SUMMARY OF SAFETY AND EFFECTIVENESS DATA

I. General Information

Device Generic Name:	High-Frequency Ventilator
Device Trade Name:	SensorMedics Model 3100B High-Frequency Oscillatory Ventilator
Sponsor Name and Address:	SensorMedics Corporation 22705 Savi Ranch Parkway Yorba Linda, CA 92887-4645
PMA Number:	P890057/S14
Date of Panel Recommendation:	July 16, 2001
Date of Notice of Approval:	September 24, 2001

II. Indications for Use

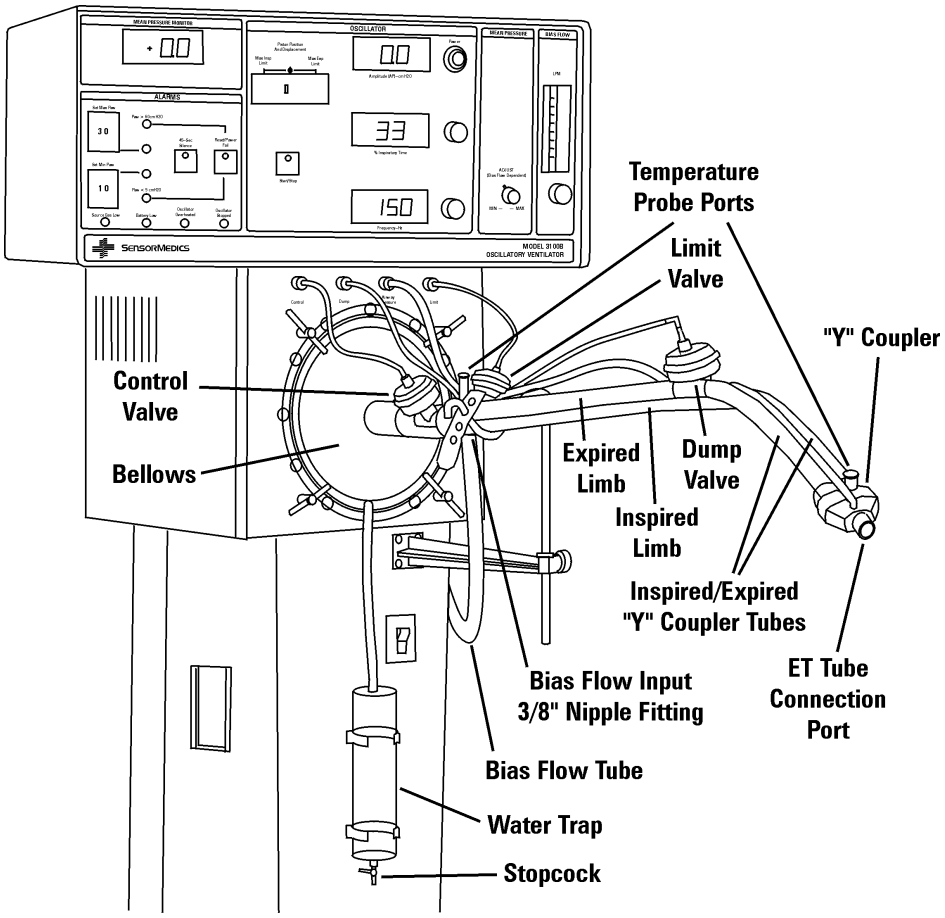
The SensorMedics 3100B is indicated for use in the ventilatory support and treatment of selected patients 35 kilograms and greater with acute respiratory failure.

III. Contraindications

This Model 3100B has no specific contraindications.

IV. Device Description

The Model 3100B consists of six subsystems, and is used with an external air/oxygen blender and an external humidifier. The six subsystems are: (1) pneumatic logic and control; (2) patient circuit; (3) oscillator subsystem; (4) airway pressure monitor; (5) electronic control and alarm subsystem; and (6) electrical power supply. During use with a patient in acute respiratory failure, the Model 3100B maintains a positive mean airway pressure, upon which pressure oscillations are superimposed at a rate between approximately 3 and 15 per second. The pressure oscillations achieve ventilation of the patient.



Pneumatic Logic and Control

The pneumatic logic and control subsystem receives pressurized, blended gas from the external air/oxygen blender. The subsystem includes three controls:

1. A bias flow control sets the continuous rate at which the blended gas flows from the external blender, through the bias flow tube and the patient circuit, and past the tracheal tube connection port. The bias flow can be set as high as 60 L/min.

2. A mean pressure adjust control opens and closes a variable-restriction control valve to set the mean pressure on which the oscillatory waveform is superimposed.

3. A patient circuit calibration set screw is used to calibrate the pressure limit valve control when the patient circuit is replaced or when the control valve diaphragm of the patient circuit is replaced.

Patient Circuit

The patient circuit provides the gas flow required for ventilation of the patient. In conjunction with the oscillator subsystem and the airway pressure

monitor (described below), the patient circuit provides: (1) means to convey bias flow from the humidifier, and to maintain a positive mean airway pressure; (2) means to convey pressure oscillations from the oscillator subsystem; (3) a pressure sensing port; and (4) pressure limiting valves.

1. During normal operation, blended, humidified gas flows from the external humidifer, through the bias flow tube and into a continuous flow line on the inspiratory limb of the patient circuit. The bias flow passes through a wye ("Y") connector including a tracheal tube connector, and into the expiratory limb of the patient circuit. Carbon dioxide is removed from the tracheal tube by the gas mixing that occurs at the "Y" connector. The expiratory limb includes two flow paths. At the end of one path is the control valve which is used to set the mean airway pressure. The other path terminates in a fixed orifice which provides an additional exit for gas regardless of the setting of the control valve.

2. The inspiratory limb of the patient circuit conveys the oscillatory pressure from the diaphragm of the oscillator subsystem to the patient through the "Y" connector and the tracheal tube.

3. An airway pressure sensing port is provided in the "Y" connector.

4. The patient circuit includes two valves which limit the mean airway pressure:

    a. The first valve is a limit valve controlled by the pressure limit control described below. If the mean airway pressure exceeds the set pressure limit, the limit valve opens to release the excess pressure. When the mean airway pressure falls to approximately 80% of the set pressure limit, the limit valve closes again.

    b. The second valve is an electrically-controlled dump valve, which opens if the mean airway is greater than 60 cm H_2O or less than 5 cm H_2O. When the dump valve opens, it remains open until the over-pressure or under-pressure condition is resolved and the ventilator is reset.

Oscillator Subsystem

The oscillator subsystem comprises an air-cooled linear motor driven by an electronic square-wave driver. If the coil temperature reaches 150°C, a panel "caution" is illuminated. If the coil temperature reaches 175°C, the oscillator shuts down and an audible alarm sounds. The coil drives a diaphragm to produce pressure oscillations which are conveyed to the patient through the patient circuit. The electronic square-wave driver is controlled by the electronic control and alarms subsystem: the oscillatory frequency can be set between 3 and 15 Hz; and

the inspiratory time can be set between 30 and 50%. Two mechanical stops limit the displacement of the diaphragm in the "full inspiration" and "full expiration" directions. The entire stroke volume from "full expiration" to "full inspiration" is approximately 365 mL.

Airway Pressure Monitor

The airway pressure monitor senses the pressure within the patient circuit through a tube that runs from the Y connector of the patient circuit. A dry gas flow of 500 mL/min flows through the sensing tube to keep it free of water vapor. The mean airway pressure is obtained by low-pass filtering of the instantaneous pressure signal. The pressure oscillation amplitude (ΔP) is computed by subtracting the oscillatory trough pressure from the oscillatory peak pressure.

Electronic Control and Alarm Subsystem

The electronic control and alarm subsystem includes: (1) oscillator subsystem controls and indicators; and (2) alarm indicators and controls.

1. The oscillator subsystem controls provide input to the electronic square-wave driver which drives the diaphragm in the oscillator subsystem to produce pressure oscillations in the patient circuit.

    a. A start/stop control enables and disables the oscillator subsystem.

    b. A power control sets the pressure oscillation amplitude, ΔP, which is displayed on a digital indicator.

    c. A frequency control sets the frequency of the oscillations produced by the oscillator subsystem between 3 and 15 per second. The set frequency is displayed on a digital indicator.

    d. An inspiratory time control sets the percent inspiratory time between 30 and 50%. The percent inspiratory time is displayed on a digital indicator. At high oscillator frequencies, a decrease in the percent inspiratory time can decrease the pressure oscillation amplitude because the shorter inspiratory times may not give the diaphragm sufficient time to reach its final inspiratory position.

2. The ventilator is provided with the following alarms, some of which have adjustable levels:

    a. The maximum mean airway pressure can be set between 0 and 59 cm H_2O. If the mean airway pressure is greater than the set level, audible and visible alarms are annunciated and the limit valve opens to release the excess pressure. When the mean airway pressure falls to approximately 80% of the set level, the audible alarm resets and the

limit valve closes again. The visible alarm remains annunciated until the alarm reset is activated.

b. The minimum mean airway pressure can be set between 0 and 59 cm H_2O. If the mean airway pressure is less than the set level, audible and visible alarms are annunciated. When the alarm condition is corrected, the audible and visible alarms automatically reset.

c. If the mean airway pressure exceeds 60 cm H_2O for more than 1.5 seconds, audible and visible safety alarms are annunciated; the dump valve opens; and the oscillator subsystem automatically shuts down. The dump valve remains open and the pressure in the patient circuit approaches the ambient pressure. The bias flow tube continues to provide fresh gas to the patient through the patient circuit. The dump valve remains open, and the alarms continue to annunciate until the alarm reset is activated.

d. If the mean airway pressure is less than 5 cm H_2O, audible and visible safety alarms are annunciated; the dump valve opens; and the oscillator subsystem automatically shuts down. The dump valve remains open and the pressure in the patient circuit approaches the ambient pressure. The bias flow tube continues to provide fresh gas to the patient through the patient circuit. When the alarm condition is corrected, the audible alarm resets. The dump valve remains open and the visible alarm continues to annunciate until the alarm reset is activated.

e. If the oscillator is enabled and the magnitude of pressure oscillations is less than approximately 7 cm H_2O, audible and visible “oscillator stopped” alarms annunciate. When the alarm condition is corrected, the alarms reset.

f. If the temperature of the oscillator coil reaches 150°C, a visible caution annunciates to indicate that the coil is overheating, but the device continues to operate. When the caution condition is corrected, the caution resets. If the temperature of the coil reaches 175°C, the oscillator shuts down, and the oscillator stopped alarm (described in item e, above) annunciates.

g. If the electrical power to the device is lost, audible and visible power failure alarms annunciate. The alarms continue to annunciate until the alarm reset is activated.

h. If the voltage on the battery that supplies the power failure alarms is low, a visible caution annunciates to indicate that the battery should be changed as soon as possible to ensure continued operation of the

power failure alarm. When the caution condition is corrected, the caution resets.

i. If the gas pressure at the "inlet from blender" connection or the "air cooling" connection is less than 30 psig, a visible caution is annunciated. When the caution condition is corrected, the caution resets.

j. An alarm silence button can be used to silence audible alarms for a period of 45 seconds. During this time, a visible caution is annunciated, but no audible alarms will sound.

k. An alarm reset button resets the safety alarms and the power failure alarm when pressed. To begin operation of the device after a safety alarm, the alarm condition must be corrected, the oscillator must be enabled and the alarm reset button must be pressed until the dump valve in the patient circuit closes and the mean airway pressure is greater than 5 cm H_2O.

V. Warnings and Precautions

Please refer to the device labeling.

VI. Alternative Practices and Procedures

Conventional mechanical ventilation is an alternative treatment for acute respiratory failure.

VII. Adverse Effects on Health

Observed Adverse Events

A prospective clinical study of the Model 3100B in patients with acute respiratory distress syndrome (ARDS) was conducted at ten sites. The 148 patients enrolled in the study were randomly assigned to one of two groups: a treatment (i.e., "high-frequency") group, in which patients were treated with the Model 3100B; or a control (i.e., "conventional") group, in which patients were treated with a conventional ventilator. Treatment outcomes and adverse events were determined at one and six months. Table 1 summarizes the adverse events observed during the study.

Table 1: Observed adverse events

Adverse event	# (%) of patient who had this event in the treatment group, N=75
Mucus-plugged ET tube	2 (3%)
Inadequate Oxygenation	4 (5%)
Respiratory acidosis	4 (5%)
New or worsening air leak syndrome	7 (9%)
Intractable hypotension	0 (0%)

Potential adverse events

The adverse events associated with the use of high-frequency ventilation include: atelectasis, inadequate oxygenation, intractable hypotension, mucus-plugging of the tracheal tube, necrotizing tracheobronchitis, new or worsening air leak syndrome, over-humidification, under-humidification, over-ventilation, under-ventilation, pneumothorax, pneumopericardium, pneumomediastinum, pneumoperitoneum, pulmonary interstitial emphysema and respiratory acidosis.

VIII. Marketing History

On March 29, 1991, a PMA application was approved for use of the SensorMedics Model 3100 High-Frequency Oscillatory Ventilator in treatment of neonates with respiratory failure and barotrauma. On September 15, 1995, a PMA supplement was approved expanding the indications for use of the Model 3100A to include selected pediatric patients who are failing conventional ventilation. The Model 3100A has been in international commercial distribution since 1991.

The Model 3100B High-Frequency Oscillatory Ventilator is a modification of the approved high-frequency ventilator, the Model 3100A—which is, in turn, a modification of the Model 3100. The Model 3100B has been shipped to countries outside of the United States since 1993. Approximately 100 units have been shipped internationally. Model 3100B units have been marketed in: Austria, Belgium, France, Germany, Italy, the Netherlands, Norway, Qatar, Saudi Arabia, South Africa, Spain, Sweden, Switzerland and the United Kingdom.

The Model 3100, Model 3100A and Model 3100B have not been withdrawn from the market in any country for any reason related to the safety and effectiveness.

IX. Summary of Studies

Non-Clinical Testing

Performance testing

Proper operation of the Model 3100B was verified through non-clinical performance testing. The non-clinical performance tests, the acceptance criteria, and the results of the testing are summarized in Table 2, below.

Table 2: Performance testing performed for two Model 3100B units.

Performance test	Nominal value	Acceptance criteria	Result
Maximum mean airway pressure that can be set	59 cm H_2O	59 cm H_2O	Both pass
Pressure at which the alarms are activated and limit valve is opened when maximum mean airway pressure is set to 59 cm H_2O:	59 cm H_2O	59±2.2 cm H_2O	Both pass
Pressure at which the over-pressure alarms are activated and the dump valve is opened:alarms are activated and dump valve is opened:	60 cm H_2O	60±2.2 cm H_2O	Both pass
Time delay between activation of over pressure alarms and opening of dump valve:	1.5 s	1.5±0.5 s	Both pass
Pressure at which the under-pressure alarms are activated and dump valve is opened:	5 cm H_2O	5±1 cm H_2O	Both pass
Time delay between activation of under-pressure alarms and opening of dump valve:	1.5 s	1.5±0.5 s	Both pass
Maximum bias flow:	60 L/min	60±6 L/min	Both pass
Cooling gas flow:	25 L/min	25 +3/-0 L/min	Both pass
Piston centering:	Compared to manual	Dependent on freq. settings.	Both pass
Maximum pressure oscillations:		Dependent on I:E time and freq. settings.	Both pass

The performance testing included measurement of tidal volumes attained with tracheal tubes of various diameters (5, 7, and 9 mm) and various oscillator frequencies (3 and 15 Hz), I:E ratios and amplitudes. The greatest tidal volume, obtained with a 9 mm endotracheal tube, an oscillator frequency of 3 Hz and amplitude of 10 (uncalibrated) was 260 mL. The results of this testing are more completely summarized by the detailed graphs provided on pages 20-24 of the operator's manual.

Finally, the performance testing included estimation of the mean time between failure of the driver diaphragm in the oscillator subsystem. Four units were allowed to run continuously at an oscillatory frequency of 3 Hz, and at 50% power. The mean time between failure of the diaphragm was 2680 hours for this test. During the clinical study, the mean time between failure was 1828 hours. Therefore, the sponsor revised the maintenance schedule to recommend replacement of the diaphragm as necessary, but at least once every 1500 hours.

Electrical safety and electromagnetic compatibility

The electrical safety of the Model 3100B was demonstrated by its conformance to *IEC 60601-1: Medical electrical equipment, Part 1: General requirements for safety* and *IEC 60601-2-12: Medical electrical equipment, Part 2: Particular requirements for the safety of lung ventilators for medical use*.

The electromagnetic compatibility of the Model 3100B was demonstrated by its conformance to *EN 60601-1-2: Medical electrical equipment, Part 1: General requirements for safety; 2. Collateral standard: Electromagnetic compatibility—Requirements and tests.* In addition, Model 3100B was subjected to the recommended tests outlined in the Reviewer Guidance for Premarket Notification Submission. The results demonstrated that the device met all acceptance criteria.

Biocompatability

The parts of this device which contact the patient directly or indirectly are made of the identical materials used in the Model 3100A.

Clinical Study

A prospective clinical study of the Model 3100B in patients with acute respiratory distress syndrome (ARDS) was conducted at ten sites. The 148 patients enrolled in the study were randomly assigned to one of two groups: a treatment (i.e., "high-frequency") group, in which patients were treated with the Model 3100B; or a control (i.e., "conventional") group, in which patients were treated with a conventional ventilator.

Inclusion and Exclusion Criteria

Patients were eligible for inclusion in the study if they met the following criteria:

- at least 16 years of age;
- at least 35 kilograms;
- $PaO_2/FiO_2 < 200$;
- bilateral pulmonary infiltrates not resulting from left atrial hypertension; and
- positive end-expiratory pressure (PEEP) of at least 10 cm H_2O.

Patients were excluded if any of the following were true:

- informed consent could not be obtained;
- patient had been treated with FiO_2 greater than 80% for at least 48 hours;
- patient had severe persistent air leak;
- patient had non-pulmonary terminal prognosis;
- patient had severe chronic obstructive pulmonary disease
- patient had asthma; or
- patient had been recently enrolled in another ARDS or septic shock investigation.

Methods

The general treatment goal for the high-frequency group and the conventional group was the same: to maintain an O_2 saturation of at least 88%; and to maintain a pH of greater than 7.15, while minimizing peak pressures and treating metabolic acidosis. The mean airway pressure was maintained until FiO_2 had been reduced to less than 60%, after which mean airway pressure and FiO_2 were given equal priority for reduction.

In the high-frequency group, the Model 3100B was initially set to provide pressure oscillations at a frequency of 5 Hz, with the mean airway pressure set 5 cm H_2O higher than the ventilator setting used before the patient was enrolled in the study, and with the oscillation amplitude (?P) set for adequate chest wall vibration. If ventilation was inadequate, ?P was increased. If ventilation was still inadequate with maximum ?P, the frequency of pressure oscillations was reduced in 1 Hz steps. When mean airway pressure had been decreased to less than 30 cm H_2O, or when there was no progress in weaning with the Model 3100B, ventilator weaning continued using a conventional ventilator. A patient assigned to the high-frequency group was treated with the Model 3100B protocol until: consent was withdrawn; the patient had died or been weaned from mechanical ventilation; the patient had been ventilated for 30 days; or the patient met defined treatment failure criteria and would, in the opinion of their physician, benefit from conventional ventilation.

In the conventional group, patients were treated with conventional pressure-controlled, volume-limited ventilation with an inspiratory to expiratory (I:E) ratio of approximately 1:2. Tidal volumes nominally between 6 and 10 mL/kg were used. (The average tidal volume delivered was 10.2 mL/kg of ideal body weight.) If oxygenation was inadequate, PEEP was increased in increments of up to 5 cm H_2O to improve oxygenation. If oxygenation was still inadequate with PEEP greater than or equal to 18 cm H_2O, the I:E ratio was increased incrementally. A patient assigned to the conventional ventilation was treated in the study with the conventional ventilator until: consent was withdrawn; the patient had died or been weaned from mechanical ventilation; or the patient had been ventilated for 30 days.

Patient outcomes were determined after one month and six months. The possible outcomes were:

- death;
- survival with respiratory support; or
- survival without respiratory support.

In this trial, "respiratory support" was defined to include mechanical ventilation, CPAP or supplemental oxygen. Only survival without respiratory support was considered a successful outcome. Outcome data were analyzed using an "intention to treat" analysis.

Hypothesis

The primary hypothesis was that the proportions of patients in the high-frequency and conventional groups with unsuccessful one-month outcomes would be equivalent.

Statistically stated, the hypothesis was that the proportion of patients with an unsuccessful one-month outcome—i.e., the proportion of patients who died or were still receiving respiratory support after one month—would be no more than 10% greater in the high-frequency group than in the conventional group, with 95% confidence.

Study Population

In this trial, 75 patients were assigned to the high-frequency group, and 73 patients were assigned to the conventional group. The patient demographics, the pre-enrollment diagnoses, the pre-enrollment ventilator settings and the pre-enrollment clinical indicators were similar for the two groups (Table 3).

Table 3: Patient demographics, pre-enrollment ventilator settings and pre-enrollment clinical indicators.

Category	Parameter	Mean ± std. dev. Treatment group	Mean ± std. dev. Control group	Units
Patient demographics	Age	48±17	51±18*	years
	Weight	78±25	81±26*	kg
	Gender (% male)	52	64	%
Pre-enrollment ventilator settings	Peak inspiratory pressure	39±7	38±8	cm H_2O
	Positive end-expiratory pressure	13±3	14±3	cm H_2O
	Mean airway pressure	22±5*	24±7*	cm H_2O
	Tidal volume per kilogram of actual body weight	8.2±3*	7.8±3*	mL/kg
	FiO_2	71±19	72±19	%
Pre-enrollment clinical indicators	PaO_2	76±20	73±18	mm Hg
	$PaCO_2$	44±12	45±12	mm Hg
	pH	7.37±0.09*	7.34±0.11	
	PaO_2/FiO_2	114±37	111±42	
	Oxygenation index[1]	24±15*	27±19*	
	Mean blood pressure	80±14*	76±12*	mm Hg
	Cardiac output	7±2*	7±3*	L/min
	APACHE II score[2]	22±6*	22±9*	

* Denotes that values for this parameter were not available for all patients.

[1] Oxygenation index = 100 × mean airway pressure / (PaO_2/FiO_2)

[2] APACHE II is a disease severity score.

Results

The one-month outcomes in this trial are summarized in Table 4, below. The patients in the high-frequency group had unsuccessful one-month outcomes with greater frequency than did the patients in the conventional group. Based on the 95% confidence interval computed from the one-month outcomes, the treatment in the high-frequency group could fail as much as 20% more often. Therefore, the prospectively defined hypothesis was not met. However, the mortality rate in the high-frequency group was lower than the mortality rate in the conventional group. The observed six-month outcomes are summarized in Table 5. Both the unsuccessful treatment rate and the mortality rate were lower in the high-frequency group than in the conventional group. The lower one-month and six-month mortality rates, and the lower six-month unsuccessful treatment rate, in the high-frequency group provide reasonable assurance that the Model 3100B is safe and effective.

Table 4: One-month outcomes

One-month outcome	Treatment group, *N* =75	Control group, *N* =73	Difference	
			Absolute	95% CI
Unsuccessful	78%	73%	+5%	-10% to +20%
Death	37%	52%	-15%	

Table 5: Six-month outcomes

Six-month outcome	Treatment group, *N* =75	Control group, *N* =73
Unsuccessful	47%	62%
Death	47%	59%

Observed Treatment Failures

Likely types of treatment failure were prospectively identified. The frequency with which each type of failure occurred was similar for the two groups, as shown in Table 6, below.

Table 6: Observed treatment failures

Treatment failure	Treatment group, *N* =75	Control group, *N* =73
Mucus-plugged ET tube	3%	1%
Inadequate oxygenation	5%	8%
Respiratory acidosis	5%	8%
New or worsening air leak syndrome	9%	12%
Intractable hypotension	0%	2%

Causes of Death

The causes of death were identified for those patients who died while being treated with a ventilator. Deaths due to withdrawal of mechanical ventilation were also identified. For many patients, more than one cause of death was identified. The causes of death included cardiac arrhythmia, multiple organ failure, sepsis and profound hypoxemia. The causes of death in each group occurred with similar frequency (Table 7).

Table 7: Causes of death observed for patients who died while being treated with a ventilator

Causes of death	# (%) of patients who died while being treated with a ventilator	
	Treatment group, *N*=75	Control group, *N*=73
Total	8 (11%)	15 (21%)
Cardiac arrhythmia	3 (4%)	6 (8%)
Multiple organ failure	3 (4%)	5 (7%)
Sepsis	6 (8%)	8 (11%)
Profound hypoxemia	3 (4%)	6 (8%)
Other	1 (1%)	2 (3%)

X. Conclusions Drawn from the Study

Patients in the two groups were similar at study entry and analysis of outcomes was by intention to treat . For the primary outcome variable (death, mechanical ventilation, CPAP, or O2 or at 30 days) HFOV is worse (79%) vs Conventional (74%). However, death was less frequent in the HFOV group. The failure, relative to the prospective hypothesis, does not preclude HFOV as reasonably safe and effective in adults.

The death rate for patients in the HFOV group at 30 days was 37% as compared to 52% in the conventional ventilation group. Observed mortality at 6 months was also better, 47% HFOV vs 59% conventional. However, the observed mortality difference was not statistically significant. A post-hoc combined variable was constructed (death or mechanical ventilation at 30 days) which would have been statistically significant if it were a prospective hypothesis.

The FDA concluded that the data provides reasonable assurance of the safety and effectiveness of this device when used as indicated.

XI. Panel Recommendation

An open meeting of the Anesthesiology and Respiratory Therapy Devices Panel was held on July 16, 2001 to discuss the safety and effectiveness information provided for the Model 3100B, and to obtain a recommendation from the Panel. The Panel recommended that the PMA supplement be found approvable with the following conditions:

- That the labeling clearly state that severe COPD and asthma were specific exclusion criteria for the trial, and that the benefits and risks

of use of the Model 3100B to treat patients with severe COPD or asthma are unknown; and

- That the labeling clearly state that there are no data to suggest that aerosols can be effectively delivered during high-frequency oscillatory ventilation.

XII. FDA Decision

The conditions of approval recommended by the Panel have been met by appropriate modification of the labeling for the Model 3100B. FDA has determined that the information provided in the PMA supplement provides reasonable assurance of the safety and effectiveness of this device when used as indicated in the labeling, and has issued an approval order on September 24, 2001.