

Polyvalent Bacterial Vaccines with "no U.S. Standard of Potency," manufactured by Hollister-Stier Laboratories, LLC, U.S. license 1272, became effective August 3, 2000. The revocation of the biologics license for the manufacture of Diphtheria and Tetanus Toxoids and Pertussis Vaccine Adsorbed, Diphtheria and Tetanus Toxoids Adsorbed, Diphtheria Toxoid Adsorbed, and Tetanus Toxoid Adsorbed, manufactured by BioPort Corp., U.S. license 1260, became effective November 20, 2000. Other products under these licenses are not affected by this revocation.

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

SUPPLEMENTARY INFORMATION: In a notice published in the *Federal Register* of May 15, 2000 (65 FR 31003), FDA issued a proposed order to accept the conclusions and recommendations of the Vaccines and Related Biological Products Advisory Committee (VRBPAC) and the Panel on Review of Allergenic Extracts (the Allergenic Panel) concerning the safety, effectiveness, and labeling of certain bacterial vaccines and related biological products that were previously classified into Category IIIA (remaining on the market pending further studies in support of effectiveness). On the basis of the Allergenic Panel and the VRBPAC findings, FDA proposed to reclassify certain Category IIIA products into Category I (safe, effective, and not misbranded) or Category II (unsafe, ineffective, or misbranded). This action was taken under the reclassification review procedures specified in 21 CFR 601.26. The proposed order also announced the agency's intention to revoke the biologics licenses for those bacterial vaccines and related products classified as Category II (unsafe, ineffective, or misbranded).

Certain Category IIIA bacterial vaccines and toxoids with standards of potency listed in the proposed order were classified into two categories based upon their use as a primary immunogen or as a booster. Diphtheria and Tetanus Toxoids Adsorbed, and Tetanus Toxoid Adsorbed manufactured by BioPort Corp. were recommended by the VRBPAC for classification into Category II (unsafe, ineffective, or misbranded) for primary immunization and Category I (safe, effective, and not misbranded) for booster immunization.

Similarly, certain bacterial vaccines and related biological products listed in

the proposed order were recommended for classification into Category II for both diagnosis and immunotherapy by the Allergenic Panel. Polyvalent Bacterial Vaccines with "no U.S. Standard of Potency," manufactured by Hollister-Stier Laboratories, LLC, was recommended for classification into Category II for both diagnosis and immunotherapy by the Allergenic Panel.

FDA agreed with the recommendations of the VRBPAC and the Allergenic Panel to reclassify the above cited products into Category II for their respective indications, and in the proposed order provided notice of the agency's intent to revoke the licenses to manufacture these products. On June 19, 2000, Hollister-Stier Laboratories, LLC, submitted a letter to FDA voluntarily requesting revocation of its license to manufacture Polyvalent Bacterial Vaccines with "no U.S. Standard of Potency." On August 9, 2000, BioPort Corp. submitted a letter to FDA voluntarily requesting revocation of its license to manufacture Diphtheria and Tetanus Toxoids Adsorbed, and Tetanus Toxoid Adsorbed. In its August 9, 2000, letter, BioPort Corp. also voluntarily requested revocation of its license to manufacture Diphtheria and Tetanus Toxoids and Pertussis Vaccine Adsorbed, and Diphtheria Toxoid Adsorbed, although these products were not included in the proposed order.

The proposed order announced that the agency would publish a notice of opportunity for a hearing on the revocation of the license of each product classified in Category II. BioPort Corp. and Hollister-Stier Laboratories waived their opportunity for a hearing when they voluntarily requested license revocation for their reclassified Category II products.

Accordingly, under the provisions of 21 CFR 601.5(a), section 351 of the Public Health Service Act, and under authority delegated to the Commissioner of Food and Drugs (21 CFR 5.10) and redelegated to the Director, Center for Biologics Evaluation and Research (21 CFR 5.68), FDA revoked the biologics license issued to Hollister-Stier Laboratories, LLC, U.S. license 1272, for the manufacture of Polyvalent Bacterial Vaccines with "no U.S. Standard of Potency," effective August 3, 2000; and FDA revoked the biologics license issued to BioPort Corp., U.S. license 1260, for the manufacture of Diphtheria and Tetanus Toxoids and Pertussis Vaccine Adsorbed, Diphtheria and Tetanus Toxoids Adsorbed, Diphtheria Toxoid Adsorbed, and Tetanus Toxoid Adsorbed effective November 20, 2000.

Dated: May 9, 2001.

Kathryn C. Zoon,

Director, Center for Biologics Evaluation and Research.

[FR Doc. 01-13306 Filed 5-25-01; 8:45 am]

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. 96P-0484]

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 August 13, 2001.

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:

I. Background (Regulatory Authorities)

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 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 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.

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

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>.

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>.

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 August 13, 2001. 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: May 17, 2001.

Margaret M. Dotzel,

Associate Commissioner for Policy.

[FR Doc. 01-13302 Filed 5-25-01; 8:45 am]

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

Science Advisory Board to the National Center for Toxicological Research; Notice of Meeting

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

This notice announces a forthcoming meeting of a public advisory committee of the Food and Drug Administration (FDA). At least one portion of the meeting will be closed to the public.

Name of Committee: Science Advisory Board to the National Center for Toxicological Research (NCTR).

General Function of the Committee: The board advises the Director, NCTR, in establishing, implementing, and evaluating the research programs that assist the Commissioner of Food and Drugs (the Commissioner) in fulfilling regulatory responsibilities. The board provides an extra-agency review in ensuring that the research programs at NCTR are scientifically sound and pertinent.

Date and Time: The meeting will be held on June 11, 2001, 1 p.m. to 5:30 p.m., and June 12, 2001, 8:30 a.m. to 1 p.m.

Location: NCTR, Bldg. #12, Conference Center, Jefferson, AR.

Contact: Leonard M. Schechtman, NCTR (HFT-10), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301-827-6696, or FDA Advisory Committee Information Line, 1-800-741-8138 (301-443-0572 in the Washington, DC area), code 12559. Please call the Information Line for up-to-date information on this meeting.

Agenda: The board will be presented with progress reports on the implementation of recommendations made by the board at its last meeting on NCTR's research programs in endocrine disrupter knowledge base and microbiology. The NCTR director will provide a center update and a discussion of future research directions. A proposal will be made to the board that it consider establishing a subcommittee on scientific opportunities to improve regulatory science through collaboration with external stakeholders. A report will be provided to the board on the activities of an existing subcommittee with a similar focus (Advisory Committee for Pharmaceutical Science, Nonclinical Studies Subcommittee) NCTR division directors will discuss the accomplishments and future directions for their divisions.

Procedure: On June 11, 2001, from 1 p.m. to 5:30 p.m., and June 12, 2001, from 8:30 a.m. to 12 noon, the meeting is open to the public. Interested persons may present data, information, or views, orally or in writing, on issues pending before the committee. Written submissions may be made to the contact person by May 18, 2001. Oral presentations from the public will be scheduled between approximately 11 a.m. and 12 noon on June 12, 2001. Time allotted for each presentation may be limited. Those desiring to make formal oral presentations should notify the contact person before May 18, 2001, and submit a brief statement of the general nature of the evidence or arguments they wish to present, the

names and addresses of proposed participants, and an indication of the approximate time requested to make their presentation.

Closed Committee Deliberations: On June 12, 2001, from 12 noon to 1 p.m., the meeting will be closed to permit discussion where disclosure would constitute a clearly unwarranted invasion of personal privacy (5 U.S.C. 552b(c)(6)). This portion of the meeting will be closed to permit discussion of information concerning individuals associated with the research programs at NCTR.

The Commissioner approves the scheduling of meetings at locations outside the Washington, DC area on the basis of the criteria of 21 CFR 14.22 of FDA's regulations relating to public advisory committees.

Notice of this meeting is given under the Federal Advisory Committee Act (5 U.S.C. app. 2).

Dated: May 22, 2001.

Linda A. Suydam,

Senior Associate Commissioner.

[FR Doc. 01-13378 Filed 5-25-01; 8:45 am]

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

Proposed Collection: Comment Request; a Study of Motivations and Deterrents to Blood Donation in the United States

SUMMARY: In compliance with the requirement of section 3506(c)(2)(A) of the Paperwork Reduction Act of 1995, for opportunity for public comment on proposed data collection projects, the National Heart, Lung, and Blood Institute (NHLBI), the National Institutes of Health (NIH), will publish periodic summaries of proposed projects to be submitted to the Office of Management and Budget (OMB) for review and approval.

Proposed Collection

Title: A Study of Motivations and Deterrents to Blood Donation in the United States. *Type of Information Collection Request:* NEW. *Need and Use of Information Collection:* There are serious blood shortages in the U.S. and the situation is predicted to worsen unless corrective measures are initiated. Through a randomized, anonymous mail survey of individuals who have donated blood at one of the five blood centers participating in the NHLBI Retrovirus Donor Study (REDS), this study will examine the personal, or