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(54) **BREATH AEROSOL MANAGEMENT AND COLLECTION SYSTEM**

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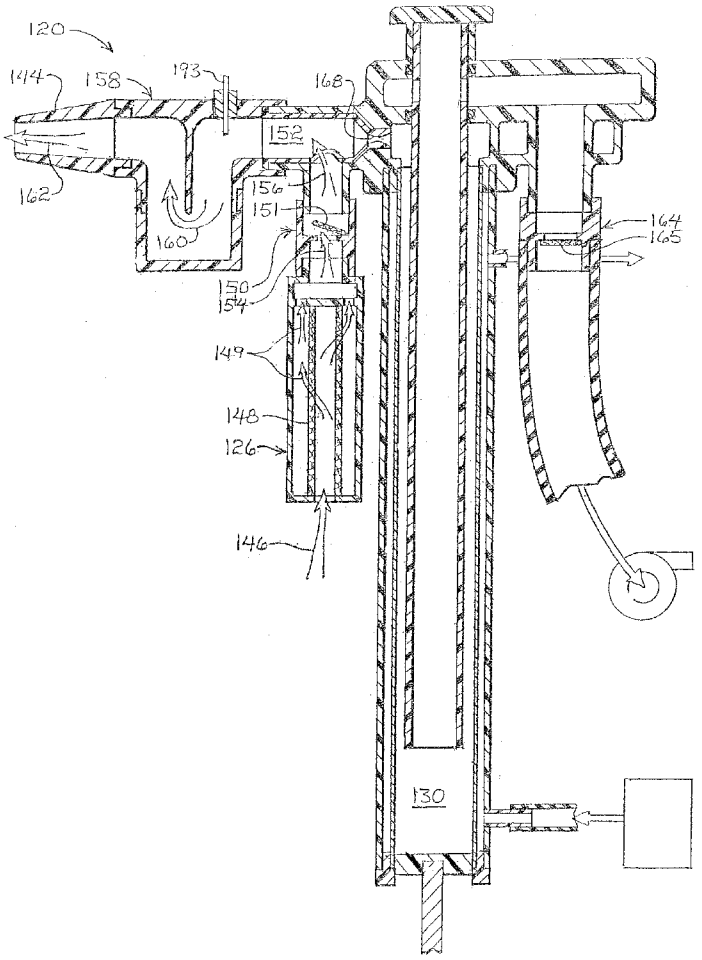
(57) **ABSTRACT**

Aerosol collectors **10**, **120** include pre-collection filters **100**, **126**, aerosol collection chambers **30**, **130**, and other exhaled breath conditioning and control features for providing not only accurate and efficient, but also reliable and reproducible aerosol collections that can be used in standardizations and can be compared in meaningful ways to other exhaled breath aerosol collections from the same test subject and from different test subjects. The aerosol collector **10** example includes electrostatic collection components **34**, **40**, and the aerosol collector **120** includes nucleating condensation components **168**, **172** and vortex collection components **132**, **138**. Both include analyte extraction apparatus **50**, **124**.



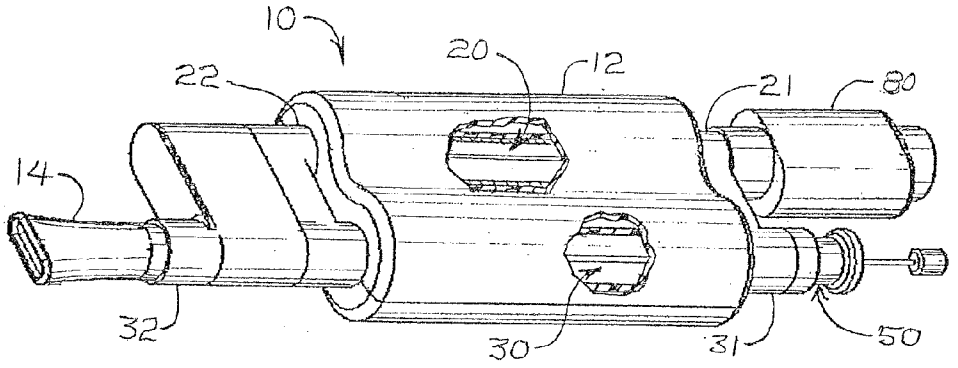


FIG. 1

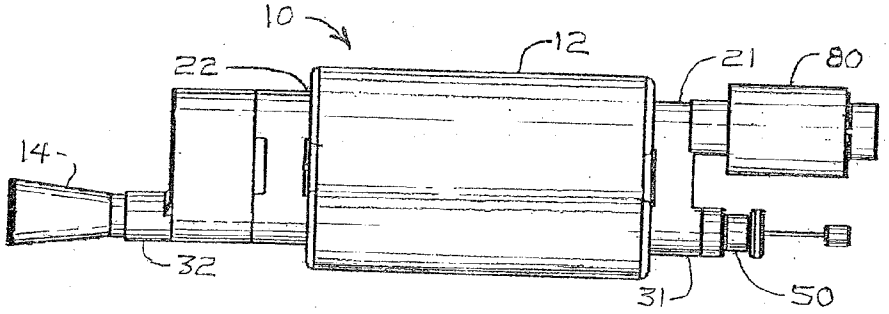


FIG. 2

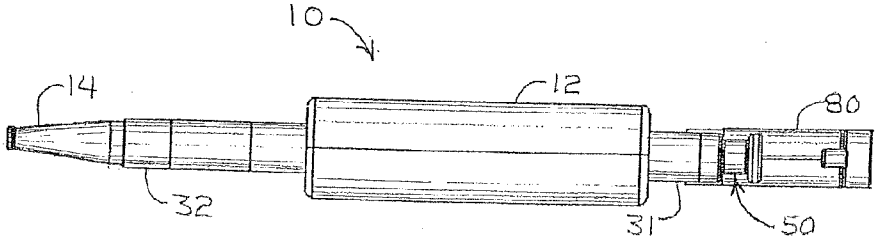


FIG. 3

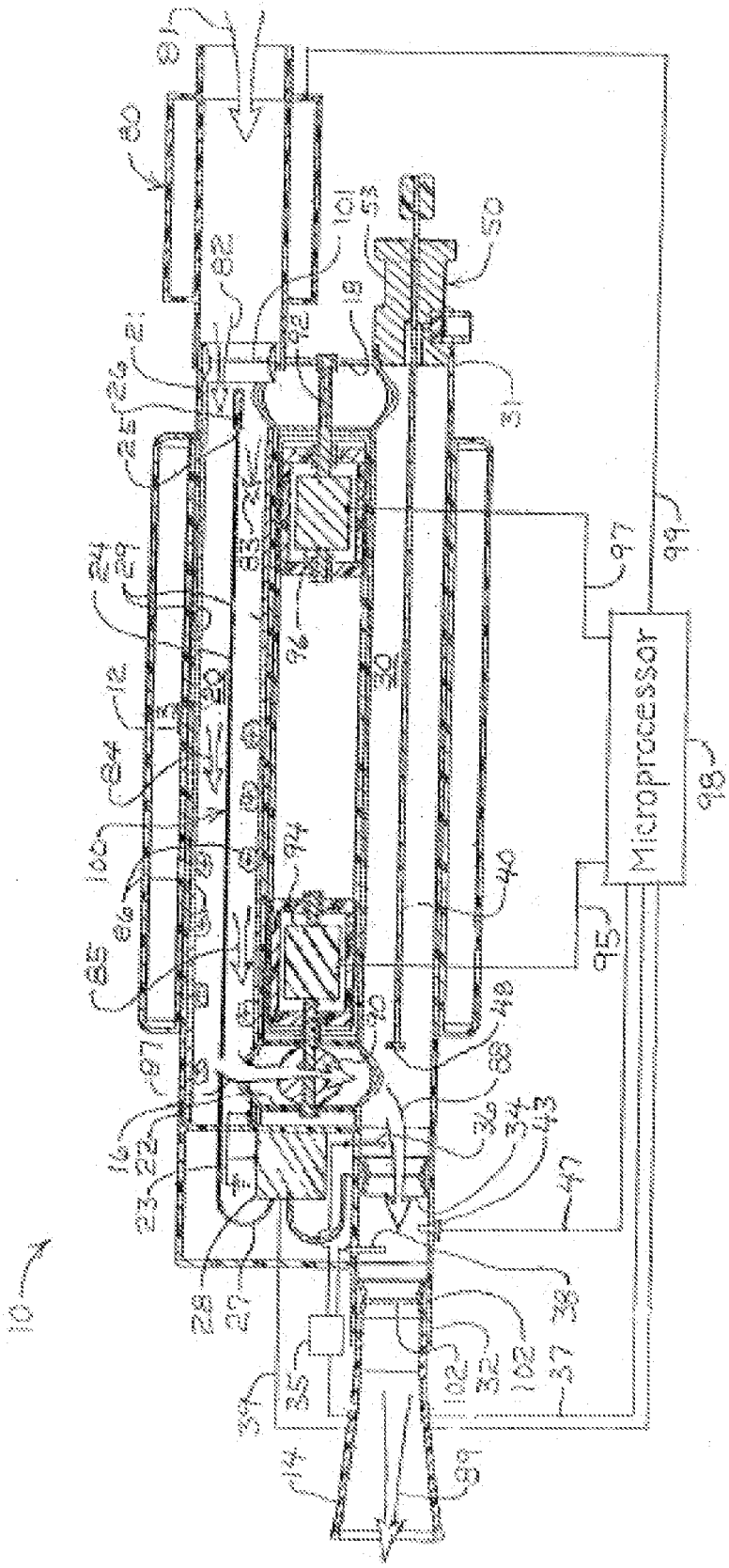


FIG. 4

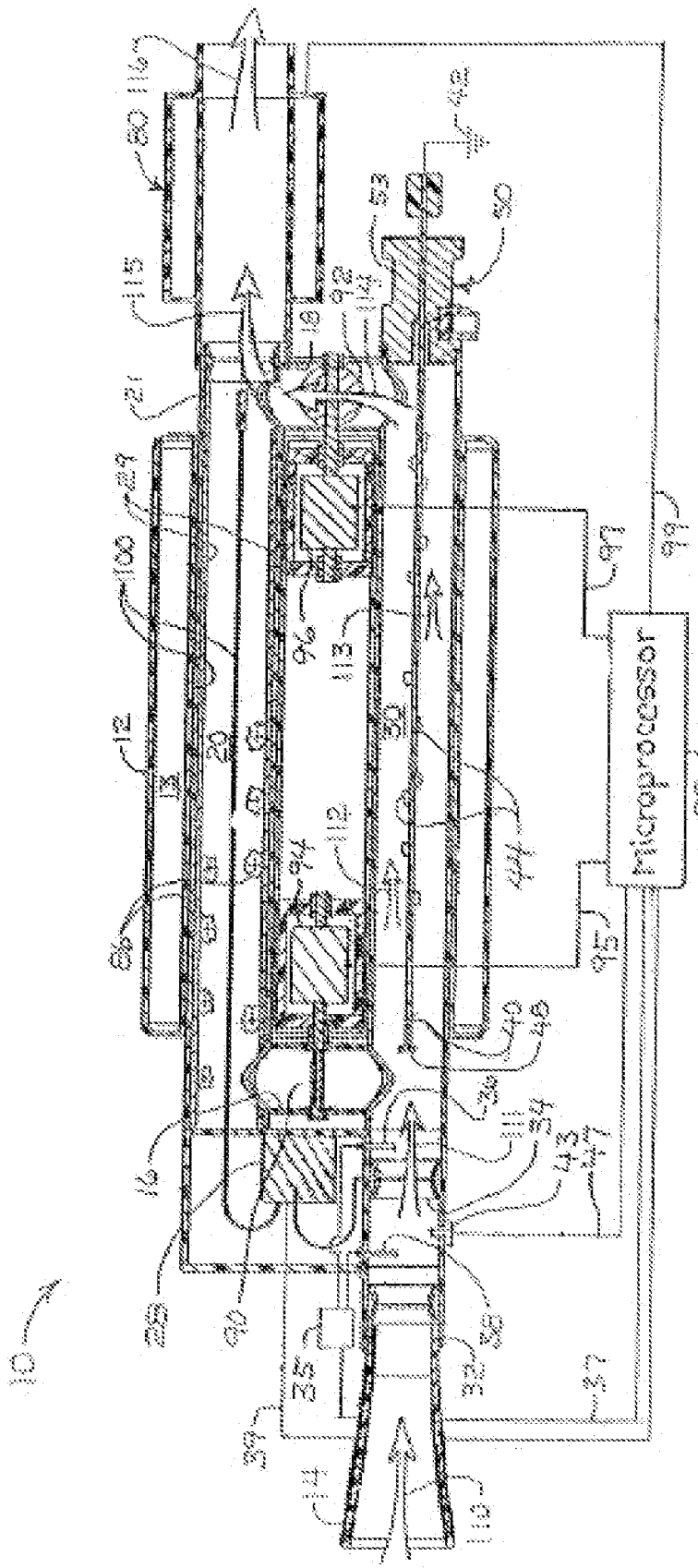

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FIG. 5

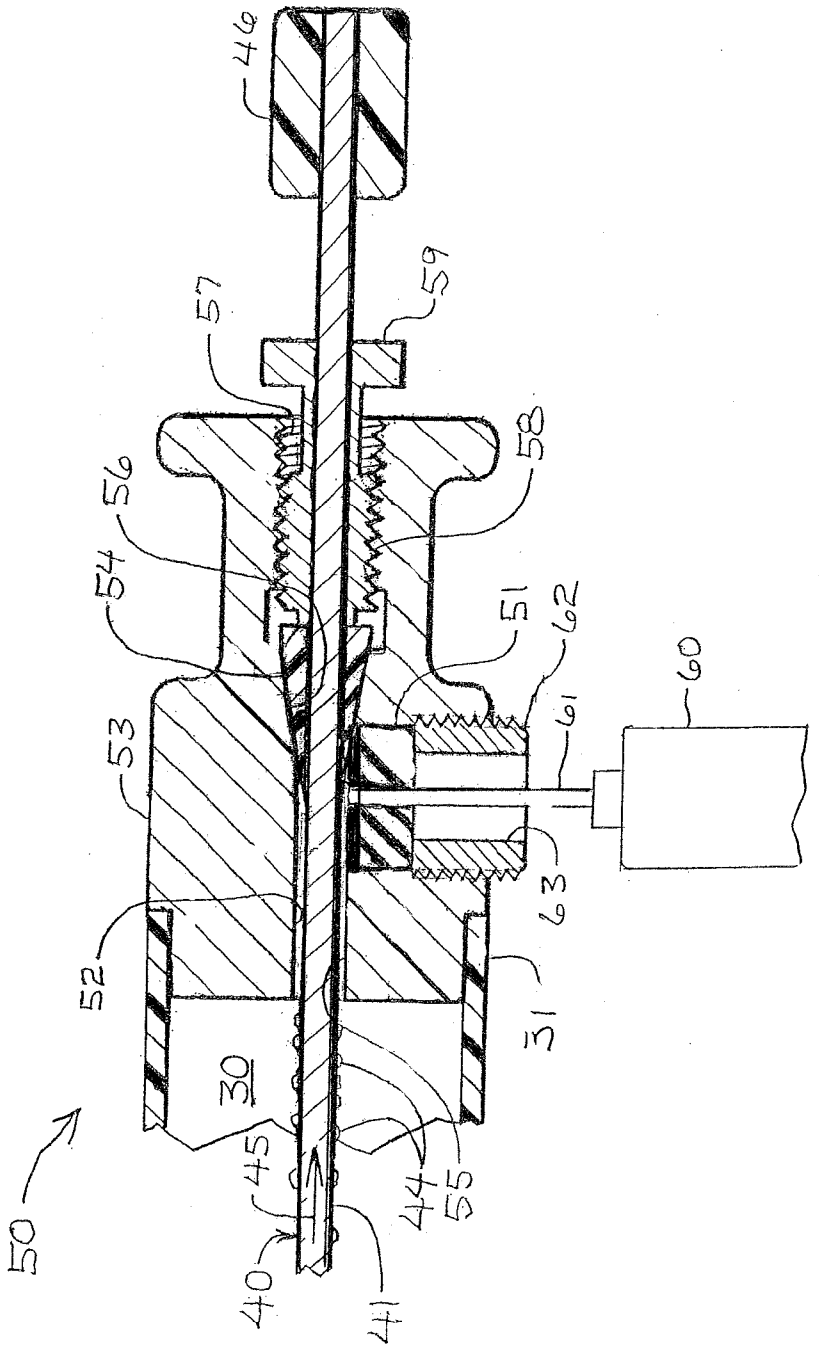

FIG. 6

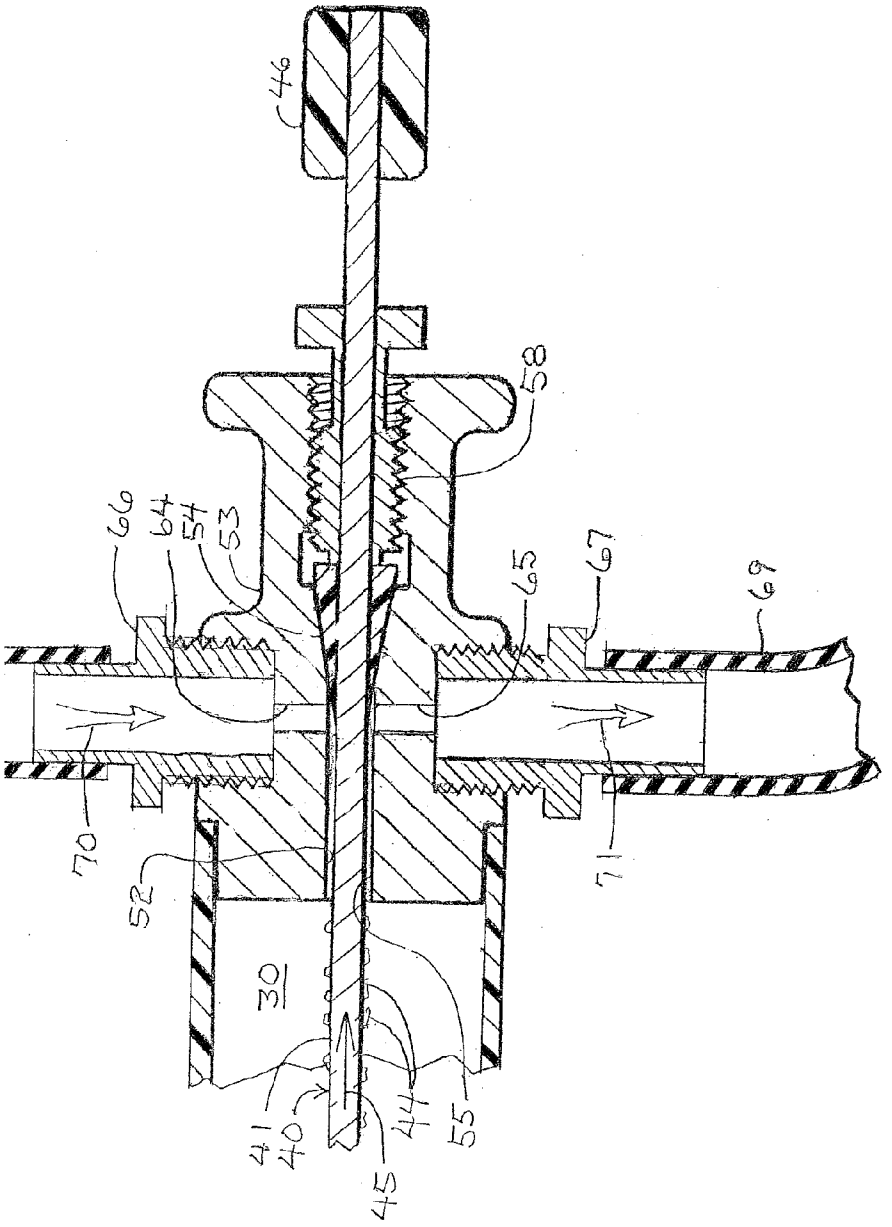

FIG. 7

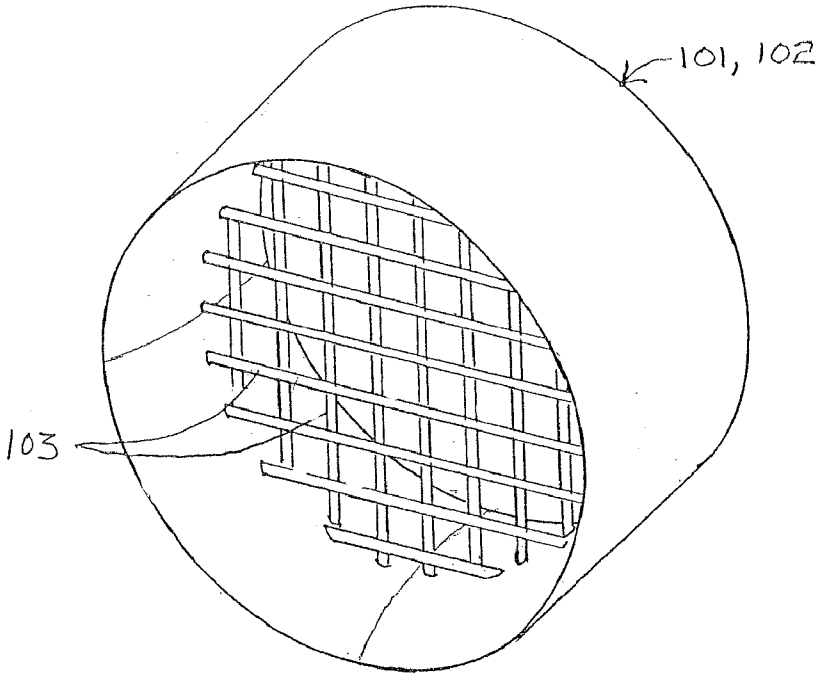

FIG. 8

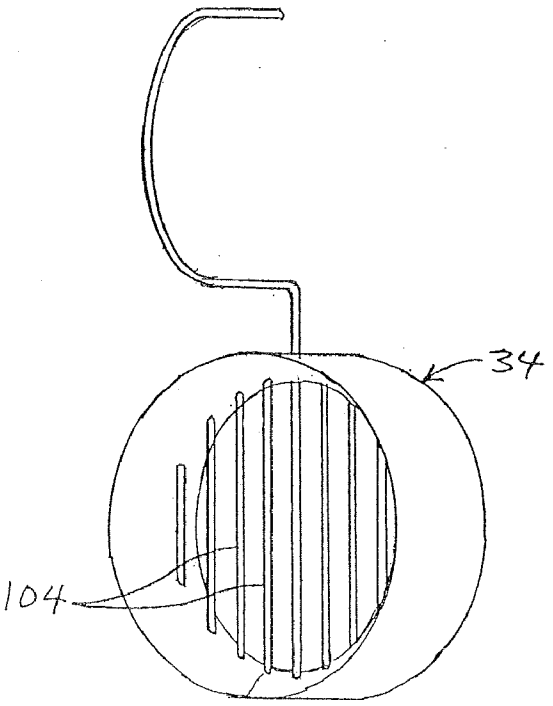

FIG. 9

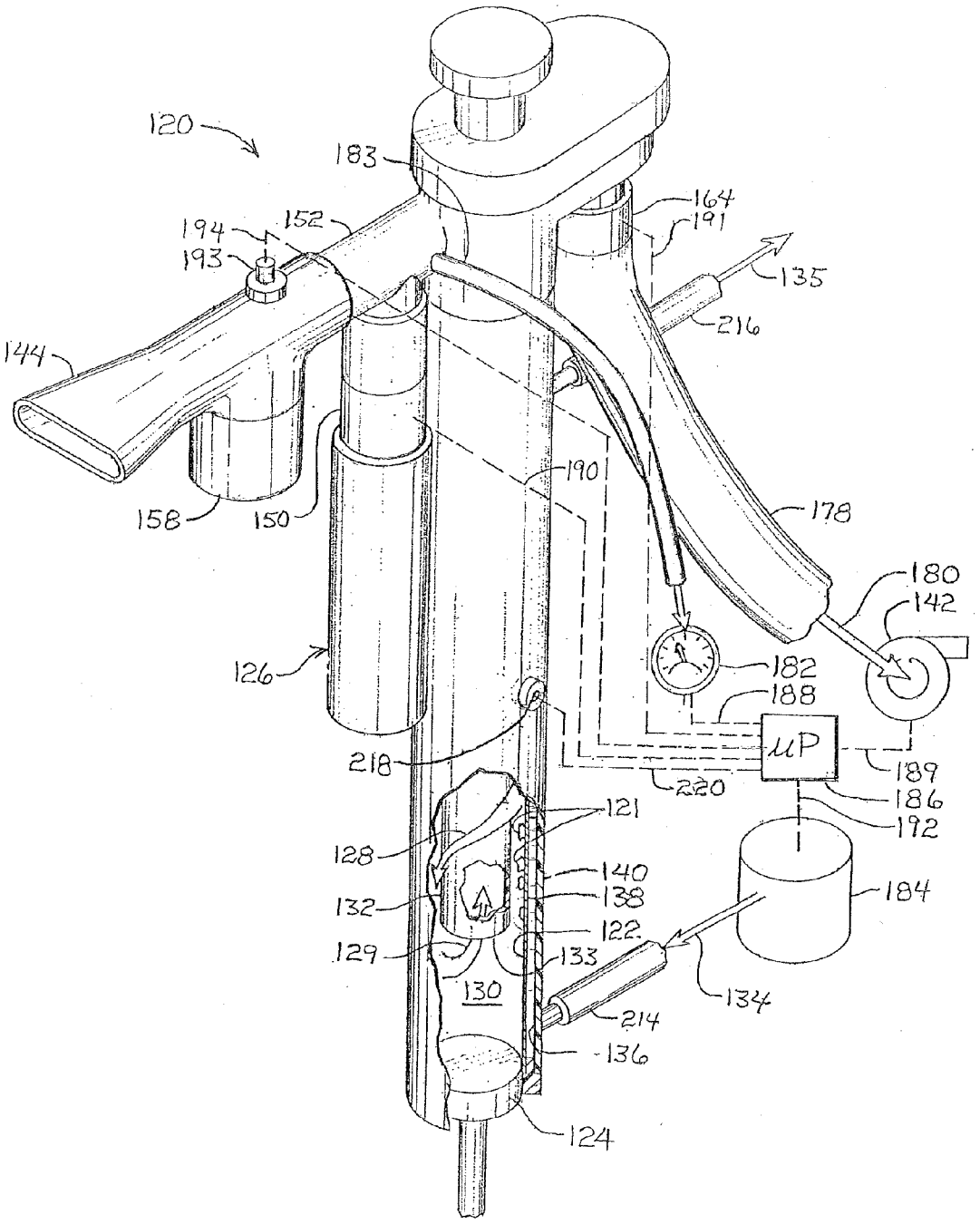
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FIG. 10

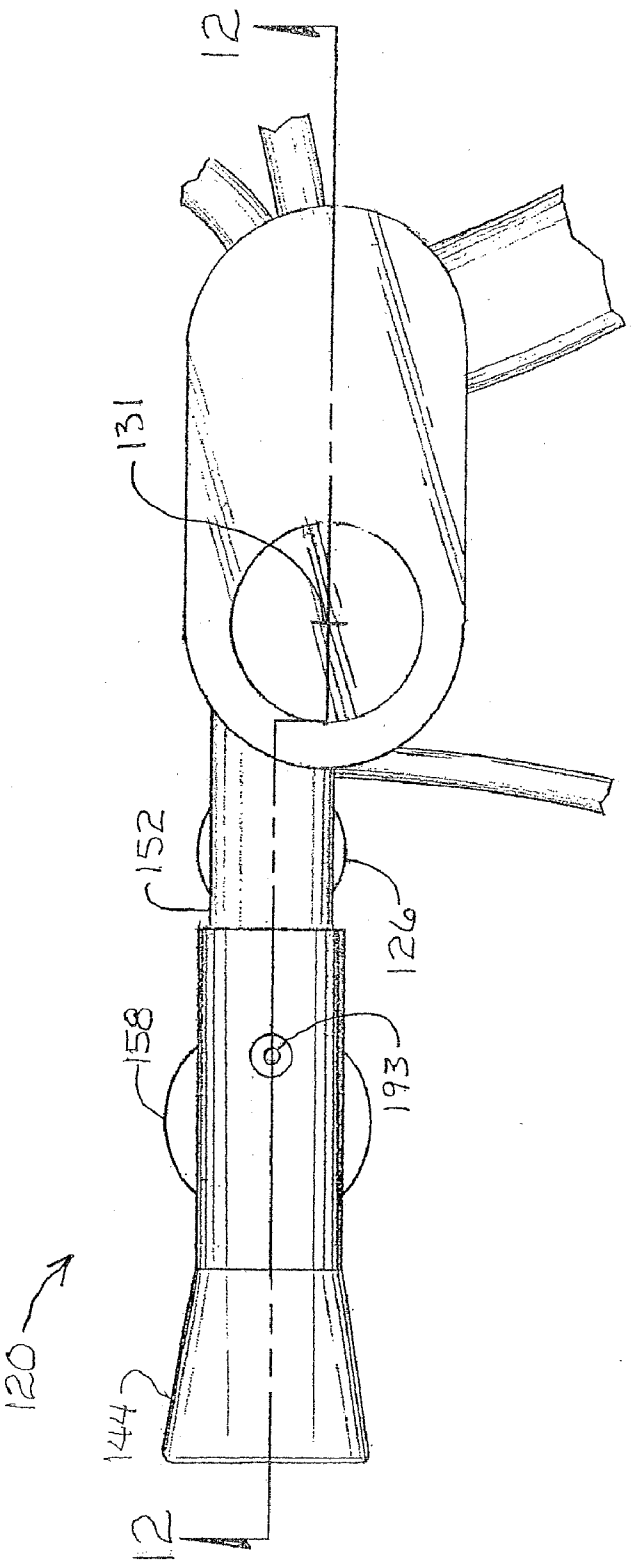

FIG. 11

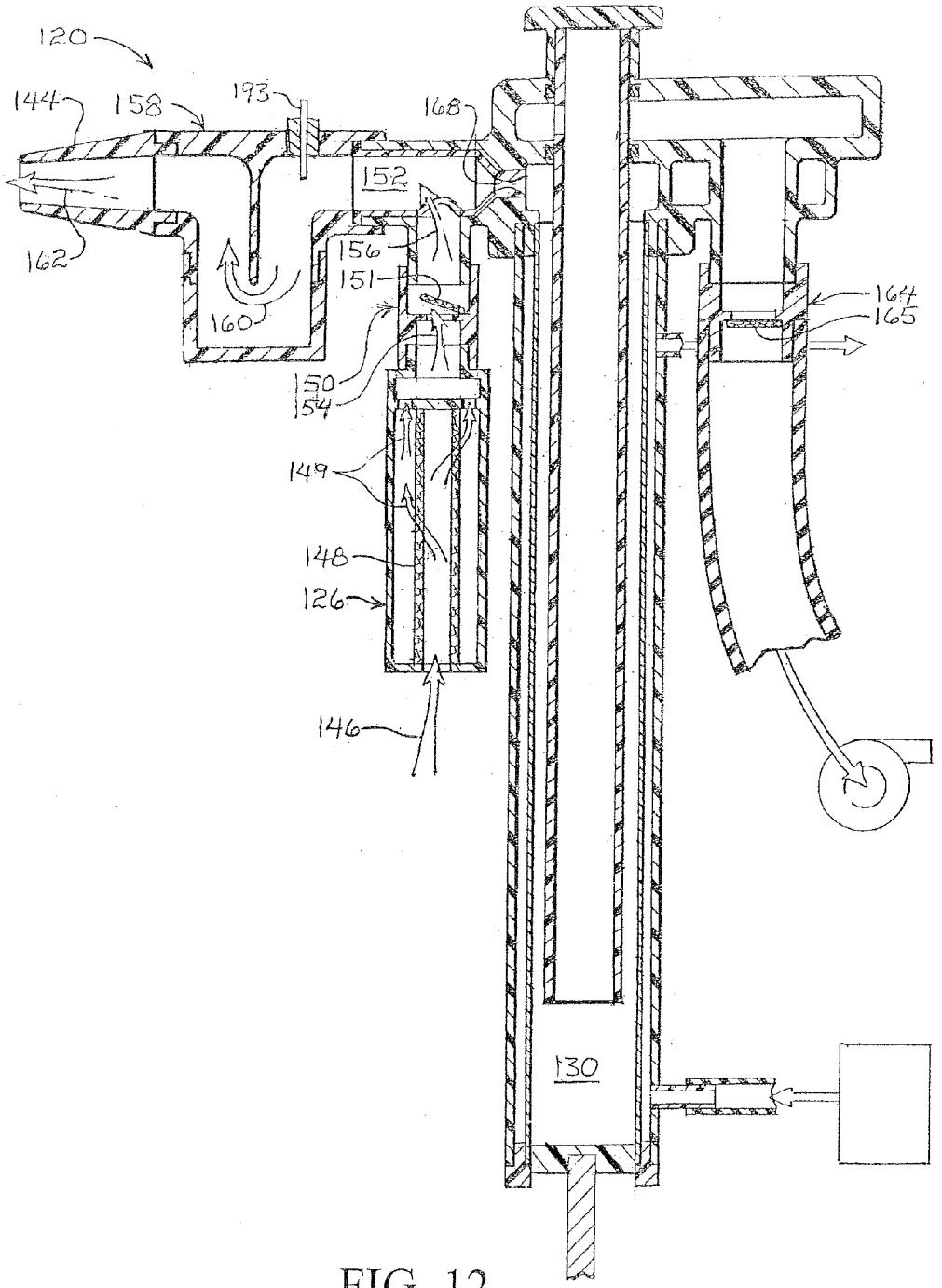
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FIG. 12

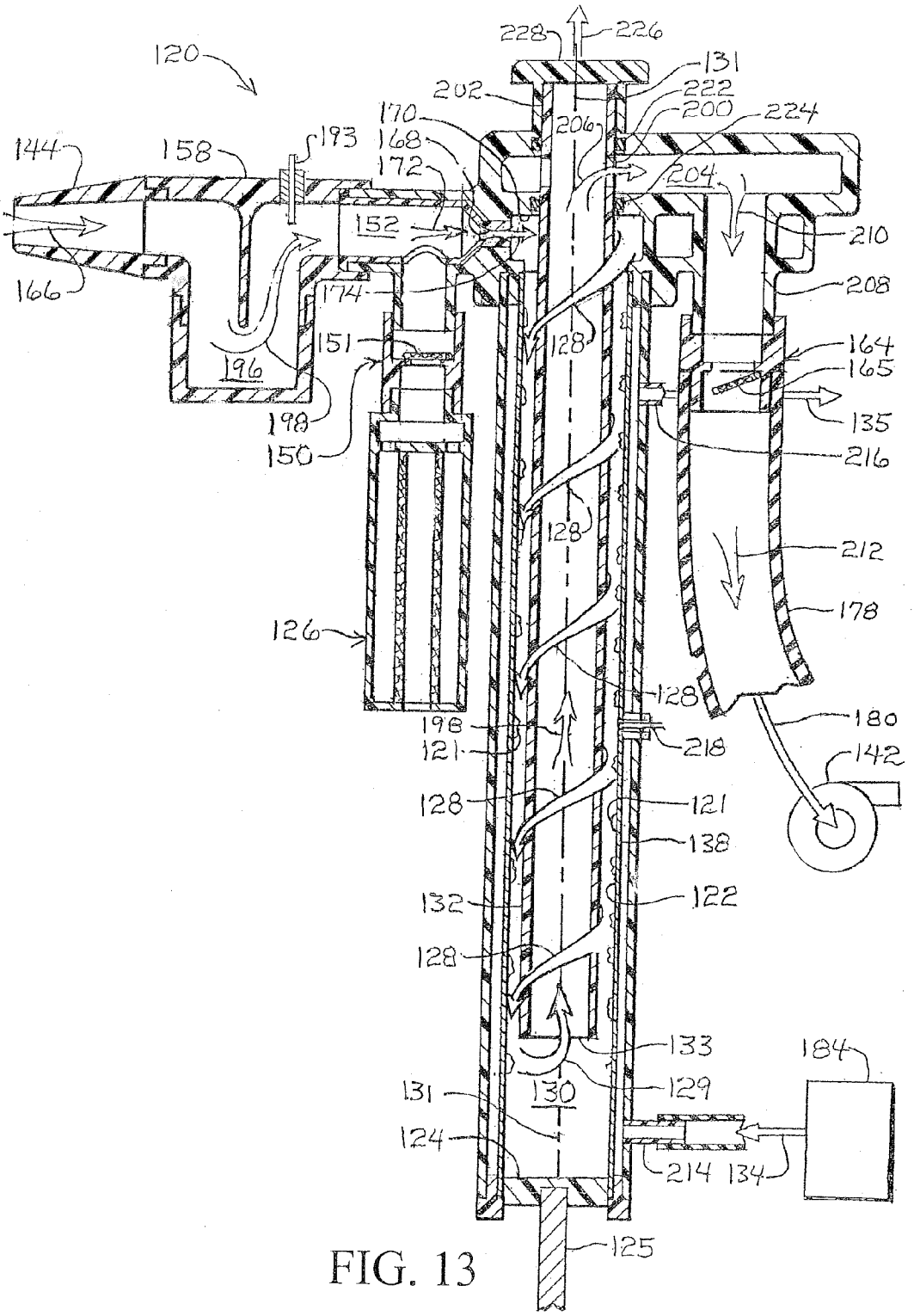
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FIG. 13

BREATH AEROSOL MANAGEMENT AND COLLECTION SYSTEM

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application is a continuation of U.S. patent application Ser. No. 10/745,331, entitled "Breath Aerosol Management and Collection System," filed on Dec. 22, 2003, which claims the benefit of U.S. Provisional Patent Application No. 60/435,804 entitled "Breath Aerosol Management Method and System," filed on Dec. 20, 2002. The aforementioned applications are both incorporated herein by reference for all purposes.

BACKGROUND OF THE INVENTION

[0002] 1. Field of the Invention

[0003] This invention is related generally to aerosol traps, and, more particularly, to methods and apparatus for collecting aerosols in exhaled breath in a reliable and reproducible manner for diagnostic and other purposes.

[0004] 2. State of the Prior Art

[0005] Exhaled breath comprises gaseous materials, such as carbon dioxide, oxygen, water vapor, and others, and non-gaseous materials, such as liquid droplets, insoluble substances, and mixtures of the two. Materials in the exhaled breath that are not in the gaseous state at the opening of the mouth or nose when exhaled are considered to be aerosols for the purposes of this discussion. Some examples of such aerosols may include airborne solid particulates, such as dust and smoke, as well as liquid droplets that comprise drugs, biological materials, and other chemicals that can be subjected to analysis, i.e., analytes.

[0006] Most standard clinical analytes, i.e., substances that are the subjects of analyses, are not volatile, thus do not evaporate, at normal physiological (body) temperatures. Nevertheless, research investigators have observed such non-volatile components as drugs, proteins, electrolytes, and other analytes in condensates from exhaled breath. In 1987, Fairchild et al., "Particle Concentration in Exhaled Breath," Am. Ind. Hyg. Assoc. J., Vol. 48, 1987, pp. 948-949, demonstrated that exhaled breath contains very finely divided and very sparse aerosols of suspended materials, with the smallest particles being smaller than 100 nanometers. Some research investigators presume, therefore, that non-gaseous materials recoverable from exhaled breath are transported in the breath by means of such aerosols in the breath.

[0007] There are numerous reports of studies in which such non-gaseous constituents (analytes) of exhaled breath have been collected along with water condensate from the breath in cold-surface condensers. In cold-surface condenser processes, exhaled breath from deep in the lungs is saturated with water vapor. Air within the upper airway of the body is slightly less humid, but it does gain some humidity over ambient air from the surrounding tissues in the airway between the lungs and lips. Thus, exhaled breath, which is a mixture of such saturated air from deep in the lungs along with such slightly less humid air in the upper airway, is quite humid. When such humid, exhaled air is directed against a cold surface, for example, a cold surface in a cold-surface condenser, the water vapor in the exhaled air condenses to liquid water, and it has been noted that the condensed water dissolves some of the non-volatile, aerosol constituents (analytes) from exhaled air that happen to come into contact with the condensed water. Unfortunately, however, such inclusion of non-volatile constituents in solution with the condensate occurs only if the non-volatile constituents happen to contact the condensation and is too inconsistent to be used for reliable, reproducible, and comparable non-volatile analyte collections.

[0008] Some non-gaseous substances in the exhaled breath are capable of indicating one or more physiological conditions of a person or animal, thus may be analytes with potential for diagnostic and other research and clinical purposes. For example, exhaled air contains some blood-borne substances and may be rich in markers that are useful in diagnosis of lung or airway diseases. One particularly interesting marker in exhaled breath, adenosine, may have the potential of indicating whether a person suffers from oxygen shortage to heart muscle (cardiac ischemia), which, if unresolved, may lead to the death of heart muscle cells, i.e., heart attack.

[0009] Unfortunately, however, measurements of aerosol analytes in exhaled breath captured by condensation and other methods prior to this invention have shown excessively high variance from one measurement to the next and have been very inconsistent. Therefore, they have not been reliable or useful for detecting or discriminating one pathological or physiological state from another. Some causes of such extreme variances in, for example, surface and other condenser methods may include: (i) Collector efficiency variations from one collection apparatus to another and even from one collection event to another with the same apparatus; (ii) The volume and flow rate of exhaled breaths may be highly variable from one person to another and even from the same person from one breath to another, thus presenting the collector apparatus with an irreproducible flow of breath material from which to collect samples; (iii) Surface condensation captures aerosol analytes only indirectly, thus previous state-of-the-art collectors may capture only non-predictable and non-verifiable portions of the aerosol analytes in the exhaled breath; (iv) Condensation may cause very high dilution of dissolved analytes, thereby leading to large and irregular losses.

SUMMARY OF THE INVENTION

[0010] Accordingly, it is an object of this invention to provide improved methods and apparatus for collecting exhaled breath aerosols.

[0011] Another object of this invention is to provide methods and apparatus for reproducible and consistent collection of specimens of exhaled breath aerosol analytes that are comparable from one test to another.

[0012] Another object of the present invention is to provide methods and apparatus for reproducible and consistent collection of specimens of exhaled breath aerosol analytes that are comparable between test values and standardized reference values for various useful analytes.

[0013] Still another object of the invention is to provide methods and systems that can be used to standardize reference values for useful breath aerosol analytes.

[0014] Other objects or uses of the invention may be perceived from the description below.

[0015] Additional objects, advantages, uses and novel features of the invention are set forth in part in the description that follows and others will become apparent to those skilled in the art upon examination of the following description and figures or may be learned by practicing the invention.

[0016] To further achieve one or more of the foregoing and other objects and uses of the invention, the apparatus may include, but are not limited to, the specific example implementations explained in the detailed description of the preferred embodiments below.

[0017] While the example collectors described herein implement the method of utilizing specific aerosol property enhancements and application of specific forces directed to those property enhancements (e.g., electrostatic charge and electrostatic force in collector **10** and mass accretion and centrifugal force in collector **120**) to collect aerosols from exhaled breath, there are many other possible property enhancements that can be used and forces that can be applied, such as thermophoretic force, magnetic force, gravitational force, inertia, and aerodynamic force comprising motion imposed by a moving fluid acting against an aerodynamic drag of non-gaseous aerosols. Also, while these example collectors are designed for collecting exhaled breath aerosols, the principles of this invention are also applicable to collecting other aerosols for other purposes, for example, for biowarfare defense, environmental air quality controls, and many others.

[0018] Another feature of this invention, which is supported by the example collectors described herein, includes the air flow conditioning and control capabilities that not only enhance the aerosol collection efficiency and effectiveness, but also make the aerosols collected quantifiable in a reliable and reproducible manner that can be compared in a meaningful way to other such exhaled breath aerosol collections from the same test subject or from other test subjects and to be standardizable for studies, possible indications of disease or absence of disease, and the like. One such parameter, aerosol collected from a certain volume of exhaled breath has been suggested as one control parameter (see Jaeger, GmbH, "Info—Special Edition, "Breath Condensate", Company-assembled compendium of research using commercial surface condenser, 1st Edition, April 2001). However, while exhaled breath volume is a useful parameter, it is not sufficient for the purposes discussed above, because there are still too many inconsistencies in the collection efficiencies as well as in the aerosol content itself without further conditioning and controls.

[0019] For example, as discussed, if ambient aerosol is drawn into the test subject's airway during inhalation, which is highly probable without pre-collection filtering, such ambient aerosols will most likely also be in the exhaled breath and thereby contaminate, and skew any exhaled breath aerosol collections, regardless of exhaled breath volume control. Therefore, conditioning the exhaled breath by pre-collection filtering of the inhaled breath to remove ambient aerosols from the inhaled breath, as discussed herein, is an important feature provided by this invention.

[0020] Flow rate of the exhaled breath is also an important parameter, because it affects collection efficiencies of the collection process. Therefore, if flow rate of the exhaled breath through the collector is not controlled and kept within predetermined ranges for a particular collector apparatus and process, the collection results will be skewed or inconsistent, regardless of exhaled breath volume control. Further, simply instructing the test subject to "breathe normally" is insufficient, because normal breathing is different for different test subjects and is affected by the environment, stress, physical condition, illness, and even by the collection process itself. Therefore, machine control of the exhaled breath flow rate, such as is provided by the example collectors described herein, is another important feature provided by this invention.

[0021] It is also important to remove large-mass artifacts from the exhaled breath, such as food particles, sputum, expectorate, saliva, and the like, before collecting the exhaled breath aerosols, because such artifacts can also contaminate and skew aerosol collection results, regardless of exhaled breath volume control. The exhaled breath aerosol collection procedures described herein can also provide for conditioning the exhaled breath by removal of such artifacts before exposing the exhaled breath to the aerosol collection apparatus and processes.

[0022] Some fractions of an exhaled breath can yield different concentrations of certain aerosols than other fractions. For example, the first one-third to one-half of an exhaled breath comprises mostly air that has been inhaled into the test subject's upper airway, but never gets into the deep lungs, where gas exchange takes place. Therefore, concentrations of aerosols that originate in the deep lungs are higher in later fractions of the exhaled breath than in earlier fractions. Therefore, for some types of aerosols targeted for use as analytes, it may be desirable to select only the later fractions of the exhaled breaths for aerosol collections and to divert the earlier fractions away from the aerosol collection apparatus or processes. This feature of the invention can be implemented in a number of ways, including, but not limited to, detection and use of markers, for example, carbon dioxide concentration, which is also higher in the later fractions of the inhaled breath, to control such flow diversions or to turn aerosol collection apparatus and processes on and off. It can also be implemented by measuring volume fractions, for example, by measuring and diverting the first 30 percent, 50 percent, or whatever, away from the aerosol collection apparatus or process or turning on the aerosol collection apparatus or process for the remaining exhaled breath fraction. Another implementation may be time, by timing breaths and activating aerosol collection after a selected time interval from the start of a breath.

[0023] Velocity of exhaled breath flow can also influence aerosol collection results, for example, if higher velocity air flow dislodges and/or carries more of a certain aerosol out of the lungs than a lower velocity air flow. In such situations, monitoring exhaled breath velocity, which is not necessarily the same as flow rate (volumetric or mass flow rate), and activating the aerosol collection process only when velocity of flow is within certain desired ranges. However, flow velocity can be derived from flow-rate measurements and other parameters, as is within the capabilities of persons skilled in the art.

BRIEF DESCRIPTION OF THE DRAWINGS

[0024] The accompanying drawings, which are incorporated in and form a part of the specification, illustrate the preferred embodiments of the present invention, and together with the written description and claims, serve to explain the principles of the invention. In the drawings:

[0025] FIG. **1** is an isometric view of an electrostatic breath aerosol analyte collector according to this invention;

[0026] FIG. **2** is a top plan view of the electrostatic breath aerosol analyte collector of FIG. **1**;

[0027] FIG. **3** is a side elevation view of the electrostatic breath aerosol analyte collector of FIG. **1**;

[0028] FIG. **4** is a cross-section view of the electrostatic breath analyte collector of FIGS. **1-3** taken along section plane **4-4** in FIG. **3** and illustrating an inhalation operational mode;

[0029] FIG. **5** is a cross-section view similar to FIG. **4**, but illustrating an exhalation operation mode;

[0030] FIG. **6** is an enlarged cross-section view of the extractor assembly of FIGS. **4** and **5**;

[0031] FIG. **7** is a cross-section view similar to FIG. **6**, but illustrating a continuous solvent flow variation of the extractor assembly;

[0032] FIG. **8** is an isometric view of an example mesh assembly component;

[0033] FIG. **9** is an isometric view of an example ionizer assembly;

[0034] FIG. **10** is an isometric view of an enhanced condensation analyte collector according to this invention;

[0035] FIG. **11** is a top plan view of the enhanced condensation analyte collection of FIG. **10**;

[0036] FIG. **12** is a cross-section view of the enhanced condensation analyte collector of FIGS. **10** and **11** taken along the section plane **12-12** of FIG. **11** and showing the valve positions set for inhalation mode; and

[0037] FIG. **13** is a cross-section view similar to FIG. **12**, but with the valve positions reversed for exhalation mode.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

[0038] The example breath aerosol analyte collector **10** illustrated in FIGS. **1-3** is based on electrostatic particle collection technology and provides a suitable platform for a description of some of the salient features of the invention as well as of certain details that are beneficial, albeit not essential, to the practice of the invention. Other enabling technologies and collector embodiments including, but not limited to, enhanced condensation, are described below. For this electrostatic embodiment **10** as well as other embodiments some or all of the following concepts are used to solve the problems of efficient, effective, reliable, and repeatable exhaled breath aerosol analyte collection: (1) Minimizing or eliminating contamination or skewed results from aerosols in ambient inhaled air; (2) Flow control of exhaled breath to minimize variations in aerosol analyte collection efficiencies, effectiveness, reliability, or repeatability that can result from different flow rates, pressures, time of flow, and the like; (3) Capturing substantially all aerosol materials, including smaller than 100 nanometers in mean equivalent diameter and preferably as low as 10 nanometers in mean equivalent diameter, which would include viruses; and (4) Collecting exhaled breath aerosol analytes in concentrations as high as practical for ease of detection, analysis, and other uses.

[0039] The example electrostatic breath aerosol analyte collector **10** illustrated in FIGS. **1-3** has a main housing **12** that encloses a pre-collection filter conduit or chamber **20** for removing ambient aerosol from inhaled air and a collection conduit or chamber **30** for removing exhaled aerosol analytes from exhaled breath, as will be explained in more detail below. The collection chamber is a section of the conduit **30** that surrounds the collection rod **40**, so collection conduit and collection chamber are sometimes used interchangeably in relation to that section. The first end of the collection chamber is the end where exhaled breath enters the collection chamber and the second end is the opposite end. Upstream means opposite the flow direction of exhaled breath and downstream means the same direction as the flow of exhaled breath. Ambient aerosol as used herein means non-gaseous, air-borne materials in the environment around the test subject and collector, and test subject means a person or animal from which analytes are being collected. A mouthpiece **14** at one end **22** of the collection conduit **30** facilitates a test subject's inhalation of air through the pre-collection filter conduit **20** and exhalation of breath air through the collection conduit **30**, although the mouthpiece **14** could be positioned at the end **22** of the pre-collection filter conduit **20** or at a variety of other locations and orientations, as will become apparent to persons skilled in the art, once they understand the principles of this invention. Suffice it to say that inhaled air is drawn through the pre-collection filter conduit or chamber **20**, and exhaled breath is directed through the collection conduit or chamber **30**, and the mouthpiece **14** or any number of mouthpieces can be positioned at any location or locations that facilitate those functions.

[0040] An exhaled aerosol analyte extraction assembly **50** is located at the other end **31** of the collection conduit **30** for extracting aerosol analytes that are removed from the exhaled breath in the collection conduit **30**, as will be explained in more detail below. An optional flow meter **80** is also shown on the breath aerosol analyte collector **10**, which can be used to control flow rate of the inhaled or exhaled breath air as well as to provide flow rate measurements used for volume control, collection of aerosol from selected fractions of exhaled breath, and other control functions, as will also be explained in more detail below.

[0041] Referring now primarily to FIG. **4** with secondary reference to FIGS. **1-3**, air during inhalation of a breath is drawn into the breath aerosol analyte collector **10** through the flow meter **80** and into the inlet end **21** of the pre-collection filter conduit **20**, as indicated by the flow arrows **81**, **82**. The flow meter **80** is optional, but flow rate measurements from it or some other flow measuring or flow controlling device can be useful in controlling and/or characterizing or quantifying breath flow through the collector **10** for comparing results of collections of exhaled aerosol analytes from one test subject with results from other collections from the same test subject, with results from collections from other test subjects, and with standardized results or quantified indicators of presence or absence of physiological diseases, symptoms, or other problems or concerns. Some flow control can be provided by the test subject in trying to, for example, inhale and exhale in as ordinary a manner as possible during an aerosol analyte collection procedure, but control of the exhale air flow with the collection apparatus **10** itself may provide more consistency, even if the test subject is uncooperative, unconscious, or unable to comply with collection operation instructions. The flow meter **80** as described herein facilitates implementation of such control.

[0042] If a flow meter **80** is not used or if it is positioned in another location, which is an option for this invention, the air can be drawn directly into the pre-collection filter conduit **20**. A pre-collection filter **100**, which, in this embodiment **10**, is an electrostatic filter but can be any other kind of filter that meets the pre-collection filter performance goals and/or functions described herein, is positioned in the pre-collection filter conduit **20** primarily for the purpose of removing any aerosols in ambient air flowing into the collector **10**. The goal is that only exhaled breath aerosols, not aerosols from the ambient air (i.e., ambient aerosols), get collected in the collection conduit or chamber **30**, which will be described in more detail

below. In other words, if the air inhaled by the test subject contains ambient aerosols, at least some of those ambient aerosols are likely to also be in the exhaled breath and would probably be caught and collected in the collection conduit **30**, which is preferably designed and made to collect as much of the aerosol in the exhaled breath as possible in order to collect the analytes from the exhaled breath in sufficient concentrations and quantities to be useable and meaningful. Since an object of this invention is to collect analytes in the exhaled breath that are produced in or derived from the lungs of the test subject, existence of ambient aerosols in the aerosols collected in the collection conduit would be considered contaminants. One of the objects of this invention is to minimize, if not eliminate such contamination.

[0043] It is well known, for example, that ambient air contains aerosolized solids and liquid droplets, such as dust, soot, and smoke. Less obvious, but of great concern nonetheless are living organisms and viruses, such as those associated with communicable diseases by means of airborne exposure. These kinds of ambient bio-aerosols have particular importance when dealing with collection and measurement of extremely small amounts of bio-materials contained in exhaled breath aerosol, and it is best to eliminate them from the airstream before they even get into exhaled air where they would likely be collected along with the aerosol analytes from the test subject's lungs. For example, it is typical that a first portion of exhaled air volume, when a test subject is at rest, comprises reflux of inhaled air with little modification. This first portion or fraction represents the volume of inhaled air that travels no deeper than the upper airways (mouth and nasal passages, pharynx, trachea, and upper bronchi) and never gets into the test subject's lungs. These upper airway structures do not participate in gas exchange and present a high ratio of volume to surface area relative to that seen within the lungs at the alveolar (gas exchange) level. Therefore, inhaled air that traverses no further than the upper airway remains substantially unmodified except for gain of some relative humidity from water that evaporates from the liquid film in the linings of these passageways. In addition, these large diameter structures of the upper airway provide little or no filtering of aerosols from inhaled air, especially if the test subject does not inhale through the nasal passages, which do provide some small amount of filtering, but not enough to remove all or even most ambient aerosols. Consequently, some proportion of aerosols borne in inhaled gas, such as ambient air, will remain suspended in the first one-third to one-half of the breath volume that is subsequently exhaled. These ambient aerosols in the exhaled breath are very likely to be collected along with aerosol analytes produced in or derived from the test subjects lungs (endogenous aerosol) in the collection conduit **30** of the collector **10**, and, in typical situations, the total mass of such ambient aerosol contaminants far exceeds the mass of endogenous aerosol generated when the test subject exhales. Furthermore, the mass of particles attributable to actively metabolizing bacteria and biocontaminants such as viruses and spores may produce bio-molecules that directly increase or metabolically reduce the measured quantity of the endogenous aerosol analytes that are the targets of the collection process. Therefore, a pre-collection filter, such as the pre-collection filter **100** in the example collector **10**, placed between the source of inhalant gas (e.g., ambient air inlet **21**) and the test subject's mouth or nose can minimize, if not eliminate such ambient aerosol contaminants.

[0044] While many variations and structures of electrostatic and other kinds of filter apparatus are available and can be adapted for use in this invention, the example electrostatic filter **100** in this embodiment **10** comprises a small diameter electric wire **24** (sometimes called a "corona wire"), which extends longitudinally through the pre-collection filter conduit or chamber **20** and is surrounded by an electrically conductive side wall **29** of or on the conduit or chamber **20**. The pre-collection filter conduit **20** and the components of the electrostatic filter **100** are preferably sized to introduce little, if any perceivable resistance to the test subject's inhalation efforts, which is one benefit of this single wire **24** design. The wire **24** is anchored at one end **25** to a non-conductive cross-bar **26** and the other end **27** is connected to a high voltage power supply **28**. The inside wall of the pre-collection filter conduit **20** comprises an electrically conductive material **29**, such as metal (for example, stainless steel), conductive plastic, or other conductive material and is connected electrically to the opposite pole of the high voltage power supply **28**. As explained in more detail below, it is preferred, but not essential, that the corona wire **24** be connected to the positive (+) voltage supply terminal, so the conductive wall material **29** is connected to the negative (−) voltage supply terminal, which is often called "ground", as indicated symbolically at **23**. The conductive material **29** can be a separate component, a coating on the wall, or the wall material itself. When the wire **24** is charged with a high voltage, for example, in a range of 2,000 to 12,000 volts, depending on the diameter of the corona wire **24**, size of the conduit or chamber **20**, and other factors, and the side wall **29** is at opposite in polarity (ground) to the wire **24**, it creates corona around the wire **24** that ionizes molecules in the air, which imparts a static electric charge to aerosols in the air that flows, as indicated by flow arrows **84**, **85**, through the pre-collection filter conduit **20**. Consequently, such charged aerosols will cling to the grounded or opposite polarity of the inside wall **29**, as indicated in exaggerated scale at **86**. The wire **24** is preferably positive, so that ozone production is minimized, although it could be negative, if desired. Consequently, when the air flow, indicated flow arrows **87**, **88**, **89**, reaches the mouthpiece **14** and is inhaled by a test subject (not shown) drawing a breath through the collector **10**, it is substantially free of aerosols. Therefore, aerosols collected from the exhaled breath, which will be described below, will include substantially only aerosols introduced by the test subject's lungs and by the airway between the test subject's lungs and lips (not shown). An optional grounded mesh **102** in the end **32** of the conduit **30** just before the air flow is inhaled through the mouthpiece **14** neutralizes any remaining ions and collects any remaining aerosol that did not get captured on the wall **29** of the electrostatic filter **100**. It also prevents someone from poking a finger or instrument into the high voltage ionizer assembly **34**, which will be described below, and thereby prevent possible damage to the apparatus as well as electric shock to the test subject or other user.

[0045] As indicated by the flow arrow **87**, a first valve **90**, which is illustrated as a butterfly valve in FIG. **4**, in the aft cross-over conduit **16** is positioned in a manner that does not impede the flow of air to the mouthpiece **14** during the inhalation of air by the test subject. At the same time, a second valve **92**, also illustrated as a butterfly valve, in the fore cross-over tube **18** is closed during inhalation to prevent the

ambient air from by-passing the filter **100** in the pre-collection filter conduit **20** by flowing through the collector conduit **30** to the mouthpiece **14**.

[0046] The first and second valves **90**, **92** do not have to be butterfly valves. On the contrary, they could be any of myriad active or passive air control valves, including, but not limited to, one-way, self-actuating check valves, as is understood by persons skilled in the art. However, the butterfly valves **90**, **92** have some advantages in that they are simple and inexpensive, yet can be activated for partial closure, full closure, or full open, thus can be used to control flow rate as well as to simply open and close the air flow. In the example of FIG. **4**, each butterfly valve **90**, **92** is operated by a separate, single-turn brushless actuator or motor **94**, **96**, such as those manufactured by Saia-Burgess of Murten, Switzerland.

[0047] The flow meter **80**, as mentioned above, is optional. However, flow rate measurements during inhalation and exhalation can provide a number of benefits in addition to the use for flow rate control, as mentioned above. For example, a test subject's inhalation pattern might affect the generation of exhaled breath aerosol. Relevant characteristics of the inhalation pattern may include flow rates, depth of inhalation, time between inhalation and exhalation (e.g., "holding" one's breath), timing and counting number of breaths in a collection period, or exhalation preceding the tested inhalation, pressure variations, or other properties. Flow rates multiplied by time can provide volumes of breaths or fractions of breaths and can be provided by the microprocessor **98** on a real time basis for control of collector functions during inhalation and exhalation as well as being recorded for post-collection analysis purposes. Therefore, data about inhalation flow rates and other patterns, in addition to enabling collector control functions may also enable correction or compensation, or at least explanations for deviations in, analytical data from the collected exhaled breath aerosol analyte specimens.

[0048] The flow meter **80** can be a hot wire anomometer or any other flow meter type that measures gas flow rates accurately. If desired, the flow meter **80** can be connected to a microprocessor, illustrated schematically at **98**, or any other circuit or device for recording, displaying, or outputting flow rate measurements and/or for controlling the opening, closing, and flow metering functions of the valves **90**, **92**, as is within the capabilities of persons skilled in the art, once they understand this invention. The actual microprocessor **98**, electrical connections **95**, **97**, **99**, and other electric circuits and components can be positioned in the annular space **13** enclosed by the housing **12** or in any other convenient locations.

[0049] After the breath of air with the ambient aerosols removed is inhaled through the collector **10** by the test subject (person or animal), the test subject exhales the breath into the mouthpiece **14**, as indicated by the flow arrow **110** in FIG. **5**. In the exhale mode, the first butterfly valve **90** is closed, and the second butterfly valve **92** is opened to allow the exhaled air to flow, as indicated by flow arrows **111**, **112**, **113**, **114**, **115**, **116**, through the collection chamber **30**, flow meter **80**, and out of collector **10**.

[0050] Also, in the exhale mode, an ionizer assembly **34** positioned in the collection conduit **30** upstream from a grounded (i.e., negative voltage potential) collection rod **40** is turned on to ionize exhaled air and thereby create electrostatic charges in any aerosols, including analytes in the exhaled breath. The corona wires **104** of the ionizer system **34** (FIG. **9**) are preferably connected to the positive (+) terminal of the high voltage power supply **28**, so, as explained above, the term "grounded" for the collection rod **40** means it is connected electrically to the negative (−) terminal of the power high voltage power supply **28**, as indicated by the "ground" symbol **42**. Again, since practically all of the ambient aerosol **86** was removed from the inhaled air in the pre-collection filter **100**, as explained above, substantially all of the aerosols in the exhaled air are derived from the test subject's lungs and airway. As the positive charged, ionized air flow **112**, **113** from the ionizer system **34** continues through the collection tube **30**, the airborne, positive charged aerosols from the test subject's lungs flow past the collection rod **40**, which extends from the extraction assembly **50** toward the ionizer assembly **34**. As mentioned above, the collection rod **40** is at negative (−) potential (i.e., grounded, as indicated by the ground symbol **42**, so the positive charged aerosol are attracted to, and cling to, the negative charged collection rod **40**, as illustrated in somewhat exaggerated sizes at **44**. Preferably, most, if not all, of the aerosol analytes in the exhaled breath are collected on the collection rod **40** before the exhaled air flows out of the collection chamber **30**. The longer the collection conduit **30** and rod **40**, and the slower the exhaled air flow through the collection conduit **30**, the more complete the aerosol analyte removal from the exhaled air will be. Therefore, it may be desirable to control the velocity or flow rate (volumetric and/or mass flow rate) of exhaled air flow **112**, **113** through the collection conduit **30** as well as the volume of exhaled air for accuracy and efficiency as well as for standardization, reliability, reproducibility, and other purposes. In the example collector **10**, flow rate measurements by the flow meter **80** can be fed by the connection or link **99** to the microprocessor **98** for use in adjusting the valve **92** in the fore cross-over conduit **18** to maintain the exhaled air flow velocity or flow rate in the collection conduit **30** in a desired range.

[0051] There is no significant detriment to lack of moisture in electrostatic collection of aerosol particles, so there is no need for provisions in collector **10** to maintain humidity in the exhaled air before and during collection of aerosol on the collection rod **40**. In fact, there are advantages to dryer airflow and dryer aerosols for electrostatic collections, so it may be desirable in some applications to add some kind of dryer, such as a heater (not shown) to the collector **10**, for example, between the grounded mesh assembly **102** and the ionizer assembly **34** to dry the exhaled air and aerosols before undergoing the electrostatic aerosol collection.

[0052] Any desired number of breaths can be inhaled and exhaled by the test subject through the collector **10** as the exhaled breath aerosol analytes are collected on the collection rod **40**. If the valves **90**, **92** are of a type that have to be driven from closed to open positions and vice versa, as opposed to self-actuated, one-way check valves, some kind of sensor may be used to facilitate actuation of the valves **90**, **92** to open and close the cross-over conduits **16**, **18** as required to direct inhale air flow through the pre-collection filter conduit **20** and to direct exhaled air flow through the collection conduit **30**. While myriad sensor systems would work for this purpose, the collector **10** is illustrated, for example, with a pair of ion detectors **36**, **38** positioned on opposite sides of the ionizer assembly **34**. The second ion detector **38** is grounded. If there are ions in the air flow that contacts the first ion detector, a current can be detected by an ammeter **35** or other suitable detector. The ionizer assembly **34** can be at least at a low level that produces enough ions in the air flow to be detected by the ion detectors **36**, **38**. Because most, if not virtually all of the

ions in the air flow through either conduit **20** or conduit **30** get eliminated by the grounded components **29**, **40**, air flow past the first ion detector probe **36** during inhalation will produce little or no current at ammeter **35**. This condition can be used to indicate inhalation and, for example, can be communicated to the microprocessor **98** via connection or link **37** for use in generating control signals on links **95**, **97** to the valve actuators **94**, **96** to open valve **90** and close valve **92** for the inhalation mode, i.e., to direct inhalation air through the pre-collection filter conduit **20** and not through the collection conduit **30**. Conversely, when air is being exhaled by the test subject, air flow through the ionizer assembly **34**, as indicated by flow arrow **111** in FIG. **5**, causes ionized air to contact the ion detector problem **36** to produce a current at ammeter **35**. This condition can be communicated to the microprocessor **98** or other suitable circuit to activate the exhale mode, i.e., to close the valve **90** and open the valve **92** to direct exhaled air flow through the collection conduit **30** and not through the pre-collection filter conduit **20**. The microprocessor **98** can also communicate via a link **39** to an appropriate circuit associated with the high voltage power supply **28** to turn up the power on the ionizer assembly **34** during exhaled breath for better aerosol analyte collection during exhalation and to turn down the power on the ionizer assembly **34** during inhalation.

[0053] As mentioned above, because exhaled breath aerosols are few and difficult to collect, analyze, quantify, characterize, and standardize, it is helpful to collect them in the highest practical concentrations. As also mentioned above, the first one-third to one-half of a typical exhaled breath is reflux of inhaled air that never reaches the lungs where alveolar gas exchange occurs and aerosol analytes of interest are produced. Therefore, it is known, for example, that carbon dioxide exchanged during respiration appears at highest concentrations in the later fractions of an exhalation, and it is quite probable, albeit not yet proven, that higher concentrations of exhaled breath aerosols are also highest in the later fractions of exhaled breaths. Consequently, it may be desirable to have the capability of starting collection of exhaled breath aerosol only when the later fractions of the exhaled breaths pass through the collection conduit or chamber **30**.

[0054] This kind of collection procedure can be implemented in a number of different ways. For example, it can be done by manually turning on the electrostatic collection components, e.g., the ionizer system **34**, for the collection conduit or chamber **30** only after a first fraction (e.g., one-third to one-half) of the exhaled breath has been released. It can also be accomplished by turning on the same components with a timer, for example associated with the microprocessor **98**, after a preset time has elapsed from detection of the start of an exhalation. A similar effect can be attained by delaying the opening of the second valve **92** and closing the first valve **90** to prevent collection of aerosol from the first fraction of the exhaled breath on the collection rod **40**. Volume, calculated with flow-rate measurements and time, can also be used as an input criteria, either alone or with other input data or criteria to control the collector **10** component functions for this purpose. Another approach (not shown) may be to provide another outlet port from the collection conduit or chamber **30**, such as a lateral side port, along with a valve that can be opened when the marker, e.g., carbon dioxide, level is below the desired collection concentration level or threshold to simply vent the first portion or fraction of the exhaled breath out of the system until the marker level rises to a threshold at which collection of aerosol is desired. However, a more precise and automated system for collection of exhalation from a more aerosol-rich fraction of the exhaled breath, instrumental sensing of a suitable marker in the exhaled breath, for example, but not for limitation, carbon dioxide, can be used to start and/or stop certain collection components, such as the ionizer system **34** or valve actuators **94**, **96**, a valve (not shown) to vent the first fraction of the exhaled breath out of the system until the marker rises to a desired level or concentration for collection, or the like. Therefore, for example, a carbon dioxide detector **43** is shown near the entrance end **32** of the collection conduit **30** for sensing concentration of the carbon dioxide in exhaled breaths for use in starting exhaled breath aerosol collection only after carbon dioxide concentrations reach some predetermined threshold level. The carbon dioxide detector **43** can be connected to the microprocessor **98**, as indicated schematically by link **47**, if desired so that the threshold and responsive functions can be processed and controlled, as is within the capabilities of person skilled in the art, once they understand the principles of this invention. A suitable carbon dioxide detector for this purpose may be, for example, a respiratory capnometer, such as the model V8200 manufactured by Harvard Apparatus of Hollister, Mass., or any other carbon dioxide detector operated on a suitable circuit as is within the capabilities of persons skilled in the art.

[0055] As can be seen from the example exhaled breath aerosol collector **10** described above, it implements one of the principles of improved exhaled breath aerosol collection according to this invention, i.e., identifying a property of exhaled breath aerosol that can be enhanced to become more responsive to application of a force that enables improved collection and then applying such a force to the exhaled breath aerosol. In the electrostatic collection example of collector **10**, the property, a possible electrostatic charge of some of the aerosols, is enhanced to a strong and more uniform electrostatic charge of known polarity for most, if not all, of the exhaled breath aerosol particles and/or droplets, which can be accomplished by surrounding the aerosol particles and/or droplets with charged ions which impart charges to the exhaled breath aerosol and then applying electrostatic force to collect the aerosol particles and/or droplets on the collection rod **40**.

[0056] When the predetermined number of breaths or other desired criteria, such as volume of breath processed by the collection chamber at a desired or regulated flow rate, have been met to terminate the exhaled breath aerosol analyte collection, the collector **10** can be removed from the mouth of the test subject to extract the collected aerosol analytes for further processing and/or analysis. Again, there are myriad ways that such extraction can be done, but the collector **10** described above has an extractor assembly **50** at one end of the collection conduit, as shown in FIGS. **1-5**. The extractor assembly **50** is best seen in FIG. **6**, which is an enlarged cross-section of the extractor assembly **50** similar to the cross-section in FIGS. **4** and **5**.

[0057] Essentially, to extract the exhaled aerosol analytes **44**, which are captured on the surface **41** of the collection rod **40**, as described above, a blunt needle **61** of a syringe **60** is pushed through a septum **51** to inject just enough liquid solvent to fill an annular space **52** around the rod **40** in the body **53** of the extraction assembly **50**. The liquid solvent will usually be a kind of high purity water, such as high performance liquid chromatography (HPLC) grade water, although other suitable solvents can be used, for example, but not for

limitation, any of a number of buffer solutions that are widely used in bio-chemical analysis techniques and procedures. If desired, the collector **10** can be turned and held with the bore **55** in the body in a vertical orientation during this extraction phase so that gravity helps to retain the liquid solvent in the annular space **52**, although capillary action may be sufficient to retain the liquid solvent in the space **52** in other orientations. Then, the collection rod **40** is pulled longitudinally through a seal **54**, as indicated by arrow **45**, which wipes or scrapes the analytes **44** off the surface **41** of rod **40**, where they are retained and dissolved into the liquid solvent in the annular space **52**.

[0058] When enough of the rod **40** has been pulled through the seal **54** to wipe or scrape substantially all of the analytes **44** off the rod surface **41**, the solvent along with the dissolved analytes can be drawn by the syringe **60** out of the space **52**. The analytes can then be recovered from the solution in the syringe **60** by conventional laboratory or commercial processes for whatever further analysis or study is desired. An optional limit stop, such as a flange **48** (FIG. **5**), can be provided on the end of collection rod **40**, if desired, to prevent accidental removal of the rod **40** from the body **53** of the extractor assembly **50**.

[0059] As illustrated in FIG. **6**, the extraction assembly can be made with an initial axial bore **55** extending longitudinally through the body **53** with a diameter that is large enough to leave the annular space **52** between the collection rod **40** and the body **53**, when the rod **40** is positioned in the bore **55**. The bore **55** then widens in the mid-section of the body at **56** to accommodate the seal **54**. The seal **54** and corresponding widened bore **56** can be cylindrical or any other convenient shape, but a preferred shape is tapered or conical, as illustrated in FIG. **6**, to accommodate uniform snugging of the seal **54** onto the rod **40** for an effective seal against solvent leakage and for effective wiping or scraping of the analytes off the surface of the rod **40**. A distal end portion **57** of the bore can be threaded to receive a threaded gland **58** for tightening and retaining the seal **54** in place. The more the gland **58** is tightened against the seal **54**, the more the tapered surface of the bore section **56** squeezes the seal **54** against the rod **40**. The seal **54** can be made of any of a number of suitable materials, such as PEEK™ (polyaryletherketone), which is available from Upchurch Scientific, of Oak Harbor, Wash. PEEK™ is preferred because of its strength, rigidity, chemical and physical inertness, high dielectric strength as an insulator, and compatibility with sterilization techniques. A flange **59** on the distal end of the gland **58** can be shaped to accommodate a tool, such as a wrench (not shown) for tightening, and it can serve in combination with a knob **46** on the end of the collection rod **40** as a limit stop to limit longitudinal movement of the rod **40** into the conduit **30**. The collection rod **40** can be made of stainless steel or other suitable electrically conductive material, and it is preferred to have a surface roughness of no more than 200 nanometers so that the seal **54** can effectively wipe or scrape the small analyte particles **44** off the rod surfaces. Longitudinal, rather than radial scratches or roughness is also helpful in this regard, although any scratching or roughness is preferably minimized as much as practical.

[0060] The septum **51**, which is preferably resilient elastomeric or flexible latex or some other resilient material that accommodates puncturing by the needle **61** and that will seal around the needle **61** to prevent leakage and reseal itself when the needle is removed, can be held in place in a transverse bore by a hollow gland **62** screwed, as shown in FIG. **6**, or glued or friction held (not shown) in the body **53**. The hollow bore **63** in the gland **62** accommodates insertion of the needle **61** into the septum **51**. If desired, the septum **51** can be pre-split to accommodate insertion of a blunt needle **61**. Also, a valve, such as those used in intravenous connections could be used in place of the septum **51**.

[0061] An alternative to the septum **51** and syringe **60** can be the arrangement shown in FIG. **7**, wherein there are two conduits **64**, **65** extending radially in different directions from the bore **55**. A pair of fittings **66**, **67** fastened to the body **53** in alignment with the conduits **64**, **65** connect tubes **68**, **69** to the respective conduits **64**, **65**, so that the liquid solvent can be flowed transversely, as indicated by arrows **70**, **71** through the bore **55** adjacent the seal **54** as the collection rod **40** is drawn through the seal **54** or after the rod **40** is drawn through the seal **54**. As the analytes **44** are scraped or wiped off the surface **41** of the collection rod **40**, the solvent flow **70**, **71** dissolves them and carries them through the downstream tube **69** to any suitable receptacle or process (not shown), where they can be recovered by conventional techniques for further analysis, classification, or study.

[0062] Referring again primarily to FIGS. **4** and **5**, a first grounded mesh assembly **101** is positioned at the entrance to the pre-collection filter conduit **20** and a second mesh assembly **102** is positioned at the entrance to the collection conduit **30**. These grounded mesh assemblies **101**, **102** prevent a person from inserting an object or finger into the high voltage ionizer elements **24**, **34**, respectively. They can also stop large particles, such as dust, insects, food particles, saliva, sputum, expectorate, and the like from entering the conduits **20**, **30**. Generally, these and other artifacts, which are larger than about 10 microns mean equivalent diameter are prevented from entering the collection chamber by the mesh assembly **102** or by any other convenient trap or device. An example grounded mesh assembly **101**, **102** as shown in FIG. **8** (not to scale), and an example ionizer assembly **34** is shown in FIG. **9** (not to scale). Both are made of electrically conductive materials. The screen **103** of the mesh assembly **101**, **102** can be, for example, 100 mesh fabricated with 500 micrometer tungsten or stainless steel wire, which conveniently has no more than 10% blockage of flow area through the screen **100**, which may be desirable so that the test subject does not feel significant resistance by the collector **50** to exhalation effort, but is not a requirement. Of course, the flow regulation provided by the flow meter **80**, microprocessor **98**, valves **90**, **92**, and other components may present some resistance to exhalation by the test subject, especially if the test subject tries to exhale too rapidly or otherwise outside the breath flow criteria applied by these components for accuracy, reproducibility, standardization, comparability, and the like. The ionizer **34** can comprise a plurality of small diameter tungsten wires **104** (e.g., 250 micrometers) positioned parallel to each other and perpendicular to the air flow **88** (FIG. **5**). They are raised to a positive potential sufficient to produce an ionized field in air, for example, 2,000 to 12,000 volts, or about 70 kV/m. The positive potential for the ionized air flow is preferred over negative to reduce ozone production, but negative may be more useful for some applications.

[0063] There are many other possible variations that can be devised to practice this invention. For example, but not for limitation, the inhaled air and exhaled air do not have to be routed through the same flow meter **80**, which is optional, or even through the same entrance end **21**. In fact, the pre-

collection filter conduit **20** and the collection conduit **30** could be separate, each with its own respective mouthpiece, which would simply require the test subject to inhale from one of the mouthpieces through the separate pre-collection filter conduit or chamber **20** and then to exhale through the other of the mouthpieces into the collection conduit. While this maneuver would add a slight complexity for the test subject, it could eliminate the valves from the apparatus and still accommodate practicing the invention. Also, such mouthpieces **14** can have any convenient shape or structure other than that shown in FIGS. **1-5**, such as a face mask with a breath port, an endotrachial tube, or any other device for capturing the air flow of a test subject's breath and channeling it through components in collector **10**.

[0064] Also, as mentioned above, there are many possible valve variations that can be used to practice the invention. For example, but not for limitation, the electrostatic collection rod **40** could be replaced with any other shape or apparatus that will collect the charged aerosol analytes and from which such analytes can be recovered to practice this invention. Also, the butterfly valves **90**, **92** could be mounted on a common shaft, but rotated 90 degrees in relation to each other, and actuated by one actuator or motor. In such an arrangement, rotation of the shaft in one direction would open one valve **90** as the other valve **92** is closed, and vice versa. Also, the valves could be operated manually. Such manual operation would add some complexity for the user, but the apparatus would be less complex and less expensive. On the other hand, further automation can be added to practice the invention. For example, but not for limitation, the collection rod **40** could be a continuous wire drawn automatically through the collection chamber **30** and extraction assembly **50**, especially in combination with the continuous solvent flow **70**, **71** of the alternate embodiment shown in FIG. **7**.

[0065] Another example breath aerosol analyte collector **120**, illustrated in FIGS. **10-12**, enhances a different property of the exhaled breath aerosol, its mass, and then applying centrifugal force to the aerosol to facilitate collection of the exhaled breath aerosol analytes. More specifically, in this embodiment breath aerosol analyte collector **120**, the conditions are created to enhance condensation of the water vapor in the exhaled breath on the aerosol particles and/or droplets to increase the mass of the aerosol, as will be explained in more detail below, and then applying centrifugal force to the aerosol with enhanced mass to enhance collection of the aerosol **121** on a condensation surface **122**, as will also be described in more detail below. Then some extraction means, for example, the wiper **124**, is used to extract the collected aerosol **121** from the collection surface **122**, as will also be explained in more detail below.

[0066] Essentially, ambient air is preferably inhaled by the test subject (not shown) through a pre-collection filter assembly **126** to remove any ambient aerosols for the reasons explained above. Then, the breath or air is exhaled by the test subject through flow constriction, such as a jet nozzle or orifice (explained below), to create a jet stream flow into an expansion chamber and/or collection chamber (explained below) to expand, cool, and cause condensation of water vapor in the exhaled breath, and to create a spiral flow of the exhaled breath, indicated by flow arrows **128**, through the collection chamber **130** to force aerosol against the tubular collection surface **122**. The aerosol in the expansion chamber nucleates the water vapor condensation to add mass, as will be explained in more detail below. The spiral flow **128** creates centrifugal forces on the aerosol and condensed water, and it creates turbulences that help to break down boundary layers of fluid flow on the collection surface **122**. Both of these effects enhance probability that the aerosols and condensed water in the exhaled breath will contact and be retained by the collection surface **122**, as illustrated in exaggerated scale at **121**. The exhaled air flow, stripped of most, if not all, of the exhaled aerosols then turns as indicated by flow arrow **129** and exhausts out of the collection chamber **130** through an exhaust tube **132**, which extends longitudinally through the collection chamber **130**, where the tube **132** also helps to shape and maintain the spiral flow **128**. An optional cooling fluid **134** can be flowed through a space **136** between the collection tube **138** and outer shell **140** to help maintain the collection surface **122** in a desired temperature range for efficient condensation and collection of water and aerosols **121** on the collection surface **122**. It is preferred, but not essential, that the exhalation of the breath be assisted by a vacuum pump **142** in order to help maintain enough of a pressure drop to enhance nucleation and condensation through the jet nozzle or orifice (explained below) without extraordinary exhaling effort by the test subject. The exhaust tube **132** is removable from the collection chamber **130** to accommodate extraction of the collected aerosols **122** by pushing the wiper **124** longitudinally through the collection chamber **130**.

[0067] With reference now primarily to FIG. **12** along with secondary reference to FIG. **10**, a mouthpiece **144** is provided for the test subject to inhale and exhale breaths through the aerosol analyte collector **120**. Again, the mouthpiece **144** can have any shape or structure and can be part of a face mask (not shown), an endotrachial tube or any other device for capturing a test subject's breath and channeling it through components in the collector **120**. Inhalation of a breath draws ambient air through the pre-collection filter assembly **126**, as indicated by flow arrow **146** to remove ambient aerosols from the air being inhaled so that any aerosol analytes **121** collected on the collection surface **122** will be derived from the test subject's lungs and airway and will not be contaminated by ambient aerosols. The pre-collection filter assembly **126** is depicted for example in FIG. **12** as having a paper or cloth filter element **148** to catch ambient aerosols, but any other kind of filter technology or apparatus that is effective to catch and remove ambient aerosols from the air being inhaled can also be used for this purpose. A suitable pre-collection filter **126** for this purpose may be, for example, an Air Life™ Bacterial Viral Filter, manufacturer's part no. 001851, available from Cardinal Health, Inc. of Dublin, Ohio.

[0068] The air flows as indicated by arrows **149** through the filter assembly **126**, through a first one-way check valve assembly **50** or any other suitable valve type, and into the main air duct **152**, as indicated by flow arrows **154**, **156**. An example one-way check valve that will work for this purpose is part no. 1664 "one-way valve" available from The Hudson RCI Company, of Temecula, Calif. From the main air duct **152**, the air flows backward through a classifier or trap **158**, which will be explained in more detail below, and through the mouthpiece **144**, as indicated by arrows **160**, **162**, to be inhaled by the test subject (not shown). The mouthpiece, trap, main air duct, and connecting sections are sometimes jointly or severally referred to herein as a conduit. The first valve assembly **150** opens during inhalation, as depicted diagrammatically by the open valve member **151** to allow inflow of air through the filter assembly **126**, while a second one-way

check valve assembly **164** closes, as indicated by the closed valve closure member **165**, to prevent backflow of air through the collection chamber **130** during inhalation. Because of the small size of the jet nozzle or orifice **168**, which will be explained in more detail below, the second one-way check valve may not be needed. However, if a valve **164** is needed to prevent backflow, it can be any suitable valve type to perform that function, not just a one-way check valve.

[0069] Next, after inhalation as described above, the test subject exhales breath, which flows through the collector **120**, as best seen in FIG. **13** with continuing secondary reference to FIG. **10**. As shown in FIG. **13**, the exhaled breath enters the collector **120** through the mouthpiece **144**, as indicated by flow arrow **166**. Upon this reversal of airflow from inhalation to exhalation, the first valve assembly **150** closes, as indicated diagrammatically by the closed valve member **151**, and the second valve assembly **164** opens, as indicated diagrammatically by the opened valve member **165**. This reversal of valve assemblies **150**, **164** prevents the exhaled air from flowing backward through the pre-collection filter assembly **126** and directs the flow instead from the main air duct **150** through the nozzle, orifice or other flow constrictor **168** and into the expansion chamber **170** and/or collection chamber **130**, as indicated by flow arrows **172**, **174**. As mentioned above, an optional vacuum source can be connected to an exhaust outlet conduit **178**, as indicated diagrammatically by vacuum pump **142** and arrow **180**, to increase and/or maintain an adequate pressure drop across nozzle **168**, i.e., pressure differential between the main air duct plenum **152** and the expansion chamber **170** to get the desired cooling and nucleated condensation effect in the expansion chamber **170** without requiring extraordinary exhaling effort by the test subject. An optional pressure transducer **182** or pressure conduit **183** to such a pressure transducer (illustrated diagrammatically by pressure transducer **182** in FIG. **10**) can be tapped into the main air duct plenum **152** to sense the build-up of pressure in the plenum **152** upon the start of exhalation by the test subject for any of a number of control functions. Another pressure sensor (not shown) can be tapped into the expansion chamber **170** and/or collection chamber **130** to monitor pressure in these chambers **130**, **170** or pressure drop across the jet nozzle **168** for feedback control to the vacuum source **142** to increase or decrease the pressure in the expansion chamber **170** and/or collection chamber **130** as needed for the desired amount of jet cooling effect. Temperature sensors (not shown) can also be added in the plenum **152** and expansion chamber **170** for achieving the desired gas temperature differentials for a good balance between enough nucleated condensation for good exhaled breath aerosol collection without too much condensate that dilutes the collected analyte specimens. For example, the pressure increase in plenum **152** from the start of exhalation can be used to activate the vacuum source **142**, to activate the cooling fluid source **184**, to actuate valve **150**, **164** (if they are of a type that require motive force for activation), and myriad other functions that may occur to persons skilled in the art, once they understand the principles of this invention. A microprocessor **186** can be used to facilitate these and other functions, as illustrated schematically by phantom lines **188**, **189**, **190**, **191**, **192** in FIG. **10**, or by analog or other methods. Such implementations are well within the capabilities of persons skilled in the art and need not be described here for an understanding of this invention. Likewise, a number of other sensor and/or transducer technologies, such as flow meters, manual switches, and others can be used to implement these functions, as will also be understood by persons skilled in the art, once they understand the principles of this invention. For example, a carbon dioxide sensor **193** can be used to detect increase in carbon dioxide, which may indicate exhaled breath to start one or more of the functions of the collector **120**. The link **194** to the microprocessor **186** in FIG. **10** is a schematic indication of control functions based on carbon dioxide detection in the air flow. One particular advantage of a carbon dioxide detector **193** is that it can distinguish between exhaled air that has been no deeper than the test subject's airway, which has near normal air content of carbon dioxide, from air that is exhaled from deep in the lungs, which has higher carbon dioxide content. Thus, for example, if the valves **150**, **164** are actively controllable or actuateable, as opposed to self-actuating one-way check valves, they can be switched on or off to allow exhaled air to flow into the collection chamber **130** only when an increase in carbon dioxide indicates that breath exhaled from deep in the lungs has reached the collector **120**. If it is determined that part or all of an exhaled breath is not to be accepted in the collection chamber **130** for this reason or for any other control reason (e.g., insufficient velocity or flow rate, volume control, etc.), the exhaled flow can be directed back through the pre-collection filter assembly **126** to the atmosphere, or another outlet port and valve (not shown) can be provided anywhere upstream of the jet nozzle **168** for redirecting the exhaled air out of the collector **120**. For example another outlet port and valve (not shown) could be connected into or out of the main plenum **152** or the valve **150** could be a 3-way valve connected to another outlet port to divert such unwanted flow out of the system, if it is preferred to avoid such backward flow through the filter assembly **126**. Of course, the microprocessor **136** or other control systems used can reverse those functions discussed above when the pressures, flows, carbon dioxide, temperatures, and the like reverse or get out of desired ranges for the functions.

[0070] Referring again primarily to FIG. **13** with secondary reference to FIG. **10**, the exhaled breath **166** is preferably directed first through a classifier or trap **158** to stop and retain any large materials or artifacts (e.g., greater than about 10 microns mean equivalent diameter) in the exhaled air, such as bits of food, sputum, expectorate, saliva, and the like, which could skew collection and/or measurements of collected aerosol analytes of interest. The trap **158** in FIG. **13** is illustrated, for example, as a simple U-shaped air conduit **196**, in which such large materials would be trapped, because they would have too much mass to make the U-turn illustrated by flow arrow **198** and defy gravity to get into the main air duct plenum **150**. However, many other types of traps or classifiers would also work for this purpose.

[0071] As mentioned above, from the main air duct plenum **152**, the air flow **172**, **174** is directed through a jet nozzle or orifice **168** into the expansion chamber **170** and/or collection chamber **130**. The jet nozzle or orifice **168** (not drawn to scale) is very much smaller in diameter than the plenum **152**, so air flow through the jet orifice accelerates to a high velocity and then escapes in a jet stream into the lower pressure expansion chamber **170**. The result of this effect is an adiabatic expansion and cooling of the fluid as it expands into the lower pressure expansion chamber **170**, which causes super-saturation of water vapor in the stream of exhaled breath.

[0072] Water vapor in a rapidly cooling, super-saturated volume of carrier gas condenses upon solid and/or liquid aerosols suspended in the air flow, i.e., on the exhaled breath

aerosols, which nucleate the condensation. Of course, condensation also occurs on the interior walls of the expansion chamber **170** and on the interior surface **122** of the collection chamber **130**. However, a significant feature of this implementation of the invention is the creation of conditions that enhance such nucleated condensation on the exhaled breath aerosols, which adds mass to the aerosols and, thereby, renders them more susceptible to a collection force.

[0073] One of the collection forces used in this implementation of the invention is centrifugal force applied to the aerosols, which has a greater effect on the aerosols that, along with condensed water on them, have increased mass. The centrifugal force is applied in this embodiment **120** by directing the jet stream flow **174** tangentially, or offset from the longitudinal axis **131** of the collection chamber **130**, into the expansion chamber **170**, which, along with the low pressure created by the vacuum source **142**, causes a vortical stream of the exhaled breath spiraling down the annulus between the exhaust tube **132** and the collection tube **138**, as indicated by flow arrow **128**. The collection chamber **130** is preferably in the shape of a figure of revolution, such as a cylinder, with a longitudinal axis **131**, and the jet stream flow **174** is directed in offset relation, to the longitudinal axis **131** into the expansion chamber **170**, which is merely a top part and/or top extension of the collection chamber **130**. The components of the main air duct or conduit **152** intersecting the expansion chamber **170** and/or the collection chamber in a tangential manner with or without the constriction or nozzle **168** are sometimes referred to as a vortex generator. The vacuum source **142** is not essential, because the exhaled breath in the plenum **152** itself raises the pressure in the plenum above the pressure in the expansion chamber **170** and collection chamber **130**, but the vacuum source **142** enhances this process and reduces the feeling of resistance to exhalation felt by the test subject. The resulting vortex **128** creates a powerful centrifugal force on the aerosol suspended in the vortical stream **128**, especially those aerosols that are laden with the additional mass of the nucleated condensation, as explained above. The dwell time of the exhaled breath stream **128** in the collection chamber **130**, i.e., the amount of time that it takes for an average air molecule to spiral down the vortex **128** from the expansion chamber **170** to the entrance **133** of the exhaust tube **132**, depends on dimensions of the collection chamber **130** and operating pressures in the collector **120**, but the centrifugal force acts on any aerosols in the vortical stream **128** all the way down the annular space to the exhaust tube entrance **133**. These centrifugal forces accelerate the particles toward the condensation surface **122** of the collection tube **138**. The more mass an aerosol has, the more it is accelerated toward the collection surface **122**.

[0074] As mentioned above, there is also some condensation of water vapor from the exhaled breath on the collection surface **122**, depending on the temperature difference between the water vapor in the exhaled breath and the collection surface **122**. However, this implementation of the invention requires only enough difference in temperature between the water vapor entering the expansion chamber **170** and the temperature in the expansion chamber **170** and continuing into the collection chamber **130** (the expansion chamber **170** is merely an upper portion and/or extension of the collection chamber **130**) to enable mass accretion on aerosol particles and droplets by nucleated condensation to assure capture of a consistent and majority of aerosol particles and droplets on the collection surface **122**. Further increase in that temperature differential will only increase condensation of water vapor directly on the collection surface **122** and, thereby, increase dilution of the captured exhaled breath aerosol analytes on the collection surface **122** by the additional condensed water on the collection surface **122** without proportionally increasing the collected quantity of aerosol analytes. Therefore, to enable consistency and repeatability of aerosol analyte collection that can be analyzed and/or compared in a meaningful manner to other aerosol analyte collections from the same test subject and/or from other test subjects or to standards and the like, it may be important to maintain the temperature of the collection surface **122** and collection chamber **130** within a desired or prescribed temperature range. Therefore, a temperature control system may be desirable and, in the example collector **120**, is illustrated as a temperature controlled cooling fluid jacket or chamber **136** between the collection tube **138** and an outer shell **140** to maintain a temperature controlled collection surface **122**. The cooling fluid can be circulated from a source **184** through an inlet tube **214** into the jacket **136** and out from the jacket **136** through an outlet tube **216** at another location, as indicated by arrows **134**, **135**, respectively. The cooling fluid can be water supplied by a thermostatic circulator manufactured by Recirculating Chiller, Neslab Instruments, Waltham, Mass., or similar device. Any suitable thermostat **218**, such as a thermocouple or other technology can be used to measure temperature of the exhaled breath flowing in the collection chamber **130** and to feed such measurements back to the microprocessor **192** or other suitable controller, as indicated schematically by link **220** (FIG. **10**), to control the source **184** to produce more or less cooling as necessary to maintain the desired or prescribed temperature.

[0075] Upon entering the exhaust tube **132**, as indicated by flow arrow **129**, the exhaled breath flow, stripped of most, if not all, of the aerosol analytes **121**, which cling to the collection surface **122**, continues its flow through the exhaust tube **132**, as indicated by flow arrow **198**. One or more ports **200** near the top **202** of the exhaust tube **132** allow the exhaled breath to flow into an exhaust manifold chamber **204**, as indicated by flow arrow **206**. From the exhaust manifold chamber **204**, the exhaled breath flows through an exhaust port fitting **208**, as indicated by flow arrow **210**, through the valve **164** and exhaust outlet conduit **178**, as indicated by flow arrow **212**, to the vacuum source **142**. All of these exhaust components from the exhaust tube **132** to the exhaust port fitting **208** are sometimes referred to as an exhaust outlet.

[0076] Upon completion of a collection period, the exhaust tube **132**, which is slidably sealed by a pair of O-rings **222**, **224** or other appropriate seals, can be pulled longitudinally out of the collection chamber **130**, as indicated by arrow **226** above the pull knob **228** at the top end **202** of the exhaust tube **132**. Then, with the exhaust tube **132** pulled out of the collection chamber **130**, the wiper **124** can be pushed by a rod **125** or other suitable device, either manually or with some machine actuator, spring, pneumatic or hydraulic actuator, etc., upwardly through the collection chamber **130** to wipe the analytes **121** off the collection surface **122**. In addition to the analytes **121**, there will be a significant amount of condensed water on the collection surface **122**, which gets wiped along with the analytes off the surface **122** by the wiper **124** and will usually be adequate to dissolve the analytes **121** and retain them in solution. As the wiper **124** approaches the top end of the collection chamber **130**, any suitable appliance or apparatus can be used to extract the condensed water and analytes

from the collector **120** for further study, analysis, or other use. For example, a syringe or pipette (not shown) can be used to draw the solution containing the analytes out of the collection chamber **130** through the opening left by the removal exhaust tube **132**, as will be understood by persons familiar with those kinds of instruments, or more sophisticated or automated equipment can be devised for this purpose.

[0077] The criteria for selecting particular physical dimensions and operating parameters for the collector **120** should preferably balance the efficiency and effectiveness of the aerosol collection against the dilution caused by the condensed water. It may be preferable, but not essential, that the temperature differential discussed above be increased only to the extent that further increase no longer increases the amount of detectable analytes in the collected specimen. Further, the collection chamber **130**, while shown to be cylindrical, can also be conical, spherical, or any other shape, but is preferably a figure of revolution. Also, all of the control features described above, including, but not limited to, those described for the collector **10** of FIGS. **1-9** can be used in this collector embodiment **120**, as will be understood by persons skilled in the art, once they understand the principles of this invention.

[0078] The foregoing description is considered as illustrative of the principles of the invention. Furthermore, since numerous modifications and changes will readily occur to those skilled in the art, it is not desired to limit the invention to the exact construction and process shown and described above. Accordingly, resort may be made to all suitable modifications and equivalents that fall within the scope of the invention. The words "comprise," "comprises," "comprising," "include," "including," and "includes" when used in this specification are intended to specify the presence of stated features, integers, components, or steps, but they do not preclude the presence or addition of one or more other features, integers, components, steps, or groups thereof.

What is claimed is:

1. A method of collecting a sample of non-gaseous aerosol in exhaled breath, comprising:

inhaling a breath of air through a filter to remove ambient aerosols from the breath of air;

exhaling the breath of air through a collector and collecting aerosols from the exhaled breath.

2. The method of claim **1**, including controlling flow rate of the exhaled air through the collector to a desired flow rate.

3. The method of claim **2**, including limiting flow rate of the exhaled air through the collector to a desired flow rate.

4. The method of claim **3**, including assisting the exhaled breath of air through the collector with a pump.

5. The method of claim **1**, including inhaling the breath of air through a first conduit that contains the filter and exhaling the breath of air through a second conduit that contains the collector.

6. A method of collecting a sample of non-gaseous aerosol in exhaled breath, comprising:

enhancing a property of the aerosol in the exhaled breath in a manner that renders the aerosol more susceptible to a collection force; and

applying the collection force to the targeted aerosol to facilitate collection of the aerosol.

7. The method of claim **6**, including:

enhancing a property of the aerosol in the exhaled breath by charging the aerosol with an electrostatic charge; and

creating a different electrostatic charge on a collection component to create an electrostatic attractive force between the aerosol and the collection component and applying such electrostatic force to attract the aerosol to the collection component.

8. The method of claim **6**, including:

enhancing mass of the aerosol in the exhaled breath by super cooling air and water vapor in the exhaled breath to cause condensation of water vapor on the aerosol; and

applying centrifugal force to the aerosol enhanced with the additional mass of the condensed water to increase probability of contact of the aerosol with a collection surface.

9. A method for the collection of non-gaseous substances suspended in exhaled breath from a human or animal test subject, comprising the steps of:

causing the subject to exhale into a receiving chamber, and

applying an urging force directly to said non-gaseous substances suspended in said exhaled breath within said receiving chamber, and

presenting a collecting surface to the interior of said receiving chamber, said collecting surface comprising a solid or a liquid to which the force urges the suspended non-gaseous substances to collect thereupon, and

removing the collected non-gaseous substances for further processing, and

displacing residual exhaled air, substantially depleted of said non-gaseous substances, with a new volume of exhaled breath,

whereby the collected material is useful for analysis and comprises substantially all of the useful said non-gaseous substances suspended in said exhaled breath but only a minor fraction of exhaled vapors.

10. The method of claim **9**, wherein said urging force is selected from the group comprised of gravitational force, centrifugal force, electrostatic force, thermophoretic force, magnetic force, and aerodynamic force comprising motion imposed by a moving fluid acting against an aerodynamic drag of said non-gaseous substances suspended in said exhaled breath.

11. The method of claim **9**, further comprising a step prior to step (b) of augmenting a property of said non-gaseous substances upon which said urging force acts, whereby said augmenting increases the rapidity with which or the probability that the suspended non-gaseous substances will be urged to said collecting surface and collect thereupon.

12. The method of claim **11**, wherein:

said property of said non-gaseous substances comprises electrical charge, and

said augmenting comprises an ionizing means to impart an electrical charge of known polarity to said non-gaseous substances, and

said collecting surface has a polarity opposite that of said electrical charge, and

said urging force comprises electrostatic force,

whereby imparting said electrical charge on the suspended non-gaseous substances increases the strength of said electrical force upon the substances, increasing the rapidity with which or the probability that said non-gaseous substances will be urged to said collecting surface and collect thereupon.

13. The method of claim **12**, wherein:

said ionizing means comprises a first electrode comprised of an electrically conductive material and situated within the inlet end of said receiving chamber, and

said first conductive electrode having a physical shape causing high charge accumulation on an exposed feature, and

said first conductive electrode connects electrically to a pole of a direct current voltage source, and

said collecting surface within said receiving chamber comprising an electrically conductive material, and

said collecting surface connecting electrically to said direct current power source at a pole of opposite polarity to that connected to said first conductive electrode, and

said direct current power source having a voltage causing a corona field around said presenting feature of said first conductive electrode,

whereby said corona field imparts said electrical charge of known polarity to said non-gaseous substances as said exhaled breath flows around said first conductive electrode.

14. The method of claim **11**, wherein:

said property of said non-gaseous substances comprises physical mass, and

said augmenting comprises accreting physical mass to said non-gaseous substances.

15. The method of claim **14**, wherein:

said accreting said physical mass of said non-gaseous substances comprises nucleation condensing of condensable gases in said exhaled breath upon substantially all nucleation centers within said receiving chamber, and

said nucleation centers comprising said non-gaseous substances.

16. The method of claim **15**, wherein said nucleation condensing comprises a super-saturating means acting upon said condensable gases within said exhaled breath.

17. The method of claim **16**, wherein said super-saturating means comprises a means to rapidly expand the volume of said exhaled breath within said receiving chamber.

18. The method of claim **17**, wherein:

said means to rapidly expand said the volume comprises a constricting means in a flow conduit that conducts said exhaled breath, followed by an enlargement of the internal diameter of said flow conduit, and

said constricting means creating a jet flow in which the flow velocity of said exhaled breath through said constricting means becomes substantially greater within said constricting means than the velocity of said exhaled breath in said flow conduit means providing said exhaled breath to said constricting means, and

said enlargement causing adiabatic expansion and thereby cooling of the gas volume to cause super-saturating of said condensable vapors in said exhaled breath, causing said condensable vapors in said exhaled breath to condense upon said nucleation centers comprising said non-gaseous substances suspended in said exhaled breath.

19. The method of claim **18**, further comprising a step of providing a negative pressure difference between said test subject's mouth and said conduit enlargement sufficient to present a resistance to exhalation that said test subject perceives as being substantially comfortable.

20. The method of claim **14**, further comprising a step of:

controlling the temperature of said collecting surface, and

preventing said temperature from rising more than five degrees Centigrade above the ambient temperature, and

preventing said temperature from falling more than five degrees Centigrade below the ambient temperature.

21. The method of claim **14**, wherein said urging force comprises centrifugal force.

22. The method of claim **21**, wherein generating said centrifugal force comprises a means to impart rapid rotational motion to said exhaled breath.

23. The method of claim **22**, wherein:

said means to impart rotational motion comprises introducing said exhaled breath into said receiving chamber by means of a constriction in a flow conduit that conducts said exhaled breath to the inlet of said receiving chamber, and

directing the flow of said exhaled breath from the outlet of said constriction substantially at a tangent to the inner diameter of said receiving chamber, and

providing an outlet from said receiving chamber to allow an exit for exhaled breath depleted of said non-gaseous substances suspended in said exhaled breath after application of said centrifugal force, and

providing a time period for the rotationally moving said exhaled breath adequate to assure substantially complete collection of said non-gaseous substances suspended in said exhaled breath.

24. The method of claim **23**, wherein:

said receiving chamber further comprises a geometric form having an internal configuration that is selected from the group comprised of substantially cylindrical, ellipsoidal, conical, or spiral form, and

said receiving chamber further including a dimension between inlet and outlet adequate to provide said time period for residence of said rotationally moving said exhaled breath, and

said collecting surface of said receiving chamber further comprises a material having thermal conductivity sufficient to assure adequate thermal regulation, and

said collecting surface further communicating thermally to a thermal mass whose temperature is regulated by a thermal controlling means.

25. The method of claim **24**, further comprising a step of providing a negative pressure difference between said test subject's mouth and said conduit enlargement sufficient to present a resistance to exhalation that said test subject perceives as being substantially comfortable.

26. A method for the collection of non-gaseous substances suspended in exhaled breath from a human or animal test subject, comprising the steps of:

causing the subject to exhale into a receiving chamber, and

applying an electrostatic force directly to said non-gaseous substances suspended in said exhaled breath within said receiving chamber, and

presenting a collecting surface to the interior of said receiving chamber, said collecting surface comprising a solid or a liquid to which said electrostatic force urges the suspended non-gaseous substances to collect thereupon, and

removing the collected non-gaseous substances for further processing, and

displacing residual exhaled air, substantially depleted of said non-gaseous substances, with a new volume of exhaled breath,

whereby the collected material is useful for analysis and comprises substantially all of the useful said non-gaseous substances suspended in said exhaled breath but only a minor fraction of exhaled vapors.

27. The method of claim **26**, further comprising a step prior to step (b) of imparting an electrical charge of known polarity to said non-gaseous substances suspended in said exhaled breath, whereby said electrical charge urged by said electrostatic force increases the rapidity with which or the probability that the suspended non-gaseous substances will be urged to said collecting surface and collect thereupon.

28. The method of claim **27**, wherein said imparting said electrical charge comprises an ionizing means.

29. The method of claim **28**, wherein:

said ionizing means comprises a first electrically conductive electrode composed of an electrically conductive material, and

said first conductive electrode is situated in near the inlet of said receiving chamber, and

said first electrically conductive electrode is electrically connected to a pole of a direct current power supply, and

said collecting surface is composed of an electrically conductive material, and

said collecting surface is electrically connected to the pole of said direct current power supply that is the opposite polarity of the pole that is electrically connected to said first electrically conductive electrode, and

said direct current power supply has a voltage sufficient to cause a corona field around said first electrically conductive electrode,

whereby said corona field has strength sufficient to impart said electrical charge of intensity sufficient to result in said electrostatic force urging said non-gaseous substances to readily collect on said collecting surface.

30. The method of claim **29** wherein said first electrically conductive electrode has at least one physical feature, exposed to the influent exhaled breath, that causes high electrical charge accumulation on said physical feature.

31. A method for the collection of non-gaseous substances suspended in exhaled breath from a human or animal test subject, comprising the steps of:

causing the subject to exhale into a receiving chamber, and

applying a centrifugal force directly to said non-gaseous substances suspended in said exhaled breath within said receiving chamber, and

presenting a collecting surface to the interior of said receiving chamber, said collecting surface comprising a solid or a liquid to which said centrifugal force urges the suspended non-gaseous substances to collect thereupon, and

removing the collected non-gaseous substances for further processing, and

displacing residual exhaled air, substantially depleted of said non-gaseous substances, with a new volume of exhaled breath,

whereby the collected material is useful for analysis and comprises substantially all of the useful said non-gaseous substances suspended in said exhaled breath but only a minor fraction of exhaled vapors.

32. The method of claim **31**, wherein generating said centrifugal force comprises a means to impart rapid rotational motion to said exhaled breath.

33. The method of claim **32**, wherein:

providing said means to impart rotational motion comprises introducing said exhaled breath into said receiving chamber by means of a constriction in a flow conduit that conducts said exhaled breath to the inlet of said receiving chamber, and

directing the flow of said exhaled breath from the outlet of said constriction substantially at a tangent to the inner diameter of said receiving chamber, and

providing an outlet from said receiving chamber to allow an exit for exhaled breath depleted of said non-gaseous substances suspended in said exhaled breath after application of said centrifugal force, and

providing a time period for the rotationally moving said exhaled breath adequate to assure substantially complete collection of said non-gaseous substances suspended in said exhaled breath.

34. The method of claim **33**, wherein:

said receiving chamber further comprises a geometric form having an internal configuration that is selected from the group comprised of substantially cylindrical, ellipsoidal, conical, or spiral form, and

said receiving chamber further including a dimension between inlet and outlet adequate to provide said time period for residence of said rotationally moving said exhaled breath, and

said collecting surface of said receiving chamber further comprises a material having thermal conductivity sufficient to assure adequate thermal regulation, and

said collecting surface further communicating thermally to a thermal mass whose temperature is regulated by a thermal controlling means.

35. The method of claim **34**, further comprising a step of providing a negative pressure difference between said test subject's mouth and said conduit enlargement sufficient to present a resistance to exhalation that said test subject perceives as being substantially comfortable.

36. The method of claim **31**, further comprising a step prior to step (b) of accreting additional physical mass to said non-gaseous substances suspended in said exhaled breath, whereby said additional physical mass urged by said centrifugal force increases the rapidity with which or the probability that the suspended non-gaseous substances will be urged to said collecting surface and collect thereupon.

37. The method of claim **36**, wherein:

said accreting said physical mass of said non-gaseous substances comprises nucleation condensing of condensable gases in said exhaled breath upon substantially all nucleation centers within said receiving chamber, and

said nucleation centers comprising said non-gaseous substances.

38. The method of claim **37**, wherein said nucleation condensing comprises a super-saturating means acting upon said condensable gases within said exhaled breath.

39. The method of claim **38**, wherein said super-saturating means comprises a means to rapidly expand the volume of said exhaled breath within said receiving chamber.

40. The method of claim **39**, wherein:

said means to rapidly expand said the volume comprises a constricting means in a flow conduit that conducts said exhaled breath, followed by an enlargement of the internal diameter of said flow conduit, and

said constricting means creating a jet flow in which the flow velocity of said exhaled breath through said constricting means becomes substantially greater within said constricting means than the velocity of said exhaled breath in said flow conduit means providing said exhaled breath to said constricting means, and

said enlargement causing adiabatic expansion and thereby cooling of the gas volume to cause super-saturating of

said condensable vapors in said exhaled breath, causing said condensable vapors in said exhaled breath to condense upon said nucleation centers comprising said non-gaseous substances suspended in said exhaled breath.

41. The method of claim **40**, further comprising a step of providing a negative pressure difference between said test subject's mouth and said conduit enlargement sufficient to present a resistance to exhalation that said test subject perceives as being substantially comfortable.

42. The method of claim **31**, further comprising a step of:

controlling the temperature of said collecting surface, and

preventing said temperature from rising more than five degrees Centigrade above the ambient temperature, and

preventing said temperature from falling more than five degrees Centigrade below the ambient temperature.

43. A method to assure reproducibility of the collection of non-gaseous substances suspended in exhaled breath from a human or animal test subject, comprising the steps of:

providing a removing means to eliminate substantially all suspended non-gaseous particles and liquid aerosol droplets from ambient air drawn into an inlet conduit, and

conducting the cleaned intake air within said conduit to a first connecting means to said test subject's respiratory airway, and

providing a first one-way valve means causing air to flow in a direction from said inlet conduit to said first connecting means, said first one-way valve means being situated at any effective location in the inlet conduit, and

causing the subject to inhale said cleaned intake air, and

conducting the consequent exhaled breath through an exhalation conduit, and

providing a second one-way valve means causing air to flow in a direction from said first connecting means through said exhalation conduit, said second one-way valve means being situated at any effective location in said exhalation conduit,

thereby substantially eliminating substances external to said test subject from being inhaled by said test subject, and assuring that substantially all non-gaseous substances suspended in said exhaled breath comprise only those arising from said test subject's respiratory system.

44. The method of claim **43**, further comprising the steps of:

optionally, measuring the flow rate over time of said intake air within said inlet conduit, and

optionally, providing data derived from said measuring to a recording means, and

optionally, providing data derived from said measuring to a controlling means,

thereby enabling the operator of said collection means to correlate the subject's inhalation performance with analyses of said collected substances, and to select the portion of consequent exhaled breath conducted to said collection means.

45. The method of claim **43**, wherein said removing means is any highly efficient device selected from one of the group comprised of filters, scrubbers, precipitators, impactors, aerosol classifiers, and collectors.

46. The method of claim **43**, wherein said first connecting means is selected from one of the group comprised of a respiratory facemask, a respiratory mouthpiece, a conduit such as an endotracheal tube inserted within the subject's upper airway, a tracheostomy portal, a component of a ventilator breathing circuit, and a component of any other respiratory support device.

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