Guidance for Industry and FDA Staff

Class II Special Controls Guidance Document: Automated Blood Cell Separator Device Operating by Centrifugal or Filtration Separation Principle

Additional copies of this guidance are available from the Office of Communication, Outreach and Development (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 athttp://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/default.htm.

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U.S. Department of Health and Human Services
Food and Drug Administration
Center for Biologics Evaluation and Research
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See additional PRA statement in Section VIII of this guidance.

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NOTE: This guidance is revised to update the November 2007 version as follows:

- On the cover page, provided updated information on the website address, office title, and office contact information;
- Deleted website addresses where appropriate; and
- Other changes made consistent with the Federal Register of March 28, 2011 (76 FR 17135)

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I. PURPOSE

We, FDA, are issuing this guidance document in conjunction with a *Federal Register* final rule reclassifying from class III to class II the automated blood cell separator device operating on a centrifugal separation principle intended for the routine collection of blood and blood components. This guidance document serves as the special control to support the reclassification.

This guidance document also serves as the special control for the automated blood cell separator device operating on a filtration separation principle intended for the routine collection of blood and blood components reclassified as class II on February 28, 2003 (68 FR 9530). Special controls, when combined with general controls, ordinarily address the risks associated with use of the device.

Following the effective date of a final rule reclassifying the device, any firm submitting a 510(k) premarket notification for an automated blood cell separator device operating by centrifugal or filtration separation principle intended for the routine collection of blood and blood components will need to address the issues covered in this special controls guidance. However, the firm need only show that its device meets the recommendations of this guidance or in some other way provides equivalent assurances of safety and effectiveness.

The firm must show that its device addresses the issues of safety and effectiveness identified in this guidance, either by meeting the recommendations of this guidance or by some other means that provides equivalent assurances of safety and effectiveness. (Section 513 (a)(1)(B) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) (21 U.S.C. 360c(a)(1)(B)).

II. BACKGROUND

FDA believes that special controls, when combined with general controls, will be sufficient to provide reasonable assurance of the safety and effectiveness of the automated blood cell separator device operating on a centrifugal or filtration separation principle and intended for the routine collection of blood and blood components. A manufacturer that intends to market a device of this generic type should (1) conform to the general controls of the Federal Food, Drug, and Cosmetic Act (the Act), including the

premarket notification requirements described in Title 21 Code of Federal Regulations (CFR), Part 807, Subpart E, (2) address the specific risks to health associated with the automated blood cell separator device identified in this guidance, and (3) obtain a substantial equivalence determination from FDA prior to marketing the device (see also 21 CFR 807.85).

This guidance document identifies the relevant classification regulation, which provides a description of the applicable automated blood cell separator device (refer to section IV. – Device Description, below). In addition, other sections of this special controls guidance document list the risks to health identified by FDA and describe measures that, if followed by manufacturers and combined with general controls, will ordinarily address the risks associated with these automated blood cell separator devices.

This document supplements the specific content requirements of a premarket notification submission under 21 CFR 807.87 and other FDA documents on this topic (e.g., **Device Advice - Premarket Notification [510(k)]**; and, **The New 510(k) Paradigm – Alternate Approaches to Demonstrating Substantial Equivalence in Premarket Notifications; Final Guidance**, March 20, 1998. A manufacturer may submit a Traditional 510(k) premarket notification or has the option of submitting either an Abbreviated 510(k) or a Special 510(k) (see The New 510(k) Paradigm). We believe an Abbreviated 510(k) provides the least burdensome means of demonstrating substantial equivalence for a new device, particularly once a special controls guidance has been issued. Manufacturers considering modifications to their own cleared devices may lessen the regulatory burden by submitting a Special 510(k) (see The New 510(k) Paradigm at page 3).

III. THE LEAST BURDENSOME APPROACH

We recommend that you address the following issues identified in this guidance before your device can be marketed. In developing this guidance, we carefully considered the relevant statutory criteria for FDA decision-making. We also considered the burden that may be incurred in your attempt to comply with the statutory and regulatory criteria in a manner suggested by this guidance and in your attempt to address the issues we have identified. We think that we have provided the least burdensome approach to resolving these issues. If, however, you believe there is a less burdensome way to address the issues, please follow the procedures outlined in the document, *The Least Burdensome Provisions - Activities Related to Implementation.*

IV. DEVICE DESCRIPTION

Title 21 CFR 864.9245 provides the classification for automated blood cell separators. The automated blood cell separator is a device that operates on a centrifugal or a filtration separation principle intended for the routine collection of blood and blood components. The device automatically withdraws whole blood from a donor, separates

the whole blood into blood components, collects one or more of the blood components, and returns to the donor the remainder of the whole blood and blood components (apheresis donation). The blood components collected are transfused or used for further manufacture.

This guidance applies to automated blood cell separator devices that operate by either centrifugal or filtration separation principles and where the intended use is for the routine collection of blood and blood components. FDA has classified these automated blood cell separator devices as class II (special controls).

V. RISKS TO HEALTH

In order to provide assurances for the safe and effective use of the device, we first identify risks to health associated with the device's intended use. Then, we determine if the general and special controls will sufficiently address the identified risks. Presently, we have identified the following risks associated with apheresis blood donation and processing:

- potential loss of blood due to leaks,
- thrombosis due to activation of factors by foreign surfaces,
- moderate-severe toxic reaction to citrate anticoagulant (e.g., tetany, seizures, cardiac arrhythmias),
- damage to red blood cells, activation of complement, and denaturation of proteins,
- potential for sepsis and fever due to bacterial contamination of the donor's blood returned to the donor,
- infectious disease risk to the donor or to the operator due to leaks,
- electrical shock hazard,
- donor stress reaction due to removal or loss of blood,
- air embolism,
- hemolysis, and
- reservoir rupture causing risk to the donor and operator.

VI. SPECIAL CONTROLS

For currently marketed products not approved under the premarket approval (PMA) process, you, the manufacturer should file with FDA for three consecutive years an annual report on the anniversary date of the device reclassification from class III to class II, or, on the anniversary date of 510(k) clearance. Any subsequent change to the device requiring the submission of a premarket notification in accordance with section 510(k) of the Act should be included in the annual report. Also, a manufacturer of a device determined to be substantially equivalent to the automated blood cell separator device operating by centrifugal or filtration separation principle intended for the routine

collection of blood and blood components, should comply with the same general and special controls.

This guidance (special controls) recommends that each annual report include, at a minimum, the following information:

1. A summary of anticipated and unanticipated adverse events that have occurred and that are not required to be reported by manufacturers under Medical Device Reporting (MDR).[1] We recommend that you summarize and report adverse events such as those required under 21 CFR 606.160(b)(1)(iii)[2, 3] to be recorded and maintained by the facility[4] using the device to collect blood and blood components. Under 21 CFR 803.50(b)(3), you are responsible for conducting an investigation of each event and evaluating the cause of the event. Therefore, this information should be available to you to summarize and provide to FDA in your annual report. We emphasize that safety information submitted to FDA is not to be considered an admission of causation or liability (October 27, 1994, 59 FR 54046 at 54051).

2. Any subsequent change to the device requiring the submission of a premarket notification in accordance with section 510(k) of the Act. (See Ref. 1).

3. Any subsequent change to the preamendments class III device requiring a 30-day notice in accordance with 21 CFR 814.39(f).

MDR reportable events may include operator infection or injury; equipment failures, including software, hardware, and disposable item failures; thrombosis; sepsis; and shock resulting from blood loss. You do not have to include the MDR reports in the annual report. If not reportable under MDR, please refer to 1. above, under this section.

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[1] 21 CFR 803.1(a) – "If you are a manufacturer or importer, you must report deaths and serious injuries that your device has or may have caused or contributed to, you must report certain device malfunctions, and you must establish and maintain adverse event files . . . ."

[2] 21 CFR 606.160(b) – "Records shall be maintained that include, but are not limited to, the following when applicable: . . . (1)(iii) Donor adverse reaction complaints and reports, including results of all investigations and followup."

[3] In separate proposed rulemaking (Safety Reporting Requirements for Human Drug and Biological Products; Proposed Rule (68 FR 12405, March 14, 2003), FDA has proposed amending 21 CFR 606.170 to require the investigation and recording by blood establishments of any complaint of a serious adverse reaction related to the collection or transfusion of blood or blood components.

[4] "Facility" means any area used for the collection, processing, compatibility testing, storage or distribution of blood and blood components (21 CFR 606.3(h)). Also, applicable is "device user facility" under 21 CFR 803.3(f), meaning "a hospital, ambulatory surgical facility, nursing home, outpatient diagnostic facility, or outpatient treatment facility . . . ." (Note: The donor becomes a patient when he or she experiences and is treated for an adverse event contributed to or caused by the medical device).

VII. CONCLUSION

This guidance contains recommendations with regard to the reporting of adverse events that typically are not reported under the MDR regulation. The reporting of adverse events summarized in an annual report will alert FDA to trends or clusters of events that might be a safety issue otherwise unreported under the MDR regulation. These special controls along with the general controls should provide reasonable assurance of the safety and effectiveness of the device.

VIII. PAPERWORK REDUCTION ACT OF 1995

This guidance contains information collection provisions that are subject to review by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (44 U.S.C. 3501-3520).

The time required to complete this information collection is estimated to average 5 hours per response, including the time to review instructions, search existing data resources, gather the data needed, and complete and review the information collection. Send comments regarding this burden estimate or suggestions for reducing this burden to:

Food and Drug Administration
Center for Biologics Evaluation and Research (HFM-99)
1401 Rockville Pike, suite 200N
Rockville, MD 20852-1448

This guidance also refers to previously approved collections of information found in FDA regulations. The collections of information in §§ 864.9245, 803.50, 803.50(b)(2), and 803.53 have been approved under OMB Control Numbers 0910-0120, and 0910-0437.

An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number. The OMB control number for this information collection is 0910-0594 (expires 09/30/2012).

IX. REFERENCES

1. Guidance - *Deciding When to Submit a 510(k) for a Change to an Existing Device*, January 10, 1997.

2. Guidance for Industry, *Recommendations for Collecting Red Blood Cells by Automated Apheresis Methods*, January 2001; Technical Correction February 2001.

3. Medical Device Reporting Guidance, *Medical Device Reporting for Manufacturers*, March 1997.