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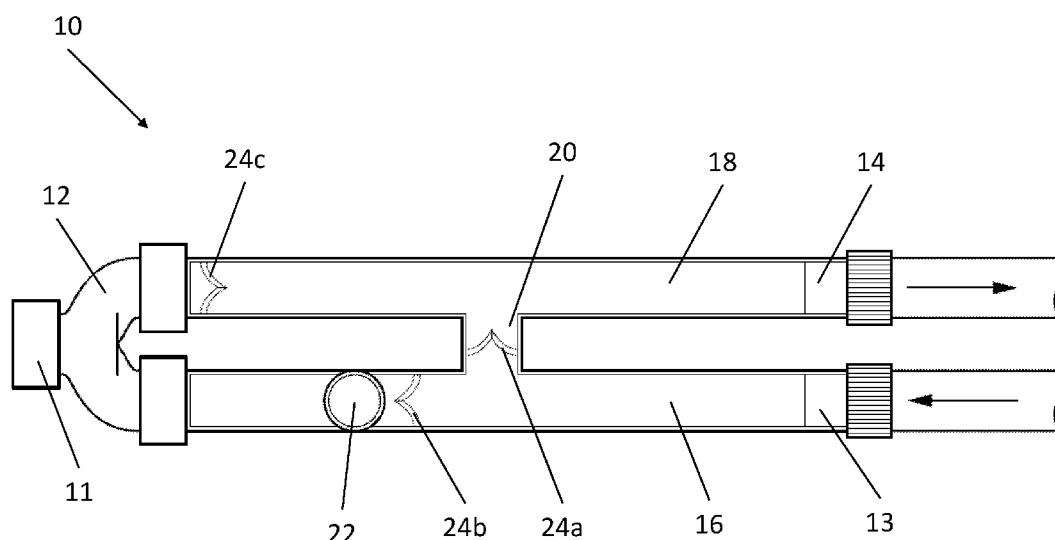


Figure 1A

(57) Abstract: The present invention provides a respiratory adapter for inhaled media deposition in the lungs and airways. The respiratory adapter provides an inspiratory arm and an expiratory arm, wherein the two arms are joined by a bypass flow bridge. A system of valves, such as one-way valves, directs the flow of gas and media through the respiratory adapter to improve media deposition efficiency and to prevent re-breathing of exhaled gas.



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TITLE
RESPIRATORY ADAPTER AND METHOD OF USE

CROSS-REFERENCE TO RELATED APPLICATIONS

5 This application claims priority to U.S. Provisional Patent Application No. 62/324,034 filed April 18, 2016, the contents of which are incorporated by reference herein in their entirety.

BACKGROUND OF THE INVENTION

10 In recent years, with the development of expensive therapeutics, biomarkers, and tracers for inhaled delivery to the lung, there is a need for improving deposition of these media in the lung while minimizing loss of these media during administration with supplemental flow. Most systems of administering inhaled agents are performed with systems that are used in continuous modes for various time durations.

15 Despite the advent of newer patient or ventilator triggered devices for output only during the inspiratory cycle, there remains loss to media both during inspiration and expiration due to flow through the media reservoir and adjustments to supplemental flow associated pressure and/or volume controlled respiratory assist devices (e.g., ventilators, continuous positive airway pressure machines, etc.).

20 A typical circuit for administering inhaled agents includes a positive pressure media generator connected by tubing to a patient interface, such as a mask, nasal prongs, or an endotracheal tube, and an exhalation path, such as tubing that allows discharge of the expired gases (e.g., to the ventilator if the patient requires active support, to a mode of the ventilator known as continuous positive airway pressure (CPAP) or to an

25 underwater receptacle known as “bubble” CPAP if the patient requires end expiratory lung volume stabilization, or directly to the environment if the patient is freely spontaneously breathing requiring no additional support). In the situation when respiratory assist devices are used, such as a ventilator or with CPAP, the inspiratory and expiratory tubes are typically connected to the patient interface via a “Y” connector,

30 which contains a port for attaching each of the inspiratory and expiratory tubes, as well as

a port for the patient interface, and typically, a port for attaching a pressure and/or temperature sensor.

The media delivery reservoir is usually positioned in the inspiratory arm of the circuit, as close to the patient interface as practical. Clinically, administration time of media is based on visualizing the media reservoir; administration time is stopped when no more media is observed in the reservoir. However, this does not mean that the media has been delivered to the lung. In this regard, whether media delivery flow is triggered by patient or assist devices, there is divergent loss of media from the lung during inspiration and expiration. This occurs even if the devices are triggered “on” only during inspiration because there is entraining of media through the device during continual and adjusted supplemental flow associated with pressure and/or volume supported/controlled respiratory devices. These issues divert device-emitted drug away from the lung and diminishes the amount delivered to the patient. The end effect of these challenges is an unknown amount of actually administered drug as well as under administration of media.

There is a need in the art for improved devices and methods for depositing media into a lung with assistive devices. The present invention meets this need.

SUMMARY OF THE INVENTION

In one aspect, the present invention relates to a respiratory adapter for inhaled media deposition comprising: an inspiratory arm having a first end connectable to a ventilator and a second end connectable to a subject/patient breathing interface; an expiratory arm having a first end connectable to a ventilator and a second end connectable to the subject/patient breathing interface; a bypass flow bridge fluidly connecting the inspiratory arm and the expiratory arm between their first and second ends; a media port positioned in the inspiratory arm between its second end and the bypass flow bridge; and one or more valve positioned in each of the bypass flow bridge, in the inspiratory arm, and in the expiratory arm.

In one embodiment, the one or more valve positioned in the inspiratory arm is a one-way valve between the media port and the bypass flow bridge and directs gas to flow in the direction of the media port. In one embodiment, the one or more valve

positioned in the expiratory arm is a one-way valve between the second end of the expiratory arm and the bypass flow bridge and directs gas to flow in the direction of the bypass flow bridge. In one embodiment, the one or more valve positioned in the bypass flow bridge is a one-way valve and directs gas to flow in the direction of the expiratory arm.

In one embodiment, the media port is configured to fit a media reservoir, a media driver, or any combination thereof. In one embodiment, a media reservoir is integrated into the media port. In one embodiment, a media driver is integrated into the media port.

In one embodiment, the connector is a Y-connector. In one embodiment, the adapter further comprises at least one low flow sample port fluidly connected to the inspiratory arm. In one embodiment, the adapter further comprises at least one low flow sample port fluidly connected to the expiratory arm. In one embodiment, the adapter further comprises a sensor selected from the group consisting of: a pressure sensor, a flow sensor, a temperature sensor, an oxygen sensor, a carbon dioxide sensor, a media concentration sensor, and a humidity sensor. In one embodiment, the adapter is disposable. In one embodiment, the adapter is reusable.

In one embodiment, the adapter further comprises a housing encasing the inspiratory arm, the expiratory arm, and the bypass bridge, and having at least four ports to accommodate the first end of the inspiratory arm, the first end of the expiratory arm, the MRD port, and the connector port.

In another aspect, the present invention relates to a respiratory adapter for inhaled media deposition comprising: an inspiratory arm having a first end connectable to a ventilator and a second end connectable to a tube; an expiratory arm having a first end connectable to a ventilator and a second end connectable to a tube; a bypass flow bridge fluidly connecting the inspiratory arm and the expiratory arm between their first and second ends; a media reservoir and driver (MRD) port positioned in the inspiratory arm between its second end and the bypass flow bridge; one or more valve positioned in each of the bypass flow bridge and in the inspiratory arm; a housing encasing the inspiratory arm, the expiratory arm, and the bypass bridge, and having at least five ports to

accommodate the first and second end of the inspiratory arm, the first and second end of the expiratory arm, and the MRD port; a connector having a connector port, an inspiratory port, an expiratory port, and one or more valve positioned between the breathing port and the expiratory port.

5 In one embodiment, the one or more valve positioned in the inspiratory arm is a one-way valve between the media port and the bypass flow bridge and directs gas to flow in the direction of the media port. In one embodiment, the one or more valve positioned in the connector is a one-way valve and directs gas to flow in the direction of the expiratory port. In one embodiment, the one or more valve positioned in the bypass
10 flow bridge is a one-way valve and directs gas to flow in the direction of the expiratory arm.

 In one embodiment, the media port is configured to fit a media reservoir, a media driver, or any combination thereof. In one embodiment, a media reservoir is integrated into the media port. In one embodiment, a media driver is integrated into the
15 media port.

 In one embodiment, the connector is a Y-connector. In one embodiment, the adapter further comprises at least one low flow sample port fluidly connected to the inspiratory arm. In one embodiment, the adapter further comprises at least one low flow sample port fluidly connected to the expiratory arm. In one embodiment, the adapter
20 further comprises a sensor selected from the group consisting of: a pressure sensor, a flow sensor, a temperature sensor, an oxygen sensor, a carbon dioxide sensor, a media concentration sensor, and a humidity sensor. In one embodiment, the adapter is disposable. In one embodiment, the adapter is reusable.

25 BRIEF DESCRIPTION OF THE DRAWINGS

 The following detailed description of embodiments of the invention will be better understood when read in conjunction with the appended drawings. It should be understood, however, that the invention is not limited to the precise arrangements and instrumentalities of the embodiments shown in the drawings.

Figure 1A and Figure 1B are top-down schematics depicting exemplary respiratory adapter configurations and flow patterns.

Figure 2A and Figure 2B are perspective views of two exemplary respiratory adapters in housing units.

5 Figure 3A depicts an experimental respiratory adapter with a pneumotachometer in the inspiratory arm during ventilation of an artificial lung and aerosolization of saline. The components include 1) pneumotachometer, 2) bypass flow bridge, 3) media driver, 4) one-way valve.

10 Figure 3B depicts a monitor screen displaying real-time air-flow tracing in the device of Figure 3A measured by pneumotachometry.

Figure 4A depicts an experimental respiratory adapter with a pneumotachometer in the bypass flow bridge during ventilation of an artificial lung and aerosolization of saline. The components include 1) pneumotachometer, 2) bypass flow bridge, 3) media driver, 4) one-way valve.

15 Figure 4B depicts a monitor screen displaying real-time air-flow tracing in the device of Figure 4A measured by pneumotachometry.

Figure 5A depicts an experimental respiratory adapter with a pneumotachometer in the inspiratory arm during ventilation of an artificial lung and aerosolization of saline. The components include 1) pneumotachometer, 2) bypass flow bridge, 3) media driver, 4) one-way valve.

20 Figure 5B depicts a monitor screen displaying real-time air-flow tracing in the device of Figure 5A measured by pneumotachometry.

Figure 6A depicts a conventional respirator without a bypass flow bridge, wherein accumulation of emitted media is visible in the inspiratory line.

25 Figure 6B depicts an experimental respiratory adapter with a bypass flow bridge, demonstrating more sustained aerosolization of emitted media and reduced accumulation in the inspiratory line.

DETAILED DESCRIPTION

The present invention provides a respiratory adapter for inhaled media deposition in the lungs and airway. The respiratory adapter provides an inspiratory arm and an expiratory arm, wherein the two arms are joined by a bypass flow bridge. A system of valves, such as one-way valves, directs the flow of gas and media through the respiratory adapter to improve media deposition efficiency and to prevent re-breathing of exhaled gas.

Definitions

It is to be understood that the figures and descriptions of the present invention have been simplified to illustrate elements that are relevant for a clear understanding of the present invention, while eliminating, for the purpose of clarity, many other elements typically found in the art. Those of ordinary skill in the art may recognize that other elements and/or steps are desirable and/or required in implementing the present invention. However, because such elements and steps are well known in the art, and because they do not facilitate a better understanding of the present invention, a discussion of such elements and steps is not provided herein. The disclosure herein is directed to all such variations and modifications to such elements and methods known to those skilled in the art.

Unless defined elsewhere, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which this invention belongs. Although any methods and materials similar or equivalent to those described herein can be used in the practice or testing of the present invention, the exemplary methods and materials are described.

As used herein, each of the following terms has the meaning associated with it in this section.

The articles “a” and “an” are used herein to refer to one or to more than one (i.e., to at least one) of the grammatical object of the article. By way of example, “an element” means one element or more than one element.

“About” as used herein when referring to a measurable value such as an amount, a temporal duration, and the like, is meant to encompass variations of $\pm 20\%$,

$\pm 10\%$, $\pm 5\%$, $\pm 1\%$, and $\pm 0.1\%$ from the specified value, as such variations are appropriate.

Throughout this disclosure, various aspects of the invention can be presented in a range format. It should be understood that the description in range format is merely for convenience and brevity and should not be construed as an inflexible limitation on the scope of the invention. Accordingly, the description of a range should be considered to have specifically disclosed all the possible subranges as well as individual numerical values within that range. For example, description of a range such as from 1 to 6 should be considered to have specifically disclosed subranges such as from 1 to 3, from 1 to 4, from 1 to 5, from 2 to 4, from 2 to 6, from 3 to 6, etc., as well as individual numbers within that range, for example, 1, 2, 2.7, 3, 4, 5, 5.3, 6, and any whole and partial increments there between. This applies regardless of the breadth of the range.

Respiratory Adapter

There is a widespread need for administering media (e.g., therapeutic or diagnostic) through the inhaled pulmonary pathway. Because of physiologic compensation of the pulmonary circulation to constrict with certain disease states, it is difficult for agents that are given systemically to reach the lungs. To overcome this challenge, systemically administered lung targeted drugs are given at higher than needed doses. The direct pulmonary administration approach provides the greatest opportunity to diagnose/treat the lung or use the lung to enhance delivery of drugs systemically. A wide range of therapeutics, biomarkers, and tracers for inhaled delivery to the lung have been developed for both lung and systemic organ application.

Because of loss through circuit delivering, procedurally, the method of administration to the patient is characterized by the amount emitted by devices, rather than that delivered to the lung, and the “effect” is determined by other assessment methods. For example, despite the advent of patient or ventilator triggered devices for output only during the inspiratory cycle, there remains loss of these media both during inspiration and expiration due to flow through the media reservoir and adjustments to the supplemental flow associated pressure and/or volume controlled respiratory assist devices

(e.g., ventilators, CPAP etc.). The present invention addresses the problems faced by conventional respiratory assist methods in at least 3 aspects: 1) greater possibility of administering actual doses, rather than device “emitted doses” to the lung; 2) minimized amounts of media needed, thus providing more cost-effective approaches; 3) minimized
5 loss of media to the circuit and into the environment.

Referring now to Figure 1A and Figure 1B, an exemplary respiratory adapter 10 is depicted. Respiratory adapter 10 comprises inspiratory arm 16 having a first end connected to inspiratory port 13 and a second end connected to connector 12, and expiratory arm 18 having a first end connected to expiratory port 14 and a second end
10 connected to connector 12. As will be understood by those having skill in the art, inspiratory port 13 and expiratory port 14 are universal ports that can connect to any respiratory assist device or ventilation system, such as a continuous positive airway pressure (CPAP) or bi-level positive airway pressure (BPAP) machine, or any other driver of gas flow to and from a patient. Connector 12 can be any suitable connector
15 used in the art that connects to a breathing interface to deliver a gas to and from a patient through one or more connector ports 11, such as a Y-connector. It should be understood that the gas can be any gas (such as air, oxygen, therapeutic gas mixtures, and the like), and that gas encompasses all inhaled and exhaled gas mixtures within the context of the present invention. Connector 12 can further comprise any number of valves to control
20 exhaled flow toward expiratory arm 18 (not shown). Inspiratory arm 16 and expiratory arm 18 are fluidly connected between their respective first and second ends by bypass flow bridge 20. A media reservoir and driver (MRD) port 22 is positioned between the second end of inspiratory arm 16 and bypass flow bridge 20. MRD port 22 may be compatible with and be engaged to any suitable media storage and dispensing mechanism
25 commonly used in the art. In some embodiments, a media reservoir and/or driver may be integrated directly into respiratory adapter 10 as a single unit.

Respiratory adapter 10 comprises several valves, such as one-way valves that direct or otherwise permit gas and media flow in one desired direction only. In various embodiments, respiratory adapter 10 has at least one or more one-way valves 24a
30 positioned in bypass flow bridge 20. The one or more one-way valve 24a directs flow

from inspiratory arm 16 into expiratory arm and blocks expired gas from entering inspiratory arm 16 to prevent re-breathing. The one or more one-way valve 24a also permits gas to bypass MRD port 22 when a patient is not inhaling, thereby conserving media. In various embodiments, respiratory adapter 10 has one or more one-way valve 5 24b positioned in inspiratory arm 16 between MRD port 22 and bypass flow bridge 20. The one or more one-way valve 24b directs flow from the first end of inspiratory arm 16 towards the second end of inspiratory arm 16 and prevents media from escaping into expiratory arm 18 and bypassing a patient during exhalation. In various embodiments, respiratory adapter 10 has one or more one-way valve 24c positioned in expiratory arm 10 18 between the second end of expiratory arm 18 and bypass flow bridge 20. The one or more one-way valve 24c directs flow from the second end of expiratory arm 18 towards the first end of expiratory arm 18 and blocks expired gas flow in expiratory arm 18 from returning to a patient during inhalation. In various embodiments, respiratory adapter 10 can further comprise multiple valves 24d, 24e, or more to supplement flow direction 15 guidance (Figure 1B).

In some embodiments, the one-way valves of the present invention open mechanically in response to a gas pressure difference across the valve. For example, respiratory adapter 10 can comprise one or more one-way valve 24b and/or one-way valve 24c having a higher activation pressure than the one or more one-way valve 24a. 20 When a patient is in an inspiratory hold, gas flowing into inspiratory arm 16 is at a pressure sufficient to open the one or more one-way valve 24a but insufficient to open the one or more one-way valve 24b. During inhalation, the pressure drop upstream of media port 22 opens the one or more one-way valve 24b while keeping the one or more one-way valve 24c closed to direct at least a portion of incoming gas into connector 12. During 25 exhalation, the increase in pressure upstream of media port 22 keeps the one or more one-way valve 24b closed while opening the one or more one-way valve 24c to direct exhaled gas into expiratory arm 18.

In other embodiments, the present invention uses one- or two-way valves that are electronically controlled. For example, respiratory adapter 10 can comprise 30 valves that are toggled to be open or closed according to a separate controller responding

to a breath sensor, synced to a ventilator, or linked to any other respiratory driver. As described elsewhere herein, the valves can be controlled to open and close in a pattern in accordance to in an inhalation phase, an exhalation phase, and an inspiratory hold phase. In the inhalation phase, the valves in inspiratory arm 16 can be controlled to be open, and
5 all other valves controlled to be closed. In the exhalation phase, the valves in expiratory arm 18 can be controlled to be open, and all other valves can be controlled to be closed. In an inspiratory hold phase, the valves in bypass flow bridge 20 can be open, and valves leading to media port 22 can be controlled to be closed. Exemplary one-way and two-way valves include duckbill valves, umbrella valves, ball valves, dome valves. Belleville
10 valves, cross-slit valves, combination valves and the like.

In certain embodiments, respiratory adapter 10 can comprise any suitable sensors, such as pressure sensors, flow sensors, temperature sensors, oxygen sensors, carbon dioxide sensors, media concentration sensors, humidity sensors, and the like. The one or more sensors can be positioned in one or more low flow sample port to measure
15 inhaled or exhaled gas. For example, one or more sensors can be positioned in sample port 26a positioned within inspiratory arm 16 to measure inhaled gas composition, or sample port 26b positioned within expiratory arm 18 to measure exhaled gas composition (Figure 1B). The one or more sensors can also be positioned for sensing directly in inspiratory arm 16 and/or in expiratory arm 18. Sample port 26a and 26b can each have
20 at least one valve 24f and/or 24g, respectively, to toggle an amount of gas to be analyzed.

Referring now to Figure 2A and Figure 2B, two exemplary configurations of respiratory adapter 10 are depicted. Figure 2A depicts an all-in-one unit, wherein the entirety of the layout of respiratory adapter 10 are encased within housing 30a. Housing 30a presents at least four openings corresponding to connector port 11 of connector 12,
25 MRD port 22, inspiratory port 13, and expiratory port 14. Figure 2B depicts an extendable unit, wherein connector 12, comprising connector port 11, third one-way valve 24c, inspiratory port 13c, and expiratory port 14c, is remote from the rest of the components of respiratory adapter 10 encased within housing 30b. Housing 30b presents at least five openings corresponding to MRD port 22, inspiratory port 13a, inspiratory
30 port 13b, expiratory port 14a, and expiratory port 14b. An extendable respiratory adapter

10 enables inspiratory arm 16 and expiratory arm 18 to be extended by any lengths of tubes connecting inspiratory port 13c with inspiratory port 13b and expiratory port 14c with expiratory port 14b. It should be understood that the embodiments depicted in Figure 2A and Figure 2B are amenable to any suitable modification for alternative port placement. For example, the various ports can be positioned on any suitable surface of housing 30a and housing 30b. Housing 30a and housing 30b can each further comprise one or more additional ports to accommodate one or more additional sample ports. In certain embodiments, respiratory adapter 10 can include one or more labeling features to indicate which port corresponds to inspiration or expiration. For example, housing 30a and housing 30b may include direct labeling, such as "From Ventilator" for inspiratory port 13a and "To Ventilator" for expiratory port 14a. Housing 30a and housing 30b may also include color indicators, such as a clear or white coloring for inspiratory ports 13a, 13b, and 13c, and blue coloring for expiratory ports 14a, 14b, and 14c. Housing 30a and housing 30b can have any suitable shape, and can include any separable attachment components as desired, such as one or more clips, hooks, hangers, mounting points, and the like. Housing 30a and housing 30b can be constructed from an opaque material or from an at least partially transparent material. The transparent material can be plastic or glass and can help a user visualize the internal components of respiratory adapter 10 to ascertain orientation or to identify malfunctions.

20 In various embodiments, housing 30a and housing 30b package respiratory adapter 10 in a small form factor for enhanced portability. Respiratory adapter 10 can thereby be deployed in any number of uses, such as in the field for military or emergency applications, or in a hospital or home facility. Respiratory adapter 10 and its several components may be disposable or reusable.

25 The devices of the present invention can be made using any suitable method known in the art. The method of making may vary depending on the materials used. For example, components substantially comprising a plastic or polymer may be milled from a larger block or injection molded. Likewise, components substantially comprising a metal may be milled, cast, etched, or deposited by techniques such as chemical vapor deposition, spraying, sputtering, and ion plating. In some embodiments,

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the devices may be made using 3D printing techniques commonly used in the art. The ports, connectors, and valves may be of standard or universal designs as would be understood by those skilled in the art.

5 Method of Use

 The respiratory adapter of the present invention is suitable for integration within any respiratory circuit commonly used in the art. As shown in Figure 1A and 1B, the respiratory adaptor receives driving flow through inspiratory arm 16 (such as a ventilator) which is connected through a “T” junction to bypass flow bridge 20 and MRD
10 port 22. As described elsewhere herein, bypass flow bridge 20 comprises one-way valve 24a to divert flow away from the MRD during inspiration in situations of inspiratory holds, or expiration in situations of variable flow, thereby reducing loss of media from the media reservoir. One-way valve 24a also prevents carbon dioxide-rich expiratory flow from the patient from reentering the inspiratory circuit and causing re-breathing of
15 expired gas. One-way valve 24b positioned between MRD port 22 and the “T” junction at bypass flow bridge 20 prevents the driving flow from reversing backwards into inspiratory arm 16 at the end of inspiration. This would offset condensation, settling, and eventual loss of media at this point. One-way valve 24c positioned in expiratory arm 18 between connector 12 and the “T” junction at bypass flow bridge 20 prevents re-
20 breathing of exhaled gas.

EXPERIMENTAL EXAMPLES

 The invention is further described in detail by reference to the following experimental examples. These examples are provided for purposes of illustration only,
25 and are not intended to be limiting unless otherwise specified. Thus, the invention should in no way be construed as being limited to the following examples, but rather, should be construed to encompass any and all variations which become evident as a result of the teaching provided herein.

 Without further description, it is believed that one of ordinary skill in the
30 art may, using the preceding description and the following illustrative examples, utilize

the present invention and practice the claimed methods. The following working examples therefore, specifically point out exemplary embodiments of the present invention, and are not to be construed as limiting in any way the remainder of the disclosure.

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Example 1: Respiratory adapter improves flow efficiency and reduces loss of media

Bench top studies were performed using the respiratory adapter with a pneumotachometer at various locations to demonstrate sparing of flow and media contact, which effectively reduces loss of media during both inspiratory and expiratory flow cycles. As shown in Figure 3A, a pneumotachometer was placed in line with the inspiratory arm, distal to the media generator and bypass flow bridge. As shown in Figure 3B, this configuration supports flow only in the inspiratory phase. In addition to this configuration, pneumotachometers were placed in two additional locations: the bridge and the expiratory arm distal to the artificial lung (not shown). In these configurations, the flow tracings demonstrated flow and media sparing at the appropriate phases of respiration. For example, when positioned in the expiratory arm, no flow was observed during inspiration as all flow was directed either into the artificial lung or across the bridge. When placed in the bridge, no flow was observed during expiration, demonstrating sparing of flow recycling through the bridge onward through the media driver.

In addition to the configuration in Figure 3A, the pneumotachometer was positioned in two additional locations: the bridge (Figure 4A) and in the expiratory arm (Figure 5A) just distal to the artificial lung. In these configurations, the flow tracings demonstrated flow, and therefore media sparing at the appropriate phases of respiration. For example, when the pneumotachometer was positioned in the bridge, expiratory flow from the artificial lung that traversed the bridge (Figure 4B, left circle) was “blocked” by the one-way valve at the circled intersection (Figure 4A) located in the inspiratory line between the bridge and media generator. In addition, when placed in the bridge, no flow was observed during expiration (Figure 4B, right circle), demonstrating sparing of flow recycling through the bridge onward through the media driver. This demonstrates

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prevention of expiratory carbon dioxide rich gas from mixing with and/or entering the inspiratory arm, thereby preventing re-breathing of expiratory gas as well as decreasing loss of media by entrainment, thus preserving media within the reservoir.

As shown in Figure 5A, when the pneumotachometer was positioned in the expiratory arm, there was no flow observed during inspiration (Figure 5B, circle; no downward signal on second tracing) demonstrating inspiratory flow directed into the artificial lung with flow occurring only in the expiratory phase. This has the effect of improving the potential for deposition of media from the media generator into the lung during inspiration with loss of media due only to what is exhaled from the lung.

As shown in Figure 6A and Figure 6B, the respirator adapter has the effect of mitigating the loss of emitted media to the inspiratory circuit itself. These studies were performed with a dye added to the saline, which was then aerosolized without (Figure 6A) or with (Figure 6B) the respiratory adapter in place. As shown in Figure 6A, there was substantial condensation and accumulation of emitted media in the inspiratory line as compared to the respiratory adapter in place. The presence of emitted media in aerosolized form was substantially maintained in the inspiratory flow and accumulation along the walls of the inspiratory line was greatly reduced.

Example 2: A respiratory bridge adapter (RBA) for improved inhaled media delivery

Despite the use of patient or ventilator triggered aerosol/nebulizer (A/N) devices for delivery during inspiration, media loss remains during both inspiration (I) and expiration (E) due to bias flow through the media reservoir and flow adjustments associated with pressure and/or volume controlled respiratory assist devices. As such, the recommended dose is not delivered and targeted dosing is often “to effect”. Furthermore, with the development of expensive therapeutics, biomarkers, and tracers for inhaled delivery, there is an additional economic need for maximizing delivery and deposition of these media in the lung.

The RBA design is based on an (I) and (E) arm, each with a proximal and distal end. A bypass flow bridge connects the (I) and (E) arms near their distal ends and a media reservoir/driver (MRD) port is positioned in the (I) arm between its proximal end

and the bypass flow bridge. One-way valves are positioned in the (I) and (E) arms, and the bypass bridge directs flow of gas and media. The RBA design was bench tested with pneumotachometers in the (I), (E), and bypass bridge arms during pressure and/or volume controlled ventilation (neonatal and adult) of an artificial lung and aerosolization of aqueous, dyed media. Flows, pressures and visualization (videography) of aerosol mist were monitored throughout ventilation cycles. Since MRD media delivery efficiency is media property, MRD, and ventilator property specific, *in vivo* testing of the RBA was performed in parallel with pressure controlled ventilation during continuous aerosolization of saline in an adult sheep hemorrhage/pneumonectomy model, and volume controlled ventilation during ventilator triggered aerosolization of plasminogen activators in an adult sheep smoke inhalation model.

Experimental flow data and videos of aerosol mist patterns demonstrated more sustained aerosolized emitted media, reduced media accumulation in the (I) line, and reduced media loss in the (E) line. Time required to deliver a complete aerosol dose increased ($\geq 25\%$) due to sparing of media via the (E) limb. Targeted ventilator flows, volumes, and pressures were unchanged with the RBA in-line.

The disclosures of each and every patent, patent application, and publication cited herein are hereby incorporated herein by reference in their entirety. While this invention has been disclosed with reference to specific embodiments, it is apparent that other embodiments and variations of this invention may be devised by others skilled in the art without departing from the true spirit and scope of the invention. The appended claims are intended to be construed to include all such embodiments and equivalent variations.

25

CLAIMS

What is claimed is:

1. A respiratory adapter for inhaled media deposition comprising:
an inspiratory arm having a first end connectable to a ventilator and a second end connectable to a subject/patient breathing interface;
an expiratory arm having a first end connectable to a ventilator and a second end connectable to the subject/patient breathing interface;
a bypass flow bridge fluidly connecting the inspiratory arm and the expiratory arm between their first and second ends;
a media port positioned in the inspiratory arm between its second end and the bypass flow bridge; and
one or more valve positioned in each of the bypass flow bridge, in the inspiratory arm, and in the expiratory arm.
2. The adapter of claim 1, wherein the one or more valve positioned in the inspiratory arm is a one-way valve between the media port and the bypass flow bridge and directs gas to flow in the direction of the media port.
3. The adapter of claim 1, wherein the one or more valve positioned in the expiratory arm is a one-way valve between the second end of the expiratory arm and the bypass flow bridge and directs gas to flow in the direction of the bypass flow bridge.
4. The adapter of claim 1, wherein the one or more valve positioned in the bypass flow bridge is a one-way valve and directs gas to flow in the direction of the expiratory arm.
5. The adapter of claim 1, wherein the media port is configured to fit a media reservoir, a media driver, or any combination thereof.

6. The adapter of claim 1, wherein a media reservoir is integrated into the media port.
7. The adapter of claim 1, wherein a media driver is integrated into the media port.
8. The adapter of claim 1, wherein the connector is a Y-connector.
9. The adapter of claim 1, further comprising at least one low flow sample port fluidly connected to the inspiratory arm.
10. The adapter of claim 1, further comprising at least one low flow sample port fluidly connected to the expiratory arm.
11. The adapter of claim 1, further comprising a sensor selected from the group consisting of: a pressure sensor, a flow sensor, a temperature sensor, an oxygen sensor, a carbon dioxide sensor, a media concentration sensor, and a humidity sensor.
12. The adapter of claim 1, wherein the adapter is disposable.
13. The adapter of claim 1, wherein the adapter is reusable.
14. The adapter of claim 1, further comprising a housing encasing the inspiratory arm, the expiratory arm, and the bypass bridge, and having at least four ports to accommodate the first end of the inspiratory arm, the first end of the expiratory arm, the MRD port, and the connector port.
15. A respiratory adapter for inhaled media deposition comprising:
 - an inspiratory arm having a first end connectable to a ventilator and a second end connectable to a tube;
 - an expiratory arm having a first end connectable to a ventilator and a second end connectable to a tube;
 - a bypass flow bridge fluidly connecting the inspiratory arm and the

expiratory arm between their first and second ends;

a media reservoir and driver (MRD) port positioned in the inspiratory arm between its second end and the bypass flow bridge;

one or more valve positioned in each of the bypass flow bridge and in the inspiratory arm;

a housing encasing the inspiratory arm, the expiratory arm, and the bypass bridge, and having at least five ports to accommodate the first and second end of the inspiratory arm, the first and second end of the expiratory arm, and the MRD port;

a connector having a connector port, an inspiratory port, an expiratory port, and one or more valve positioned between the breathing port and the expiratory port.

16. The adapter of claim 15, wherein the one or more valve positioned in the inspiratory arm is a one-way valve between the media port and the bypass flow bridge and directs gas to flow in the direction of the media port.

17. The adapter of claim 15, wherein the one or more valve positioned in the connector is a one-way valve and directs gas to flow in the direction of the expiratory port.

18. The adapter of claim 15, wherein the one or more valve positioned in the bypass flow bridge is a one-way valve and directs gas to flow in the direction of the expiratory arm.

19. The adapter of claim 15, wherein the media port is configured to fit a media reservoir, a media driver, or any combination thereof.

20. The adapter of claim 15, wherein a media reservoir is integrated into the media port.

21. The adapter of claim 15, wherein a media driver is integrated into the media port.

22. The adapter of claim 15, wherein the connector is a Y-connector.

23. The adapter of claim 15, further comprising at least one low flow sample port fluidly connected to the inspiratory arm.

24. The adapter of claim 15, further comprising at least one low flow sample port fluidly connected to the expiratory arm.

25. The adapter of claim 15, further comprising a sensor selected from the group consisting of: a pressure sensor, a flow sensor, a temperature sensor, an oxygen sensor, a carbon dioxide sensor, a media concentration sensor, and a humidity sensor.

26. The adapter of claim 15, wherein the adapter is disposable.

27. The adapter of claim 15, wherein the adapter is reusable.

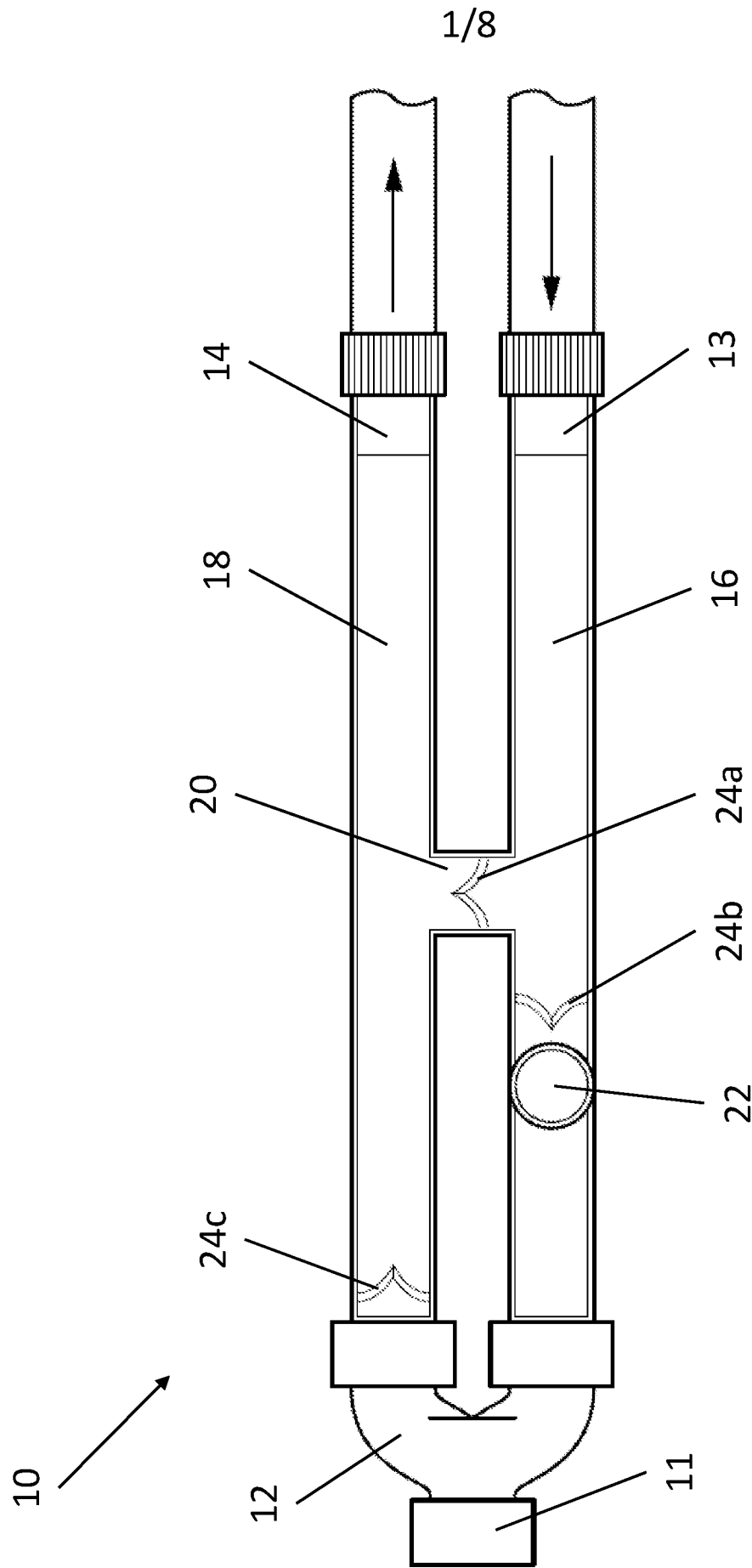


Figure 1A

2/8

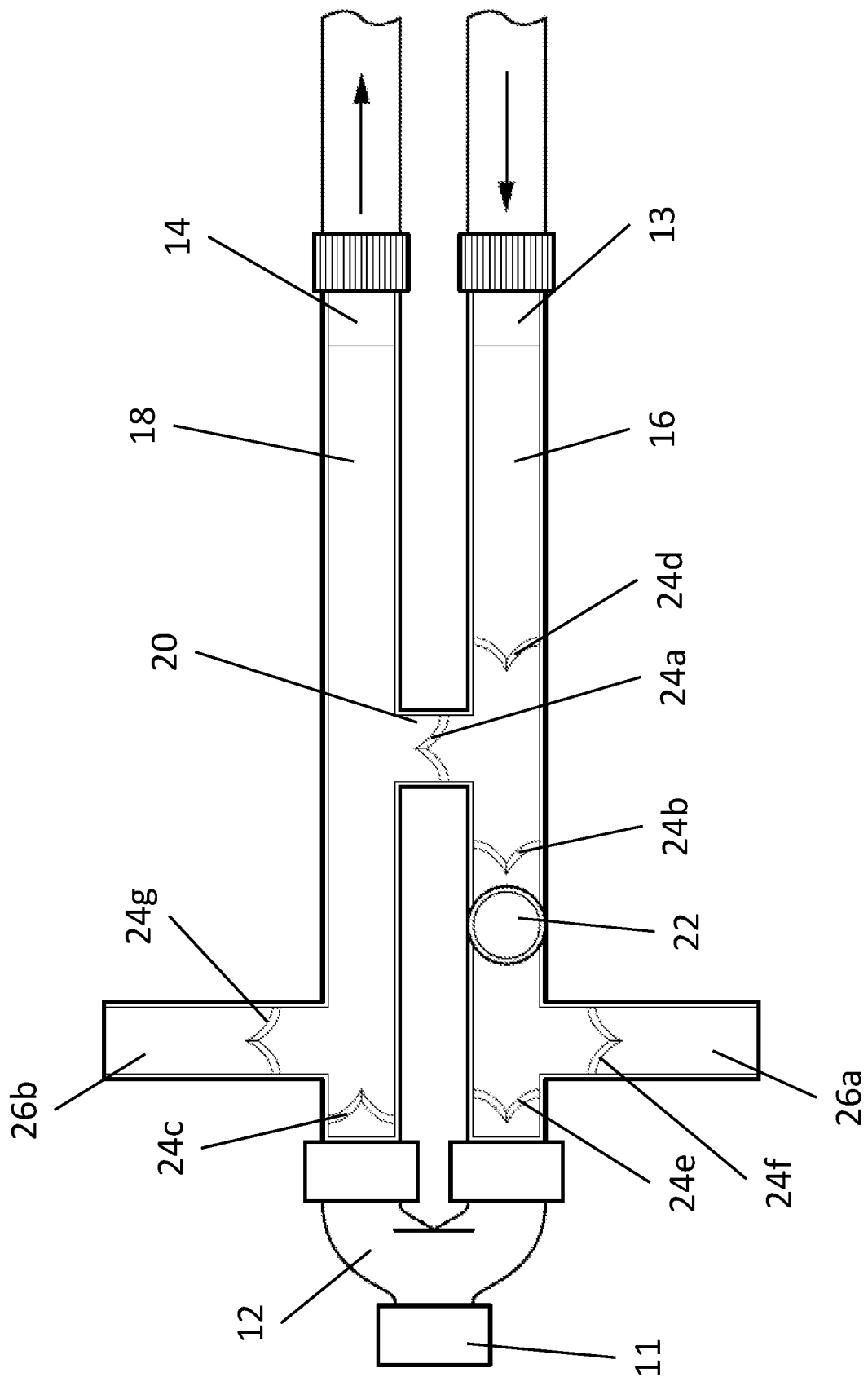


Figure 1B

3/8

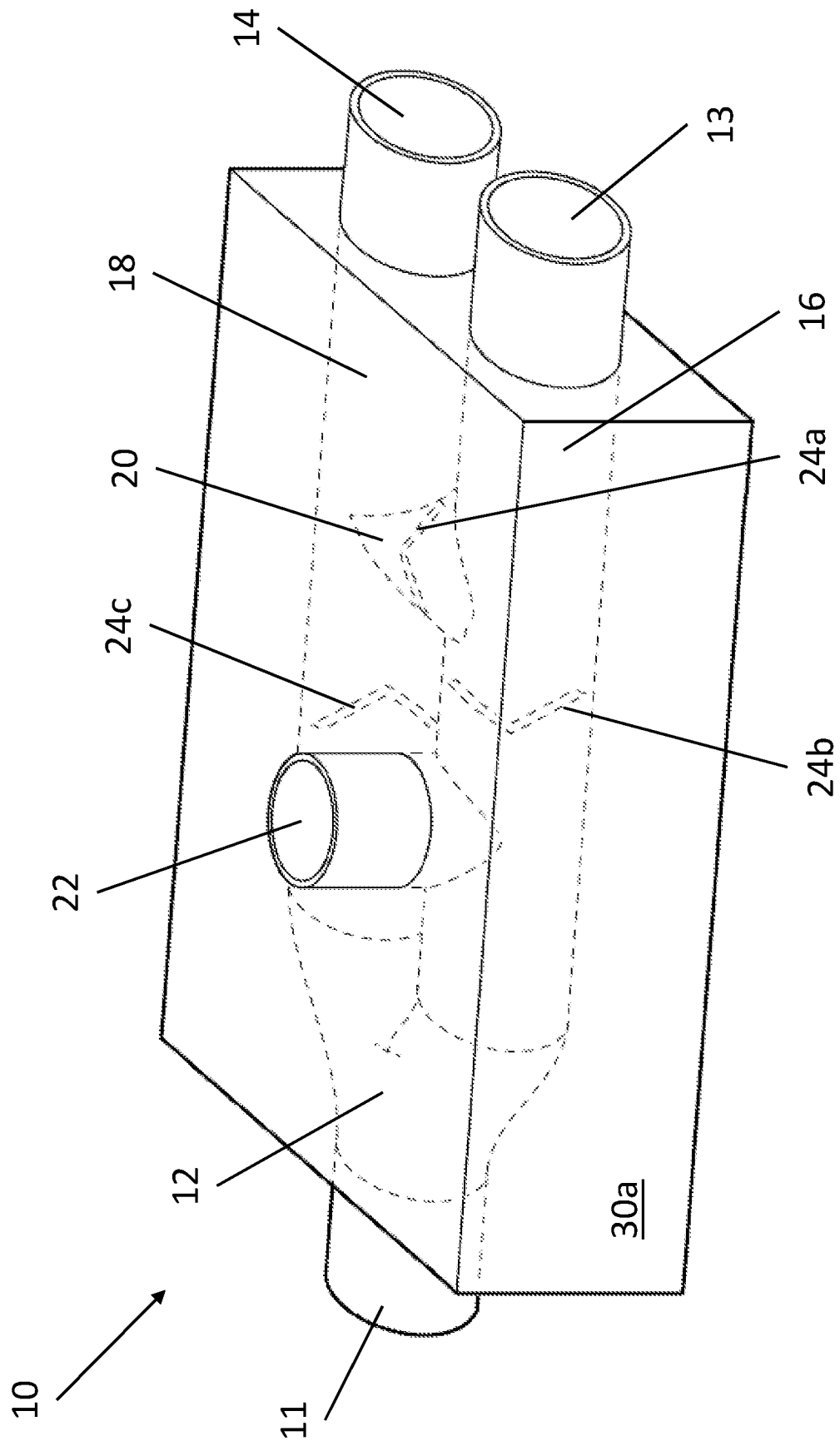


Figure 2A

4/8

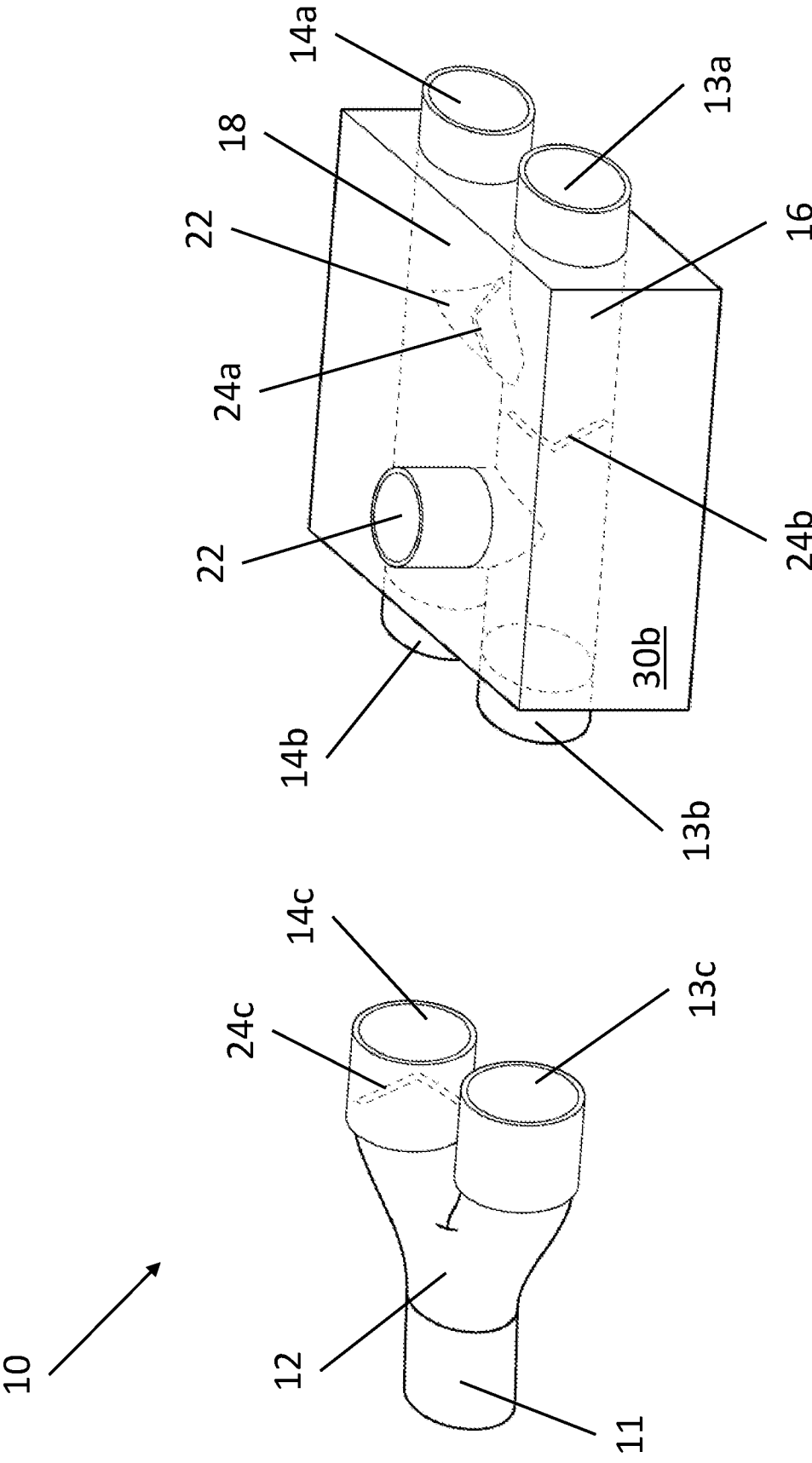


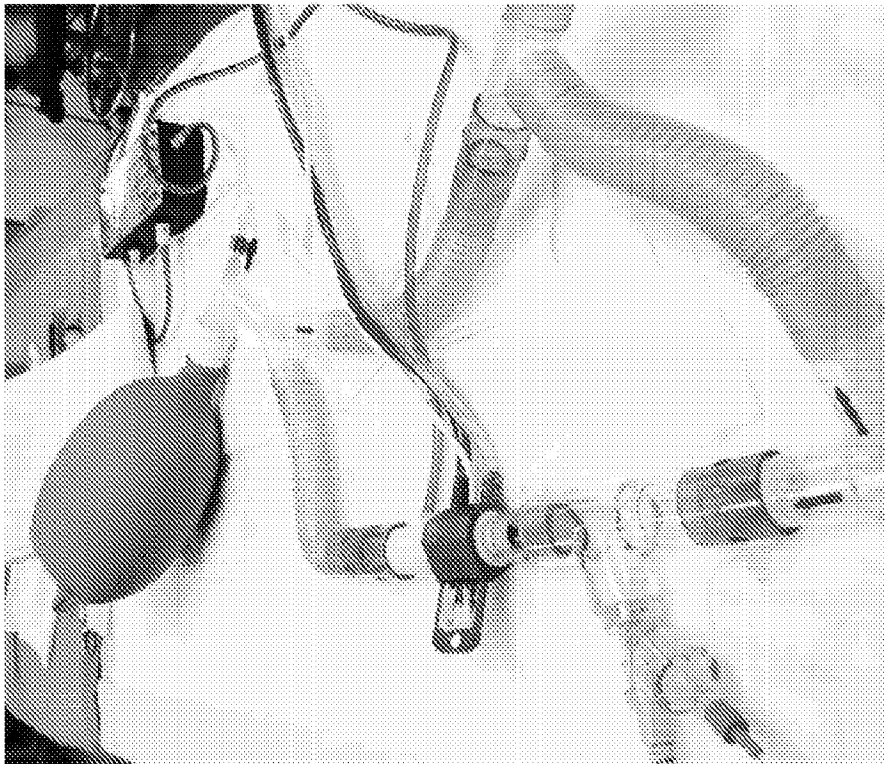
Figure 2B

5/8

Figure 3B



Figure 3A



6/8

Figure 4B

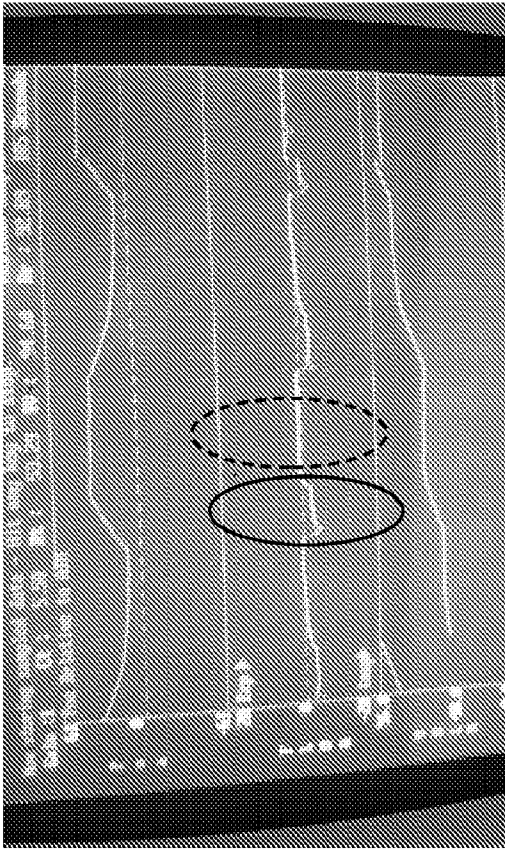


Figure 4A

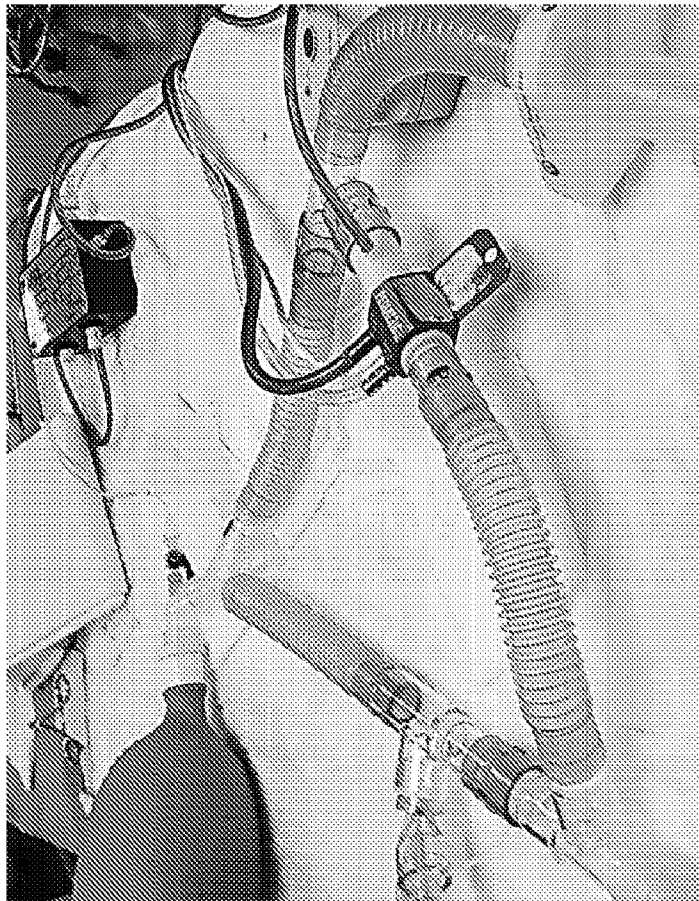
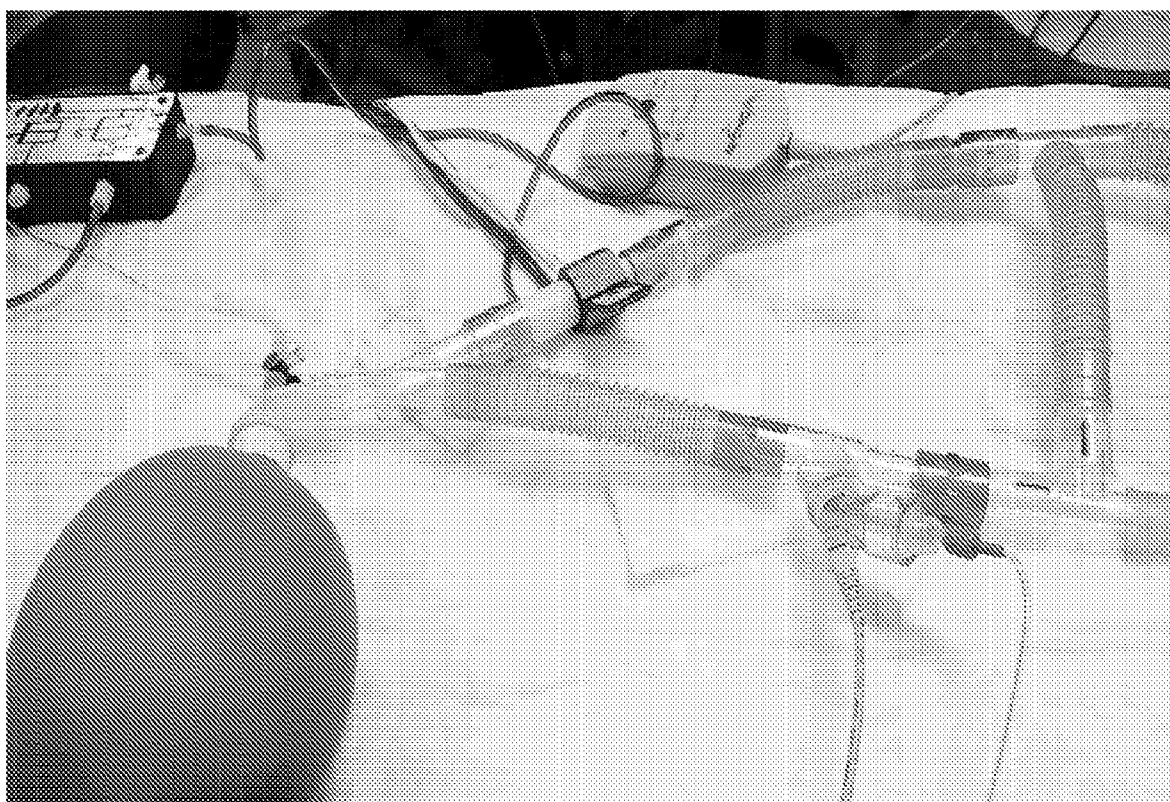


Figure 5B



Figure 5A



8/8

Figure 6B

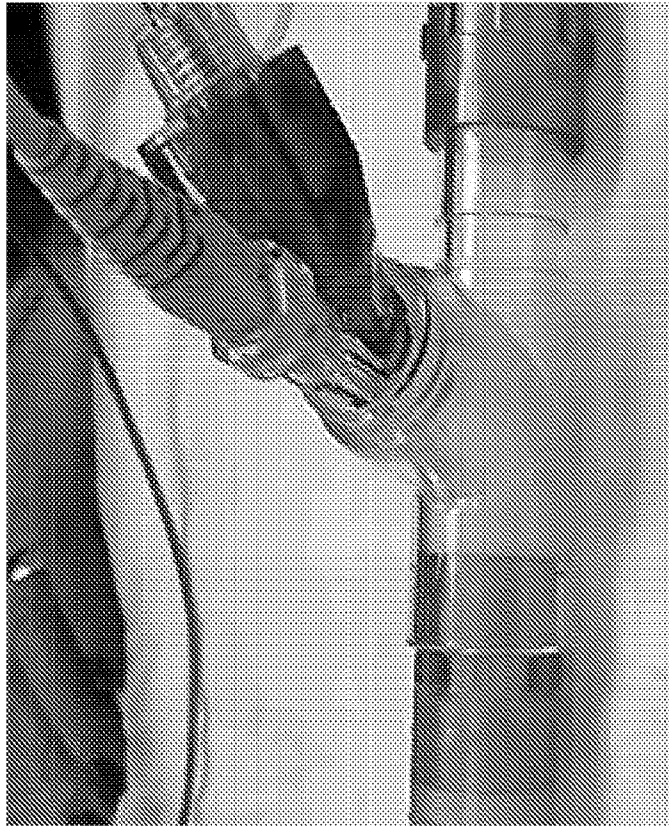
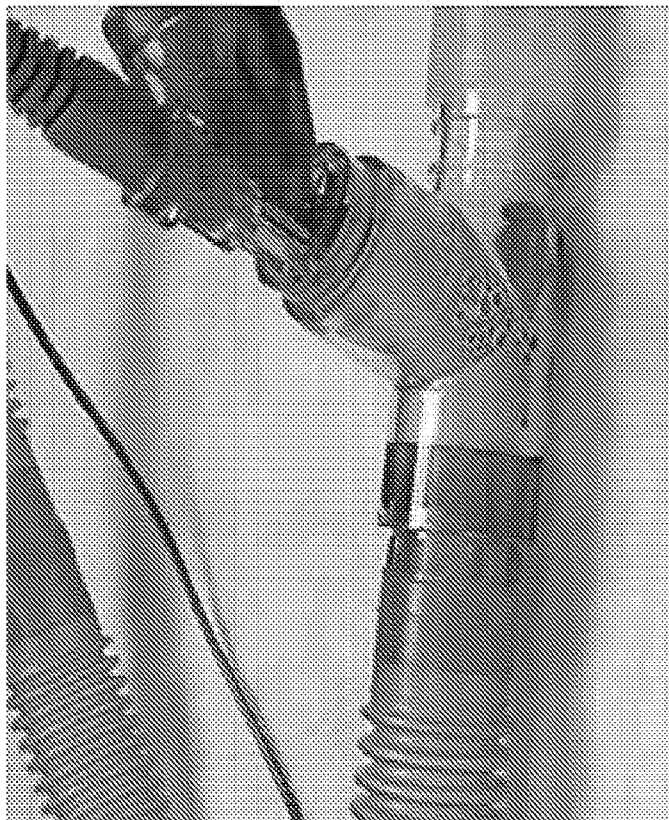


Figure 6A



INTERNATIONAL SEARCH REPORT

International application No.

PCT/US2017/028038

A. CLASSIFICATION OF SUBJECT MATTER

IPC(8) - A61M 16/00; A61M 16/04; A61M 16/08 (2017.01)

CPC - A61M 16/0054; A61M 16/0463; A61M 16/0465; A61M 16/0488; A61M 16/049; A61M 16/0493; A61M 16/0495; A61M 16/0816; A61M 16/0825; A61M 16/0833; A61M 16/0841; A61M 16/085; A61M 16/0858; A61M 16/20 (2017.02)

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

See Search History document

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

USPC - 128/200.24; 128/204.17; 128/204.18; 128/204.21; 128/204.22; 128/204.23; 128/205.24; 600/538 (keyword delimited)

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

See Search History document

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2007/0062534 A1 (FISHER et al) 22 March 2007 (22.03.2007) entire document	1, 4-13
A	US 6,209,539 B1 (LOESCHER et al) 03 April 2001 (03.04.2001) entire document	1-27
A	US 2013/0345586 A1 (THORNHILL SCIENTIFIC INC) 26 December 2013 (26.12.2013) entire document	1-27
A	US 2010/0031964 A1 (TUREK et al) 11 February 2010 (11.02.2010) entire document	1-27

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

* Special categories of cited documents:

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"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search

09 June 2017

Date of mailing of the international search report

03 JUL 2017

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