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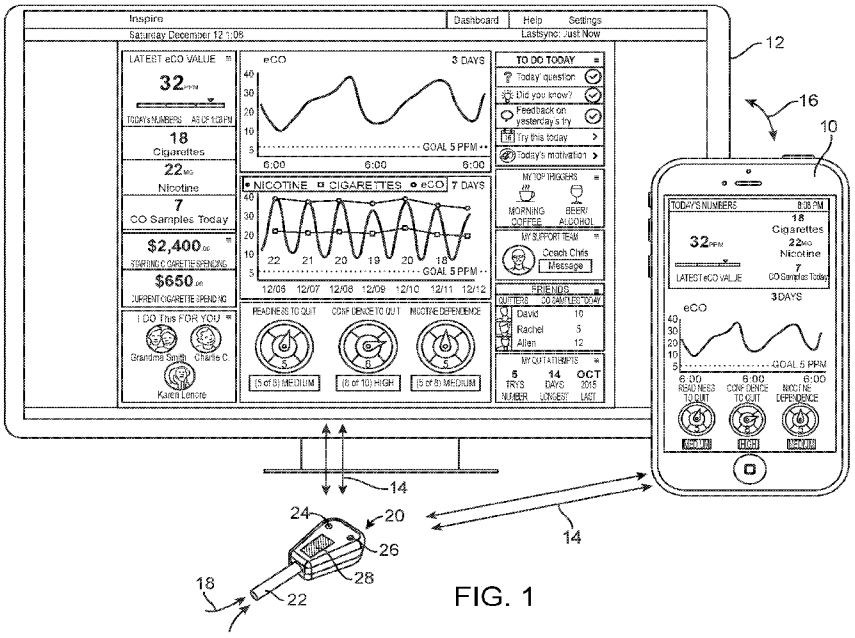


FIG. 1

(57) Abstract: Breath sensor apparatus and methods of use are described herein where a flow control apparatus may generally comprise a sampling chamber defining a volume and one or more openings into the sampling chamber, at least one sensor in fluid communication with the sampling chamber, wherein the at least one sensor is configured to detect the analyte. The sampling chamber may also be configured to receive the breath sample into the sampling chamber and into contact with the at least one sensor via diffusion into the sampling chamber.

[Continued on next page]

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BREATH SENSOR APPARATUS AND METHODS OF USE

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application is a continuation of U.S. Patent Application No. 15/782,718 filed October 12, 2017, and is incorporated by reference herein in its entirety.

FIELD OF THE INVENTION

[0002] The present invention relates to apparatus and methods for receiving and detecting biological parameters from breath samples. In particular, the present invention relates to apparatus and methods of use for receiving and detecting biological parameters from breath samples exhaled from a subject and into a portable breath sensor apparatus.

BACKGROUND OF THE INVENTION

[0003] The health problems associated with tobacco smoking are well known. Cigarette smoke contains nicotine as well as many other chemical compounds and additives. Tobacco smoke exposes an individual to carbon monoxide as well as these other compounds, many of which are carcinogenic and toxic to the smoker and those around the smoker. The presence and level of carbon monoxide in the exhaled breath of the smoker can provide a marker for identifying the overall smoking behavior of that individual as well as provide a marker for their overall exposure to the other toxic compounds.

[0004] In order to sample the exhaled breath, a portable breath sensor which is readily carried by the user and which is unobtrusive is desirable. However, the relatively reduced size of the breath sensor also brings a number of challenges in capturing and accurately measuring samples of the exhaled breath. Factors such as moisture content in the breath as well as breath temperature may affect the accuracy of the sensors used to measure the parameters due to the relatively small size.

[0005] There remains a need for a breath sensor which is able to sample and accurately detect parameters from exhaled breath while being readily portable.

SUMMARY OF THE INVENTION

[0006] Personal sampling unit may generally comprise a housing having a shape which allows for the user to hold and manipulate the unit with a single hand. The housing may incorporate the input trigger as well as one or more indicators such as indicator. The collection tube may be comprised of a tube defining a lumen and which extends from the housing. Within the housing, a

first sensor and second sensor which in turn may be mounted upon a substrate such as a printed circuit board. Although in other variations, one or more sensors may be used depending upon the parameters being detected. A power port and/or data access port may also be integrated with the printed circuit board and readily accessible by a remote device such as a computer, server, smartphone, or other device. The sensors may include any number of different sensor types including chemical gas sensors, electrochemical gas sensors, etc. for detecting agents such as carbon monoxide in the case of detecting smoking related inhalation.

[0007] When detecting agents from breath samples from a subject, it is generally desirable to avoid temperature and humidity impacts on the sensors particularly in breath sensing devices which are compact as temperature swings and humidity may interfere with the detected signals in the sensors. Larger breath sensing devices are able to readily contend with temperature and humidity variances due to their relatively larger mass and longer flow paths as the sampled breath temperature is reduced and moisture is removed prior to the breath sample reaching the sensor.

[0008] One variation of a flow control apparatus for measuring an analyte from a breath sample of a subject may generally comprise a sampling chamber defining a volume and one or more openings into the sampling chamber, at least one sensor in fluid communication with the sampling chamber, wherein the at least one sensor is configured to detect the analyte, and wherein the sampling chamber is configured to receive the breath sample into the sampling chamber and into contact with the at least one sensor via diffusion into the sampling chamber.

[0009] Another variation of a flow apparatus for measuring a concentration of an analyte of interest from an individual's breath may generally comprise a sampling chamber including at least one opening to receive a portion of the breath, wherein a remainder of the breath is diverted and vented, at least one sensor positioned in fluid communication with the sampling chamber, wherein the at least one sensor is configured to detect the analyte of interest, and wherein the sampling chamber is configured such that a majority of the portion of the breath in contact with the sensor is introduced via diffusion, rather than flow, into the sampling chamber.

[0010] One variation of a method of extrapolating a final value of a parameter from a breath sample may generally comprise obtaining a calibration curve of a gas having a known parameter concentration, recording at least a portion of the calibration curve as a function of time, measuring an input response curve of the parameter from the breath sample over a period of time, associating the input response curve to the calibration curve, and extrapolating the final value of the

parameter from the breath sample based on the calibration curve associated with the input response curve.

[0011] Another variation of a flow control assembly may generally comprise a proximal receiving channel sized to receive a fluid sample, a dispersion channel fluidly connected to the proximal receiving channel, a main receiving channel, wherein the dispersion channel is configured to divert a portion of the fluid sample to the main receiving channel and a majority of the fluid sample to one or more secondary channels for venting from the assembly, and one or more sampling chambers fluidly connected to the main receiving channel via one or more openings.

[0012] Another method of measuring a fluid sample may generally comprise receiving the fluid sample within a proximal receiving channel, diverting a majority of the fluid sample to one or more secondary channels, diverting a portion of the fluid sample into a main receiving channel, and introducing the portion of the fluid sample into contact with one or more sensors for determining a parameter from the fluid sample.

[0013] In order for a relatively smaller device such as the personal sampling unit described herein to accurately detect breath samples, one or several mechanisms may be employed to filter out moisture from the breath sample as well as reduce its temperature. A flow control assembly may be incorporated into the housing for controlling the flow of a breath sample to the sensors. The assembly may have a receiving channel into which the collection tube may be inserted and retained. The lumen of the collection tube may be fluidly connected through the receiving channel and into a dispersion channel which extends into and is fluidly coupled to one or more secondary channels which define corresponding second fluid pathways extending away from the dispersion channel, e.g., at an angle relative to the dispersion channel.

[0014] One or more primary channels may further extend away from and fluid coupled with the dispersion channel so that the primary channels open into a receiving channel which is defined by a barrier formed around the receiving channel. The dispersion channel helps to divert a majority of the sampled breath into the secondary channels so that a relatively smaller portion of the breath passes through the primary channels and into the receiving channel. For instance, about 80% of the breath sample may be diverted into the secondary channels where it may then be vented out from of the housing. The remaining, e.g., 20% of the breath sample, may then enter into the receiving channel so that the diverted flow helps to decrease the moisture level in the sampled breath. In other variations, more than 50% of the breath sample may be diverted so that less than

50% of the breath sample enters into the receiving channel. Additionally, the relatively larger volume defined by the receiving channel may further help to reduce the temperature of the sampled breath.

[0015] The openings extending into the respective first and second sampling chambers are sized to be relatively smaller and may number from a single opening to multiple openings which help to further maintain the flow rate of the sampled breath entering the sampling chambers to a minimum flow rate of, e.g., about 4 mL/sec.

[0016] Contained within the first and second sampling chambers are respective first and second filters which further help to remove any additional moisture from the sampled breath. Additionally, respective first and second seals may surround the sampling chambers to contain the sampled breath over the sensors for detection. These first and second filters help to diffuse the flow path through a matrix, e.g., porous material, which not only removes moisture but also helps to further reduce the temperature of the sampled breath due to their additional thermal mass. The filters may be comprised of various materials that also filter out various chemicals such as alcohols, sulfur compounds, carbon monoxide, etc.

[0017] Another variation for reducing moisture and cooling the sampled breath may include incorporating a tortuous flow path which increases the surface area in contact with the sampled breath. This may include a coiled path or a maze which helps to drop the temperature and further allows for moisture to condense out of the breath and onto the surface area. In yet another variation, rather than utilizing barriers or baffles to create a tortuous flow path, tubing may be used for flowing the breath sample.

[0018] Alternatively, moisture may be removed from the sample by utilizing, e.g., a moisture-permeable membrane along the flow path or a hygroscopic material such as silica that may absorb the moisture from the sample. In these variations where moisture is condensed or absorbed along the flow path, the condensed water is desirably removed from the flow assembly. Removal may be accomplished in one variation by increasing a number of vent holes from the flow path to the environment while in another variation, a water transport membrane, e.g., Nafion or another water-permeable solid, may be used to transport the water away from the flow assembly.

[0019] In yet another variation, an active mechanism such as a pump may be used to draw a portion of the sample from the flow path after the initial exhalation from the subject is introduced into the unit.

[0020] Once the breath sample has been introduced through the openings and past the filter, the sample may be introduced within a sensing chamber contained within an interior of the sampling chamber where it comes into contact with the sensor. The surface of the sensor generally presents a planar face against which a contact region of the sampling chamber may be positioned against. The sample breath within the sensing chamber is desirably maintained within for prolonging contact against the sensor surface and also to prevent the sample breath from escaping into the rest of the housing by sealing the contact region with an interface such as a seal which encircles the sensing chamber. Preventing the breath sample from escaping into the rest of the housing not only may provide for better signal sensing and response speed but also avoids the contact against the other electronics contained within the housing.

[0021] However, due to the assembly tolerances of the flow control assembly, which may have a positional tolerance with respect to the sensor surface of up to, e.g., +/- 0.010 in., the seal may be positioned upon a tapered surface which may be formed in an annular configuration around the sampling chamber. The tapered surface may be angled so that the tapered surface extends away from the contact region. When the seal is positioned upon the tapered surface, the seal is urged to push against the sensor surface with a spring constant in proportion to the angle of the tapered surface. This also allows for the seal to press against the sensor surface while providing sealing with a flatter force response than what a conventional compression gasket could provide by providing a relatively lower force across the geometric gap range especially if the sensor is pressure sensitive.

[0022] When a subject blows into the collection tube for submitting a breath sample, predicting a terminal value of the sensors in a limited-duration breath test may be difficult due to the stabilization time typically needed for many types of sensors to accurately detect parameters from the breath sample. For instance, gas sensors (such as CO sensors) may take up to 10-30 seconds of sampling time to stabilize and yield a final value. However, subjects may not be able to (or should not need to) exhale for more than 5-10 seconds into the collection tube in order to obtain an accurate reading. Hence, the final value may be estimated based upon the transient signals obtained from the sensor. The rate of stabilization may also be complicated due to various known or unknown variables such as current temperature or humidity levels at the time of sampling, previous dwell temperature or humidity levels, etc.

[0023] Hence, if the rates of stabilization are fixed or can be estimated accurately based on other known parameters, e.g. temperature, then the following process may be used in one variation. For

instance, the sensor electronics in the unit may be calibrated using a gas of known concentration (e.g. 50 ppm CO) and the entire calibration curve may be recorded as a function of time, e.g., the sensor response may be recorded as a function of time. Alternatively, rather than the entire calibration curve, a sufficient portion of the calibration curve (and not just the terminal and plateau values) may be recorded and stored in memory.

[0024] During a test, the input response sensor curve may be associated with the calibration curve. The association may be accomplished using a number of different methods. In one variation, the sensor value at test time t = t1 may be compared to the calibration value at t = t1, where t1 is a selected to be a time of interest, e.g., time at the peak, time at the end of the test, or a specific time during the test (e.g. 10 seconds, etc.). In another variation, a least-squares fit may be performed of the input sensor curve to the calibration curve multiplied by a constant, and optimizing for that constant. For example, a constant of 0.6 would mean the input value is calculated to be 0.6 * the calibration value. The calibration constant is calculated for each device and may be based on the calibrated input from the subject. Finally, the final value may be determined by extrapolating the sample result based the calibrated curve.

[0025] If the rate of stabilization is not sufficiently well known for a sensor but the shape of the calibration curve is known, in particular an exponential settling function of the type $y(t) = y_{terminal} * (1 - e^{-t/\tau})$, then the following process may be used. During a calibration test or a field test, any compensations may be performed (heuristical or theoretical) that allow the input curve to better fit a simple analytical function such as the exponential settling function. For example, the early part of the curve may be adjusted to compensate for diffusion speed to the sensor. Default values may be assumed for constants associated with the analytical function. In the case of the exponential settling function, a default value for tau, τ, may be assumed. The goodness of fit of the (compensated) input data to the analytical function may be assessed and a determination may be made as to whether the good of fit is sufficient. Assuming goodness of fit is insufficient, an adjustment may be made of the value of the analytical function constants, τ, based on the disparity between the input data and analytical function, e.g. overshoot or undershoot and steps may be repeated using an optimizing algorithm (e.g., binary search, executed on the constant tau) to evaluate for the best fit to the analytical function. Once the goodness of fit is sufficient, the optimized analytical function and input data may be used to predict the value of input analyte (CO), e.g., by estimating the terminal value. When performing calibration, this procedure may be

used to set the sensitivity (yterminal / COppm) and when performing a test, this procedure may be used and the terminal value may be divided by the sensitivity to calculate the analyte level.

[0026] Over time, the sensors may begin to degrade with repeated use and the calibration data initially used may no longer be valid after some amount of time has passed. Thus, aging data may be used to determine typical behavior over time and also used to compensate the calibration data accordingly. For example, the approximate degradation of certain sensors may be known to be, e.g., 0.6% per month for the first six months and then 0.3% per month thereafter. With this known degradation rate, these parameters may be used to compensate the analysis of each measured value thereafter based upon the amount of time which has elapsed since the device was calibrated.

[0027] In another variation of the sampling unit, the device may additionally and/or alternatively incorporate one or more spirometers for monitoring or screening for various conditions, e.g., COPD, asthma, etc. The spirometer may be incorporated into the unit so that it is in fluid communication with a sample breath passing through the flow path to detect and/or monitor parameters. The spirometer may be wired to a processor within the unit or it may be wirelessly in communication with the personal electronic device or computer. Additionally, the flow path may include a flow switch to increase or decrease flow resistance along the flow path. When the subject breaths into the device, they may be instructed to exhale as vigorously as possible and the device may translate measured pressure into a flow rate to calculate, e.g., forced vital capacity (FVC) or forced expiratory volume, 1 second test (FEV1).

BRIEF DESCRIPTION OF THE DRAWINGS

[0028] FIG. 1 illustrates a variation of a system which is able to receive the exhaled breath from a subject and detect various parameters and which can communicate with a one or more remote devices.

[0029] FIG. 2 illustrates a perspective view of one variation of a portable breath sensor.

[0030] FIG. 3 illustrates one variation of the internal circuitry and sensors contained within the housing of the breath sensor.

[0031] FIG. 4A illustrates a graph of a humid gas and the effects of humidity upon the readings.

[0032] FIG. 4B illustrates a graph of a humid gas introduced at a relatively higher flow rate.

[0033] FIG. 4C illustrates a graph of a humid gas with diffusion pathways implemented.

[0034] FIG. 5A illustrates a top view of one variation of a flow path control device.

[0035] FIG. 5B illustrates a bottom view of the flow path control device of FIG. 4A.

[0036] FIG. 6 illustrates a top view of the flow path control device positioned over the sensors.

[0037] FIG. 7 illustrates a top view of the flow path control device with the various flow paths shown.

[0038] FIG. 8 illustrates a top view of another variation of a flow path control device showing how the flow path may be configured to be tortuous through the breath sensor.

[0039] FIG. 9 illustrates a top view of another variation of a flow path control device showing another configuration of a tortuous flow path.

[0040] FIG. 10A illustrates a top view of another variation of a flow path control device which may utilize tubing coiled in any number of configurations.

[0041] FIG. 10B illustrates an exemplary side view of a variation of a flow path incorporating a moisture-permeable membrane.

[0042] FIG. 10C illustrates an exemplary side view of another variation of a flow path incorporating an active pumping mechanism.

[0043] FIG. 11A illustrates a cross-sectional perspective view of a sensor enclosed by a seal which is urged into contact via a tapered interface.

[0044] FIG. 11B illustrates the tapered interface of FIG. 11A with the seal removed for clarity.

[0045] FIG. 11C illustrates a cross-sectional detail perspective view of another variation of a sampling chamber.

[0046] FIG. 12 illustrates a diagram of one method for estimating a final value of a sensor based on calibrated information.

[0047] FIG. 13A illustrates a graph of a calibration curve of a gas having a known CO concentration.

[0048] FIG. 13B illustrates a graph of a test sample obtained where the sample time is less than the calibration curve.

[0049] FIG. 13C illustrates an association between the known calibration curve and the obtained test sample for determining a final output value.

[0050] FIG. 14 illustrates a diagram of one method for compensation when the rate of stabilization is not well known for a sensor.

[0051] FIG. 15 illustrates an exemplary side view of a sampling unit incorporating an optional spirometer.

DETAILED DESCRIPTION OF THE INVENTION

[0052] In engaging individuals who smoke and quantifying their smoking behavior, methods and systems may be implemented to allow for improved measuring and quantifying of a smoker's behavior. Once the individual smoker is identified, the same methods and systems may allow for a learn and explore phase where the individual's specific smoking behavior can be tracked and quantified and the individual's behavioral data may also be tracked to identify potential triggers to smoking or simply to educate the individual on the extent of their smoking. These methods and systems also allow for a more active monitoring of the individual that has decided to engage in a quit program, where such monitoring allows the individual to self-monitor as well as monitoring by peers, coaches, or counselors.

[0053] Certain biometric data of the subject may be obtained by non-invasively detecting and quantifying the smoking behavior for a patient based on measuring one or more of the patient's biometric data such as CO level or exhaled CO level. However other biometric data can also be used. Such measurements or data collection can use a portable measuring unit or a fixed measuring unit, either of which communicates with one or more electronic devices for performing the quantification analysis. Alternatively, the analysis can be performed in the portable/fixed unit. For example, the portable unit can be coupled to a keychain, to the individual's cigarette lighter, cell phone, or other item that will be with the individual on a regular basis. Alternatively, the portable unit can be a stand-alone unit or can be worn by the individual.

[0054] Systems and methods for assisting a subject in quantifying and quitting their smoking behavior as well as details of how such a breath sensing device may be used or incorporated into such systems and methods are described in further detail in U.S. Pat. App. 15/092,475 filed April 6, 2016 (U.S. Pat. Pub. 2017/0055572) and U.S. Pat. App. 15/258,921 filed September 7, 2016 (U.S. Pat. Pub. 2017/0055573), each of which is incorporated herein by reference in its entirety and for any purpose.

[0055] For instance, FIG. 1 illustrates one variation of a system and/or method in which a plurality of samples of biometric data are obtained from the individual and analyzed to quantify the individual's exposure to cigarette smoke such that the quantified information can be relayed to the individual, a medical caregiver, and/or other parties having a stake in the individual's health. The example discussed below employs a portable device 20 that obtains a plurality of samples of exhaled air from the individual with commonly available sensors that measure an amount of carbon monoxide within the sample of exhaled air (also referred to as exhaled carbon monoxide or eCO). However, the quantification and information transfer is not limited to exposure of

smoking based on exhaled air. As noted above, there are many sampling mechanisms to obtain an individual's smoking exposure. The methods and devices described in the present example can be combined or supplemented with any number of different sampling mechanisms where possible while still remaining within the scope of the invention.

[0056] The measurement of exhaled CO level has been known to serve as an immediate, non-invasive method of assessing a smoking status of an individual. The levels of eCO levels for non-smokers can range between, e.g., 0 ppm to 6 ppm, or more particularly between, e.g., 3.61 ppm and 5.6 ppm.

[0057] As shown, a portable or personal sampling unit 20 may communicate with either a personal electronic device 10 or a computer 12. Where the personal electronic device 10 includes, but is not limited to a smart phone, cellular phone, or other personal transmitting device designed or programmed for receiving data from the personal sampling unit 20. Likewise, the computer 12 is intended to include a personal computer, local server, remote server, etc. Data transmission 14 from the personal sampling unit **20** can occur to both or either the personal electronic device **10** and/or the computer **12**. Furthermore, synchronization **16** between the personal electronic device **10** and the computer **12** is optional. Either the personal electronic device **10**, the computer **12**, and/or the personal sampling unit 20 can transmit data to a remote server for data analysis as described herein. Alternatively, data analysis can occur, fully or partially, in a local device (such as the computer or personal electronic device). In any case, the personal electronic device 10 and/or computer 12 can provide information to the individual, caretaker, or other individual as shown in FIG. 1.

[0058] The personal sampling unit 20 receives a sample of exhaled air 18 from the individual via a collection tube 22. Hardware within the personal sampling unit 20 may include any commercially available electrochemical gas sensor that detects carbon monoxide (CO) gas within the breath sample, commercially available transmission hardware that transmits data 14 (e.g., via Bluetooth, cellular, or other radio waves to provide transmission of data). The transmitted data and associated measurements and quantification are then displayed on either (or both) a computer display 12 or a personal electronic device 10. Alternatively, or in combination, any of the information can be selectively displayed on the portable sampling unit 20.

[0059] The personal sampling unit 20 (or personal breathing unit) can also employ standard ports to allow direct-wired communication with the respective devices 10 and 12. In certain variations, the personal sampling unit 20 can also include memory storage, either detachable or built-in, such

that the memory permits recording of data and separate transmission of data. Alternatively, the personal sampling unit can allow simultaneous storage and transmission of data. Additional variations of the device 20 do not require memory storage. In addition, the unit 20 can employ any number of GPS components, inertial sensors (to track movement), and/or other sensors that provide additional information regarding the patient's behavior.

[0060] The personal sampling unit 20 can also include any number of input trigger (such as a switch or sensors) 24, 26. As described below, the input trigger 24, 26 may allow the individual to prime the device 20 for delivery of a breath sample 18 or to record other information regarding the cigarette such as quantity of cigarette smoked, the intensity, etc. In addition, variations of the personal sampling unit 20 also associate a timestamp of any inputs to the device 20. For example, the personal sampling unit 20 can associate the time at which the sample is provided and provide the measured or inputted data along with the time of the measurement when transmitting data 14. Alternatively, the personal sampling device 20 can use alternate mechanisms to identify the time that the sample is obtained. For example, given a series of samples rather than recording a timestamp for each sample, the time periods between each of the samples in the series can be recorded. Therefore, identification of a timestamp of any one sample allows determination of the time stamp for each of the samples in the series.

[0061] In certain variations, the personal sampling unit 20 may be designed such that it has a minimal profile and can be easily carried by the individual with minimal effort. Therefore the input triggers 24 can comprise low profile tactile switches, optical switches, capacitive touch switches, or any commonly used switch or sensor. The portable sampling unit 20 can also provide feedback or information to the user using any number of commonly known techniques. For example, as shown, the portable sampling unit 20 can include a screen 28 that shows select information as discussed below. Alternatively or in addition, the feedback can be in the form of a vibrational element, an audible element, and a visual element (e.g., an illumination source of one or more colors). Any of the feedback components can be configured to provide an alarm to the individual, which can serve as a reminder to provide a sample and/or to provide feedback related to the measurement of smoking behavior. In addition, the feedback components can provide an alert to the individual on a repeating basis in an effort to remind the individual to provide periodic samples of exhaled air to extend the period of time for which the system captures biometric (such as eCO, CO levels, H2 etc.) and other behavioral data (such as location either entered manually or via a GPS component coupled to the unit, number of cigarettes, or other triggers). In certain

cases, the reminders can be triggered at higher frequency during the initial program or data capture. Once sufficient data is obtained, the reminder frequency can be reduced.

[0062] In obtaining the breath sample with the sampling unit 20, instructions may be provided on the personal electronic device 10 or computer display 12 for display to the subject in a guided breath test for training the subject to use the unit 20. Generally, the subject may be instructed, e.g., on the electronic device 10, to first inhale away from the unit 20 and then to exhale into the unit 20 for a set period of time. The unit 20 may optionally incorporate one or more pressure sensors fluidly coupled with, e.g., check valves, to detect if the subject inhales through the unit 20.

[0063] Turning now to the personal sampling unit **20** itself, FIG. 2 illustrates a perspective view of one variation of the unit **20** which may generally comprise a housing 30 having a shape which allows for the user to hold and manipulate the unit 20 with a single hand. The housing may incorporate the input trigger 24 as well as one or more indicators such as indicator 32 which is shown as a light. The collection tube 22 may be comprised of a tube defining a lumen 34 and which extends from the housing 30.

[0064] FIG. 3 shows a portion of the housing 30 and collection tube 22 removed to show a top view of the sensors contained within. In this variation, a first sensor 38 and second sensor 42 (either or both of the sensors 38, 42 may include CO and H2 sensors) are shown optionally positioned upon respect respective sensor platforms 36, 40 which in turn may be mounted upon a substrate such as a printed circuit board 44. Although in other variations, one or more sensors may be used depending upon the parameters being detected. In other variations, the one or more sensors may be mounted directly upon the printed circuit board 44. A power port and/or data access port 46 may also be seen integrated with the printed circuit board 44 and readily accessible by a remote device such as a computer, server, smartphone, or other device. As shown, multiple sensors 38, 42 or a single sensor may be used to detect the parameters from the sampled breath.

[0065] In other variations, at least one CO sensor or multiple CO sensors may be implemented alone. Alternatively, one or more CO sensors may be used along with one or more H2 sensors in combination. If both a CO and H2 sensor are used, the readings from the H2 sensor may be used to account for or compensate for any H2 signals detected by the CO sensor since many CO sensors have a cross-sensitivity to H2 which is frequently present in sufficient quantity to potentially affect CO measurement in the breath of people. If a CO sensor is used without an H2 sensor, various methods may be applied to reduce any H2 measurement interference to a nominally acceptable level. However, the use of an H2 sensor to directly measure and

compensate for the presence of H2 may facilitate CO measurement. The sensors may also include any number of different sensor types including chemical gas sensors, electrochemical gas sensors, etc. for detecting agents such as carbon monoxide in the case of detecting smoking related inhalation.

[0066] When detecting agents from breath samples from a subject, it is generally desirable to avoid temperature and humidity impacts on the sensors 38, 42 particularly in breath sensing devices which are compact as temperature swings and humidity may interfere with the detected signals in the sensors 38, 42. Larger breath sensing devices are able to readily contend with temperature and humidity variances due to their relatively larger mass and longer flow paths as the sampled breath temperature is reduced and moisture is removed prior to the breath sample reaching the sensor.

[0067] As an example of the effects of humidity upon the sensors, FIGS. 4A to 4C illustrate how sensor readings may be affected if humidity is not mitigated. A humid gas with no gas analyte was passed over sensors and the CO level 43 and H2 level 45 were measured at a medium flow rate and charted in graph 41, as shown in FIG. 4A. FIG. 4B illustrates graph 47 when the gas is introduced at a relatively higher flow rate. As shown, the CO level 43 and H2 level 45 result in more chaotic effects due not only to the humidity but also from the flow dynamics. The graphs 41, 47 demonstrate some of the difficulties in compensating for humidity as well as the flow dynamics. While differential temperature of the breath and device can affect the sensor readings, condensation can also create large signal differentials as variability due to moisture effects may be relative high in sample-to-sample readings if the moisture effects are not mitigated. In contrast, FIG. 4C shows graph 49 of the CO level 43 and H2 level 45 measurements at a medium flow rate with diffusion pathways implemented, as described herein.

[0068] Hence, the diffusion pathways that the sampled breath follows to the sensors 38, 42 helps to minimize the equivalent signal from breath humidity. Additionally, the implementation of algorithmic extrapolation of relatively short breaths still enable accurate approximation of true values, as described in further detail herein. While creating diffusion resistance may reduce the effects of humidity, diffusion resistance may also increase the sensor equilibration time which may make extrapolation relatively more difficult, e.g., by increasing the time required to achieve a certain level of accuracy. However, within the context of a relatively small sampling unit 20, the implementation of these mechanisms or processes enable the detection and processing of optimal signals.

[0069] In order for a relatively smaller device such as the personal sampling unit 20 described herein to accurately detect breath samples, one or several mechanisms may be employed to filter out moisture from the breath sample as well as reduce its temperature. FIGS. 5A and 5B illustrate respective top and bottom views of a flow control assembly 50 which may be incorporated into the housing 30 for controlling the flow of a breath sample to the sensors **38**, **42**. The assembly **50** may have a proximal receiving channel **52** into which the collection tube **22** may be inserted and retained. The lumen **34** of the collection tube **22** may be fluidly connected through the proximal receiving channel **52** and into a dispersion channel **54** which extends into and is fluidly coupled to one or more secondary channels **56**, **58** which define corresponding second fluid pathways 60, 62 extending away from the dispersion channel 54, e.g., at an angle relative to the dispersion channel 54. While two secondary channels 56, 58 are shown extending opposite to one another away from the dispersion channel 54, other variations may incorporate a single channel or more than two channels.

[0070] One or more primary channels 64, 66 may further extend away from and fluid coupled with the dispersion channel 54 so that the primary channels 64, 66 open into a main receiving channel 68 which is defined by a barrier 78 formed around the receiving channel 68. The illustration shows two primary channels 64, 66 in parallel which divide the flow into at least two different paths; however, a single primary channel or more than two primary channels may be used in other variations. Regardless, the receiving channel 68 may be in fluid communication with the first and second sensors 38, 42 through openings 72, 76 extending into respective first and second sampling chambers 70, 74 which are formed as individual chambers for receiving the sample breath directly over the sensors 38, 42.

[0071] The dispersion channel 54 helps to divert a majority of the sampled breath into the secondary channels 56, 58 so that a relatively smaller portion of the breath passes through the primary channels 64, 66 and into the receiving channel 68. For instance, about 80% of the breath sample may be diverted into the secondary channels 56, 58 where it may then be vented out from of the housing 30. The remaining, e.g., 20% of the breath sample, may then enter into the receiving channel 68 so that the diverted flow helps to decrease the moisture level in the sampled breath. Additionally, the relatively larger volume defined by the receiving channel 68 may further help to reduce the temperature of the sampled breath.

[0072] The openings 72, 76 extending into the respective first and second sampling chambers 70, 74 are sized to be relatively smaller and may number from a single opening to multiple openings

which help to further maintain the flow rate of the sampled breath entering the sampling chambers 70, 74 to a minimum flow rate of, e.g., about 4 mL/sec.

[0073] Contained within the first and second sampling chambers 70, 74 are respective first and second filters 80, 84 which further help to remove any additional moisture from the sampled breath. Additionally, respective first and second seals 82, 86 may surround the sampling chambers 70, 74 to contain the sampled breath over the sensors for detection. These first and second filters 80, 84 help to diffuse the flow path through a matrix, e.g., porous material, which not only removes moisture but also helps to further reduce the temperature of the sampled breath due to their additional thermal mass. The filters 80, 84 may be comprised of various materials that also filter out various chemicals such as alcohols, sulfur compounds, carbon monoxide, etc.

[0074] FIG. 6 shows a top view of the flow control assembly 50 incorporated into the housing 30 and sealed into positioned over the sensors 38, 42 such that the sampled air entering through the lumen 34 is contained within the assembly 50. As illustrated, the first and second sampling chambers 70, 74 are positioned over their respective first and second sensors 38, 42. FIG. 7 illustrates an example of the flow path that a sampled breath may follow. The initial breath 90 is shown entering the lumen 34 when exhaled by the subject. The breath enters the dispersion chamber 54 where a majority of the sample 92, 96, e.g., about 80%, is diverted through the chamber 54 and into respective second fluid pathways 60, 62 defined by secondary channels 56, 58. The remaining sample 100, 102, about 20%, enters through the primary channels 64, 66 and into the receiving channel 68 where the breath may then enter through the openings 72, 76 and into contact with the sensors 38, 42. In other variations, more than 50% of the breath sample may be diverted so that less than 50% of the breath sample enters into the receiving channel.

[0075] Another variation for reducing moisture and cooling the sampled breath may include incorporating a tortuous flow path which increases the surface area in contact with the sampled breath. This may include a coiled path or a maze which helps to drop the temperature and further allows for moisture to condense out of the breath and onto the surface area. FIG. 8 shows an example of how the breath sample passing from the dispersion chamber 54 may be forced into an exemplary tortuous flow path such as a circuitous loop 110 within the housing 30. The variation shown is intended to be illustrative and any number of tortuous flow paths may be configured. FIG. 9 shows another variation where the flow path is configured into a maze pattern. The sampled breath may leave the dispersion chamber **54** and encounter one or more barriers or baffles **112** which form the tortuous flow path **114**. The sampled breath may pass through one or

more channels **116** and enter a chamber **118** for entry through one or more openings **120** for sampling, as described herein.

[0076] In yet another variation, rather than utilizing barriers or baffles to create a tortuous flow path, tubing **122** may be used for flowing the breath sample. The tubing 122, as illustrated in FIG. 10A, may be coiled in any number of configurations and the tubing itself may be fabricated from a material such as a synthetic polymer, e.g., sulfonated tetrafluoroethylene based fluoropolymer-copolymer such as Nafion, which may facilitate moisture removal. Alternatively, moisture may be removed from the sample by utilizing, e.g., a moisture-permeable membrane 124 along the flow path 123 or a hygroscopic material such as silica that may absorb the moisture from the sample 125, as shown in FIG. 10B. In these variations where moisture is condensed or absorbed along the flow path, the condensed water is desirably removed 126 from the flow assembly. Removal may be accomplished in one variation by increasing a number of vent holes (e.g., vent holes 130 as shown below in FIG. 11A) from the flow path to the environment while in another variation, a water transport membrane, e.g., Nafion or another water-permeable solid, may be used to transport the water away from the flow assembly.

[0077] In yet another variation, an active mechanism such as a pump 126 may be used to draw a portion 128 of the sample 125 from the flow path 123 after the initial puff from the subject is introduced into the unit. FIG. 10C shows an example of how the portion 128 of exhaled breath may be drawn from the sample 125 by actuating the pump 126 after the breath is initially introduced through the flow path 123. This process may help to reduce the amount of moisture in the portion 128 before it is measured by the sensor.

[0078] Once the breath sample has been introduced through the openings 76 and past the filter 84, the sample may come be introduced within a sensing chamber 134 contained within an interior of the sampling chamber 74 where it comes into contact with the sensor 38, as illustrated in the cross-sectional detail perspective view of FIG. 11A. The gas diffusion into the sampling chambers may depend in part upon the size and number of openings into the sensing chambers and the presence of the one or more filters 84 may function as a capacitor for humidity. Hence, the sample breath passing over the sampling chambers may be diffused at a relatively slower rate into the sensing chamber 134 and into contact against the sensor 38. Despite the sample breath passing over the one or more openings 76, the net flow of the sample breath passing into the sampling chamber 74 is zero as the chamber 74 remains a sealed environment aside from the

openings 76. The sample breath that does arrive within the sensing chamber 134 and into contact with the sensor 38 does so by via diffusion through the openings 76 and the one or more filters 84.

[0079] The surface 132 of the sensor 38 generally presents a planar face against which a contact region 136 of the sampling chamber 74 may be positioned against. The sample breath within the sensing chamber 134 is desirably maintained within for contacting against the sensor surface 132 and also to prevent the sample breath from escaping into the rest of the housing 30 by sealing the contact region 136 with an interface such as a seal 86 which encircles the sensing chamber 134. Preventing the breath sample from escaping into the rest of the housing 30 not only may provide for better signal sensing and response speed but also avoids the contact against the other electronics contained within the housing. The sample breath is prevented from escaping from the receiving channel 68 by the barrier 140 which may be sealed against the housing interior by a seal 142.

[0080] It is still desirable to divert or vent a majority of the sample breath flow as a greater flow over the diffusion chambers may increase net moisture content and hence increase the dew point, Td, whereas a reduction of the dew point may increase the sensor response.

[0081] Due to the assembly tolerances of the flow control assembly 50, which may have a positional tolerance with respect to the sensor surface 132 of up to, e.g., +/- 0.010 in., the seal 86 may be positioned upon a tapered surface 138 which may be formed in an annular configuration around the sampling chamber 74. The tapered surface 138 may be angled so that the tapered surface 138 extends away from the contact region 136 as shown in FIG. 11B which illustrates the interface of FIG. 11A with the seal 86 removed for clarity purposes only. When the seal 86 is positioned upon the tapered surface 138, the seal 86 is urged to push against the sensor surface 132 with a spring constant in proportion to the angle of the tapered surface 138. This also allows for the seal 86 to press against the sensor surface 132 while providing sealing with a flatter force response than what a conventional compression gasket could provide by providing a relatively lower force across the geometric gap range especially if the sensor **38** is pressure sensitive. Furthermore, the use of the seal **86** upon the tapered surface **138** helps to accommodate displacement due to tolerances of the contact region **136** and/or flow control assembly **50** for up to half the cross-sectional diameter of the seal 86, e.g., 0.070 in. FIG. 11C illustrates a cross-sectional detail perspective view of another variation of a sampling chamber 74 having multiple (e.g., four or more) filter layers contained within for filtering out the sampled breath.

[0082] With respect to the sampling chambers, its volume for receiving the sampled breath through the openings 76 may vary. In one variation, the volume may be, e.g., approximately 0.13 mL with 3 x 1.2 mm diameter openings 76 (3.4 mm2). A larger or smaller sampling chamber may be used and the area or size of the openings may change linearly with chamber volume. Thus, a ratio of opening area per chamber volume may be used as an indicator for determining optimal opening size and sampling chamber volume. This ratio of, e.g., about 25 mm2 / mL, works well for CO and the ratio may change with the target gas as a smaller ratio may be more effective in blocking water. For instance, H2 diffuses relatively faster than CO and so a ratio of about 10 mm2 / mL would be effective if H2 were the main gas of interest.

[0083] The sampling chamber may be filled with a porous or fibrous material that functions as a filter that can absorb moisture. This will not only remove some moisture from the gas diffusing through, but will also preferentially slow down the diffusion of moisture that does ultimately diffuses to the sensor. Furthermore, the filter material may be selected so that it removes unwanted contaminants, such as volatile organic compounds (VOCs). Materials such as activated carbon may be selected as it removes moisture and also many contaminants including alcohol which is particularly applicable for breath sensing.

[0084] Additionally, the ideal diffusion chamber geometry may also depend on the sensor. For instance, a relatively fast sensor may be able to handle a "slower" diffusion chamber characteristic, but a sensor with faster detection characteristics may be limited by the type and construction of the sensor.

[0085] When a subject blows into the collection tube 22 for submitting a breath sample, predicting a terminal value of the sensors 38, 42 in a limited-duration breath test may be difficult due to the stabilization time typically needed for many types of sensors to accurately detect parameters from the breath sample. For instance, gas sensors (such as CO sensors) may take up to 10-30 seconds of sampling time to stabilize and yield a final value. However, subjects may not be able to (or should not need to) exhale for more than 5-10 seconds into the collection tube 22 in order to obtain an accurate reading. Hence, the final value may be estimated based upon the transient signals obtained from the sensor.

[0086] During a test 156, the input response sensor curve may be associated with the calibration curve. The association may be accomplished using a number of different methods. In one variation, the sensor value at test time t = t1 may be compared to the calibration value at t = t1, where t1 is a selected to be a time of interest, e.g., time at the peak, time at the end of the test, or a

specific time during the test (e.g. 10 seconds, etc.). In another variation, a least-squares fit may be performed of the input sensor curve to the calibration curve multiplied by a constant, and optimizing for that constant. For example, a constant of 0.6 would mean the input value is calculated to be 0.6 * the calibration value. The calibration constant is calculated for each device and may be based on the calibrated input from the subject. Finally, the final value may be determined 158 by extrapolating the sample result based the calibrated curve.

[0087] Hence, if the rates of stabilization are fixed or can be estimated accurately based on other known parameters, e.g. temperature, then the process illustrated in the diagram 150 of FIG. 12 may be used in one variation. For instance, the sensor electronics in the unit 20 may be calibrated 152 using a gas of known concentration (e.g. 50 ppm CO) and the entire calibration curve may be recorded 154 as a function of time, e.g., the sensor response may be recorded as a function of time. Alternatively, rather than the entire calibration curve, a sufficient portion of the calibration curve (and not just the terminal and plateau values) may be recorded and stored in memory. The rate of stabilization may also be complicated due to various known or unknown variables such as current temperature or humidity levels at the time of sampling, previous dwell temperature or humidity levels, etc.

[0088] FIG. 13A illustrates an example of a graph 151 showing a calibration curve 153 of a gas having a known CO concentration and a curve 155 of a known H2 concentration as described above in steps 152 and 154. The calibration curve may be obtained with a sample of, e.g., 50 ppm CO, measured over a period of, e.g., about 30 sec. This calibration curve may be used as a baseline where 129 mV = 50 ppm is derived. FIG. 13B shows the graph **157** with a sample curve **159** of a test sample where 50 ppm CO for approximately 15 sec. Because the obtained test result is less than the length of the calibration curve **153** (e.g., if the subject is unable to continue blowing the sample breath), the detected signal may register a peak value **161** relatively early and begin to show a decrease **163**. With the known calibrated curve **153**, the sample curve **159** may be compared and associated with the calibrated curve 153, as described in step 156 and as shown in FIG. 13C. The sample curve 159 when compared against the calibrated curve 153 illustrates how the peak value 161 (for 50 ppm) is unable to reach the full sensor signal value in the recorded time of 15 seconds yet the algorithm may fit the data 165 to the exponential function, described herein, and determine that the final value as described in steop 158.

[0089] If the rate of stabilization is not sufficiently well known for a sensor but the shape of the calibration curve is known, in particular an exponential settling function of the type y(t) =

yterminal * (1 – e-t/τ), then the process illustrated in diagram 160 of FIG. 14 may be used. During a calibration test or a field test, any compensations 162 may be performed (heuristical or theoretical) that allow the input curve to better fit a simple analytical time function such as the exponential settling function. For example, the early part of the curve may be adjusted to compensate for diffusion speed to the sensor. Default values may be assumed 164 for constants associated with the analytical time function. In the case of the exponential settling function, a default value for an analytical function time constant tau, τ, may be assumed. The goodness of fit of the (compensated) input data to the analytical function may be assessed 166 and a determination 168 may be made as to whether the good of fit is sufficient. Assuming goodness of fit is insufficient, an adjustment 170 may be made of the value of the analytical function constants, τ, based on the disparity between the input data and analytical function, e.g. overshoot or undershoot and steps 166, 168, 170 may be repeated using an optimizing algorithm (e.g., binary search, executed on the constant tau) to evaluate for the best fit to the analytical function. Once the goodness of fit is sufficient, the optimized analytical function and input data may be used 172 to predict the value of input analyte (CO), e.g., by estimating the terminal value. When performing calibration, this procedure may be used to set the sensitivity (yterminal / COppm) and when performing a test, this procedure may be used and the terminal value may be divided by the sensitivity to calculate the analyte level.

[0090] Compensation in step 162 may be done in either of the following situations. The first situation is when the input breath sample does not immediately propagate to the sensor due to the device geometry but the gas concentration at the sensor surface can be modeled for example by an exponential decay function. The second situation is when a subject's CO level in their breath is not evenly distributed throughout the sample breath, but is actually highest at the end of the exhaled breath. Compensation may be done by adjusting the slope up in the analysis, essentially amplifying the early part of the curve. Several constants that were derived experimentally by optimizing using existing datasets may be utilized.

[0091] Over time, the sensors may begin to degrade with repeated use and the calibration data initially used may no longer be valid after some amount of time has passed. Thus, aging data may be used to determine typical behavior over time and also used to compensate the calibration data accordingly. For example, the approximate degradation of certain sensors may be known to be, e.g., 0.6% per month for the first six months and then 0.3% per month thereafter. With this known degradation rate, these parameters may be used to compensate the analysis of each

measured value thereafter based upon the amount of time which has elapsed since the device was calibrated.

[0092] In another variation of the sampling unit 20, the device may additionally and/or alternatively incorporate one or more spirometers 180 for monitoring or screening for various conditions, e.g., COPD, asthma, etc. The spirometer 180 may be incorporated into the unit 20 so that it is in fluid communication with a sample breath 125 passing through the flow path 123 to detect and/or monitor parameters, as shown in FIG. 15. The spirometer 180 may be wired to a processor within the unit 20 or it may be wirelessly in communication with the personal electronic device 10 or computer 12. Additionally, the flow path 123 may include a flow switch to increase or decrease flow resistance along the flow path. When the subject breaths into the device, they may be instructed to exhale as vigorously as possible and the device may translate measured pressure into a flow rate to calculate, e.g., forced vital capacity (FVC) or forced expiratory volume, 1 second test (FEV1).

[0093] While illustrative examples are described above, it will be apparent to one skilled in the art that various changes and modifications may be made therein. Moreover, various apparatus or procedures described above are also intended to be utilized in combination with one another, as practicable. The appended claims are intended to cover all such changes and modifications that fall within the true spirit and scope of the invention.

CLAIMS

What is claimed is:

1. A flow control apparatus for measuring an analyte from a breath sample of a subject, comprising:

a sampling chamber defining a volume and one or more openings into the sampling chamber;

at least one sensor in fluid communication with the sampling chamber, wherein the at least one sensor is configured to detect the analyte, and

wherein the sampling chamber is configured to receive the breath sample into the sampling chamber and into contact with the at least one sensor via diffusion into the sampling chamber.

2. The apparatus of claim 1 wherein the sampling chamber is further configured to receive a zero net flow of the breath sample through the one or more openings.

3. The apparatus of claim 1 further comprising at least one filter element positioned within the volume and between the one or more openings and the at least one sensor.

4. The apparatus of claim 1 wherein the volume is approximately 0.13 mL.

5. The apparatus of claim 1 wherein the one or more openings comprise three openings each having a diameter of 1.2 mm.

6. The apparatus of claim 1 wherein a ratio of the one or more openings and the volume is about 25 mm^2 / mL for detecting CO levels.

7. The apparatus of claim 3 wherein the at least one filter comprises a porous or fibrous material configured to slow diffusion of moisture to the sensor.

8. The apparatus of claim 3 wherein the at least one filter is comprised of activated carbon.

9. The apparatus of claim 3 wherein the at least one filter is a CO filter.

10. The apparatus of claim 1 further comprising:

a proximal receiving channel sized to receive the breath sample;

a dispersion channel fluidly connected to the proximal receiving channel;

a main receiving channel, wherein the dispersion channel is configured to divert a portion of the breath sample to the main receiving channel and a majority of the breath sample to one or more secondary channels for venting; and

wherein the flow control apparatus is fluidly connected to the main receiving channel.

11. The apparatus of claim 10 further comprising a housing sized to contain the flow control apparatus within.

12. The apparatus of claim 10 wherein the main receiving channel is sized to receive about 20% of the breath sample.

13. The apparatus of claim 10 wherein the main receiving channel is sized to receive less than 50% of the breath sample.

14. The apparatus of claim 10 further comprising one or more seals for sealing between the sampling chamber and the at least one sensor.

15. The apparatus of claim 14 wherein the sampling chamber further defines an annular tapered surface configured to urge the one or more seals into contact against a surface of the sensor.

16. The apparatus of claim 10 wherein the main receiving channel comprises a plurality of barriers or baffles which define a tortuous flow path from the dispersion channel to the flow control apparatus.

17. The apparatus of claim 1 wherein the at least one sensor comprises one or more CO sensors.

18. The apparatus of claim 17 further comprising at least one H_2 sensor.

19. A flow apparatus for measuring a concentration of an analyte of interest from an individual's breath, comprising:

a sampling chamber including at least one opening to receive a portion of the breath, wherein a remainder of the breath is diverted and vented;

at least one sensor positioned in fluid communication with the sampling chamber, wherein the at least one sensor is configured to detect the analyte of interest, and

wherein the sampling chamber is configured such that a majority of the portion of the breath in contact with the sensor is introduced via diffusion, rather than flow, into the sampling chamber.

20. The apparatus of claim 19 wherein the at least one opening into the sampling chamber is configured so as to reduce transport of moisture to the sensor.

21. The apparatus of claim 19 further comprising at least one filter element positioned between the at least one opening and the at least one sensor.

22. The apparatus of claim 21 wherein the at least one filter is a CO filter.

23. The apparatus of claim 19 wherein the sampling chamber has a volume of approximately 0.13 mL.

24. The apparatus of claim 19 wherein the at least one opening comprises three openings each having a diameter of 1.2 mm.

25. The apparatus of claim 19 wherein a ratio of the at least one opening and a volume of the sampling chamber is about 25 mm^2 / mL for detecting CO levels.

26. The apparatus of claim 21 wherein the at least one filter comprises a porous or fibrous material configured to slow diffusion of moisture to the sensor.

27. The apparatus of claim 19 wherein the at least one sensor comprises one or more CO sensors.

28. The apparatus of claim 27 further comprising at least one H_2 sensor.

29. A method of extrapolating a final value of a parameter from a breath sample, comprising:

obtaining a calibration curve of a gas having a known parameter concentration;

recording at least a portion of the calibration curve as a function of time;

measuring an input response curve of the parameter from the breath sample over a period of time;

associating the input response curve to the calibration curve; and

extrapolating the final value of the parameter from the breath sample based on the calibration curve associated with the input response curve.

30. The method of claim 29 wherein extrapolating comprises using an iterative method to determine analytical constants to achieve a best fit of an input data to a predetermined function.

31. The method of claim 29 wherein obtaining comprises obtaining the calibration curve of a gas having a known CO concentration.

32. The method of claim 29 wherein measuring comprises measuring over the period of time which is less than a time of the calibration curve.

33. The method of claim 32 wherein the period of time is less than 15 seconds.

34. The method of claim 29 wherein associating comprises applying an exponential settling function of $y(t) = y_{terminal} * (1 - e^{-t/\tau})$, where:

τ = analytical function time constant

$y_{terminal}$ = a terminal value.

35. The method of claim 29 wherein measuring further comprises measuring the breath sample via at least one CO sensor.

36. The method of claim 35 further comprising measuring the breath sample via at least one H_2 sensor.

37. The method of claim 36 further comprising compensating for any H_2 measurement sensitivity from the at least one CO sensor with a measurement from the at least one H_2 sensor.

38. A flow control assembly, comprising:

a proximal receiving channel sized to receive a fluid sample;

a dispersion channel fluidly connected to the proximal receiving channel;

a main receiving channel, wherein the dispersion channel is configured to divert a portion of the fluid sample to the main receiving channel and a majority of the fluid sample to one or more secondary channels for venting from the assembly; and

one or more sampling chambers fluidly connected to the main receiving channel via one or more openings.

39. The assembly of claim 38 further comprising a housing sized to contain the flow control assembly within.

40. The assembly of claim 38 wherein the main receiving channel is sized to receive about 20% of the fluid sample.

41. The assembly of claim 38 wherein the main receiving channel is sized to receive less than 50% of the fluid sample.

42. The assembly of claim 38 further comprising one or more sensors in fluid communication respectively with the one or more sampling chambers.

43. The assembly of claim 42 wherein the one or more sensors comprises one or more CO sensors.

44. The assembly of claim 43 further comprising at least one H_2 sensor.

45. The assembly of claim 38 further comprising one or more seals for sealing between the one or more sampling chambers and the one or more sensors.

46. The assembly of claim 45 wherein the one or more sampling chambers further define an annular tapered surface configured to urge the one or more seals into contact against a surface of the one or more sensors.

47. The assembly of claim 38 wherein the one or more secondary channels extend from the dispersion channel at an angle.

48. The assembly of claim 38 wherein the main receiving channel comprises a plurality of barriers or baffles which define a tortuous flow path from the dispersion channel to the one or more sampling chambers.

49. The assembly of claim 38 wherein the flow control assembly further comprises a water permeable membrane.

50. The assembly of claim 38 further comprising a pump in fluid communication with the fluid sample.

51. A method of measuring a fluid sample, comprising:
receiving the fluid sample within a proximal receiving channel;
diverting a majority of the fluid sample to one or more secondary channels;
diverting a portion of the fluid sample into a main receiving channel; and
introducing the portion of the fluid sample into contact with one or more sensors for determining a parameter from the fluid sample.

52. The method of claim 51 wherein diverting a portion of the fluid sample comprises diverting about 20% of the fluid sample to the main receiving channel.

53. The method of claim 51 wherein diverting a portion of the fluid sample comprises diverting about less than 50% of the fluid sample to the main receiving channel.

54. The method of claim 51 wherein diverting a portion of the fluid sample further comprises reducing a temperature of the fluid sample.

55. The method of claim 51 wherein diverting a portion of the fluid sample further comprises removing moisture from the fluid sample.

56. The method of claim 55 wherein removing moisture comprises passing the portion of fluid sample over a water permeable membrane.

57. The method of claim 55 wherein removing moisture comprises passing the portion of fluid sample through a tortuous flow path.

58. The method of claim 51 further comprises detecting the parameter from the fluid sample via the one or more sensors.

59. The method of claim 58 wherein the detecting the parameter comprises detecting via one or more CO sensors.

60. The method of claim 59 further comprising detecting via at least one H_2 sensor.

61. The method of claim 60 further comprising compensating for any H_2 measurement sensitivity from the one or more CO sensors with a measurement from the at least one H_2 sensor.

62. The method of claim 51 further comprising calibrating the one or more sensors with a gas of known concentration.

63. The method of claim 62 further comprising recording an entire calibration curve of the gas as a function of time.

64. The method of claim 63 further comprising associating an input response from the one or more sensors to the calibration curve.

65. The method of claim 64 further comprising extrapolating a final value of the input response based on the calibration curve.

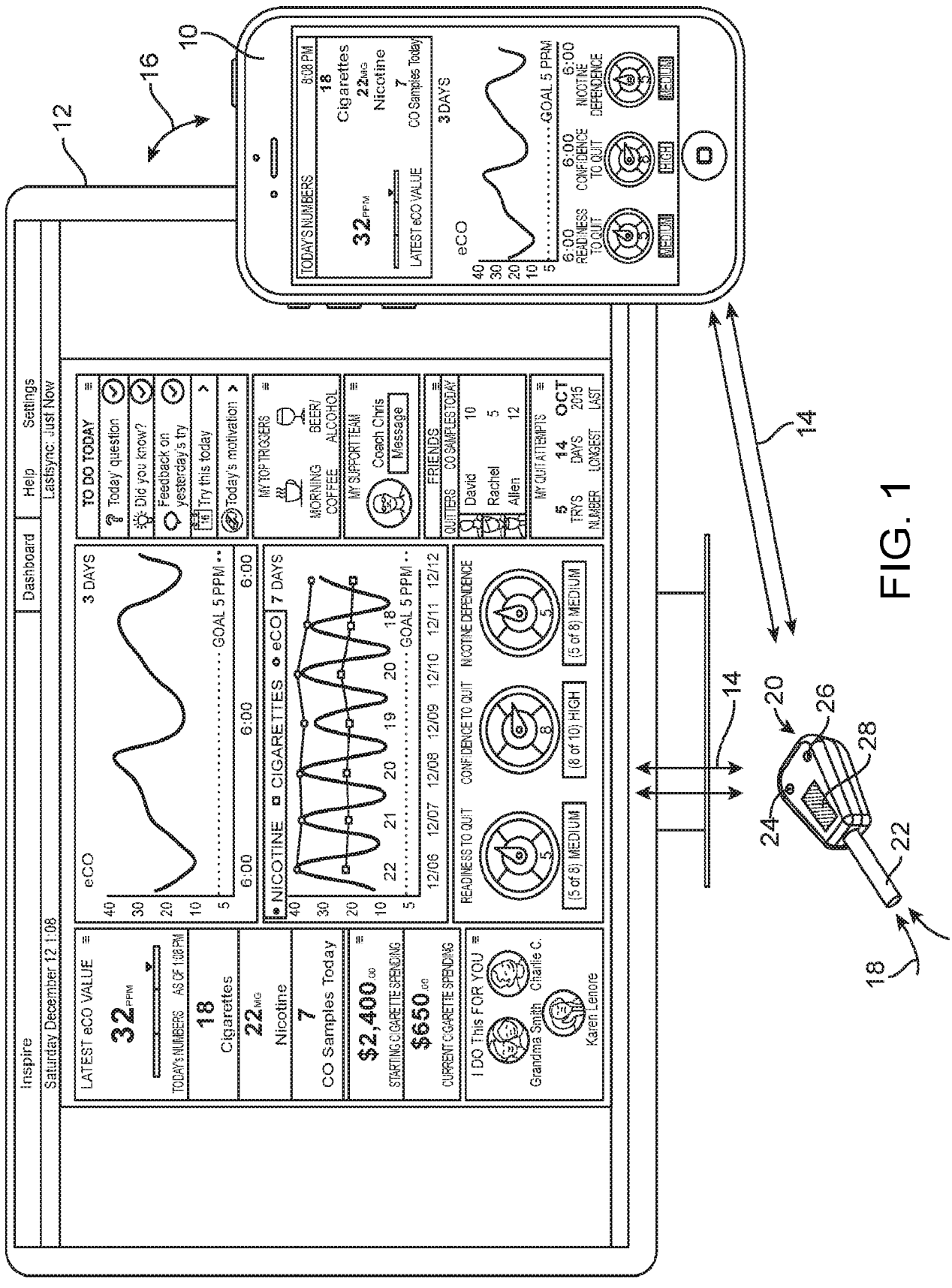

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Inspire
Dashboard
Help
Settings
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Saturday December 12 1:08
LATEST eCO VALUE
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TODAY'S NUMBERS AS OF 1:08 PM
18 Cigarettes
22 MG Nicotine
7 CO Samples Today
$2,400 00 STARTING CIGARETTE SPENDING
$650 00 CURRENT CIGARETTE SPENDING
I DO This FOR YOU
Grandma Smith
Charlie C.
Karen Lenore
eCO
3 DAYS
GOAL 5 PPM
6:00
NICOTINE CIGARETTES eCO
7 DAYS
12/06 12/07 12/08 12/09 12/10 12/11 12/12
READINESS TO QUIT
CONFIDENCE TO QUIT
NICOTINE DEPENDENCE
(5 of 8) MEDIUM
(8 of 10) HIGH
(5 of 8) MEDIUM
TO DO TODAY
Today question
Did you know?
Feedback on yesterday's try
Try this today
Today's motivation
MY TOP TRIGGERS
MORNING COFFEE
BEER/ ALCOHOL
MY SUPPORT TEAM
Coach Chris
Message
FRIENDS
QUITTERS
CO SAMPLES TODAY
David 10
Rachel 5
Allen 12
MY QUIT ATTEMPTS
5 TRYS
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3 DAYS
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MEDIUM
HIGH
MEDIUM

FIG. 1

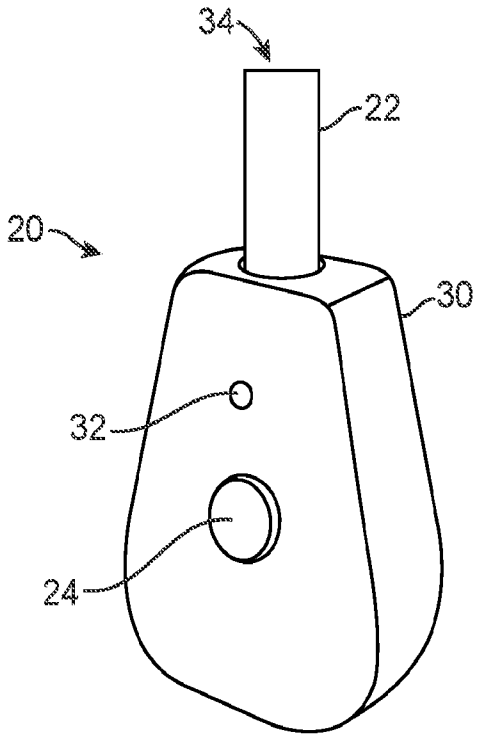


FIG. 2

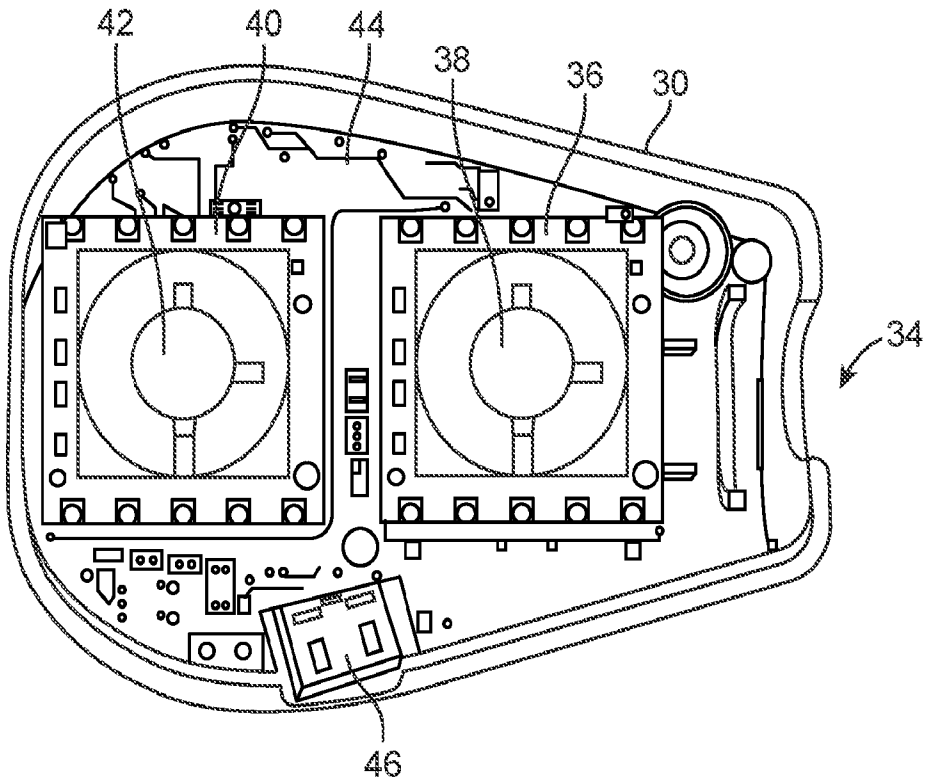


FIG. 3

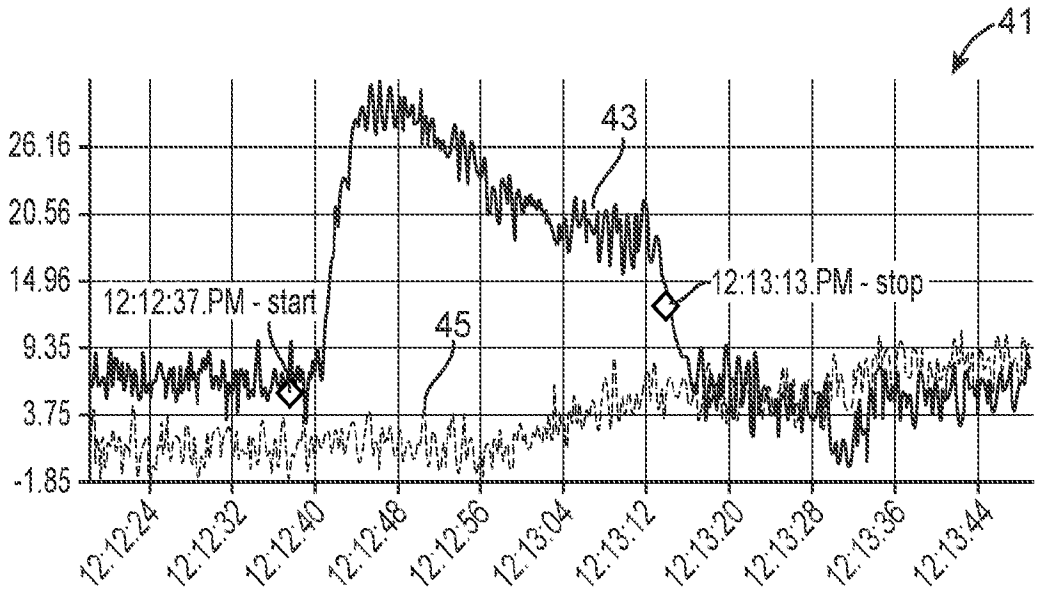


FIG. 4A

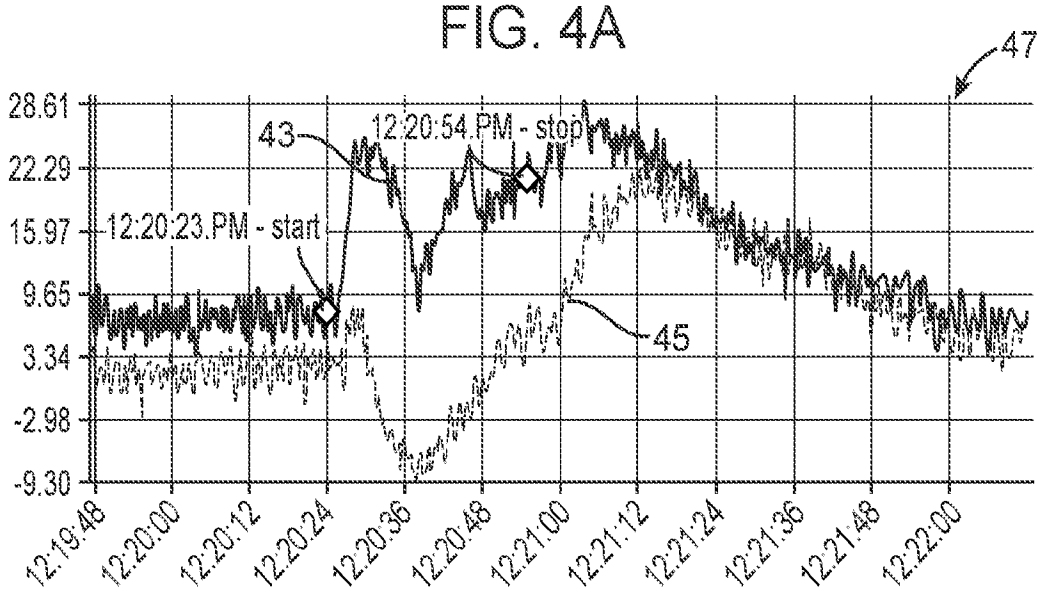


FIG. 4B

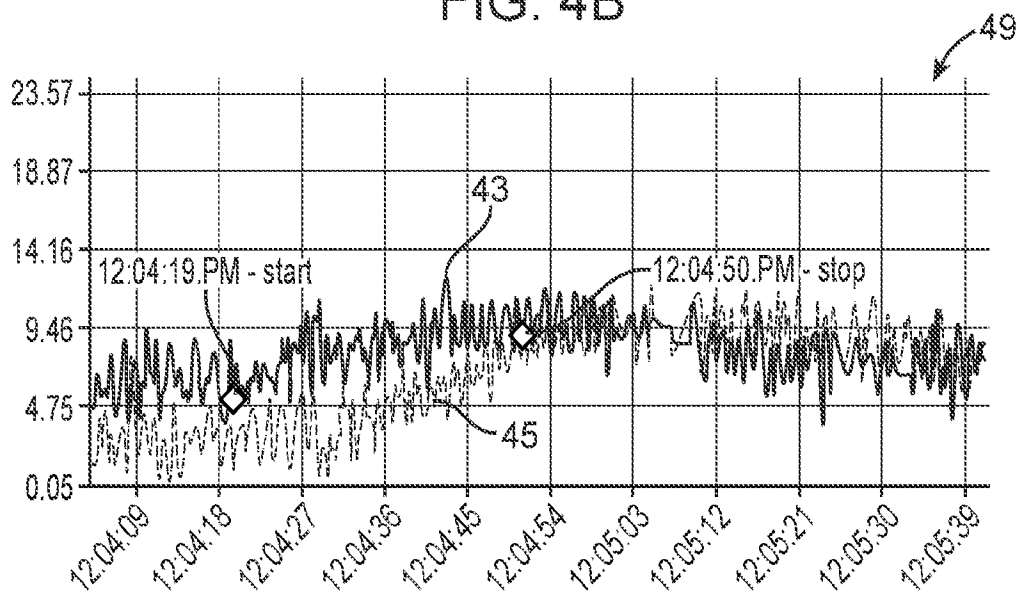


FIG. 4C

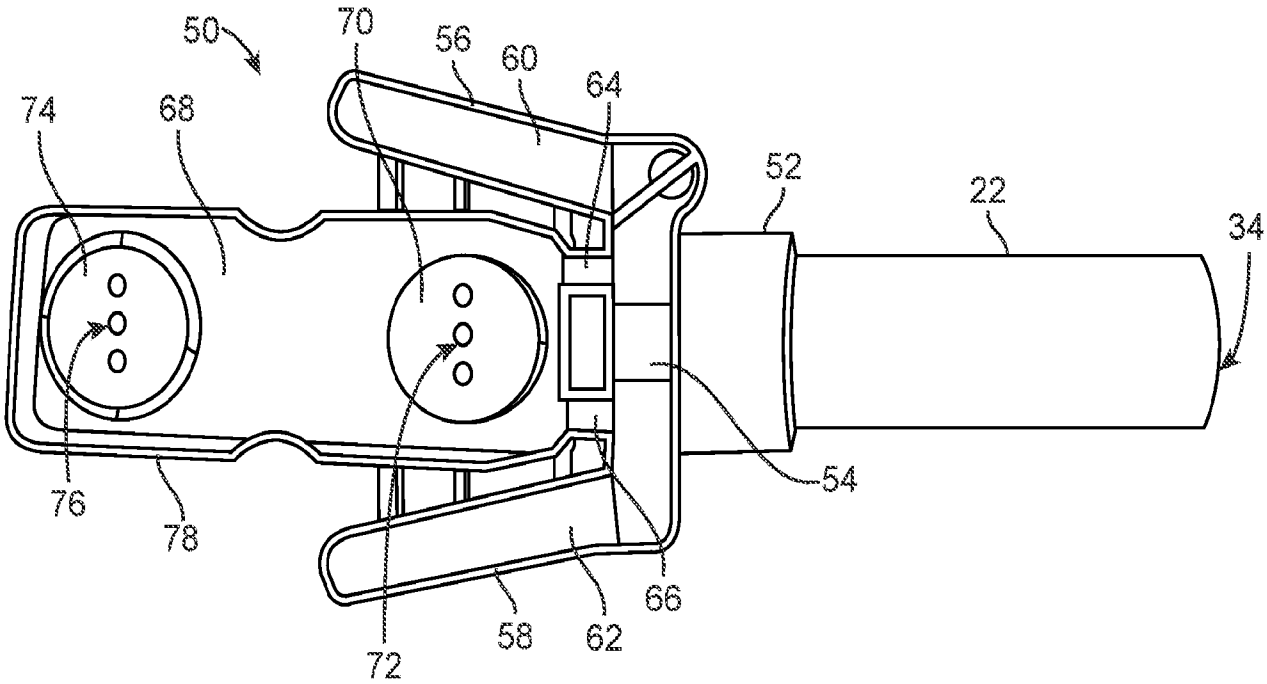

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FIG. 5A

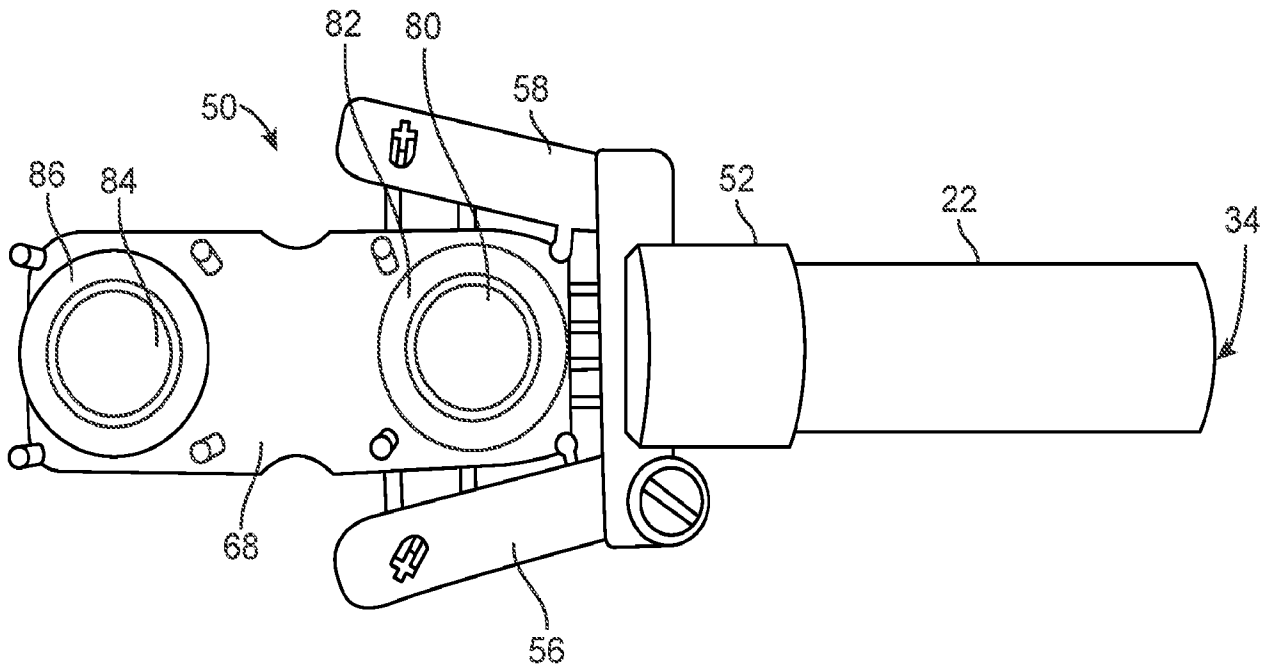

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FIG. 5B

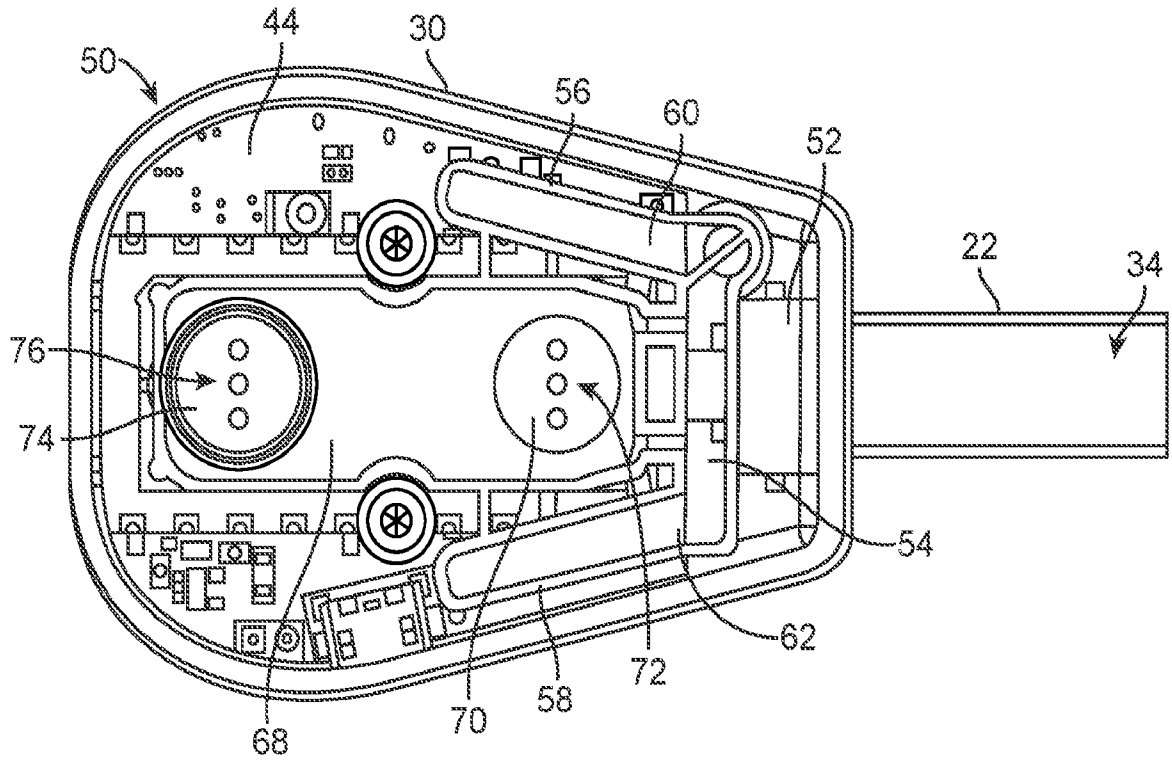

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FIG. 6

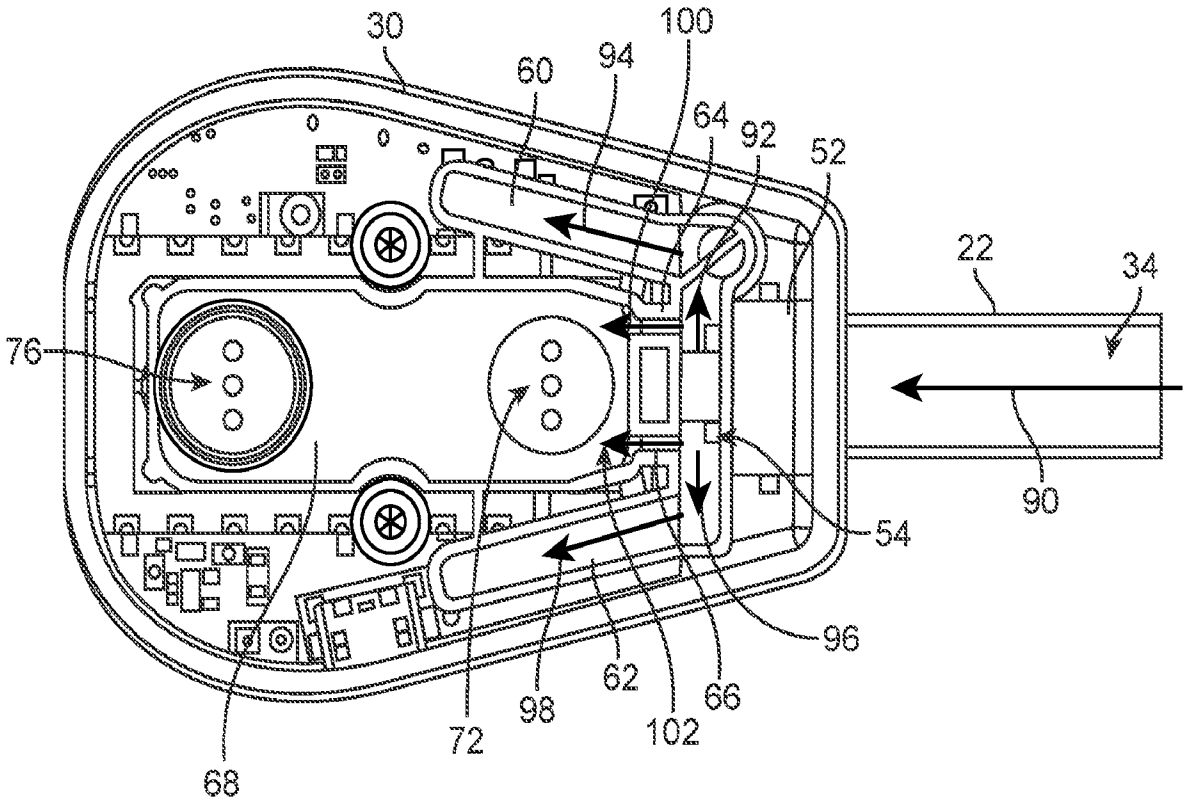

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FIG. 7

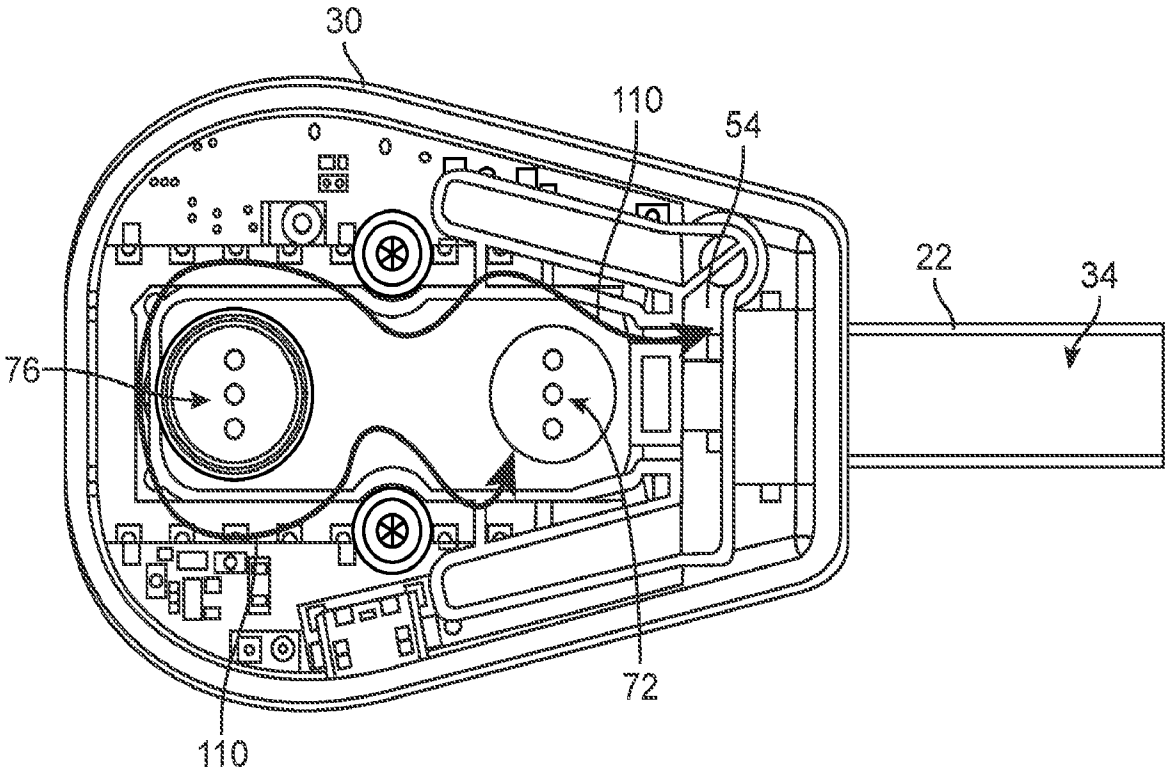


FIG. 8

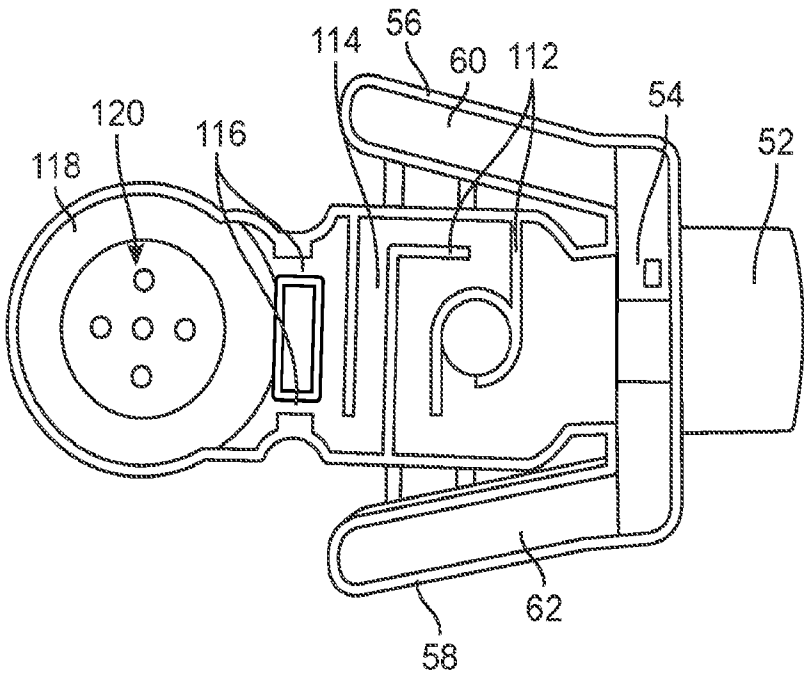


FIG. 9

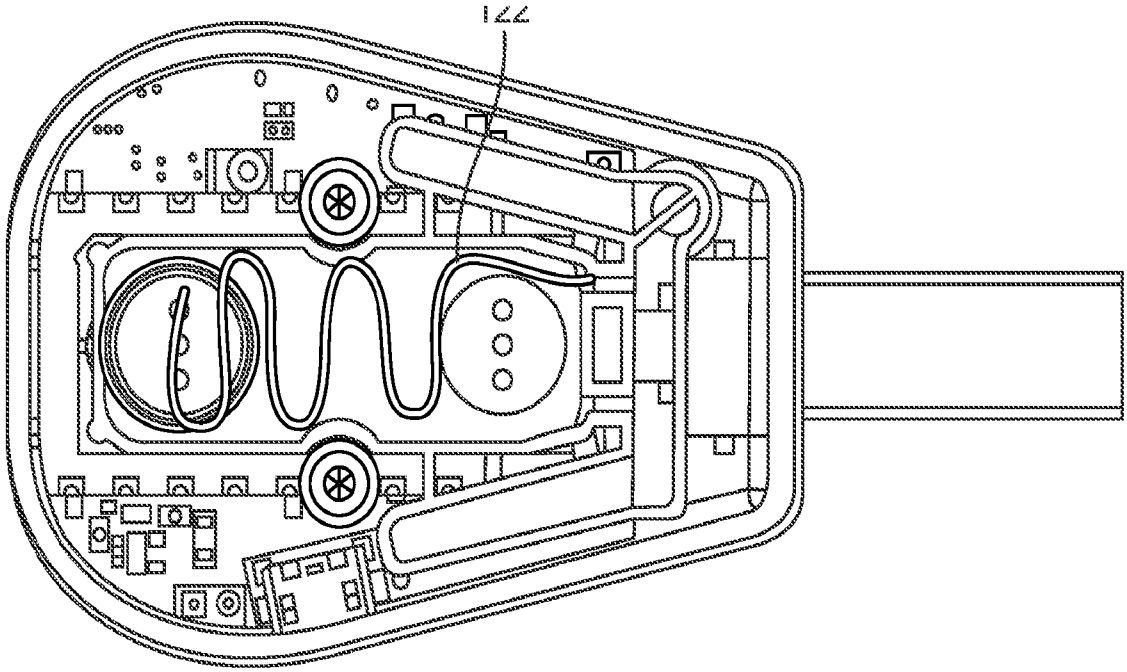


FIG. 10A

FIG. 10B

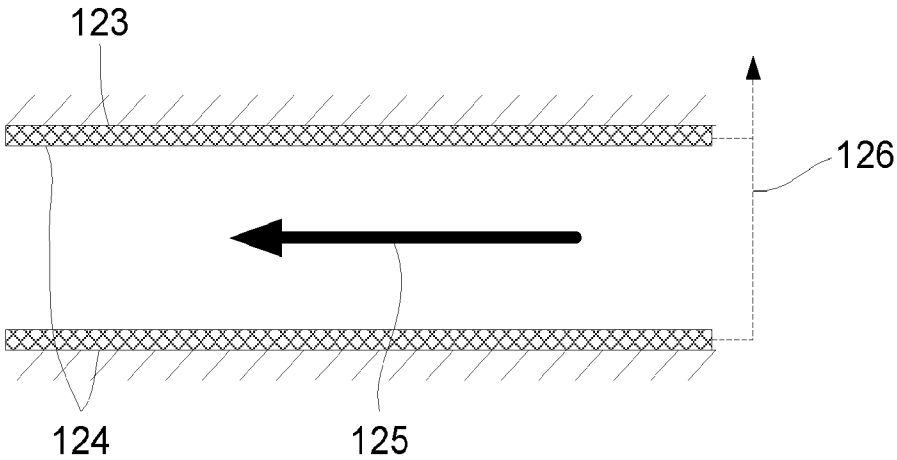
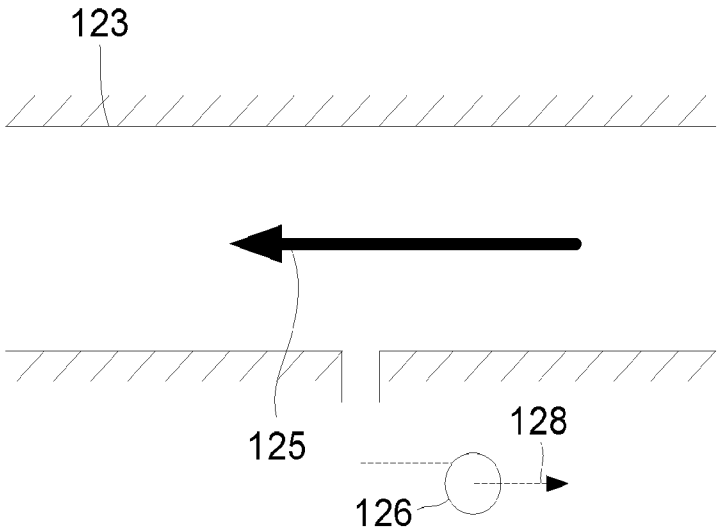


FIG. 10C



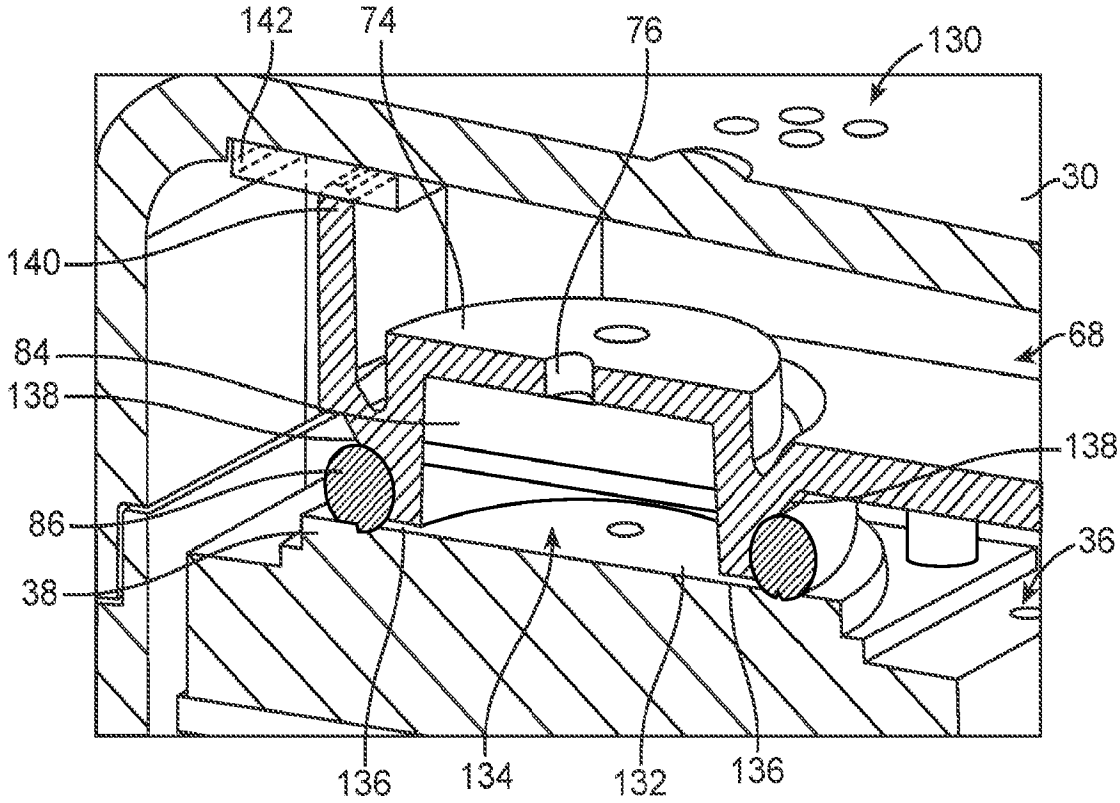


FIG. 11A

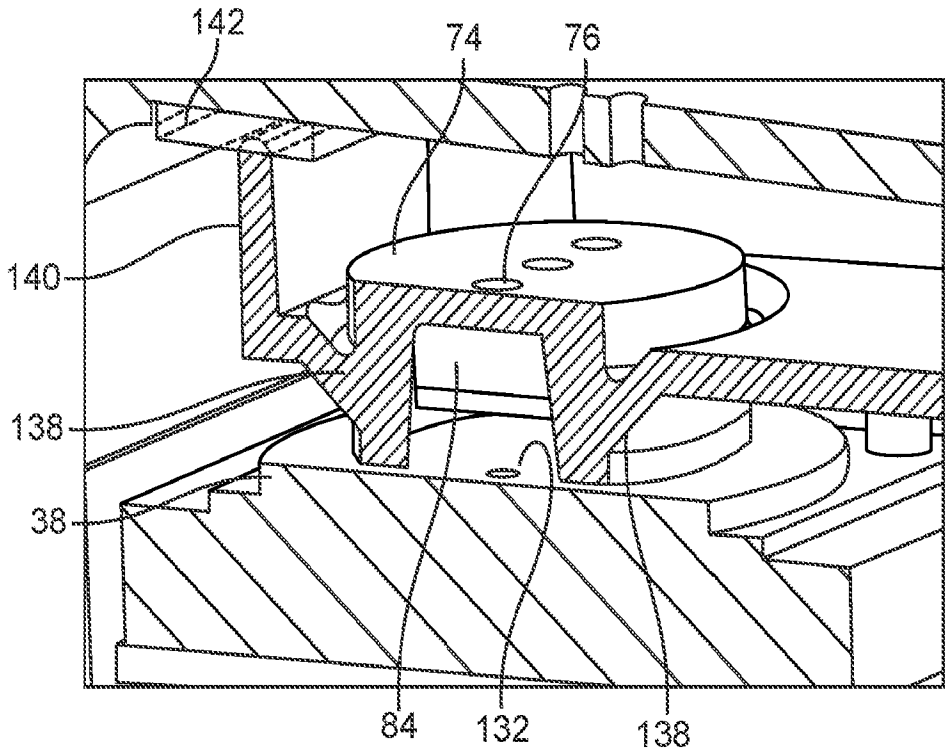


FIG. 11B

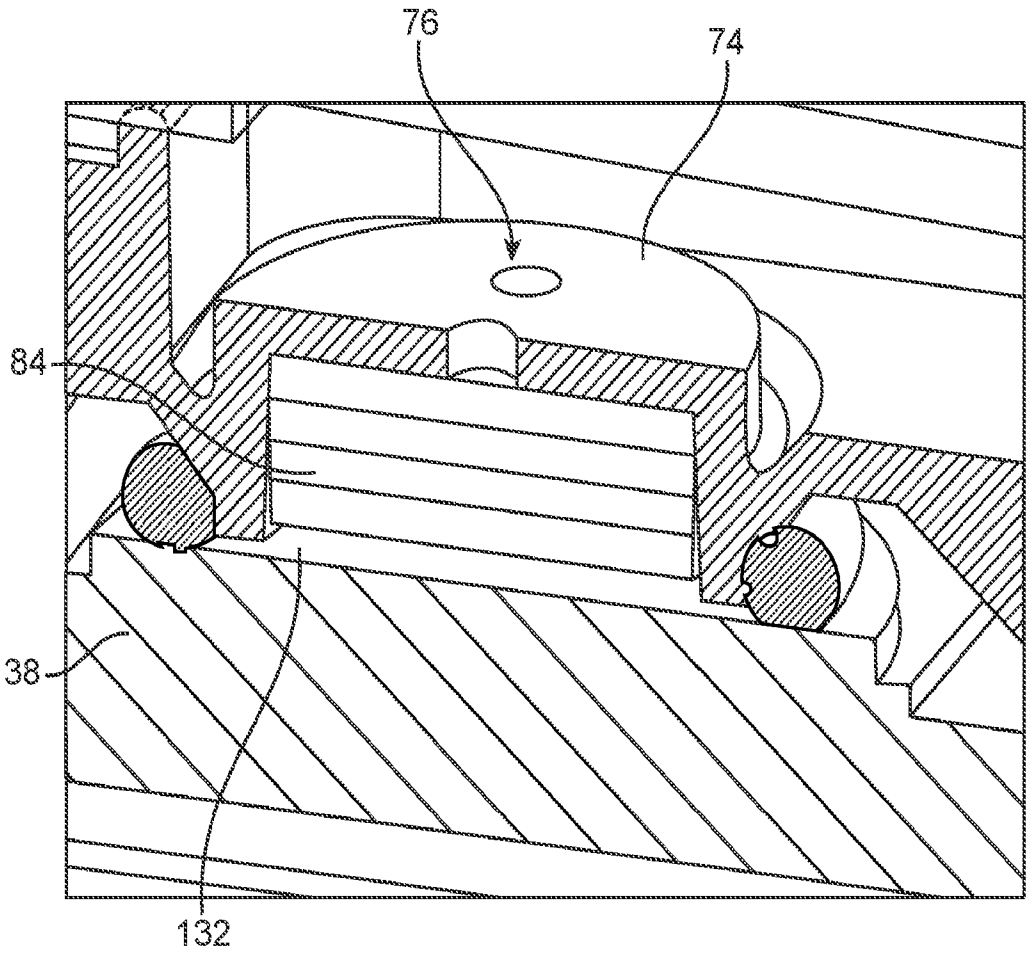


FIG. 11C

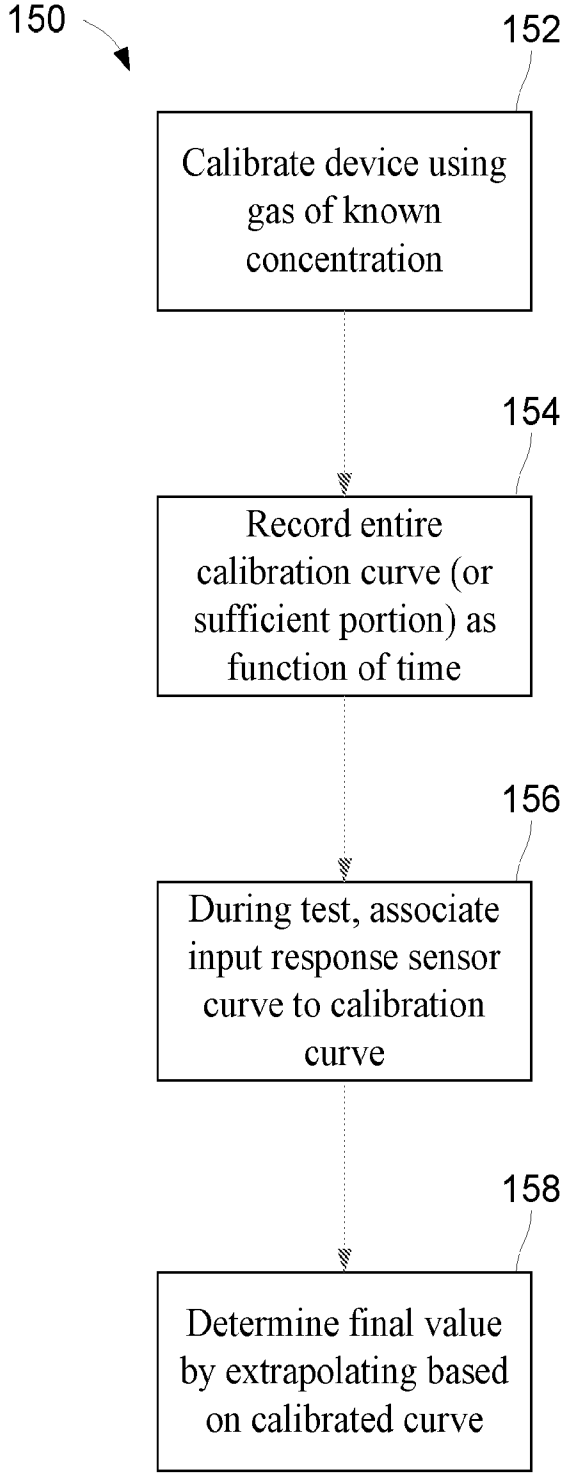

150
152
Calibrate device using gas of known concentration
154
Record entire calibration curve (or sufficient portion) as function of time
156
During test, associate input response sensor curve to calibration curve
158
Determine final value by extrapolating based on calibrated curve

FIG. 12

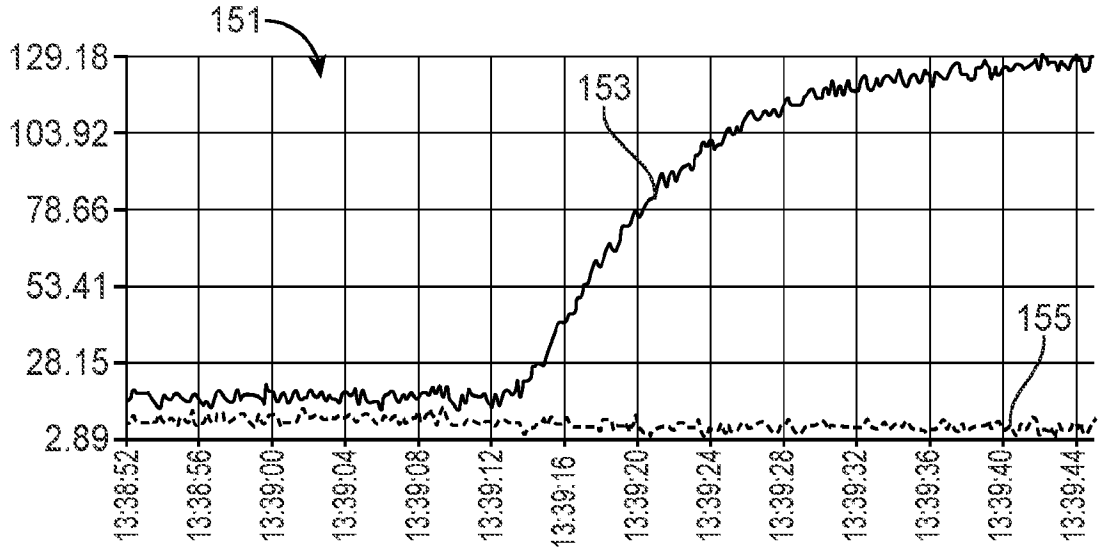


FIG. 13A

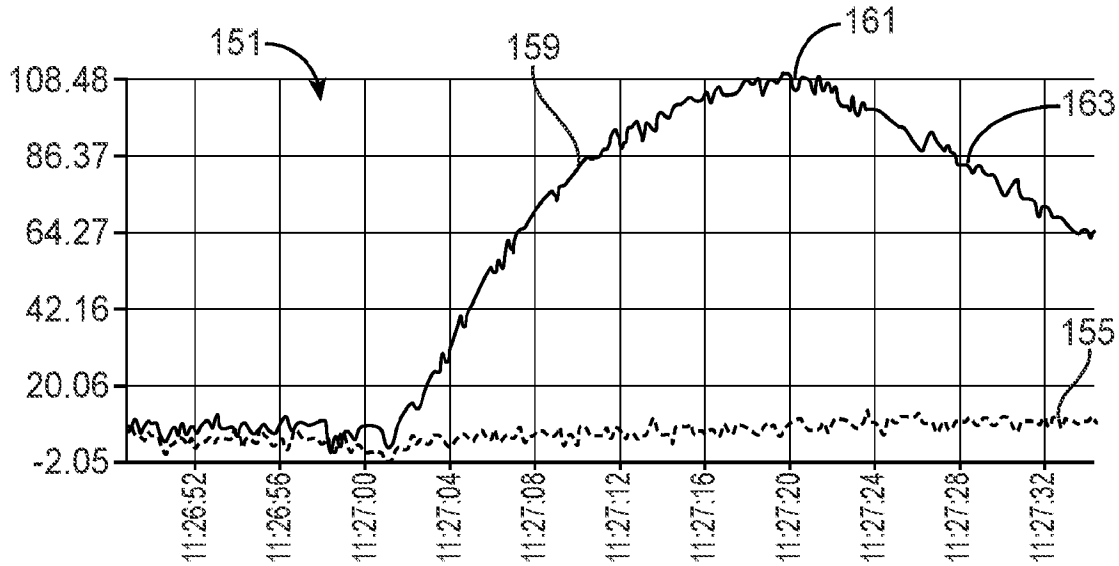


FIG. 13B

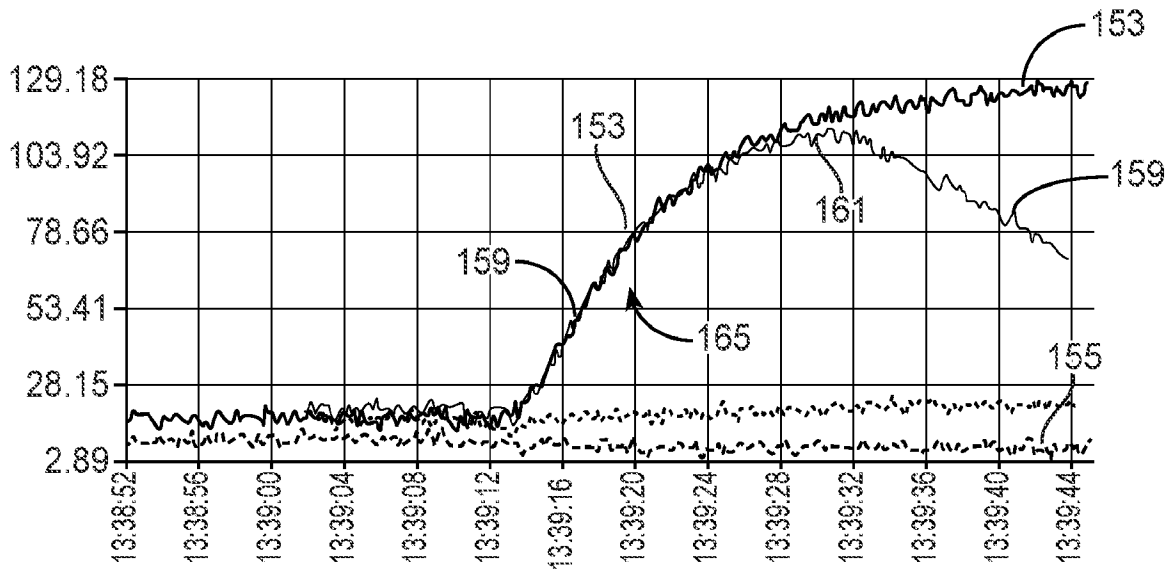


FIG. 13C

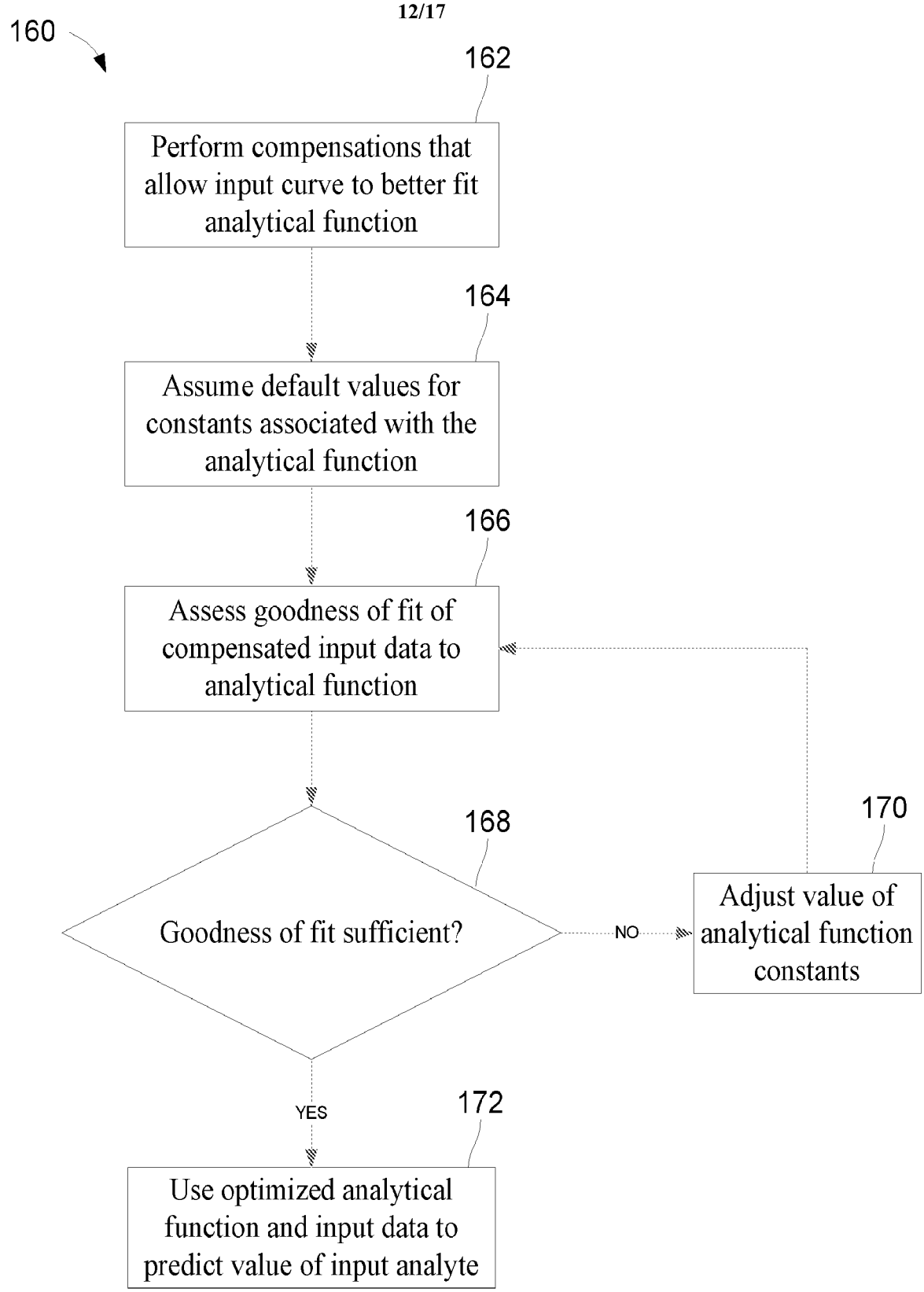

160
162
Perform compensations that allow input curve to better fit analytical function
164
Assume default values for constants associated with the analytical function
166
Assess goodness of fit of compensated input data to analytical function
168
Goodness of fit sufficient?
NO
170
Adjust value of analytical function constants
YES
172
Use optimized analytical function and input data to predict value of input analyte

FIG. 14

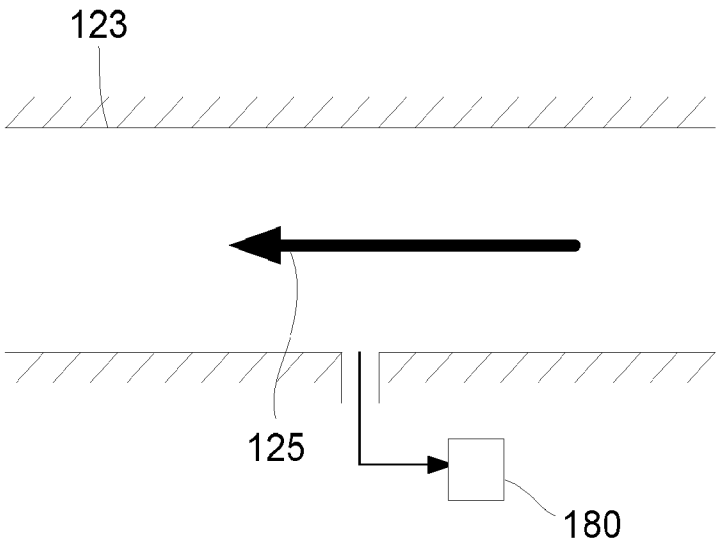


FIG. 15

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2018/052677

A. CLASSIFICATION OF SUBJECT MATTER
IPC(8) - A61B 5/097; A61B 5/08; A24F 47/00 (2019.01)
CPC - A61B 5/082; A61B 5/097; A24F 47/00 (2019.02)

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)
See Search History document

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
USPC - 600/532; 422/84 (keyword delimited)

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

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2005/0083527 A1 (FLAHERTY et al) 21 April 2005 (21.04.2005) entire document	1-4, 7, 8, 17, 19-21, 23, 26, 27
---		---
Y		5, 6, 9-16, 18, 22, 24, 25, 28, 39, 55-57
X	US 2014/0358019 A1 (AEROCRINE AB) 04 December 2014 (04.12.2014) entire document	38, 40-43, 47, 48, 50-53, 58, 59
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Y		10-16, 39, 44-46, 49, 54-57, 60-65
Y	US 2006/0266353 A1 (YAMADA et al) 30 November 2006 (30.11.2006) entire document	5, 6, 24, 25
Y	US 2015/0105684 A1 (PANASONIC HEALTHCARE CO., LTD. et al) 16 April 2015 (16.04.2015) entire document	9, 22
Y	US 2017/0265778 A1 (MYSPIROMETER LLC) 21 September 2017 (21.09.2017) entire document	14, 15, 45, 46
Y	US 2001/0049477 A1 (STONE) 06 December 2001 (06.12.2001) entire document	18, 28, 44, 60, 61
Y	US 2017/0055875 A1 (MASSACHUSETTS INSTITUTE OF TECHNOLOGY) 02 March 2017 (02.03.2017) entire document	49

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

* Special categories of cited documents:
"A" document defining the general state of the art which is not considered to be of particular relevance
"E" earlier application or patent but published on or after the international filing date
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed
"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
13 February 2019	25 FEB 2019
Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US, Commissioner for Patents P.O. Box 1450, Alexandria, VA 22313-1450 Facsimile No. 571-273-8300	Authorized officer Blaine R. Copenheaver PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2018/052677

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 2016/0073930 A1 (SPEC SENSORS, LLC) 17 March 2016 (17.03.2016) entire document	54
Y	WO 2010/005738 A1 (DUKE UNIVERSITY et al) 14 January 2010 (14.01.2010) entire document	62-65
A	US 2015/0260706 A1 (DUBLIN CITY UNIVERSITY) 17 September 2015 (17.09.2015) entire document	1-28, 38-65

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2018/052677

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:
See extra sheet(s).

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of additional fees.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
1-28, 38-65

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.

☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.

☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2018/052677

Continued from Box No. III Observations where unity of invention is lacking

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group I, claims 1-28 and 38-65, are drawn to a flow control apparatus for measuring an analyte from a breath sample of a subject, comprising: a sampling chamber defining a volume and one or more openings into the sampling chamber.

Group II, claims 29-37, are drawn to a method of extrapolating a final value of a parameter from a breath sample, comprising: obtaining a calibration curve of a gas having a known parameter concentration; recording at least a portion of the calibration curve as a function of time.

The inventions listed as Groups I-II do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: the special technical feature of the Group I invention: a sampling chamber defining a volume and one or more openings into the sampling chamber; at least one sensor in fluid communication with the sampling chamber, wherein the at least one sensor is configured to detect the analyte, and wherein the sampling chamber is configured to receive the breath sample into the sampling chamber and into contact with the at least one sensor via diffusion into the sampling chamber as claimed therein is not present in the invention of Group II. The special technical feature of the Group II invention: obtaining a calibration curve of a gas having a known parameter concentration; recording at least a portion of the calibration curve as a function of time; measuring an input response curve of the parameter from the breath sample over a period of time; associating the input response curve to the calibration curve; and extrapolating the final value of the parameter from the breath sample based on the calibration curve associated with the input response curve as claimed therein is not present in the invention of Group I.

Groups I and II lack unity of invention because even though the inventions of these groups require the technical feature a method comprising measuring a breath sample of a subject, this technical feature is not a special technical feature as it does not make a contribution over the prior art.

Specifically, US 2015/0260706 to Dublin City University teaches a method comprising measuring a breath sample of a subject (Para. [0005]).

Since none of the special technical features of the Group I or II inventions are found in more than one of the inventions, unity of invention is lacking.