Guidance for FDA Reviewers

Premarket Notification Submissions for Empty Containers for the Collection and Processing of Blood and Blood Components

Comments and suggestions regarding this document may be submitted at anytime to Dockets Management Branch (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. All comments should be identified with the title of this guidance document.

Additional copies are available from the Office of Communication, Training and Manufacturers Assistance (HFM-40), 1401 Rockville Pike, Rockville, MD 20852-1448 or by calling 1-800-835-4709 or 301-827-1800 or from the Internet at http://www.fda.gov/cber/guidelines.htm

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This guidance document represents the Agency's current thinking on the review of premarket notification submissions for empty containers for the collection and processing of blood and blood components used in blood establishments. It does not create or confer any rights, privileges, or benefits on or for any person and does not operate to bind FDA or the public. An alternate approach may be used if such approach satisfies the requirements of the applicable statutes and regulations.

I. INTRODUCTION

This guidance presents an overview of the type of information FDA reviewers should expect to be included in the premarket notifications submitted for such devices and the approach FDA reviewers normally should take in reviewing premarket submissions for empty containers for the collection and processing of blood and blood components used in blood establishments. The detailed requirements for premarket notifications in 21 CFR Part 807 should also be consulted.

The development of this document is based on information currently recognized as important for a complete and adequate review of these devices by the Regulatory Project Management Branch (RPMB) in the Office of Blood Research and Review (OBRR). The use of this document for the preparation of a 510(k) for empty containers for the collection and processing of blood and blood components is not mandatory and its use does not ensure FDA clearance of a device. However, the use of this document will help ensure that the basic elements are present to conduct an evaluation of substantial equivalence for the device(s). Certain 510(k) submissions may require additional information not described in this document. This guidance is subject to revision depending upon new technological information and regulatory requirements.

GENERAL INFORMATION

510(k) Summary or Statement. In accordance with the Safe Medical Devices Act of 1990 as amended in the Food and Drug Administration Modernization Act (FDAMA) of 1997 and 21 CFR Part 807.87(h), the applicant must submit either: (1) a summary of the safety and effectiveness information in the premarket notification submission upon which an equivalence determination could be based (i.e., a "510(k) summary"); or (2) a statement that safety and effectiveness information will be made available to interested persons upon request (i.e., a "510(k) statement"). The summary or statement should be clearly identified as a "510(k) summary" or a "510(k) statement".

Truthful and Accurate Statement. As required by 21 CFR 807.87(k), the manufacturer or applicant must also provide a statement that all data and information submitted in the premarket notification are truthful and accurate and that no material fact has been omitted.

Indications for Use Form. On January 1, 1996, FDA implemented a change in the way pre-market notifications (510(k)s) would be handled. FDA issued a letter on February 6, 1996, concerning this change to all 510(k) submitters requesting that they clearly identify the "Indications for Use" for which a substantially equivalent determination is sought using a separate page that is clearly labeled as "Indications for Use". This separate sheet should include the trade name of the device and the proposed uses for the device.

The New 510(k) Paradigm. On March 20, 1998, new guidance for the submission of 510(k)s became effective. This guidance is titled "The New 510(k) Paradigm." More information on the New 510(k) Paradigm is available at: http://www.fda.gov/cdrh/modact/modern.html.

Other documents and guidances which may be useful in the preparation of the 510(k) can be found on the CDRH home page at http://www.fda.gov/cdrh or by telephone at the [CDRH FAX on Demand at 800-899-0381].

II. DEVICE DEFINITIONS

An empty container for the collection and processing of blood and blood components is a device intended for medical purposes that is an empty plastic bag or plastic or glass bottle used to collect, store, or transfer blood and blood components for further processing (21 CFR 864.9100).

Standards

Standard for these devices that is recognized by FDA:

ANSI/AAMI/ISO 10993-1: 1997 Biological Evaluation of Medical Devices - Part 1: Evaluation and Testing

III. PRODUCT DESCRIPTIONS

The following information should be included in a 510(k) submission:

- Empty containers for the collection and processing of blood and blood components are classified in 21 CFR 864.9100 (a); PRODUCT CODE is 81 KSR. The trade name of the device must be clearly identified as required by 21 CFR 807.87(a).

- A detailed description of the product, its intended use(s), and its indication(s) for use.

- Identification of a legally marketed device to which substantial equivalence is claimed and provide a comparative analysis (descriptive or tabular) of the similarities

and differences of the device to that legally marketed device in terms of intended use, indications for use, design features, technological and mechanical properties, functional specifications, and operational parameters.

IV. DESIGN AND PERFORMANCE FEATURES

The design and performance features of the empty container for the collection and processing of blood and blood components provide the basis for understanding the intended uses and capabilities of the device. Design features address the intended uses of the device to meet the need of the user and the patient, while the performance features ensure that the device is safe and effective when used in accordance with the directions. The features listed in this section are important in determining whether the empty container for the collection and processing of blood and blood components described in the 510(k) submission is substantially equivalent to a legally marketed device. A discussion of many of these features can be found in the standards document identified in Section II of this guidance document.

Materials of construction
- U.S.P. Approved

Engineering diagrams

Functionality
- Physical durability and robustness
- Temperature range

Performance
- Quality of product prepared

Safety features
- Leachability

V. SAFETY AND EFFECTIVENESS TESTING

A. Biocompatibility of Materials

Except as noted below, biocompatibility testing is indicated for all parts of the device that have direct or indirect contact with the patient and is performed to determine the potential toxicity that can result from contact of the component materials of the device with the patient's body. The materials used in the construction of the device should not, either directly or indirectly through the release of their material constituents, (1) produce unreasonable risk of adverse local or systemic effects; (2) be carcinogenic; or (3) cause adverse reproductive and developmental effects. The evaluation of any new device intended for human use requires data from systematic testing to ensure that the benefits

provided by the final product will exceed any potential risks produced by device materials.

Biocompatibility testing is indicated when a "new" or non-conventional material or chemical component is incorporated into a device and there is no known appropriate predicate use, or for which the safety or effectiveness of the resulting formulation is in question. These materials or chemical components include plastics, metals, colorants, plasticizers, germicides, and chemical or other treatments of the device or device components.

Biocompatibility testing should be submitted on the finished product, using test conditions simulating as closely as possible actual patient use. Biocompatibility testing is not indicated for materials and chemical components that have already been incorporated in legally marketed devices with similar conditions of use, or have a demonstrated history of safety and effectiveness; however, the biocompatibility of these materials and chemical components should be fully discussed to support the lack of testing.

Refer to ISO-10993-1: 1997 Part I "Biological Evaluation of Medical Devices, Evaluation and Testing", and the FDA-modified matrix to identify the types of biocompatibility testing that should be considered in evaluating the safety-in-use of medical devices and materials. The ISO Standard, Part 1, uses an approach to test selection that is very similar to the Tripartite Biocompatibility Guidance. It also uses a tabular format (matrix) for laying out the test requirements based on the various factors discussed above. The matrix consists of two tables, "Initial Evaluation Tests for Consideration" and "Supplementary Evaluation Tests for Consideration." To harmonize biological response testing with the requirements of other countries, FDA will apply the ISO Standard, Part 1, in the review process in lieu of the Tripartite Biocompatibility Guidance.

Reviewers in OBRR should accept data developed according to ISO-10993-1: 1997, Part 1, with the matrix as modified and presented in Blue Book Memorandum #G95-1 entitled "Use of International Standard ISO-10993, Biological Evaluation of Medical Devices Part-1: Evaluation and Testing." The manufacturer or the applicant also has the option of providing a summary of the specific tests conducted in accordance with the standard.

All testing performed should either conform with the recommended standard documents or be accompanied by an explanation as to how the testing or methodology is an acceptable alternative to that of the standard. FDA reviewers should advise manufacturers or applicants to initiate discussions with the RPMB prior to the initiation of expensive, long-term testing of any new device materials to ensure that the proper testing will be conducted and unnecessary testing will not be undertaken. We also recognize that an ISO standard is a document that undergoes periodic review and is subject to revision.

B. Device Performance

The submission would normally contain data to support the safe and effective operations of the device when used according to the directions for use. However, the manufacturer or applicant now has the option of providing a declaration of conformance to a standard. A declaration of conformance to a standard obviates the need for the submission of protocols and raw data as called for by that standard. If the submission does not include a declaration of conformance to a standard, the submission should include performance data from bench testing. Additional data may include results from testing under actual conditions or in a simulated environment in which the device is expected to be used. As with the biocompatibility testing, functional testing should be performed in conformance with the recommended standards or be accompanied by a justification that the testing or methodology is an acceptable alternative to that particular standard.

FDA reviewers should advise manufacturers or applicants to initiate discussions with the RPMB prior to the initiation of extensive performance testing to ensure that proper testing will be conducted. Since standards are documents that undergo periodic review and are subject to revision, FDA reviewers should also notify manufacturers or applicants of any future revisions of any performance standards referenced here.

VI. LABELING

It is important to the user that the labeling for the empty container bear clear, accurate, and complete information for use concerning any relevant indications for use, conditions and limitations of use, hazards, contraindications, and precautions in its use.

The 510(k) should identify and discuss all known situations and events that could cause the device to malfunction or become a hazard to the user or patient when the device is being properly used. The labeling should discuss these situations and hazards in a precaution, warning, or advisory statement as appropriate.

A 510(k) submission for the empty containers for the collection and processing of blood and blood components should include the proposed package labels and labeling. Labeling refers to the package label plus other written, printed, or graphic material that accompanies the device or that is placed on either the device or any of its wrappers or containers. Advertising may be considered labeling, especially if it accompanies the device. The labeling must bear adequate directions for use and any warnings needed to ensure the safe use of the device. See sections 201 (k) and 502(f)(1) and (2) of the Federal Food, Drug, and Cosmetic Act.