Guidance for Industry

Class II Special Controls Guidance Document: Cord Blood Processing System and Storage Container

This guidance is for immediate implementation.

FDA is issuing this guidance for immediate implementation in accordance with 21 CFR 10.115(g)(3) without initially seeking prior comment because the agency has determined that prior public participation is not feasible or appropriate because of the timeframes established by section 513(f)(2) of the Federal Food, Drug, and Cosmetic Act.

FDA invites comments on this guidance. Submit written comments at anytime to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852. Submit electronic comments to http://www.fda.gov/dockets/ecomments. You should identify all comments with the docket number listed in the notice of availability that publishes in the *Federal Register*. FDA will review any comments we receive and revise the guidance when appropriate.

Additional copies of this guidance are available from the Office of Communication, Training and Manufacturers Assistance (HFM-40), 1401 Rockville Pike, Suite 200N, Rockville, MD 20852-1448, or by calling 1-800-835-4709 or 301-827-1800, or from the Internet at http://www.fda.gov/cber/guidelines.htm.

For questions on the content of this guidance, contact the Office of Cellular, Tissue, and Gene Therapies at (301) 827-5102.

U.S. Department of Health and Human Services
Food and Drug Administration
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Contains Nonbinding Recommendations

Guidance for Industry

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This guidance represents the Food and Drug Administration's (FDA'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. You can use an alternative approach if the approach satisfies the requirements of the applicable statutes and regulations. If you want to discuss an alternative approach, contact the appropriate FDA staff. If you cannot identify the appropriate FDA staff, call the appropriate number listed on the title page of this guidance.

I. INTRODUCTION

This document was developed as a special control to support the classification of a cord blood processing system and storage container into class II (special controls). This guidance is relevant to devices intended for use in the processing and the storage of cord blood.

This guidance is issued in conjunction with a *Federal Register* notice announcing the classification of a cord blood processing system and storage container into class II. Any manufacturer submitting a 510(k) (premarket notification) for a cord blood processing system and storage container will need to address the issues covered in this special controls guidance document. However, the manufacturer need only show that its device meets the recommendations of the guidance or in some other way provides equivalent assurances of safety and effectiveness.

The issues identified in this guidance document represent those that we believe should be addressed before your device can be marketed. 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 follow the statutory and regulatory criteria in the manner suggested by the guidance and in your attempt to 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 there is a less burdensome way to address the issues, you should follow the procedures outlined in the FDA document, "A Suggested Approach to Resolving Least Burdensome Issues."[1]

FDA's guidance documents, including this guidance, do not establish legally enforceable responsibilities. Instead, guidances describe the FDA's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in FDA's guidances means that something is suggested or recommended, but not required.

[1] See http://www.fda.gov/cdrh/modact/leastburdensome.html.

II. BACKGROUND

Cord blood collection is generally performed by venipuncture of the umbilical cord under aseptic conditions with drainage of the cord blood into closed bags. Various processing methods may be used to prepare the product for cryopreservation and long term storage. A functionally closed cord blood automated processing system increases processing efficiency and reduces the risk of product contamination. These products meet the definition of a medical device under section 201(h) of the Federal Food, Drug, and Cosmetic Act (the Act) and are subject to premarket notification requirements.

FDA believes that special controls, when combined with general controls, will be sufficient to provide reasonable assurance of the safety and effectiveness of a cord blood processing system and storage container. A manufacturer who intends to market a device of this type should (1) conform to the general controls of the Act, including the premarket notification requirements described in 21 Code of Federal Regulations (CFR), Part 807, Subpart E, (2) address the specific risks to health associated with a cord blood processing system and storage container identified in this guidance, and (3) obtain a substantial equivalence determination from FDA prior to marketing the device.

Section IV of this guidance document identifies the classification regulation and product code for a cord blood processing system and storage container. In addition, other sections of this guidance list the risks to health identified by FDA and describe measures that, if followed by manufacturers and combined with the general controls, will generally address the risks associated with this device and lead to a timely premarket notification (510(k)) review and clearance.

This document supplements other FDA documents regarding the specific content requirements of a premarket notification submission. You should also refer to 21 CFR 807.87 and other FDA documents on this topic, such as "Device Advice – Premarket Notification 510(k)."[2]

Under "The New 510(k) Paradigm - Alternate Approaches to Demonstrating Substantial Equivalence in Premarket Notifications, Final Guidance," dated March 1998 (Ref. 1), a manufacturer may submit either a Traditional 510(k) or an Abbreviated 510(k). An Abbreviated 510(k) provides a means to streamline the review of data in a 510(k) through a reliance on FDA-recognized consensus standards or FDA guidance documents. Alternatively, manufacturers considering modifications to their own cleared devices may lessen the regulatory burden by submitting a Special 510(k).

[2] See http://www.fda.gov/cdrh/devadvice/314.html.

FDA believes an Abbreviated 510(k) provides the least burdensome means of demonstrating substantial equivalence for a new device, particularly when FDA has issued a guidance document that provides recommendations on what should be addressed in a submission for the device. Recommendations on the content and format for abbreviated and traditional 510(k)s are available in guidance.[3] Also, see section 514(c)(1)(B) of the Act, and the FDA guidance, "Use of Standards in Substantial Equivalence Determinations."[4]

III. THE CONTENT AND FORMAT OF AN ABBREVIATED 510(K) SUBMISSION

An Abbreviated 510(k) submission must include the required elements identified in 21 CFR 807.87, including the proposed labeling for the device sufficient to describe the device, its intended use, and the directions for its use. In an Abbreviated 510(k), we recommend you include a report summarizing how this special controls guidance document was used during device development and testing (summary report). The summary report should also include a summary of the test data or description of the acceptance criteria applied to address the device risks identified in this guidance document, as well as any additional risks specific to your device.

This section provides information that you should generally include in an Abbreviated 510(k):

A. Coversheet

You should include a coversheet that clearly identifies the submission as an Abbreviated 510(k) and cites the title of this guidance document.

B. Proposed Labeling

Proposed labeling must be sufficient to describe the device, its intended use, and the directions for its use (21 CFR 807.87(e)). (Refer to Section VIII for specific information that you must include, as well as information we recommend you include, in the labeling for this type of device).

C. Summary Report

We recommend that the summary report contain the following:

- A description of the device and its intended use. You should submit an "indications for use" enclosure (Ref. 2). (Refer to Section VI for specific information that you must include, as well as information we recommend you include, in the intended use statement and device description for this type of device).

[3] See http://www.fda.gov/cdrh/ode/guidance/1567.html.
[4] See http://www.fda.gov/cdrh/ode/guidance/1131.html.

- A description of the device design. We recommend that the description include a detailed summary of all performance specifications and detailed, labeled drawings of the device and all components. Although not directly applicable to disposable single-use containers and other soft goods for cord blood processing and storage, the FDA "Guidance for FDA Reviewers: Premarket Notification Submissions for Empty Containers for the Collection and Processing of Blood and Blood Components," dated July 2001 (Ref. 3), may provide useful information about supporting data that should be submitted, such as a detailed description of final product containers that are included as components of the device, design and performance features, and safety and effectiveness testing data.

- Identification of the risk analysis method(s) used to assess the risk profile in general, as well as the risks specific to the device's design and the results of this analysis. (Refer to Section V for the risks to health generally associated with the use of this device).

- A discussion of the device characteristics that mitigate the risks identified in this class II special controls guidance, as well as any additional risks identified in your risk analysis.

- A brief description of the test method(s) used to address each performance aspect identified in Section VII of this guidance. If you follow a test method suggested in this guidance, you may cite the method rather than describing it. If you modify a test method suggested in this guidance, you may cite the method, but should provide sufficient information to explain the nature of and reason for the modification. For each test, you may either (1) present the data resulting from the test in clear and concise form, such as a table, or (2) describe the acceptance criteria that you will apply to your test results. (See also 21 CFR Part 820, Subpart C, Design Controls).

- If you choose to rely on a recognized standard for any part of the device design or testing, you should include either (1) a statement that testing will be conducted and meet specified acceptance criteria before the product is marketed, or (2) a declaration of conformity to the standard. Because a declaration of conformity is based on results from testing, you should complete the testing that the standard describes before submitting a declaration of conformity. For more information, please refer to section 514(c)(1)(B) of the Act and the FDA "Guidance for Industry and for FDA Staff: Use of Standards in Substantial Equivalence Determinations," dated March 2000 (Ref. 4).

If it is not clear how you have addressed the risks identified by FDA or if additional risks are identified through your risk analysis, we may request additional information about aspects of the device's performance characteristics. We may also request additional information needed to assess the adequacy of your acceptance criteria. Under 21 CFR 807.87(l), we will request any additional information regarding the device that is necessary to reach a determination regarding substantial equivalence to a device in commercial distribution.

As an alternative to submitting an Abbreviated 510(k), you can submit a Traditional 510(k) that provides all of the information and data required under 21 CFR 807.87 and described in this guidance. A Traditional 510(k) must include all of your methods, data, acceptance criteria, and conclusions. Manufacturers considering modifications to their own cleared devices should consider submitting Special 510(k)s.

The general discussion above applies to any device subject to a special controls guidance document. The following is a specific discussion of how you should apply this special controls guidance document to a 510(k) premarket notification for a cord blood processing system and storage container.

IV. SCOPE

The scope of this document is limited to the following devices as described in 21 CFR 864.9900 (product code OAO):

21 CFR § 864.9900 Cord blood processing system and storage container.

(a) *Identification*. A cord blood processing system and storage container is a device intended for use in the processing and the storage of cord blood. This device is a functionally closed processing system that includes containers, other soft goods, and a centrifugation system for cord blood concentration, and a final container for the cryopreservation and the storage of a cord blood product.

V. RISKS TO HEALTH

Failure of a cord blood processing system and storage container to perform as indicated, or failure of any of the hardware, plastic disposables, or other components of the device, could result in the manufacture of a cord blood product that does not provide the expected clinical effect. In the table below, FDA has identified the risks to health generally associated with the use of a cord blood processing system and storage container. The measures recommended to mitigate these identified risks are given in this guidance document, as shown in the table below. We recommend that you conduct a risk analysis prior to submitting your premarket notification, to identify any other risks specific to your device. The premarket notification should describe the risk analysis method. If you elect to use an alternative approach to address a particular risk identified in this guidance, or have identified risks in addition to those described in this guidance, you should provide sufficient detail to support the approach you have used to address that risk.

Risks Related to a Cord Blood Processing System and Storage Container

Identified risk	Recommended mitigation measures
Lack of biocompatible components Toxicity of residual chemical sterilants Toxicity of leached materials	Section VII, Safety Evaluation of Cord Blood-Contacting Materials
Insufficient mechanical strength of containers, tubing, and seals	Section VII, Physical Integrity
Contamination	Section VII, Sterility
Instability of soft goods over time	Section VII, Stability
Physical damage to or loss of cord blood product	Section VII, Physical Evaluation of Device/Cord Blood Interaction
Software failure	Section VII, Software
Operator/User Injury	Section VII, Operator/User Injury
Electromagnetic Interference	Section VII, Electromagnetic Compatibility
Electrical Hazards	Section VII, Electrical Safety Testing

VI. DEVICE DESCRIPTION

Your device description should include specific details as to the filling of the device, terminal sterilization of the system, and container closure integrity. As specified in 21 CFR 807.92(a)(4), the device description must include an explanation of how the device functions, the scientific concepts that form the basis for the device, and the significant physical and performance characteristics of the device (such as device design, material used, and physical properties). We recommend that you also provide information on the device's design specifications and range of operation.

A. Intended Use

Required information regarding the intended use statement can be found at 21 CFR 807.92(a)(5). We recommend that the statement include specific indications for use. This statement must be consistent with your labeling, advertising, and instructions for use (21 CFR 807.87(e)). Once the 510(k) review is complete, FDA intends to make available to the public the device's specific indications for use and the Substantial Equivalence (SE) letter sent to the manufacturer of the device.

B. Software

If software (and/or firmware) is a component of your instrument, we recommend that you describe the role of the software (and/or firmware) included in your device and what it controls. You should submit documentation in accordance with the FDA "Guidance for Industry and FDA Staff: Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices" (Software Guidance), dated May 2005 (Ref. 5).

VII. PERFORMANCE CHARACTERISTICS

Technical performance data for the device should demonstrate biocompatibility, absence of toxicity, physical integrity, sterility, non-pyrogenicity, and stability, as well as functional performance characteristics of the device and all associated components.

A. Functional Performance Characteristics

You should report the following functional performance characteristics, if applicable:

- clamping
- seal integrity of single use kits
- cutting
- processing times
- range of acceptable volumes of cord blood for processing and expected yields
- centrifuge function including pneumatic circuit, spill censor, separation chamber, motor, and valve system
- function of alarms, sensors, monitors, and error conditions
- methods of cord blood freezing and storage for which the container is designed, if the device includes a final product container

B. Cord Blood Characterization and Processing Performance Data

Cord blood processing performance of the device, assessed by characterization of the cord blood before and after processing, should include total nucleated cell, mononuclear cell, and specific target cell yields and viability, as well as functional data such as colony forming unit (CFU) yields.

We recommend that you analyze the cells for other relevant cell surface markers, such as cell phenotypic markers, markers of cell activation, and markers of acute cell damage, where applicable, to determine whether the use of the device affects any specific cell population. We also recommend that you perform cell recovery and function studies with products that have been frozen and thawed to determine whether the cells experience any delayed effects from the device or any of its materials.

Due to the nature of the indication(s) for use, the manufacturer may submit in vitro data, (e.g., cell viability data), for efficacy in place of clinical data.

We recommend that your submission contain the following pre-processing and post-processing data; and post-processing sterility data, if applicable.

1. Pre-Processing

   - Nucleated Cell Count (NCC – x 10^6/mL)
   - % Viability of targeted cell population
   - % Mononuclear cells
   - Total viable NCC (x 10^6/mL)
   - Total viable mononuclear cells (MCC – x 10^6/mL)
   - Phenotypic markers (such as CD34, CD90, CD38, CD61, etc.)
   - Total colony forming unit granulocyte macrophage (CFU-GM)
   - Total burst-forming-units-erythroid (BFU-E), if applicable
   - Total colony forming unit-granulocyte erythrocyte monocyte macrophage (CFU-GEMM), if applicable

2. Post-Processing

   - Nucleated Cell Count (NCC – x 10^6/mL)
   - % Viability of targeted cell population
   - % Mononuclear cells
   - Total viable NCC (x 10^6/mL)
   - Total viable MCC (x 10^6/mL)
   - % Recovery of viable NCC
   - % Recovery of viable mononuclear cells (x 10^6/mL)
   - Phenotypic markers (such as CD34, CD90, CD38, CD61, etc.)
   - Total colony forming unit granulocyte macrophage (CFU-GM)
   - Total burst-forming-units-erythroid (BFU-E), if applicable
   - Total colony forming unit-granulocyte erythrocyte monocyte macrophage (CFU-GEMM), if applicable
   - Plasma and/or buffy coat hemoglobin concentration (for hemolysis)

3. Post-Processing Sterility

   For functionally closed systems that include a dimethyl sulfoxide (DMSO) filter, you should provide:

   - data to demonstrate that filter use assures sterility of the cord blood product and maintains closure of the system
   - data to demonstrate that the filter maintains its integrity under expected conditions and concentrations of reagents used during the filtration process
   - data to demonstrate whether extractables are produced when the DMSO is filtered

- the exact identity of the filter and the specifications required for the filter
- whether the DMSO is provided with the device or whether it is to be added by the user

C. Safety Evaluation of Cord Blood-Contacting Materials

When demonstrating the efficacy of a cord blood processing system and storage container, the manufacturer should evaluate the effects from the cord blood-contacting materials and their handling (both before and after processing of the cord blood), either by comparing the effects to those of existing products or by characterizing them independently. These comparisons may include the following:

1. Biocompatibility

   For the materials used in the various components of the cord blood system (i.e., tubing, bags, etc.), the manufacturer should submit biocompatibility test results in accordance with the Blue Book Memorandum #G95-1 entitled "Use of International Standard ISO-10993, Biological Evaluation of Medical Devices Part-1: Evaluation and Testing," dated March 1995 (Ref. 6), as well as other in vitro test results for this indication. Under Standard ISO-10993, the testing category for a cord blood system is 'External Communicating Devices,' for 'Circulating Blood,' or 'Blood Path, Indirect,' with Contact Duration C (>30 days).

2. Toxicity of Chemical Sterilants

   Ethylene oxide (EtO) has been used for a number of years as a sterilant for some drug products and for medical devices. Based on animal studies, exposure to this chemical poses the potential risks of mutagenicity, carcinogencity, and teratogenicity. Hypersensitivity reactions during hemodialysis in humans have shown strong correlation with immune responses to EtO.

   When EtO is used to sterilize the components of a cord blood processing system and storage container, the EtO residue level should be measured for several hours under simulated use conditions. The acceptance criteria for the EtO residue level should be consistent with the FDA recognized consensus standard currently adopted for hemodialyzers by the Association for the Advancement of Medical Instrumentation (AAMI) (Ref. 7), in lieu of specific published standards for residue levels for a cord blood processing device. This limit is set at a maximum of 5 mg EtO/device.

3. Toxicity of Materials that Leach from or Permeate through the Plastic Components

Potential toxicity of leached materials from the plastic components of the device constitutes a risk. Additional toxicity potential may result from dyes, adhesives, solvents, other chemicals in or on labels, or other articles affixed to, or printed directly on, the plastic components. These chemicals may permeate through the plastic components over time. You should identify and provide data on the leached or permeated material extracted under conditions that mimic clinical usage. For example, cord blood or whole blood could be used as an extraction medium to determine the exposure levels of each leachate from or permeated through the plastic components of the device. In performing this testing, you should ensure that the extraction time parallels the storage time before freezing and the estimated time post-thaw, based on expected clinical use. Detailed information regarding the toxicity of the extracts or the permeates should be provided either from 1) data that you have generated, 2) data from products that used previously approved plastic formulations for cord blood, or blood and blood component storage, or 3) the scientific literature, accompanied by a risk analysis to show the safety of the device when used according to the manufacturer's instructions.

D. Physical Integrity

1. Physical Strength Testing

We recommend you submit physical strength test data, including data on the breakage and leakage of device components. In acquiring such data, you should mimic the actual use conditions for each of the following device components including an appropriate freeze/thaw cycle:

- container
- seals
- tubing
- other attachments

2. Packaging

We recommend that you submit information about packaging for the device and all components that are designed to maintain the physical integrity of the device during storage and shipping.

3. Cell Recovery

   We recommend that you provide a mechanism for recovery of the cells in the event of integrity failure of the device or its components. The procedure should be designed to assure maximal recovery of cells and minimize the risk of contamination during processing and storage.

4. Validation of Operational Parameters

   You should characterize the device's range of operation. This should include parameters, such as flow rates, pressures, centrifuge speeds, and temperatures. You should test the operation of the device under expected use conditions and worst case scenarios. The device's alarms, sensors, monitors, and error conditions should be validated, if applicable. If the device can be programmed or changed by the user (such as changing default values or performance settings), you should identify the parameters which can be programmed and their allowable range of settings. Device validations should include device component testing, as well as system-wide testing.

E. Sterility and Non-Pyrogenicity

For sterilization processes and where the article is labeled "pyrogen free," the manufacturer should submit information in accordance with the provisions in the FDA Guidance "Updated 510(k) Sterility Review Guidance K90-1," dated August 2002 (Ref. 8). Details about the microbiological challenge used, including the method used to validate the recovery of the challenge, should be included in the description of the validation method. For articles labeled "pyrogen free," the description of the method used to make that determination should include a detailed summary of the method, the specified limit, a description of how the specified limit was determined, the sample size, and a description of any sample pooling used. Where aseptic assembly is used to retain the sterility of already sterilized articles that will not be subsequently sterilized (an activity beyond the scope of K90-1), the manufacturer should submit information in accordance with the FDA "Guidance for Industry for the Submission of Documentation for Sterilization Process Validation in Applications for Human and Veterinary Drug Products," dated November 1994 (Ref. 9).

F. Stability

You should perform stability studies on the disposable, single-use components of the device. While accelerated stability studies may be performed, we recommend that you use real-time stability data to determine the shelf-life of the device components under conditions of actual storage and use. Stability studies for containers should be designed to detect effects on the plastics and seals over time. Stability studies should also detect the limits for retention of relevant physical properties such as tensile strength, flexibility, shatter resistance, and seal integrity.

G. Physical Evaluation of Device/Cord Blood Interaction

A safety evaluation of the cord blood processing system and storage container and its components should provide measures to ensure that the operation of the device does not cause physical damage to the biological elements or affect the physical integrity of the device components and cause leakage of biological material. The manufacturer should demonstrate that safety measures are in place to prevent excessive temperatures and physical forces (e.g., due to positive or sub-atmospheric pressures, centrifugal forces, and fluid shear forces), from occurring throughout the entire device treatment process.

1. Damage to Cellular Elements

   Technical and biological performance data should be provided to demonstrate that repeated operation of the device at the maximum operating conditions does not cause functional alteration or damage to the relevant cellular elements due to excessive heat production, pressures, centrifugal forces, or fluid shear stresses throughout the entire flow path. Controls should also be in place to ensure that the flow path components, during device operation, are free of abrupt transitions, sharp edges, inadvertent clamping, or kinks which may adversely affect device operation or physically damage cellular elements. These controls should be validated through evaluation of the processed cord blood products.

   The tests to detect effects on biologic performance of the cells should include in vitro measurements of markers of cell damage and assays of cell function and may include in vivo studies of clinical transplant outcomes. These studies should be performed with cord blood products unless data are provided to demonstrate the comparability of the test material with regard to the relevant biologic characteristics being assessed. Studies should include determination of levels of free hemoglobin due to lysis of red blood cells. A sufficient number of tests should be performed to allow meaningful statistical analysis of the results.

2. Physical Integrity to Prevent Cord Blood or Air Leaks

   To assess loss of the cord blood product, data should be provided to demonstrate physical integrity of the containers, seals, connectors, and tubing under the maximum operating conditions (i.e., maximum pressures, fluid flow rates, centrifugal forces, temperatures). For instance, the manufacturer should evaluate for cord blood leaks when the cord blood contacting system is exposed to pressure two times the maximum operating pressure under processing conditions in which the maximum fluid flow rates, centrifugal forces, and temperatures are attained. If the

cord blood treatment system utilizes sub-atmospheric pressures, the manufacturer should assess whether air can be inadvertently pulled into the flow path under a pressure level 1.5 times the maximum sub-atmospheric operating condition.

To test the integrity of the sterile connections, the manufacturer should evaluate the container system after it has been processed with a sterile connecting device as would occur under normal use. The manufacturer should validate the integrity of the rotating seals by contaminating the outside of the seals with bacteria and measuring any transfer of bacteria to the internal media during normal operating conditions.

H. Software Validation Activities

Please refer to the Software Guidance (Ref. 5) for a discussion of the software documentation that you should provide. As discussed in the Software Guidance, the "level of concern" is related to the possible consequences of software failure, and may be minor, moderate, or major. You should provide a clear scientific justification of the level of concern that discusses the possible consequences of a software failure.

If your device utilizes off-the-shelf (OTS) software, you should also reference the FDA "Guidance for Industry, FDA Reviewers, and Compliance on Off-the-Shelf Software Use in Medical Devices," dated September 1999 (Ref. 10).

Any hazards relating to system software and hardware operations controlled by software must be assessed. Software hazards, such as failure of alarms or error codes, sample identification, communications and interfaces, and data integrity, should be addressed.

I. Operator/User Injury

Test data should be provided to show that adequate measures have been taken for protecting the operator/user from injury from the following hazards: 1) electrical shock, 2) mechanical hazards (including rotating components), 3) infectious disease transmission risk to the operator due to leaks, 4) excessive radiation (including electromagnetic compatibility (EMC) issues), and 5) excessive temperatures. As indicated in Section III of this guidance, you may choose to rely upon a recognized standard for any part of the design or testing. Use of a standard should be indicated by either 1) a statement indicating that compliance testing will be performed, or 2) a declaration of conformity to the standard.

J. Electromagnetic Compatibility

We recommend that you demonstrate the EMC of the device by following the EMC testing methods in the FDA recognized consensus standard IEC 60601-1-2, "Medical Electrical Equipment – Part 1: General Requirements for Safety; Electromagnetic Compatibility - Requirements and Tests," (Ref. 11), or a method that provides equivalent assurance of electromagnetic compatibility.

K. Electrical Safety Testing

We recommend that you demonstrate the electrical safety of the device by following the testing in the FDA recognized consensus standard IEC 60601-1, "Medical Electrical Equipment – Part 1: General Requirements for Safety," (Ref. 12), or a method that provides equivalent assurance of electrical safety.

VIII. LABELING

The 510(k) premarket notification must include proposed labels, labeling, and advertisements sufficient to describe the device, its intended use, and the directions for its use (21 CFR 807.87(e)). We recommend the following in preparing labeling that satisfies these requirements.

A. Directions for Use

You should present clear and concise instructions that delineate the technological features of the specific device and how the device is to be used. Instructions should encourage local or institutional training programs, if available, that are designed to familiarize users with the features of the device and how to use it in a safe and effective manner.

The directions for use should include recommendations regarding the freezing temperature and fill volume, and should specify whether the intent is to store the products in the liquid or vapor phase of liquid nitrogen.

B. Intended Use

The intended use should be compatible with the performance characteristics of the cord blood processing system and storage container.

C. Design Specifications, Range of Operation, and Correct Usage

You should include in the package insert a list of the device's design specifications and range of operation (e.g., flow rates, pressures, centrifuge speeds, and temperatures). If the device may be programmed by the user (e.g., change in default values), you should provide a list of the programmable ranges. You should also include all study designs and results for studies described in Section VII of this guidance that would aid users in the correct usage of this device.

D. Alarms, Error Conditions, and Troubleshooting

The package insert should include a list of the device's alarms and error conditions, including explanations of the type of alarms (e.g., audible, visual), what may activate the alarm, the severity of the alarm or error condition, what the operator must do to resolve it, and implications for the use of the device and for the cord blood products being processed. We recommend you include instructions for device troubleshooting. This information should detail the recommended steps in addressing possible device malfunction and information on when and how to seek further help.

E. Cleaning, Disinfection, and Preventative Maintenance

This section should provide the user with detailed instructions for proper device cleaning, disinfection, and maintenance, including schedules for cleaning and maintenance.

IX. REFERENCES

1. The New 510(k) Paradigm - Alternate Approaches to Demonstrating Substantial Equivalence in Premarket Notifications, Final Guidance**,** dated March 1998. http://www.fda.gov/cdrh/ode/parad510.html

2. Guidance on Indications for Use, dated February 1996. http://www.fda.gov/cdrh/ode/indicuse.html

3. Guidance for FDA Reviewers: Premarket Notification Submissions for Empty Containers for the Collection and Processing of Blood and Blood Components, dated July 2001. http://www.fda.gov/cber/gdlns/pmacontain.htm

4. Guidance for Industry and for FDA Staff: Use of Standards in Substantial Equivalence Determinations, dated March 2000. http://www.fda.gov/cdrh/ode/guidance/1131.html

5. Guidance for Industry and for FDA Staff: The Content of Premarket Submissions for Software Contained in Medical Devices, dated May 2005. http://www.fda.gov/cdrh/ode/guidance/337.html

6. Blue Book Memorandum #G95-1, "Use of International Standard ISO-10993, Biological Evaluation of Medical Devices Part-1: Evaluation and Testing," dated March 1995. http://www.fda.gov/cdrh/g951.html

7. ANSI/AAMI RD:16 1996/A1: 2002/(R) 2005, Hemodialyzers http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfStandards/Detail.CFM?STANDARD__IDENTIFICATION_NO=16809

8. Guidance for Industry and for FDA: Updated 510(k) Sterility Review Guidance K90-1, dated August 2002. http://www.fda.gov/cdrh/ode/guidance/361.html

9. Guidance for Industry: The Submission Documentation for Sterilization Process Validation in Applications for Human and Veterinary Drug Products, dated November 1994. http://www.fda.gov/cder/guidance/cmc2.pdf

10. Guidance for Industry, FDA Reviewers, and Compliance on Off-the-Shelf Software Use in Medical Devices, dated September 1999. http://www.fda.gov/cdrh/ode/guidance/585.html

11. IEC 60601-1-2 (2001), "Medical Electrical Equipment - Part 1: General Requirements for Safety; Electromagnetic Compatibility - Requirements and Tests." http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfStandards/SimpleSearch.cfm?db=STD&id=14761

12. IEC 60601-1 (1988), "Medical Electrical Equipment - Part 1: General Requirements for Safety." http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfStandards/SimpleSearch.cfm?db=STD&id=14754