

“Guidance for Industry: Animal Drug Sponsor Fees Under the Animal Drug User Fee Act” and follow the directions. Copies of this guidance may be obtained on the Internet from the CVM home page at <http://www.fda.gov/cvm>.

Dated: September 21, 2004.

**Jeffrey Shuren,**

*Assistant Commissioner for Policy.*

[FR Doc. 04–21677 Filed 9–27–04; 8:45 am]

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## DEPARTMENT OF HEALTH AND HUMAN SERVICES

### Food and Drug Administration

[Docket No. 2004D–0410]

#### Draft Guidance for Industry and Food and Drug Administration Staff: Application User Fees for Combination Products; Availability

**AGENCY:** Food and Drug Administration, HHS.

**ACTION:** Notice.

**SUMMARY:** The Food and Drug Administration (FDA) is announcing the availability of a draft document entitled “Guidance for Industry and FDA Staff: Application User Fees for Combination Products.” This draft guidance provides guidance to industry and FDA staff on marketing application user fees for combination products. The guidance also describes how the “barrier to innovation” waiver provision under the prescription drug user fee provisions of the Federal Food, Drug, and Cosmetic Act (act) may be applied to innovative combination products in the infrequent situation where FDA requires the submission of two marketing applications.

**DATES:** Submit written or electronic comments on this draft guidance by November 29, 2004 to ensure their adequate consideration in preparation of the final guidance. General comments on agency guidance documents are welcome at any time.

**ADDRESSES:** Submit written requests for single copies of the draft guidance to the Office of Combination Products, 15800 Crabbs Branch Way, suite 200, Rockville, MD 20855. Send one self-addressed adhesive label to assist that office in processing your requests. See the **SUPPLEMENTARY INFORMATION** section for information on electronic access to the guidance.

Submit written comments on the draft guidance to the Division of Dockets Management (HFA–305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. Submit

electronic comments to <http://www.fda.gov/dockets/ecomments>.

**FOR FURTHER INFORMATION CONTACT:** Mark D. Kramer, Office of Combination Products (HFG–3), Food and Drug Administration, 15800 Crabbs Branch Way, suite 200, Rockville, MD 20855, 301–427–1934.

#### **SUPPLEMENTARY INFORMATION:**

##### **I. Background**

A combination product is a product comprised of any combination of a drug and a device; a biological product and a device; a drug and a biological product; or a drug, device and a biological product. Depending upon the type of combination product, approval, clearance or licensure may be obtained through submission of a single marketing application, or through separate marketing applications for the individual constituent parts of the combination product. For most combination products, a single marketing application is sufficient for the product’s approval, clearance, or licensure. In some cases, two marketing applications may be submitted for a combination product when one application would suffice. For example, a sponsor may choose to submit two applications when one would suffice in order to receive some benefit from having two applications. In other cases, FDA may determine that two marketing applications are necessary.

In 1992, Congress passed the Prescription Drug User Fee Act (PDUFA). PDUFA authorized FDA to collect fees from companies that produce certain human drug and biological products. The Medical Device User Fee and Modernization Act of 2002 amended the act to provide for user fees for the review of device applications. When a company requests approval of a new drug, device or biological product prior to marketing, it must submit an application along with a fee to support the review process.

This document provides guidance to industry and FDA staff on marketing application user fees for combination products as defined under 21 CFR 3.2(e). The guidance document explains that combination products for which a single marketing application is submitted will be assessed the user fee associated with that particular type of marketing application. The document explains that, if a sponsor chooses to submit two marketing applications when one would suffice, a user fee for each application would ordinarily be assessed. The document also explains that, in the infrequent situation where FDA requires two marketing

applications for a combination product, two application fees would ordinarily be assessed. However, the guidance also describes how the PDUFA “barrier to innovation” waiver provision may be applied to innovative combination products for which FDA requires the submission of two marketing applications. Such a waiver would provide a reduction in application user fees equivalent to the additional fee burden associated with the submission of two marketing applications. This guidance does not address how FDA will determine whether a single marketing application or multiple marketing applications should be submitted for a combination product. Such guidance is in development and will be provided separately for public review and comment.

##### **II. Significance of Guidance**

This draft guidance document is being issued consistent with FDA’s good guidance practices regulation (21 CFR 10.115). The draft guidance, when finalized will represent the agency’s current thinking on application user fees for combination products. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. An alternative approach may be used if such approach satisfies the requirements of the applicable statute and regulations.

##### **III. Electronic Access**

To receive “Guidance for Industry and FDA Staff: Application User Fees for Combination Products,” you may either send a fax request to 301–427–1935, or an e-mail request to [combination@fda.gov](mailto:combination@fda.gov) to receive a hard copy or electronic copy of the document.

Persons with access to the Internet may obtain the draft guidance at either <http://www.fda.gov/oc.combination/default.htm> or <http://www.fda.gov/ohrms/dockets/default.htm>.

##### **IV. Comments**

The draft guidance is being distributed for comment purposes only and is not intended for implementation at this time. Interested persons may submit to the Division of Dockets Management (see **ADDRESSES**) written or electronic comments regarding the draft guidance. Submit written or electronic comments to ensure adequate consideration in preparation of the final guidance. Submit a single copy of electronic comments or two paper copies of any mailed comments, except that individuals may submit one paper copy. Comments are to be identified with the docket number found in the

brackets in the heading of this document. A copy of the draft guidance and received comments are available for public examination in the Division of Dockets Management between 9 a.m. and 4 p.m., Monday through Friday.

Dated: September 22, 2004.

**Jeffrey Shuren,**

*Assistant Commissioner for Policy.*

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## DEPARTMENT OF HEALTH AND HUMAN SERVICES

### Food and Drug Administration

[Docket No. 2004N-0367]

#### Cumulative List of Exceptions and Alternative Procedures Approved by the Director of the Center for Biologics Evaluation and Research

**AGENCY:** Food and Drug Administration, HHS.

**ACTION:** Notice.

**SUMMARY:** The Food and Drug Administration (FDA) is announcing the availability a cumulative list of exceptions and alternative procedures to requirements regarding blood, blood components, and blood products that have been approved by the Director of the Center for Biologics Evaluation and Research (CBER). Also, FDA is announcing that this list is posted on the Internet and it will be periodically updated.

**ADDRESSES:** Copies of the cumulative list of exceptions and alternative procedures are available from the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852, and the Office of Communication, Training and Manufacturers Assistance (HFM-40), Food and Drug Administration, suite 200 N, 1401 Rockville Pike, Rockville, MD 20852-1448, 1-800-835-4709 or 301-827-1800. See the **SUPPLEMENTARY INFORMATION** section for electronic access to the cumulative list of exceptions and alternative procedures.

**FOR FURTHER INFORMATION CONTACT:** Nathaniel L. Geary, Center for Biologics Evaluation and Research (HFM-17), Food and Drug Administration, suite 200N, 1401 Rockville Pike, Rockville, MD 20852-1448, 301-827-6210.

#### **SUPPLEMENTARY INFORMATION:**

##### **I. Background**

The Director of CBER has approved exceptions or alternative procedures that have been requested by blood

establishments under § 640.120 (21 CFR 640.120). Section 640.120 grants the Director authority to approve exceptions or alternatives to any requirement in subchapter F (Biologics) of chapter I, parts 600 through 680 (21 CFR parts 600 through 680) regarding blood, blood components, or blood products.

FDA is announcing publication of a cumulative list of exceptions and alternative procedures to requirements regarding blood, blood components, and blood products that have been approved by the Director of CBER. Also, FDA is announcing that this list is posted on the Internet and it will be periodically updated.

##### **II. List of Approved Exceptions and Alternative Procedures (§ 640.120(b))**

###### **§ 600.15(a)**

- Allow use of autologous units that were transported in a shipping container without ice and exposed to temperatures of 10.0 °C to 10.5 °C for 10 minutes.

###### **§ 606.60(b)**

- Calibrate digital thermometer according to the schedule recommended by manufacturer, instead of monthly as required by regulation.

###### **§ 606.65(e)**

- Deviate from manufacturer's instructions to use the Gen-Probe Procleix HIV-1/HCV Assay and Roche COBAS Ampliscreen HIV-1 and HCV nucleic acid tests on whole blood, red blood cells (RBC), platelets, source leukocytes, therapeutic exchange plasma, and recovered plasma intended for further manufacturing.

- Deviate from manufacturer's instruction to use samples containing up to 200 milligrams (mg)/deciliters (dL) hemoglobin or 800 mg/dL triglycerides in the following assays: Abbott HIV AB HIV-1/HIV-2, (rDNA) EIA (LN3A77), Ortho Hepatitis B Core Antibody, Ortho Hepatitis B Surface Antigen ELISA System 2, and Roche Alanine Aminotransferase.

- Deviate from manufacturer's instruction to use an alternate testing algorithm for confirming repeatedly reactive HIV-1 p24 antigen test results. Specifically, a licensed HIV-1 single unit Nucleic Acid Test will be performed in place of the HIV-1 p24 antigen neutralization test and the results used for donor notification and counseling and recipient tracing.

- Deviate from manufacturer's instructions to test donor specimens that were initially reactive using Ortho HbsAg System 3, in duplicate using Genetic Systems HbsAg EIA 3.0 (shaker method). If either or both of the donor samples test reactive using Genetic Systems HbsAg EIA 3.0 (shaker

method), the donor specimen will be tested using Genetic Systems HbsAg Confirmatory 3.0 (shaker method).

###### **§ 606.121**

- Use of full face green labels for autologous use only units.
- Use of black print for all statements on container labels (omit use of statements in red print.) (Regulation revised—variance request no longer needed.)

- Use of "Autologous" on label in lieu of "Paid" or "Volunteer"

- Omit special labeling from RBC with positive antibody screens that are suspended in additive solution, if the supernatant of the additive solution was tested using approved methods and found to be negative for unexpected antibodies.

- Place ABO/Rh label and "Donor Untested" on group and type label position.

- Print the anticoagulant name after the proper product name instead of preceding it. (Done for ISBT 128 labels.)

###### **§ 606.122(m)**

- Extend the storage time of thawed Fresh Frozen Plasma (FFP) at 1 to 6 °C to 24 hours, instead of 6 hours.

###### **§ 606.151**

- Omit performing a minor side crossmatch on RBC prepared in additive solutions that have not been screened for unexpected antibodies.

- Use of a computer (electronic) crossmatch instead of a major side crossmatch. (Regulation revised—variance request no longer needed.)

- Use of a type and screen procedure as an alternative method for the antiglobulin crossmatch. (Regulation revised—variance request no longer needed.)

- Allow use of a recipient sample up to 72 hours old for pre-transfusion testing. (Regulation revised—variance request no longer needed.)

###### **§ 610.40**

- Ship source leukocytes to the manufacturer before infectious disease testing has been completed, provided the product is labeled that testing is not complete and stored in quarantine until the manufacturer has received the test results. (Regulation revised—variance request no longer needed.)

- Ship autologous blood unit to another establishment without testing unit for communicable disease agents. Testing performed on sample drawn on subsequent donation.

- Ship autologous blood unit to another establishment for processing and labeling and return to collecting facility without testing unit for communicable disease agents, provided neither facility has a crossover policy.

- Allow shipment under quarantine of untested source plasma labeled as