DEPARTMENT OF HEALTH AND HUMAN SERVICES

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[Docket No. 2005N–0017]

Medical Devices; Hematology and Pathology Devices: Reclassification of Automated Blood Cell Separator Device Operating by Centrifugal Separation Principle

AGENCY: Food and Drug Administration, HHS.

ACTION: Final rule.

SUMMARY: The Food and Drug Administration (FDA) is reclassifying from class III to class II the automated blood cell separator device operating by centrifugal separation principle and intended for the routine collection of blood and blood components. FDA is taking this action on its own initiative based on new information. Elsewhere in this issue of the **Federal Register**, FDA is announcing the availability of a guidance document that will serve as the special controls for this device, as well as the special controls for the device with the same intended use but operating on a filtration separation principle.

DATES: This rule is effective [*insert date 30 days after date of publication in the* **Federal Register**]. The reclassification date is [*insert the date of publication in the* **Federal Register**].

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SUPPLEMENTARY INFORMATION:

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I. Background

The Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 301 *et seq.*), as amended by the Medical Device Amendments of 1976 (the 1976 amendments) (Public Law 94–295), the Safe Medical Devices Act (SMDA) (Public Law 101–629), the Food and Drug Administration Modernization Act (FDAMA) (Public Law 105–115), and the Medical Device User Fee and Modernization Act (Public Law 107–250) established a comprehensive system for the regulation of medical devices intended for human use. Section 513 of the act (21 U.S.C. 360c) established three categories (classes) of devices, depending on the regulatory controls needed to provide reasonable assurance of their safety and effectiveness. The three categories of devices are as follows:

- Class I (general controls),
- Class II (special controls), and
- Class III (premarket approval).

Under the 1976 amendments, class II devices were defined as devices for which there was insufficient information to show that general controls themselves would provide reasonable assurance of safety and effectiveness, but for which there was sufficient information to establish performance standards to provide such assurance. SMDA broadened the definition of class II devices to mean those devices for which the general controls by themselves are insufficient to provide reasonable assurance of safety and effectiveness, but for which there is sufficient information to establish special controls to provide such assurance, including performance standards, post-market surveillance, patient registries, development and dissemination of guidelines, recommendations, and other appropriate actions the agency deems necessary (section 513(a)(1)(B) of the act).

Under section 513 of the act, devices that were in commercial distribution before May 28, 1976 (the date of enactment of the 1976 amendments), generally referred to as preamendment devices, are classified after FDA:

1. Receives a recommendation from a device classification panel (an FDA advisory committee);

2. Publishes the panel's recommendation for comment, along with a proposed regulation classifying the device; and

3. Publishes a final regulation classifying the device.

FDA has classified most preamendments devices under these procedures.

1. Devices that were not in commercial distribution before May 28, 1976, generally referred to as postamendments devices, are classified automatically by statute (section 513(f) of the act) (21 U.S.C. 360c(f)) into class III without any FDA rulemaking process. Those devices remain in class III and require premarket approval unless and until FDA reclassifies the device into class I or class II.

2. FDA issues an order classifying the device into class I or II in accordance with new section 513(f)(2) of the act, as amended by FDAMA; or

3. FDA issues an order finding the device to be substantially equivalent, under section 513(i) of the act (21 U.S.C. 360c(i)), to a predicate device that does not require premarket approval.

The agency determines whether new devices are substantially equivalent to previously offered devices by means of premarket notification procedures in section 510(k) of the act (21 U.S.C. 360(k)) and part 807 of the regulations (21 CFR part 807).

A preamendments device that has been classified into class III may be marketed through premarket notification procedures, without submission of a premarket approval application (PMA) until FDA issues a final regulation

under section 515(b) of the act (21 U.S.C. 360e(b)) requiring premarket approval.

Section 513(e) of the act governs reclassification of classified preamendments devices. This section provides that FDA may, by rulemaking, reclassify a device (in a proceeding that parallels the initial classification proceeding) based upon "new information." FDA can initiate a reclassification under section 513(e) or an interested person may petition FDA to reclassify a preamendments device. The term "new information," as used in section 513(e)(1) of the act, includes information developed as a result of a reevaluation of the data before the agency when the device was originally classified, as well as information not presented, not available, or not developed at that time. (See, e.g., *Holland Rantos* v. *United States Department of Health, Education, and Welfare*, 587 F.2d 1173, 1174 n.1 (D.C. Cir. 1978); *Upjohn* v. *Finch*, 422 F.2d 944 (6th Cir. 1970); *Bell* v. *Goddard*, 366 F.2d 177 (7th Cir. 1966)).

Reevaluation of the data previously before the agency is an appropriate basis for subsequent regulatory action where the reevaluation is made in light of newly available regulatory authority (see *Bell* v. *Goddard*, supra, 366 F.2d at 181; *Ethicon, Inc.* v. *FDA*, 762 F.Supp. 382, 389–91 (D.D.C. 1991)), or in light of changes in "medical science." (See *Upjohn* v. *Finch*, supra, 422 F.2d at 951). Regardless of whether data before the agency are past or new data, the "new information" to support reclassification under section 513(e)(1) of the act must be "valid scientific evidence," as defined in section 513(a)(3) of the act and 21 CFR 860.7(c)(2). (See, e.g., *General Medical Co.* v. *FDA*, 770 F.2d 214 (D.C. Cir. 1985); *Contact Lens Assoc.* v. *FDA*, 766 F.2d 592 (D.C. Cir.), cert. denied, 474 U.S. 1062 (1985)). FDA relies upon "valid scientific

evidence" in the classification process to determine the level of regulation for devices. To be considered in the reclassification process, the valid scientific evidence upon which FDA relies must be publicly available. Publicly available information excludes trade secret and/or confidential commercial information, e.g., the contents of a pending PMA. (See section 520(c) of the act (21 U.S.C. 360j(c)).

Section 510(m) of the act (21 U.S.C. 360(m)) provides that FDA exempt a class II device from the premarket notification requirements under section 510(k) of the act if FDA determines that premarket notification is not necessary to provide reasonable assurance of the safety and effectiveness of the device. FDA believes that an automated blood cell separator device operating by centrifugal separation principle should not be exempt from premarket notification under section 510(m) of the act because premarket notification is necessary to provide reasonable assurance of the safety and effectiveness of the device.

II. Regulatory History of the Device

The automated blood cell separator device operating by centrifugal separation principle intended for the routine collection of blood and blood components is a preamendments device classified into class III.

In the **Federal Register** of March 10, 2005 (70 FR 11887), based on new information with respect to the device, FDA proposed, on its own initiative, to reclassify from class III to class II the automated blood cell separator device operating by centrifugal separation principle, when the intended use of the device is for the routine collection of blood and blood components. Interested persons were invited to comment on the proposed rule by June 8, 2005. FDA

received one comment on the proposed rule and draft guidance and that comment was considered as the rule and guidance were finalized.

Also, FDA is correcting a regulatory citation in the proposed rule of March 10, 2005 (70 FR 11887), on page 11892, in the first column, starting in the second line; "21 CFR 803.50(b)(2)" is corrected to read "21 CFR 803.50(b)(3))".

FDA also identified the draft guidance entitled "Guidance for Industry and FDA Staff: Class II Special Controls Guidance Document: Automated Blood Cell Separator Device Operating by Centrifugal or Filtration Separation Principle" as the proposed special controls capable of providing reasonable assurance of safety and effectiveness for these devices.

III. Summary of Final Rule

Under section 513(e) of the act and § 860.130 (21 CFR 860.130), based on new information and on its own initiative, FDA is reclassifying from class III to class II (special controls) the automated blood cell separator device operating by centrifugal separation principle and intended for the routine collection of blood and blood components. The special controls in conjunction with general controls will provide reasonable assurance of the safety and effectiveness of the device. For all other uses, including therapeutic apheresis, the device remains in its current classification as class III. All therapeutic apheresis (blood cell separator) devices are regulated by the Center for Devices and Radiological Health and are not part of § 864.9245 (21 CFR 864.9245).

The automated blood cell separator device operating by centrifugal separation principle is assigned the generic name, automated blood cell separator. It is identified as a device that automatically withdraws whole blood from a donor, separates the blood into components, retains one or more components, and returns the remainder of the blood to the donor. This final

rule removes reference in § 864.9245, to the words that were in parentheses, specifically, red blood cells, white blood cells, plasma, and platelets. The components obtained are transfused or used for further manufacturing. The separation bowls of centrifugal blood cell separators may be reusable or disposable, as specified by the device manufacturer.

Also in this rule, we are removing from § 864.9245(b), the list of special controls for the class II automated blood cell separator device operating by filtration separation principle and intended for the routine collection of blood and blood components. The special controls guidance entitled "Guidance for Industry and FDA Staff: Class II Special Controls Guidance Document: Automated Blood Cell Separator Device Operating by Centrifugal or Filtration Principle" will provide the special controls for both filtration- and centrifugal-based automated blood cell separator devices intended for the routine collection of blood and blood components. The availability of this guidance is announced elsewhere in this issue of the **Federal Register**.

The special controls guidance document recommends that the manufacturer file with FDA for 3 consecutive years an annual report on the anniversary date of the final rule for reclassification or on the anniversary date of 510(k) clearance. Each annual report should include, at a minimum, the following information:

- A summary of anticipated and unanticipated donor adverse events that have occurred and that are not required to be reported by manufacturers under part 803 (21 CFR part 803) Medical Device Reporting (MDR);
- Any subsequent change to the device requiring the submission of a premarket notification in accordance with section 510(k) of the act;

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

For this type of device, FDA has determined that premarket notification is necessary to provide reasonable assurance of the safety and effectiveness of the device and, therefore, the type of device is not exempt from premarket notification requirements. Prior to marketing the device, persons must submit to FDA a premarket notification containing information about the automated blood cell separator device they intend to market. Following the effective date of this final rule, any firm submitting a 510(k) premarket notification for an automated blood cell separator device operating by filtration or centrifugal separation principle and intended for the routine collection of blood and blood components will need to address the issues covered in the special controls guidance. However, the firm need only show that its device meets the recommendations of the guidance or in some other way provides equivalent assurance of safety and effectiveness.

IV. Analysis of Comments on the Proposed Rule and FDA's Response

FDA received one comment on the proposed rule. The comment supported the reclassification of the automated blood cell separator device operating by centrifugal separation principle and intended for the routine collection of blood and blood components. In addition, the comment provided specific questions about the reporting requirements in the special controls guidance document and asked FDA to clarify these reporting requirements.

We first provide a general response to the comment and then respond to the questions submitted in the comment. To make it easier to identify the questions provided in the comment and our responses, the word "Comment," in parentheses, will appear before the description of the question, and the word

"Response," in parentheses, will appear before our response. We numbered the comments to distinguish the questions.

When the device is reclassified, all manufacturers of currently marketed automated blood cell separators operating by centrifugal separation principle not approved under the premarket approval process should file annual reports for 3 consecutive years on the anniversary date of reclassification of the device from class III to class II, or on the anniversary date of the 510(k) clearance. Within the 3-year reporting period, any subsequent change to the device requiring a 510(k) should be included in the annual report. The criteria for reporting changes to the device and its labeling under 510(k) are delineated in FDA's guidance "Deciding When to Submit a 510(k) for a Change to an Existing Device," January 10, 1997.

However, manufacturers of automated blood cell separator devices operating by filtration separation principle that were classified into class II (68 FR 9530, February 28, 2003) were subject to the special controls of § 864.9245 issued in 2003, requiring 3 consecutive years of submitting annual reports. These devices are not required to initiate another cycle of annual reports as a result of the change of special controls for those devices codified by this rule.

Under §§ 606.160(b)(1)(iii) and 606.170 (21 CFR 606.160(b)(1)(iii) and 606.170), the facility using the device to collect blood and blood components is required to keep records of donor adverse reaction complaints and reports, including results of all investigations and followup. Under § 803.50(b)(3), manufacturers are responsible for conducting an investigation of each event and evaluating the cause of the event. The special controls would have the

manufacturer summarize this information and submit it to FDA in the annual report.

Specific questions submitted in the comment and FDA's responses:

(Comment 1) Do you intend to request 3-year annual reporting only for the initial 510(k) clearance for the automated blood cell separator device?

(Response) Yes. The 3-year annual reporting described in the special controls guidance document recommends annual reporting only for the initial 510(k) clearance. Any subsequent change to the device within this 3-year reporting period requiring the submission of a premarket notification in accordance with section 510(k) of the act should be included in the annual report. However, the submission of this 510(k) information concerning a change to the device would not restart the 3-year reporting period.

(Comment 2) Is it correct that for a device originally approved under the PMA process, then switched to a 510(k), annual reporting would not be required?

(Response) Yes, this is correct, if an automated blood cell separator device intended for the routine collection of blood and blood components was originally approved under the PMA process.

(Comment 3) Does this reporting requirement apply to all automated blood cell separator devices operating by centrifugal or filtration separation principle intended for the routine collection of blood and blood components regardless of when the original clearance was granted? Would any preamendments devices be "grandfathered" in so that the reporting would not be required?

(Response) The reporting recommended in the special controls guidance applies to currently marketed products not approved under the PMA process. The 3-year annual reporting for these products should begin on the anniversary

date of the device reclassification from class III to class II, or, on the anniversary date of 510(k) clearance.

In this rulemaking, we are reclassifying the automated blood cell separator device operating by centrifugal separation principle from class III to class II. Therefore, the reclassification date from class III to class II for the automated blood cell separator device operating by centrifugal separation principle and intended for the routine collection of blood and blood components is the date of publication in the **Federal Register** of this final rule (see **DATES**). The reclassification date from class III to class II for the automated blood cell separator device operating by filtration separation principle and intended for the routine collection of blood and blood components is February 28, 2003.

Devices in commercial distribution before May 28, 1976, are also referred to as preamendments devices. On September 12, 1980 (45 FR 60643), FDA issued a final rule classifying these preamendment automated blood cell separator devices as class III (premarket approval). The 1976 amendments did not immediately subject preamendment devices classified in class III to the preamendment process. In the regulation (§ 864.9245), FDA did not set a deadline for the submission of premarket approval applications for the device. That regulation is amended in this rulemaking to reclassify the device from class III to class II. Therefore, preamendments devices are subject to this rulemaking, and the special controls guidance document as of the anniversary date of device reclassification from class III to class II.

V. FDA's Conclusion

Therefore, under section 513 of the act, FDA is adopting the summary of reasons for the Panel's recommendation and the summary of data upon which the Panel's recommendation is based (70 FR 11887 at 11890). FDA is also

the Panel's recommendation is based (70 FR 11887 at 11890). FDA is also adopting the risks to public health stated in the proposed rule (70 FR 11887 at 11891). Furthermore, FDA is issuing a final rule that revises § 864.9245, thereby, reclassifying the generic type of device, automated blood cell separator operated by centrifugal separation principle and intended for the routine collection of blood and blood components from class III into class II.

VI. Analysis of Impacts

FDA has examined the impacts of the final rule under Executive Order 12866 and the Regulatory Flexibility Act (5 U.S.C. 601–612), and the Unfunded Mandates Reform Act of 1995 (Public Law 104–4). Executive Order 12866 directs agencies to assess all costs and benefits of available regulatory alternatives and, when regulation is necessary, to select regulatory approaches that maximize net benefits (including potential economic, environmental, public health and safety, and other advantages; distributive impacts; and equity). The agency believes that this final rule is not a significant regulatory action under the Executive order.

The Regulatory Flexibility Act requires agencies to analyze regulatory options that would minimize any significant impact of a rule on small entities. The reclassification of automated blood cell separator devices from class III to class II will relieve manufacturers of the cost of complying with the premarket approval requirements in section 515 of the act. Although the special controls guidance document recommends that manufacturers of these devices file with FDA an annual report for 3 consecutive years, this is less burdensome than the current premarket approval requirements, including the submission of periodic reports (21 CFR 814.84). By eliminating the need for premarket approval applications, reclassification will reduce regulatory costs

with respect to these devices, impose no significant economic impact on any small entities, and may permit small potential competitors to enter the marketplace by lowering their costs. The agency therefore certifies that this final rule will not have a significant impact on a substantial number of small entities.

Section 202(a) of the Unfunded Mandates Reform Act of 1995 requires that agencies prepare a written statement, which includes an assessment of anticipated costs and benefits, before proposing "any rule that includes any Federal mandate that may result in the expenditure by State, local, and tribal governments, in the aggregate, or by the private sector, of $100,000,000 or more (adjusted annually for inflation) in any one year." The current threshold after adjustment for inflation is $127 million, using the most current (2006) Implicit Price Deflator for the Gross Domestic Product. FDA does not expect this final rule to result in any 1-year expenditure that would meet or exceed this amount.

VII. Environmental Impact

The agency has determined under 21 CFR 25.34(b) that this action is of a type that does not individually or cumulatively have a significant effect on the human environment. Therefore, neither an environmental assessment nor an environmental impact statement is required.

VIII. Federalism

FDA has analyzed this final rule in accordance with the principles set forth in Executive Order 13132. FDA has determined that the rule does not contain policies that have substantial direct effects on the States, on the relationship between the National Government and the States, or on the distribution of power and responsibilities among the various levels of government. Accordingly, the agency has concluded that the rule does not contain policies that have federalism implications as defined in the Executive

order and, consequently, a federalism summary impact statement is not required.

IX. Paperwork Reduction Act of 1995

This final rule contains no collections of information. Therefore, clearance by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (PRA) is not required. FDA concludes that the special controls guidance document contains information collection provisions that are subject to review and clearance by OMB under the PRA. Elsewhere in this issue of the **Federal Register**, FDA is publishing a notice announcing the availability of the guidance document entitled "Class II Special Controls Guidance Document: Automated Blood Cell Separator Device Operating by Centrifugal of Filtration Separation Principle." The notice contains an analysis of the paperwork burden for the guidance.

List of Subjects in 21 CFR Part 864

Blood, Medical devices, Packaging and containers.

■ Therefore, under the Federal Food, Drug, and Cosmetic Act and under authority delegated to the Commissioner of Food and Drugs, 21 CFR part 864 is amended as follows:

PART 864—HEMATOLOGY AND PATHOLOGY DEVICES

■ 1. The authority citation for 21 CFR part 864 continues to read as follows:

Authority: 21 U.S.C. 351, 360, 360c, 360e, 360j, 371.

■ 2. Section 864.9245 is revised to read as follows:

§ 864.9245 Automated blood cell separator.

(a) *Identification.* An automated blood cell separator is a device that uses a centrifugal or filtration separation principle to automatically withdraw whole

blood from a donor, separate the whole blood into blood components, collect one or more of the blood components, and return to the donor the remainder of the whole blood and blood components. The automated blood cell separator device is intended for routine collection of blood and blood components for transfusion or further manufacturing use.

(b) *Classification.* Class II (special controls). The special control for this device is a guidance for industry and FDA staff entitled "Class II Special

Controls Guidance Document: Automated Blood Cell Separator Device Operating by Centrifugal or Filtration Separation Principle."

Dated: 11/26/07
November 26, 2007.

Jeffrey Shuren

Jeffrey Shuren,
Assistant Commissioner for Policy.

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