

BREATH CONTAINER, BREATH CAPTURE DEVICE, BREATH SAMPLING SYSTEM AND FACIAL MASK

Technical Field

The present invention relates, in general terms, to devices for controlling and/or capturing exhaled breath. In particular, the present invention relates to, but is not limited to, breath containers having capture volumes with compartment(s) for containing exhaled breath.

Background

Exhaled human breath or gas analysis has shown promise for enabling non-invasive disease diagnosis. Breath analysis is a fast, non-hazardous, cost effective, point of care process for disease state monitoring and environmental exposure assessment in human beings.

VOCs/gases (Volatile Organic Compounds – a VOC from an exhaled gas is any organic compound having an initial boiling point less than or equal to 250° C measured at a standard atmospheric pressure of 101.3 kPa) in exhaled breath bear the fingerprints of metabolic and biophysical processes in the human body. Some VOCs/gases in exhaled breath are biomarkers of different diseases. The presence of those biomarkers in excess amounts is indicative poor health or adverse patient medical conditions.

Breath analysis has been proposed for early detection of diseases, particularly those that can be assessed based on biomarkers present in exhaled breath.

Exhaled breath analysis is mostly focused on breath exhaled through the mouth. However, other than VOCs of systemic origin, mouth exhaled breath contains VOCs originating from the airway, oral cavity and gut by

bacterial action from mucus and saliva. This makes disease detection and health monitoring from exhaled breath challenging. For example, acetone and isoprene are absolutely systemic in origin, ammonia, hydrogen sulphide, and ethanol are mostly mouth-generated, and methanol, propanol and other VOCs have partly systemic origins.

It would be desirable to overcome or ameliorate at least one of the above-described problems, or at least to provide a useful alternative.

Summary

The devices and systems disclosed herein are intended to provide a storage kit for major biomarkers (VOCs/gases) present in exhaled breath. By adequately storing exhaled breath, biomarkers are preserved for longer. This enables use of a broader range of analysis techniques for detection and disease monitoring. In some embodiments, mass spectrometry such as GC-MS (gas chromatography-mass spectrometry), PTR-MS (proton transfer reaction – mass spectrometry) and SIF-MS (selected ion flow tube-mass spectrometry) is used for performing analysis.

Disclosed herein is a breath container adapted for use with a breath capture device, the container comprising:

- a body comprising an inlet;
- a capture volume inside the body and comprising at least two compartments; and
- a valve assembly positioned between the inlet and compartments and having an open condition to permit a flow of breath from the breath capture device into each of the compartments and a closed condition to contain breath in the compartments.

The valve assembly comprises a valve for each compartment and may be configured to open and/or close the valve for each respective

compartment, in a predetermined sequence. The predetermined sequence may be selected to capture, in successive ones of the compartments, one of:

- successive portions of an exhaled breath; and
- a common portion, from successive breaths.

One of the capture volume and body may comprise a suction port by which suction can be applied to the capture volume or body to shrink an internal volume of the capture volume or body and thereby apply pressure to the at least two compartments.

The breath container may further comprise a humidity controller for controlling a humidity within each compartment.

Also disclosed is a breath container adapted for use with a breath capture device, the breath container comprising:

- a body comprising an inlet;
- a capture volume inside the body;
- a valve assembly positioned between the inlet and the capture volume, and having an open condition to permit a flow of breath from the breath capture device into the capture volume and a closed condition to contain breath in the capture volume; and
- a humidity controller to control a relative humidity level within the capture volume.

The humidity controller may comprise a temperature controller for controlling a temperature of at least a portion of the capture volume. The temperature controller may control the temperature to maintain a predetermined relative humidity differential between the portion of the capture volume and atmosphere outside the capture volume.

The humidity controller may comprise a desiccant filter between the capture volume and the inlet.

The humidity controller may comprise a desiccant material located in at least one of the body and the capture volume.

Also disclosed is a breath capture device for use with a breath container described above, comprising:

- a device body comprising a device inlet;
- a connector for connecting to the breath container, to admit a flow of breath from the inlet into the breath container; and
- a desiccant device positioned within the device body, between the device inlet and the connector.

Also disclosed is a breath sampling system comprising:

- a device as described above; and
- a breath container as described above, coupled to the device.

Also disclosed is a facial mask comprising:

- a mask body shaped to cover a mouth of a user;
- an air control system in communication with the mask body, comprising:
 - an inlet for air to enter the mask body during inhalation;
 - an outlet with mouthpiece that extends into the mouth, during use, through which exhaled breath exits the mask body during exhalation, the outlet being having a connection for connecting to a breath sampling system; and
 - a one-way valve assembly between the mask body and the connection.

The air control system may comprise a desiccant device positioned between the one-way valve and the outlet. The desiccant device may comprise a desiccant filter.

The outlet may be adapted to connect to mass spectrometer inlet tubing, to facilitate direct transfer of breath from the mask to a mass

spectrometer.

The outlet may be adapted to connect to the breath sampling system of 13, to facilitate direct transfer of breath from the mask to the breath sampling system.

The outlet may comprises a luer activated port for connection to a luer fitting of the breath sampling system.

The one-way valve assembly may comprise a droplet filter for removing droplets from the exhaled breath.

Advantageously, some embodiments filter off all aerosols or droplets from exhaled breath (hereinafter interchangeably referred to as "exhaled gas" and similar). This can prevent infectious virus from spreading through aerosols when exhaled gas of patient infected with contagious virus is filtered.

Advantageously, some compartments of the capture volume can carry at least 1L of exhaled gas volume and, in other embodiments, the volume is 500mL. Devices disclosed herein can store the breath at room temperature, from 25-30degC and <95%RH (relative humidity) for stability, at approximately slightly higher than atmospheric pressure. The VOCs contained in the breath stored in the compartments can remain for to 72 hours at approximately 60% of the ppbv. Moreover, VOCs stored for 24 achieve approximately 85% recovery ppbv, or higher. Notably, the present teachings have been applied to human-related VOCs (i.e. VOCs in breath exhaled from humans), but may be similarly applied to VOCs from other animals and organisms.

Advantageously, some embodiments use multiple compartments. This enables different portions of a breath, or portions from successive breaths, to be stored in separate compartments. In some cases, this enables

comparative analyses between end-tidal breath and other portions of an exhaled breath. In other cases, this facilitates repeatability of results where a portion of a first breath is analysed using a particular technique and the same portion of a second breath is analysed using a different technique or for verification of results.

The flexible pouch is compartmentize to store different exhalation breath volume up to 500ml per each compartment. This is to allow each breath of up to 500ml to be separated and collected per exhale. This allows testing repeatability and do not generally mix the collection of each breath.

Brief description of the drawings

Embodiments of the present invention will now be described, by way of non-limiting example, with reference to the drawings in which:

Figure 1 shows a breath analysis system in accordance with present teachings;

Figure 2 is an alternative breath analysis system in accordance with present teachings;

Figure 3 illustrates a mask with one-way valve;

Figure 4 shows a mask comprising a mechanical filter with a one-way valve, connected directly to a flexible pouch/capture volume;

Figure 5 shows a mask comprising a mechanical filter with a one-way valve, connected to tubing that can itself be connected to the mass spectrometer;

Figure 6 shows a mask without any filter, with a one-way valve and connected to tubing that can itself be connected to a mass spectrometer;

Figure 7 shows an embodiment of a breath container in accordance with present teachings;

Figure 8 shows a mask and tubing canister embodiment of the present invention, with the tubing canister in a collapsed condition;

Figure 9 shows the same assembly as that shown in Figure 8, with the tubing canister in a partially extended condition;

Figure 10 shows a connection between a tubing canister and breath container;

Figure 11 illustrates embodiments of a device comprising a mouthpiece connected to a tube canister embodiment of the breath container with the bottom connection having a luer activated port for connection to a mass spectrometer;

Figure 12 shows a mask with mechanical filter and a one-way valve, connectable to a mass spectrometer (referred to as an "instrument" in Figure 12);

Figure 13 illustrates a mask connected to a tube canister storage container having a bottom luer activated port for connection to a mass spectrometer vacuum suction system.

Detailed description

Devices and systems for storing exhaled breath are disclosed. The exhaled breath is used for diagnosis of diseases through detection of metabolic biomarkers. The apparatus includes a mask to cover one or both of the nose and mouth of a patient to shield or remove aerosol droplets from exhaled breath and to direct the exhaled breath into a storage container or storage collection flexible pouch or tube.

The present devices and systems enable storage of major biomarkers (VOCs/gases) present in exhaled breath for their analysis towards disease monitoring and analysis – e.g. using mass spectrometry such as GC-MS, PTR-MS and SIF-MS. The VOCs can be stable for up to 72 hours, at which point up to 60% of VOCs (concentration in ppbv) is recoverable. This is achieved using various mechanisms discussed below, including insulating the storage flexible pouch from the effects of external humidity and

temperature, and by compartmentation of the exhaled breath into at least two compartments.

Some biomarkers the present devices and system are capable of containing include ammonia, acetone, isoprene, nitric oxide, hydrogen sulphide, methane, ethane and pentane. Table 1 shows the biomarker relationship to disease and detectable at ppb level.

Biomarker	Major disease	Maximum permissible limit
Ammonia	Renal failure, liver dysfunction, cirrhosis in the liver, peptic ulcer, halitosis et cetera	250 ppb
Nitrogen oxide	Asthma, chronic obstructive literary disease, unlike diseases such as laboratory animal allergies, lung infections in aluminium pot-room workers, swine confinement workers, lung cancer et cetera	25 ppb
Hydrogen sulphide	Asthma, airway inflammation, oral malodour, dental disease et cetera	8 to 16 ppb
Acetone	Diabetes	0.9 ppm
Isoprene	Diabetes, hypercholesterolaemia	105 ppb
Methane, ethane, pentane	Intestine and colon related disease, breast cancer, liver diseases, asthma et cetera	-
Aldehydes	Cancers such as lung cancer, breast cancer, Alzheimer's disease, Parkinson's disease,	-

	Wernicke's encephalopathy et cetera	
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Table 1: biomarker versus disease

Figure 1 illustrates a breath capture system 100. The system 100 includes a mask 200, a breath capture device 300 and a breath container 400, the breath capture device 300 and breath container 400 together forming a breath sampling system 500 connected to the mask 200. The breath sampling system 500 includes a box 502. The box 502 is intended to represent either a closed end (dimensions not to scale), breath analyser (e.g. CO₂ detector) or other equipment while still ensuring there is sufficient pressure to direct breath into container 400.

The breath container 400 is adapted for use with the breath capture device 300. To that end, the container 400 may comprise a screw fitting or Luer fitting that is sized to match a cooperating screw fitting all Luer fitting on the breath capture device 300. In other embodiments, the container 400 or parts thereof may be integral with the breath capture device 300.

The container 400 broadly comprises a body 402 with inlet 404, a capture volume 406 and valve assembly 408. The body 402 presently comprises a flexible body for containing the capture volume 406. In other embodiments, the body 402 comprises a rigid flask or container made of any suitable material. The inlet 404 of the body 402 enables gear to be communicated into the capture volume 406 from the breath capture device 300.

The capture volume 406 is inside the body 402 and, in the present embodiment, comprises two compartments 410, 412 for containing the exhaled breath. In some embodiments, there may be only a single compartment or the capture volume may itself be used for containing the

exhaled breath with no compartment within the capture body. Install further embodiments, three or more compartments may be provided.

The valve assembly 408 is positioned between the inlet 404 and compartments 410, 412. The valve assembly 408 has, for each compartment 410, 412, an open condition to permit a flow of breath from the breath capture device 300 into each of the compartments 410, 412 and a closed condition to contain breath in the compartments 410, 412. To that end, valve assembly 408 may comprise a single valve, such as a leaf valve or other one-way valve, for communicating exhaled breath from the device 300 simultaneously into both compartments 410, 412. However, the valve assembly 408 presently comprises a valve (414, 416) for each compartment 410, 412.

The valve assembly 408 is configured to open and/or close the valve 414, 416 for each respective compartment 410, 412. This can be performed in a predetermined sequence, either manually or automatically – e.g. using a push button to manually activate the valve for each compartment, or making the valves from pressure-regulators that are passively actuated. The predetermined sequence can be matched to the type of analysis desired to be performed. For example, the predetermined sequence may be selected to capture, in successive ones of the compartments 410, 412, successive portions of the same exhaled breath. For example, compartment 410 capture the first or a middle portion of an exhaled breath whereas compartment 412 may capture end-tidal breath. This enables comparative analyses between end-tidal breath and other portions of an exhaled breath. The predetermined sequence may instead be selected to capture the same portion of a breath from successive breaths (i.e. a common portion from each breath). For example, compartment 410 may capture the end-tidal portion of a first breath and compartment 412 may capture the end-tidal portion of a second breath. This facilitates repeatability of results where a portion of a first breath is analysed using

a particular technique and the same portion of a second breath is analysed using a different technique or for verification of results. Moreover, this testing repeatability is achieved in a single device without mixing the breaths.

The capture volume 406 comprises a flexible pouch or bag 418 that surrounds the compartments 410, 412 – i.e. the bag 418 or its volume is compartmentalised. In other embodiments, the capture volume is itself defined by the compartments (i.e. is not a separate structure). The bag 418 is positioned between the compartments 410, 412 and the body 402. The bag 418 can be withdrawn from the body 402 when the compartments 410, 412 contained a desired volume of exhaled breath. Each of the compartments 410, 412 can be filled independently. There is no mixing between the compartments. Similarly, compartments 410, 412 can be separately evacuated (i.e. have their contents drawn out for analysis) – e.g. through respective valves 414, 416. Compartment 406 can also be filled if provided with the necessary valve in the valve assembly 408, and can be emptied via suction port 420. In the embodiment shown in Figure 2, the compartments 666, 668 are connected in series and are thus filled in sequence and some mixing may occur – mixing can potentially be avoided by entirely evacuating compartment 666 into compartment 668 before refilling compartment 666. As discussed below, these compartments 666, 668 also have valves arranged such that their contents can be separately extracted without mixing, for analysis.

The bag 418 has a suction port 420. Suction applied via the suction port 420 to the bag 418 shrinks the internal volume of the bag 418. This applies pressure to the compartments 410, 412. This pressure can serve multiple purposes: it can maintain a higher than atmospheric pressure in the compartments 410, 412; and it can force the contents of compartments 410, 412 into an analysis device such as a mass spectrometer. The contents of compartments 410, 412 will only be able to be expelled if the

respective valve 414, 416 is open. Therefore, the contents of the compartments can be selectively or sequentially taken for analysis - e.g., the contents can be drawn via vacuum suction or compression protesting, through a valve with the stock clock to a mass spectrometer. Notably, since the body 402 is flexible, the bag 418 may be omitted, and the suction port may be provided directly on the body 402.

Each compartment may have any volume suitable for the application of the container 400. Presently, each compartment as a capacity of 500 mL although 1 L compartments may be used in some applications.

The flexible pouch or bag 418 may be able to contain 1L (or more) of exhausted breath. The container 400 then stores this breath at room temp (25-30°C) and <95% RH (relative humidity) for stability at approximately slightly higher than atmospheric pressure – pressure adjustment can be achieved via suction port 420. Exhalation parameters such as expiratory flow at approximately 5L/min and breath-containment may affect VOC levels significantly. Therefore, standardisation of exhaled VOC measurements is very useful to ensure repeatability of results and to avoid confounding analysis systems. The manner in which the exhaled breath is stored in the compartments is important for VOC stability. For example, for a flexible pouch with 1 L air volume, the flexible pouch is compartmentalised into smaller volume compartments (410, 412) of up to 500 mL. Thus, when the exhaled breath is pushed into the flexible pouch, it enters a first compartment that catches the initial exhaled breath through a pressure-regulated port (part of valving assembly 408). Once the first compartment is filled, the last of the exhaled breath (i.e. the portion exhaled breath in excess of the volume of the first compartment) will enter a second compartment and fill up the second compartment. For testing of the exhaled breath, the last breath in the final compartment (i.e. the compartment filled last of all the compartments in the capture volume) will be drawn by mass spectrometer vacuum suction for analysis. The

compartment containing the initial exhaled breath can be drawn through another port on the outside of that compartment for comparison and benchmarking.

Between taking the breath sample and analysing it, the flexible pouch is placed in another outer bag – or maintained in body 402 where body 402 is resistant to penetration. The function of the body 402, which contains the outer bag 406, is to assist squeezing the flexible pouch (when the body 402 is flexible and includes a suction port) and to protect against tearing or damage to the flexible pouch during transportation. The outer bag of body may have a vacuum port such that when the flexible pouch valve ports are connected to the mass spectrometer, suction can be applied to squeeze the flexible pouch inside the bag connected to the mass spectrometer. This can be useful if the vacuum suction of the mass spectrometer ($<1 \times 10^{-6}$ mbar) is insufficient to draw the exhaled breath from.

The flexible pouch may be made from any suitable material, such as PVF (polyvinyl fluoride), PVDF (polyvinyl difluoride), PEA (poly ethanolamine), PTFE (polytetrafluoroethylene), polyether ether ketone (PEEK) and other VOC inert materials. Similar materials may be used for the tubing or any other component that will come into contact with the exhaled breath.

The dimensions of the patch may be dictated by purpose. For example, the current may be made with a 250cm² area made of 2 layers of PVF film that is heat sealed at all edges with a sealed edge of at least 8mm. The thickness of film can be 0.1um to 100 um. The human related VOCs recovery for storage in such flexible pouches, up to 72 hours after exhalation, is approximately 60% of its ppbv (parts per billion volume). The recovery for human related VOCs stored within 24 hours is above 85%. Notably, however, are flexible pouch is not the only option. For example, a Vacutainer or other device such as a plunger canister may be used.

The breath container 300 also includes a humidity controller for controlling a humidity within each compartment. In embodiments that do not have to compartments, such as those that have no compartments, will the humidity controller may control the humidity (e.g. relative humidity or absolute moisture content) within the capture volume itself.

The humidity controller can include a desiccant filter 422 between the capture volume 408 and the inlet 404. The filter 422 filters out droplets and may also filter out moisture more generally, from an exhaled breath (or part thereof) that is to be contained. As such, the filter 422 filters off some or all aerosols from exhaled breath (herein interchangeably referred to as "exhaled gas" and similar). For example, a mechanical filter may be connected to the valve assembly (alternatively, or in addition, the mechanical filter may be connected to the mask – e.g. in air control system 602 described with reference to Figure 3) for removing moisture from the exhaled breath. That moisture may otherwise affect VOC storage and testing. Thus, filtration can prevent infectious viruses from spreading through aerosols.

Alternatively, or in addition, the humidity controller may include a desiccant material located in one or more of the body 402, capture volume 406 and compartments 410, 412 – see, e.g., desiccant material 424 and 426. Each of these humidity control devices is passive – i.e. non-powered. Other humidity control devices may be powered and thus active such as a dehumidifier provided in device 300, or even a re-humidifier located at an appropriate position if humidity is determined to preserve some VOCs. Active humidity control devices will be powered by a power source, and have access to a water reservoir, in a known manner.

Often, moisture will pass through a flexible material over time if there is a sufficient humidity differential across the material. Since the capture volume 406 in some embodiments is a flexible bag or pouch, it is expected

that some moisture may pass into the capture volume 406 over time. Particular devices described herein are capable of maintaining VOCs at analysable levels for up to 72 hours, during which time there is significant opportunity for moisture to migrate into the capture volume 406. While the capture volume 406 is not designed to permit the passage of moisture through its walls, to the extent that such passage of moisture is unavoidable, the material of the capture volume is moisture permeable.

To reduce the amount of moisture passing into the capture volume 406, the community controller can include a temperature controller for controlling a temperature of at least a portion of the capture volume. Heating up the stored breath to below the boiling point of the VOCs can prevent or reduce the humidity gradient between an environmental relative humidity of, for example, 85%RH and the relative humidity level in the flexible pouch with the exhaled gas, particularly if the mechanical filter did not remove the moisture.

The capture volume is at least partially formed from a moisture permeable material, the humidity controller comprising a temperature controller for controlling a temperature of at least a portion of the capture volume. Presently, the temperature controller comprises a heating jacket or element, one of which is shown on the body (428) and the other of which is shown on the capture volume 406 itself (430). The temperature controller 428, 430 may comprise an insulating layer (to control temperature stability to maintain the stability of VOCs for storage up to 72 hours), or may be electrically heated or cooled (using means it will be evident to the skilled person in my to present teachings) to maintain the temperature within the capture volume at the desired level. Where the capture volume simply comprises the compartment or compartments, it will be understood that the temperature controller may be directly on the compartment or compartments.

The temperature controller controls the temperature to maintain a predetermined relative humidity differential across the material of the capture volume – i.e. between the portion of the capture volume which the temperature controller is applied, and atmosphere outside the capture volume. That atmosphere may be between the capture volume 406 and the body 402, or may be outside of the body 402.

The breath container 400 is adapted for use with the breath capture device as described above. One such breath capture device 300 includes a device body 302 comprising a device inlet 304, a connector 306 and a desiccant device 308. The connector 306 connects the device 300 to the breath container 400, to admit a flow of breath from the inlet 304 into the breath container 300. The desiccant device 308 is positioned within the device body 302, between the device inlet 304 and the connector 306. The desiccant device 308 may be a desiccant filter or other device for drawing droplets or moisture from the exhaled breath before it passes into the breath container 300.

While a user may breathe directly into the device 300, or even into the container 400, the present embodiment includes a facial mask 200 for capturing the exhaled breath. The mask 200 includes a mask body 202 shaped to cover the mouth of a user. Presently, the body 202 covers both the nose and mouth of the user. The mask 200 also includes an air control system 204 for controlling airflow in the mask 200.

The air control system 204 is in communication with the mask body 202. Unit control system 204 includes an inlet 206 for air to enter the mask body 202 during inhalation, and an outlet 208 for exhaled breath to exit the mask body 202 during exhalation. The outlet 208 with a mouthpiece 209 that extends into the mouth, during use. The outlet 208 has a connection 211 that is adapted to connect to the breath sampling system which can, in some embodiments, be an analysis system such as a mass

spectrometer, but presently is system 500. Since the mouthpiece may be made from VOC inert material (e.g. PEEK or other material as identified herein), the mask itself need not be made from VOC inert material. Similarly, a tube formed from VOC inert material may extend within the mouthpiece 209 all the way to the storage container 400 or analysis system, thereby removing the need for other components (e.g. the mask), that do not contact the exhaled breath, to be VOC inert. The air control system 204 also includes a one-way valve assembly 210. The valve assembly 210 is located between the mask body 202 and the outlet 208.

Air flowing into the mask 200 enters the inlet 206 and into the user's lungs where it picks up VOCs and moisture. On exhalation, the exhaled breath flows from the user into the body 202 of the mask 200 and out of the mask 200 via the one-way valve assembly 210. Although the system to which the exhaled breath then flows may itself include some mechanism for removing moisture, in the event that the mask 200 is to be directly connected to a mass spectrometer or other analysis equipment, it can be useful to remove droplet or moisture from the exhaled breath to avoid confounding results. To that end, the air control system 204 includes a desiccant device or filter 212 positioned between the one-way valve 210 and the outlet 208. Similarly, the one-way valve assembly 210 may include a droplet filter.

The outlet 208 is adapted to connect to the breath sampling system 500, via tubing 214, to facilitate direct transfer of breath from the mask 200 to the breath sampling system 500. The outlet 208 includes a Luer activated port for connection to a Luer fitting of the breath sampling system or, as shown, tubing 214.

Figure 2 shows a mask 640 including an adjustable nose clip 642 and elastic band 644 for attaching the mask 642 the face of the user. The mask 640 includes an air control system comprising an inhalation port or inlet

646 and an outlet. The outlet includes a mouthpiece 648 that extends, in use, into the mouth of the user. This enables the user to exhaled directly into the outlet rather than forcing exhaled breath into the mask generally until sufficient pressure is built up that exhaled breath exits the outlet. The outlet may also include an adapter 650 for adapting the mouthpiece 648 to a further device 652 of the outlet, the further device including one or both of a one-way valve and filter. The one-way valve will ensure that exhaled breath can only exit the mask 640 through the mouthpiece 648 and not return to the mask 640. The filter will remove viral contaminants such as droplets and/or moisture from exhaled breath. The filter may be positioned upstream or downstream of the one-way valve, as needed, in embodiments where both a one-way valve and filter are provided.

The one-way valve and/or filter 652 is connected through a connector 654 to tubing 656. While the tubing 656 may be connected via connector 658 to a system similar to system 300 of Figure 1, in the present embodiment of the tubing 656 is connected via connector 658 to a breath container 660.

In the embodiment of Figure 1, the outlet 208 includes an elbow joint connecting mouthpiece 209 to connector 211. An elbow joint increases resistance to passage of exhaled breath out of the mask 200. In contrast, the outlet of mask 640 (including mouthpiece 648, adapter 650 and one-way valve and/or filter 652) includes a straight joint. The straight joint removes much of the resistance to the passage of exhaled breath from the mask 640 when compared with the mask 200.

The breath container 660 includes a body 662 comprising an inlet 664. The inlet 664 presently comprises a stopcock. As with connector 654 and supply tubing 656, stopcock 664 connects with connector 658 via a Luer fitting. The breath container 660 also includes a capture volume inside the body 662, the capture volume comprising compartments 666 and 668. The

breath container 660 also includes a valve assembly positioned in the body 662. As above, valve assembly has an opening condition to permit flow of breath from the breath capture device (presently mask 640) into which the compartments 666, 668, and close condition to contain breath in compartments 666, 668. The valve assembly presently includes a first valve (stopcock 664) between a first of the two compartments 666 and the breath capture device. The valve assembly also includes a second valve 670 between the first compartments 666 and the second compartment 668.

Each compartment 666, 668, includes an extraction port 672, 674 respective. In some embodiments, only a single extraction port may be provided. For example, if extraction port 672 were removed, the contents of compartment 668 would be depleted first for analysis, and the contents of compartment 666 would then be fed into compartment 668 and subsequently out through extraction port 674 for subsequent analysis.

In each of the embodiments shown in Figure 1 in Figure 2, the the outlet of the mask may be connected directly to a breath analysis system (for example a mass spectrometer), a breath container (for example, the mask 650 of Figure 2 may be used to control exhalation into the device 400 of Figure 1), or to a device such as device 300 of Figure 1. In essence, the mask in each case is adapted to filter the exhaled breath of undesirable components (for example droplets or moisture) and enable direct connection between the mask and downstream processing, whether that downstream processing be for the purpose of storage or immediate analysis.

With reference to Figure 3, a mask 600 (e.g. a mouth nose mask) covers the patient's mouth and nose to shield the aerosol droplets during exhalation – i.e. ensure the droplets are contained. The mask 600 also directs the exhaled gas or breath, containing relevant VOCs, via a port

assembly or air control system 602 to an outlet 604 within the facial mask 600. The mask or port assembly allows fresh air to enter one-way through the mouth nose mask upon inhalation – e.g. a one-way valve (not shown) may be used to permit inhalation through an aperture such as that indicated by inlet circle 206 in Figure 1, while not permitting airflow out through that valve and, as a consequence, exhaled breath passes through a second one-way valve in air control system 602 and thus into tubing 606.

Concentration of VOCs exhaled from the nose have lower concentrations than those in breath. However, the nose can remove or obviate some confounding factors present in breath expelled from the mouth. Therefore, for particular applications or diseases thought to be diagnosed, the mask may cover only the nose or may, if higher concentrations of VOCs are required, cover only the mouth or both the nose and mouth as shown.

The flexible tube 606 connects the mask 600 and a storage container (not shown – e.g. system 500 comprising storage container 400). Due to the one-way valve in air control system 602, an exhaled gas or breath sample is directed in a single direction to the collection container via valve port (e.g. valve assembly 408) on the container while permitting fresh air to enter the mouth nose mask upon inhalation.

As discussed above, the container to which the mask connects is adapted to maintain humidity equilibrium (i.e. a constant humidity or humidity within a desired range). This reduces diffusion of VOCs within the flexible pouch inside the container holding the exhaled breath – the contained breath will therefore generally have lower humidity than during exhalation.

For convenience and comfort, the mask 600 also includes an elastic band 608 for holding the mask 600 onto the user's face, and a nose clip 610.

Figure 4 shows another embodiment of a facial mask 700 including a mask

body 702, and air control system 704. The air control system 704 again includes an inlet (which may be an aperture as shown in previous embodiments, or may constitute the interface between the mask body 702 and the user) and an outlet 706, with a one-way valve 708 disposed between the patient and the outlet 706. The air control system 704, and the outlet 706, is adapted to enable the mask 700 to be directly connected to a breath sampling system or breath analysis system – e.g. bio-sensor, CO₂ detector, flow rate sensor and others (similar equipment can be connected to the masks and other devices of the other embodiments described herein). The outlet 706 again includes a Luer fitting for connecting to tubing 710 that leads to the breath sampling system or breath analysis system.

Figure 5 shows another assembly of a mask 800, including air control system 802 that includes a mechanical filter 804 with a one way valve 806 and connects to a flexible pouch 808. The pouch 808 does not include any compartments. Instead it is a single storage volume with two stop cock valves 810, 812, one of which (810) is operable to selectively permit and preclude flow of exhaled air from the tube 814 into the pouch 808, and the other of which (812) is operable to selectively permit and preclude flow of stored in air from pouch 808 to an analysis system but as a mass spectrometer.

Figure 6 shows another embodiment of a mask 900 which is substantially similar to mask 800, except that the air control system includes a port 902 by which additional gas (e.g. inert gas) can be added to the exhaled breath, a CO₂ detector or other detector can be attached to the system etc. Port 902 enables manipulation of the sample being collected, and properties of the sample to be determined, in advance of storage. Notably, if the valve assembly is controlled by CO₂ content of the breath (e.g. to capture end-tidal breath), then measurements from a CO₂ sensor attached to port 902 can be used to automatically actuate valves of the valve assembly in a

manner understandable to the skilled person in view of present teachings.

The breath container may be configured as a series of containers. One such embodiment is shown in Figure 7. The breath container 680 includes a plurality of compartments, a first of which is referenced by 682 and a last of which is referenced by 684. There may be additional compartments located therebetween. The inlet 686 of the breath container 680 connects with the first compartment 682. Between successive compartments is a one-way valve 688. The one-way valve in each case permits flow to a further downstream compartment. In practice, this may permit mixing of exhaled breath between the various compartments of the breath container 680. However, pressure can be applied to upstream compartments (for example, pressure can be applied to the first compartment 682 under such a force using a vacuum port as described above) to force exhaled breath into subsequent, downstream compartments. As a result, the last compartment 684 can be made to contain the first portion of an exhaled breath, and subsequent portions of the exhaled breath will be stored in successively further upstream compartments. Moreover, the same breath container 608 thereby be made to contain multiple exhaled breaths in successive compartments, in series.

Figure 8 shows a mask 800 with an air control system that includes a mouthpiece 802 (presently a straight mouthpiece similar to that shown in Figure 2) and inhalation port 804 and an outlet 806. The outlet 806 connects directly to a tubing canister 808. The tubing canister 808 is telescopically extendable to increase its internal volume. The tubing canister 808 may therefore be extended to contain the full volume of the desired portion of an exhaled breath. The tubing canister 808 includes a one-way valve 810 at an upstream or proximal in, to contain the desired portion of exhaled breath in the tubing canister 808. At the downstream end of the canister 808 is a cap 812 and a connector 814. The connector 814 may be sealed by a as shown, thereby to prevent premature egress

exhaled breath from the canister 808.

Figure 9 shows a similar embodiment to that shown in Figure 8, with the exception that the tubing canister 690 is divided into multiple compartments, each of which is separated by a one-way valve 692. The number of compartments may be adjusted as desired, between two or greater than two compartments, in a similar manner to that shown in Figure 7.

Figure 10 shows an extrapolation of the present concept, where the canister 1000 attached to the mask (similar to canister 808 being attached to mask 800 of Figure 8) is used as a tube rather than the storage container, to convey exhaled breath from the mask to a breath container 1002. Between the canister 1000 in the breath container 1002 may be a valve 1004 valving arrangement of the container 1002.

Figure 11 shows a tubing canister 1100 with plunger pusher 1102 consisting of at least 2 valve ports with stock cock 1104 that can be used for storage of exhaled gas breath containing VOCs. The tubing canister 1100 may be divided by one-way valves in a similar manner to tubing canister 808. As such, the plunger pusher 1102 is provided by enabling the compressibility of tubing canister 1100 to reduce the internal volume of the successive containers therein in order to expel the contents of each of those containers as desired. The length can vary and be extendable depending on the required volume of exhaled breath to be stored, storage with at least 500 mL per compartment within the tubing canister being desirable – end-tidal breath is often around 500 mL for adults. An outer insulation layer 1104 for the tubing canister is required to maintain the temperature when the room temperature falls below 25°C. Tubing canister 1100 with plunger pusher can be use to push exhaled breath into MS (mass spectrometer) pipeline if the MS vacuum suction is weak. The tubing

canister 1100 can be made of VOC inert material so it enhance the stability of VOCs storage up to 72 hours for testing.

As shown in Figure 12, the one-way valve 1200 can be connected to a mechanical filter 1202 having virus filtration efficiency greater 99.999%. The filter 1202 may therefore filter virus in aerosol droplets out of the exhaled breath flowing through the circuit pipe. This can be useful where the mask is connected directly to a mass spectrometry equipment for measuring VOCs for prognosis of disease detectable by VOCs. In general, VOC levels in exhaled breath can be within limits of detection at the ppbv level (parts per billion by volume) for example. A mechanical filter is usually effective to filter particles up to 0.2 μ m size. The mechanical filter 1202 may be hygroscopic and remove the droplets that carry infectious virus or bacteria, with an efficiency of up to 99.999%. Although VOCs are around 3 μ m in size, it is possible for them to diffuse through a mechanical filter and into the mass spectrometer. The material used within the mechanical filter is important and, ideally, no active carbon should be used. Active carbon can absorb VOCs and thus exhaled breath cannot be reliably tested.

As shown in Figure 1, the mouth port 209 can be connected to an elbow shoulder/joint or, as shown in Figure 2, straight port. The port or joint may lead to a flange or manifold having one or more outlets. It may also include at least one aperture around said outlet conduit for connection to flow path, or may otherwise be configured to either provide/connect to a single flow path for exhaled breath, two flow paths or three or more flow paths as desired. Each flow path may comprise a direct connection to the relevant device or container, or connect thereto through tubing such as that discussed herein. –For example, an embodiment comprising two flow paths may include one flow path to analysis equipment such as a mass spectrometer and another flow path to a storage container, enabling immediate VOC content to be ascertained and compared with VOC levels

after storage. The mouth port (209, 648) may be 12mm to 22mm in end diameter – the end that project into the mouth. The elbow shoulder or straight port can be connected to a one-way valve facilitating the one-way passage of exhaled breath as discussed above. The elbow shoulder or straight port may have any dimensions, but are ideally 12mm to 22mm in end diameter.

The one-way valve of the outlets described above can be connected directly to a breath container, or be connected to a flexible tube. The flexible tube is connected at the opposite end to a stock cock port or valve port leading to a flexible pouch (breath container) inside which the exhaled breath is contained. In each case, the one-way valve prevents the backflow of exhale breath or gas.

For embodiments that use a tubing canister, the material of the tubing canister is ideally VOC inert. For example, the tubing canister may be made from PVF, PVDF, PEA, PTFE, PEEK or other VOC inert materials such as stainless steel. The size of the tubing canister can have OD ranging from 20mm to 40mm or other diameter as needed. The length can vary or be extendable depending on the required volume for storage with at least 500ml being desirable for each compartment within the tubing canister. Between each compartment, there is a one-way check valve allowing the first breath to fill up the compartment and not return to the adjacent chamber. If the tubing canister is made of a rigid material, an external container is not required. An outer insulation layer for the tubing canister may be used to maintain the temperature when the room temperature falls below 25°C.

Figure 13 shows various components of the system described above, including a mask 1300, outlet 1302, tubing 1304 for attachment to the outlet 1302 for conveying breath exhale into the mask 1300 into interchangeable storage canisters 1306, 1308 through one-way valve

1310. Canisters 1306, 1308 are connected via a connector 1312 to tubing 1314 that may in turn be connected to a mass spectrometer or other piece of analysis equipment.

Exhaled gas or breath sampling using the devices disclosed herein, during a fixed time, can reduce variations in breath-to-breath VOC concentrations that are otherwise reported for analyses based on a single breath. This is achieved by sampling from multiple breaths. Moreover, breath sampling using a predefined fixed volume (e.g. 500ml per exhale) facilitates repeatability.

Physico-chemical properties of individual volatiles and collecting materials affect relative VOC recoveries. Ideally, collection kit devices should be inert and/or disposable, given that many materials and cleaning agents emit VOCs with a high risk of carry-over effects even under stringent conditions. Various materials may be used for the different components of system 100, and the devices and systems described with reference to the other drawings. In general, it is desirable that polymeric materials such as silicone are used for the mask and tubes, polycarbonates, PFA (poly (fufuryl alcohol)), HDPE (high-density polyethylene) and others can be used for storing the exhaled breath VOCs, provided the material used does not interfere with VOCs such as ammonia, acetone, isoprene, nitric oxide, hydrogen sulphide, methane, ethane and pentane VOCs in ppbv level.

It will be appreciated that many further modifications and permutations of various aspects of the described embodiments are possible. Accordingly, the described aspects are intended to embrace all such alterations, modifications, and variations that fall within the spirit and scope of the appended statements.

Throughout this specification and the statements that follow, unless the context requires otherwise, the word "comprise", and variations such as "comprises" and "comprising", will be understood to imply the inclusion of

a stated integer or step or group of integers or steps but not the exclusion of any other integer or step or group of integers or steps.

The reference in this specification to any prior publication (or information derived from it), or to any matter which is known, is not, and should not be taken as an acknowledgment or admission or any form of suggestion that that prior publication (or information derived from it) or known matter forms part of the common general knowledge in the field of endeavour to which this specification relates.

CLAIMS

1. A breath container adapted for use with a breath capture device, the container comprising:
 - a body comprising an inlet;
 - a capture volume inside the body and comprising at least two compartments; and
 - a valve assembly positioned in the body and having an open condition to permit a flow of breath from the breath capture device into each of the compartments and a closed condition to contain breath in the compartments, wherein the valve assembly comprises a valve for each compartment and the valve assembly is configured to open and/or close the valve for each respective compartment, in a predetermined sequence.
2. The breath container of claim 1, wherein the predetermined sequence is selected to capture, in successive ones of the compartments, one of:
 - successive portions of an exhaled breath; and
 - a common portion, from successive breaths.
3. The breath container of claim 1 or 2, wherein one of the capture volume and body comprises a suction port by which suction can be applied to the capture volume or body to shrink an internal volume of the capture volume or body and thereby apply pressure to the at least two compartments.
4. The breath container of any one of claims 1 to 3, further comprising a humidity controller for controlling a humidity within each compartment.
5. A breath container adapted for use with a breath capture device, the breath container comprising:
 - a body comprising an inlet;

a capture volume inside the body;

a valve assembly positioned in the body and having an open condition to permit a flow of breath from the breath capture device into the capture volume and a closed condition to contain breath in the capture volume; and

a humidity controller to control a relative humidity level within the capture volume.

6. The breath container of claim 5, wherein the capture volume comprises at least two compartments, the open condition permits the flow of breath into each of the compartments and the closed condition contains breath in the compartments, wherein the valve assembly comprises a valve for each compartment and the valve assembly is configured to open and/or close the valve for each respective compartment, in a predetermined sequence
7. The breath container of claim 5 or 6, wherein the humidity controller comprises a temperature controller for controlling a temperature of at least a portion of the capture volume.
8. The breath container of claim 7, wherein the temperature controller controls the temperature to maintain a predetermined relative humidity differential between the portion of the capture volume and atmosphere outside the capture volume.
9. The breath container of any one of claims 5 to 8, wherein the humidity controller comprises a desiccant filter between the capture volume and the inlet.
10. The breath container of any one of claims 5 to 9, wherein the humidity controller comprises a desiccant material located in at least one of the body and the capture volume.

11. A breath capture device for use with a breath container according to any one of claims 1 to 10, comprising:
 - a device body comprising a device inlet;
 - a connector for connecting to the breath container, to admit a flow of breath from the inlet into the breath container; and
 - a desiccant device positioned within the device body, between the device inlet and the connector.
12. A breath sampling system comprising:
 - a device according to claim 11; and
 - a breath container according to any one of claims 1 to 10, coupled to the device.
13. A facial mask comprising:
 - a mask body shaped to cover a mouth of a user;
 - an air control system in communication with the mask body, comprising:
 - an inlet for air to enter the mask body during inhalation;
 - an outlet with mouthpiece that extends into the mouth, during use, through which exhaled breath exits the mask body during exhalation, the outlet being having a connection for connecting to a breath sampling system; and
 - a one-way valve assembly between the mask body and the connection.
14. The mask of claim 13, wherein the air control system comprises a desiccant device positioned between the one-way valve and the outlet.
15. The mask of claim 13 or 14, wherein the desiccant device comprises a desiccant filter.

16. The mask of any one of claims 13 to 15, wherein the outlet is adapted to connect to mass spectrometer inlet tubing, to facilitate direct transfer of breath from the mask to a mass spectrometer.
17. The mask of any one of claims 13 to 15, wherein the outlet is adapted to connect to the breath sampling system of claim 12, to facilitate direct transfer of breath from the mask to the breath sampling system.
18. The mask of any one of claims 13 to 17, wherein the outlet comprises a luer activated port for connection to a luer fitting of the breath sampling system.
19. The mask of any one of claims 13 to 18, wherein the one-way valve assembly comprises a droplet filter for removing droplets from the exhaled breath.