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ATTACHMENT 2

REVISED GUIDANCE FOR CARDIOPULMONARY BYPASS OXYGENATORS 510(k) SUBMISSIONS

Guidance for Industry and FDA Staff

**Guidance for Cardiopulmonary
Bypass Oxygenators 510(k)
Submissions**

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**U.S. Department of Health and Human Services
Food and Drug Administration**

Center for Devices and Radiological Health

**Circulatory Support and Prosthetic Devices Branch
Division of Cardiovascular and Respiratory Devices
Office of Device Evaluation**

Preface

Public Comment:

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Guidance¹ for Cardiopulmonary Bypass Oxygenator 510(k) Submissions

This guidance document describes a means by which cardiopulmonary bypass oxygenator devices may comply with the requirement of special controls for class II devices. The special controls discussed in this guidance document address the potential risks associated with cardiopulmonary bypass oxygenators (biocompatibility of materials; blood damage; gas embolism; particulate embolism; thromboembolism; leaks and mechanical integrity; and inadequate gas exchange) and provide a reasonable assurance of the safety and effectiveness of the device. Designation of this guidance document as a special control means that manufacturers attempting to establish that their device is substantially equivalent to a predicate cardiopulmonary bypass oxygenator device should demonstrate that the proposed device complies with either the specific recommendations of this guidance or some alternate control that provides equivalent assurances of safety and effectiveness.

1. Device Identification

“Cardiopulmonary bypass oxygenator (21 CFR 870.4350) - A cardiopulmonary bypass oxygenator is a device used to exchange gases between blood and a gaseous environment to satisfy the gas exchange needs of a patient during open-heart surgery.” The device is intended for use up to six hours in duration.

2. Purpose and Scope

This guidance document is intended to identify the minimum information to submit in support of a substantial equivalence finding for a cardiopulmonary bypass oxygenator. It also identifies testing protocols that may be followed in providing the necessary data. Since these protocols may not be applicable to all devices, manufacturers should verify that testing is conducted which provides appropriate data to determine the substantial equivalence of their oxygenator. Manufacturers should be aware that the national and international standards available on oxygenators provide details on characterization and performance testing of these devices, but they do not serve as comprehensive guides for the

¹ *This document is intended to provide guidance. It represents the Agency's current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. An alternative approach may be used if such approach satisfies the requirements of the applicable statute, regulations, or both.

Manufacturers should be aware that the national and international standards available on oxygenators provide details on characterization and performance testing of these devices, but they do not serve as comprehensive guides for the submission of data necessary for a regulatory review. (ISO 7199:1996(E) and CAN/CSA-Z364.3-M90 (1990))

3. Definitions

Test oxygenator	the oxygenator submitted for 510(k) regulatory clearance.
Aged test oxygenator	the test oxygenator after it has undergone appropriate accelerated or real time aging.
Predicate oxygenator	a similar oxygenator to the test oxygenator which has previously been cleared by FDA and is currently in commercial distribution in the United States.
Control blank circuit	a recirculation circuit that does not include an oxygenator but is otherwise identical to those circuits used to test oxygenators for blood damage.
Static control blood	a small volume of blood that is not circulated in a circuit and used to monitor autohemolysis.
Index of Hemolysis	the mass of hemoglobin released from the red blood cells per 100L of blood pumped through the device.
Modified Index of Hemolysis	the ratio of the amount of hemoglobin released into the plasma normalized by the total amount of hemoglobin pumped through the device.

4. Oxygenator Testing

To evaluate substantial equivalence of a cardiopulmonary bypass oxygenator, provide data addressing the biological, material, physical, and performance characteristics over the expected storage (shelf life) and use lifetime of the oxygenator. The potential failure modes for oxygenators, which should be investigated thoroughly, include leaks, toxicity, loss of gas transfer efficiency, gas embolism, thromboembolism, and blood damage. The oxygenator should

be tested over its entire performance specification range under expected use conditions for the labeled life of the oxygenator. *In vitro* testing should be conducted according to an established protocol using at least five devices for each test. Submit the testing protocols along with the results of the tests reported in a statistically meaningful manner. Include the range of values, mean, standard deviation and standard error of the mean for each data set. For any comparative test, provide the p-value or similar measure indicating statistical significance of the comparison. Calibrate all instruments and equipment used in conducting these tests, to minimize the limit of testing error. Accuracy of the test apparatus should conform to that in section 11.1.2 of standard CAN/CSA-Z 364.3M90 (1990) or equivalent.

4.1 Comparative Data

For all testing, the test oxygenator should be compared to a similar legally marketable oxygenator, the predicate, or to the manufacturer's specifications for the test oxygenator.

4.2 Preparation of the Test Oxygenator

For Physical Characterization/Integrity, section 4.4, and Performance Characteristics, section 4.5, testing should be performed on the oxygenators only after they have undergone appropriate accelerated or real time aging and sterilization. The purpose of the testing is to determine adverse effects that may not be apparent in recently manufactured devices.

4.3 Biological Compatibility

The blood pathway materials of the oxygenator should be tested sterile and unaged unless the material has not been previously used in a blood contacting application, for biocompatibility, e.g., cytotoxicity, irritation or intracutaneous reactivity, systemic toxicity, and hemocompatibility, in accordance with ISO 10993 (Biological Evaluation of Medical Devices) and sensitivity and genotoxicity in accordance with FDA Blue Book

Memo G95-1: Use of International Standard ISO 10993, "Biological Evaluation of Medical Devices Part 1: Evaluation and Testing" dated May 1, 1995.

4.4 Physical Characterization/Integrity

The mechanical integrity of the sterilized, aged oxygenator should be demonstrated by subjecting the blood and water pathways (integral heat exchangers) to pressures of at least 1.5 times the recommended maximum operating limit for ten minutes.

4.4.1 Blood Pathway Integrity

Using water as the test liquid, subject the blood path of the device to 1.5 times the maximum recommended pressure for 10 minutes to determine whether leakage occurs, i.e., blood side to gas side, blood side to atmosphere.

4.4.2 Heat Exchanger Fluid Pathway Integrity

Using water as the test liquid, subject the heat exchanger fluid path of the device to 1.5 times the maximum recommended pressure for 10 minutes to determine whether water leakage occurs, i.e., water side to blood side, water side to atmosphere.

4.4.3 Blood Volume Capacity of Oxygenator

Determine the static volume of blood within the device. The static priming volume is the minimum volume of fluid residing in the oxygenator after priming at zero flow.

4.5 Performance Characterization

The performance characterization of the aged test, and predicate oxygenators should be based on dynamic testing over the entire range of operating variables, as described in tables 1-3, for the aged, sterilized test and predicate oxygenator for the maximum labeled life of the device

using whole blood. Submit testing protocols with detailed descriptions and figures of the testing circuit components. Submit data in tabular and graphical forms. Both testing protocols and data should be submitted on oxygen and carbon dioxide transfer rates, blood side pressure drop, heat exchanger performance (if applicable), and blood cell damage. Atmospheric pressure during testing should be noted in the submission.

4.5.1 Blood Used for Evaluations

Use fresh whole animal blood collected and refrigerated for less than 24 hours for performance testing, unless blood is stored for more than 24 hours in which case antibiotics should be used. Although bovine blood is most commonly used, sheep, goat or pig blood may also be used. To minimize the effects of interanimal variation, it is advised that the common blood pool be composed of blood from more than one animal. FDA recommends an adequate anticoagulant protocol be used as appropriate.

4.5.2 Oxygen and Carbon Dioxide Transfer Rates/Blood Side Pressure Drop

Gas transfer and blood side pressure drop characteristics are determined by circulating blood and gas through the test oxygenator over the manufacturer's specified range of operating variables. Changes in gas transfer and blood side pressure drop over time is determined by evaluating these characteristics over the labeled life of the test oxygenator as recommended by the manufacturer.

4.5.2.1 General Testing

Identify the components of the testing circuit (described in the text and in figures) and include the following components as a minimum:

- Test oxygenator
- Conduit tubing
- Connectors
- Blood pump
- Blood reservoir
- Deoxygenator
- Heat/cooler units
- Monitors and, or transducers
- Blood gas analyzer
- CO₂ analyzer

For determining gas transfer rates, a device is used in the loop to deoxygenate the blood and maintain the same venous inlet blood conditions to the oxygenator under evaluation. Blood sampling ports directly before the inlets and directly after the outlets of each of the oxygenators are used to measure blood gases and pressure drops across the oxygenators as a function of the operating variables.

4.5.2.2 *Inlet Blood Conditions to Each Oxygenator for Gas Transfer*

Use the following venous inlet blood conditions during gas transfer testing over the labeled life of the test oxygenator:

$$PvCO_2 = 45 \pm 5 \text{ mmHg}$$

$$pH = 7.4 \pm 0.1$$

$$\text{Venous Base Excess} = 0 \pm 5 \text{ meq/l}$$

$$\text{Temperature} = 37 \pm 2^\circ \text{ C}$$

Hemoglobin concentration = 12 ± 1 g/dl

Oxyhemoglobin saturation = $65 \pm 5\%$

Oxygenator outlet backpressure should be set at a minimum of 100 mmHg during gas transfer characterization and duration testing.

The testing circuit for evaluating gas transfer should provide an identical blood condition at the inlet of each oxygenator as described. This should be checked at a minimum of baseline, 60, 180, and 360 minutes.

- Hemoglobin concentration: 12 ± 1 g/dl
- Oxyhemoglobin saturation: $65 \pm 5\%$
- $p\text{CO}_2$: 45 ± 5 mm Hg
- Base excess: 0 ± 5 mmol/L
- Temperature: $37 \pm 2^\circ\text{C}$
- pH: 7.4 ± 0.1

Since the characteristics of blood may degrade over time outside the body, the gas exchange capability of the oxygenator may be compromised. Therefore, to effectively assess the gas exchange capability of the oxygenator, circulating blood may be replaced with fresh blood after three hours of recirculation. Obtain a blood sample immediately after the blood exchange to verify that inlet blood conditions specified above are met.

4.5.2.3 Gas Transfer and Blood Pressure Drop Data Over the Operational Range of the Oxygenator

The test oxygenator should be characterized for oxygen and carbon dioxide transfer rates, blood and gas side pressure drop measurements over the manufacturer's recommended range of operation (i.e., minimum, nominal, and maximum blood flow rates). Short term testing should include gas to blood flow rate ratios of 0.5:1, 1:1, and 2:1. Testing over the labeled life of the device should be performed at a 1:1 F/Q at the maximum flow rate.

For gas exchange and blood side pressure drop measurements, cover the manufacturer's range of specified blood flow (i.e., minimum, nominal, and maximum recommended blood flows) for the labeled life of the device. At each blood flow rate, record the gas transfer (refer to Tables 1, 2, and 3) for various gas flow rates within the manufacturer's recommended range. Data should be included for gas to blood flow rate ratios of 0.5:1, 1:1, and 2:1.

To better simulate the clinical use of the device, submit data that shows the effects on gas transfer and pressure drop when the blood side outlet of the oxygenator experiences a backpressure of a minimum of 100 mmHg during use.

TABLE 1. Oxygen Gas Transfer Data Set *

Provide a table of data for each of the three different blood flow rates (minimum, nominal, and maximum) per the manufacturer's recommendation, and according to the labeling. FDA suggests the table format given below.

Minimum Blood Flow Rate = (L/min)	Gas: Blood Flow Rates (L/min)		
	F/Q = 0.5:1 Minimum	F/Q=1:1 Nominal	F/Q=2:1 Maximum
Inlet PO ₂ , % Sat, pCO ₂ , pH			
Outlet PO ₂ , % Sat, pCO ₂ , pH			
Calculate Oxygen Transfer Rate ⁺			

+ Oxygen Transfer Rate [ml O₂ (STPD)/min] Q x (CaO₂ outlet CvO₂ inlet

Q = blood flow rate in L/min.

F = gas flow rate in L/min.

CaO₂ outlet = blood O₂ content (ml O₂/L blood) calculated at the outlet

CvO₂ inlet = blood O₂ content (ml O₂/L blood) calculated at the inlet

Since CaO₂ or CvO₂ = CaO₂ (or CvO₂) bound to hemoglobin + CaO₂ or CvO₂ dissolved in the plasma, CaO₂ outlet and CaO₂ inlet can be calculated from the following formula (assuming that the total hemoglobin concentration of the blood is 12 g/dl):

CvO₂ (or CaO₂) [ml O₂/L blood] = 12 g Hb/ 100 ml blood x 1.34 ml O₂/ 1 Gm Hb x 1000 ml blood/ 1 L blood x (% O₂ saturation) + (PO₂ mmHg x 0.00314 ml O₂/ (100 ml blood) (mmHg) x 1000 ml blood/ 1 L blood)

STPD = standard temperature and pressure, dry

TABLE 2. Carbon Dioxide Gas Transfer Data Set *

* Provide a table with data for each of the three different blood flow rates (minimum, nominal, and maximum). FDA suggests the table format given below.

Blood Flow Rate = (L/min)	Gas Flow Rates (L/min)		
	F/Q = 0.5:1 Minimum	F/Q = 1:1 Nominal	F/Q = 2:1 Maximum
Inlet gas composition			
Outlet gas composition			
%ΔCO ₂ [ml CO ₂ (STPD)/L gas]			
Calculate CO ₂ Transfer Rate +			

The gas flow entering and leaving the oxygenator should be analyzed for CO₂. The CO₂ transfer rate is calculated as follows:

$$+ \text{CO}_2 \text{ Transfer Rate [ml CO}_2 \text{ (STPD)/min]} = F \times \% \Delta \text{CO}_2$$

F = gas flow rate, exiting the blood-gas exchange device, L/min.

%ΔCO₂ = the change in carbon dioxide concentration between the inlet and outlet flow [ml CO₂ (STPD)/L gas].

TABLE 3. Blood Pressure Drop Data Set*

* Provide a table of data for each of the three different blood flow rates (minimum, nominal, and maximum). Hydrostatic differences between the locations of the inlet and outlet pressure transducers should be accounted for in the table. FDA suggests the table format given below.

Blood Flow Rate = (L/min)	Minimum	Nominal	Maximum
Inlet Blood Pressure (mmHg)			
Outlet Blood Pressure (mmHg)			
Blood Pressure Drop (mmHg)			

Provide graphs along with the above tables showing gas transfer rate (O_2 and CO_2) as a function of blood flow rate and gas flow rate.

4.5.2.4 Gas Transfer and Pressure Drop Data

Change in oxygen and carbon dioxide transfer rates and blood and gas side pressure drop over time is measured at the maximum blood flow rate and at 1:1 gas flow rate. Samples are drawn at time 0 and one hour, and every three hours thereafter for the labeled life of the oxygenator.

The specified time intervals for tabular and graphical data are at baseline, 1 hr, 3 hr, and 6 hr.

4.5.2.5 Data Collection and Calculations (new)

Calculated oxygen and carbon dioxide transfer rates should be provided in tabular and graphical form as a function of blood flow rate and gas flow rate.

To Calculate Oxygen Transfer:

Oxygen Transfer Rate [ml O₂ (STPD)/min] = Q x
(CaO₂ outlet - CvO₂ inlet)

Q = blood flow rate in L/min.

F = gas flow rate in L/min.

CaO₂ outlet = blood O₂ content (ml O₂/L blood)
calculated at the outlet

CvO₂ inlet = blood O₂ content (ml O₂/L blood)
calculated at the inlet

Since CaO₂ or CvO₂ = CaO₂ (or CvO₂) bound to
hemoglobin + CaO₂ or CvO₂ dissolved in the plasma,
CaO₂ outlet and CaO₂ inlet can be calculated from
the following formula (assuming that the total
hemoglobin concentration of the blood is 12 g/dl):

CvO₂ (or CaO₂) [ml O₂/L blood] = 12 g Hb/ 100 ml
blood x 1.34 ml O₂/1 Gm Hb x 1000 ml blood/ 1 L
blood x (% O₂ saturation) + (PO₂ mmHg x 0.00314 ml
O₂/ (100 ml blood) (mmHg) x 1000 ml blood/ 1 L
blood)

STPD = standard temperature and pressure, dry

To Calculate Carbon Dioxide Transfer:

CO₂ Transfer Rate [ml CO₂ (STPD)/min] = F x %ΔCO₂

F = gas flow rate, exiting the blood-gas exchange
device, L/min.

%ΔCO₂ = the change in carbon dioxide concentration
between the inlet and outlet streams [ml CO₂
(STPD)/L gas].

Blood side pressure drop should be provided in tabular and graphical form as a function of blood flow rate.

Gas side pressure drop should be provided in tabular and graphical form as a function of gas flow rate.

4.5.2.6 Raw Data and Calculated Data Tables (new)

For change in gas transfer over time and gas transfer characterization, provide a table containing raw data. Include blood flow (Q), gas flow (F), CO₂ concentration, arterial and venous blood gases, and arterial and venous saturation.

Table 4

ARTERIAL SAMPLE							VENOUS SAMPLE			
Q	F	CCO ₂	pH	PCO ₂	PO ₂	SAT	pH	PCO ₂	PO ₂	SAT

For gas transfer characterization, provide a table containing oxygen transfer rate for each of the different F/Qs and a table containing carbon dioxide transfer rate for each of the blood flow rates.

For change in gas transfer over time, provide a table containing oxygen transfer rate over the minimum and maximum rated blood and gas flow rates and a

table containing carbon dioxide transfer rate over the minimum and maximum rated blood and gas flow rates.

For blood side pressure drop characterization and change over time, provide a table containing the pressure drop for each flow rate.

For gas side pressure drop characterization and change over time, provide a table containing the pressure drop for each gas flow rate.

5. Heat Exchanger Performance Evaluation

The performance of the oxygenator's heat exchanger is evaluated using fixed temperature differences between the inlet blood and water, fixed water flow rates, and blood flow rates spanning the recommended operating range specified by the manufacturer.

5.1 General Testing

Identify the components of the testing circuit (described in the text and in figures) and include the following components as a minimum:

- Test oxygenator
- Conduit tubing
- Connectors
- Blood pump
- Blood reservoir
- Heat exchange device acting to chill the blood
- Monitors and, or transducers

For determining the performance factor of the oxygenator's heat exchanger, a heat-exchanging device is used in the loop to maintain the same venous inlet blood temperature conditions to each of the

oxygenators under evaluation. Blood sampling ports directly before the inlets and directly after the outlets of each of the heat exchangers are used to measure the blood temperature as a function of the operating variables.

To better simulate the clinical use of the device, data may also be submitted showing the effects on heat transfer and water pressure drop when the blood side outlet of the oxygenator experiences a backpressure of a minimum of 100 mmHg during use.

5.1.1 Inlet Blood Conditions to Each Oxygenator

The blood should have total hemoglobin content of 12 ± 1 g/dl.

The inlet blood temperature to each oxygenator should be maintained at $40 \pm 1^\circ\text{C}$. The inlet water temperature to each oxygenator should be maintained at $40 \pm 1^\circ\text{C}$.

5.1.2 Heat Transfer and Water Pressure Drop Data over the Operational Range of the Oxygenator

For heat exchange measurements, cover the manufacturer's range of specified blood flow rates (i.e., minimum, nominal, and maximum recommended blood flows). At each blood flow rate, record the temperature needed to determine heat transfer (refer to Table 5) for various water flow rates within the manufacturer's recommended range.

5.1.3 Heat Transfer and Water Pressure Drop Data (Six hour duration)

TABLE 5. Heat Exchanger Data Set *

* Provide a table of data for each of the three different blood flow rates (minimum, nominal, and maximum). FDA suggests the table format given below.

Water Flow Rates (L/min)

Blood Flow Rate = (L/min)	Minimum	Nominal	Maximum
Inlet Blood Temperature (°C)			
Outlet Blood Temperature (°C)			
Inlet Water Temperature (°C)			
Outlet Water Temperature (°C)			
Calculate Performance Factor*			

Provide a graph along with the above data tables showing the heat exchanger performance factor as a function of both blood flow rate and water flow rate.

The efficiency of the heat exchanger can be expressed as a heat exchanger performance factor (R) defined as the difference between the outlet and inlet oxygenator blood temperatures divided by the difference in temperatures in °C between the water and blood at their respective inlets to the oxygenator.

$$R = (B_o - B_i) / (W_i - B_i)$$

Where B_o = blood temperature at the oxygenator outlet
 B_i = blood temperature at the oxygenator inlet
 W_i = water temperature at the oxygenator inlet

6. **Blood Damage Performance Evaluation**

The oxygenator will be evaluated for *in vitro* blood damage by monitoring the plasma hemoglobin concentration, WBC and platelets for the labeled life as recommended by the manufacturer.

6.1 **General Testing**

Identify the components of the testing circuit (described in the text and in figures) and include the following components as a minimum:

- Test oxygenator
- Conduit tubing
- Connectors
- Blood pump
- Blood reservoir
- Heater/cooler unit
- Monitors and, or transducers

The test oxygenator and the predicate oxygenator should be tested using identical circuits with the same pool of blood.

6.1.1 **Condition of Blood for Damage Testing**

Conditions of the blood for blood damage testing should be consistent with 7199.

6.1.2 **Blood Damage Testing Protocol**

A detailed protocol with figures for performing the blood damage testing should be provided. The blood flow rate to the oxygenator will be the maximum specified by the manufacturer. The back pressure on each oxygenator should be maintained at a minimum of 100 mmHg during use to simulate clinical use. Important procedures to control include:

- precise occlusivity setting of the roller pumps prior to blood introduction in every test loop (if a roller pump is used)
- priming and wetting of all surfaces of the circuits by recirculating saline through the circuits for 5 min. prior to the introduction of blood
- minimizing any air/blood interfaces, minimizing the total circuit blood volume, and
- purging each blood sampling port by withdrawing blood in a syringe prior to taking the actual blood sample using a second syringe

Inherent in this type of testing is the assumption that the blood damage caused by the other (non-oxygenator) components of the testing circuits is identical in each circuit. Experience has shown that this is not necessarily true and that precise occlusivity setting of the roller pumps (if used) using saline prior to the introduction of blood is an important step in the testing. Due to uncontrollable variations in blood, it is preferable to perform the blood damage testing on the test oxygenator circuit and the predicate oxygenator circuit at the same time using the same blood pool. However, this may not always be possible. Correlation between the blood used, the control and test circuits run for each set of data should be apparent in the final report. The total volume of blood in the test circuits should be identical and minimized so that the sensitivity of the testing for blood damage is increased. In general, the total circuit blood volume should be dependent on the maximum recommended blood flow rate.

6.1.3 Blood Damage Data Reporting

For *in vitro* blood damage testing, provide data according to the sampling schedule in Table 6. Raw data and calculated data (with respect to "baseline" values) for each device should be provided in tabular form. Calculated data should also be provided in graphical form. The plasma hemoglobin is reported as a concentration (mg/dl) that increases over time. Mean (\pm SD) results should also be tabulated and graphed for the aged, sterilized test oxygenator circuit and the predicate oxygenator circuit at the same time using the same blood pool. Correlation between the blood used with the control and test circuits run for each set of data should be apparent in the final report. Appropriate statistical testing should be performed to account for testing using different blood source pools at different times.

TABLE 6. Parameter Sampling Schedule

Sampling Schedule (minutes)

Parameter	Main Blood Pool	Baseline*	30	90	180	360
Plasma Hemoglobin Concentration	X	X	X	X	X	X
Activated Clotting Time (ACT)	X	X	X		X	X
Hematocrit	X	X	X		X	X
Platelet and White Blood Cell Count		X				X
Temperature		X	X	X	X	X
Blood Gas Values (pO ₂ , pCO ₂ , pH)		X	X	X	X	X
Blood and Gas Flow Rates		X	X	X	X	X

* "Baseline" refers to the time (at "zero minutes" on the sampling schedule) after all of the blood has been introduced into the circuit, all bubbles have been removed from the circuit, the recirculation pump has been run at the proper blood flow rate for at

least 5 minutes to insure complete mixing throughout the circuit, and the blood gas values, gas flow rate, and gas composition conditions have been established.

Although a standardized testing protocol has not been established, supplemental testing for the labeled life of the oxygenator at the manufacturer's specified minimum blood flow rate (with blood with an ACT of 300-450 seconds and a normal to high platelet count) is also recommended. In-line monitoring for microparticle formation and post-test oxygenator evaluation for evidence of areas of blood stasis, thrombus deposition, and maldistribution of flow are encouraged.

6.2 Acceptable Endpoints

The oxygenator should meet product specifications and be substantially equivalent to the predicate or other legally marketable oxygenators.

6.3 Biological/ Material Compatibility

The test oxygenator will demonstrate acceptable biological/material compatibility.

6.4 Physical Characterization/ Integrity

The test oxygenator should withstand 1.5 times maximum recommended blood and water pathway pressures.

6.5 Performance Characterization

Mean oxygenator outlet saturation, oxygen and carbon dioxide transfer rates, and blood side pressure drop should be comparable to the predicate.

7. Packaging

7.1 Performance Evaluation

- Perform a sterilization validation to ensure that the sterilization process is capable of providing the Sterility Assurance Limit (SAL) of

10-6, in accordance with suitable guidance (e.g., ANSI/AAMI VP20-1994, Section 4.5 (Sterility), ANSI/AAMI/ISO 11134-1993, ANSI, AAMI/ISO 11135-1994, and ANSI/AAMI/ISO 11137-1994). Alternate sterilization methods should be validated to an appropriate SAL.

- Describe the sterilization method that will be used; the method that used to validate the sterilization cycle, and the SAL.
- Describe how the packaging serves to maintain the device sterility. For ETO sterilization, state the maximum levels of residues of ethylene oxide, ethylene chlorohydrin, and ethylene glycol. State whether the product is non-pyrogenic, and describe the method used to make that determination. For radiation sterilization; state the radiation dose used. See also, Sterility Review Guidance, and Revision of 11/18/90 #K90-1.

7.2 Labeling 510(k) Certifications

- The 510(k) will contain a statement that biological testing (including pyrogen and nonpyrogenic or fluid path nonpyrogenic testing) will be or has been performed to assess acceptable limits of biological contaminants.
- The 510(k) will include a statement that package shelf life validation will be or has been performed.

7.3 Labeling Requirements

- State that the product is supplied sterile on the product package label and in the Instructions for Use.
- Instruct the user that sterility cannot be assured if the packaging has been opened or damaged.

- State that the health care provider must observe aseptic technique in preparation and use of the device.
- The labeling should contain a statement cautioning the user against use of the oxygenator with liquid volatile anesthetics.