

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 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.

Any change in the indication for use, i.e., for therapeutic use, would require a PMA because devices for therapeutic use are not included in this reclassification action.

#### IV. 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 syncope 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.

In addition to the potential risks of the AUTOPHERESIS-C SYSTEM and subsequent generic types of filtration-based blood cell separators, 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 show no evidence of cellular or protein damage to the donor blood; the procedure is well tolerated by the donor; and the instrument is 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 potential adverse event that were reported to Baxter.

#### V. Panel Recommendation

The Panel reviewed the data and information contained in the petition and provided by FDA, and considered the open discussions during the Panel meeting. The Panel consisted of members with personal knowledge of and clinical experience with the device. At a public meeting on September 27, 1996, the Panel unanimously recommended that the AUTOPHERESIS-C SYSTEM and subsequent membrane-based blood cell separators substantially equivalent to this device, intended for routine collection of blood and blood components, be reclassified from class III to class II. 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.

#### VI. Special Controls

FDA believes that, in addition to general controls, the special controls described below address these risks and provide reasonable assurance of the safety and effectiveness of the device. FDA described the special controls in the **Federal Register** of May 29, 2001 (66 FR 29149 at 29151), and provided an opportunity for public comment. FDA did not receive any comments on the special controls. Therefore, on September 5, 2001, FDA issued an order to the petitioner reclassifying the AUTOPHERESIS-C SYSTEM, and substantially equivalent devices of this generic type, from class III to class II subject to the special controls described below (Ref. 3). Through this final rule, FDA is codifying the reclassification of this device by revising 21 CFR 864.9245. By listing the contents of the special controls, new manufacturers of substantially equivalent devices can comply with the same special controls.

In addition to general controls of the act, automated blood cell separator devices operating by filtration principle are subject to the following special controls in order to provide reasonable assurance of the safety and effectiveness of the 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 equivalent to the AUTOPHERESIS-C SYSTEM, intended for routine

collection of blood and blood components, also is required to comply with the same general and special controls. 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.

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.

#### 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. Analysis of Impacts

FDA has examined the impacts of the final rule under Executive Order 12866, the Regulatory Flexibility Act (5 U.S.C. 601–612), and the Unfunded Mandates Reform Act of 1995 (2 U.S.C. 1501 *et seq.*). 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 consistent with the regulatory philosophy and principles identified in the Executive order. In addition, the final rule is not a significant regulatory action as defined by the Executive order and so is not subject to review under the Executive order.

Under the Regulatory Flexibility Act, if a rule has a significant economic impact on a substantial number of small entities, an agency must consider alternatives that would minimize the economic impact of the rule on small