

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. 96P-0484]

Display Date	5-25-01
Publication Date	5-29-01
Certifier	Womoni Owey

Blood Products Advisory Committee, Medical Devices Panel; Reclassification of Autopheresis-C® System From Class III to Class II

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice of panel recommendation.

SUMMARY: The Food and Drug Administration (FDA) is issuing for public comment the recommendation of the Blood Products Advisory Committee, Medical Devices Panel (the Panel) to reclassify the Autopheresis-C® System, intended for routine collection of blood and blood components, from class III to class II. The Panel made this recommendation after reviewing the reclassification petition submitted by Baxter Healthcare Corp. (Baxter). FDA is also issuing for public comment its tentative findings on the Panel's recommendation. After considering any public comments on the Panel's recommendation and FDA's tentative findings, FDA will approve or deny the reclassification petition by order in the form of a letter to the petitioner. FDA's decision on the reclassification petition will be announced in the **Federal Register**.

DATES: Submit written comments by [*insert date 75 days after date of publication in the Federal Register*].

ADDRESSES: Submit written comments to the Dockets Management Branch (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.

FOR FURTHER INFORMATION CONTACT: Paula S. McKeever, Center for Biologics Evaluation and Research (HFM-17), Food and Drug Administration, 1401 Rockville Pike, Rockville, MD 20852-1448, 301-827-6210.

SUPPLEMENTARY INFORMATION:

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I. Background (Regulatory Authorities)

The Federal Food, Drug, and Comestic 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 of 1990 (Public Law 101–629), and the Food and Drug Administration Modernization Act of 1997 (Public Law 105–115), 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 class I (general controls), class II (special controls), and class III (premarket approval).

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 preamendments devices, are classified after FDA has: (1) Received a recommendation from a device classification Panel (an FDA advisory committee); (2) published the Panel's recommendation for comment, along with a proposed regulation classifying the device; and (3) published a final regulation classifying the device. FDA has classified most preamendments devices under these procedures.

Devices that were not in commercial distribution prior to May 28, 1976, generally referred to as postamendments devices, are classified automatically by statute (section 513(f) of the act) into class III without any FDA rulemaking process. Those devices remain in class III and require premarket approval, unless and until the device is reclassified into class I or II or FDA issues an order finding the device to be substantially equivalent, under section 513(i) of the act, 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 21 CFR part 807 of the regulations.

A preamendments device that has been classified into class III may be marketed, by means of 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.

Reclassification of classified postamendments devices is governed by section 513(f)(3) of the act. This section provides that FDA may initiate the reclassification of a device classified into class III under section 513(f)(1) of the act, or the manufacturer or importer of a device may petition the Secretary of Health and Human Services (the Secretary) for the issuance of an order classifying the device in class I or class II. FDA's regulations in § 860.134 (21 CFR 860.134) set forth the procedures for the filing and review of a petition for reclassification of such class III devices. In order to change the classification of the device, it is necessary that the proposed new class have sufficient regulatory controls to provide reasonable assurance of the safety and effectiveness of the device for its intended use.

Under section 513(f)(3)(B)(i) of the act, the Secretary may, for good cause shown, refer a petition to a device classification panel. The Panel shall make a recommendation to the Secretary respecting approval or denial of the petition. Any such recommendation shall contain: (1) A summary of the reasons for the recommendation, (2) a summary of the data upon which the recommendation is based, and (3) an identification of the risks to health (if any) presented by the device with respect to which the petition was filed.

II. Regulatory History of the Device

The Autopheresis-C® System, intended for the routine collection of blood and blood components, is a postamendments device classified into class III under section 513(f)(1) of the act. Therefore, the device can not be placed in commercial distribution for the routine collection of blood and blood components unless it is reclassified under section 513(f)(3) of the act, or subject to an approved PMA under section 515 of the act. This action is taken in accordance with section 513(f)(3) of the act and § 860.134 of the regulations, based on information submitted in a petition for reclassification by Baxter on June 17, 1996, requesting reclassification of the Autopheresis-C® System, intended for routine collection of blood and blood components, from class III to class

II. Although Baxter submitted its petition for reclassification under section 513(e) of the act, the request should have been submitted under section 513(f)(3), and therefore FDA has considered the petition filed under section 513(f)(3). Consistent with the act and the regulation, FDA referred the petition to the Panel for its recommendation on the requested change in classification. The Panel met on September 26, 1996, at a public meeting.

III. Device Description

The Autopheresis-C® System, intended for routine collection of blood and blood components, is an automated plasmapheresis system. It utilizes a spinning membrane separation device to achieve rapid and gentle separation by filtration of whole blood into concentrated cellular components for reinfusion and into plasma for collection.

The instrument uses a system of pumps and sensors controlled by a microprocessor and it incorporates a variety of safety and alarm system functions. It uses a fully automated processing program to collect a preset volume of plasma from a donor. Plasma collection in the Autopheresis-C® System involves sequential phases of collection of plasma from the donor and reinfusion of the residual red blood cell concentrate back to the donor.

The Autopheresis-C® System is currently employed in commercial plasma centers where it is used to collect Source Plasma, and it is also found in blood centers and hospital blood banks where it is used for the collection of plasma for preparation of fresh frozen plasma.

IV. Recommendations of the Panel

At a public meeting on September 27, 1996, the Panel unanimously recommended that the Autopheresis-C® System, intended for routine collection of blood and blood components, be reclassified from class III to class II. The Panel also recommended that subsequent membrane-based blood cell separators be classified as class II devices, if in the opinion of FDA they are substantially equivalent to the Autopheresis-C® System, the predicate device. The Panel believed that class II with the special controls of a periodic report filed annually for a minimum of 3 years

with emphasis on adverse reactions would provide reasonable assurance of the safety and effectiveness of the device.

V. Risks to Health

FDA has identified the following risks associated with apheresis blood donation and processing: (1) The potential loss of blood due to leaks; (2) thrombosis due to activation of factors by foreign surfaces; (3) toxic reaction to citrate or heparin anticoagulant; (4) damage to red cells, activation of complement, and denaturation of proteins; (5) potential for sepsis and fever due to bacterial contamination of the donor's blood returned to the donor; (6) infectious disease risk to the donor or to the operator due to leaks; (7) electrical shock hazard; (8) donor stress reaction due to removal or loss of blood; and (9) reservoir rupture.

Some of the reported adverse donor reactions are: (1) Allergic reaction; (2) vasovagal or syncopal reaction; (3) citrate toxicity; (4) hematoma; (5) hematuria or hemoglobinuria; (6) hypovolemic reaction; (6) myocardial infarct in three cases unrelated to the donation procedure; (7) mesenteric thrombosis unrelated to the donation procedure; (8) chest pains; (9) high blood pressure; (10) blood clotting; (11) nonresponsive donor during or after the donation procedure; (12) death of a donor several days following an apheresis unrelated to the procedure; (13) blood spray; and (14) tubing separation.

VI. Summary of Reasons for Recommendation

After reviewing the data and information contained in the petition and provided by FDA, and after consideration of the open discussions during the Panel meeting and the Panel members' personal knowledge of and clinical experience with the device, the Panel gave the following reasons in support of its recommendation to reclassify the Autopheresis-C® System, intended for routine collection of blood and blood components, as the predicate device and the subsequent generic type of filtration-based blood cell separator for use in routine collection of donor plasma from class III to class II.

The Panel believes that the Autopheresis-C® System and subsequent generic type of filtration-based blood cell separator should be reclassified into class II because special controls, in addition to general controls, provide reasonable assurance of the safety and effectiveness of the device, and there is sufficient information to establish special controls to provide such assurance.

VII. Summary of Data Upon Which the Panel Recommendation Is Based

In addition to the potential risks of the Autopheresis-C® System and subsequent generic types of filtration-based blood cell separators described above, there is sufficient information about the benefits of the device. Specifically, the Autopheresis-C® System has been used since 1986, and the data presented by Baxter showed no evidence of cellular or protein damage to the donor blood; the procedure was well tolerated by the donor; and the instrument was safe and effective for plasma collection. The period from 1986 to 1996 showed that a 0.03 percent of donations were associated with some type of event which were reported to Baxter.

Based on the available information, FDA believes that the special controls discussed below are capable of providing reasonable assurance of the safety and effectiveness of the Autopheresis-C® System, intended for routine collection of blood and blood components, and subsequent generic types of filtration-based blood cell separators with regard to the identified risks to health of this device.

VIII. Special Controls

In addition to general controls, FDA believes that the following special control is adequate to address the risks to health described for this device. The manufacturer must file an annual report with FDA on the anniversary date of reclassification for 3 consecutive years. A manufacturer of a device determined to be substantially equivalent¹ to the Autopheresis-C® System, intended for routine collection of blood and blood components, also is required to comply with the same general

¹ For assistance see the guidance document entitled "The New 510(k) Paradigm: Alternate Approaches to Demonstrating Substantial Equivalence in Premarket Notifications," March 1998, at <http://www.fda.gov/cdrh>.

and special controls. Any subsequent change to the device requiring the submission a premarket notification in accordance with section 510(k)² of the act, should be included in the annual report.

Unless FDA specifies otherwise, each annual report (special control) must include:

1. A summary of adverse donor reactions reported by the users to the manufacturer that do not meet the threshold for medical device reporting under 21 CFR part 803;
2. Any change to the device, including but not limited to:
 - new indications for use of the device;
 - labeling changes, including operation manual changes;
 - computer software changes, hardware changes, and disposable item changes, e.g., collection bags, tubing, filters;
3. Equipment failures, including software, hardware, and disposable item failures, e.g., collection bags, tubing, filters.

IX. FDA's Tentative Findings

The Panel and FDA believe that the Autopheresis-C[®] System, intended for routine collection of blood and blood components, and subsequent generic types of filtration-based blood cell separators should be classified into class II because special controls, in addition to general controls, would provide reasonable assurance of the safety and effectiveness of the device, and there is sufficient information to establish special controls to provide such assurance.

However, any change in the indication for use, i.e., for therapeutic purposes, would require a PMA since these devices are not included in the reclassification action.

² For assistance see the guidance document entitled "Deciding When to Submit a 510(k) for a Change to an Existing Device," January 1997, at <http://www.fda.gov/cdrh>.

X. References

The following references have been placed on display in the Dockets Management Branch and may be seen by interested persons between 9 a.m. and 4 p.m., Monday through Friday.

1. Petition for reclassification of the Autopheresis-C® System from class III to class II by Baxter Healthcare Corp., June 17, 1996.
2. Transcript of the Blood Products Advisory Committee, 52d Meeting, September 27, 1996.

XI. 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.

XII. Analysis of Impacts

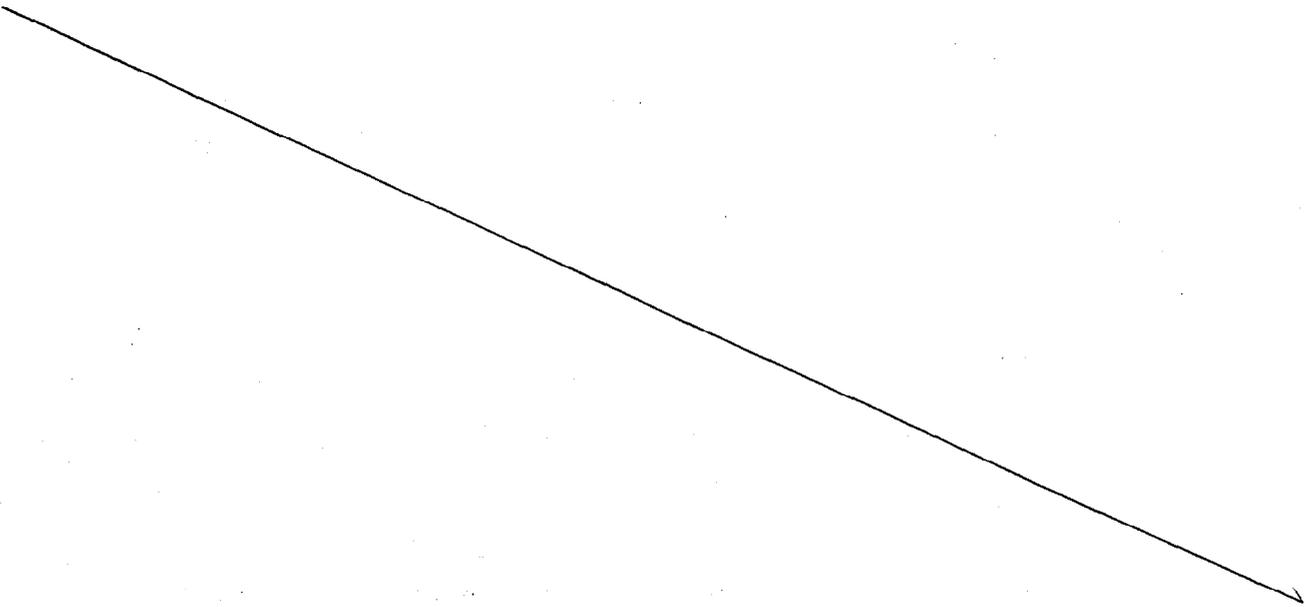
FDA has examined the impacts of the notice under Executive Order 12866 and the Regulatory Flexibility Act (5 U.S.C. 601–612) (as amended by subtitle D of the Small Business Regulatory Fairness Act of 1996 (Public Law 104–121), and the Unfunded Mandates Reform Act of 1995 (Public Law 104–4). Executive 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 reclassification action is consistent with the regulatory philosophy and principles identified in the Executive order. In addition, the reclassification action is not a significant regulatory action as defined by the Executive order and so is not subject to review 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. Reclassification of the device 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. Because reclassification will reduce regulatory costs with

respect to this device, it will impose no significant economic impact on any small entities, and it may permit small potential competitors to enter the marketplace by lowering their costs. The agency therefore certifies that this reclassification action, if finalized, will not have a significant economic impact on a substantial number of small entities. In addition, this reclassification action will not impose costs of \$100 million or more on either the private sector or State, local, and tribal governments in the aggregate, and therefore a summary statement of analysis under section 202(a) of the Unfunded Mandates Reform Act of 1995 is not required.

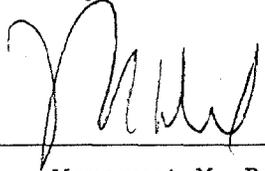
XIII. Request for Comments

Interested persons may submit to the Dockets Management Branch (address above) written comments regarding this document by [*insert date 75 days after date of publication in the **Federal Register***]. Two copies of any comment are to be submitted, except that individuals may submit one copy. Comments are to be identified with the docket number found in brackets in the heading of this document. Received comments may be seen in the Dockets Management Branch between 9 a.m. and 4 p.m., Monday through Friday.



Dated: 5/17/01
May 17, 2001.

cb0027



Margaret M. Dotzel,
Associate Commissioner for Policy.

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COPY OF THE ORIGINAL**



[FR Doc. 01-????? Filed ??-??-01; 8:45 am]

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