upper and lower surfaces of the substrate.

71. The method of claim 69, wherein in step i) the substrate is provided having an upper surface and a lower surface, wherein in step ii) a conductive material is disposed on at least one of the upper and lower surfaces of the substrate by non-impact printing to form at least one electrode, and wherein in step iii) a bead is formed on at least one of the upper and lower surfaces of the substrate to produce a sensor.

72. The method of claim 69, wherein in step i) the substrate is provided having an upper surface and a lower surface, wherein in step ii) a film or sheet comprising a conductive material is provided, and the conductive material from the film or sheet is transferred to the substrate to form at least one sensor electrode, and wherein in step iii) a bead is formed on at least one of the upper and lower surfaces of the substrate.

73. A sensor produced by the method of claim 14.

74. A sensor set comprising:

a) a mounting base adapted for mounting onto a patient's skin;

b) a sensor as claimed in claim 73;

c) a cannula protruding from the mounting base and having a portion of the sensor; and

d) an insertion needle carried by the mounting base to protrude from the mounting base and having at least a portion of the cannula nested within the insertion needle, the insertion needle defining a longitudinally extending slot along one side to permit sliding withdrawal of the insertion needle from the mounting base and the nested portion of the cannula.

75. A sensor produced by the method of claim 41.

76. A sensor set comprising:

a) a mounting base adapted for mounting onto a patient's skin;

b) a sensor as claimed in claim 75;

c) a cannula protruding from the mounting base and having a portion of the sensor; and

d) an insertion needle carried by the mounting base to protrude from the mounting base and having at least a portion of the cannula nested within the insertion needle, the insertion needle defining a longitudinally extending slot along one side to permit sliding withdrawal of the insertion needle from the mounting base and the nested portion of the cannula.

77. A sensor produced by the method of claim 46.

78. A sensor set comprising:

a) a mounting base adapted for mounting onto a patient's skin;

b) a sensor as claimed in claim 77; and

c) an insertion needle carried by the mounting base to protrude from the mounting base and having at least a portion of the bead of the sensor nested within the insertion needle, the insertion needle defining a longitudinally extending slot along one side to permit sliding withdrawal of the insertion needle from the mounting base and the nested portion of the sensor.

79. A sensor produced by the method of claim 65.

80. A sensor set comprising:

a) a mounting base adapted for mounting onto a patient's skin;

b) a sensor as claimed in claim 79; and

c) an insertion needle carried by the mounting base to protrude from the mounting base and having at least a portion of the bead of the sensor nested within the insertion needle, the insertion needle defining a longitudinally extending slot along one side thereof to permit sliding withdrawal of the insertion needle from the mounting base and the nested portion of the sensor.

81. A sensor produced by the method of claim 70.

82. A sensor set comprising:

a) a mounting base adapted for mounting onto a patient's skin;

b) a sensor as claimed in claim 81; and

c) an insertion needle carried by the mounting base to protrude from the mounting base and having at least a portion of the bead of the sensor nested within the insertion needle, the insertion needle defining a longitudinally extending slot along one side to permit sliding withdrawal of the insertion needle from the mounting base and the nested portion of the sensor.

83. A sensor produced by the method of claim 71.

84. A sensor set comprising:

a) a mounting base adapted for mounting onto a patient's skin;

b) a sensor as claimed in claim 83; and

c) an insertion needle carried by the mounting base to protrude from the mounting base and having at least a portion of the bead of the sensor nested within the insertion needle, the insertion needle defining a longitudinally extending slot along one side to permit sliding withdrawal of the insertion needle from the mounting base and the nested portion of the sensor.

85. A sensor produced by the method of claim 71.

86. A sensor set comprising:

a) a mounting base adapted for mounting onto a patient's skin;

b) a sensor as claimed in claim 85; and

c) an insertion needle carried by the mounting base to protrude from the mounting base and having at least a portion of the bead of the sensor nested within the insertion needle, the insertion needle defining a longitudinally extending slot along one side thereof to permit sliding withdrawal of the insertion needle from the mounting base and the nested portion of the sensor.

87. The method of claim 30, wherein an additional metal layer is applied to the sensor electrode where the coating was removed.

88. The method of claim 41, wherein an additional metal layer is applied to the sensor electrode where the coating was removed.

89. A sensor set comprising:

a) a mounting base adapted for mounting onto a patient's skin;

b) a sensor as claimed in claim 1; and

c) an insertion needle carried by the mounting base to protrude from the mounting base and having at least a portion of the sensor nested within the insertion needle, the insertion needle defining a longitudinally extending slot along one side to permit sliding withdrawal of the insertion needle from the mounting base and the nested portion of the sensor and to accept the necked down region of the substrate.

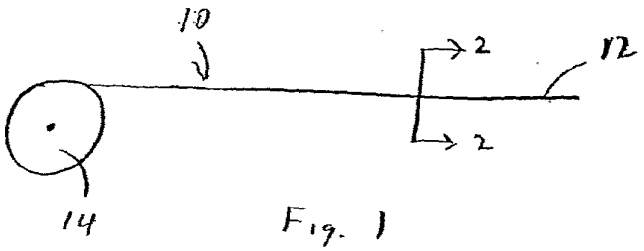


Fig. 1

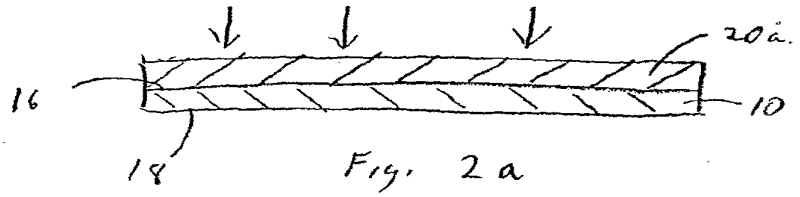


Fig. 2a

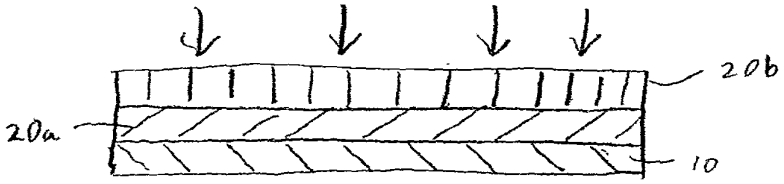


Fig. 2b

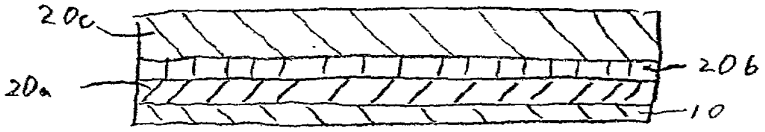


Fig. 2c

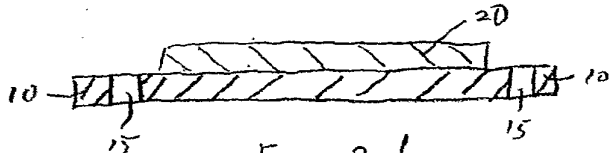


Fig. 2d

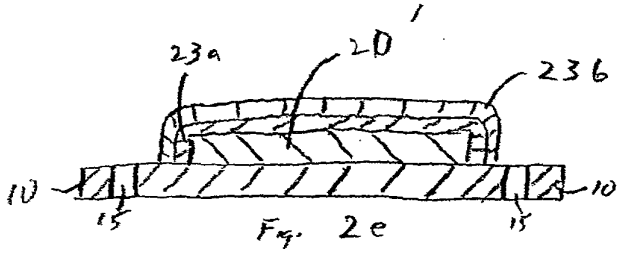


Fig. 2e

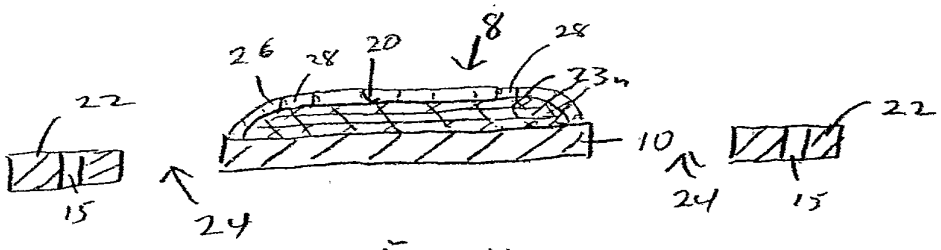


Fig. 4

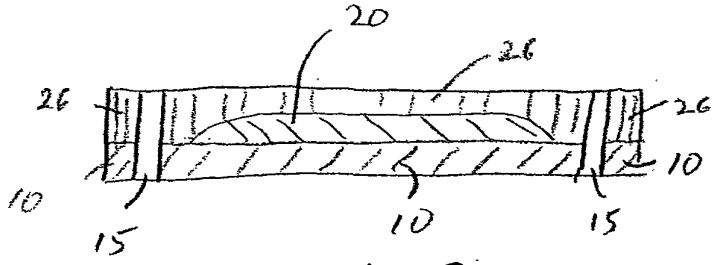


Fig. 3a

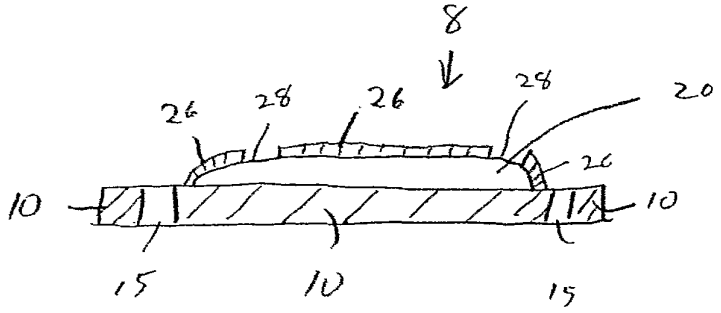


Fig. 3 b

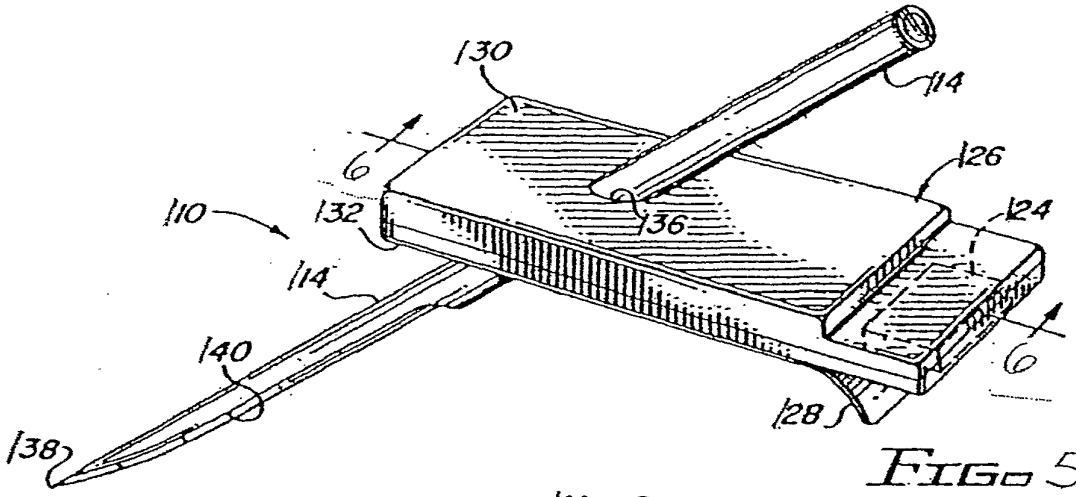


FIG. 5

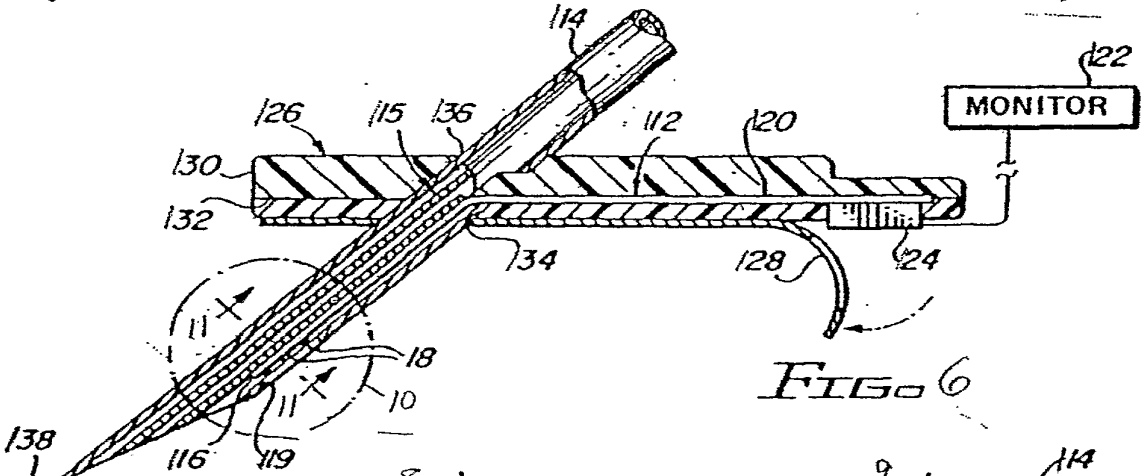


FIG. 6

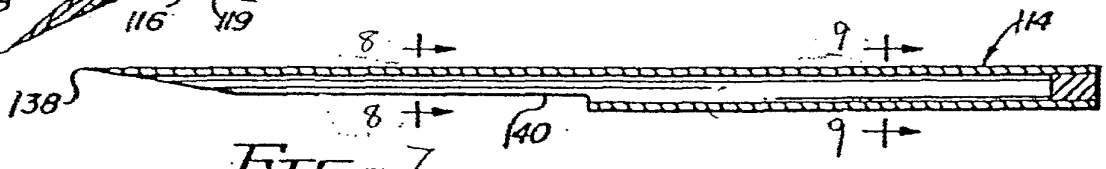


FIG. 7

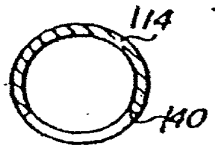


FIG. 8



FIG. 9

FIG. 10

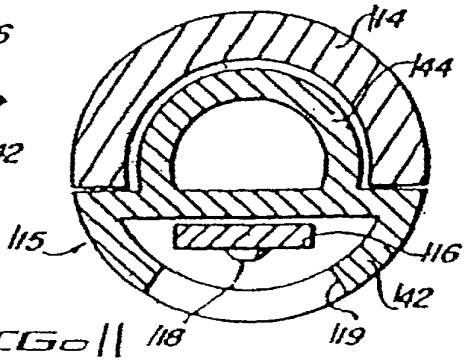


FIG. 11

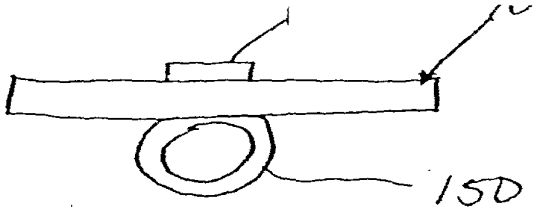


Fig. 12a

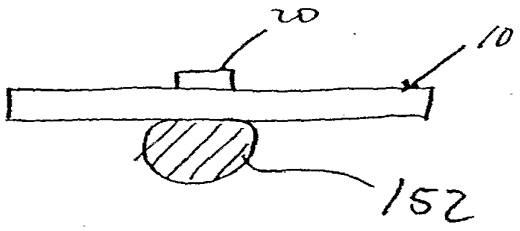


Fig. 12b

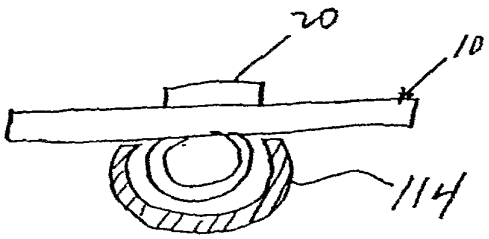


Fig. 13

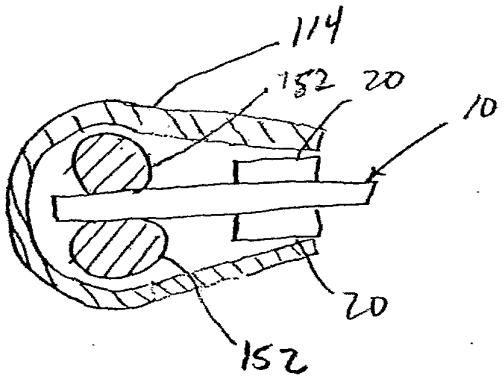


Fig. 14

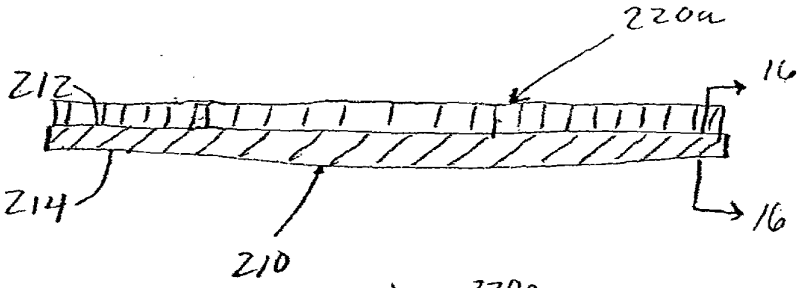


Fig. 15a

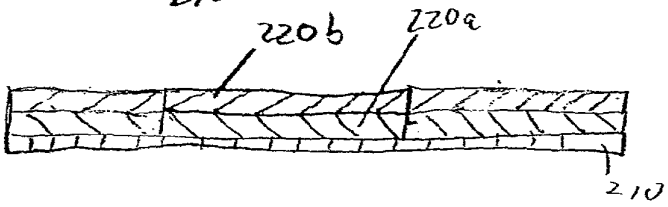


Fig. 15b

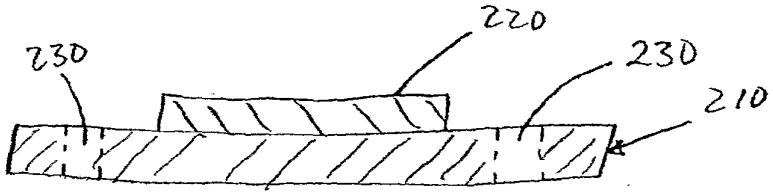


Fig. 16

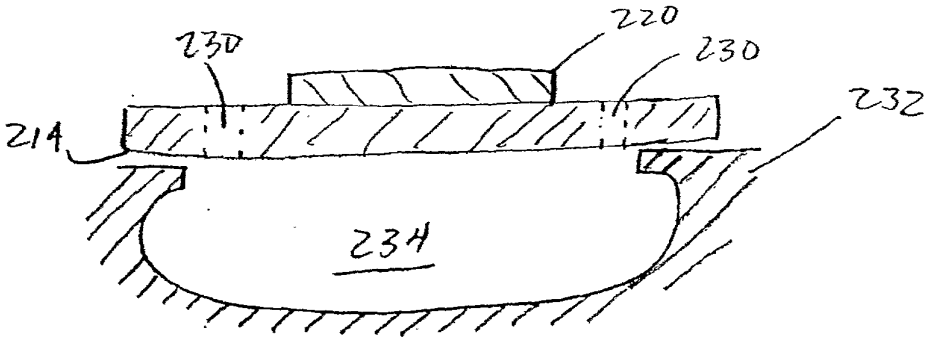


Fig. 17

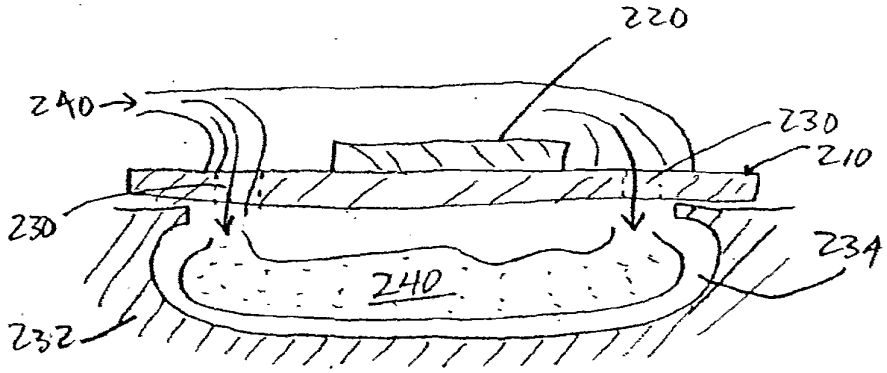


Fig. 18c

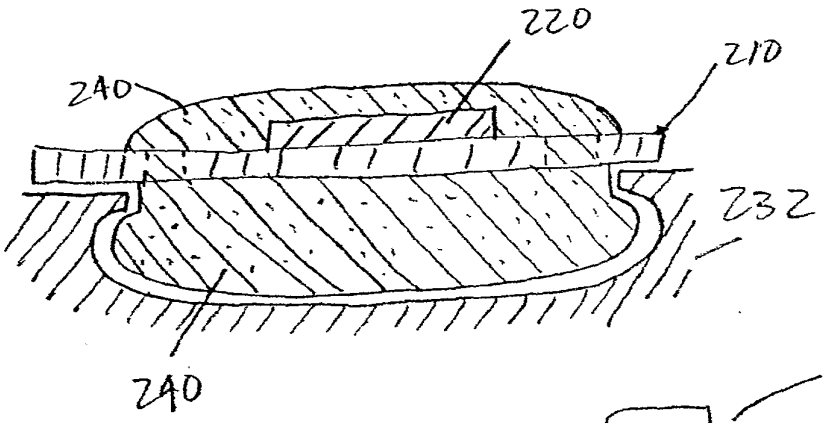


Fig. 18b

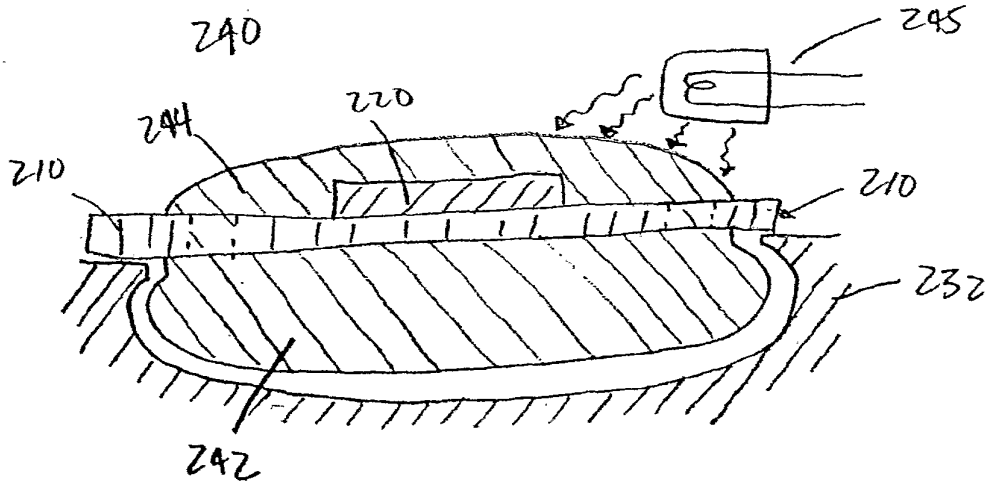


Fig. 19

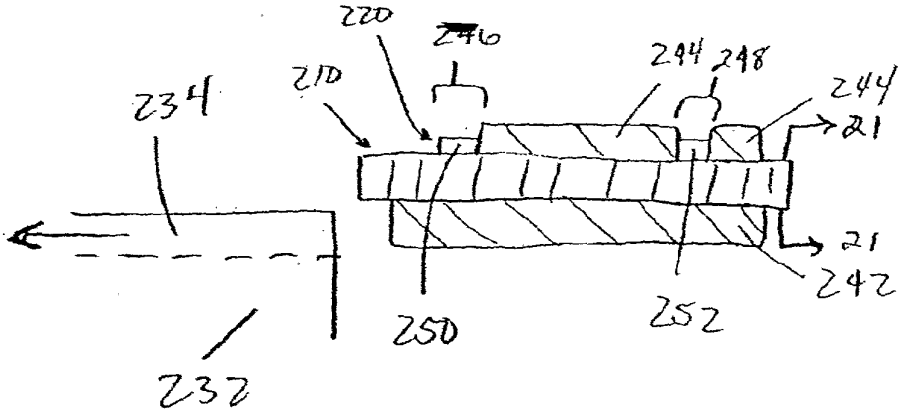


Fig. 20

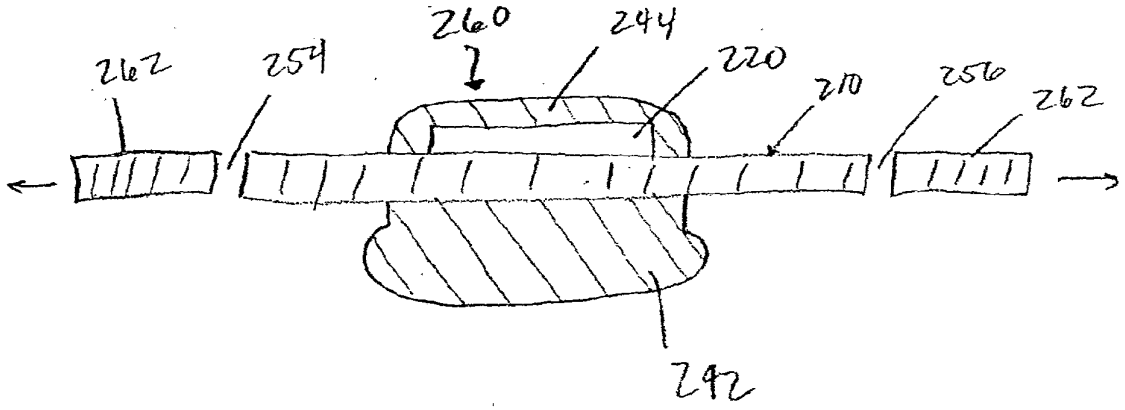


Fig. 21

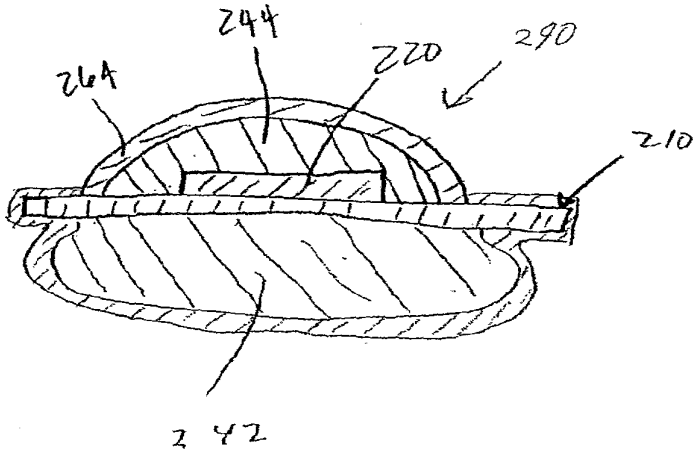


Fig. 22

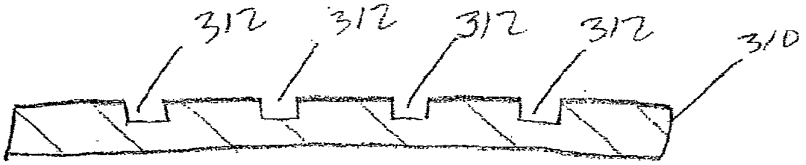


FIG. 23a

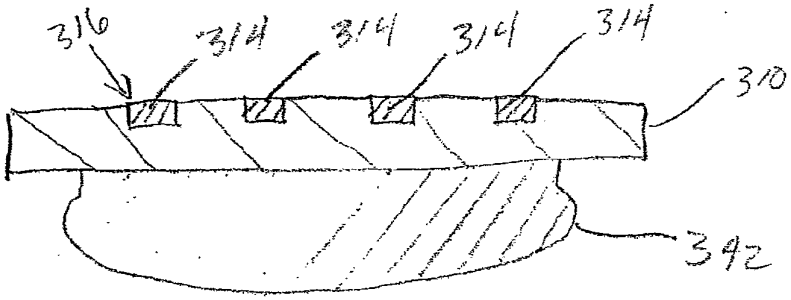


FIG. 23b

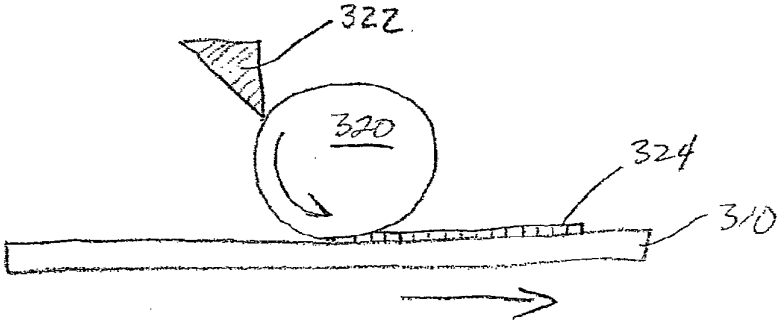


FIG. 24

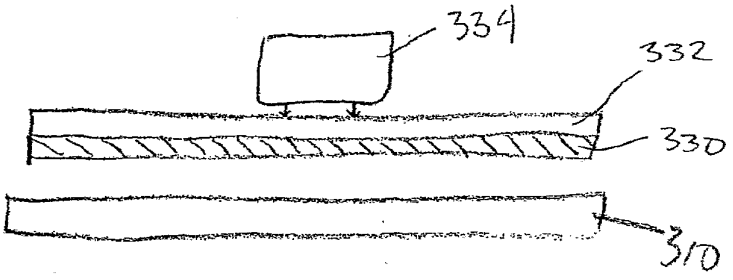


FIG. 25a

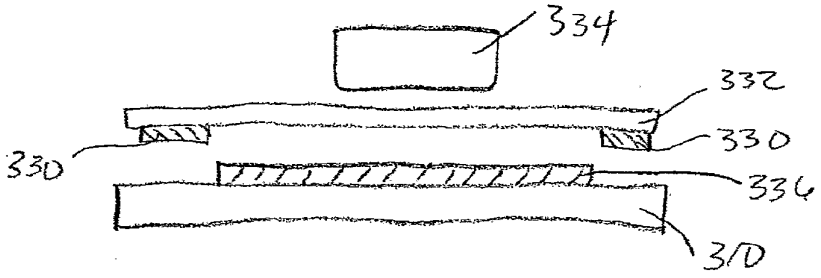


FIG. 25b

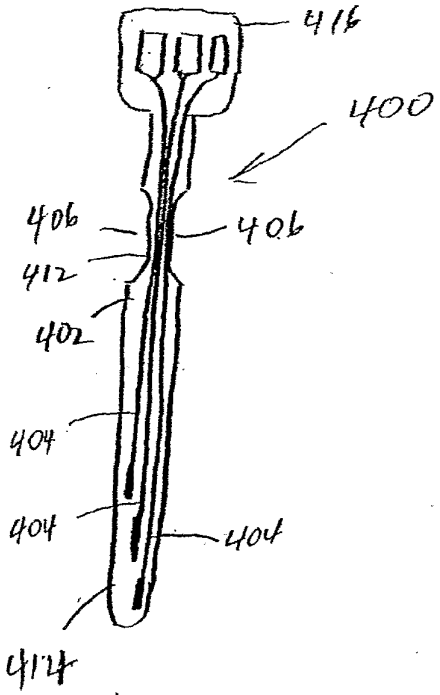


Fig. 26

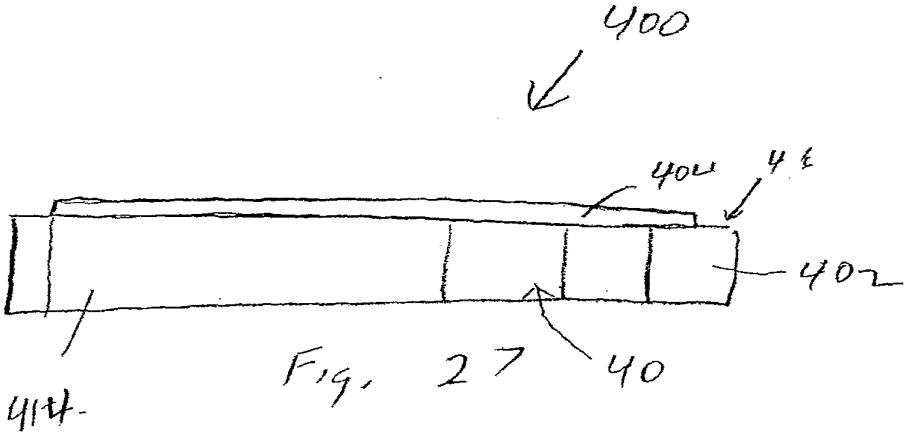


Fig. 27

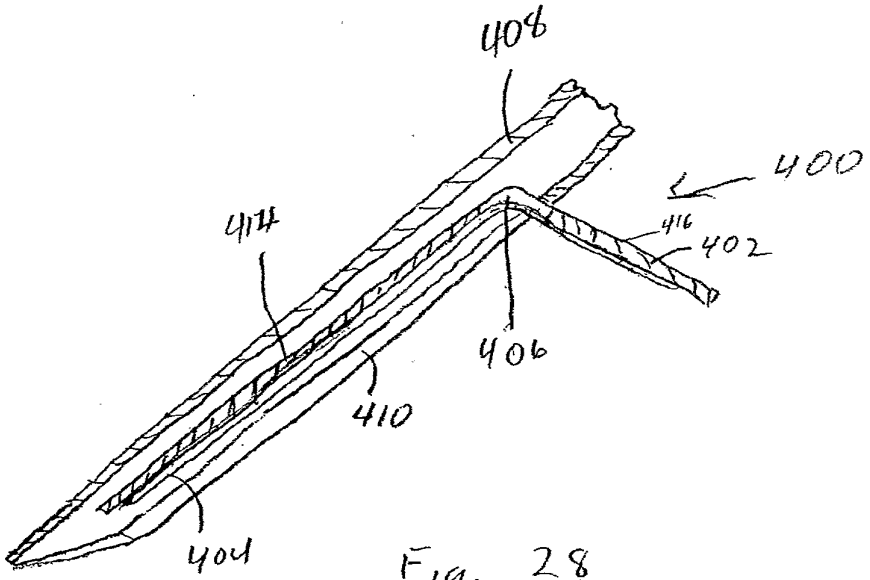


Fig. 28

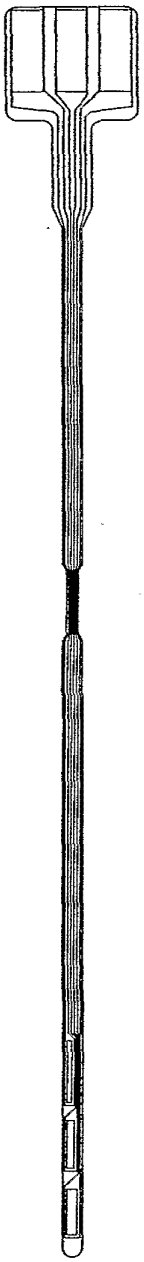


Fig. 29

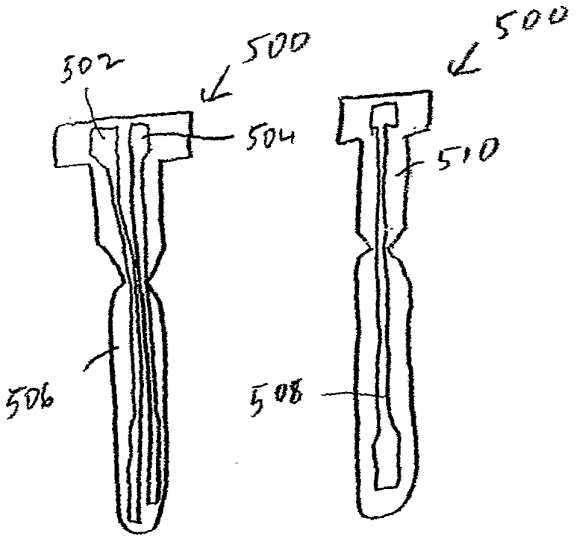


Fig. 30(a) Fig. 30(b)

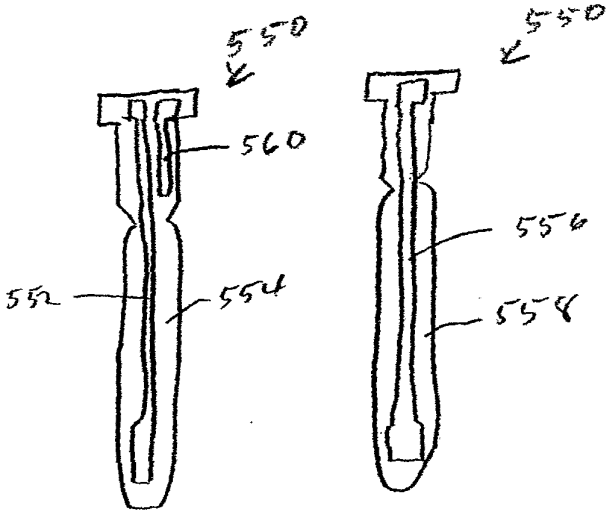


Fig. 31(a) Fig. 31(b)

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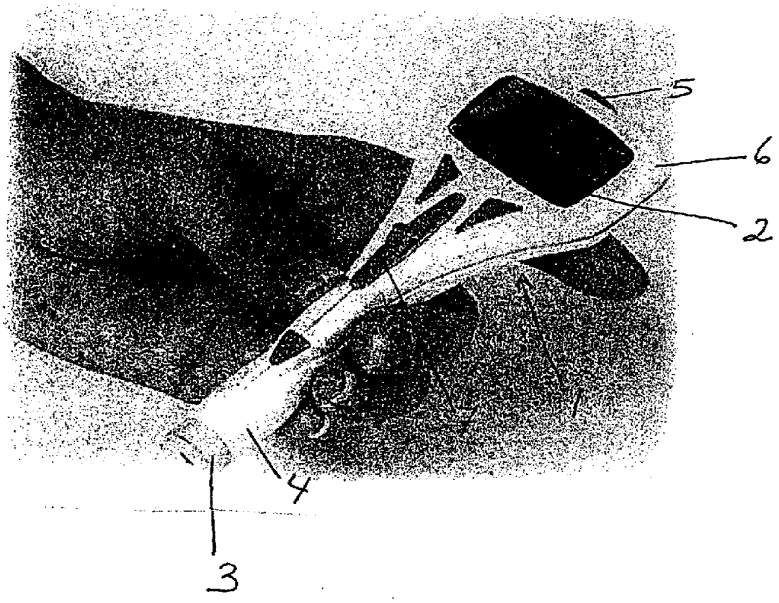
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(54) Title: COMBINED LANCET AND ELECTROCHEMICAL ANALYTE-TESTING APPARATUS



(57) Abstract: An apparatus for detection and quantitation of an electrochemically-detectable analyte, such as glucose, in blood or interstitial fluid includes a meter unit, a lancet and an electrochemical sensor. Of these components, the meter is preferably reusable, while the lancet and the electrochemical sensor are preferably incorporated in assemblies intended for single-use. The meter unit has a housing, within which a lancet is engaged with a mechanism for moving then lancet; a connector disposed within the housing for engaging an electrochemical sensor specific for the analyte and transmitting a signal indicative of the amount of analyte, and a display operatively-associated with a connector for displaying the amount of the analyte to user. The electrochemical sensor is adapted for detection of a particular analyte.

WO 01/64105 A1

COMBINED LANCET AND ELECTROCHEMICAL ANALYTE-TESTING APPARATUS

Field of the Invention

This application relates to an electrochemical apparatus for the detection of analytes, and particularly glucose, in blood or interstitial fluid.

Background of the Invention

Glucose monitoring is a fact of everyday life for diabetic individuals, and the accuracy of such monitoring can literally mean the difference between life and death. To accommodate a normal life style to the need for frequent monitoring of glucose levels, a number of glucose meters are now available which permit the individual to test the glucose level in a small amount of blood. Many of these meters detect glucose in a blood sample electrochemically, by detecting the oxidation of blood glucose using an enzyme such as glucose oxidase provided as part of a disposable, single-use electrode system. Examples of devices of this type are disclosed in European Patent No. 0 127 958, and US Patents Nos. 5,141,868, 5,286,362, 5,288,636, and 5,437,999 which are incorporated herein by reference.

To use these meters, the user pricks a finger or other body part to produce a small sample of blood or interstitial fluid which is then transferred to the disposable electrode system. This can cause problems, because of the need to take several measurements a day. The biggest drawback to routinely drawing small blood samples is the pain inflicted by the currently available lancets or finger-sticking devices. The most favored site of sampling is the rich capillary bed of the skin of the finger tip which readily yields a drop of blood from a small cut. The finger tip is also rich in pain receptors, and the pain is increased when the incision is too deep, or is too close to a recent incision, or is not deep enough requiring an additional incision. The pain maybe also be increased if the cutting blade penetrates slowly or is withdrawn slowly. Furthermore, the user may be forced to make a larger incision than is necessary in order to get a drop of blood to form for transfer to the measuring strip. Because of this, different designs for lancing devices have been proposed which are designed to facilitate use of the device and limit the pain

associated with the procedure. Examples of lancing devices are described in US Patents Nos. 4,924,879, 5,201,324, 5,318,584, 5,879,311, and 5,879,367 which are incorporated herein by reference.

International Patent Publication No. WO95/10223 describes a device for collection of interstitial fluid. The device can include a membrane on which sample is collected and dried. This membrane is then transferred to an external device for analysis.

Each of these known devices for the electrochemical monitoring of glucose by a diabetic involves a two-step process, in which the skin is first pierced to obtain a sample and this sample is transferred to a sensor for analysis. This presents several drawbacks. First, the user must transfer blood into the detection apparatus which requires a measure of dexterity to align the drop of blood on the finger with the sample-receiving opening of the sensor or meter. Second, because of this transfer, the amount of blood or fluid extracted from the patient may be inappropriate for the sensor, either being too little to provide an accurate measurement or too much, which can increase the amount of pain associated with the procedure.

US Patent No. 4,637,403 discloses a self-contained device for lancing and testing blood glucose using colorimetry. US Patent No. 5,054,499 discloses a colorimetric device in which a lancet punctures an absorbent member which includes reagents for the colorimetric detection of glucose prior to puncturing the skin. US Patents Nos. 5,682,233 and 5,823,973 disclose a sampling device which is sized to allow it to be mated with a testing apparatus for optical analysis of a sample. US Patent No. 5,746,217 discloses a lancet in which a capillary tube is used to capture sample, which is there analyzed by infrared spectroscopy in the capillary. US Patent No. 5,879,310 discloses a device in which a lancet punctures the skin and the sample resulting sample of body fluid is transported for analysis in an optical system.

US Patent No. 4,953,552 discloses a device for electrochemical glucose detection in which reagents for generating the electrochemical signal are coated directly onto the lancet, and thus come into contact with the sample without further user intervention. In this device, there is no spring action to drive the needle, and the needle is simply pressed in by the user. This makes control of the puncture difficult. Furthermore,

replacement of the lancet and reagent are inconvenient in the device as disclosed, and mass production of sensors would be difficult.

Thus, there remains room for improvement in the manner in which fluid samples are collected and analyzed.

Summary of the Invention

The present invention provides an improved apparatus for detection and quantitation of an electrochemically-detectable analyte, such as glucose, in blood or interstitial fluid. The apparatus comprises a meter unit, a lancet and an electrochemical sensor. Of these components, the meter is preferably reusable, while the lancet and the electrochemical sensor are preferably intended for single-use.

The meter unit comprises a housing, means disposed within the housing for engaging a lancet and moving an engaged lancet, a connector disposed within the housing for engaging an electrochemical sensor specific for the analyte and transmitting a signal indicative of the amount of analyte, and a display operatively-associated with a connector for displaying the amount of the analyte to user. The electrochemical sensor is adapted for detection of a particular analyte. In addition, the electrochemical sensor comprises an sample uptaking or accepting member for uptake of a sample of blood or interstitial fluid. In one embodiment of the invention, when a lancet is engaged in the apparatus, the means for engaging and moving the lancet moves the lancet from a initial position to a piercing position in which skin of the user is pierced and optionally back to a retracted position, which may be the same as or different from the initial position. The electrochemical sensor is disposed such that the sample uptaking or accepting member takes up a sample from the pierced skin of the user when it is pierced by the lancet. In an alternative embodiment, the lancet is a hollow cannula through which blood or interstitial fluid is transported from the puncture site to an absorbent portion of the electrochemical sensor. Thus, in either embodiment, the invention provides an apparatus with single-step operation in which sample acquisition and analysis occur as a result of the single action of pressing the apparatus against the users skin without necessitating movement of the housing. The invention further provides a method including a single step procedure in which both sample acquisition and analysis are achieved.

Another aspect of the invention relates to disposable sensor assemblies for use in a meter in accordance with the invention. Such disposable sensor assemblies may contain just the sensor in a support suitable for attachment to the meter or both the sensor and the lancet. In the latter case, the disposable sensor assembly may contain one sensor and one or more lancets, or it may contain a plurality of lancet/sensor pairs.

Brief Description of the Drawings

Fig. 1 shows an exterior view of an apparatus in accordance with the invention;

Figs. 2A-C show sectional views of a device in accordance with the invention;

Figs. 3A-C show a schematic representation of an arrangement of the sensor and the lancet in accordance with one embodiment of the invention;

Figs. 3D and E show a sensor for use in an alternative embodiment of the invention;

Fig. 4 shows an exemplary sensor assembly for electrochemical detection of an analyte;

Figs. 5A-C show a specific embodiment of a sensor 32 for incorporation in a sensor assembly in accordance with the invention;

Fig. 5D shows an further embodiment of a sensor assembly in accordance with the invention;

Figs. 6A-C show an schematic representation of an alternative embodiment of the invention;

Fig. 7 shows a cross-section of an embodiment of a sensor assembly for use in the embodiment of the invention shown in Fig. 6;

Figs 8A-G show a further embodiment of the invention;

Figs. 9A and B show the preparation of a sensor with multiple electrode sites;

Fig. 9C shows an apparatus in accordance with the invention; and

Fig. 10 shows a schematic representation of the electronics which can incorporated in an apparatus in accordance with the invention.

Detailed Description of the Invention

The apparatus of the present invention is an integrated lancing and analysis device which does not require a separate action for the transfer of the sample from the puncture site to a strip for analysis. This apparatus includes a meter unit, in which the electronics for analysis of a sample and display of a result are located, a cutting member (i.e, a lancet or hollow needle) and an electrochemical sensor. The electrochemical sensor includes an "sample uptaking or accepting member" for the uptake of sample. As used in the specification and claims hereof, the term "sample uptaking or accepting member" encompasses various methods for achieving the direct transfer of a liquid sample from the sampling site to the electrochemical sensor, including but not limited to absorptive materials, such as a wick, sponge or absorptive pad, which take up liquid and cannula's through which liquid is transferred. The uptake of liquid may be a result of inherent capillarity or surface tension forces resulting from the structure of the absorptive material or the size of the analysis chamber or cannula, or it may be an active absorption stimulated by application of suction. In fact, the term "sample uptaking or accepting member" should be understood to encompass any means that enables transfer of sample from the sample site to the electrode of the sensor. For example, the sample uptaking or accepting member could be the active portion of the sensor itself. The size or volume-uptaking capcity of the sample uptaking or accepting member would be influenced by the volume of sample to be analyzed, which would typically be on the order of 100 nl to 10 µl.

Fig. 1 shows an exterior view of an embodiment of an apparatus in accordance with the invention, although it will be appreciated that the overall shape of the device is a matter of design choice and is thus provided here solely for purposes of illustration. The device as shown allows for an easy grip by one hand, while providing good visibility of the display. In addition, it is easy to handle when sampling from alternative sites like the palm of the hand, the arm or the abdomen.

As shown, the device comprises a housing 1 of a size easily held in one hand. A display 2 is visible to the user on the outside of the housing 1. A skin-contact ring 3 is disposed at the sample end 4 of the device, while a button 8 for activating a sample/measurement cycle is disposed at the opposite end 6. Ejector slide 7 ejects used

lancets and electrochemical sensors when it is shifted towards the sample end 4, and is also used to lock the device. Optional button 5 is used to set the penetration depth of the lancet.

Figs. 2A-C show sectional views of the device of Fig 1 showing the internal mechanism for engaging and moving the lancet 20, the electronics 21 for transfer of an electrical signal from a sensor (not shown in Fig. 2) to the display 2. An electrical contact 22 is provided near the end of the housing 1 for making electrical contact with a sensor, and is connected to the electronics via a conductive element 23. The three figures illustrate the operation of the device.

In Fig. 2A, the device is shown in a rest position, prior to sampling. There is no tension on the spring 20. Plunger 24 is attached to the lancet holder 29 and to a cocking button 27. The spring is attached to the lancet and bears on the lancet to allow both pushing out on the lancet from the cocked position and retraction of the lancet from a piercing position. Pores 28 allow air to move out of the space defined by a valve 26 and skin pressed against the skin-contact ring 3. The valve is a one-way valve which permits the flow of air from this space, but not into it. Catch 29 holds the cocking button 27 in place until released manually. To cock the device the cocking button 27 is pushed up to the catch 29, causing the lancet assembly and the valve to move upwards, compressing spring 20 as shown in Fig. 2B. The cocked device is then pressed against the skin and catch 29 is released. This results in the lancet assembly being driven downwards to puncture the skin as shown in Fig. 2C. During this downwards movement, pressure does not increase in the region between the plunger 24 and the skin because of the one-way valve 26. However, because the spring passes through its equilibrium position, there is a backwards motion of the lancet assembly after the skin is pierced and this motion results in the creation of reduced pressure in this region.

An important feature of the device of the present invention which enables true one-step operation is use of an arrangement of the lancet and sensor to allow "in situ" sampling without movement of the apparatus. Figs. 3A-C show a schematic representation of one such arrangement. Fig. 3A shows the device in a ready-to-use state. The lancet 31 is disposed within the housing 1 and is engaged with the means for moving the lancet (not shown). The sensor strip 32 is part of a sensor assembly 33 that includes

the skin-contact ring 3 and a collar 34 for coupling the assembly to the housing 1. The skin-contact ring 3 is pressed against the skin of the user, which causes an upwelling of tissue in the region surrounded by the skin-contact ring. When the device is activated, the lancet device 31 moves downward, piercing first the sensor 32 and then the skin as shown in Fig. 3B. The lancet 31 is then retracted, and blood or fluid flowing from the pierced skin wicks into the sensor. (Fig. 3C). The sensor may be designed such that the lancet pierces the sensor through a weak spot 98 (see Fig. 3D). This weak spot, which is an integral part of the sensor, may be the sample accepting uptake means.

According to an alternative embodiment of the invention, the lancet device pierces the skin without first piercing the sensor assembly. The sensor is designed to be placed in close proximity to the sample which is obtained by this piercing, so that transfer of the sample to the sensor occurs as part of a single-step sample acquisition and analysis process without movement of the housing. In such an embodiment, the sensor is positioned in relation to the cutting device, and therefore in relation to the position of the sample, such that the sample uptaking or accepting means would be in close proximity to or touching the sample formed as a consequence of the cutting device piercing the skin, such that transfer of the sample to the sensor is enabled. The sample uptaking and accepting member could be an integral part of the sensor, for example as illustrated in Fig. 3D, or it could be an external part of the sensor, for example wick 97 as shown in Fig. 3E. The angle of the sensor with respect to the sample can be varied, and can be any angle which facilitates efficient sample transfer.

In the embodiment of the invention as shown in Figs. 3A-3C, the lancet 31 and the sensor assembly 33 are separate. The lancet used in this embodiment may be of conventional design compatible with the means for moving the lancet and the size of the housing. Various forms of lancets and associated means for moving the lancet are known in the art, including for example in US Patents Nos. 4,924,879; 5,196,025; 5,304,193 and 5,318,583 , which are incorporated herein by reference. The sensor assembly is a novel component adapted for use in the present invention, and itself forms an aspect of the invention. Fig. 4 shows a cross section in greater detail of an exemplary sensor assembly for electrochemical detection of an analyte. As shown, the sensor 32 has a reagent pad 41 disposed in approximate alignment with one edge of the opening 42 defined by the skin-

contact ring 3. The collar 34 has a lip 43 against which the housing 1 of the meter bears when the sensor assembly is attached to the meter. Electrical contacts 44 and 45 are accessible through an opening in the lip 43 . An insulating pad may be provided so that conductivity between the connectors only occurs in the vicinity of the reagent pad when a liquid sample is present. When the housing 1 of the meter is inserted in the sensor assembly, electrical contact is made via electrical contacts 44 and 45.

In the sensor assembly of Fig. 4, the sensor 32 is disposed adjacent to the skin-contact ring 3 and extends across one end of the open space 42 defined with the skin-contact ring. The sensor comprises reagents 41 and electrodes for generation of an electrochemical signal in response to the presence of analyte and an adsorptive member for absorbing fluid placed within the central opening of the ring and transporting the fluid into reactive proximity to the reagents, and an electrical contact for transmitting the electrochemical signal from the sensor. The reagents are selected to provide an electrochemical signal in response to the presence of analyte. In the case of glucose, suitable reagents would include an enzyme capable of oxidizing glucose (for example glucose oxidase), and a mediator compound which transfers electrons from the enzyme to the electrode resulting in a measurable current when glucose is present. Representative mediator compounds include ferricyanide, metallocene compounds such as ferrocene, quinones, phenazinium salts, redox indicator DCPIP, and imidazole-substituted osmium compounds. Working electrodes have been formulated using materials of this type in a number of ways. For example, mixtures of conductive carbon, glucose oxidase and a mediator have been formulated into a paste or ink and applied to a substrate. See, EP 0 127 958 and US 5,286,362 which are incorporated herein by reference.

Figs. 5A-C show the assembly of a specific embodiment of a sensor 32 for incorporation in a sensor assembly in accordance with the invention. Contacts 53 and leads 55 are formed on a non-conductive substrate 51. In the embodiment shown in Fig. 5A, three set of contacts and three sets of leads are formed to create two working electrodes with reagents 52 and one reference electrode. The contacts and leads are suitably formed from conductive carbon inks, although other conductive materials may also be used. The electrodes may be formed by printing. Groups of sensors are suitably formed on a sheet of material and then cut apart for use.

The substrate 51 may advantageously be formed from a material which is sufficiently strong that the lancet will not pierce through the substrate material. This avoids contamination issues in the event of faulty lancet alignment. In this case, however, the substrate 51 needs to have an opening 54 or a weak spot through which the lancet can pass. Suitable materials for the substrate include polyester strips, high density polyethylene and ABS.

After the electrodes have been formed, a wick layer 56 is placed over the opening 54 and the electrodes, including the reagent pads 52 (Fig. 5B). This wick acts as an absorbent member to draw sample into the sensor and guide it to the electrodes. Suitable materials include nylon mesh. In some cases, however, no separate wick is necessary, as when the hole 54 in the substrate 51 inherently provides a capillary channel to the reagent pads 52 of the electrodes. Polymer film layers could also be used instead of or in combination with a wick to define a capillary channel for absorption of the sample to the electrodes.

Over the wick (if present) and the electrodes a print of an insulation ink 57 is provided. The insulation ink holds the wick in place, and defines the path through which sample can migrate. Thus, the insulation ink includes an opening having a hole 571 in alignment with the hole 54 and a contiguous region 572 extending over the reagent pads 52 of the electrodes. Contacts 53 remain exposed outside the edges of the insulating ink print 57 for making contact with the meter. Optionally, a top cover can be added to protect the reactants. Such a top cover could be made form a polymeric film such as polyester.

The sensor of Figs. 5A-C may be assembled with a skin contact ring and collar as shown in the Fig. 4. Fig. 5D shows an alternative configuration. Sensor 32 is supported on a skin contact ring 3. A collar 534 is affixed to the edge of the skin contact ring 3 and sized to receive the distal end 535 of the meter unit. O-rings 536 provide a tight seal between the collar 534 and the distal end of the meter unit 535. A contact 522 on the distal end of the meter unit 535 makes electrical contact directly with the contact portions of the sensor (for example contacts 53 in Fig. 5A).

Figs. 6A and 6 B show a schematic representation of an alternative embodiment of the invention. In this case, the lancet 61 is a hollow cannula disposed

adjacent to the sensor 62. The lancet 61 and the sensor 62 can be fabricated as a single unit which is loaded into a housing 1 for use. The housing desirably includes a skin-contact ring 3 which creates pressure to displace blood or interstitial fluid out of a puncture created by the lancet 61. When the device is activated, the lancet and the sensor are driven downwards as a unit to puncture the skin. (Fig. 6B) The sample is then drawn up through the lancet to the sensor. The dwell time in the piercing position is long enough to permit sufficient sample to be drawn into the sensor. Alternatively, the movement of the lancet may be in only one direction, with the entire device being moved away when sufficient sample has been collected. As discussed in more detail below, this latter option can be facilitated by the use of a device which provides an audible or other signal to the user when sufficient sample has been collected.

Fig. 6C shows an apparatus in accordance with the invention including a sensor assembly of the type shown in Figs. 6A and 6B. In this apparatus, the sensor 62 has an integral lancet 61, and is slidably received in a first housing portion 67. The distal end 3 of the first housing portion 67 is pressed against the skin of the user, causing the compression of spring 66 and the exposure of the lancet for piercing of the users skin. When the apparatus is removed from the skin, the spring 66 causes the first housing portion 67 to move outward, to once again shield the end of the lancet. The sensor 62 is in electrical contact with a contact 22 which in turn is in electrical contact with the electronics 21 via a connector 23. A vacuum plunger 24 is disposed within a second part of the housing 68 for creating a suction to draw in blood or fluid.

Fig. 7 shows a cross-section of an embodiment of a sensor assembly for use in the embodiment of the invention shown in Fig. 6. The assembly includes a collar portion 71 and a base portion 72. These portions can be made as a continuous piece of material or they may be made from separate pieces joined together, for example with an adhesive. A hollow lancet 73 passes through the base portion 72, such that the hollow interior 74 of the lancet is in contact with the sensor 75. The sensor may extend over a greater area than the collar portion, as shown, or a lip extending from the interior surface of the collar may be utilized to hold the sensor 75 in place. The second portion of the housing 68 may bear on this lip, or in the embodiment shown in Fig. 7 on an annular surface 79 surrounding the collar 71. Electrical contact is made through an opening in this

annular surface 79, for example via contacts 77, 78. Contacts 77, 78 may also be formed on the interior wall of the collar portion. The sensor 75 may have the same type of structure as shown in Fig. 5. Reagents may also be disposed directly on the lancet, or in a lancet lumen.

Figs. 8A-G shows a further embodiment of the invention. The device can operate manually (no automatic timing function) or perform a test procedure on demand from the meter. In the latter case, the meter housing 81 contains a plurality of lancet/sensor pairs and a timing mechanism for automatically using the pairs at pre-defined time intervals. The length of the pre-defined time interval is related to the number of lancet/sensor pairs and to the frequency with which testing for the target analyte is desired. For example, in a device for testing for blood glucose, with twelve lancet/sensor pairs, the time interval is suitably between one and four hours. This results in a need to replace the lancet/sensors at reasonable intervals, for example twice a day, once a day, or once every other day. The timing can also be shorter, for example every minute, or can be selected using a logic circuit. Thus, for example, in the case of a rapidly changing glucose level (as determined by the difference between two successive measurements), the logic circuit in the meter may be configured to decrease the interval between subsequent measurements until such time as the glucose level stabilizes. The meter may also be configured to take several initial readings at short time intervals to determine a suitable baseline test interval based on the degree of variations in the results. This baseline test interval may be used for all subsequent measurements in the test cycle, or it may be shortened as described above in response to changes in glucose levels.

A suitable format for an embodiment of the invention in which the housing contains a plurality of lancet/sensor pairs is the watch-type format as shown in Figs. 8A and 8B. The apparatus comprises the housing 81 and a strap 82. The housing has a bottom side 83, through which contact is made between the lancets and the skin of the user (shown in Fig. 8A), and a top side 841 (shown in Fig. 8B) on which the test results are displayed. The device may be strapped like a watch around the wrist of a user, as shown in Fig. 8B, or about the forearm or upper arm. Once in place, the device is activated and a number of tests may be automatically performed without further action by the user and the result are displayed, individually or as a summary of a number of tests on the display.

Alternatively, the device or the sensor disk may be self-attaching (for example using a skin-compatible adhesive). This provides utility on any body surface, and eliminates the need for a strap.

Figs. 8C-F show an exploded view of the component parts of an apparatus in accordance with this embodiment of the invention. Closest to the bottom side 83 of the apparatus is a sensor disk 84. The sensor disk 84 comprises a substrate 810 on which are formed a plurality of sensors 812. Each sensor includes a reagent pad 814 in contact with a pair of electrodes 816, 818. The sensor disk 84 has a central opening to allow the trigger mechanism (the spindle/ramp) to pass through. The sensor as a whole is bonded together with glue, ultrasonic welding or with snap-together fittings.

Above and coaxial with the sensor disk 84 is placed a spacer ring 85 (Fig. 8D). The spacer ring 85 provides a defined area surrounding each sensor 812, so that fluids contacting one sensor will not interact with adjacent sensors. Alternatively, the insulation print or capillary channels can provide this isolation. As shown, sensor ring 85 has a hub 820, a rim 822 and a plurality of spokes 824. The separator ring 85 is placed over the sensor disk 84 such that one sensor 812 is positioned in the space between each adjacent pair of spokes 824. The rim may include electrical contacts for conducting signal indicative of the amount of analyte from the electrodes 816, 818 of each sensor pair.

Over and coaxial with the separator ring 85 is placed a cam ring 86 (Fig. 8E). The cam ring has a ramp portion 830, such that rotation of the cam ring 85 results in an increase in the thickness of the cam ring 86 when viewed at a fixed location. The cam ring 86 has a central opening through which a screw or similar fastener is inserted to assemble the completed device. The opening preferably has a faceted or toothed edge, however, to allow engagement of the cam ring 86 with a drive mechanism for rotating the cam ring.

Over and coaxial with the cam ring 86 is a lancet ring 87. The lancet ring 87 has a rim 840 and a plurality of lancet spokes 842, each of which has a free center end. The lancet ring 87 is positioned such that each lancet spoke 842 is aligned with a space between the spokes 824 of the separator ring 85. The lancet spokes 842 are made of a flexible material with substantial memory such as spring steel. A lancet 844 is attached to each lancet spoke 842 near the center-end of the lancet spoke 842, oriented in a downward

direction so that the point of the lancet 844 is directed towards the sensor disk 84. The lancet spokes 842 are of a length such that they interact with the cam ring 86 lying beneath the lancet spokes. When the device is first assembled, one of the lancet spokes (arbitrarily referred to as the first lancet spoke) is substantially aligned with highest part of the ramp portion 830 and is thus deflected upwards from its neutral or rest position. When the cam ring 86 is rotated a partial turn, this first lancet spoke is moved off the end of the ramp and springs downward, piercing through the underlying sensor disk 84 and the skin of the user. At the same time, the "second" lancet spoke is moved into position at the highest part of the ramp portion 830, and each of the other lancet spokes is shifted to a position of increased deflection. Thus, each partial rotation of the cam ring 86 brings about one sampling and measurement activity.

Fig. 8 G shows a cross section of an assembled device incorporating a sensor system assembly of the type shown in Figs. 8A-F. Spacer ring 85 is received within an opening on the bottom of a housing 801. Sensor disk 84 is disposed exterior to the housing, and has a larger diameter than the spacer ring 85 such that it can make electrical contact with contacts 802 disposed on the bottom of the housing. A small motor 803, such as a stepper motor, is engaged with the cam ring 86 to rotate it with respect to the sensor assembly, thereby sequentially activating the lancets associated with the sensors. The motor 803 is controlled by electronics 804, which also receive signal from the contacts 802, process the signal and transmit instructions for an appropriate display to the display 805. A small vacuum pump 806 (for example a membrane pump or actuator pump) is also disposed within the housing 801 to create a suction which draws sample into the sensors. This pump may be on continuously, or it may be controlled by the electronics to be active for a period of time spanning the activation of the motor to rotate the cam ring. Alternatively, the vacuum pump could be activated prior to lancing, with a sufficient underpressure acting as a signal to start the lancing cycle.

The sensor disk 84 can be fabricated in much the same way as the sensor shown in Figs. 5A-C. Thus, as illustrated in Figs. 9A and B, contacts 91 are deposited around the periphery of a electrodes are deposited on substrate 92 in sets of three radially outwards from openings (or weak spots) 93. One of the electrodes in each set is a reference electrode, while the other two are working electrodes which include reagents

appropriate for generating a signal indicative of the amount of the target analyte. Next, a mesh strip 94 is applied over each opening 93 and each set of electrodes. Over the top of the mesh an insulation layer 95 is formed. Once the sensor disk is formed, it is assembled with the other components to form the complete device.

Fig. 9C provides a further view of such a device, which includes a skin contact ring 96 on the lower surface. The skin contact ring 96 surrounds an opening 97 through which the lancets 98 pass to pierce the skin of the user. This opening 96 moves with the rotation of the spindle 99, such that comes successively into alignment with each of the electrode sets. In the embodiment shown in Fig. 9C, the lancets are pre-tensioned by the spindle when the sensor assembly is put together. Slot 990 in the top of the spindle 99 allows the aligned lancet to drop through the spindle, to pierce the underlying skin. The upper case 901 of the assembly seals to the base portion 902 with an O-ring 903 seal. Electrical contact is made between this upper case 901 and contacts 91 via contact 904. This allow the analytical electronics to be located away from the sensor disk where they are not at risk of being exposed to fluid, and where they can be reused. Because of the sealing engagement of the upper case 901 with the base portion 902, the contact 904 also rotates and comes into contact with one electrode set at a time. In the case of a device "permanently" attached to the skin there would be as many skin-contact rings as there are sensors. Only the spindle moves, testing with a fresh lancet and a fresh sensor at a different sampling site each time.

Fig. 10 shows a schematic representation of the electronics which can incorporated in a device in accordance with the invention. As shown, input signals are provided from the sensors and from any included skin-contact or sufficient-sample detector systems to a signal processing system. These signals are transmitted via analog circuitry to a processor which performs data analysis. This processor provides a signal to display driver which is connected (via a wired or wireless connection) to an output display. The processor may also provide a signal via a wired or wireless connection to an alarm generator. The display and the alarm generator together constitute the output portion of the device. The data analysis processor also communicates with a memory device, for example an EEPROM, in which information including calibration information and previous results may be stored. A timer is also provided which is activated by the data

analysis software. This timer provides functional output signals to control a steeper motor (for rotating the sensor disk or spindle) and a vacuum generator (if present). Values from the timer may also be stored in the memory EEPROM for utilization by the data analysis processor.

The foregoing descriptions of various embodiments of the invention address show specific combinations of features. These descriptions and combinations should be viewed as merely exemplary, however, and do not exclude alternative implementations. For example, while the lancet ring 87 is shown with the free-ends of the lancets towards the center of the ring, it will be appreciated that an alternative geometry could be used in which the lancet ring has a star-like configuration in which the free-ends are pointed outwards. Similarly, the lancet ring could be pre-tensioned, in which case the cam ring would act to release rather than create tension. A further alternative is the use of a single actuating cam or hammer to activate the lancets. one-by-one, in turns, as they rotate through the position of the actuator.

The devices of the present invention may incorporate a variety of additional features which enhance the characteristics of the device and make it easier to use. For example, the devices may include an audible or otherwise detectable alarm which alerts the user that it is time to take a measurement. In the case of the device shown in Fig. 1, this alarm would indicate to the user that they need to insert a new lancet and sensor (if not already done) and take a measurement. In the case of a device such as that shown in Figs 8 or 9, the alarm may actually precede the taking of a sample, so that the user will not be surprised by the lancet and will know to look at the display to observe the result.

The device, particularly the device of the type shown in Fig. 1, may also or additionally include an audible or otherwise detectable alarm which alerts the user that sufficient sample has been collected, and that the device can be removed. An audible alarm could take the form of a click, caused by the release of a detent within the device, or might be a beep generated electronically in the device. One way to achieve sufficient-sample indication is to assume that a pre-defined period of time is sufficient to collect the sample. In this case, the first appearance of a signal between one of the working electrodes and the reference, or between the separate sample-monitoring pair of electrodes starts a timer and the sufficient-sample indication is given some pre-defined period of time

(for example 2 seconds) later. Sufficient sample may also be determined using an electrode pair having a spatial location and separation such that an electrical signal is only possible between the electrodes when sufficient sample is present. In either case, the signal which is collected can be any type of electronic signal, including signals based on conductivity, potential differences, or current flow (amperometric).

While the embodiment shown in Fig. 1 incorporates a skin-contact ring as a means to help with the expression of blood or fluid from the puncture, this skin-contact ring is optional, and can be replaced with other components such as a suction force generated by a mechanical or electrical pump for accomplishing the same function. A variable, user-selected vacuum force can be used to ensure sufficient bulging of the skin. A feedback mechanism tells the user that the skin made contact with the sensor. Two simple contacts bridged by the skin can achieve this. In an apparatus where the user is creating the vacuum (for example by drawing on a plunger), once the apparatus has detected the skin, the user is alerted, for example by an audible or visual signal that no more vacuum has to be created. In an automated apparatus, the pump mechanism can be shut down in response to this signal.

The device may include capacity for providing counseling to a user when abnormal readings are obtained for the analyte. Such counseling might be in the form of a prompt to call a physician, or might in appropriate cases instruct the user to administer medications. The audible signal can function as a hypoglycemic alarm, particularly in the multiple test embodiments. Such devices can also be used for overnight surveillance to alert the user or other concerned individual (for example a partner, parent or nurse) to changes in glucose levels.

The devices of the present invention offer a variety of advantages over existing devices for the measurement of glucose levels. To advantages flow directly from the incorporation of sampling and analysis functions in a single device. First, such devices require the user to perform fewer steps. Second, the user is not required to manipulate a small electrode into a slot in the meter. This allows for the utilization of smaller electrodes, which (as described in US Patent Application No. 09/228,855, which is incorporated herein by reference) are both less expensive to make and more accurate in providing glucose measurements. Moreover, for embodiments in which there are a

plurality of lancet/sensor pairs, the sampling site can be automatically varied throughout the course of a day, thus reducing injury resulting from repetitive punctures in the same location. The invention also allows the utilization of very small samples, which might otherwise be difficult to transfer to a sensor strip. This not only facilitates the taking of measurements with less pain, it can also provide for a more accurate result because of the benefits associated with small-sample measurements. In addition, the taking of a small sample which is optimally utilized by the device reduces or eliminates disposal issues for sample-contaminated waste.

CLAIMS

1. An apparatus for detection and quantitation of an electrochemically-detectable analyte in blood or interstitial fluid, comprising:

(a) a meter unit comprising a housing, means disposed within the housing for engaging a cutting member and moving an engaged cutting member, a connector disposed within the housing for engaging an electrochemical sensor specific for the analyte and transmitting a signal from the sensor indicative of the amount of analyte, and a display operatively-associated with the connector for displaying the amount of the analyte to user;

(b) a cutting member engaged within the housing;

(c) an electrochemical sensor comprising an sample uptaking or accepting member for the uptake of a sample of blood or interstitial fluid, wherein the means for engaging and moving the cutting member moves the cutting member in a cycle from an initial position to a piercing position in which skin of the user is pierced, and wherein the electrochemical sensor is disposed such that the sample uptaking or accepting member takes up a sample from the pierced skin of the user when it is pierced by the lancet without movement of the apparatus.

2. An apparatus for detection and quantitation of an electrochemically-detectable analyte in blood or interstitial fluid, comprising:

(a) a meter unit comprising a housing, means disposed within the housing for engaging a cutting member and moving an engaged cutting member, a connector disposed within the housing for engaging an electrochemical sensor specific for the analyte and transmitting a signal from the sensor indicative of the amount of analyte, and a display operatively-associated with the connector for displaying the amount of the analyte to user;

(b) a cutting member engaged within the housing, wherein the means for engaging and moving the cutting member moves the cutting member in a cycle from an initial position to a piercing position in which the skin of the user is pierced at a point of entry, and wherein the connector is positioned in relationship to the cutting

member and the point of entry such that when a sensor or plurality of sensors comprising a sample uptake or accepting member are engaged with the connector, the sensor or plurality of sensors are able to take up or accept sample generated at the point of entry as a consequence of piercing of the skin without movement of the apparatus.

3. The apparatus of claim 1 or 2, wherein the electrochemical sensor and the cutting member are disposed such that the means for engaging and moving the cutting member causes the cutting member to pierce the sensor prior to piercing the skin of the user.

4. The apparatus of any of the preceding claims, wherein the means for moving the cutting member moves the cutting member back to a retracted position which may be the same or different from the initial position after piercing the skin of the user.

5. The apparatus of any of the preceding claims, further comprising a skin-contact ring disposed to apply pressure to an area surrounding the piercing of the skin when the apparatus is pressed against the skin of the user.

6. The apparatus of any of the preceding claims, further comprising a vacuum mechanism disposed within the housing to accelerate extraction of sample after piercing when the apparatus is pressed against the skin of the user.

7. The apparatus of claim any of the preceding claims, comprising a plurality of electrochemical sensors and an equal plurality of cutting members.

8. The apparatus of any of claim 7, wherein the plurality of electrochemical sensors are provided on a disk.

9. The apparatus of claim 8, wherein the housing is a flattened disk having a top and a bottom surface, and further comprising means for holding the bottom surface of the housing against the skin of a user, wherein the electrochemical sensors are

disposed adjacent to the bottom surface and the cutting members move to pierce the skin adjacent to the bottom surface.

10. The apparatus of claim 9, wherein the means for holding the bottom surface of the housing against the skin of the user is a strap.

11. The apparatus of claim 9 or 10, wherein the display is visible to the user when the bottom surface is held against the skin of the user.

12. The apparatus of any of claims 1, 2, 4, 5 or 6, wherein the cutting member is a hollow cannula having a proximal end and a distal end, and wherein the proximal end is in juxtaposition with the electrochemical sensor to permit absorption of fluid passing through the hollow cannula by the sample uptaking or accepting member.

13. The apparatus of claim 12, comprising a plurality of electrochemical sensors.

14. The apparatus of claim 13, wherein the plurality of electrochemical sensors are provided on a disk.

15. The apparatus of any of claims 7-11, 13 or 14, further comprising a timer operatively connected to the plurality of cutting members for automatically taking and evaluating a sample at pre-defined time intervals.

16. The apparatus of claim 15, wherein the time intervals are adjusted in response to amounts of analyte as determined by the apparatus.

17. The apparatus of any preceding claim, further comprising an sample alarm for indicating to the user that sufficient sample has been collected.

18. The apparatus of any preceding claim, further comprising an testing alarm for indicating to the user that it is time to take a sample.

19. The apparatus of any preceding claim, further comprising an results alarm for indicating measured levels of analyte which are above or below preestablished thresholds.

20. The apparatus of claim 19, wherein the results alarm transmits a signal to a remote receiver.

21. A sensor assembly for electrochemical detection of an analyte when associated with a meter unit, said assembly comprising a collar member, a skin-contact ring and an electrochemical sensor, wherein

the skin-contact ring comprises a wall member having a central opening with first and second open ends formed therethrough,

the electrochemical sensor is disposed adjacent to the skin-contact ring and extends across the first open end of the skin-contact ring, said sensor comprising reagents for generation of an electrochemical signal in response to the presence of analyte and an adsorptive member for absorbing fluid placed within the central opening of the ring and transporting the fluid into reactive proximity to the reagents, and an electrical contact for transmitting the electrochemical signal from the sensor; and

the collar member comprises a wall member having a central opening for receiving a portion of the meter unit and holding it in position with respect to the electrochemical sensor and the skin-contacting portion.

22. The sensor assembly of claim 21, wherein the sensor is disposed between the skin contact ring and the collar member, and wherein the collar member further comprising an electrical connector in contact with the electrical contact portion of the electrochemical sensor for transmitted an electrical signal from the electrical contact to an electrical contact in a meter unit received within the collar member.

23. A sensor assembly for electrochemical detection of an analyte when associated with a meter unit, said assembly comprising a housing formed from a collar portion and a base portion, a cutting member in the form of a hollow tube and an electrochemical sensor, wherein

the electrochemical sensor is disposed in contact with a first surface of the base portion, said sensor comprising reagents for generation of an electrochemical signal in response to the presence of analyte and an adsorptive member for absorbing and transporting fluid into reactive proximity to the reagents, and an electrical contact for transmitting the electrochemical signal from the sensor;

the cutting member passes through the base portion thereby forming a channel for passage of fluid between the electrochemical sensor disposed in contact with the first surface of the base portion and a second opposed surface of the base portion, and

the collar portion comprises a wall member having a central opening for receiving a portion of the meter unit and an electrical connector in contact with the electrical contact of the sensor for transmitting an electrical signal from the electrical contact to an electrical contact in the meter.

24. A method for detection and quantification of an electrochemically-detectable analyte in blood or interstitial fluid, comprising the steps of:

(a) positioning an apparatus against the skin of a test subject, said apparatus comprising

a meter unit comprising a housing, means disposed within the housing for engaging a cutting member and moving an engaged cutting member, a connector disposed within the housing for engaging an electrochemical sensor specific for the analyte and transmitting a signal from the sensor indicative of the amount of analyte, and a display operatively-associated with the connector for displaying the amount of the analyte to user;

a cutting member engaged within the housing;

an electrochemical sensor comprising an sample uptaking or accepting member for the uptake of a sample of blood or interstitial fluid, wherein the means for engaging and moving the cutting member moves the cutting member in a cycle from an initial position to a piercing position in which skin of the user is pierced, and wherein the electrochemical

sensor is disposed such that the sample uptaking or accepting member takes up a sample from the pierced skin of the user when it is pierced by the lancet without movement of the apparatus;

(b) triggering the cutting member to initiate piercing of the skin of the test subject, whereby acquisition and analysis are performed as a result of triggering of the cutting member without further need to move the housing until the analysis has been performed.

25. The method of claim 24, wherein the apparatus is an apparatus in accordance with any of claims 3-20.

26. The method of claim 25, wherein the apparatus comprises a sensor assembly in accordance with any of claims 21-23.

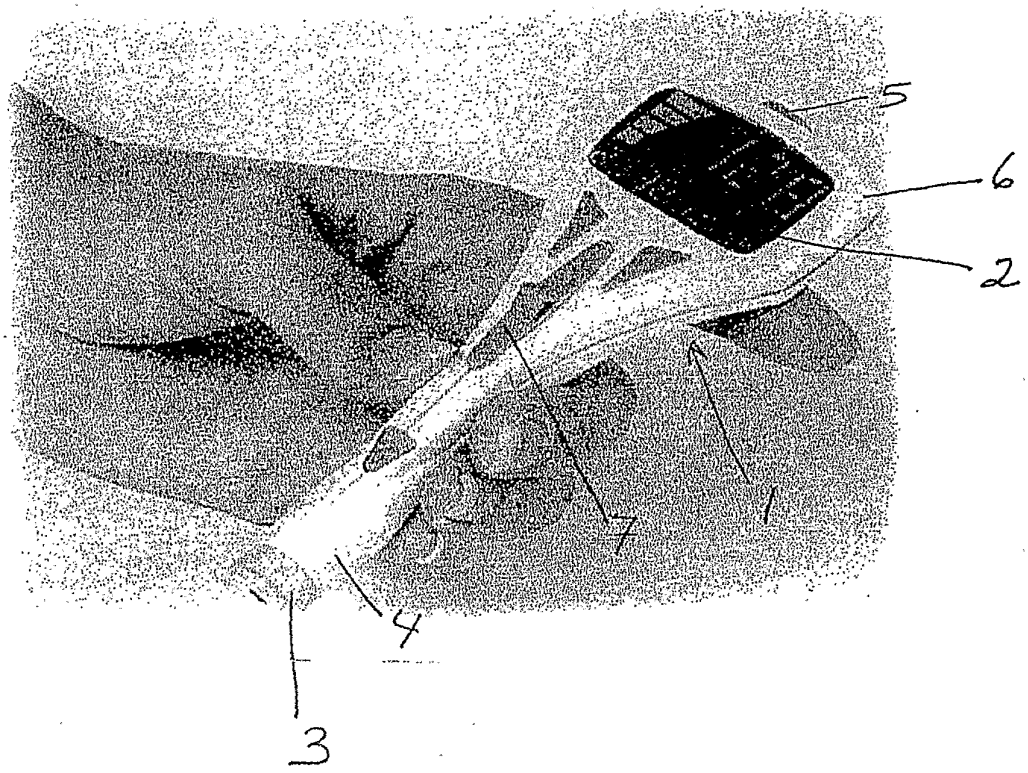


Fig. 1

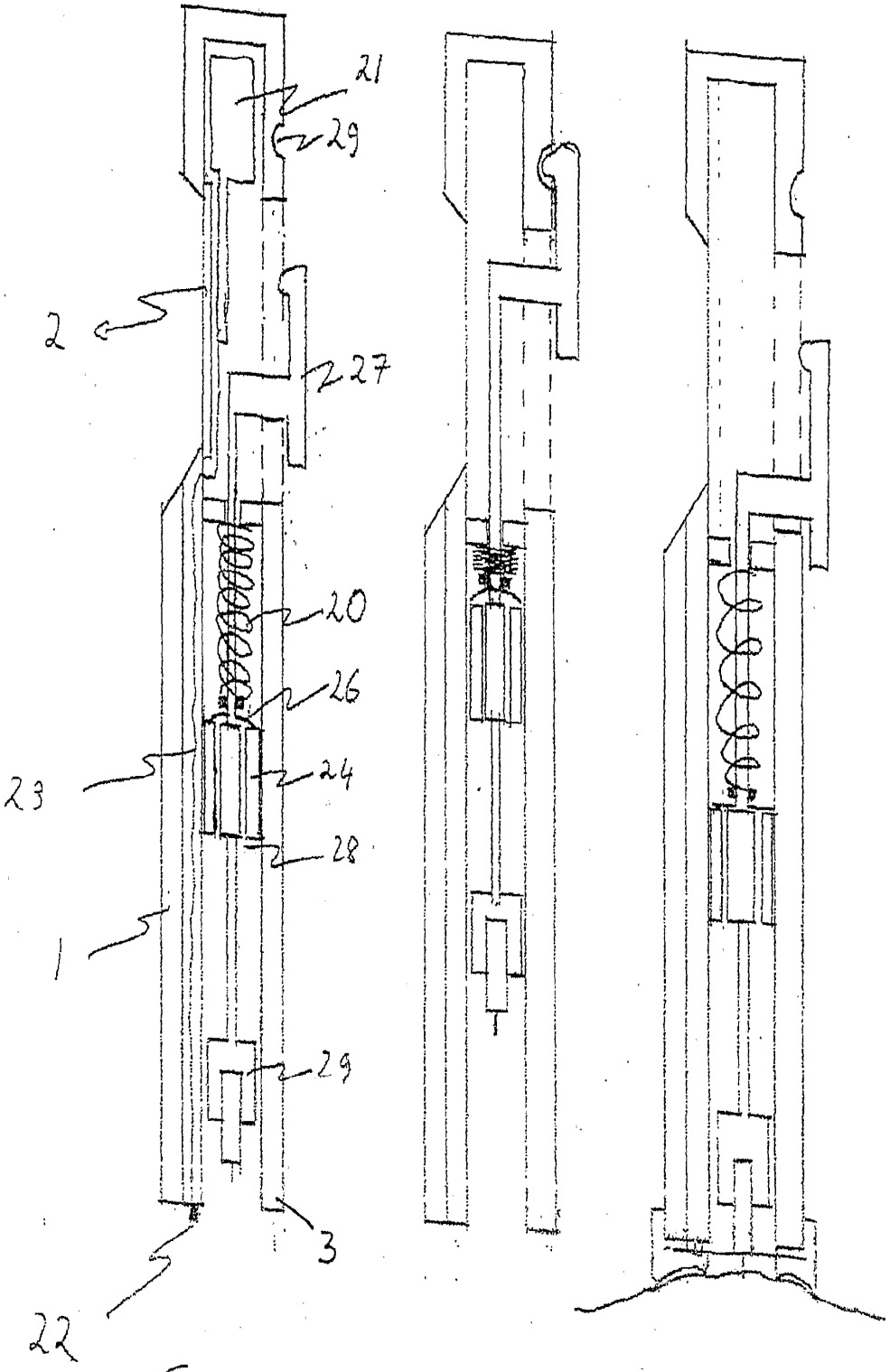


Fig2A Fig.2B Fig.2C

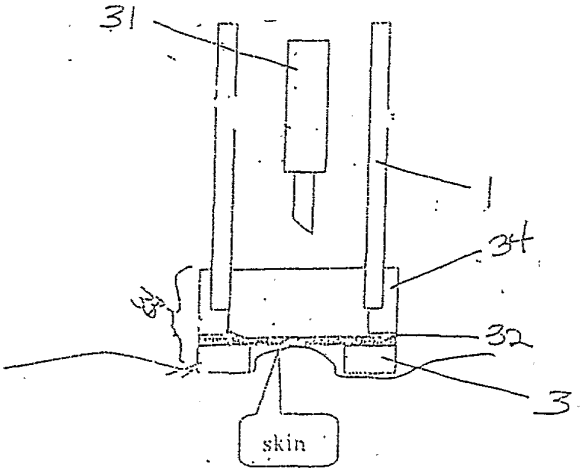


Fig. 3A

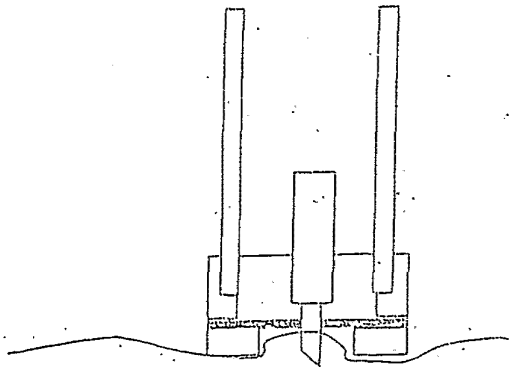


Fig. 3B

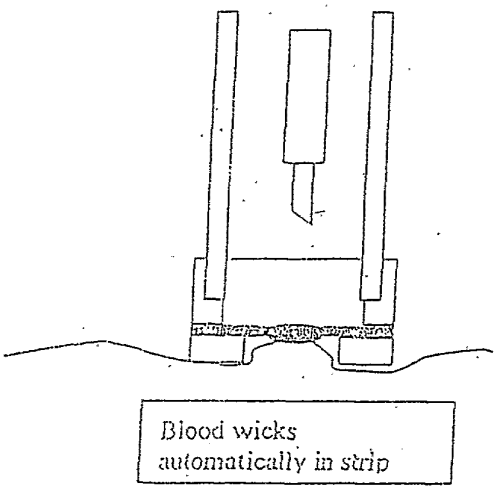


Fig. 3C

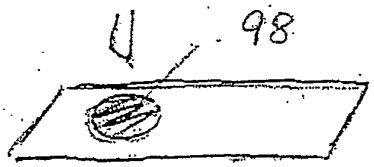


Fig 3D

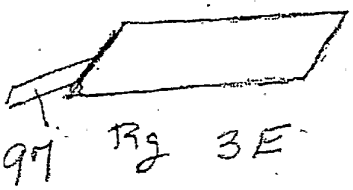


Fig 3E

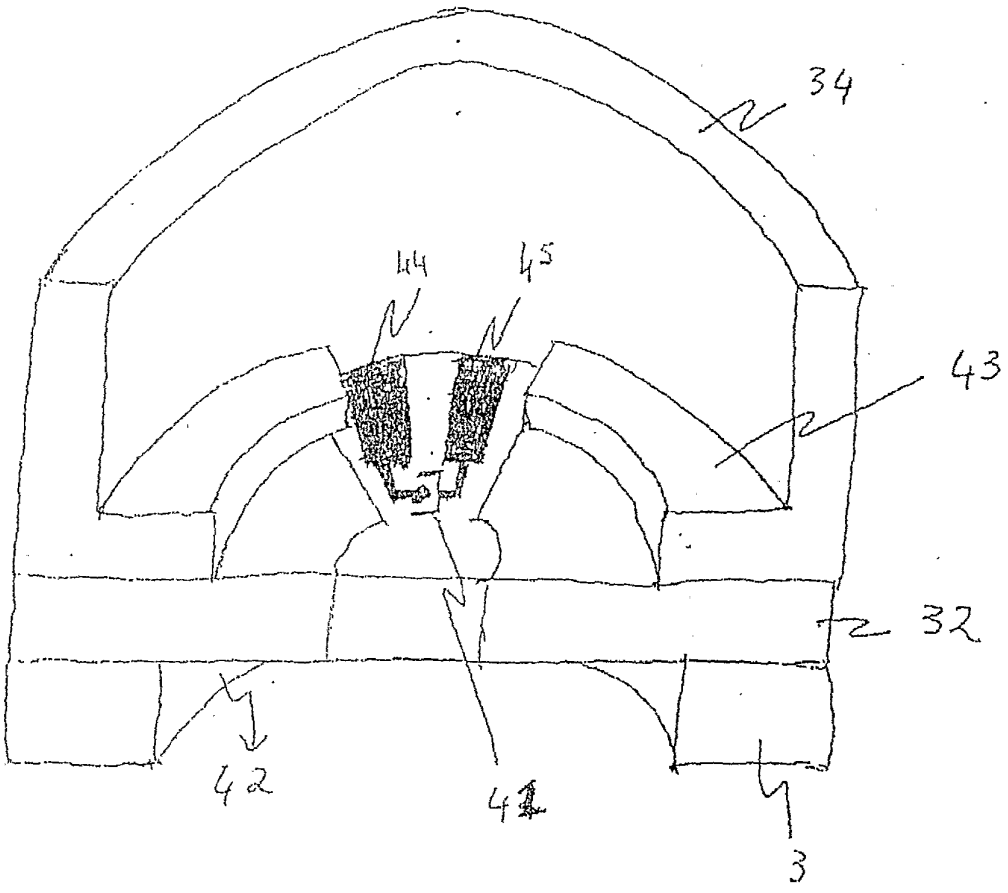


Fig 4

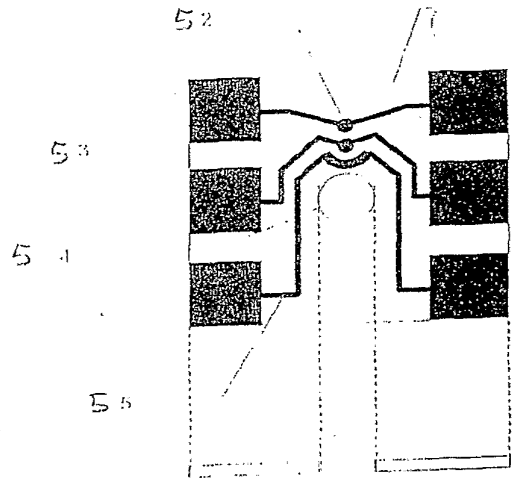


Fig 5A

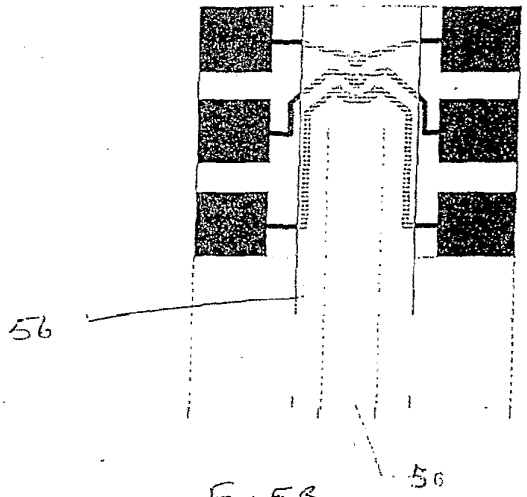


Fig 5B

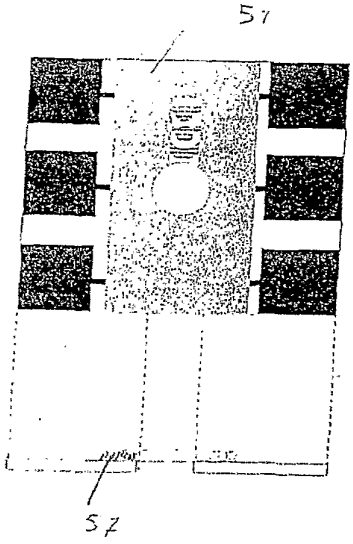


Fig 5C

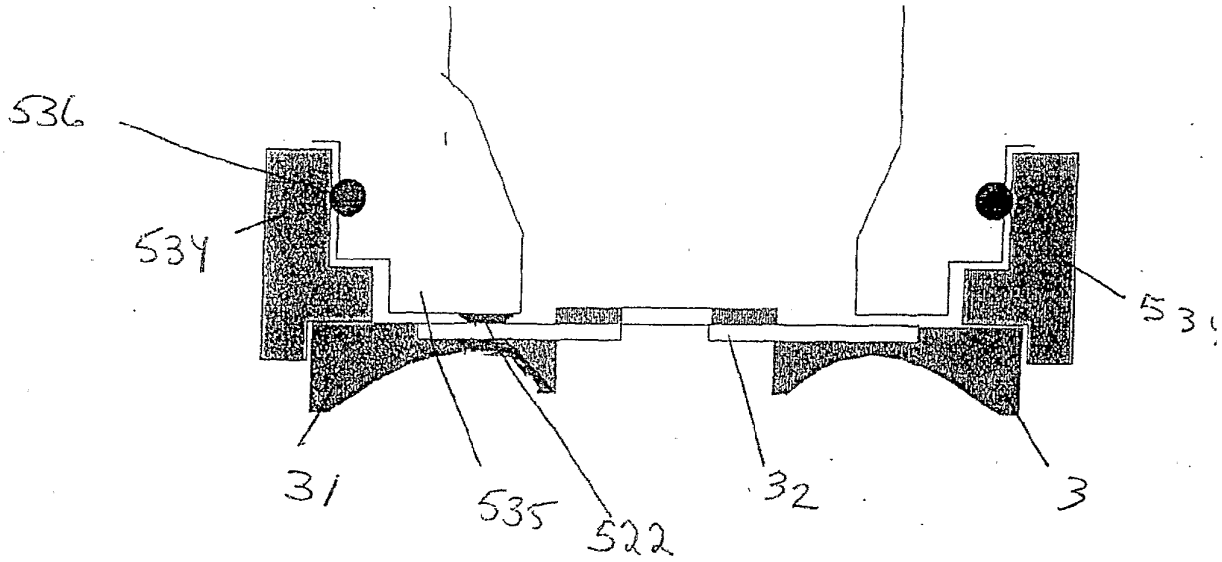


Fig. 5D

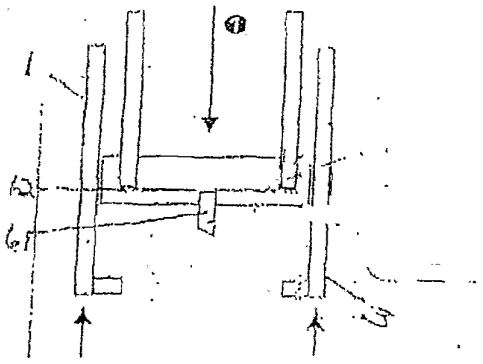


Fig. 6A

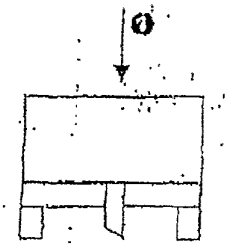


Fig 6B

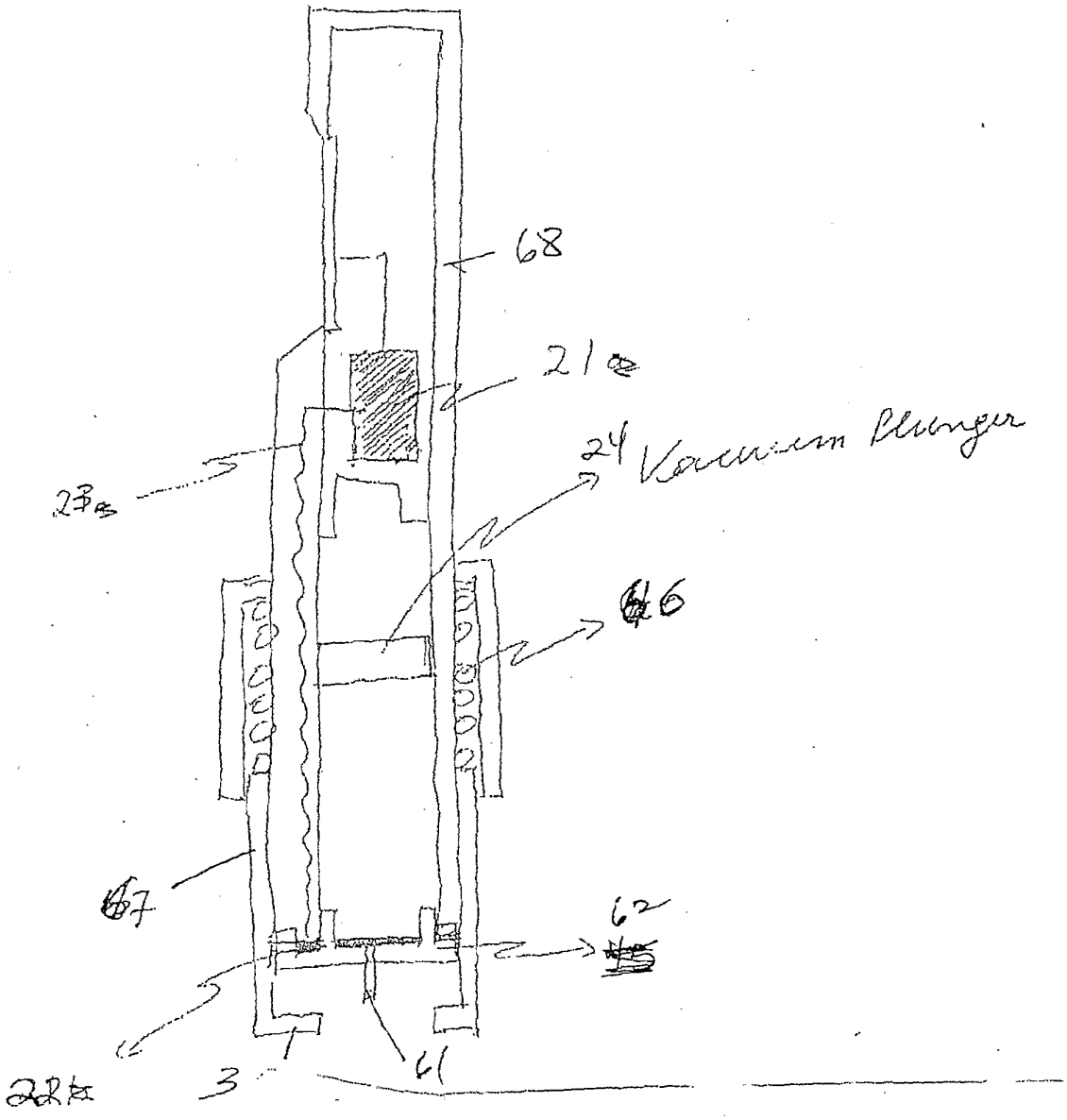


Fig. 6C

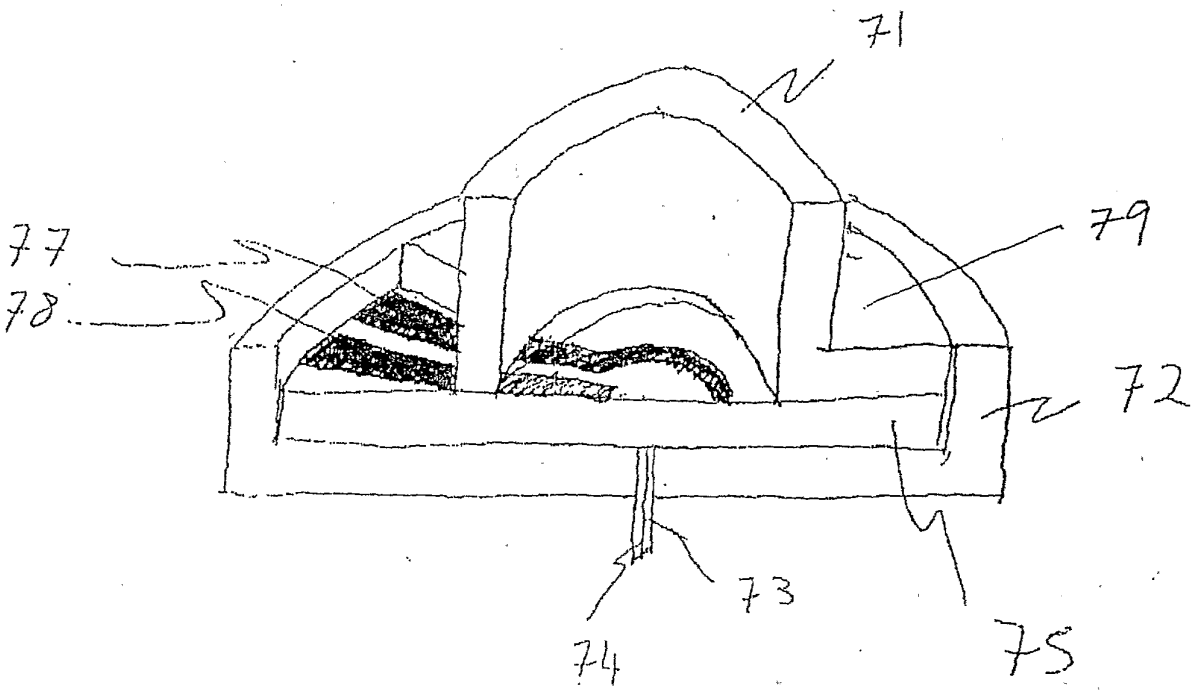


Fig. 7

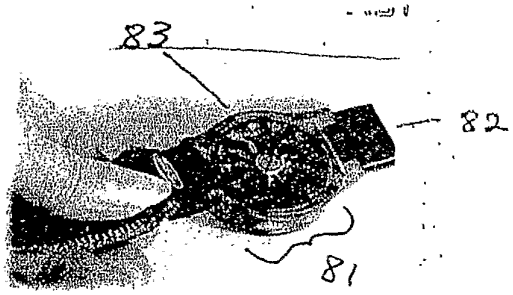


Fig 8A

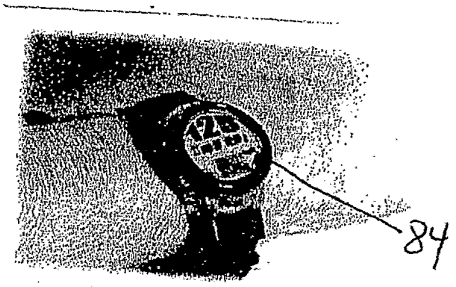


Fig 8B

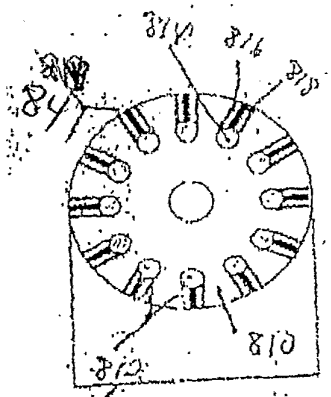


Fig. 8C

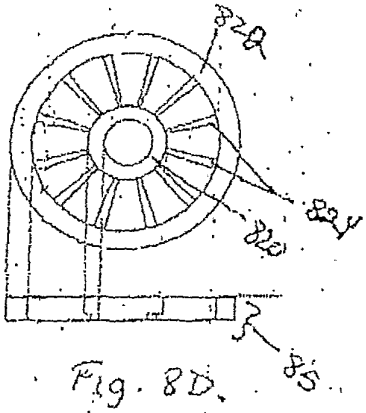


Fig. 8D

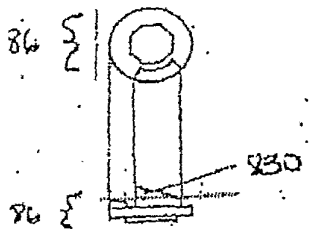


Fig. 8E

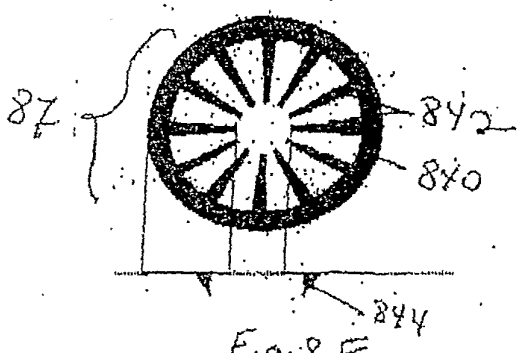


Fig 8F

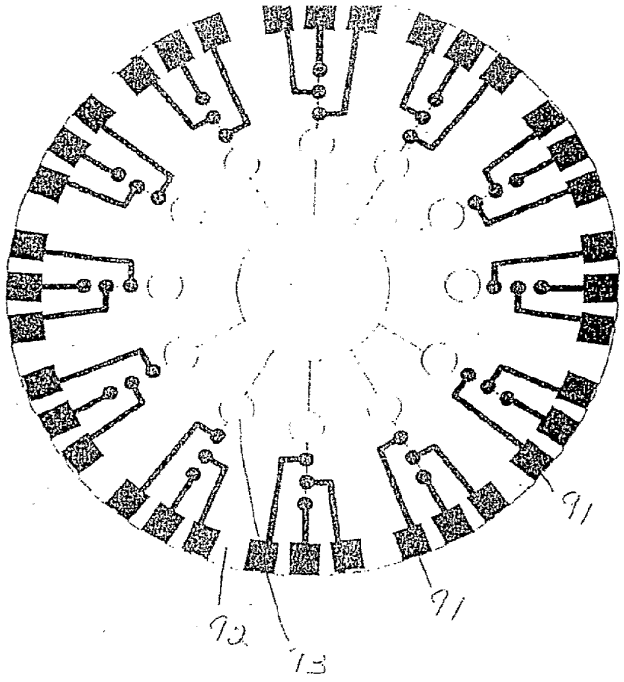


Fig 9A

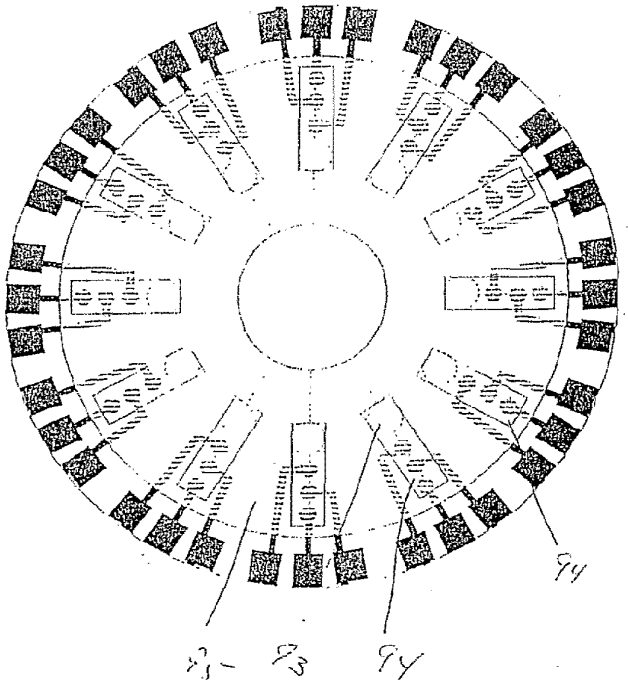


Fig 9B

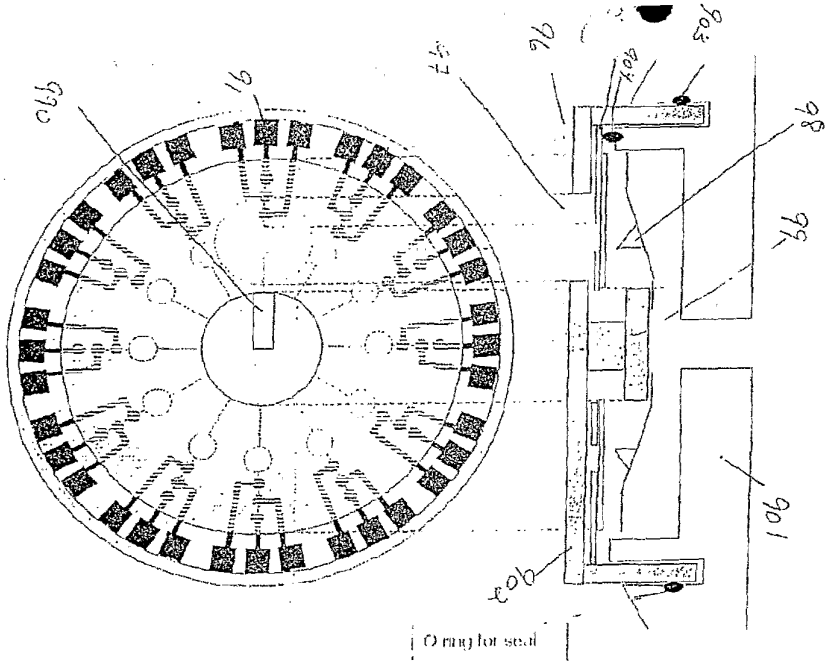

O ring for seal

Fig 9c

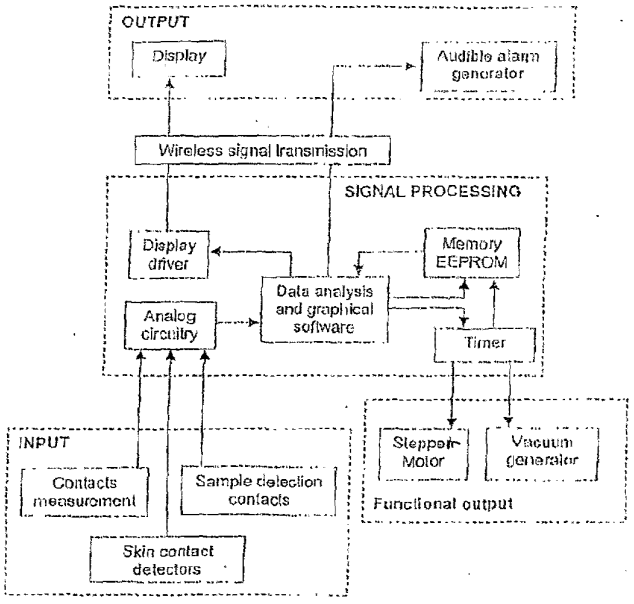

OUTPUT
Display
Audible alarm generator
Wireless signal transmission
SIGNAL PROCESSING
Display driver
Memory EEPROM
Data analysis and graphical software
Analog circuitry
Timer
INPUT
Contacts measurement
Sample detection contacts
Skin contact detectors
Stepper Motor
Vacuum generator
Functional output

Fig 10

INTERNATIONAL SEARCH REPORT

tional Application No
PCT/US 01/07169

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61B5/15 A61B5/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A61B

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

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, WPI Data, PAJ

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 97 42882 A (MERCURY DIAGNOSTICS INC) 20 November 1997 (1997-11-20)	1-5,12, 24
Y		7,8,13, 14
A	page 9, line 18 -page 11, line 21 page 11, line 34 -page 13, line 27; tables 1-5	21,23

Y	WO 97 19344 A (WILGUS ERIC S ;WARD W KENNETH (US); LEGACY GOOD SAMARITAN HOSPITAL) 29 May 1997 (1997-05-29)	7,8,13, 14
A	page 9, line 17 -page 11, line 7 page 15, line 21 -page 17, line 11; tables 1-3,7-9	16-20

	-/--	

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

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

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"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

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"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
7 August 2001	16/08/2001

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Weihs, J

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INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 01/07169

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication,where appropriate, of the relevant passages	Relevant to claim No.
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X A	WO 98 24366 A (CHAMBERS GEOFFREY R ;HUGHES GRAHAM J (GB); WATKIN JARED L (GB); GO) 11 June 1998 (1998-06-11) abstract page 7, line 21 -page 9, line 3 page 43, line 17 -page 52, line 31; tables 1-10,21,29	1-6 21,23,24
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1

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Int ational Application No
PCT/US 01/07169

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Information on patent family members

International Application No
PCT/US 01/07169

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For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

WO 02/15778 A1

(54) Title: ANALYTE MONITORING DEVICE ALARM AUGMENTATION SYSTEM

(57) Abstract: The present invention relates to a device for augmenting an alarm signal generated by an analyte monitoring device, e.g., the Gluco Watch® (Cygnus, Inc., Redwood City, CA) biographer glucose monitoring device, for improving the alarm signal's effectiveness in alerting the user, and/or for communicating the signal to a person or person(s) other than the user, or to a trained assistance animal.

Analyte Monitoring Device Alarm Augmentation System

TECHNICAL FIELD

The present invention generally relates to a system for augmenting an alarm signal from an analyte monitoring device, e.g., the GlucoWatch® (Cygnus, Inc., Redwood City, CA) biographer glucose monitoring device.

An exemplary device for use with the present invention is the GlucoWatch biographer, a device which monitors glucose levels in an individual user and generates an aural alert signal upon sensing glucose levels outside of a predetermined range, thereby alerting the user that he or she is hypo- or hyper-glycemic, and that corrective action is necessary. Further, the device sounds an alert if glucose levels are falling too rapidly. The device comprises two primary elements, a durable element (comprising a watch-type housing, display element, microprocessor element, electrical connector elements, and may further comprise a power supply) and a consumable element (e.g., an AutoSensor component involved in sampling and signal detection).

In some cases, however, an aural signal provided by an analyte monitoring device may be inadequate to alert an individual user of an analyte monitoring device that the analyte amount or concentration is not within the normal predetermined range. For example, the user may be asleep or physically impaired. Alternately, the user may be a small child or animal who is unable to take the action required, e.g., administering glucose, insulin, or alerting an adult who may provide assistance. In a worst-case scenario, the detected analyte abnormality may render the user incapable of perceiving the signal or of seeking help, such as in the case of insulin shock or diabetic coma.

In such cases, augmentation and/or transmission of the alarm signal to another person or to emergency personnel is desirable.

However, until now, an alarm augmentation system for an analyte monitoring device, e.g., the GlucoWatch biographer, has not been described or suggested.

SUMMARY OF THE INVENTION

The present invention relates to an augmented alarm system for use with an analyte monitoring device.

In a first aspect of the invention, the augmented alarm system constitutes an improvement to a pre-existing analyte monitoring device (for example, a glucose monitoring device) that provides an alert or alarm, e.g., when analyte values (or predicted analyte values) fall outside of a predetermined range. The improvement results from modification of the device's circuitry which renders the device capable of producing a auditory, visual, tactile (or kinesthetic), olfactory, or gustatory stimulus, or variations or combinations thereof. That stimulus serves as the augmented alarm signal.

In one embodiment of this first aspect of the invention, the analyte monitoring device is the GlucoWatch biographer. Typically modification of the device's system comprises changes to the durable element of the system, although the consumable component of the Glucowatch biographer (i.e., the AutoSensor) may also be modified. For example, the iontophoretic channels of the monitoring device's durable element are modified to deliver an electrical current, typically delivered through the ionically conductive material of the consumable element, so as to provide a tactile stimulus that serves as the augmented alarm signal.

In a second aspect of the invention, the augmented alarm system constitutes an improvement to a pre-existing analyte monitoring system, for example, a glucose monitoring device. In this second aspect of the invention, the improvement results from modification of the device's circuitry, typically of the durable element, to provide a connection to a first and/or second signaling component for producing alarm signals to alert a user of the monitoring device (or to alert others) to analyte levels outside of a predetermined range.

In one embodiment of this second aspect of the invention, the analyte monitoring device is the GlucoWatch biographer glucose monitoring device. Some modifications to provide a connection to a first and/or second signaling component include, but are not limited to, modifications to the following elements of the durable component: reconfiguring the confidence loop of the analyte monitoring device, modifying the transmission and receipt lines, modifying the sweat probes, or adding a serial port, which is placed in operative communication with the analyte monitoring device. In one aspect, the connection may be via a wire-like connector or alternately, via a telemetering system. The telemetering system may take a variety of forms, including but not limited to, electromagnetic radiation,

capacitance coupling, inductive coupling, infrared coupling, and may further include variations and combinations thereof. In yet another embodiment, the first signaling component may be an auditory stimulus generator, a visual stimulus generator, a tactile stimulus generator (including but not limited to a kinesthetic stimulus generator), an olfactory stimulus generator, a gustatory stimulus generator, or variations or combinations thereof.

In a third aspect of the invention, the augmented alarm system may be an integral part of an analyte monitoring device, for example, a glucose monitoring device. The analyte monitoring device may comprise (a) an acquisition unit capable of at least sensing or detecting analyte concentrations or amounts in a subject; (b) a display unit, operably linked to said acquisition unit, wherein (i) the display unit comprises means to provide an audible alert when an analyte level, in a subject being monitored, is outside of a predetermined range, and (ii) the acquisition unit and the display units are separately housed; and (c) an alarm augmentation system comprising a first signaling component, capable of producing alarm signals to alert a subject in response to analyte levels outside of a predetermined range. The first signaling component is typically operably linked to the display unit. In this embodiment the acquisition unit and the display unit, each operably connected to the other, are typically separately housed. The augmented alarm system may be housed with the display unit, or separately housed as well. In one embodiment, the display unit comprises at least a first signaling component, operably connected to the display unit, for producing augmented alarm signals to alert a user in response to analyte levels outside of a predetermined range.

In one embodiment of this third aspect of the invention, the first signaling component is a stimulus generator capable of generating auditory, visual, tactile (including but not limited to kinesthetic), olfactory or gustatory stimuli, or variations or combinations thereof. In one exemplary embodiment, the first signaling component is an auditory stimulus generator which provides a volume control for varying the volume of auditory stimuli.

In another embodiment of this third aspect, the display unit further includes a transmitter component that is operably linked to the display unit, for transmitting alarm signals to at least one external communication target; it may also provide an operative link

between the display unit and the first signaling component. The transmitter component may take the form of a serial port and a wire-like connector, the port being capable of connecting with one or more external communication targets; alternately, the transmitter component may be a telemetering system. A variety of possible telemetering systems may be employed, which include but are not limited to electromagnetic radiation, capacitance coupling, inductive coupling, infrared coupling, and may further include variations or combinations thereof.

In yet another embodiment of the third aspect of the invention, the telemetering system may be capable of connecting with other alarm augmentation system components, including but not limited to first and/or second signaling components.

In still another embodiment, the analyte monitoring device with alarm augmentation system may further include a second signaling component, for example, operably linked to the transmitter component via a telemetering system, for producing alarm signals to alert a person or persons other than the user of the analyte monitoring device to analyte levels outside of a predetermined range. The second signaling component may be an auditory, visual, tactile (including, but not limited to kinesthetic), olfactory, or gustatory stimulus generator, or variations or combinations thereof.

In a further embodiment of the third aspect of the invention, the analyte monitoring device may further include a processor component, which is operably linked to the acquisition unit, the display unit, the transmitter component, and the first and second signaling components. The processor component may be capable of receiving and processing information received from the acquisition unit and the first and second signaling components, and may further be capable of controlling the operation of the transmitter component as well as the first and second signaling components.

These and other embodiments of the present invention will readily occur to those of ordinary skill in the art in view of the disclosure herein.

BRIEF DESCRIPTION OF THE FIGURE

Figure 1 presents a schematic of an exploded view of exemplary components comprising one embodiment of an AutoSensor for use in an analyte monitoring system.

DESCRIPTION OF THE INVENTION

1. Definitions

It is to be understood that the terminology used herein is for the purpose of describing particular embodiments only, and is not intended to be limiting. As used in this specification and the appended claims, the singular forms "a", "an" and "the" include plural referents unless the context clearly dictates otherwise. Thus, for example, reference to "a reservoir" includes a combination of two or more such reservoirs, reference to "an analyte" includes mixtures of analytes, and the like.

Unless defined otherwise, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which the invention pertains. Although other methods and materials similar, or equivalent, to those described herein can be used in the practice of the present invention, the preferred materials and methods are described herein.

In describing and claiming the present invention, the following terminology will be used in accordance with the definitions set out below.

The term "microprocessor" refers to a computer processor contained on an integrated circuit chip, such a processor may also include memory and associated circuits. A microprocessor may further comprise programmed instructions to execute or control selected functions, computational methods, switching, etc. Microprocessors and associated devices are commercially available from a number of sources, including, but not limited to, Cypress Semiconductor Corporation, San Jose, CA; IBM Corporation, White Plains, New York; Applied Microsystems Corporation, Redmond, WA; Intel Corporation, Chandler, Arizona; and, National Semiconductor, Santa Clara, CA.

The terms "analyte" and "target analyte" are used to denote any physiological analyte of interest that is a specific substance or component that is being detected and/or measured in a chemical, physical, enzymatic, or optical analysis. A detectable signal (e.g., a chemical signal or electrochemical signal) can be obtained, either directly or indirectly, from such an analyte or derivatives thereof. Furthermore, the terms "analyte" and "substance" are used interchangeably herein, and are intended to have the same meaning, and thus encompass any substance of interest. In preferred embodiments, the

analyte is a physiological analyte of interest, for example, glucose, or a chemical that has a physiological action, for example, a drug or pharmacological agent.

A "sampling device," "sampling mechanism" or "sampling system" refers to any device and/or associated method for obtaining a sample from a biological system for the purpose of determining the concentration of an analyte of interest. Such "biological systems" include any biological system from which the analyte of interest can be extracted, including, but not limited to, blood, interstitial fluid, perspiration and tears. Further, a "biological system" includes both living and artificially maintained systems. The term "sampling" mechanism refers to extraction of a substance from the biological system, generally across a membrane such as the stratum corneum or mucosal membranes, wherein said sampling is invasive, minimally invasive, semi-invasive or non-invasive. The membrane can be natural or artificial, and can be of plant or animal nature, such as natural or artificial skin, blood vessel tissue, intestinal tissue, and the like. Typically, the sampling mechanism is in operative contact with a "reservoir," or "collection reservoir," wherein the sampling mechanism is used for extracting the analyte from the biological system into the reservoir to obtain the analyte in the reservoir. Non-limiting examples of sampling techniques include iontophoresis, sonophoresis (see, e.g., International Publication No. WO 91/12772, published 5 September 1991; U.S. Patent No. 5,636,632), suction, electroporation, thermal poration, passive diffusion (see, e.g., International Publication Nos.: WO 97/38126 (published 16 October 1997); WO 97/42888, WO 97/42886, WO 97/42885, and WO 97/42882 (all published 20 November 1997); and WO 97/43962 (published 27 November 1997)), microfine (miniature) lances or cannulas, biolistic (e.g., using particles accelerated to high speeds), subcutaneous implants or insertions, and laser devices (see, e.g., Jacques et al. (1978) J. Invest. Dermatology 88:88-93; International Publication WO 99/44507, published 1999 September 10; International Publication WO 99/44638, published 1999 September 10; and International Publication WO 99/40848, published 1999 August 19). Iontophoretic sampling devices are described, for example, in International Publication No. WO 97/24059, published 10 July 1997; European Patent Application EP 0942 278, published 15 September 1999; International Publication No. WO 96/00110, published 4 January 1996; International Publication No. WO 97/10499, published 2 March 1997; U.S. Patent

Numbers 5,279,543; 5,362,307; 5,730,714; 5,771,890; 5,989,409; 5,735,273; 5,827,183; 5,954,685 and 6,023,629. Further, a polymeric membrane may be used at, for example, the electrode surface to block or inhibit access of interfering species to the reactive surface of the electrode.

The term "physiological fluid" refers to any desired fluid to be sampled, and includes, but is not limited to, blood, cerebrospinal fluid, interstitial fluid, semen, sweat, saliva, urine and the like.

The term "artificial membrane" or "artificial surface," refers to, for example, a polymeric membrane, or an aggregation of cells of monolayer thickness or greater which are grown or cultured in vivo or in vitro, wherein said membrane or surface functions as a tissue of an organism but is not actually derived, or excised, from a pre-existing source or host.

A "monitoring system" or "analyte monitoring device" refer to a system useful for obtaining frequent measurements of a physiological analyte present in a biological system. Such a device is useful, for example, for monitoring the amount or concentration of an analyte in a subject. Such a system may comprise, but is not limited to, a sampling mechanism, a sensing mechanism, and a microprocessor mechanism in operative communication with the sampling mechanism and the sensing mechanism. Such a device typically provides frequent measurement or determination of analyte amount or concentration in the subject and provides an alert or alerts when levels of the analyte being monitored fall outside of a predetermined range. Such devices may comprise durable and consumable (or disposable) elements. The term "glucose monitoring device" refers to a device for monitoring the amount or concentration of glucose in a subject. Such a device typically provides a frequent measurement or determination of glucose amount or concentration in the subject and provides an alert or alerts when glucose levels fall outside of a predetermined range. One such exemplary glucose monitoring device is the GlucoWatch biographer available from Cygnus, Inc., Redwood City, CA, US. The GlucoWatch biographer comprises two primary elements, a durable element (comprising a watch-type housing, circuitry, display element, microprocessor element, electrical connector elements, and may further comprise a power supply) and a consumable, or disposable, element (e.g., an AutoSensor component involved in sampling and signal

detection, see, for example, WO 99/58190, published 18 November 1999). This and similar devices is described, for example, in the following publications: Tamada, et al., (1999) *JAMA* 282:1839-1844; U.S. Patent No. 5,771,890, issued 30 June 1998; U.S. Patent No. 5, 735,273, issued 7 April 1998; U.S. Patent No. 5,827,183, issued 27 October 1998; U.S. Patent No. 5,954,685, issued 21 September 1999; U.S. Patent No. 5,989,409, issued 23 November 1999; U.S. Patent No. 6,023,629, issued 8 February 2000; EP Patent Application EP 0 942 278 A2, published 15 Sept. 1999; PCT International Application WO 96/001100, published 4 January 1996; PCT International Application WO 99/58190, published 18 November 1999. The GlucoWatch biographer provides a device for frequent sampling of glucose from a subject the application of low intensity electric fields across the skin (iontophoresis) to enhance the transport of glucose from body tissues to a sampling chamber. In addition, when the concentration or amount of glucose has been determined to be outside of a predetermined range of values the GlucoWatch biographer produces an alert or alarm signal. Such an alert or alarm is a component of the GlucoWatch biographer.

In a further embodiment, the analyte monitoring device of the present invention may comprise an "acquisition unit" and a "display unit." An "acquisition unit" is a device that is capable of at least sensing or detecting analyte concentrations or amounts (e.g., a sensing device, or an analyte monitoring device comprising sampling and sensing devices) and of transmitting that data to a "display unit." In turn, a "display unit" is a device capable of receiving data from an acquisition unit and exhibiting that data using, e.g., an LCD screen. The acquisition unit and display unit may be contained together in a single housing, or separately housed.

The terms "alarm augmentation system," and "alarm system" are used interchangeably herein, and refer to the analyte monitoring device alarm augmentation system that is the subject of the present invention, for example, the GlucoWatch biographer provides an alert to the user and a glucose monitoring device alarm augmentation system may be used to provide an enhanced alarm as described herein.

A "component" is a conceptual part of the entire alarm augmentation system of the present invention which performs a particular function. Thus, a "component" may comprise more than one physical part or device. Similarly, a "sub-component" is a

conceptual sub-part of a component which performs a particular function. As is the case for a component, a "sub-component" may comprise more than one physical part or device.

"Signaling components" are devices capable of augmenting the analyte monitoring device alert or alarm signal, for example, the GlucoWatch biographer's alert signal, by generating a sensory stimulus, and thereby alerting persons to analyte levels outside of a predetermined range. A "first signaling component" typically serves to alert the user of the monitoring device or someone in close proximity; a "second signaling component" typically serves to alert persons other than the user. In general, signaling components are capable of generating sensory stimuli of at least one of the following types: (i) auditory; (ii) visual; (iii) tactile, including but not limited to kinesthetic; (iv) olfactory; (v) gustatory; and (vi) variations and combinations thereof.

A "transmitter component" is a device capable of communicating an alarm signal to an external communication target, and/or to first and/or second signaling components, when present.

A "processor component" refers to a component capable of integrating alarm signals received from the GlucoWatch biographer and from the other alarm system components, as well as controlling the functioning of the other components.

The term "housing" refers to a structure that physically contains a component or components of the alarm augmentation system of the present invention. The housing may be of any suitable material, including plastic. "Components within a single housing" are those contained within a single structure, as distinguished from "components within several housings" or "components each within individual housings," etc.

"Operably connected" means any kind of telemetric or hard link by which data may be communicated between or among the analyte monitoring device and/or the component(s) of the alarm augmentation system of the present invention.

The terms "wire-like," "cable-like," and "hard link" are terms that refer to tangible connections capable of transmitting data. Transmission may occur electronically or by other methods, e.g., via transmission of light pulses along fiber optic cables. In contrast, the terms "wireless" or "telemetric" intend devices capable of transmitting data without a tangible connection. Examples of telemetric communication methods include

electromagnetic waves and infrared radiation, and are further described in the subsection entitled "Intra- and inter-system communication" appearing below.

A "measurement cycle" typically comprises extraction of an analyte from a subject, using, for example, a sampling device, and sensing of the extracted analyte, for example, using a sensing device, to provide a measured signal, for example, a measured signal response curve. A complete measurement cycle may comprise one or more sets of extraction and sensing.

The term "frequent measurement" refers to a series of two or more measurements obtained from a particular biological system, which measurements are obtained using a single device maintained in operative contact with the biological system over a time period in which a series of measurements (e.g., second, minute or hour intervals) is obtained. The term thus includes continual and continuous measurements.

The term "subject" encompasses any warm-blooded animal, particularly including a member of the class Mammalia such as, without limitation, humans and nonhuman primates such as chimpanzees and other apes and monkey species; farm animals such as cattle, sheep, pigs, goats and horses; domestic mammals such as dogs and cats; laboratory animals including rodents such as mice, rats and guinea pigs, and the like. The term does not denote a particular age or sex and, thus, includes adult and newborn subjects, whether male or female. A "user" or "subject" refers to a person or animal whose analyte levels are being monitored by an analyte monitoring device. Thus, for example, a user or subject of the GlucoWatch biographer, glucose monitoring device is one whose glucose levels are being monitored by that device.

The terms "another" and "others" refer to a person or to persons, respectively, other than a "user" or "subject" as defined above. Further, these terms may refer to an animal that, for example, is trained as an assistance animal (e.g., guide dogs, service dogs, seizure alert dogs, etc.).

The term "emergency personnel" refers to persons such as paramedics, firepersons, policepersons, and others trained to respond to medical emergencies who are available to respond and who may respond upon being summoned.

An "external communication target" is an entity that is the target of data communicated by the transmitter component of the alarm system. Such targets may

include, but are not limited to, the following: (1) pagers, for example, pagers carried by a significant other, parent, relative or other care giver, or by the user's physician; (2) computers, such as the computer of the user's physician or of a health-care facility; and (3) phone lines, such as 911 emergency response lines, the phone line of a physician or of a parent, significant other, relative or care-giver. Additional targets may be apparent to persons of ordinary skill in the art, in light of the teachings of the present specification.

The term "transdermal" includes both transdermal and transmucosal techniques, i.e., extraction of a target analyte across skin, e.g., stratum corneum, or mucosal tissue. Aspects of the invention which are described herein in the context of "transdermal," unless otherwise specified, are meant to apply to both transdermal and transmucosal techniques.

The term "transdermal extraction," or "transdermally extracted" refers to any sampling method, which entails extracting and/or transporting an analyte from beneath a tissue surface across skin or mucosal tissue. The term thus includes extraction of an analyte using, for example, iontophoresis (reverse iontophoresis), electroosmosis, sonophoresis, microdialysis, suction, and passive diffusion. These methods can, of course, be coupled with application of skin penetration enhancers or skin permeability enhancing technique such as various substances or physical methods such as tape stripping or pricking with micro-needles. The term "transdermally extracted" also encompasses extraction techniques which employ thermal poration, laser microporation, electroporation, microfine lances, microfine cannulas, subcutaneous implants or insertions, combinations thereof, and the like.

The term "iontophoresis" refers to a method for transporting substances across tissue by way of an application of electrical energy to the tissue. In conventional iontophoresis, a reservoir is provided at the tissue surface to serve as a container of (or to provide containment for) material to be transported. Iontophoresis can be carried out using standard methods known to those of skill in the art, for example by establishing an electrical potential using a direct current (DC) between fixed anode and cathode "iontophoretic electrodes," alternating a direct current between anode and cathode iontophoretic electrodes, or using a more complex waveform such as applying a current with alternating polarity (AP) between iontophoretic electrodes (so that each electrode is

alternately an anode or a cathode). For example, see U.S. Patent Nos. 5,771,890 and 6,023,629 and PCT Publication No. WO 96/00109, published 4 January 1996.

The term "reverse iontophoresis" refers to the movement of a substance from a biological fluid across a membrane by way of an applied electric potential or current. In reverse iontophoresis, a reservoir is provided at the tissue surface to receive the extracted material, as used in the GlucoWatch® (Cygnus, Inc., Redwood City, CA) biographer glucose monitor (See, e.g., Tamada, et al. (1999) JAMA 282:1839-1844).

"Electroosmosis" refers to the movement of a substance through a membrane by way of an electric field-induced convective flow. The terms iontophoresis, reverse iontophoresis, and electroosmosis, will be used interchangeably herein to refer to movement of any ionically charged or uncharged substance across a membrane (e.g., an epithelial membrane) upon application of an electric potential to the membrane through an ionically conductive medium.

The term "sensing device," or "sensing mechanism," encompasses any device that can be used to measure the concentration or amount of an analyte, or derivative thereof, of interest in a subject. Preferred sensing devices for detecting analytes generally include electrochemical devices, optical and chemical devices and combinations thereof. Examples of electrochemical devices include the Clark electrode system (see, e.g., Updike, et al., (1967) Nature 214:986-988), and other amperometric, coulometric, or potentiometric electrochemical devices, as well as, optical methods, for example UV detection or infrared detection (e.g., U. S. Patent No. 5,747,806).

A "biosensor" or "biosensor device" includes, but is not limited to, a "sensor element" that includes, but is not limited to, a "biosensor electrode" or "sensing electrode" or "working electrode" which refers to the electrode that is monitored to determine the amount of electrical signal at a point in time or over a given time period, which signal is then correlated with the concentration of a chemical compound. The sensing electrode comprises a reactive surface which converts the analyte, or a derivative thereof, to electrical signal. The reactive surface can be comprised of any electrically conductive material such as, but not limited to, platinum-group metals (including, platinum, palladium, rhodium, ruthenium, osmium, and iridium), nickel, copper, and silver, as well as, oxides, and dioxides, thereof, and combinations or alloys of the

foregoing, which may include carbon as well. Some catalytic materials, membranes, and fabrication technologies suitable for the construction of amperometric biosensors are described by Newman, J.D., et al.(1995) Analytical Chemistry 67:4594-4599.

The "sensor element" can include components in addition to the sensing electrode, for example, it can include a "reference electrode" and a "counter electrode." The term "reference electrode" is used to mean an electrode that provides a reference potential, e.g., a potential can be established between a reference electrode and a working electrode. The term "counter electrode" is used to mean an electrode in an electrochemical circuit that acts as a current source or sink to complete the electrochemical circuit. Although it is not essential that a counter electrode be employed where a reference electrode is included in the circuit and the electrode is capable of performing the function of a counter electrode, it is preferred to have separate counter and reference electrodes because the reference potential provided by the reference electrode is most stable when it is at equilibrium. If the reference electrode is required to act further as a counter electrode, the current flowing through the reference electrode may disturb this equilibrium. Consequently, separate electrodes functioning as counter and reference electrodes are preferred.

In one embodiment, the "counter electrode" of the "sensor element" comprises a "bimodal electrode." The term "bimodal electrode" typically refers to an electrode which is capable of functioning non-simultaneously as, for example, both the counter electrode (of the "sensor element") and the iontophoretic electrode (of the "sampling mechanism") as described, for example, U.S. Patent No. 5,954,685.

The terms "reactive surface," and "reactive face" are used interchangeably herein to mean the surface of the sensing electrode that: (1) is in contact with the surface of an ionically conductive material which contains an analyte or through which an analyte, or a derivative thereof, flows from a source thereof; (2) is comprised of a catalytic material (e.g., a platinum group metal, platinum, palladium, rhodium, ruthenium, or nickel and/or oxides, dioxides and combinations or alloys thereof) or a material that provides sites for electrochemical reaction; (3) converts a chemical signal (for example, hydrogen peroxide) into an electrical signal (e.g., an electrical current); and (4) defines the electrode surface area that, when composed of a reactive material, is sufficient to drive

the electrochemical reaction at a rate sufficient to generate a detectable, reproducibly measurable, electrical signal that is correlatable with the amount of analyte present in the electrolyte.

An "ionically conductive material" refers to any material that provides ionic conductivity, and through which electrochemically active species can diffuse. The ionically conductive material can be, for example, a solid, liquid, or semi-solid (e.g., in the form of a gel) material that contains an electrolyte, which can be composed primarily of water and ions (e.g., sodium chloride), and generally comprises 50% or more water by weight. The material can be in the form of a hydrogel, a sponge or pad (e.g., soaked with an electrolytic solution), or any other material that can contain an electrolyte and allow passage of electrochemically active species, especially the analyte of interest. Some exemplary hydrogel formulations are described in WO 97/02811, published Jan. 30, 1997. The ionically conductive material may comprise a biocide. For example, during manufacture of an AutoSensor assembly, one or more biocides may be incorporated into the ionically conductive material. Biocides of interest include, but are not limited to, compounds such as chlorinated hydrocarbons; organometallics; hydrogen releasing compounds; metallic salts; organic sulfur compounds; phenolic compounds (including, but not limited to, a variety of Nipa Hardwicke Inc. liquid preservatives registered under the trade names Nipastat®, Nipaguard®, Phenosept®, Phenonip®, Phenoxetol®, and Nipacide®); quaternary ammonium compounds; surfactants and other membrane-disrupting agents (including, but not limited to, undecylenic acid and its salts), combinations thereof, and the like.

The term "buffer" refers to one or more components which are added to a composition in order to adjust or maintain the pH of the composition.

The term "electrolyte" refers to a component of the ionically conductive medium which allows an ionic current to flow within the medium. This component of the ionically conductive medium can be one or more salts or buffer components, but is not limited to these materials.

The term "collection reservoir" is used to describe any suitable containment method or device for containing a sample extracted from a biological system. For example, the collection reservoir can be a receptacle containing a material which is

ionically conductive (e.g., water with ions therein), or alternatively it can be a material, such as a sponge-like material or hydrophilic polymer, used to keep the water in place. Such collection reservoirs can be in the form of a hydrogel (for example, in the shape of a disk or pad). Hydrogels are typically referred to as "collection inserts." Other suitable collection reservoirs include, but are not limited to, tubes, vials, strips, capillary collection devices, cannulas, and miniaturized etched, ablated or molded flow paths.

A "collection insert layer" is a layer of an assembly or laminate comprising a collection reservoir (or collection insert) located, for example, between a mask layer and a retaining layer.

A "laminate" refers to structures comprised of, at least, two bonded layers. The layers may be bonded by welding or through the use of adhesives. Examples of welding include, but are not limited to, the following: ultrasonic welding, heat bonding, and inductively coupled localized heating followed by localized flow. Examples of common adhesives include, but are not limited to, chemical compounds such as, cyanoacrylate adhesives, and epoxies, as well as adhesives having such physical attributes as, but not limited to, the following: pressure sensitive adhesives, thermoset adhesives, contact adhesives, and heat sensitive adhesives.

A "collection assembly" refers to structures comprised of several layers, where the assembly includes at least one collection insert layer, for example a hydrogel. An example of a collection assembly as referred to in the present invention is a mask layer, collection insert layer, and a retaining layer where the layers are held in appropriate functional relationship to each other but are not necessarily a laminate (i.e., the layers may not be bonded together. The layers may, for example, be held together by interlocking geometry or friction).

The term "mask layer" refers to a component of a collection assembly that is substantially planar and typically contacts both the biological system and the collection insert layer. See, for example, U.S. Patent Nos. 5,735,273, 5,827,183, and 6,201,979.

The term "gel retaining layer" or "gel retainer" refers to a component of a collection assembly that is substantially planar and typically contacts both the collection insert layer and the electrode assembly.

The term "support tray" typically refers to a rigid, substantially planar platform and is used to support and/or align the electrode assembly and the collection assembly. The support tray provides one way of placing the electrode assembly and the collection assembly into the sampling system.

An "AutoSensor assembly" refers to a structure generally comprising a mask layer, collection insert layer, a gel retaining layer, an electrode assembly, and a support tray. The AutoSensor assembly may also include liners where the layers are held in approximate, functional relationship to each other. Exemplary collection assemblies and AutoSensor structures are described, for example, in International Publication WO 99/58190, published 18 November 1999; and U.S. Patent Numbers 5,735,273 and 5,827,183. The mask and retaining layers are preferably composed of materials that are substantially impermeable to the analyte (chemical signal) to be detected; however, the material can be permeable to other substances. By "substantially impermeable" is meant that the material reduces or eliminates chemical signal transport (e.g., by diffusion). The material can allow for a low level of chemical signal transport, with the proviso that chemical signal passing through the material does not cause significant edge effects at the sensing electrode.

The terms "about" or "approximately" when associated with a numeric value refers to that numeric value plus or minus 10 units of measure (i.e. percent, grams, degrees or volts), preferably plus or minus 5 units of measure, more preferably plus or minus 2 units of measure, most preferably plus or minus 1 unit of measure.

By the term "printed" is meant a substantially uniform deposition of an electrode formulation onto one surface of a substrate (i.e., the base support). It will be appreciated by those skilled in the art that a variety of techniques may be used to effect substantially uniform deposition of a material onto a substrate, e.g., Gravure-type printing, extrusion coating, screen coating, spraying, painting, electroplating, laminating, or the like.

The term "physiological effect" encompasses effects produced in the subject that achieve the intended purpose of a therapy. In preferred embodiments, a physiological effect means that the symptoms of the subject being treated are prevented or alleviated. For example, a physiological effect would be one that results in the prolongation of survival in a patient.

"Parameter" refers to an arbitrary constant or variable so appearing in a mathematical expression that changing it give various cases of the phenomenon represented (McGraw-Hill Dictionary of Scientific and Technical Terms, S.P. Parker, ed., Fifth Edition, McGraw-Hill Inc., 1994). In the context of the GlucoWatch biographer, a parameter is a variable that influences the value of the blood glucose level as calculated by an algorithm.

"Decay" refers to a gradual reduction in the magnitude of a quantity, for example, a current detected using a sensor electrode where the current is correlated to the concentration of a particular analyte and where the detected current gradually reduces but the concentration of the analyte does not.

2. Modes of Carrying Out the Invention

Before describing the present invention in detail, it is to be understood that this invention is not limited to particular combinations or process parameters, as such may, of course, vary. It is also to be understood that the terminology used herein is for the purpose of describing particular embodiments of the invention only, and is not intended to be limiting.

2A. General Overview of the Invention

The present invention relates to a system for augmenting an alert or alarm signal from an analyte monitoring device, in particular, a glucose monitoring device, wherein the improvement comprises an augmented alarm system. Embodiments of the augmented alarm system may comprise at least (a) a first signaling device, for producing an augmented alarm signal and thereby improving the effectiveness of the GlucoWatch biographer in alerting the user. Embodiments may additionally include (b) a transmitter component, for transmitting an augmented alarm signal to external communication targets and to the first signaling component. These individual components are described in further detail below, as are specific embodiments of an enhanced GlucoWatch biographer of the present invention. Modifications of the GlucoWatch biographer are typically, but not necessarily, made to the durable element of the system. In some aspects of the present invention modifications are made to the circuitry of the durable element of the system.

In the enhanced GlucoWatch biographer of the present invention, the first signaling component and the transmitter component are in operative communication with the GlucoWatch biographer and with each other, either by hardware or telemetric device(s). Details of inter- and intra-system communication are described in further detail below.

The present invention further relates to an alarm augmentation system for an analyte monitoring device, wherein the analyte monitoring device comprises an acquisition and a display unit. The alarm augmentation system comprises at least (a) a first signaling component for producing an alarm signal to alert the user of the analyte monitoring device to analyte levels outside of a predetermined range, and/or (b) a transmitter component for transmitting an alarm signal to external communication targets and to the first signaling component, when present. Some embodiments may include both.

Other embodiments may also include (c) a second signaling component, for producing alarm signals to alert a person or persons other than the user of said analyte monitoring device to analyte levels outside of a predetermined range. Further embodiments may additionally comprise (d) a processor component for receiving and integrating information received from both the analyte monitoring device and from the other components of the augmented alarm system, and for controlling the operation of those components. Specific embodiments of the augmented alarm system are described in further detail below.

The components of the augmented alarm system are in operative communication with each other and with the analyte monitoring device; further, the transmitter component, when present, is in operative communication with external communication targets. The specifics of these intra- and inter-system communications are described in further detail below.

2A(i). First Signaling Component and Second Signaling Component

Embodiments of the present invention may include a first signaling component and/or a second signaling component. Preferred embodiments may include at least a first signaling component, and may further include both.

The first signaling component comprises a sensory stimulus generator for generating an augmented alarm signal and thereby improving the effectiveness of the alarm signal

generated by the analyte monitoring device (e.g. the alert signal of the GlucoWatch biographer) in alerting a user. Similarly, the second signaling component comprises a sensory stimulus generator for alerting a person or persons other than the user.

Both the first and second signaling components comprise at least one sensory stimulus generator, including but not limited to the following:

1) an aural stimulus generator, which may merely amplify the alarm sound produced by the analyte monitoring device (e.g., the alert signal of the GlucoWatch biographer) or alternately generate sounds different from those produced by the device;

2) a visual stimulus generator, for example, one which turns on or flashes the lights in the room where the user of the GlucoWatch biographer is located, or which independently produces colored or flashing light;

3) a tactile stimulus generator, which, for example, generates pressure, vibration, changes in temperature or mild electrical shocks. Such a tactile stimulus generator may comprise a kinesthetic stimulus generator, which produces movement of the user relative to his/her surroundings. An example would be a vibrator which causes vibration of a chair or bed in which the user is sitting or reclining;

4) an olfactory stimulus generator, which releases various odorant compounds; and

5) a gustatory stimulus generator, which causes the release of salty, sweet, sour or bitter compounds in the mouth, or a combination of those compounds.

Both the first and second signaling components, when present, are in operative communication with the analyte monitoring device, and with the other alarm augmentation system components, either directly and/or via a processor component when such is present.

For example, in embodiments of the analyte monitoring device of the present invention wherein the display unit of that device comprises a first signaling component, that component may be in direct operative communication with the acquisition unit. In embodiments wherein the display unit comprises both a transmitter component and a first signaling component, the first signaling component may be in direct operative communication with both the acquisition device and the transmitter component; alternately, there may be a serial connection from the acquisition unit to the transmitting component to the first signaling component. Communication may be either uni- or bi-directional between these various components.

Similarly, in embodiments comprising a second signaling component in addition to a transmitting component and a first signaling component , the second signaling component may be in operative communication with both the acquisition unit and the first signaling component, directly and/or indirectly, for example, by virtue of a connection from the acquisition unit to the transmitter component, and subsequent parallel connections between the transmitting component and the first and second signaling components.

In general, communication between the signaling component(s) and the analyte monitoring device, as well as among the signaling component(s) and the other alarm augmentation system components, may be mediated either by hardware (e.g., a port and a wire-like connector) or by intangible, telemetric device(s) as described in greater detail in the sub-section entitled "Intra- and Inter-System Communication" appearing below.

Both the first and second signaling components may be responsive to alarm signals generated by the analyte monitoring device via the operative connections just described.

For example, in one embodiment, the first signaling component comprises a sound amplifier which directly detects an audio alert or alarm signal generated by the analyte monitoring device, e.g., via a microphone component. The microphone may further include a filtering sub-component that limits the range of audio alarm signals detectable by the amplifier's microphone.

Alternately, there may be an intermediate processor component that receives input from the analyte monitoring device, integrates that input, and on the basis of a predetermined hierarchy of response, activates, for example, one, both or neither of a first signaling component and a second signaling component.

The signaling components may also be responsive to user inputs. For example, both the first and second signaling components may further comprise an alarm turn-off mechanism, which provides a way for input from the user or others to indicate that responsive action has been taken. In this regard, the alarm signal of both the first and second signaling components may be graded, and may increase in intensity and/or frequency if not answered. In some embodiments, a processor sub-component may be present that is capable of monitoring whether the user (in the case of the first signaling component) and/or person(s) other than the user (in the case of the second signaling

component) has activated the turn-off mechanism, and increasing the alarm frequency and/or intensity if the user/other has failed to do so.

Activity of the signaling component(s) may be simultaneous with the monitoring device's alarm, may occur sequentially, or in any predetermined sequence. Similarly, when both a first and a second component are present, either one or both may be active; when both are active, their activity may be either simultaneous or sequential.

2A(ii). Transmitter Component

Some embodiments of the alarm augmentation system of the present invention comprise a transmitter component for communicating the alarm signal to external communication targets. In some embodiments, the transmitter component may further communicate alarm signals to the first and second signaling components, when such components are present.

The transmitter component is in operative communication with the analyte monitoring device and with the other components of the alarm augmentation system, when such are present, either directly or via an intermediate processor component when present. Modes of communication between the analyte monitoring device and the transmitter component, as well as between the transmitter and other components of the alarm augmentation system of the present invention, are discussed in further detail.

The transmitter component is responsive to alarm signals generated by the analyte monitoring device, via the operative links referred to above, either directly, via a receiver sub-component of the transmitter; alternately, it may be detected initially by another component of the alarm system and subsequently communicated to the transmitter component.

The transmitter component may comprise at least one of a variety of different types of devices, including but not limited to the following: (1) a wire or wire-like connection such as a cable; (2) a modem, (3) a radio transmitter; (4) a microwave transmitter; (5) a sound transmitter (subsonic, sonic, or ultrasonic); and (6) an infrared (IR) transmitter. Other suitable devices may be apparent to persons of ordinary skill in the art, in light of the teachings of the present specification.

In response to an alarm signal, the transmitter component contacts an external

communication target (e.g., a first and/or second signaling component). External communication targets may include, but are not limited to, the following: (1) pagers, for example, pagers carried by a significant other, parent, other relative or care giver, or the user's physician; (2) computers, such as the computer of the user's physician or of a health-care facility; and (3) phone lines, such as 911 emergency response lines, the phone line of a physician or of a parent, significant other, relative or care-giver. Additional targets may be apparent to persons of ordinary skill in the art, in light of the teachings of the present specification.

In some embodiments of the invention, the transmitter component may further be capable of receiving input from remote sources, such as a telephone line or computer, and communicating them to the other components of the alarm augmentation system, either directly or via a processor component, when one is present.

Modes of communication between the transmitter component of the alarm augmentation system and external communication targets, and between remote sources of input and the transmitter, are discussed in further detail below.

In another embodiment of the present invention, the alarm augmentation system comprises a transmitting component capable of relaying the initial alarm signal to a second signaling component remote from the analyte monitoring device. Upon receipt of that signal, the second signaling component produces an augmented alarm at the remote location. For example, a relay unit (comprising the transmitting component) may be placed proximal to the acquisition unit. The acquisition unit emits an alert or alarm signal, this signal is communicated (for example, by a wire or wire-like connection such as a cable; a modem, a radio transmitter; a microwave transmitter; a sound transmitter (subsonic, sonic, or ultrasonic); and/or an infrared (IR) transmitter) to the relay unit. The relay unit then communicates the signal to a second, remote, signaling component (which may also include a display unit to show, for example, the analyte amount or concentration or a trend of analyte amount or concentration, e.g., a hyper- or hypo-glycemic trend). Communication with the second signaling component may be via any of the above described modes, as well as via, for example, phone lines, the internet, and/or an intranet. The second signaling component may, for example, be used to alert a doctor, home practitioner, parent, significant other, or medical emergency personnel.

2A(iii). Processor Component

Some embodiments of the alarm augmentation system of the present invention also comprise a processor component, e.g., for evaluating the incoming alarm signal, integrating user inputs, coordinating the alarm augmentation system's response to the alarm signal, and controlling the other alarm system components.

The processor component may comprise a variety of devices, including but not limited to one or more microprocessors.

The processor component is typically responsive to the alarm signal generated by the analyte monitoring device . As discussed above, the GlucoWatch biographer alert signal may be detected by the processor component directly, via a receiver sub-component of the processor, or it may be detected initially by another component of the alarm system and subsequently communicated to the transmitter component. Modes of communication between the GlucoWatch biographer and the processor component, as well as between the processor component and other components of the alarm augmentation system of the present invention, are discussed in further detail below.

Further, the processor component is typically capable of receiving and integrating a variety of inputs in addition to the analyte monitoring device alarm signal, including but not limited to the following: (1) inputs from the other alarm augmentation system components, including user inputs made into those other components; (2) user inputs made directly into the processor component, e.g., via sensitivity controls; and (3) inputs from remote sources, either via the transmitter component or alternately directly via a second receiver sub-component . Other possibilities may be apparent to persons of ordinary skill in the art, in light of the teachings of the present specification.

The processor component may further be capable of controlling the other components of the alarm augmentation system, including but not limited to the following capabilities: (1) determining which of the various components to activate, and the order in which they are activated; and (2) controlling the functioning of the various components, including (a) the frequency and/or intensity of the augmented alarm signals generated by the signaling components; (b) determining whether the transmitter component may communicate with external communication targets, which targets the transmitter component may communicate with, the order in which the communication may occur, and the nature of

the communication; (c) determining whether the transmitter component may receive inputs from external sources; and (d) controlling the sensitivity of the system to the analyte monitoring device alarm signal. Other capabilities may be apparent to persons of ordinary skill in the art, in light of the teachings of the present specification.

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2A(iv). Intra- and Inter-System Communication

The analyte monitoring device is in operative communication with the alarm augmentation system. Likewise, in embodiments of the alarm augmentation system comprising more than one component, the components are in operative communication with
10 each other. In turn, in embodiments of the invention comprising a transmitter component, the alarm augmentation system is in operative communication with external communication targets, and may further be able to receive input from remote data sources.

With respect to those embodiments that do not possess a processor component, the analyte monitoring device is in direct operative communication with the signaling and/or
15 transmitter components included in specific embodiments. In those embodiments which do include the processor component, the GlucoWatch biographer is in direct operative communication with the processor component, which in turn is in operative communication with the remaining component or components. Alternately, it is also possible for the analyte monitoring device to be in simultaneous communication with the processor component and
20 with the signaling and/or transmitter components.

The operative communication can include, for example, the following: both one-way and bi-directional communication from the analyte monitoring device to the alarm augmentation system, and both one-way and bi-directional communication among the various components of the alarm augmentation system. There may further be both one-way
25 and bi-directional communication among the alarm augmentation system components, and between external communication targets and external data sources, e.g., healthcare providers, 911 emergency services telephone lines, emergency transport services, pagers, computers, etc.

Communication between the acquisition unit (e.g., the analyte monitoring device)
30 and the alarm augmentation system of the present invention, among the system components, between the system and external communication targets, and between external data sources

and the system, may be via a wire or cable-like connection and/or via a telemetric connection. Communications between the various components described herein may, for example, be:

1) One-way communication from the analyte monitoring device to the alarm augmentation system and/or among the alarm augmentation system components. The alarm augmentation system can include components for data storage, user inputs, and the ability to upload information to a host computer, i.e., the system can include a processor component, e.g., one or more microprocessor and associated algorithms or protocols, and a transmitter component, e.g., a modem. Alternately, one or more of the individual system components may include a processor sub-component capable of performing those functions.

2) Two-way communications (send and receive) between the analyte monitoring device and the alarm augmentation system, and/or among the alarm components or components, where data storage, user inputs, and upload to a remote computer can be divided in any combination among the monitor device and the components.

3) A mixture of one-way and two-way (i.e., unidirectional and bi-directional) communication among components. For example, communication between the analyte monitoring device, a processor component, and a first signaling component may be bi-directional and communication between the processor component and a transmitter component in operative communication with a second signaling component may be unidirectional.

4) uni- and/or bi-directional communication, with wireless communications link between the analyte monitoring device and the alarm system, and/or among the alarm system components.

5) uni- and/or bi-directional communication, with wired or wireless communications to a remote communication target, e.g., for data upload or automatic reporting to healthcare provider via telephone, Internet, or wireless communications. For example, the alarm system may include a transmitter component, e.g., a bedside receiver/radio transmitter that automatically reports to a patient's personal physician. Alternately, the transmitter component may be a telephonic or wireless modem that performs this function.

Examples of wireless communications technologies include, but are not limited to the following (for example, short range communication, i.e., less than or equal to 3 meters, or longer range):

- Low frequency electromagnetic waves (frequency range about 1 Hz - 1 Mega Hz);
- Medium frequency electromagnetic waves (frequency range about 1 Mega Hz - 500 Mega Hz);
- High frequency electromagnetic waves (frequency range about 500 Mega Hz - 5 Giga Hz);
- Capacitance coupling between, for example, a subject's body and the environment/air (frequency range about 1 Hz - 1 Mega Hz);
- Inductive coupling (i.e., time varying magnetic field; not freely propagating electromagnetic wave);
- Close coupled inductive (i.e., inductive but so weak that it works only at very short range). This would likely require bringing the two components (e.g., a display device and sensor electronics) in close proximity whenever the data needs to be displayed.
- Brief electrical contact whenever data is needed at the display.
- Infrared coupling (using infrared light, e.g., as in low speed communications links to computers and personal digital assistants), and
- High frequency acoustic energy, as well as,
- Combinations and modifications of the above.

One embodiment of the alarm augmentation system of the present invention comprises, a glucose monitoring device, a processing component, a first signaling component, a second signaling component, and a transmitter component. Upon detection of abnormal glucose levels or trends, an alarm signal is generated by the glucose monitoring device, which signal is then be communicated to the alarm augmentation system. The alarm signal may initially be communicated to the processor component. The processor component may subsequently communicate with the first signaling component and cause it to generate an augmented alarm signal in order to alert the user. The user may then press a button on the first signaling component, which turns off the augmented alarm signal.

After a time period, which may have either been preset or previously determined by user input, receipt of additional alarm signals from the analyte monitoring device may again

cause the processor to communicate with the first signaling component, and again cause it to generate an augmented alarm signal. It may further communicate with the second signaling component and cause it to communicate the alarm signal to a person or persons other than the user. It may further communicate with the transmitter component, which may then communicate the alarm signal to remote targets, e.g., the user's physician, emergency medical personnel, etc.

Alternately, the user may fail to respond to the initial augmented alarm signal. The user's failure to turn off the first signaling component may be communicated to the processor component, which may then communicate to the second signaling component, causing an augmented alarm signal to be generated in order to alert a person or persons other than the user. The processor may also communicate with the transmitter component, which may in turn communicate with remote targets, e.g., the user's physician, emergency personnel, etc.

In a further embodiment, the processor component may additionally be capable of receiving data from the analyte monitoring device , of storing the data, and of communicating the data to the transmitter component. In addition, the processor component may be capable of performing further functions, such as data analysis, to, for example, predict trends based on the data provided by the analyte monitoring device. Further, the transmitter component may be capable of transmitting the data to remote targets, and of uploading the data to remote targets such as a pager device or a computer.

In one embodiment, the wireless connection or link may be established using a technology called Personal Area Network (PAN; WO 96/36134, N. Gershenfeld, et al., published 14 November 1996). This technology is an example of capacitance coupling involving the use of the human body to carry current, and thus information, from one device to another. These devices have to be either in direct contact, or in close proximity, to the body. A low frequency carrier is used to transmit the information.

Other examples may be apparent to persons of ordinary skill in the art, in light of the teachings of the present specification.

2A(v). Housings for the Alarm Augmentation System Components

The components of an alarm augmentation system of the present invention may be

contained in separate and independent housings. Alternately, the components may be contained within a single housing. In some embodiments, the alarm augmentation system may have a modular character, and be capable of accommodating a variable number of processing, signaling and transmitter components; in such embodiments, each of the components can be housed independently. In all cases, the components may be in operative communication (i.e., operatively connected) with each other as described above.

In one embodiment, both the analyte monitoring device and the components of the alarm augmentation system of the present invention may all be contained in a single housing. In another embodiment, the analyte monitoring device may be in close proximity to the alarm augmentation system, for example, the analyte monitoring device may be a watch-like device and the alarm augmentation system (or components thereof) may be worn as a similar device adjacent to the analyte monitoring device. In yet another embodiment, the alarm augmentation system may be worn on a different part of the body. In a further embodiment, the alarm augmentation system may be remote to the analyte monitoring device, for example, at a fixed location in the home.

The housings may comprise a variety of materials known in the art, including but not limited to the following: a wide variety of plastic polymers; metals and metal alloys; fiberglass; ceramic materials; and composite materials such as plastic polymers impregnated with graphite or silicon nitride fibers.

2B. Exemplary Monitoring Systems and Analytes

2B(i). Exemplary Analyte Monitoring Systems

Numerous analyte monitoring systems can be used in the practice of the present invention. Typically, the analyte monitoring system used to monitor the level of a selected analyte in a target system comprises a sampling device, which provides a sample comprising the analyte, and a sensing device, which detects the amount or concentration of the analyte or a signal associated with the analyte amount or concentration in the sample.

One exemplary analyte monitoring system (the GlucoWatch biographer) is described herein for monitoring glucose levels in a biological system via the transdermal extraction of glucose from the biological system, particularly an animal subject, and then

detection of signal corresponding to the amount or concentration of the extracted glucose. Transdermal extraction is carried out by applying an electrical current or ultrasonic radiation to a tissue surface at a collection site. The electrical current is used to extract small amounts of glucose from the subject into a collection reservoir. The collection reservoir is in contact with a sensor element (e.g., a biosensor) which provides for measurement of glucose concentration in the subject. As glucose is transdermally extracted into the collection reservoir, the analyte reacts with the glucose oxidase within the reservoir to produce hydrogen peroxide. The presence of hydrogen peroxide generates a current at the biosensor electrode that is directly proportional to the amount of hydrogen peroxide in the reservoir. This current provides a signal which can be detected and interpreted (for example, employing a selected algorithm) by an associated system controller to provide a glucose concentration value or amount for display.

In the use of the sampling system, a collection reservoir is contacted with a tissue surface, for example, on the stratum corneum of a subject's skin. An electrical current is then applied to the tissue surface in order to extract glucose from the tissue into the collection reservoir. Extraction is carried out, for example, frequently over a selected period of time. The collection reservoir is analyzed, at least periodically and typically frequently, to measure glucose concentration therein. The measured value correlates with the subject's blood glucose level.

To sample the analyte, one or more collection reservoirs are placed in contact with a tissue surface on a subject. The ionically conductive material within the collection reservoir is also in contact with an electrode (for reverse iontophoretic extraction) which generates a current sufficient to extract glucose from the tissue into the collection reservoir. Referring to Figure 1, an exploded view of exemplary components comprising one embodiment of an AutoSensor for use in an iontophoretic sampling system is presented. The AutoSensor components include two biosensor/iontophoretic electrode assemblies, **104** and **106**, each of which have an annular iontophoretic electrode, respectively indicated at **108** and **110**, which encircles a biosensor electrode **112** and **114**. The electrode assemblies **104** and **106** are printed onto a polymeric substrate **116** which is maintained within a sensor tray **118**. A collection reservoir assembly **120** is arranged over the electrode assemblies, wherein the collection reservoir assembly comprises two

hydrogel inserts **122** and **124** retained by a gel retaining layer **126** and mask layer **128**. Further release liners may be included in the assembly, for example, a patient liner **130**, and a plow-fold liner **132**. In one embodiment, the electrode assemblies include bimodal electrodes. A mask layer **128** (for example, as described in PCT Publication No. WO 97/10356, published 20 March 1997, and US Patent Nos. 5,735,273, 5,827,183, 6,141,573, and 6,201,979) may be present. Other AutoSensor embodiments are described in WO 99/58190, published 18 November 1999.

The mask and retaining layers are preferably composed of materials that are substantially impermeable to the analyte (e.g., glucose) to be detected (see, for example, U.S. Patent Nos. 5,735,273, and 5,827,183). By "substantially impermeable" is meant that the material reduces or eliminates analyte transport (e.g., by diffusion). The material can allow for a low level of analyte transport, with the proviso that the analyte that passes through the material does not cause significant edge effects at the sensing electrode used in conjunction with the mask and retaining layers. Examples of materials that can be used to form the layers include, but are not limited to, polyester, polyester derivatives, other polyester-like materials, polyurethane, polyurethane derivatives and other polyurethane-like materials.

The components shown in exploded view in Figure 1 (i.e., an exemplary AutoSensor) are intended for use in a automatic sampling system which is configured to be worn like an ordinary wristwatch, as described, for example, in PCT Publication No. WO 96/00110, published 4 January 1996. The AutoSensor in this case is a consumable element. A durable element, that is the wristwatch housing into which the AutoSensor is inserted, is also provided. The durable element can further include suitable electronics (e.g., one or more microprocessor(s), memory, display and other circuit components) and power sources, for example, for operating the automatic sampling system. The durable element also provides means to provide an audible alert when glucose levels in a subject being monitored are outside of a predetermined range. The one or more microprocessors may control a variety of functions, including, but not limited to, control of a sampling device, a sensing device, aspects of the measurement cycle (for example, timing of sampling and sensing, and alternating polarity between electrodes), connectivity, computational methods, different aspects of data manipulation (for example, acquisition,

recording, recalling, comparing, and reporting), etc. The durable component of the GlucoWatch biographer provides a variety of electronic configurations (i.e., circuitry) that may be modified to accommodate components of the alarm augmentation system of the present invention. Such modifications include but are not limited to (a) reconfiguring the confidence loop circuitry of the GlucoWatch biographer; (b) modifying the transmission and receipt lines or transmission and receipt line circuitry of the GlucoWatch biographer, and (c) modifying the sweat probe or sweat probe circuitry of the GlucoWatch biographer. Other modifications may be apparent to persons of ordinary skill in the art in light of the teachings of the present invention.

The sensing electrode can be, for example, a Pt-comprising electrode configured to provide a geometric surface area of about 0.1 to 3 cm^2, preferably about 0.5 to 2 cm^2, and more preferably about 1 cm^2. This particular configuration is scaled in proportion to the collection area of the collection reservoir used in the sampling system of the present invention, throughout which the extracted analyte and/or its reaction products will be present. The electrode composition is formulated using analytical- or electronic-grade reagents and solvents which ensure that electrochemical and/or other residual contaminants are avoided in the final composition, significantly reducing the background noise inherent in the resultant electrode. In particular, the reagents and solvents used in the formulation of the electrode are selected so as to be substantially free of electrochemically active contaminants (e.g., anti-oxidants), and the solvents in particular are selected for high volatility in order to reduce washing and cure times. Some electrode embodiments are described in European Patent Publication 0 942 278 A2, published Sept. 15, 1999.

The reactive surface of the sensing electrode can be comprised of any electrically conductive material such as, but not limited to, platinum-group metals (including, platinum, palladium, rhodium, ruthenium, osmium, and iridium), nickel, copper, silver, and carbon, as well as, oxides, dioxides, combinations or alloys thereof. Some catalytic materials, membranes, and fabrication technologies suitable for the construction of amperometric biosensors were described by Newman, J.D., et al. (Analytical Chemistry 67(24), 4594-4599, 1995).

Any suitable iontophoretic electrode system can be employed, an exemplary system uses a silver/silver chloride (Ag/AgCl) electrode system. The iontophoretic electrodes are formulated typically using two performance criteria: (1) the electrodes are capable of operation for extended periods, preferably periods of up to 24 hours or longer; and (2) the electrodes are formulated to have high electrochemical purity in order to operate within the present system which requires extremely low background noise levels. The electrodes must also be capable of passing a large amount of charge over the life of the electrodes. With regard to operation for extended periods of time, Ag/AgCl electrodes are capable of repeatedly forming a reversible couple which operates without unwanted electrochemical side reactions (which could give rise to changes in pH, and liberation of hydrogen and oxygen due to water hydrolysis). The Ag/AgCl electrode is thus formulated to withstand repeated cycles of current passage in the range of about 0.01 to 1.0 mA per cm^2 of electrode area. With regard to high electrochemical purity, the Ag/AgCl components are dispersed within a suitable polymer binder to provide an electrode composition which is not susceptible to attack (e.g., plasticization) by components in the collection reservoir, e.g., the hydrogel composition. The electrode compositions are also typically formulated using analytical- or electronic-grade reagents and solvents, and the polymer binder composition is selected to be free of electrochemically active contaminants which could diffuse to the biosensor to produce a background current.

The automatic sampling system can transdermally extract the sample over the course of a selected period of time using reverse iontophoresis. The collection reservoir comprises an ionically conductive medium, preferably the hydrogel medium described hereinabove. A first iontophoresis electrode is contacted with the collection reservoir (which is typically in contact with a target, subject tissue surface), and a second iontophoresis electrode is contacted with either a second collection reservoir in contact with the tissue surface, or some other ionically conductive medium in contact with the tissue. A power source provides an electrical potential between the two electrodes to perform reverse iontophoresis in a manner known in the art. As discussed above, the biosensor selected to detect the presence, and possibly the level, of the target analyte (for example, glucose) within a reservoir is also in contact with the reservoir. Typically, there

are two collections reservoirs, each comprising glucose oxidase, and each in operative contact with iontophoretic electrode and a sensing electrode. The iontophoretic electrode may be a bimodal electrode that also serves, non-concurrently, as a counter electrode to the sensing electrode (see, for example, U.S. Patent No. 5,954,685).

In practice, an electric potential (either direct current or a more complex waveform) is applied between the two iontophoresis electrodes such that current flows from the first electrode through the first conductive medium into the skin, and back out from the skin through the second conductive medium to the second electrode. This current flow extracts substances through the skin into the one or more collection reservoirs through the process of reverse iontophoresis or electroosmosis. The electric potential may be applied as described in PCT Publication No. WO 96/00110, published 4 January 1996. Typically, the electrical potential is alternated between two reservoirs to provide extraction of analyte into each reservoir in an alternating fashion (see, for example, U.S. Patent Nos. 6,023,629, 5,954,685). Analyte is also typically detected in each reservoir.

As an example, to extract glucose, the applied electrical current density on the skin or tissue can be in the range of about 0.01 to about 2 mA/cm^2. In order to facilitate the extraction of glucose, electrical energy can be applied to the electrodes, and the polarity of the electrodes can be, for example, alternated so that each electrode is alternately a cathode or an anode. The polarity switching can be manual or automatic. A device and method for sampling of substances using alternating polarity is described in U.S. Patent No. 5,771,890, issued June 30, 1998.

When a bimodal electrode is used (e.g., U.S. Patent No. 5,954,685, issued Sept. 21, 1999), during the reverse iontophoretic phase, a power source provides a current flow to the first bimodal electrode to facilitate the extraction of the chemical signal into the reservoir. During the sensing phase, a separate power source is used to provide voltage to the first sensing electrode to drive the conversion of chemical signal retained in reservoir to electrical signal at the catalytic face of the sensing electrode. The separate power source also maintains a fixed potential at the electrode where, for example hydrogen peroxide is converted to molecular oxygen, hydrogen ions, and electrons, which is compared with the potential of the reference electrode during the sensing phase.

While one sensing electrode is operating in the sensing mode it is electrically connected to the adjacent bimodal electrode which acts as a counter electrode at which electrons generated at the sensing electrode are consumed.

The electrode subassembly can be operated by electrically connecting the bimodal electrodes such that each electrode is capable of functioning as both an iontophoretic electrode and counter electrode along with appropriate sensing electrode(s) and reference electrode(s).

A potentiostat is an electrical circuit used in electrochemical measurements in three electrode electrochemical cells. A potential is applied between the reference electrode and the sensing electrode. The current generated at the sensing electrode flows through circuitry to the counter electrode (i.e., no current flows through the reference electrode to alter its equilibrium potential). Two independent potentiostat circuits can be used to operate the two biosensors. For the purpose of the present invention, the electrical current measured at the sensing electrode subassembly is the current that is correlated with an amount of chemical signal corresponding to the analyte.

The detected current can be correlated with the subject's blood glucose concentration (e.g., using a statistical technique or algorithm or combination of techniques) so that the system controller may display the subject's actual blood glucose concentration as measured by the sampling system. Such statistical techniques can be formulated as algorithm(s) and incorporated in one or more microprocessor(s) associated with the sampling system. Exemplary signal processing applications include, but are not limited to, those taught in the following U.S. Patent Nos. 6,144,869, 6,233,471, 6,180,416.

In a further aspect of the present invention, the sampling/sensing mechanism and user interface may be found on separate components. Thus, the monitoring system can comprise at least two components, in which a first component comprises sampling mechanism and sensing mechanism that are used to extract and detect an analyte, for example, glucose, and a second component that receives the analyte data from the first component, conducts data processing on the analyte data to determine an analyte concentration and then displays the analyte concentration data. Typically, microprocessor functions (e.g., control of a sampling device, a sensing device, aspects of

the measurement cycle, computational methods, different aspects of data manipulation or recording, etc.) are found in both components. Alternatively, microprocessing components may be located in one or the other of the at least two components. The second component of the monitoring system can assume many forms, including, but not limited to, the following: a watch, a credit card-shaped device (e.g., a "smart card" or "universal card" having a built-in microprocessor as described for example in U.S. Patent No. 5,892,661), a pager-like device, cell phone-like device, or other such device that communicates information to the user visually, audibly, or kinesthetically.

Further, additional components may be added to the system, for example, a third component comprising a display of analyte values or an alarm related to analyte concentration, may be employed. In certain embodiments, a delivery unit is included in the system. An exemplary delivery unit is an insulin delivery unit. Insulin delivery units, both implantable and external, are known in the art and described, for example, in U.S. Patent Numbers 5,995,860; 5,112,614 and 5,062,841. Preferably, when included as a component of the present invention, the delivery unit is in communication (e.g., wire-like or wireless communication) with the extracting and/or sensing mechanism such that the sensing mechanism can control the insulin pump and regulate delivery of a suitable amount of insulin to the subject.

Advantages of separating the first component (e.g., including the biosensor and iontophoresis functions) from the second component (e.g., including some microprocessor and display functions) include greater flexibility, discretion, privacy and convenience to the user. Having a small and lightweight measurement unit allows placement of the two components of the system on a wider range of body sites, for example, the first component may be placed on the abdomen or upper arm. This wider range of placement options may improve the accuracy through optimal extraction site selection (e.g., torso rather than extremities) and greater temperature stability (e.g., via the insulating effects of clothing). Thus, the collection and sensing assembly will be able to be placed on a greater range of body sites. Similarly, a smaller and less obtrusive microprocessor and display unit (the second component) provides a convenient and discrete system by which to monitor analytes. The biosensor readouts and control signals will be relayed via wire-like or wireless technology between the collection and sensing

assembly and the display unit which could take the form of a small watch, a pager, or a credit card-sized device. This system also provides the ability to relay an alert message or signal during nighttime use, for example, to a site remote from the subject being monitored.

In one embodiment, the two components of the device can be in operative communication via a wire or cable-like connection. Operative communications between the components can be wireless link or connection, i.e. provided by a "virtual cable," for example, a telemetry link. This wireless link can be uni- or bi-directional between the two components. In the case of more than two components, links can be a combination of wire-like and wireless.

2B(ii). Exemplary Analytes

The analyte can be any one or more specific substance, component, or combinations thereof that one is desirous of detecting and/or measuring in a chemical, physical, enzymatic, or optical analysis.

Analytes that can be measured using the methods of the present invention include, but are not limited to, amino acids, enzyme substrates or products indicating a disease state or condition, other markers of disease states or conditions, drugs of abuse (e.g., ethanol, cocaine), therapeutic and/or pharmacologic agents (e.g., theophylline, anti-HIV drugs, lithium, anti-epileptic drugs, cyclosporin, chemotherapeutics), electrolytes, physiological analytes of interest (e.g., urate/uric acid, carbonate, calcium, potassium, sodium, chloride, bicarbonate (CO_2), glucose, urea (blood urea nitrogen), lactate and/or lactic acid, hydroxybutyrate, cholesterol, triglycerides, creatine, creatinine, insulin, hematocrit, and hemoglobin), blood gases (carbon dioxide, oxygen, pH), lipids, heavy metals (e.g., lead, copper), and the like. Analytes in non-biological systems may also be evaluated using the methods of the present invention.

In preferred embodiments, the analyte is a physiological analyte of interest, for example glucose, or a chemical that has a physiological action, for example a drug or pharmacological agent.

In order to facilitate detection of the analyte, an enzyme (or enzymes) can be disposed within the one or more collection reservoirs. The selected enzyme is capable of

catalyzing a reaction with the extracted analyte to the extent that a product of this reaction can be sensed, e.g., can be detected electrochemically from the generation of a current which current is detectable and proportional to the amount of the analyte which is reacted. In one embodiment of the present invention, a suitable enzyme is glucose oxidase, which oxidizes glucose to gluconic acid and hydrogen peroxide. The subsequent detection of hydrogen peroxide on an appropriate biosensor electrode generates two electrons per hydrogen peroxide molecule creating a current that can be detected and related to the amount of glucose entering the device. Glucose oxidase (GOx) is readily available commercially and has well known catalytic characteristics. However, other enzymes can also be used singly (for detection of individual analytes) or together (for detection of multiple analytes), as long as they specifically catalyze a reaction with an analyte or substance of interest to generate a detectable product in proportion to the amount of analyte so reacted.

In like manner, a number of other analyte-specific enzyme systems can be used in the invention, which enzyme systems operate on much the same general techniques. For example, a biosensor electrode that detects hydrogen peroxide can be used to detect ethanol using an alcohol oxidase enzyme system, or similarly uric acid with urate oxidase system, cholesterol with a cholesterol oxidase system, and theophylline with a xanthine oxidase system.

In addition, the oxidase enzyme (used for hydrogen peroxidase-based detection) can be replaced or complemented with another redox system, for example, the dehydrogenase-enzyme NAD-NADH, which offers a separate route to detecting additional analytes. Dehydrogenase-based sensors can use working electrodes made of gold or carbon (via mediated chemistry). Examples of analytes suitable for this type of monitoring include, but are not limited to, cholesterol, ethanol, hydroxybutyrate, phenylalanine, triglycerides, and urea.

Further, the enzyme can be eliminated and detection can rely on direct electrochemical or potentiometric detection of an analyte. Such analytes include, without limitation, heavy metals (e.g., cobalt, iron, lead, nickel, zinc), oxygen, carbonate/carbon dioxide, chloride, fluoride, lithium, pH, potassium, sodium, and urea. Also, the sampling system described herein can be used for therapeutic drug monitoring, for example,

monitoring anti-epileptic drugs (e.g., phenytoin), chemotherapy (e.g., adriamycin), hyperactivity (e.g., ritalin), and anti-organ-rejection (e.g., cyclosporin).

Preferably, a sensor electrode is able to detect the analyte that has been extracted into the one or more collection reservoirs when present at nominal concentration levels. Suitable exemplary biosensor electrodes and associated sampling systems as described in are described in PCT Publication Nos. WO 97/10499, published 20 March 1997 and WO 98/42252, published 1 October 1998.

A single sensor may detect multiple analytes and/or reaction products of analytes. For example, a platinum sensor could be used to detect tyrosine and glucose in a single sample. The tyrosine is detected, for example, by direct electrochemical oxidation at a suitable electrode potential (e.g., approximately 0.6V vs. Ag/AgCl). The glucose is detected, e.g., using glucose oxidase and detecting the hydrogen peroxide reaction product.

Different sensing devices and/or sensing systems can be employed as well to distinguish between signals. For example, a first gel containing glucose oxidase associated with a first platinum sensor can be used for the detection of glucose, while a second gel containing uricase associated with a second platinum sensor can be used for the detection of urea.

2C. Exemplary Embodiments of the Alarm Augmentation System

The alarm augmentation system of the present invention may exist as a singe unit device, or alternatively, may comprise multiple units.

2C(i). Single Unit Devices

The augmented alarm system may exist as a single unit device combined with an analyte monitoring device.

In an exemplary device, the alarm augmentation system is incorporated into a durable element of the analyte monitoring device. In one embodiment of this exemplary device, an aspect of the durable element of the GlucoWatch biographer circuitry is modified to provide an augmented alarm signal, which may be (i) auditory, (ii) visual, (iii) tactile, including but not limited to kinesthetic, (iv) olfactory, (v) gustatory, and also be (vi)

variations and combinations thereof. Other types of signals, sensory or otherwise, are also possible. For example, the iontophoretic channels (or leads) of the durable component of GlucoWatch biographer are modified so as to be capable of delivering an electrical current to provide a tactile stimulus to the user. Corresponding modifications to the consumable element of the GlucoWatch biographer may be made as well, for example, increasing the size or surface area of the hydrogels in order to provide a suitable stimulus to the user. Further, the consumable component of the GlucoWatch biographer (i.e., an AutoSensor, or similar structures in other analyte monitoring devices) may be modified to include components of an alarm augmentation system, for example, including a speaker device capable of providing an amplified signal in the AutoSensor assembly. Exemplary AutoSensor assemblies are described, for example, in WO 99/58190, published 18 November 1999. Other modifications are also possible, and may be apparent to persons of ordinary skill in the art in light of the teachings of the present specification.

In the case of an augmented alarm system and an analyte monitoring device within a single housing, the analyte monitoring device typically comprises an acquisition unit and a display unit, which are contained within a single housing. The display unit may further comprise a first signaling component; in some embodiments, the first signaling component may be an aural stimulus generator. Preferably, the display unit may further comprise a volume control for varying the intensity of the aural alarm signal.

Other embodiments may be apparent to persons of ordinary skill in the art in light of the teachings of the present specification.

2C(ii). Multiple Unit Systems

Some embodiments of the augmented alarm system of the present invention may have a modular character, and be capable of accommodating a variable number of processing, signaling and transmitter components. In such embodiments, at least one of the components may be housed independently of the acquisition unit (e.g., an analyte monitoring device) and/or of other components comprising the alarm augmentation system. In all cases, the components may be in operative communication with each other as described above.

Multiple-unit alarm augmentation systems for use with an enhanced GlucoWatch biographer include but are not limited to the following examples. In some exemplary embodiments, the enhanced GlucoWatch biographer may comprise a transmitter component, wherein the transmitter itself may comprise a port that provides a connection to a first signaling component of an alarm augmentation system. The first signaling component of this exemplary embodiment may comprise an auditory stimulus generator, and preferably one with a volume control.

The port may comprise a serial port that is added to the GlucoWatch biographer, being placed in operative connection therewith, and a wire-like or cable-like connector for connecting the GlucoWatch biographer and a first signaling component. Alternately, the port may comprise a modification to some aspect of the GlucoWatch biographer's circuitry. Such modifications include but are not limited to (a) reconfiguring the confidence loop circuitry of the GlucoWatch biographer; (b) modifying the transmission and receipt lines or transmission and receipt line circuitry of the GlucoWatch biographer, and (c) modifying the sweat probe or sweat probe circuitry of the GlucoWatch biographer. Other modifications may be apparent to persons of ordinary skill in the art in light of the teachings of the present invention.

Multiple-unit versions of the augmented alarm system for an analyte monitoring device include but are not limited to the following. Common to the embodiments of this aspect of the invention is an analyte monitoring device that comprises an analyte monitoring unit and a display unit. Such units (or components) of an analyte monitoring device may be contained within a single housing; or in another aspect, they are contained in different housings, and operably connected by either hardware or telemetric device(s), preferably telemetric. The GlucoWatch biographer is an example of an analyte monitoring device where the sampling device, sensing device, microprocessors, controls, and display are combined into a single unit to worn like a wrist watch. Examples of multi-component analyte monitoring devices are provided in WO 00/47109, published 17 August 2000. In one exemplary embodiment, the acquisition unit is worn by the user, and the display unit is separable, so that it may be placed, for example, at a different physical location on the user, on a night stand, or a desk, etc. Such a display unit may comprise at least either (a) a

transmitting component or (b) a first signaling component. More preferred embodiments may include both.

In an exemplary embodiment, the acquisition unit, the display unit and the transmitting component may all be contained within a single housing, while the first signaling component may be contained in an independent housing. The user may therefore place the first signaling component in a location that maximizes the effectiveness of the alarm signal in alerting him or her to the existence of abnormal analyte levels. For example, in cases where the first signaling component generates a sound alarm signal, it may be placed on a night stand nearer to the user's ears.

In another exemplary embodiment, the acquisition unit, the display unit and the transmitting component may all be contained within a single housing while both the first signaling component and the second signaling component may each be contained within separate independent housings. Thus, it is possible to place the second signaling component in a location remote from the user where it can alert a person or person(s) other than the user (e.g., a significant other, parent, other family member, or caretaker) to the existence of abnormal analyte levels.

In still another alternate embodiment, the augmented alarm system may further comprise a processor component. In one example of these embodiments, the processor component may be contained within a single housing along with the acquisition unit, the display unit and the transmitter component, while the first and second signaling components may be housed separately, as described above.

As is apparent to one of skill in the art, various modification and variations of the above embodiments can be made without departing from the spirit and scope of this invention. Such modifications and variations are within the scope of this invention.

What is Claimed Is:

1. An improved glucose monitoring device, said device comprising a durable element and a consumable element, said durable element comprising circuitry and means to provide an audible alert when glucose levels in a subject being monitored are outside of a predetermined range, wherein the improvement comprises modification of the circuitry of the durable element of said device to provide an augmented alarm signal capable of alerting a user of said device to glucose levels outside of a predetermined range, said alarm signal selected from the group consisting of (i) tactile stimulus, (ii) auditory stimulus, (iii) visual stimulus, and (iv) variations and combinations thereof.

2. The improved glucose monitoring device of claim 1, wherein said glucose monitoring device comprises a transdermal sampling device, a sensing device, a display, and means to provide an audible alert when glucose levels in a subject being monitored are outside of a predetermined range.

3. The improved glucose monitoring device of claim 1, further comprising said durable element operably linked to said consumable element.

4. The improved glucose monitoring device of claim 3, wherein said consumable element is an AutoSensor.

5. The improved glucose monitoring device of any of claims 1-4, wherein said device comprises iontophoretic channels, and said iontophoretic channels are modified to be capable of delivering an electrical current to provide a tactile stimulus.

6. An improved glucose monitoring device, said device comprising a durable element and a consumable element, said durable element comprising circuitry and means to provide an audible alert when glucose levels in a subject being monitored are outside of a predetermined range, wherein the improvement comprises modification of the circuitry of the durable element of said device to provide a connection to a first signaling component for

producing alarm signals capable of alerting a user of said device to glucose levels outside of the predetermined range.

7. The improved glucose monitoring device of claim 6, wherein said glucose monitoring device comprises a transdermal sampling device, a sensing device, a display, and means to provide an audible alert when glucose levels in a subject being monitored are outside of a predetermined range.

8. The improved glucose monitoring device of claim 6, further comprising said durable element operably linked to the consumable element.

9. The improved glucose monitoring device of claim 8, wherein said consumable element is an AutoSensor.

10. The improved glucose monitoring device of any of claims 6-9, wherein said glucose monitoring device comprises confidence loop circuitry and said modification comprises reconfiguring the confidence loop circuitry of said glucose monitoring device to provide said connection.

11. The improved glucose monitoring device of any of claims 6-9, wherein said glucose monitoring device comprises transmission and receipt lines, and said modification comprises modifying the transmission and receipt lines of said glucose monitoring device to provide said connection.

12. The improved glucose monitoring device of any of claims 6-9, wherein said glucose monitoring device comprises a sweat probe, and said modification comprises modifying the sweat probe of said glucose monitoring device to provide said connection.

13. The improved glucose monitoring device of any of claims 6-9, wherein said modification comprises adding a serial port to said glucose monitoring device, said port

being in operative communication with said glucose monitoring device and providing said connection.

14. The improved glucose monitoring device of any of claims 6-9, wherein the connection is via a wire-like connector.

15. The improved glucose monitoring device of any of claims 6-9, wherein the connection is via a telemetering system, wherein said telemetering system is selected from the group consisting of (i) electromagnetic radiation; (ii) capacitance coupling; (iii) inductive coupling; (iv) infrared coupling; and (v) variations and combinations thereof.

16. The improved glucose monitoring device of any of claims 6-9, wherein said first signaling component is selected from the group consisting of (i) an auditory stimulus generator; (ii) a visual stimulus generator; (iii) a tactile stimulus generator; (iv) an olfactory stimulus generator; and (v) variations and combinations thereof.

17. An alarm augmentation system for an analyte monitoring device, comprising

an analyte monitoring device, said analyte monitoring device comprising

an acquisition unit capable of at least sensing or detecting analyte concentrations or amounts in a subject; and

a display unit, operably linked to said acquisition unit, wherein (i) said display unit comprises means to provide an audible alert when an analyte level, in a subject being monitored, is outside of a predetermined range, and (ii) said acquisition unit and said display units are separately housed; and

an alarm augmentation system comprising a first signaling component, capable of producing alarm signals to alert a subject in response to analyte levels outside of a predetermined range, said first signaling component operably linked to said display unit.

18. The alarm augmentation system of claim 17, wherein said first signaling component is selected from the group consisting of (i) an auditory stimulus generator; (ii) a

visual stimulus generator; (iii) a tactile stimulus generator; (iv) an olfactory stimulus generator; (v) a gustatory stimulus generator; and (vi) variations and combinations thereof.

19. The alarm augmentation system of claim 17, wherein said first signaling component comprises an auditory stimulus generator, and said auditory stimulus generator provides a volume control for varying the volume of auditory stimuli generated thereby.

20. The alarm augmentation system of claim 17, further comprising a transmitter component, operably linked to said display unit, said transmitter component capable of transmitting alarm signals to at least one external communication target.

21. The alarm augmentation system of claim 20, wherein said transmitter further provides an operative link between said display unit and said first signaling component.

22. The alarm augmentation system of claim 20, wherein said transmitter component comprises a serial port and a wire-like connector, said port and said connector capable of connecting with at least one external communication target.

23. The alarm augmentation system of claim 20, wherein said transmitter component comprises a telemetering system selected from the group consisting of (i) electromagnetic radiation; (ii) capacitance coupling; (iii) inductive coupling; (iv) infrared coupling; and (v) combinations and variations thereof.

24. The alarm augmentation system of claim 23, wherein said telemetering system is capable of connecting with said first signaling component and said external communication target.

25. The alarm augmentation system of claim 23, wherein (a) said external communication target is a second signaling component, capable of producing alarm signals to alert a person or persons other than the user of said analyte monitoring device to analyte levels outside of the predetermined range, (b) said second signaling component is selected

from the group consisting of (i) an auditory stimulus generator; (ii) a visual stimulus generator; (iii) a tactile stimulus generator; (iv) an olfactory stimulus generator; (v) a gustatory stimulus generator; and (vi) variations and combinations thereof, and (c) said second signaling component is operably linked to said transmitter component via said telemetering system.

26. The alarm augmentation system of claim 25, further comprising

a processor component, wherein said processor component is (i) operably linked to said display unit, said acquisition unit, said transmitter component, and said first and second signaling components, (ii) capable of receiving and processing information received from said display unit, said acquisition unit, and said first and second signaling components, and (iii) capable of controlling the operation of said transmitter component and said first and second signaling components.

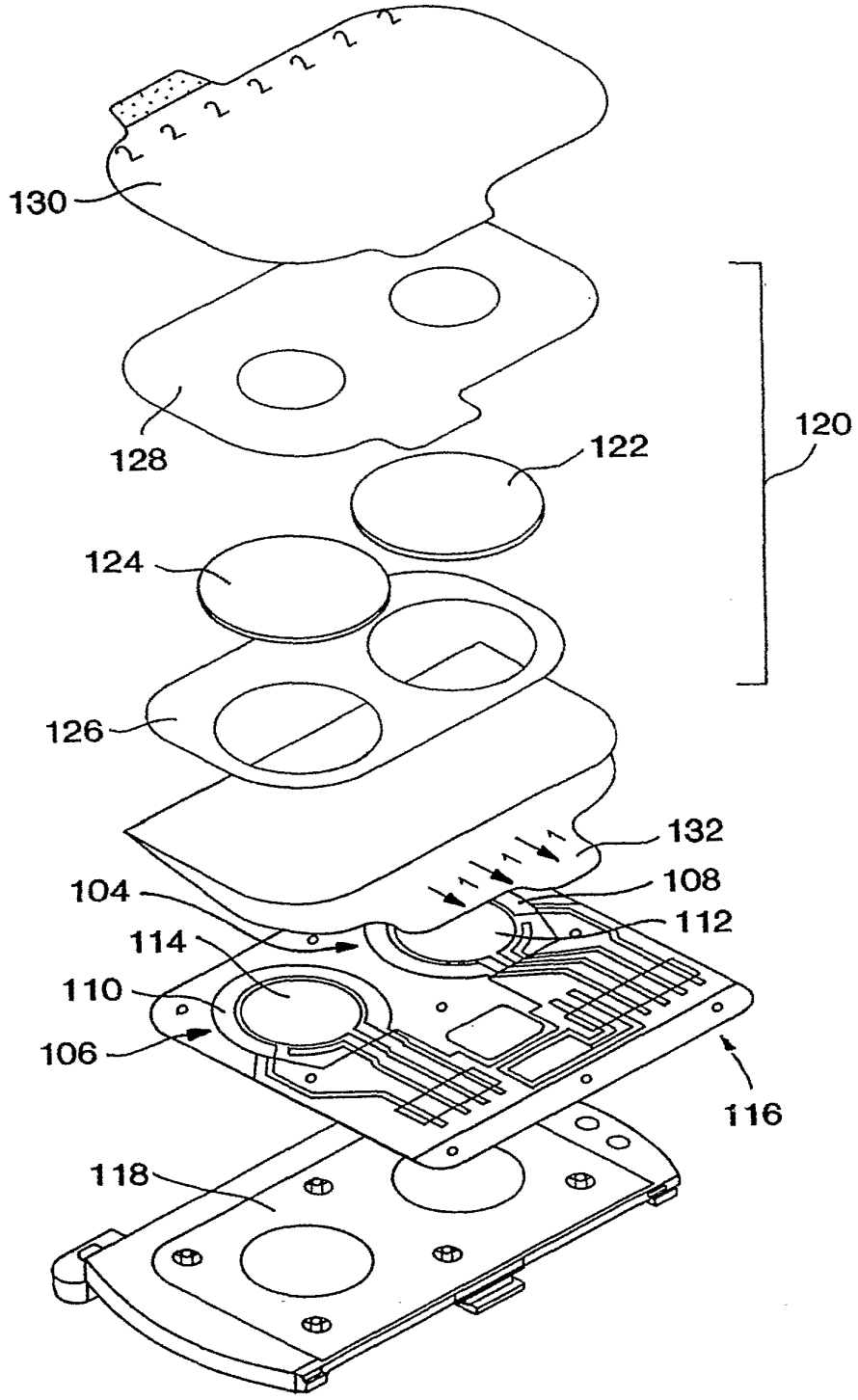


FIG. 1

INTERNATIONAL SEARCH REPORT

Inter nal Application No
PCT/US 01/25152

A. CLASSIFICATION OF SUBJECT MATTER
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According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

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IPC 7 A61B

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

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, PAJ, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 96 00110 A (CYGNUS THERAPEUTIC SYSTEMS) 4 January 1996 (1996-01-04) page 18, line 18-25 page 30, line 33 -page 31, line 12	1,6,17
A	WO 00 47109 A (CYGNUS THERAPEUTIC SYSTEMS) 17 August 2000 (2000-08-17) page 29, line 15-21 page 12, line 27 -page 13, line 15	1,6,17
A	US 4 509 531 A (WARD JOHN W) 9 April 1985 (1985-04-09) column 15, line 51 -column 16, line 24	1,6,17
A	US 4 178 916 A (MCNAMARA ELGER W) 18 December 1979 (1979-12-18)	

☐ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

° Special categories of cited documents :

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"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
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Name and mailing address of the ISA	Authorized officer
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INTERNATIONAL SEARCH REPORT

Information on patent family members

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(54) Title: MICRO-BAND ELECTRODE

(57) Abstract: The invention concerns an electrochemical cell which, either alone or together which a substrate onto which it is placed, is in the form of a receptacle. The electrochemical cell contains a working electrode and a counter electrode, the working electrode being in a wall of the receptacle. At least one of the electrodes has at least one dimension of less than 50μm. The electrochemical cell is principally intended for use as a micro-electrode suitable for screening water, blood, urine or other biological or non-biological fluids.

MICRO-BAND ELECTRODE

Field of the Invention

The present invention relates to an electrochemical cell, typically a micro-electrode for electrochemical detection, a process for manufacturing such a cell and a method for electrochemically testing a substance using the micro-electrode.

Background to the Invention

Micro-electrodes are used for the electrochemical detection of various parameters of a substance. For example, a micro-electrode may be used to detect, or measure the concentration of, a particular compound in a test substance. Typically, micro-electrodes contain an electrode which has at least one dimension which is equal to or less than 50μm, and frequently a dimension of from 1 to 25μm. The use of these systems as sampling devices brings a number of potential benefits including speed of operation, accuracy and minimal sample requirement.

The common forms of large scale production fabricated micro-electrodes are either micro-disc, micro-band or interdigitated electrodes. A micro-disc electrode is a plate like electrode with a diameter of less than about 25μm whereas the micro-band electrode consists of a stripe with a thickness or smallest dimension of less than about 25μm. The interdigitated electrode has a more complex form of two combs with their teeth inter meshed.

By using these micro-electrodes in conjunction with enzymes or other electro-active substances it is possible to create sensors that provide quantitative measurement of target parameters through reactions with the corresponding electro-active substance.

However, several problems occur when using the micro-electrodes known in the art in conjunction with an electro-active substance. Firstly, difficulties are frequently experienced in fixing the electro-active substance to the electrodes and movement of

the substance away from its desired location is often seen. Systems containing several micro-electrodes on a single substrate are particularly susceptible to problems in this regard, since enzymes which are not sufficiently attached to their electrode become loose and migrate from one sensor to another causing cross-contamination. This type of problem is exacerbated by the effect of the sample flowing over the micro-electrode, which tends to wash the electro-active substance off the electrode.

A common manner of immobilizing the electro-active substance, at least to some extent, is to dry it in position on the electrode. However, this is typically not sufficient to hold the electro-active substance in place. Furthermore, drying the electro-active substance on top of the micro-electrode can cause electrical fouling of the electrode.

It is therefore an object of the present invention to provide a micro-electrode which is capable of holding an electro-active substance at the electrode ready for sample testing and which will restrict movement of any such electro-active substance whilst the sample flows over the micro-electrode. It is also desired that the problems of electrode fouling which occur when an electro-active substance is dried to the electrodes will be avoided or reduced.

Summary of the Invention

The present inventors have found that the problems discussed above can be minimised when the micro-electrode is in the form of a receptacle. The receptacle comprises a working electrode in the wall of the receptacle, typically having a small surface area. A counter electrode is also present, this electrode typically having a much larger surface area than that of the working electrode, generally a surface area which is at least an order of magnitude larger than that of the working electrode. The electro-active substance may be placed into the receptacle and is optionally dried into position. The sample is then applied to the receptacle in order that testing can be carried out.

Such a micro-electrode is thus ideally suited to containing the electro-active substance and preventing its movement away from the electrodes. Furthermore, the effect of the sample flowing over the micro-electrode is much reduced and is unlikely to cause the enzyme to be washed away from its position in the base of the receptacle.

The electro-active substance will typically not contact the working electrode in the wall of the receptacle during storage and therefore fouling of this electrode is minimised. Furthermore, the electro-active substance will typically contact only a small proportion of the counter electrode and in some embodiments (discussed below) contact with the counter electrode can be totally avoided. Therefore, if fouling does occur, this will only be to a relatively small area of the electrode. The remaining, unaffected areas of the counter electrode may still operate as normal.

Accordingly the present invention provides an electrochemical cell which, either alone or in combination with a substrate onto which it is placed, is in the form of a receptacle, said cell comprising a counter electrode and a working electrode, wherein at least one electrode has at least one dimension not exceeding 50μm, the working electrode being in a wall of the receptacle. The present invention in particular provides an electrochemical cell in the form of a receptacle, said cell comprising a counter electrode and a working electrode, wherein at least one electrode has at least one dimension not exceeding 50μm, the working electrode being in a wall of the receptacle.

The present invention also provides a process for producing an electrochemical cell such as is described above, which process comprises the steps of:

(a) forming a first part comprising an insulating material which is optionally coated with a counter electrode layer;

(b) forming a second part comprising a laminate of a working electrode layer between two layers of an insulating material;

(c) creating a hole in the second part; and

(d) bonding said first part to said second part to form a receptacle.

Where a counter electrode layer is present in the first part, step (d) comprises bonding the counter electrode layer of said first part to said second part to form a receptacle.

The process of the invention provides a simple and efficient way of producing the micro-electrodes of the invention. Furthermore, the step of creating a hole in the part containing the working electrode may eliminate the need for a separate step to activate the carbon, or other working electrode.

The present invention also provides a multi-analyte device which comprises a plurality of micro-electrodes in a single device. This device enables different types of measurement to be taken for a single sample by using different electro-active substances in the various micro-electrodes. Alternatively, the multi-analyte device can be used to carry out the same test on a single sample several times in order to detect or eliminate errors in results. The multi-analyte device of the present invention also ensures complete segregation of different electro-active substances since each micro-electrode is self-contained.

The present invention also provides a method of electrochemically testing a substance, the method comprising the steps of:

(a) inserting the sample into an electrochemical cell or multi-analyte device of the invention;

(b) applying a voltage or a current between the working and counter electrodes of the micro-electrode; and

(c) measuring the resulting current, voltage or charge across the micro-electrode.

Brief Description of the Figures

Figure 1 depicts an electrochemical cell according to a first embodiment of the invention;

Figure 2 depicts an electrochemical cell containing separate counter and reference electrodes in accordance with a second embodiment of the invention;

Figure 3 depicts an electrochemical cell having multiple working electrodes in accordance with a third embodiment of the invention;

Figure 4 depicts an electrochemical cell having capiliary flow channels in accordance with a fourth embodiment of the invention;

Figure 5 depicts an electrochemical cell in which the counter electrode is in a wall or walls of the cell;

Figure 6 depicts an alternative embodiment of the invention in which the cell itself is not in the form of a receptacle but forms a receptacle when placed on a substrate;

Figures 7, 8 and 9 show a multi-analyte device containing four electrochemical cells of the present invention;

Figure 10 illustrates a process for producing the electrochemical cells of the invention;

Figure 11 illustrates a modified process for producing the electrochemical cells of the invention; and

Figures 12 to 20 illustrate the results of amperometric and cyclic voltammetric experiments carried out using electrochemical cells according to the invention.

Detailed Description of the Invention

An electrochemical cell comprises a working electrode and a counter electrode which are connected to one another electrically. When in use, electrochemical reactions occurring at each of the electrodes cause electrons to flow to and from the electrodes, thus generating a current. An electrochemical cell can be set-up either to harness the electrical current produced, for example in the form of a battery, or to detect electrochemical reactions which are induced by an applied current or voltage.

Embodiment 1

A first embodiment of the present invention is depicted in Figure 1. In this embodiment, the electrochemical cell has a micro-electrode. A micro-electrode has at least one dimension not exceeding 50μm. Microelectrodes exhibit a typical microelectrode response when using cyclic voltammetry. The microelectrodes of the invention may have one or more dimensions which are macro in size, i.e. which are greater than 50μm. Due to these macro dimensions, the electrochemical cells of the invention may exhibit some characteristics which are not usually associated with microelectrodes. For example, the electrochemical cells of the invention may exhibit some degree of Cottrell current. For the purposes of the present specification therefore, the term microelectrode is taken to include any electrode have at least one dimension not exceeding 50μm.

Typically, the micro-electrode will be suitable for screening water (such as river water), blood, urine or other biological fluids or liquids such as beer and wine for determination of their contents. The cell is in the form of a receptacle or a container. The receptacle may be in any shape as long as it is capable of containing a liquid which is placed into it. For example, the receptacle may be cylindrical. Generally, a receptacle will contain a base 1 and a wall or walls 2 which surround the base. In one embodiment of the invention, which is described further below, the cell itself does not have a base and thus is not, alone, a receptacle. However, the cell is designed such that when placed against a separate substrate, the cell together with the

substrate forms a receptacle. In this embodiment, the cell comprises a wall or walls 2 which surround an open "base". The open "base" may be placed against the substrate to form a receptacle, such that the substrate forms the true base of the receptacle thus formed.

Typically, the receptacle will have a depth (i.e. from top to base) of from 50 to 1000μm, preferably from 200 to 800μm, for example from 300 to 600μm. The length and width (i.e. from wall to wall), or in the case of a cylindrical receptacle the diameter, of the receptacle is typically from 0.1 to 5mm, for example 0.5 to 1.5mm, such as 1mm.

The open end of the receptacle 3 may be partially covered by an impermeable material as long as at least part of the open end is uncovered, or covered by a permeable material, such as a permeable membrane. Preferably, the open end of the receptacle is substantially covered with a permeable membrane 4. The membrane 4 serves to prevent dust or other contaminants from entering the receptacle, and helps to keep any electro-active substance which might be inserted into the receptacle in position.

The membrane 4 is preferably made of a material through which the sample to be tested can pass. For example, if the sample is a blood sample, the membrane should be permeable to blood. Suitable materials for use as the membrane include polyester, cellulose nitrate, polycarbonate, polysulfone, microporous polyethersulfone films, PET, cotton and nylon woven fabrics, coated glass fibres and polyacrylonitrile fabrics. These fabrics may optionally undergo a hydrophilic or hydrophobic treatment prior to use. Other surface characteristics of the membrane may also be altered if desired. For example, treatments to modify the membrane's contact angle in water may be used in order to facilitate flow of the desired sample through the membrane. The membrane may comprise one, two or more layers of material, each of which may be the same or different. For example, conventional double layer

membranes comprising two layers of different membrane materials may be used.

The membrane may also be used to filter out some components of the sample which are not desired to enter the cell. For example, some blood products such as red blood cells or erythrocytes may be separated out in this manner such that these particles do not enter the cell. Suitable filtration membranes, including blood filtration membranes, are known in the art. An example of a blood filtration membrane is Presence 200 of Pall filtration.

The electrochemical cell of the invention contains a working electrode 5 which is situated in a wall of the receptacle. The working electrode is, for example, in the form of a continuous band around the wall(s) of the receptacle. The thickness of the working electrode is typically from 0.01 to 25 μm, preferably from 0.05 to 15μm, for example 0.1 to 20μm, more preferably from 0.1 to 10μm. Thicker working electrodes are also envisaged, for example electrodes having a thickness of from 0.1 to 50 μm, preferably from 5 to 20 μm. The thickness of the working electrode is its dimension in a vertical direction when the receptacle is placed on its base. The working electrode is preferably formed from carbon, palladium, gold or platinum, for example in the form of a conductive ink. The conductive ink may be a modified ink containing additional materials, for example platinum and/or graphite. Two or more layers may be used to form the working electrode, the layers being formed of the same or different materials. For example, a layer of Ag/AgCl may be present beneath the working electrode layer.

The counter electrode 6 typically forms at least a part of either the base or the top of the receptacle, although the counter electrode may also be present in the wall or walls of the receptacle. In the present embodiment, the counter electrode 6 forms the base of the receptacle. The counter electrode is typically made from $Ag/AgSO_4$ carbon, Ag/AgCl, palladium, gold, platinum, $Cu/CuSO_4$, $Hg/HgCl_2$ or $Hg/HgSO_4$. It is preferably made from carbon, Ag/AgCl, palladium, gold, platinum, $Cu/CuSO_4$,

$Hg/HgCl_2$ or $Hg/HgSO_4$. Each of these materials may be provided in the form of a conductive ink. The conductive ink may be a modified ink containing additional materials, for example platinum and/or graphite. Typically, the electrochemical cell of the invention contains only one counter electrode.

The counter electrode 6 typically has a surface area which is of a similar size to, or which is larger than, for example substantially larger than, that of the working electrode 5. Typically, the ratio of the surface area of the counter electrode to that of the working electrode is at least 1:1, such as at least 5:1, 10:1, preferably at least 20:1, more preferably at least 25:1. The counter electrode may, for example, be a macroelectrode. Preferred counter electrodes have a dimension of 0.01mm or greater, for example 0.1mm or greater. This may be, for example, a diameter of 0.1mm or greater. Typical areas of the counter electrode are from $0.001mm^2$ to $10mm^2$, preferably about $5mm^2$. The minimum distance between the working electrode and the counter electrode is preferably from 10 to 1000μm, for example from 10 to 300μm.

In a typical cell according to the invention, each electrode will be separated from the neighbouring electrode by a distance of from 10 to 1000μm, for example from 50 to 200μm or from 75 to 150μm. In order that the cell can operate, the electrodes must each be separated by an insulating material 7. The insulating material is typically a polymer, for example, an acrylate, polyurethane, PET, polyolefin, polyester or any other stable insulating material. Polycarbonate and other plastics and ceramics are also suitable insulating materials. The insulating layer may be formed by solvent evaporation from a polymer solution. Liquids which harden after application may also be used, for example varnishes. Alternatively, cross-linkable polymer solutions may be used which are, for example, cross-linked by exposure to heat or UV or by mixing together the active parts of a two-component cross-linkable system. Dielectric inks may also be used to form insulating layers where appropriate.

The electrodes of the electrochemical cell may be connected to one another and to any required measuring instruments by any suitable means. Typically, the electrodes will be connected to electrically conducting tracks which are themselves connected to one another and to the required measuring instruments.

The cell of the present invention may contain an electro-active substance 8. The electro-active substance 8 may be any substance which is capable of causing an electrochemical reaction when it comes into contact with a sample. Thus, on insertion of the sample into the cell and contact of the sample with the electro-active substance, electrochemical reaction may occur and a measurable current, voltage or charge may occur in the cell.

The electro-active substance 8 comprises an electrocatalyst. Typically the electro-active substance 8 comprises an electrocatalyst and a mediator. A mediator is a chemical species that has two or more oxidation states of distinct electro-active potentials that allow a reversible mechanism of transferring electrons/charge to an electrode. The mediator reacts with the sample in the electrochemical reaction, the reaction being catalysed by the electro-catalyst. Typical examples of an electro-catalyst are enzymes, for example lactate oxidase, cholesterol dehydrogenase, lactate dehydrogenase, glycerol kinase, glycerol-III-phosphate oxidase and cholesterol oxidase. Ionic species and metal ions, for example cobalt, may also be used as the electrocatalyst. Examples of suitable mediators are ferricyanide, ferrocyanide and ruthenium compounds such as ruthenium (III) hexamine.

The electro-active substance 8 is typically inserted into the receptacle in such a position that the electro-active substance is not in contact with the working electrode. This ensures that fouling of the working electrode is minimised or avoided. The electro-active substance may be dried to ensure that it remains in position. In a preferred embodiment of the invention, the electro-active substance is pre-coated onto the substrate which forms the base of the receptacle. This may be done either

by directly coating the electro-active substance onto a flat substrate, or by forming a well in the substrate and dispensing an electro-active substance into the well. Typically, the electro-active substance is then dried into position and the thus-coated substrate is joined to the walls of the receptacle. Where the electro-active substance is inserted into a well in the substrate, the well typically has a cross-section which is identical to that of the final electrochemical cell. Thus, the well creates the bottom part of the receptacle formed by the electrochemical cell. Where the counter electrode is on the base of the receptacle, the electro-active substance is pre-coated onto the counter electrode layer.

This embodiment has the advantage that the electro-active substance is kept remote from the working electrode at all times during manufacture of the cell. Contact between electro-active substance and working electrode is therefore minimised before the cell is used. This in turn minimises fouling of the working electrode.

In an alternative preferred embodiment, the electro-active substance is impregnated into a membrane which is placed onto the substrate either before or after, preferably before, the substrate is joined to the walls of the receptacle. The electro-active substance may equally be impregnated into the membrane 4 which covers the cell. This embodiment also avoids contact between the electro-active substance and the working electrode and minimises fouling.

The receptacle forming the micro-electrode of the present invention may, for example, contain one or more small air-holes in its base or its wall or walls (not depicted in Figure 1). These holes allow air to escape from the receptacle when sample enters the receptacle. If such air-holes are not present, the sample may not enter the receptacle when it flows over the open end, or it may enter the receptacle only with difficulty. The air holes typically have capiliary dimensions, for example, they may have an approximate diameter of 1-25μm. Typically, from 1 to 4 air holes may be present.

Embodiment 2

A second embodiment of the invention, which is the same as the first embodiment except as described below, is depicted in Figure 2. In this embodiment, the cell contains one or more reference electrodes 9 in addition to the working and counter electrodes. In the case that no reference electrode is present (as in the first embodiment described above), the counter electrode acts as a reference or pseudo reference electrode. Typically, the reference electrode will be located in a wall of the receptacle 2. For example, the reference electrode may be in the form of a continuous band. The counter and working electrodes 6 and 5 may be positioned such that the reference electrode 9 is located between them, as is depicted in Figure 2, or the counter and working electrodes 6 and 5 may be adjacent. The reference electrode is typically made from $Ag/AgSO_4$, carbon, Ag/AgCl, palladium, gold, platinum, $Cu/CuSO_4$, $Hg/HgCl_2$ or $Hg/HgSO_4$. It is preferably made from carbon, Ag/AgCl, palladium, gold, platinum, $Cu/CuSO_4$, $Hg/HgCl_2$ or $Hg/HgSO_4$. Each of these materials may be provided in the form of a conductive ink. The conductive ink may be a modified ink containing additional materials, for example platinum and graphite.

Embodiment 3

A third embodiment of the invention, which is the same as either the first or second embodiments except as described below, is depicted in Figure 3. This embodiment of the invention is a multi-ring electrode which contains one or more further electrodes 10, 10' in addition to the working, counter and optionally reference electrodes. The one or more further electrodes 10, 10' typically act as additional working electrodes. Preferably, the counter electrode 6 acts as both the counter and the reference electrode and a separate reference electrode, as described in embodiment 2, is not present.

Typically, the receptacle comprises no more than 10 electrodes in total, including

working, counter and reference electrodes. Preferably no more than 7 electrodes, more preferably no more than 5 electrodes are present. More preferred receptacles contain 2, 3 or 4 electrodes. Where more than one working and/or reference electrode is present, these are typically located one above the other in the wall(s) of the receptacle.

The additional working electrodes 10, 10' allow different measurements to be carried out simultaneously on the same sample by applying different potentials across two or more of the working/counter electrode pairs. Alternatively, the same potential may be applied to each working electrode and the same measurement recorded several times for the same sample. This helps to eliminate or detect errors in the measurements taken.

In one particular example of this embodiment, one of the working electrodes is present on the base of the receptacle, i.e. in the position in which the counter electrode 6 is depicted in Figure 3. In this case, the counter electrode is present either in the wall(s) of the receptacle as described below with reference to embodiment 5, or in the top of the receptacle as described below with reference to embodiment 4.

Embodiment 4

A fourth embodiment of the invention, which is the same as the first, second or third embodiments except as described below, is depicted in Figure 4. In this embodiment, the cell comprises one or more capiliary channels 11 to allow sample to enter the receptacle. The capiliary channels are, for example, covered by a capiliary film. Examples of suitable capillary films are PET films such as Melinex or ARcare®, adhesive coated films by Adhesive Research, and hydrophilic coated films such as ARcare® 8877, which can offer better capillary performance. In this embodiment, the receptacle is preferably covered by a substantially impermeable material 12. The impermeable material 12 is typically a capiliary film as described

above. One or more capiliary channels 11 are provided, for example in a wall or walls of the receptacle 2, through which the sample may enter the receptacle. Typically, as is depicted in Figure 4, the capiliary channel 11 is located at the point where the wall 2 meets the impermeable material 12.

In order that air can escape from the receptacle and allow the sample liquid to enter, one or more air holes must be present in this embodiment. Typically, an air hole will be positioned at the point where the base meets the wall of the receptacle, as indicated by the label 12a in Figure 4. The air hole(s) preferably have the dimensions described above and preferably from 1 to 4 air holes are present.

This embodiment has the advantage that the top of the receptacle is closed and thus the counter electrode may either be located at the top 3, at the base 1, or in the wall(s) 2 of the receptacle. The counter electrode 6 is depicted at the top of the receptacle in Figure 4. This is achieved by bonding the counter electrode 6 to the impermeable material 12 prior to its attachment to the receptacle. In this way, the electro-active substance 8, which is typically located on the base 1 of the receptacle, is not in contact with either the working or the counter electrodes and thus electrode fouling is significantly reduced or eliminated. It is possible to locate the electro-active substance on the top 3 of the receptacle, typically by pre-coating the substance onto the substrate which is to form the top 3 prior to its attachment to the receptacle.

A further advantage of placing the counter electrode at the top of the receptacle is that the base of the receptacle may be coated, or adapted in another way, to make it more suitable to receive the electro-active substance which is typically dried onto the base. For example, the base may be made of a particular material, such as carbon (provided that the carbon is electrically insulated from the electrodes), which is suitable for depositing enzymes on. Alternatively, the base may be coated with a hydrophilic coating.

If desired, the base of the cell may be formed from a permeable membrane which may be of the same type as the membrane 4 discussed above. The membrane is typically impregnated with an electro-active substance prior to attachment to the cell. This avoids electrode-fouling caused by contact between electro-active substance and working electrode during insertion of the electro-active substance.

Embodiment 5

An alternative embodiment of the invention is depicted in Figure 5. This embodiment is the same as any one of embodiments 1 to 4 discussed above except as described below. The counter electrode 6 in the cell of this embodiment is located in a wall or walls 2 of the receptacle. The counter electrode is, for example, in the form of a continuous band around the wall(s) of the receptacle.

The thickness of the counter electrode in this embodiment is typically from 0.1 μm to 1 mm, preferably from 5 to 500μm, for example from 5 to 100μm, more preferably from 5 to 50μm. The thickness of the counter electrode in this embodiment is its dimension in a vertical direction when the receptacle is placed on its base. The ratio of the surface area of the counter electrode to that of the working electrode may, in this embodiment, be less than the preferred value of 25:1 which applies for counter electrodes located in the base or top of the receptacle. Preferred ratios for this embodiment are in the range 1:1 to 10:1, preferably 2:1 to 5:1.

Embodiment 6

A further embodiment of the invention, which is depicted in Figure 6, relates to a modification of the above described electrochemical cell in which the receptacle is completed when the cell is placed on a substrate 21. In this manner, the substrate 21 forms the base of the receptacle. The cell of this embodiment alone is not necessarily in the form of a receptacle since it has an opening at the position of the base 1. However, when placed onto a separate substrate 21, the cell together with the substrate forms a receptacle.

This embodiment therefore relates to an electrochemical cell comprising a counter electrode and a working electrode, wherein at least one electrode has a dimension of less than 50 μm, and wherein the cell has a shape such that, when placed on a substrate, the cell, together with the substrate on which it is placed, forms a receptacle, the working electrode being in a wall of the receptacle.

The electrochemical cell of this embodiment is at least partially open at its base 1. In this context, the term "open" includes a total absence of a base material and also the presence of a material which allows sample liquid to pass through it. Typically, the cell's base 1 is either at least partially uncovered or at least partially covered with a permeable membrane. The permeable membrane is optionally impregnated with an electro-active substance prior to its attachment to the walls of the receptacle.

The top of the cell 3 may be totally or partially covered with a permeable membrane 4 (as depicted) or with an impermeable material. If the cell is at least partially covered with an impermeable material, the counter electrode may be located at the top of the cell coated onto the impermeable material as described with reference to embodiment 4 above. This is achieved by bonding the counter electrode 6 to the impermeable material 12 prior to its attachment to the walls of the receptacle. An electro-active substance (not depicted), as described above, may also be bound to the counter electrode prior to its attachment to the walls of the receptacle. If the cell is totally covered with an impermeable material, air-holes, as described with reference to embodiment 4, are preferably present in order to facilitate entry of a sample liquid into the cell. Alternatively, the counter electrode 6 may be located in the wall(s) of the cell as described in embodiment 5 above and as depicted in Figure 6. Where the top of the cell 3 is open or covered only with a permeable membrane, the counter electrode is located in the wall(s) of the cell as here depicted.

The sample liquid to be tested enters the cell either through the top of the receptacle (where the top is not totally covered by an impermeable membrane), or, more

usually, through the open base. This is typically achieved by placing the cell onto a substrate which is already coated with the sample liquid. Alternatively, the cell may be placed onto the substrate, either directly or through a permeable membrane, and the substrate then pierced within the receptacle in order to introduce a liquid sample present under the substrate surface into the receptacle. For example, the substrate may be the skin and the sample liquid blood. Alternatively, the substrate may be a pre-packaged container in which a sample liquid is present, the sample liquid being released when the container is pierced.

A non-limiting example of a use of the cell of this embodiment is as a self-testing blood analysis kit. A diabetic user for example might employ such a cell to carry out glucose analysis tests on samples of their blood. This can be done by (i) piercing the skin, e.g. a finger, which is optionally covered with a permeable membrane, (ii) placing the cell over the blood spot produced such that the skin, or the permeable membrane as relevant, together with the cell form a receptacle, and (iii) operating the cell in the usual manner. Alternatively, the cell may first be placed onto the skin or permeable membrane and the skin subsequently pierced through an open part of the receptacle. In the same manner, the cell can also be used for other types of blood test.

The remaining features of the cell are typically as described above with regard to the other embodiments of the invention.

Multi-analyte Device

The present invention also provides a multi-analyte device which comprises two or more micro-electrodes of this invention, for example in accordance with any one of embodiments 1 to 6 above. The micro-electrodes of the multi-analyte device may each be of the same or different designs. Typical multi-analyte devices according to the invention are described in Figures 7, 8 and 9. The multi-analyte device will typically comprise a plate or strip 14 which contains one or more micro-electrodes

13a, b, c and d. Each micro-electrode may contain the same or different electro-active substances such that when a sample is inserted into each receptacle, several different tests may be carried out or the same test may be repeated several times in order to detect or eliminate errors in the measurements taken. Furthermore, the micro-electrodes may be set at different potentials, again providing different measurements for the same sample.

The micro-electrodes are typically separated by a distance of from 250μm to 550μm, for example from 250μm to 425μm.

A multi-analyte device can also be made with a "vertical" arrangement of cells as an alternative to Embodiment 3.

In this arrangement the sample in the first micro-electrode passes to a further micro-electrode below it, for example, using a permeable membrane in the base of the first micro-electrode, for a determination of a different component in the sample. The permeable membrane may be impregnated with an electro-active substance.

The electrical tracks 15 of the multi-analyte device are typically on the top surface of the device. Filled vias are used to connect the counter, optional reference and working electrodes to the surface tracks 15 which then mate with a measuring instrument 16, or the laminated back/counter can be arranged to mate with the instrument directly.

The multi-analyte device may contain one or more blank electrodes 17 as is depicted in Figure 8. The blank electrode(s) do not contain a counter electrode. This embodiment may, for example, be useful where the electro-active substance has a working potential which conflicts with that of the counter electrode system. In this situation, reduction or oxidation of the mediator contained in the electro-active substance may occur. Thus, for example, where the counter electrode is a Ag/AgCl

couple and the mediator is ferricyanide, the redox state of the mediator is such that it interacts with the Ag/ACl, forming a battery system or galvanic cell in which reactions occur spontaneously as soon as there is liquid connection between them.

The multi-analyte device may also comprise capiliary channels 18 as are depicted in Figure 9. These capiliary channels are preferably of the type described in embodiment 4 above. Thus, each receptacle is provided with a capiliary channel which may optionally be connected to a single channel from which the sample is drawn.

Process for Producing Electrochemical Cells

A process for producing the electrochemical cells of the first embodiment of the present invention is depicted in Figure 10. The cells may be produced by a process which comprises the steps of:

(a) forming a first part 18 comprising an insulating material 18a which is optionally coated with a counter electrode layer 18b;

(b) forming a second part 19 comprising a laminate of a working electrode layer 19a between two layers 19b and c of an insulating material;

(c) creating a hole 19d in the second part; and

(d) bonding said first part 18 to said second part 19 to form a receptacle.

The materials, dimensions and other properties of the electrochemical cell are as described above.

Where the counter electrode is in the base of the receptacle, the first part comprises an insulating material 18a which is coated with a counter electrode layer 18b as depicted in Figure 10. In this case, step (d) comprises bonding the counter electrode layer 18b of said first part 18 to said second part 19 to form a receptacle.

Alternatively, when the counter electrode is in a wall or walls of the electrode as

described in embodiment 5 above, the counter electrode layer may be absent from the first part and the second part comprises a counter electrode layer between two layers of insulating material.

Step (c) in which a hole is created in the second part may be carried out by any suitable means. For example, the hole may be punched or drilled or formed by die-cutting, ultra-sonic cutting or laser drilling. This step has the advantage that the electrode surfaces are automatically cleaned by the action of creating the hole, thus reducing the requirement for a separate step of cleaning the electrodes.

A suitable technique for creating the hole is to punch the second part with a pneumatic or hydraulic press tool. Holes of 0.1 to 5mm, preferably 0.5 to 1.5, more preferably about 1mm diameter are preferred. The hole should extend down through all of the printed layers and the substrate. The punching tool can be coated with hardening materials such as titanium and may or may not have an angled cutting edge. For example, the tool may be Ti coated with a 2° angle from the horizontal cutting edge.

The bonding step (d) may be carried out by any suitable bonding technique. For example, bonding may be performed using pressurized rollers. A heat sensitive adhesive may be used, in which case an elevated temperature is needed. Room temperature can be used for pressure sensitive adhesive.

If desired, air channels may be created in the micro-electrode at the joint between the first part 18 and the second part 19. This can be achieved, for example, by creating grooves in either the bottom side of the second part 19b or the top side of the first part 18a prior to bonding these two parts together.

Carbon or other inks may, for example, be printed onto the insulating material 18a, 19b, 19c using a screen printing, ink jet printing, thermal transfer or lithographic or

gravure printing technique, for example the techniques described in GB 0106417.9. The insulating layer 19c may also be formed by printing an insulating material onto the working electrode layer. Other techniques for forming the insulating layer include solvent evaporation of a solution of the insulating material or formation of an insulating polymer by a cross-linking mechanism.

Each electrode is typically printed, or otherwise coated, onto the relevant insulating layer in a chosen pattern. For the working electrode or other electrodes which are to be formed in the wall of the receptacle, the pattern selected should be such that at least a part of the electrode layer is exposed when hole 19d is created. Preferably the pattern chosen is such that the electrode layer is exposed around the whole perimeter of hole 19d.

In one embodiment, two or more printing or other coating steps are carried out to create an electrode layer. One or more steps, preferably one step, uses a pattern which deposits conductive material in the area which will form the perimeter of hole 19d as well as, for example, areas which are to form conductive tracks. This layer is exposed when hole 19d is created and forms the electrode. One or more further steps uses a pattern which deposits conductive material, for example, in areas which are to form conductive tracks but deposits no material in the area which will form the perimeter of hole 19d. These areas are not exposed when hole 19d is made. Thus, a thin electrode layer is formed around hole 19d, leading to a thin electrode in the wall of the finished receptacle, whilst a thicker layer is formed away from hole 19d. This thicker layer has a lower resistance and thus leads to a more efficient functioning of the electrochemical cell. This use of a double layer is particularly preferred with regard to the working electrode.

If desired, the one or more layers may be formed of different materials. For example, the layer which will be exposed at hole 19d may be formed of carbon whilst a further layer, for example a sub-layer, of a different material may be used.

The working electrode, counter electrode and reference electrode may all be produced by printing ink containing the desired material onto the substrate. Insulating layers may also be produced in this manner by printing an ink containing an insulating material onto a substrate or onto a conductive layer. Screen printing is a preferred manner in which this is carried out. Typically, a conductive layer will be printed onto a substrate and a dielectric layer will be printed onto the conductive layer.

Screen printing is generally carried out on polyester, polycarbonate, or other plastic/ceramic substrate. Types of substrates used are for example, DuPont films of Mylar A, Mylar ADS, Melinex, Kaladex, Tejin Tetoron, Purex, Teonex. Substrates used are preferably surface treated to improve adhesion of the ink to the substrate, for example by corona discharge or chemical modification. Substrates are also preferably laminated on one side, for example with either heat sensitive or pressure sensitive adhesive in the thickness range 20μm to 200μm, preferably about 40μm. A preferred embodiment employs 250μm thick Mylar ST535 with 40μm thermally activated adhesive laminate as a substrate.

A screen is selected from stock with the carbon stencil defined with photosensitive emulsion with a thickness of 10μm to 20μm, preferably about 13μm. The required thickness of the print is determined by the mesh count of the screen. Typically this is within the range of 83t/inch to 330t/inch, preferably 305t/inch for both carbon Ag/AgCl inks, and about 195t/inch for dielectric ink. The ink is typically forced through the mesh using a squeegee rubber of 65 to 85 shore hardness, preferably 75-shore hardness.

Suitable mesh counts are as follows:

Approx thickness of print when using 330t/inch / = 7μm

305t/inch / 120t/cm = 10μm
195t/inch / 77t/cm = 15μm
156t/inch / 61t/cm = 20μm
83t/inch / = 25μm

The printed layer is typically dried using the ink manufacturer recommendations. It is typically stoved in an oven for 2 minutes to 4 hours, preferably 1 hour, at about 70-130°C. Air drying, or air forced tunnel drying for 2-3 minutes at 90-130°C may also be used.

The screen printed dielectric layer can be replaced by a laminate of polyester, polycarbonate or similar (preferably Mylar ST535) which covers the carbon layer and with thickness in the range 10μm to 200μm, preferably 10μm to 30μm.

Suitable inks for use in the screen printing processes are as follows:

Carbon Inks:

1. Coates carbon 26-8203
2. Ercon G449
3. Du-pont L881

Dielectric Inks:

1. Ronseal ultra tough hardglaze clear varnish.
2. Ercon E6165-116 blue insulator.
3. Du-Pont 5036 encapsulant
4. Coates screen flex coverlay.

Silver/Silver chloride Inks:

1. Gem ag/agcl
2. Ercon E0430-128

3. Du-Pont 5874 conductor

After forming the receptacle, an electro-active substance as described above may be inserted into the micro-electrode, for example, using micropipetting or enzyme jet printing. The electro-active substance may then be dried by any suitable technique. Alternatively, the electro-active substance may be pre-coated onto the base before bonding step (d) takes place. To achieve this, the electro-active substance is typically coated onto layer 18b, dried into position and subsequently parts 18 and 19 are bonded together as described above. A further option is to impregnate the electro-active substance into a membrane which can be placed on, or fixed onto, layer 18b prior to or after bonding step (d).

If desired, a permeable membrane may then be placed over the receptacle (as in Figure 1). Membrane structures are applied to the top surface of the device using double sided adhesive or screen printed pressure sensitive adhesive. Attachment of the membrane 20 may, for example, be carried out by using a pressure sensitive adhesive (which has been cast) that has been die cut to remove the adhesive in the area over the receptacle. In the embodiments in which the electro-active substance is impregnated into membrane 4, impregnation of the desired substance is typically carried out before the membrane is attached to the receptacle.

If one or more capiliary channels are desired, these are preferably formed by creating one or more grooves in the top of the second part 19c, the grooves being connected to the hole 19d, or the top of the receptacle. The grooves may conveniently be created during the same process as creating the hole in the second part. For example, using a technique of pressing, punching, die-cutting, ultra-sonic cutting or other suitable film fabrication technique. The second part may then be coated with an impermeable material, for example a capiliary film as described above, thus creating a capiliary channel connected to the receptacle and which allows a sample to enter the receptacle.

A modified process may be used when the electro-active substance is to be pre-coated into a well in the substrate which forms the base of the receptacle. This modified process is depicted in Figure 11.

In this process, step (a) comprises, if desired, coating insulating layer 18a with counter electrode layer 18b as described above. A further insulating layer 18c is provided which has a pre-formed hole 18d. Hole 18d is typically of the same size as hole 19d and may be formed by the techniques mentioned above with reference to hole 19d. Insulating layer 18c is bonded to layer 18b thus creating a well in the position of hole 18d. An electro-active substance is then dispensed into this well, for example using micro-pipetting or enzyme jet printing. The electro-active substance may then be dried by any suitable technique. Following addition of the electro-active substance, Part B (18) may be used in bonding step (d) in the manner described above.

An alternative process may be used when the invention is to be produced in accordance with embodiment 4 above. In this embodiment, the process comprises the steps of:

(a) forming a first part comprising an insulating material;

(b) forming a second part comprising a laminate of a working electrode layer between two layers of an insulating material;

(c) creating, in the second part, a hole and a capiliary channel to allow a sample to enter said hole;

(d) bonding said first part to said second part to form a receptacle;

(e) placing an electro-active substance as described above into the receptacle and optionally drying the electro-active substance; and

(f) bonding to the open end of said receptacle a layer which is optionally coated with a counter electrode material.

The materials, dimensions and other properties of the electrochemical cell are as described above. Step (c), comprising forming a hole and a capiliary channel in the second part may be carried out as described above. In this process, the impermeable

material or capiliary film is typically coated on the underside with a counter electrode material before it is bonded. Thus, when this layer is coated to the top of the receptacle, a counter electrode is formed. Alternatively, when the counter electrode is in a wall or walls of the electrode as described in embodiment 5 above, the counter electrode layer may be absent from the layer used in step (f) and instead the second part comprises a counter electrode layer between two layers of insulting material.

In a modification of the above process, the electro-active substance may be pre-coated onto either the base or the top of the receptacle by any desired technique, for example those discussed above, thereby eliminating the need for step (e). Thus, an alternative preferred process comprises steps (a), (b), (c), (d) and (f) above and employs (i) a first part which comprises an electro-active substance on its surface and/or (ii) a layer for use in step (f) comprising an electro-active substance on its surface. Where said layer for use in step (f) comprises a counter electrode layer, the electro-active substance is typically coated onto the counter electrode layer. Following bonding step (f), a receptacle is thus formed having an electro-active substance coated to the interior surface of either the base or the top. If desired, the electro-active substance may be placed into a well in the substrate as discussed above in relation to Figure 11.

In one embodiment, the insulating material of the first part is a permeable membrane as described above. The membrane is optionally impregnated with an electro-active substance prior to bonding step (d).

In order to form the electrochemical cell described in Embodiment 6 above, a modified version of any of the above described processes is used in which the step of bonding the first part to the second part is omitted. Thus, the process comprises :

(a) forming a second part 19 comprising a laminate of a working electrode layer 19a between two layers 19b and c of an insulating material;

(b) creating a hole 19d in the second part; and optionally

(c) bonding to said second part a layer which is coated with a counter electrode

material.

Steps (a) and (b) are carried out as described above with reference to corresponding steps. The process may optionally comprise a further step, which may be carried out before or after step (c), of attaching to the bottom of the second part a permeable membrane which may optionally have an electro-active substance impregnated into it. If the counter electrode is present in the top of the cell, step (c) above is carried out. If the counter electrode is present in a wall of the cell, step (c) may be omitted and the second part additionally comprises a layer of counter electrode material between two layers of insulating material.

An electro-active substance may be coated onto the counter electrode layer, if desired and alternatively or additionally to the electro-active substance bound to any permeable membrane present. This coating process may be carried out as described above.

In order to form the multi-analyte devices of the present invention, the step (c) described in one of the two processes above is extended to include the formation of two or more holes in the second part. Thus, when the bonding step (d) is carried out, two or more receptacles are formed. Where capiliary channels are used, these may be formed as described above at each of the receptacles. Thus, samples may be drawn into each micro-electrode by capiliary action.

Typical Uses of the Electrochemical Cell

The electrochemical cell of the present invention is intended principally for use as a micro-electrode for screening purposes, i.e. for screening liquid samples. For example, the cell may be used for determining the content of various substances in water, beer, wine, blood or urine samples, or samples of other biological or non-biological fluids. The cells may, for example, be used to determine the pentachlorophenol content of a sample for environmental assessment; to measure cholesterol, HDL, LDL and triglyceride levels for use in analysing cardiac risk, or for measuring glucose levels, for

example for use by diabetics. A further example of a suitable use for the cells of the invention is as a renal monitor for measuring the condition of a patient suffering from kidney disease. In this case, the cells could be used to monitor the levels of creatinine urea, potassium and sodium in the urine.

Whilst the major use envisaged for the electrochemical cells of the invention is as a microsensor, the cells may also be used for any other purpose in which electrochemical measurement or the harnessing of electrochemical energy takes place. For example, the electrochemical cell of the invention may be used as a battery. The cell may also be used to process an electro-active substance such as an intercalating material used for detection of electrolytes such as sodium, potassium, calcium and phosphates. Such processing may involve electro-cycling of the substance in order to develop a consistent thin layer on the electrodes.

Examples

Example 1: Manufacture of Electrochemical Cell

A base film of 125μm thick PET was printed with the counter / reference electrode using a silver/silver chloride printing ink, and then dried at 90°C for 30 minutes.

A middle film of 250μm PET was coated with heat seal. The film was then printed on the reverse side to the heat seal coating with a conductive carbon ink in a pattern that defines the conductive tracks. This was then dried at 90°C for 1 hour. The carbon ink print was subsequently over printed with a dielectric ink, except for the part of the tracks that were required to mate with the connector in the measuring instrument, where over printing was not carried out. The dielectric ink was then dried at 60°C for 20 minutes.

Several holes were then formed in the middle layer using a punch that forms the holes using a shearing action. This punch comprised metal dies or pins having a diameter

equal to that of the required holes. The metal dies or pins were used to shear the film which was supported by metal or wooden plates having holes that match the formation of the punch in order to allow the punch to slide.

Following punching of the holes, the middle film was laminated to the base film using heat. During the heating step, the heat seal on the underside of the middle film melts and bonds to the base film.

The desired electro-active substances were then dispensed into the wells formed. The substances were then dried using room temperature airflow over the surface.

Over some of the wells, a blood separation membrane was added that is capable of removing the larger cellular particles from whole blood. For these electrodes, a blood separation membrane such as Presence 200 by Pall filtration was attached to the top most surface of the electrodes covering the wells. Attachment of the membranes was accomplished by using a screen printed pressure sensitive adhesive cast around the wells onto the middle layer.

Example 2: Use of Electrochemical Cell

Electrodes were constructed from a 250 μm PET layer on which a 15 μm Coates carbon ink 26-8203 layer had been screen-printed followed by a 30 μm layer of Ronseal ultra tough hardglaze clear varnish (a polyurethane bsed on Baxenden trixine containing polyurethane and isocyanates). This layer was punched to produce a 1 mm diameter hole. A PET base layer was produced consisting of a 125 μm PET layer having a common Ag/AgCl counter reference on the top. The PET base layer was then adhered to the punched layer using ARcare 7841 sheet adhesive. Various tests were carried out using this electrochemical cell as described below at Examples 2a to 2f.

Example 2a

Cyclic voltammetric current was measured at -0.45 V vs. Ag/AgCl after addition of concentrations of 2, 5, 10, 15 and 20 mmol dm^{-3} ruthenium hexaamine in 0.1 mol dm^3 Tris buffer at pH 9 containing 0.1 mol dm^{-3} KCl. Results are shown in Figure 12.

Example 2b

Amperometric current was measured 1 second after the application of a -0.50 V vs. Ag/AgCl potential step after addition of concentrations of 2, 5, 10, 15 and 20 mmol dm^{-3} ruthenium hexaamine in 0.1 mol dm^{-3} Tris buffer at pH 9 containing 0.1 mol dm^{-3} KCl. Results are shown in Figure 13.

Example 2c

Cyclic voltammetric current was measured at 0.15 V vs. Ag/AgCl immediately after addition of 2, 4, 6, 8 and 10 mmol dm^{-3} NADH in 0.1 mol dm^{-3} Tris buffer at pH 9 containing 0.1 mol dm^{-3} KCl to electrodes on which 0.2 mL of a solution containing 0.2 mol dm^{-3} ruthenium hexaamine and 650 KU /mL putadiaredoxin reductase has been dried. Results are shown in Figure 14.

Example 2d

Amperometric current was measured 1 second after the application 0.15 V vs. Ag/AgCl on the addition of 2, 4, 6, 8 and 10 mmol dm^{-3} NADH in 0.1 mol dm^{-3} Tris buffer at pH 9 containing 0.1 mol dm^{-3} KCl to electrodes on which 0.2 mL of a solution containing 0.2 mol dm^{-3} ruthenium hexaamine and 650 KU/mL putadiaredoxin reductase has been dried. Results are shown in Figure 15.

Example 2e

Amperometric current was measured 60 seconds after the application of a 0.20 V vs. Ag/AgCl potential step after addition of concentrations of 2, 5, 7.5, 10, 12.5 and 15 mmol dm^{-3} glycerol in 0.1 mol dm^{-3} Tris buffer at pH 9 containing 0.1 mol dm^{-3} KCl

obtained at electrodes on which 0.3 mL of a solution containing 150 U/mL glycerol dehydrogenase, 100 mmol dm^{-3} of NAD, 100 mmol dm^{-3} of ruthenium hexaamine, 100 mmol dm^{-3} of ammonium sulphate, 100 mmol dm^{-3} of potassium chloride has been dried. Results are shown in Figure 16.

Example 2f

Ratio of amperometric current was measured 60 seconds after the application of a -0.50 V vs. Ag/AgCl potential step after addition of concentrations of 2, 5, 7.5, 10, 12.5 and 15 mmol dm^{-3} glycerol in 0.1 mol dm^{-3} Tris buffer at pH 9 containing 0.1 mol dm^{-3} KCl obtained at electrodes on which 0.3 mL of a solution containing 150 U/mL glycerol dehydrogenase, 100 mmol dm^{-3} of NAD, 100 mmol dm^{-3} of ruthenium hexaamine, 100 mmol dm^{-3} of ammonium sulphate, 100 mmol dm^{-3} of potassium chloride has been dried. Results are shown in Figure 17.

Example 3

Electrodes were constructed from a 250 μm PET layer on which a 7 μm Coates carbon ink 26-8203 layer had been screen-printed followed by a 30 μm Ronseal layer. This layer was punched to produce a 1 mm diameter hole. A base layer was formed by printing a 10 μm Ag/AgCl layer onto a 125 μm PET base layer. The base layer was then adhered to the punched layer using ARcare 7841 sheet adhesive. Various tests were carried out using this electrochemical cell which are described in Examples 3a and 3b below.

Example 3a

Amperometric current was measured 120 sec after the application of a -0.25 V vs. Ag/AgCl potential step. Showing the effect of additions of 1.5, 2.25, 3.0, 4.5, 6.0 mmol dm^{-3} cholesterol to a solution comprising 1 KU/mL cholesterol oxidase, 200 KU/mL horseradish peroxidase, 33 mmol dm^{-3} potassium ferrocyanide in 0.1 mol dm^{-3} potassium phosphate buffer at pH 7.4 containing 0.1 mol dm^{-3} KCl to electrodes

with a common counter/reference electrode configured at the bottom of the well. Results are shown in Figure 18.

Example 3b

Amperometric current was measured 120 sec after the application of a -0.25 V vs. Ag/AgCl potential step. Showing the effect of additions of 1.5, 2.25, 3.0, 4.5, 6.0 mmol dm^{-3} cholesterol to a solution comprising 1KU/mL cholesterol oxidase, 200KU/mL horseradish peroxidase, 33 mmol dm^{-3} potassium ferrocyanide in 0.1 mol dm^{-3} potassium phosphate buffer at pH 7.4 containing 0.1 mol dm^{-3} KCl to electrodes with a common counter/reference electrode configured on the top of the strip. Results are shown in Figure 19.

Example 4

Electrodes were constructed from a 250 µm PET layer on which a 7 µm Ercon carbon ink G449C layer had been screen-printed followed by a 30 µm Ercon E65615-116D dielectric layer. This was then punched to produce a 1 mm diameter hole. A 125 µm PET base layer was coated with a common Ag/AgCl counter reference layer (using Ercon E6165-128). The base layer as formed was then adhered to the punched layer using heat lamination.

Amperometric current was measured 1 second after the application 0.15 V vs. Ag/AgCl on the addition of 2, 4, 6, 8 and 10 mmol dm^{-3} NADH in 0.1 mol dm^{-3} Tris buffer at pH 9 containing 0.1 mol dm^{-3} KCl to electrodes on which 0.2 mL of a solution containing 0.2 mol dm^{-3} ruthenium hexaamine and 650 KU/mL putadiaredoxin reductase has been dried. Results are shown in Figure 20.

CLAIMS

1. An electrochemical cell which, either alone or in combination with a substrate onto which it is placed, is in the form of a receptacle, said cell comprising a counter electrode and a working electrode, wherein at least one electrode has at least one dimension of less than 50μm, the working electrode being in a wall of the receptacle.

2. An electrochemical cell according to claim 1 which is in the form of a receptacle.

3. An electrochemical cell according to claim 1 or 2, wherein the working electrode is in the form of a continuous band.

4. An electrochemical cell according to any one of the preceding claims, which further comprises a reference electrode.

5. An electrochemical cell according to any one of the preceding claims, wherein the ratio of the surface area of the counter electrode to the surface area of the working electrode is at least 25:1.

6. An electrochemical cell according to any one of the preceding claims, wherein the working electrode has at least one dimension in the range of 0.1 to 20μm.

7. An electrochemical cell according to any one of the preceding claims, wherein the receptacle has a width of from 0.1 to 5mm.

8. An electrochemical cell according to any one of the preceding claims, wherein the minimum distance between the counter electrode and the working electrode is from 10 to 1000μm.

9. An electrochemical cell according to any one of the preceding claims, wherein a base and/or a wall or walls of the receptacle contain one or more air-outlet channels.

10. An electrochemical cell according to any one of the preceding claims, wherein the receptacle contains an electro-active substance.

11. An electrochemical cell according to claim 10, wherein the electro-active substance has been dried.

12. An electrochemical cell according to claim 10 or 11, wherein the electro-active substance comprises an enzyme.

13. An electrochemical cell according to any one of claims 10 to 12, wherein the base of the receptacle comprises an electro-active substance.

14. An electrochemical cell according to any one of claims 10 to 12, wherein the base of the receptacle comprises a membrane, said membrane comprising an electro-active substance.

15. An electrochemical cell according to any one of the preceding claims, wherein the open end of the receptacle is at least partly covered by a permeable membrane.

16. An electrochemical cell according to claim 15 wherein the permeable membrane comprises an electro-active substance.

17. An electrochemical cell according to any one of the preceding claims, wherein the receptacle comprises one or more capiliary flow channels through which a sample may enter.

18. An electrochemical cell according to any one of the preceding claims, wherein the counter electrode forms at least a part of a base of the receptacle.

19. An electrochemical cell according to claim 17, wherein the receptacle is covered by a layer containing the counter electrode.

20. An electrochemical cell according to any one of claims 1 to 17, wherein the counter electrode is in a wall or walls of the receptacle.

21. An electrochemical cell according to any one of the preceding claims which is suitable for screening liquid samples.

22. A multi-analyte device comprising a plurality of electrochemical cells according to any one of claims 1 to 21.

23. A process for producing an electrochemical cell according to any one of claims 1 to 22, which process comprises the steps of:

(a) forming a first part comprising an insulating material which is optionally coated with a counter electrode layer;
(b) forming a second part comprising a laminate of a working electrode layer between two layers of an insulating material;
(c) creating a hole in the second part; and
(d) bonding said first part to said second part to form a receptacle.

24. A process according to claim 23 wherein the second part comprises a laminate of a counter electrode layer between two layers of insulating material.

25. A process according to claim 23 wherein the first part comprises an electro-active substance.

26. A process according to claim 23 or 24 which further comprises placing an electro-active substance as defined in claim 10 or 12 into the receptacle and optionally drying the electro-active substance.

27. A process according to any one of claims 23 to 26, which further comprises placing a membrane over at least a part of the open end of the receptacle.

28. A process according to any one of claims 23 to 27, wherein step (c) comprises forming two or more holes in said second part, in order to form a multi-analyte device.

29. A process for producing an electrochemical cell according to any one of claims 1 to 22, which comprises the steps of:

(a) forming a second part comprising a laminate of a working electrode layer between two layers of an insulating material;

(b) creating a hole in the second part; and optionally

(c) bonding to said second part a layer which is coated with a counter electrode material.

30. A process according to claim 29, wherein the second part comprises a laminate of a counter electrode layer between two layers of insulating material.

31. A process according to claim 23 or 24 which comprises the steps of:

(a) forming a first part comprising an insulating material;

(b) forming a second part comprising a laminate of a working electrode layer between two layers of an insulating material;

(c) creating, in the second part, a hole and a capiliary channel to allow a sample to enter said hole;

(d) bonding said first part to said second part to form a receptacle;

(e) placing an electro-active substance into the receptacle and optionally drying the electro-active substance; and

(f) bonding to the open end of said receptacle a layer which is optionally coated with a counter electrode material.

32. A process according to claim 31, wherein step (c) comprises forming, in said second part, two or more holes and two or more capiliary channels to allow a sample to enter said two or more holes, and wherein step (e) comprises inserting an electro-active substance, which may be identical or different, into one or more of the receptacles formed in step (d), in order to form a multi-analyte device.

33. A modification of the process of claim 31 or claim 32 which comprises the steps (a), (b), (c), (d) and (f) as defined in claim 31 or claim 32 and in which the first part comprises an electro-active substance.

34. A process according to any one of claims 23 to 33, wherein one or more of the electrodes is formed by screen or inkjet printing onto a substrate.

35. A method of electrochemically testing one or more compounds of a sample, the method comprising the steps of:

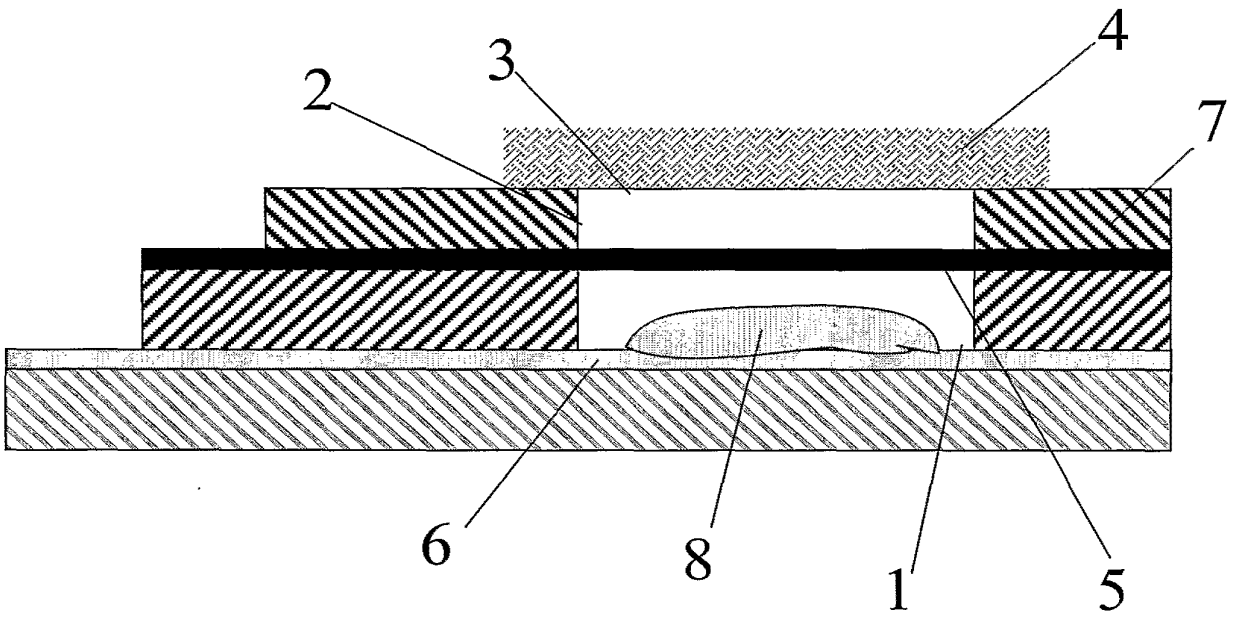
(a) inserting the sample into an electrochemical cell according to any one of claims 1 to 21 or a multi-analyte device according to claim 22;

(b) applying a voltage or a current between the working and counter electrodes of the micro-electrode; and

(c) measuring the resulting current, voltage or charge across the micro-electrode.

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FIG. 1



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FIG. 2

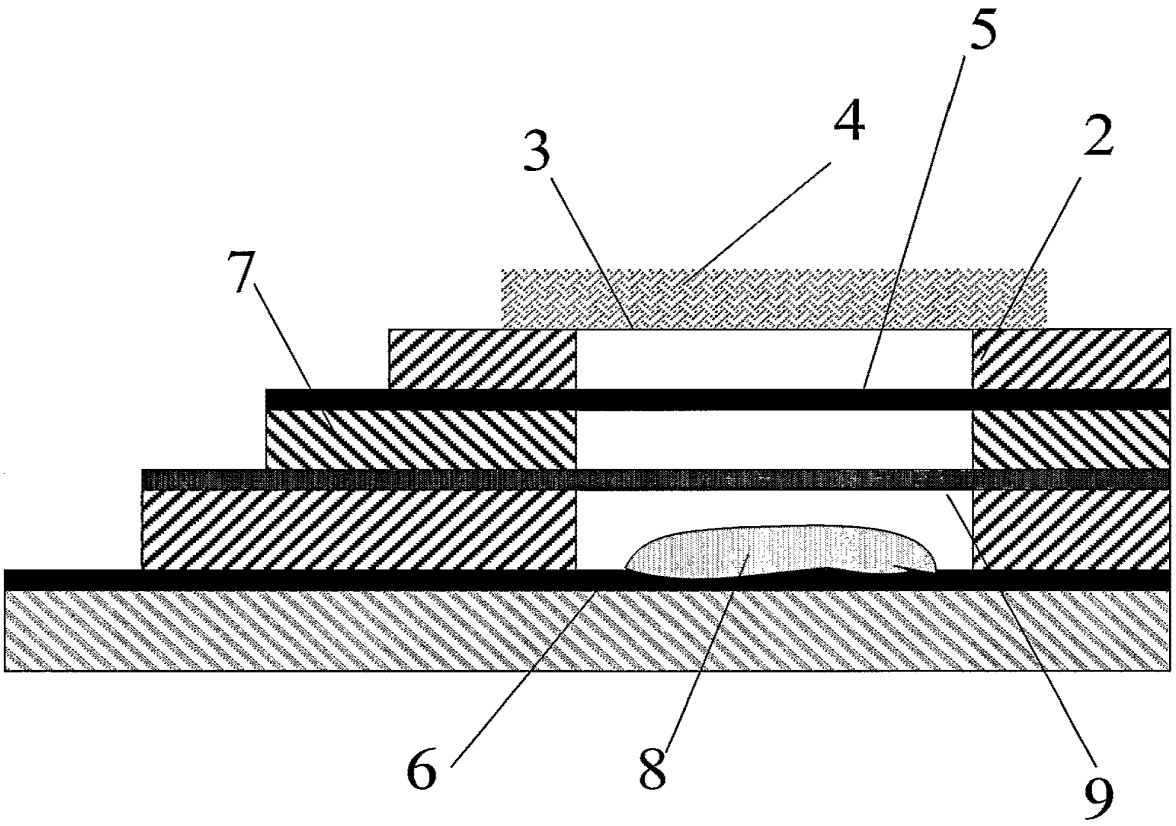


FIG. 3

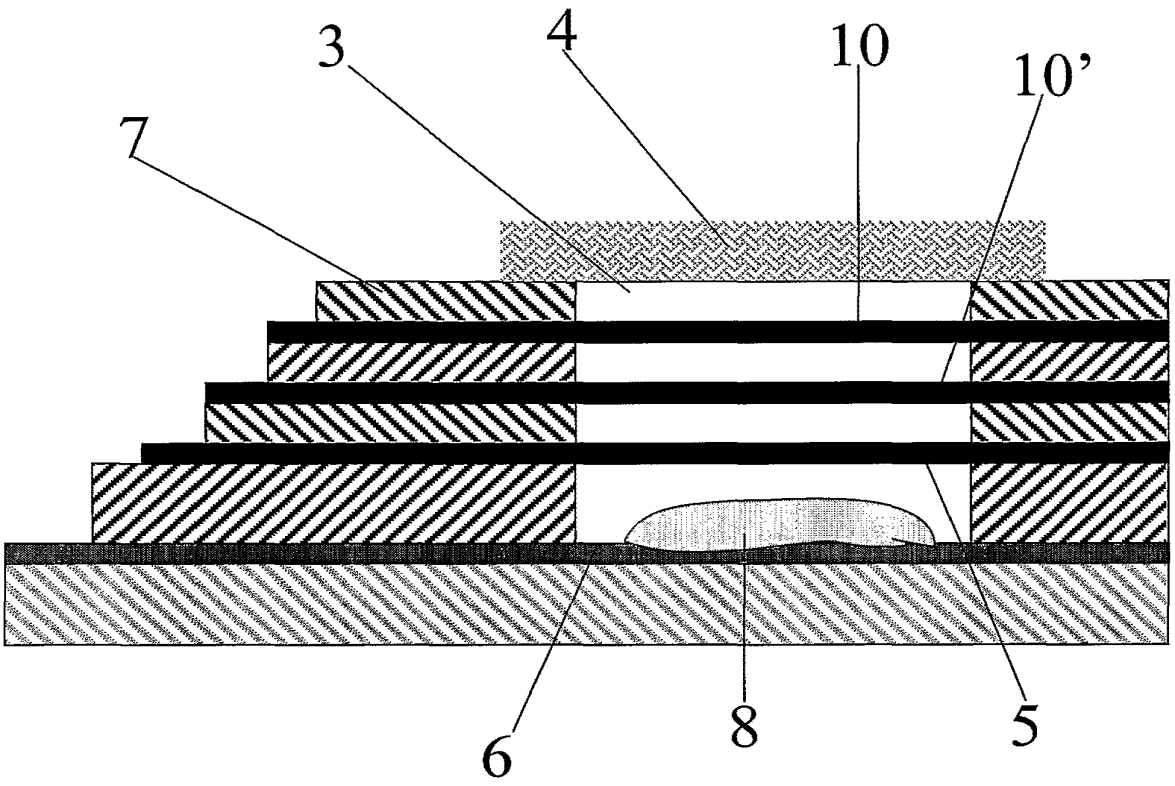


FIG. 4

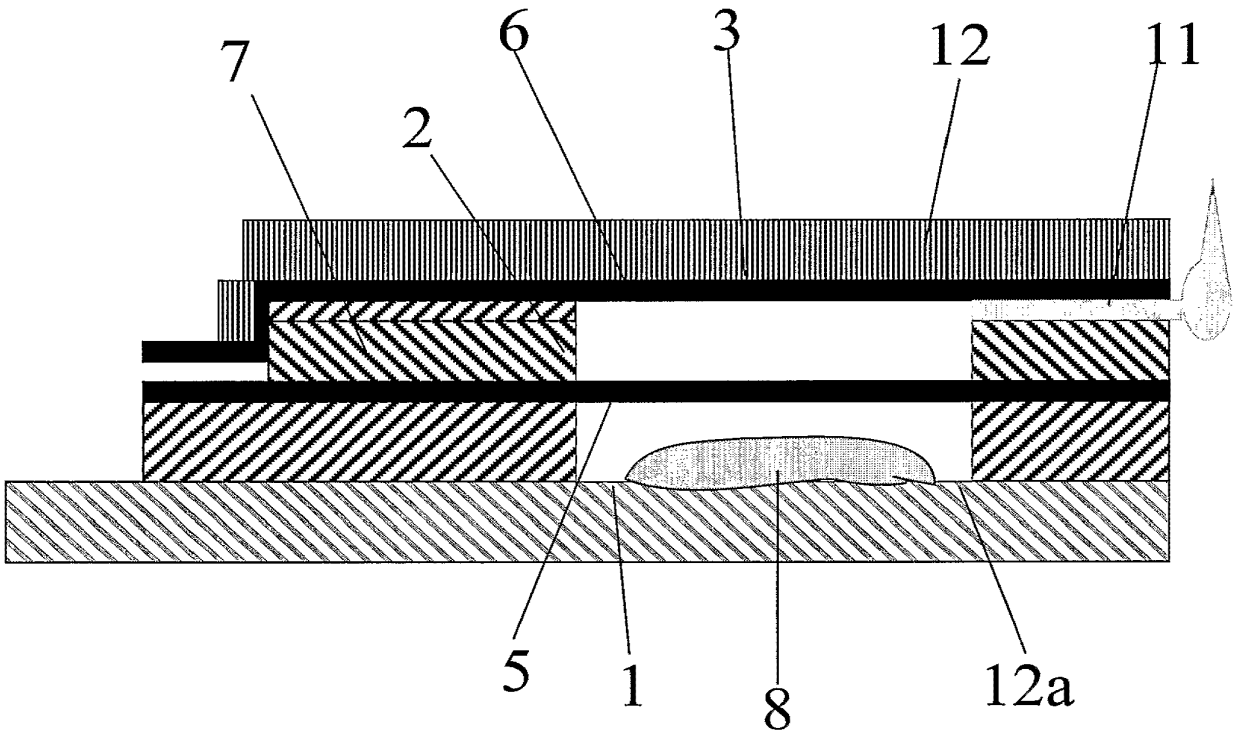


FIG. 5

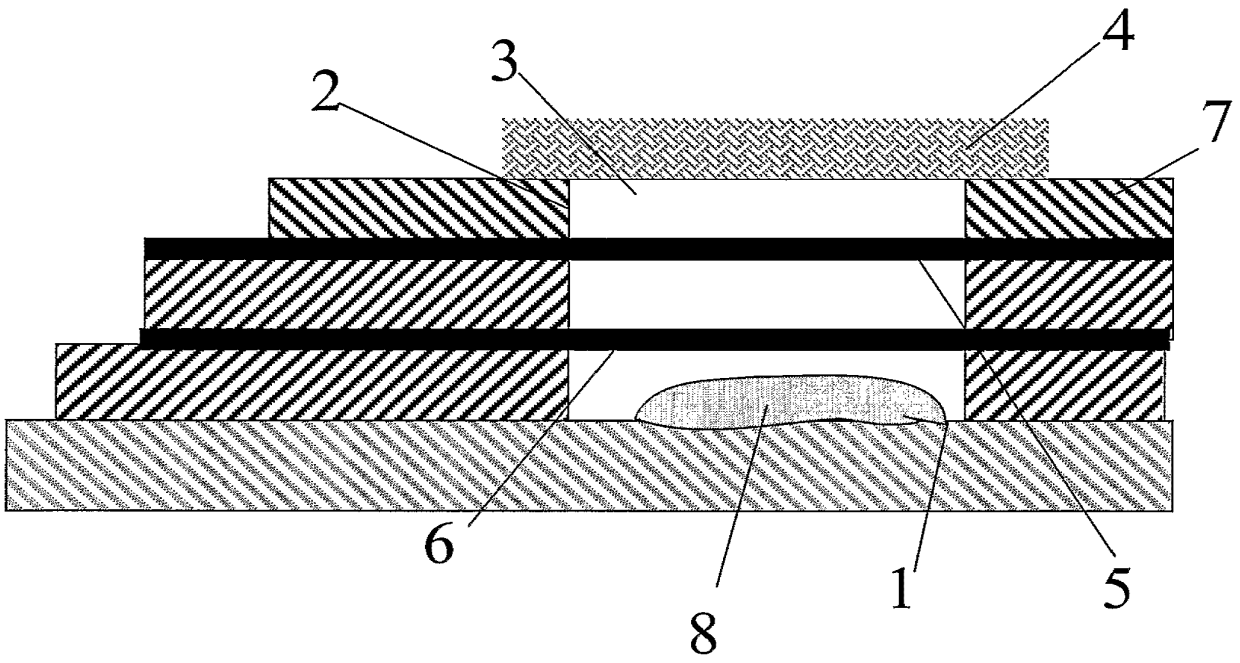


FIG. 6

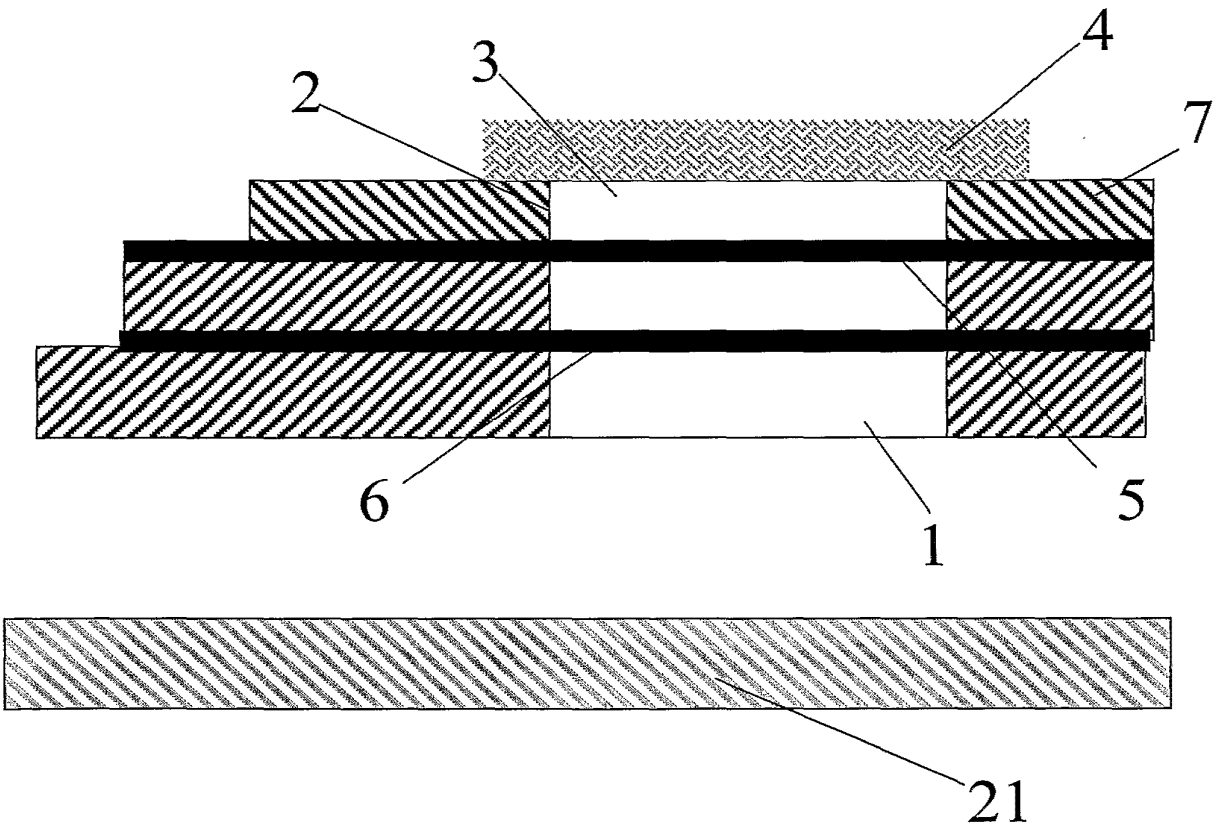


FIG. 7

