

# **Guidance for Extracorporeal Blood Circuit Defoamer 510(k) Submissions; Final Guidance for Industry and FDA**

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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 Respiratory and Neurology Devices  
Office of Device Evaluation**

# Preface

## Public Comment

Comments and suggestions may be submitted at any time for Agency consideration to Dockets Management Branch, Division of Management Systems and Policy, Office of Human Resources and Management Services, Food and Drug Administration, 5630 Fishers Lane, Room 1061, (HFA-305), Rockville, MD, 20852. When submitting comments, please refer to the exact title of this guidance document. Comments may not be acted upon by the Agency until the document is next revised or updated.

For questions regarding the use or interpretation of this guidance contact Catherine Wentz at (240) 276-4141 or by e-mail at [catherine.wentza@fda.hhs.gov](mailto:catherine.wentza@fda.hhs.gov).

## Additional Copies

Additional copies are available from the Internet, on the CDRH home page at <http://www.fda.gov/cdrh/ode/guidance/1632.pdf> or CDRH Facts on Demand at 1-800-899-0381 or 301-827-0111 from a touch-tone telephone. Press 1 to enter the system and enter the document number 1632 followed by the pound sign (#). Follow the remaining voice prompts to complete your request.

# Guidance for Extracorporeal Blood Circuit Defoamer 510(k) Submissions; Final Guidance for Industry and FDA

*This document is intended to provide guidance. It represents the Agency's current thinking on the above. 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.*

## Introduction:

This guidance document describes a means by which cardiopulmonary bypass defoamer devices may comply with the requirement of special controls for class II devices. 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 defoamer 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.

This guidance document has been developed as a special control to support a change in classification from class III to class II. It identifies relevant material on preclinical studies and labeling to include in a 510(k) premarket notification application. We intend it be used in conjunction with other identified special controls, [Use of International Standard ISO-10993](#), [Biological Evaluation of Medical Devices Part 1: Evaluation and Testing](#), dated May 1, 1995, and [510\(k\) Sterility Review Guidance](#) (February 12, 1990). All FDA requirements regarding premarket notification submissions are not repeated in this document.

### **The Least Burdensome Approach:**

The issues identified in this guidance document represent those that we believe need to be addressed before your device can be approved/cleared for marketing. In developing the guidance, we carefully considered the relevant statutory criteria for Agency decision-making. We also considered the burden that may be incurred in your attempt to comply with the guidance and address the issues we have identified. We believe that we have considered the least burdensome approach to resolving the issues presented in the guidance document. If, however, you believe that information is being requested that is not relevant to the regulatory decision for your pending application or that there is a less burdensome way to address the issues, you should follow the procedures outlined in the “A Suggested Approach to Resolving Least Burdensome Issues” document. It is available on our Center webpage at:

<http://www.fda.gov/cdrh/modact/leastburdensome.html>

### **Scope:**

An extracorporeal circuit blood defoamer (21 CFR 870.4230) is a device used to remove gas bubbles from the blood for up to six hours. It may be used on the arterial side of a extracorporeal circuit distal to the oxygenator during cardiopulmonary bypass surgery. It may also be used on the venous side before the oxygenator during cardiopulmonary bypass procedures, and in open and closed autotransfusion procedures. The device when used on the venous side is usually an integral part of the cardiopulmonary bypass blood reservoir (21 CFR 870.4400).

The following table sets forth the risks to health associated with this device that were identified in the proposed classification ruling (dated February 26, 1979), as well as additional adverse event reporting since the classification ruling. Next to each risk is a description of the special control suggested to address the risk.

RISKS TO HEALTH	SPECIAL CONTROLS
<p><b>1. Thromboembolism, Embolism complications, Blood damage</b></p>	<p><u>Blood Studies</u>: Evaluate hemolysis and cell depletion (i.e., blood cell counts) over a 6 hour circulation period for the subject, predicate and dynamic control circuits. In addition, blood component (platelet) functionality should be performed if new technology, materials, or surface characteristics are introduced. Blood studies should be performed at the maximum labeled flow rate. In some cases where flow dynamics at low flow rates may play a role in blood trauma, the data should also be presented for the minimum labeled flow rate</p> <p>Visual Inspection: Gross inspection for thromboemboli.</p>
<p><b>2. Inadequate blood flow, Excessive pressure gradients, Structural integrity</b></p>	<p><u>Pressure Integrity Testing</u>: Perform burst pressure for test device using sustained static pressure at 1.5 times the maximum anticipated pressure for the intended use for 6 hours. Observe for leaks, tears, and structural integrity. Use Water or saline as the test medium.</p> <p><u>Pressure Drop</u>: Perform pressure drop testing to steady state, on the test and predicate devices, at highest rated flow rate. Use blood or a blood analog as the testing medium.</p>
<p><b>3. Structural damage under intended use conditions</b></p>	<p><u>Leak testing</u>: Assess mechanical integrity by testing under static pressure conditions as noted in pressure testing above. Test and state the pull strength required to separate the connections or bonds (if applicable).</p>
<p><b>4. Gaseous emboli</b></p>	<p><u>Defoaming testing</u>: Demonstrate the ability of the defoamer to eliminate foam as indicated in the labeling, at the flow rates indicated in the labeling, e.g., 0.5, 1.0, and 1.5 liters/min. Describe the acceptance criteria, e.g., the complete absence of foam in the reservoir.</p> <p><u>Labeling</u>: Recommend the use of the <a href="#">attached Checklist</a>.</p> <p>For those defoamers used on the arterial side of the circuit, the use of a bubble detector downstream from the defoamer, both during testing and in clinical use, is strongly recommended.</p>

RISKS TO HEALTH	SPECIAL CONTROLS
<p><b>5. Excessive pressure gradients; i.e., blood damage, inadequate blood flow</b></p>	<p><u>Flow rate capacity</u>: Determine the flow rate limitation(s) to assure safe and effective performance.</p>
<p><b>6. User error</b></p>	<p><u>Labeling</u>: Include clear, concise instructions for use. Describe the human factors review e.g., inclusion of a troubleshooting guide, easy formatting of instructions for use, etc. Use the <a href="#">attached Checklist</a> as a guide.</p> <p>Provide flow rate, duration of use (e.g., 6 hours), and other pertinent information obtained through performance testing within the labeling, to facilitate correct use of the device.</p> <p>For those defoamers used on the arterial side of the circuit, the use of a bubble detector downstream from the defoamer is strongly recommended.</p>
<p><b>7. Blood incompatibility</b></p>	<p><u>Biocompatibility testing</u>: Perform testing on aged product, as recommended in the FDA guidance on ISO 10993: <a href="#">Use of International Standard ISO 10993, Biological Evaluation of Medical Devices Part 1: Evaluation and Testing, dated May 1, 1995</a> to assure that the materials used are non-toxic for the intended use. Include sensitization, pyrogenicity, acute systemic toxicity, mutagenicity, cytotoxicity, irritation, and hemocompatibility/hemolysis testing.</p> <p>If biocompatibility testing is performed on the unaged product, then submit an FT-IR and results of cytotoxicity testing on the aged product as well, that demonstrates that the physical and chemical properties of the material(s) have not changed.</p>

RISKS TO HEALTH	SPECIAL CONTROLS
<p><b>8. Incompatibility of the product when exposed to circulating blood; and infection.</b></p>	<p><u>Sterilization</u>: Perform sterilization validation to ensure that the sterilization process is capable of providing a Sterility Assurance Limit (SAL) of <math>10^{-6}</math>. Perform biological indicator (as applicable), pyrogen, and bioburden testing to ensure acceptable limits of biological contaminants.</p>
<p><b>9. Insufficient device performance, material incompatibility, and lack of sterility over a period of time</b></p>	<p><u>Shelf-life</u>: Submit the protocol and data from real or accelerated aging studies for the intended labeled shelf-life for the device. If accelerated studies are used, validate (for your own files) the results with real-time data.</p> <p>Perform package integrity and barrier property assessment: use validated physical and microbial-based methods.</p>

## ATTACHMENT: Human Factors/Instruction for Use Checklist

This Checklist is a human factors tool to aid the manufacturer when designing the device and developing the instructions for use manual. Using this checklist will reduce many of the risks to health discussed in this guidance; especially those that can be addressed by adequate instructions for use.

### **1. EQUIPMENT ASSEMBLY**

- Mount motor drive correctly, relative to venous reservoir.
- Check that all electrical connections are secure.
- Test control module power and display.
- Check date and integrity of sterile centrifugal pump (and disposable probe) package(s).
- Check that flow transducer/sensor (and disposable probe) are sized properly.
- Assemble perfusion circuit in a sterile manner.
- Allow sufficient tubing length for standby pumping unit.
- Connect flow transducer/sensor (and disposable probe) to circuit in correct location and flow direction.

### **2. PRIME PUMP AND CIRCUIT**

- CO<sub>2</sub> flush pump and circuit, if indicated; turn off CO<sub>2</sub>.
- Gravity-prime and debubble pump and perfusion circuit.
- Check pump for leaks, irregular motion, and noise.
- Check circuit for visible air.
- Check that all tubing connections are secure.
- Clamp pump outlet line completely.
- Clamp venous return line completely.

### **3. OPERATING PARAMETERS**

- Calibrate transducers/sensors according to manufacturer's instructions.
- Set low/high flow alarms.
- Verify flow alarms.

### **4. EMERGENCY BACKUP EQUIPMENT**

- Backup power available..
- Hand crank available.
- Pump (and disposable probe) available.
- Control module or roller pump available.

### **5. PERFUSION**

- Achieve minimum pump speed prior to unclamping lines.
- Monitor control module for messages and alarms.
- Monitor perfusion circuit for visible air.
- Maintain minimum pump speed prior to clamping lines.

### **6. CLEANUP**

- Turn off power.
- Discard disposable components.
- Cover magnetic motor drive.
- Clean console and transducer/sensor.

## **7. CHECK EQUIPMENT**

- Inspect and verify that equipment is operational.
- Maintain indicated preventive maintenance schedule
- Recharge batteries to full capacity (if necessary).