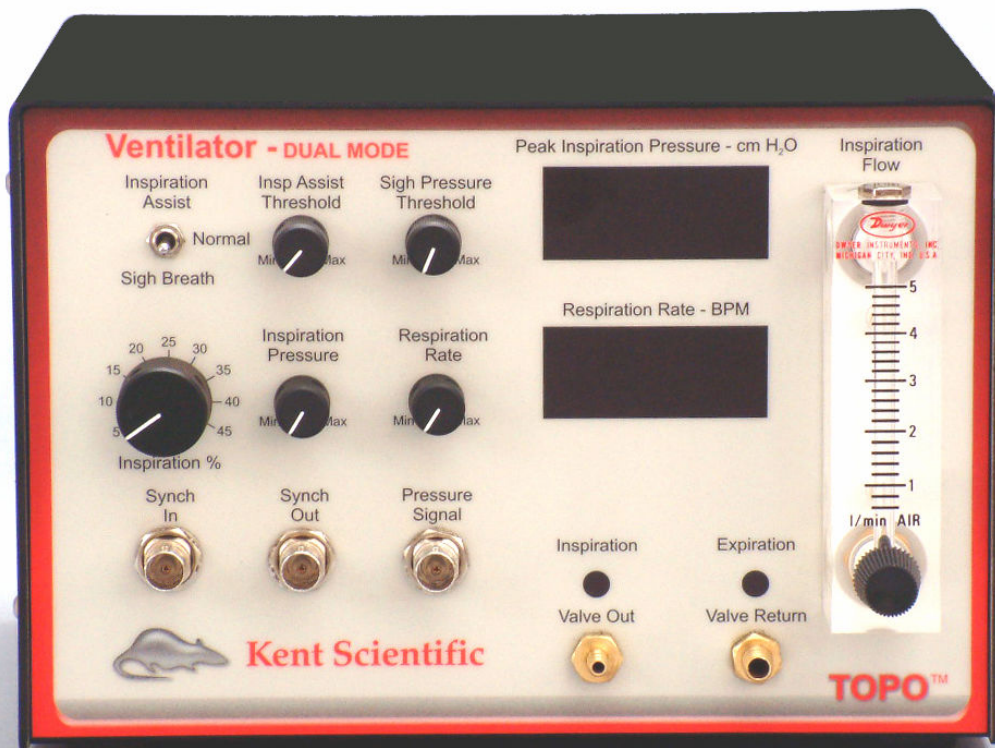




Kent Scientific Corporation

TOPO

DUAL MODE VENTILATOR



Operating Manual

July 2005



Kent Scientific Corporation

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NOTE: In January of 2004, the front and rear nameplates of the TOPO were changed to reflect the new name (TOPO). Consequently, if you received a unit manufactured prior to January 2004, some of the labeling on the front of the ventilator may not completely match the digital photographs in this manual. The functionality however is completely the same. Descriptions of each control as described in the text, has remained unchanged.

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1.0. General Information

Thank you for purchasing our TOPO Dual Mode Ventilator System. To truly appreciate and properly operate this product, we highly suggest you read this manual in detail.

1.1. Please contact us for any further assistance:

Kent Scientific Corporation
1116 Litchfield St.,
Torrington, CT 06790
Tel: 860-626-1172 (Toll Free: 1-888-5RATTUS)
Fax: 860-626-1179
e-mail: kentsci2@kentscientific.com

1.2. Disclaimer

Kent Scientific Corporation makes no representations or warranties, expressed, statutory or implied, regarding the fitness or merchantability of the components of this system for any particular purpose. Further, Kent Scientific Corporation is not liable for any damages, including but not limited to, lost profits, lost savings, or other incidental or consequential damages arising from ownership or use of these products, or for any delay in the performance of its obligations under the warranty due to causes beyond its control. Kent Scientific Corporation also reserves the right to make any improvements or modifications to these products described in this manual at any time, without notice of these changes. All brand and product names used in this manual are the trademarks of their respective owners.

Kent Scientific products are not designed, intended, or authorized for use in human applications

1.3. Warranty

Kent Scientific Corporation provides a one-year warranty including parts and labor. Glassware and plastic components are warranted for 30 days. The warranty commences on the date of shipment from Kent Scientific facility.

Repairs: Kent Scientific Corporation requires a Return Manufacturer Authorization (RMA) number before the product can be shipped to our facility. It is the option of the manufacturer to replace or repair a defective part or product.

This warranty does not cover damage by any cause including, but not limited to, any malfunction, defect or failure caused by or resulting from unauthorized service or parts, improper maintenance, operation contrary to furnished instructions, shipping or transit accidents, modifications or repair by the user, harsh environments, misuse, neglect,



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abuse, accident, incorrect line voltage, fire, food, other natural disasters, or normal wear and tear. Changes or modifications not approved by Kent Scientific Corporation could void the warranty. The foregoing is in lieu of all other expressed warranties. Kent Scientific Corporation does not assume or authorize any party to assume for it any other obligation or liability.

1.4. Customer Satisfaction Information

We, at Kent Scientific, would like to provide you with information and contact with researchers that may be performing research studies of interest to you. In addition, our current customers would benefit from your research. If you are willing to share the results of your studies with the research community, we will be pleased to disseminate your research to our list of references.

Customer feedback is very important to us. We value your opinion and would greatly appreciate your recommendations in order to continually improve the quality of our products.

2.0 Specifications

<u>Voltage</u>	<u>120 / 220 VAC</u>
<u>Current Draw</u>	<u>Approx. .5 Amp</u>
<u>Respiration rate</u>	<u>Approx 10-200 BPM</u>
<u>Pressure Transducer</u>	<u>-10 to +30 cm H2O</u>
<u>Pressure signal BNC</u>	<u>1-5 VDC</u>
<u>Inspiration Pressure cutoff</u>	<u>-10 to +30 cm H2O</u>
<u>Sigh Pressure</u>	<u>-10 to +30 cm H2O</u>
<u>Respiration Assist</u>	<u>-10 to +30 cm H2O</u>
<u>External Trigger</u>	<u>5-12 VDC for > 1 ms</u>
<u>Sync Out</u>	<u>5 VDC Following Exp Valve</u>
<u>Inspiration Flow</u>	<u>0-5 Liters Per Minute</u>

3.0 Overview of Features

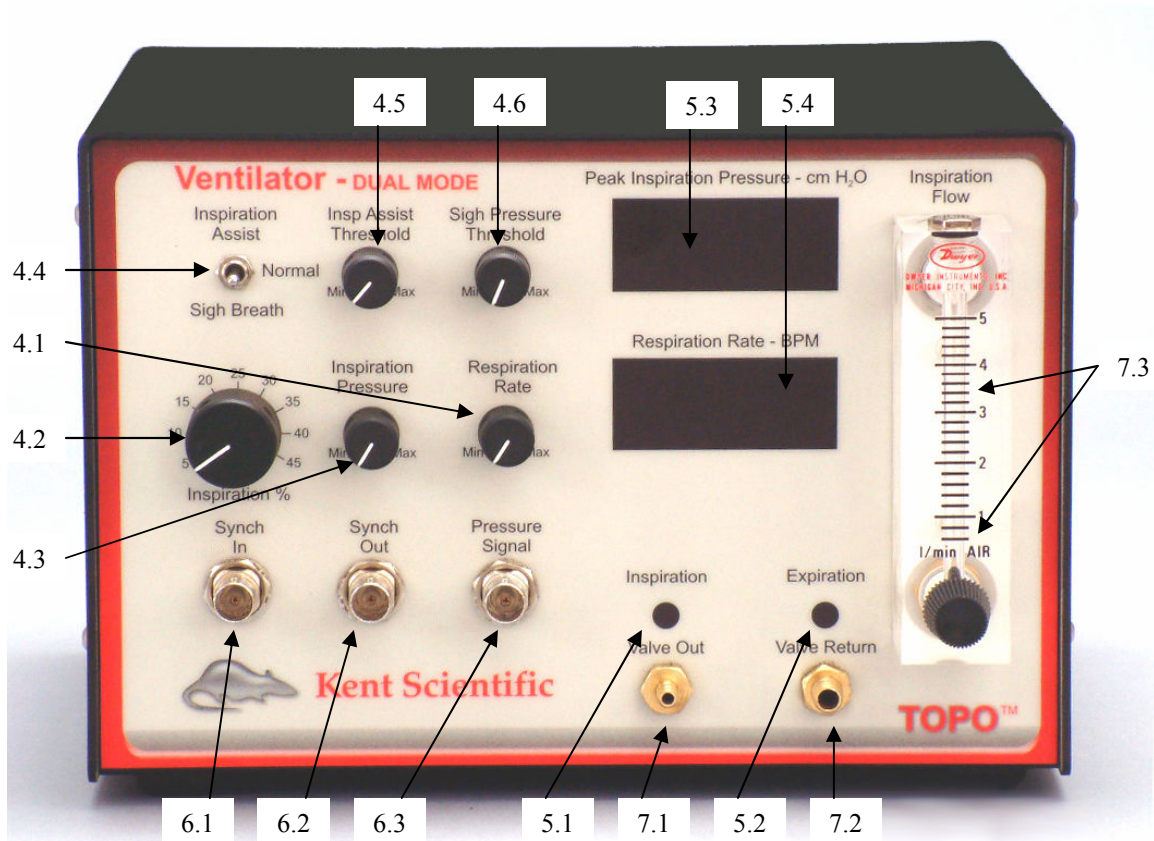
The TOPO Dual Mode Ventilator provides the most physiologic respiration possible. Over pressurizing and damaging the lungs, which can easily occur with fixed volume ventilators, is eliminated. The main features of the TOPO include: variable respiration rate, selectable inspiratory time, variable inspiratory assist threshold, extra sigh breaths, inspiratory assist mode (for spontaneous breathing animals), and external signal trigger controlled respiration.



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4.0 Front Panel Controls



4.1 Respiration Rate – The rate control provides a continuously variable setting of the respiration rate from approximately 10 to 200 breaths per minute. Turning the knob clockwise increases the rate.

4.2 Inspiration % - The inspiration % control allows the selection of the percentage of time allowed for inspiration of the total respiratory cycle time. The values range from 5 to 45% in increments of 5%. The percent inspiration value remains the same regardless of the respiration rate.

4.3 Inspiration Pressure – The inspiration pressure sets the cutoff point where active inspiration will cease. This value is usually set in the range of 5-20 cm of water pressure.



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As the inspiratory portion of respiration is initiated, the expiratory valve closes to prevent air escape and the inspiratory valve opens to pump fresh air into the animal.

Active inspiration continues until either the inspiratory pressure setting reaches its cutoff threshold, or the inspiration % is reached. If the pressure threshold is crossed, the inspiratory valve closes, thus ceasing active inspiration. The expiratory valve remains closed until the inspiratory time is reached. The time between the inspiratory valve closing and the expiratory valve opening is considered the inspiratory pause. This pause helps achieve a more natural respiration pattern.

After the inspiratory valve closes, it cannot be activated again until the start of the next inspiration cycle, even if the airway pressure should drop below the inspiration pressure threshold.

Should the airway pressure remain above the inspiration pressure (cutoff) threshold (for whatever reason, such as blockage of the expiratory tube) the inspiratory valve will not open during the next cycle. This prevents the animal from being over inflated.

CAUTION:

IT IS ESSENTIAL THAT THE EXPIRATORY TUBE DOES NOT BECOME BLOCKED WHILE THE TOPO VENTILATOR IS IN USE. A FATAL OVER PRESSURIZATION OF THE ANIMALS LUNGS CAN OCCUR

Important: The inspiration control valve on the flow meter should be adjusted to allow an inspiratory flow rate that causes active inspiration to end before the total inspiratory time is completed. This means that the inspiration pressure threshold should be reached and the inspiratory valve closes (as shown by the inspiratory valve LED) before the expiratory valve opens (as shown by the expiratory valve LED). This will ensure that the animal has attained full inspiratory pressure and pauses for a brief moment before expiration occurs. Should both the inspiratory and expiratory LED's go out at the same time, the animal may not reach full inspiratory pressure and may become hypoxic. This is remedied by increasing the inspiratory flow rate until the inspiratory LED begins to go off before the expiratory LED.

4.4 Sigh Breath – Inspiration Assist – The Sigh Breath Inspiration assist toggle switch selects the mode in which the TOPO ventilator will operate. With the switch in the center position, normal timed respiration occurs. Pushing the toggle switch down into the sigh breath position causes a sigh inspiration to occur. The termination of sigh inspiration occurs when the sigh pressure threshold is crossed causing the inspiratory valve to close and the expiratory valve to open. As long as the toggle switch is pushed in the sigh breath position, the normal timed respiration cycle is suspended.

The sigh switch is very useful in keeping the animal's breathing efficient. The sigh breath threshold is usually set to a value higher than the normal inspiration pressure threshold. Thus, when a sigh breath is given, the lungs expand to a greater capacity and redistribute



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the lung surfactant that tends to puddle in the alveoli during normal respiration. A sigh breath is part of normal respiration and helps prevent atelectasis.

Should periods of apnea be desired, keeping the toggle switch depressed will interrupt the timed respiration cycle. When the toggle switch is released the timed respiratory cycle commences with the expiratory portion of the cycle first. This insures that full expiration occurs before another inspiratory cycle can occur.

Inspiration Assist – When the switch is in the respiration assist position, either assisted respiration or external signal respiration can occur. Assisted respiration uses two thresholds to control respiration, the respiration assist threshold to trigger inspiration and the sigh threshold to terminate inspiration.

In using the respiratory assist mode, the animal is usually breathing spontaneously but the breaths are shallow and the animal may become hypoxic. The respiration assist threshold is set to detect a slightly negative pressure generated as the animal tries to inhale. The negative pressure need only be a few millimeters of water below atmosphere to trigger the inspiration. The inspiration is terminated when the sigh threshold is crossed. In this mode the sigh threshold is normally set at the normal inspiratory pressure. Another inspiration will not occur until the slight negative pressure is again sensed.

External signal respiration - occurs when a momentary 5 to 12 VDC signal is applied to the Sync In BNC connector for a few milliseconds. This will commence the inspiration cycle, which is terminated by the sigh pressure threshold. Signals generated by the phrenic nerve, muscle contraction, external clock etc. can be used to control respiration frequency. The inspiration assist threshold should be set in the lowest position to prevent interference with the external signal respiration.

4.5 Inspiration Assist Threshold - The inspiration assist control sets the pressure threshold at which inspiration will commence in the inspiration assist mode. All the thresholds have the same working range and can be set to positive and negative working pressures.

4.6 Sigh Pressure Threshold – The sigh pressure control sets the pressure threshold at which the inspiration in the sigh or respiratory assist mode will be terminated.

5.0 Front Panel displays

5.1 Inspiration valve LED – When the inspiration valve LED is lit, the inspiration valve is open allowing air to be pumped out the inspiration outlet.



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5.2 Expiration Valve LED - When the expiration valve LED is lit, the expiration valve is closed preventing air from passing through the expiration port. This indicates that the inspiratory part of the respiration cycle is occurring.

5.3 Peak Inspiration Pressure Display – The peak inspiration LED displays the peak inspiration value for each inspiration cycle. These values represent cm H₂O. The meter updates at the termination of active inspiration as indicated by the inspiration LED turning off. By adjusting the inspiration pressure control, the actual peak inspiratory pressure can be viewed on the meter.

5.4 Respiration Rate Display BPM – The respiration rate LED displays the respiration rate in beats per minute. This display only monitors the timed respiration rate.

Refer to the table below for the ventilation rate determination based on the body weight and tidal volume

RESPIRATION CHART

**Table 1: Ventilation rates determination based on the tidal volume and body weight*
(apparatus dead volume must be added)**

Tidal Volume (ml at ambient temperature)	Body Weight (Grams)	Breaths per minute
0.4	70	100
0.45	100	90
0.5	150	80
0.6	200	70
0.7	250	60
0.8	300	50
1	350	40
2	400	40
3	450	40
4	500	40
5	550	30-40
6	600	30
8	650	30
10	700	30

*Derived from the graph constructed by Leonard Kleinman, M.D. and Edward Radford JR., M.D.



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6.0 BNC Connections

6.1 Sync IN – The Sync in BNC connector provides for an input signal 5-12 VDC to control the inspiration cycle when the ventilator is placed in the inspiration assist mode. Signals should be in the millisecond range and can come from nerve pulse discriminators, muscle contraction signals, external clocks etc.

6.2 Sync Out – The Sync Out BNC connector allows monitoring of respiration. The signal shows the action of the expiratory valve. When the valve is closed a 5 VDC signal is present.

6.3 Pressure Signal – The pressure signal BNC connector allows monitoring of the airway pressure signal from the internal transducer. The transducer range is -10 to +30 cm H₂O and the signal output is 1-5 VDC.

7.0 Air Flow

7.1 Valve out - This air outlet port is used to deliver inspiration air to the animal.

7.2 Valve return - This inlet port is the return path for the expiratory air.

7.3 Inspiration Flow Meter – The inspiration Flow meter and valve show and control the actual inspiratory flow that occurs during respiration. The pump continuously pumps air through the flow meter, the ball in the flow meter displays flow rate. The inspiratory valve directs the air flow either out of the inspiration port to the animal during active inspiration, or back to the pump air inlet to be recycled. In this way, if special gas mixtures are used, only the actual amount that the animal breathes is used; even though the pump is on continuously.



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8.0 Rear Panel



8.1 Air Inlet – The air in port is the inlet to the pump. The air can be either normal room air or a special gas mixture. When using a gas mixture, the gases should flow into a large container such as a 5 liter bottle. The Ventilator should draw from this container as the gases are flowing into it. Remember that the ventilator only delivers the inspired air to the animal while the rest of the air is diverted back to the inlet and recycled.

CAUTION: Under No Circumstances Are Explosive Gas Mixtures To Be Used.

8.2 Exhaust Port – The exhaust port passes the expired air from the animal to the outside. This port can be connected to a collector for analysis or scavenging. Be sure that any connections are made with large tubing forming a low resistance pathway as not to interfere with the normal expiration of the animals, which is passive.



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8.3 Power Switch & Power Receptacle – The Power Switch is for turning the unit on and off. Pressing the I part of the switch (red showing) turns the unit on. The AC receptacle allows the cord to be detached and also houses a 1 amp fuse. Be sure to observe the voltage rating on the rear label. The TOPO Ventilator is available in 120 & 220 VAC versions. Conversions can be preformed at the factory if required. Appropriate American / European line cords are also available.

9.0 Connecting the Animal to the Ventilator

The TOPO Ventilator can be connected to the animal in several different ways. Many researchers have their own procedure. One method is as follows: Semi rigid PE or Tygon tubing of the proper outside diameter is selected and cut to fit the animal's trachea either by intubation (through the mouth) or by cannulation (tracheotomy). This tubing is connected to a plastic Y fitting as close to the animal as possible. The expiratory and inspiratory lines are connected to the arms of the Y fitting. Connecting the Y fitting as close as possible to the animal will help decrease any dead volume between the inspiratory and expiratory pathways. The size and length of the inspiration is not extremely critical. On the other hand the expiratory should be as short and as large in diameter as possible to decrease any resistance to the expiratory airflow. Since expiration is controlled completely by the animal, higher expiratory airway resistance makes exhalation more difficult and can cause a buildup of CO₂ in the lower airways. See section 11.0 for step by step startup.

10.0 Operation

CAUTION:

IT IS ESSENTIAL THAT THE EXPIRATORY TUBE DOES NOT BECOME BLOCKED WHILE THE TOPO VENTILATOR IS IN USE. A FATAL OVER PRESSURIZATION OF THE ANIMALS LUNGS CAN OCCUR

The TOPO Ventilator has four modes of operation: Normal timed response, sigh breath, Inspiration assist, and external signal.

10.1 Normal Timed Response Mode – This mode provides total artificial respiration, % inspiration time, and inspiratory pressure can all be set in this mode. (See appropriate description of the front panel controls).

To set the inspiration pressure threshold initially connect the inspiration port to the animal with a short length of tube. Select a respiration rate for the animal size. Select the proper % inspiration to generate the desired I:E ratio. Select a flow rate fast enough to



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provide an “inspiratory pause”, i.e. a flow rate that causes the inspiration valve to close before the expiratory valve opens. Monitor the peak inspiration pressure meter and adjust the inspiration pressure control to give the desired peak inspiratory pressure.

10.2 Sigh Breath Mode - To set the sigh breath threshold make all the proper tubing connections, set a low respiration rate and a low inspiratory flow rate and depress the sigh switch repeatedly. The peak inspiration meter will display the value of the cutoff pressure during the expiratory cycle.

To insert a sigh breath during a timed respiration, depress the sigh until inspiration is terminated then release the switch.

Should periods of apnea be desired, maintaining the switch depressed will cause the timed respiration to be interrupted. When the switch is released the timed respiration cycle begins again with expiration followed by inspiration.

10.3 Inspiration Assist Mode – The respiratory assist mode is designed to aid an animal when its breathing is shallow or labored. This mode operates when the inspiration assist toggle switch is placed in the up position and uses the inspiration assist control to trigger an inspiration cycle.

To set the Inspiration assist threshold, first be sure all the proper connections are made to the animal. Next turn the respiration assist threshold knob completely counter-clockwise. Slowly turn the knob clockwise until a respiration cycle is initiated each time the animal tries to inhale. As the animal attempts to inhale, a slight negative airway pressure is generated below atmospheric pressure. Set the threshold such that inspiration is triggered off this negative pressure.

If the threshold pressure is set too high, the respiration assist mode will trigger on a positive airway pressure. The higher the airway is set the faster the respiratory cycle will occur. The time between the sigh threshold terminating inspiration and the respiration assist initiating a new inspiration, is shortened because both thresholds are set in the positive pressure range. This type of configuration may be useful in studies that require ultra high respiration and maintained elevated airway pressures.

The sigh threshold is used to terminate inspiration and is set as described above.

10.4 External Signal Respiration Mode – The external signal mode operates in the same manner as the respiratory assist but it allows an external signal of 5 to 12 VDC to be applied to the Sync IN BNC connector for a few milliseconds. This signal will trigger inspiration, which will terminate based on the sigh pressure threshold.

To prevent double triggering inspiration assist control should be turned completely counter-clockwise. This will set the threshold too low to be triggered. The external signal



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can come from a variety of places, most common are nerve impulses, muscle contraction signals, external clocks, etc. The Kent respiration strap can be quite useful in generating signals from muscle contractions.

11.0 Using the TOPO Ventilator

CAUTION:

IT IS ESSENTIAL THAT THE EXPIRATORY TUBE DOES NOT BECOME BLOCKED WHILE THE TOPO VENTILATOR IS IN USE. A FATAL OVER PRESSURIZATION OF THE ANIMALS LUNGS CAN OCCUR

Since the TOPO ventilator operates on the basis of constant pressure and dynamic volume, the dead space in the tubing connections before the tee at the tracheal tube is not very relative to the performance. In fact, in cases where the animal is small such as a baby mouse or the lung volumes change dramatically as in an induced pneumothorax, larger dead space is more desirable. This allows more consistent inspirations.

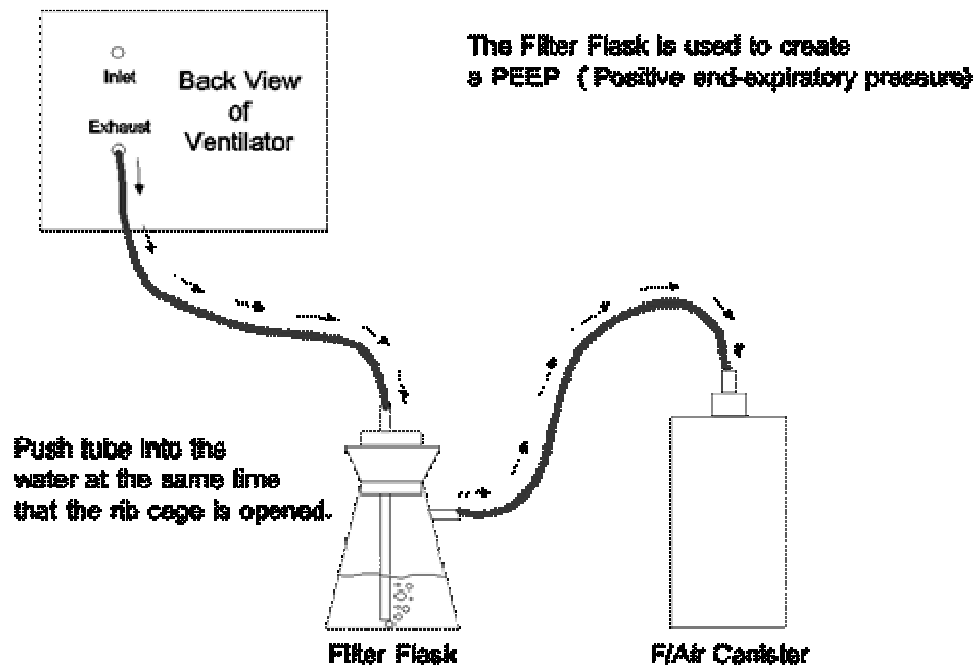
1. Make all the connections from the TOPO ventilator to the tee of the tracheal tube or cannula. Do not connect the animal yet. Allow ample tubing before the tee on the tracheal tube to provide at least a 1:1 or more dead space to lung volume ratio.
2. Block the end of the tracheal tube.
3. Turn the TOPO ventilator on. Select the desired respiration rate and % inspiration.
4. Adjust the inspiration pressure to the desired inspiratory airway pressure.
5. During the inspiratory phase of the respiration cycle, both the inspiration valve and expiratory valve LED's are lit at the same time. Now adjust the inspiration flow rate until the inspiration flow LED turns off slightly before the Expiratory LED. This will yield an "inspiratory pause" to the respiration sequence.
6. Connect the animal and adjust the flow rate as needed to maintain the inspiratory pause as described in step 5.
7. If the respiration rate is changed, the flow rate should be checked to maintain the correct rate of inspiration. It is important to maintain the proper inspiratory pause (the time between the inspiration valve LED going off and the expiratory LED going off).



11.1 TOPO Standard Protocol: Open Chested Animals

The following diagram is designed for the open chest procedures performed on mice or rats.

Figure 1



The space between of the inside of the chest cavity, diaphragm, and the outside of the lungs is covered by the pleura and in called the intrapleural space. There is always a pressure difference between the intrapleural pressure and atmospheric pressure to keep the lungs inflated. Opening the chest causes the intrapleural pressure to equal the atmospheric pressure and can collapse the lungs. Because there is no restriction on the expiratory cycle of the TOPO to the exhaust port on the rear of the ventilator, all air from the lungs can escape and the lungs can collapse.

To overcome the collapse of the lungs a PEEP (Peak End Expiratory Pressure) is used. A PEEP is accomplished by causing a resistance on the Exhaust port of the ventilator. This is usually done by placing a section of tubing under water.



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Refer to the diagram above: A tube from the rear of the ventilator is placed through a hole in a stopper and placed in a filter flask partially filled with water. The tube is placed under 4-6 cm of water, the depth of the tube equals the PEEP in cmH₂O.

If gas anesthesia is used, the side vacuum port of the filter flask is connected to an absorption canister or used is a vent hood.

Even with the PEEP attached, inflating collapsed lungs can take significant pressure initially. Using a sigh breath set to a higher pressure can help. Be sure to have the PEEP attachment in place before opening the chest cavity to avoid lung collapse.

11.2 TOPO Standard Protocol: Close Chested Animals

1. Anesthetizing the animal

1.1 The animal must be anesthetized enough to completely inhibit normal breathing. If it is desired that the animal be allowed to breath on its own, the ventilator is to be placed in the **Inspiration assist** mode. If the animal fails to breath adequately on it's own in this mode, the ventilator must be placed in the **Normal** mode or loss of the animal can occur.

1.2 Average pumps per minute for the Rat is 60-80 breaths. For the mouse it is 100-150 (120) breaths.

2. Setting parameters

2.1 **Inspiration %**. Inspiration % is the ratio of Inspiration to Expiration (I/E). An I:E of 1:2 is desirable for a close chested animal and is achieved by a setting the Inspiration % at 30-35%. 1:3 ratio is approximately 25% I/E and the 1:1 E/I is 45%.

3. Modes of Operation

3.1 There are 2 operating modes, **Constant Volume & Constant Pressure**. The experimental procedure will determine the mode type.

3.2 Constant volume sets the volume at the constant rate, while allowing the pressure to vary.

3.3 Constant Pressure sets the pressure at a constant rate while allowing the volume to vary.



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3.4 To operate in the **constant volume mode**, turn the inspiration pressure to max, also adjust the flow meter to be set close to zero flow.

Increase the flow is then as desired. The setting is correct if the inspiration LED goes out, just before the expiratory LED does.

NOTE: It is possible to overflow the animal if the flow is not regulated correctly. This is evident by the inspiratory LED coming on in a short burst, and going out at the same time as the expiratory LED.

3.5 To operate at **constant pressure mode**, adjust the inspiration pressure as desired (10-15 cm H₂O) Begin with the flow at nearly zero and increase the volume until the inspiration LED light goes out right before the expiration LED light goes out. The audible sound of the valves operating will become familiar, allowing the operator to know when the ventilator is set correctly by listening to its sound.

NOTE: Restriction in the animal's airway may occur. This becomes evident by observing the animal's breathing pattern. If the ventilator reaches pressure without a noticeable expansion of the chest, it is likely that the animal is not getting an adequate flow volume. This can also occur when the flow rate is set too high. In such a case, reduce the flow. If the problem isn't corrected, check the tracheal tube and animal's airway.

4. Anesthesia Considerations:

4.1 Regulation:

Regulator is necessary between the anesthesia bottle and the inlet of the ventilator. A standard arrangement will be an anesthesia supply into a flow meter (which offers flow regulation) with a Compliance bag connected in series, terminating into the inlet.

4.2 The flow meter is adjusted such that the compliance bag is partially inflated, and neither inflates further or deflates.

4.3 Inspiration assist mode during anesthesia is used for animals breathing on their own. This mode is used primarily for large animals. The inspiration % has no effect in this mode.



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12.0 Important MRI Considerations

All units made after November 2003 are MRI compatible. These units are easy to identify by the word TOPO on the lower right corner of the front nameplate. Units made prior to November 2003 are generally not MRI compatible unless specifically requested by the customer at the time of purchase. Older ventilators can be converted upon request. Contact the factory for more information.

13.0 Constant Volume Ventilation

The TOPO Ventilator can also be used in a constant volume mode as follows:

1. Connect the animal to the ventilator as outlined on page 11.
2. Set the respiration rate to the proper frequency for the animal.
3. Turn the inspiration pressure to the maximum (clockwise).
4. Turn the valve on the flow meter until the reading on the peak inspiration pressure meter reads in a physiologic range (usual 8-12 cmH₂O). The ventilator is now giving a constant volume, which is enough to reach the desired airway pressure. Should airway resistance increase or tidal volume decrease, the peak inspiration pressure will show a proportional increase following the ideal gas law, $P_1 * V_1 / T_1 = P_2 * V_2 / T_2$

Operating in this manner the ventilator will give a constant volume. The reading that is presented is, however, not volume but pressure.

14.0 TOPO accessory kit

Components:

1. Squirt bottle with the measurement scale
2. Compliance bag (available in 0.5L and 1.0L)
3. Tubing attached to one of the following:
 - a) Tracheal
 - b) Nose Cone
 - c) Chamber

All components are individually wrapped and placed into the plastic bag with the Part Number and a company logo.