Proposed Rules

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This section of the FEDERAL REGISTER contains notices to the public of the proposed issuance of rules and regulations. The purpose of these notices is to give interested persons an opportunity to participate in the rule making prior to the adoption of the final rules.

DEPARTMENT OF AGRICULTURE

Animal and Plant Health Inspection Service

9 CFR Part 3

[Docket No. 93–076–14]

Animal Welfare; Marine Mammals

AGENCY: Animal and Plant Health Inspection Service, USDA.

ACTION: Notice of reopening and extension of comment period.

SUMMARY: We are reopening and extending the comment period for our proposed rule to amend the Animal Welfare Act regulations concerning the humane handling, care, treatment, and transportation of marine mammals in captivity. This action will allow interested persons additional time to prepare and submit comments.

DATES: We invite you to comment on Docket No. 93–076–11. We will consider all comments that we receive by May 26, 1999.

ADDRESSES: Please send your comment and three copies to: Docket No. 93–076–11, Regulatory Analysis and Development, PPD, APHIS, Suite 3C03, 4700 River Road, Unit 118, Riverdale, MD 20737–1238.

Please state that your comment refers to Docket No. 93–076–11.

You may read any comments that we receive on this docket in our reading room. The reading room is located in room 1141 of the USDA South Building, 14th Street and Independence Avenue, SW., Washington, DC. Normal reading room hours are 8 a.m. to 4:30 p.m., Monday through Friday, except holidays. To be sure someone is there to help you, please call (202) 690–2817 before coming.

APHIS documents published in the **Federal Register**, and related information, including the names of organizations and individuals who have commented on APHIS rules, are available on the Internet at http://www.aphis.usda.gov/ppd/rad/webrepor.html.

FOR FURTHER INFORMATION CONTACT: Dr. Barbara Kohn, Senior Staff Veterinarian, Animal Care, APHIS, 4700 River Road Unit 84, Riverdale, MD 20737–1228, (301) 734–7833.

SUPPLEMENTARY INFORMATION:

Background

On February 23, 1999, we published in the **Federal Register** (64 FR 8735–8755, Docket No. 93–076–11) a proposal to amend the Animal Welfare Act regulations concerning the humane handling, care, treatment, and transportation of marine mammals in captivity. The proposed regulations were developed by the Marine Mammal Negotiated Rulemaking Advisory Committee.

Comments on the proposed rule were required to be received on or before April 26, 1999. We are reopening and extending the comment period on Docket No. 93–076–11 for 30 days to May 26, 1999. This action will allow interested persons additional time to prepare and submit comments.

Authority: 7 U.S.C. 2131–2159; 7 CFR 2.22, 2.80, and 371.2(d).

Done in Washington, DC, this 10th day of April 1999.

Joan M. Arnoldi,

Acting Administrator, Animal and Plant Health Inspection Service.

[FR Doc. 99–12236 Filed 5–13–99; 8:45 am]

BILLING CODE 3410–34–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Parts 207, 607, and 807

[Docket No. 98N–1215]

Foreign Establishment Registration and Listing

AGENCY: Food and Drug Administration, HHS.

ACTION: Proposed rule.

SUMMARY: The Food and Drug Administration (FDA) is proposing to amend its regulations pertaining to the registration of foreign establishments and the listing of human drugs, animal drugs, biological products, and devices. The proposal would require foreign establishments whose products are imported or offered for import into the United States to register with FDA. The proposal would also require foreign establishments to identify a United States agent and would describe some of the agent's responsibilities. The agency is proposing these changes to implement section 417 of the Food and Drug Administration Modernization Act of 1997 (FDAMA) as it pertains to foreign establishment registration.

DATES: Written comments by July 28, 1999. Written comments on the information collection requirements by June 14, 1999.

ADDRESSES: Submit written comments to the Dockets Management Branch (HFA–305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. Submit written comments on the information collection requirements to the Office of Information and Regulatory Affairs, Office of Management and Budget (OMB), New Executive Office Bldg., 725 17th St. NW., rm. 10235, Washington, DC 20502, Attn: Wendy Taylor, Desk Officer for FDA.

FOR FURTHER INFORMATION CONTACT: Philip L. Chao, Office of Policy (HF–23), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301–827–3380.

SUPPLEMENTARY INFORMATION:

I. Introduction

On November 21, 1997, the President signed FDAMA into law (Pub. L. 105–115). Section 417 of FDAMA amended section 510(i) of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 360(i)) to require, in part, that:

(1) Any establishment within any foreign country engaged in the manufacture, preparation, propagation, compounding, or processing of a drug or a device that is imported or offered for import into the United States shall register with the Secretary the name and place of business of the establishment and the name of the United States agent for the establishment.

(2) The establishment shall also provide the information required by subsection (j).

* * *

(Section 510(j) of the act pertains to product listing.)

Generally speaking, before FDAMA's enactment, foreign establishments could, but were not required to, register with FDA. Foreign establishments were required, however, to list their products regardless of whether the foreign establishment was registered (see, e.g.,

former section 510(i) of the act, § 207.40(a) (21 CFR 207.40(a)) (38 FR 6258 at 6267, March 7, 1973)). This generated confusion and resulted in foreign establishments not complying with the listing requirement. Moreover, in some cases, the lack of registration information on foreign establishments made it difficult to determine the source of specific imported products, particularly products that were impure, counterfeit products, or products whose safety or efficacy had not been established.

In contrast, before FDAMA was enacted, the act required—and continues to require—all domestic establishments to register unless they are specifically exempted from the registration requirement and to list their products.

FDAMA changed this situation by requiring all foreign establishments engaged in the manufacture, preparation, propagation, compounding, or processing of a drug or a device that is imported or offered for import into the United States to register. It also emphasized that foreign establishments must list their products. Thus, under the act, as revised by FDAMA, both foreign and domestic establishments must now register and list their products.

II. Description of the Proposed Rule

The proposed rule would amend the establishment registration and listing regulations in part 207 (21 CFR part 207) (human and animal drugs), part 607 (21 CFR part 607) (human blood and blood products), and part 807 (21 CFR part 807) (devices). In general, the proposal would remove the distinctions between domestic and foreign establishments where appropriate, would require foreign establishments to identify a United States agent, and would describe some of the United States agent's duties.

The proposal would also make minor technical amendments, such as updating addresses of FDA offices and the names of marketing applications, to be consistent with current FDA practices.

The proposed rule would not affect veterinary biologics because such products are regulated by the U.S. Department of Agriculture.

A. Proposed Changes to Part 207 (Human Drugs and Animal Drugs)

1. Section 207.3—Definitions

a. *Definition of ''commercial distribution''*. Section 207.3(a)(5) currently defines ''commercial distribution'' as:

> any distribution of a human drug except for investigational use under part 312 of this chapter, and any distribution of an animal drug or an animal feed bearing or containing an animal drug for noninvestigational uses, but the term does not include internal or interplant transfer of a bulk drug substance between registered domestic establishments within the same parent, subsidiary, and/or affiliate company.

The proposed rule would add a new sentence to this definition to clarify that, for foreign establishments, commercial distribution does not include distribution of a human or animal drug that is neither imported nor offered for import into the United States. This change is intended to reflect the statutory language limiting the registration requirement to those foreign establishments that are ''engaged in the manufacture, preparation, propagation, compounding, or processing of a drug or a device that is imported or offered for import *into the United States*'' (emphasis added), as well as the definition of ''interstate commerce'' in section 201(b) of the act (21 U.S.C. 321(b)).

b. *Definition of ''United States agent''*. The proposed rule would define ''United States agent,'' at new § 207.3(a)(11), as ''a person residing or maintaining a place of business in the United States whom a foreign establishment designates as its agent.'' *Black's Law Dictionary* defines ''reside'' as ''live, dwell, abide, sojourn, stay, remain, lodge'' and ''to settle oneself or a thing in a place, to be stationed, to remain or stay, to dwell permanently or continuously * * *'' (see *Black's Law Dictionary* 1308 (6th ed. 1990)) and defines ''place of business,'' in part, as ''The location at which one carries on his business or employment'' (*id*. at 1149). Thus, by using the term ''residing'' and referring to a ''place of business,'' proposed § 207.3(a)(11) would permit a foreign establishment to designate, as its United States agent, either an individual who lives in the United States or a firm or company in the United States where an individual or individuals conduct business or are employed. The definition of United States agent would exclude mailboxes, answering machines or services, or other places where an individual acting as the foreign establishment's agent is not physically present.

Additionally, FDA emphasizes that it interprets section 510(i)(1) of the act as allowing for only one United States agent for each foreign establishment, for purposes of section 510(i) of the act. This interpretation is both efficient (because FDA would communicate or interact with only one United States agent rather than multiple agents who represent or purport to represent the same foreign establishment) and consistent with section 510(i)(1) of the act because the act refers to the United States agent in singular, rather than plural, terms.

2. Section 207.7—Establishment Registration and Product Listing for Human Blood and Blood Products and for Medical Devices

Section 207.7(a) currently states, in part, that owners and operators of human blood and blood product establishments are to register and list their products in accordance with part 607.

The proposal would revise the address for the office in the Center for Biologics Evaluation and Research that receives the registration and listing information.

3. Section 207.10—Exemptions for Domestic Establishments

Currently, § 207.10 exempts various domestic entities or persons from the registration requirements. Some exemptions reflect the statutory language in section 510(g) of the act, whereas others were exempted by FDA because registering such persons would not be necessary to protect the public health.

The proposed rule would amend § 207.10 to delete the word ''domestic'' from its title, so that the provision pertains to exemptions for both foreign and domestic establishments. FDA is proposing this change because the establishment registration requirements now apply to both domestic and foreign establishments, so no further distinction is necessary in the heading of § 207.10.

However, the exemptions currently found in § 207.10(a) and (b) (pertaining to pharmacies operating under applicable local laws and to hospitals, clinics, and public health agencies that maintain establishments in conformance with local laws regulating the practice of pharmacy or medicine) would remain limited to establishments in the United States and its territories. FDA is not proposing to extend these exemptions to foreign pharmacies, hospitals, clinics, and public health agencies because the statutory exemption for pharmacies in section 510(g)(1) of the act does not extend to foreign pharmacies and because FDA has limited experience with or access to foreign laws on the practice of pharmacy or medicine and, therefore, cannot readily determine whether these foreign establishments are in compliance with such laws. The agency also lacks sufficient information to make a finding, under section 510(g)(5) of the act, that registration by such foreign establishments is not

necessary to protect the public health. However, it is unlikely that many foreign pharmacies, hospitals, clinics, or public health agencies export or offer to export drugs or devices to the United States, so few of these foreign establishments should be subject to the registration requirement. Those that do export to the United States should be in FDA's inventory of registered foreign establishments for the efficient administration and enforcement of the act.

4. Section 207.20—Who Must Register and Submit a Drug List

Section 207.20(a) currently requires ''owners and operators of all drug establishments, not exempt under section 510(g) of the act or subpart D of this part 207, that engage in the manufacture, preparation, propagation, compounding, or processing of a drug or drugs'' to register and list every drug in commercial distribution. The rule also states that owners and operators must register and list every drug in commercial distribution ''whether or not the output of such establishment or any particular drug so listed enters interstate commerce * * *.'' However, under the current rule, drug listing is not required ''at this time for the manufacturing, preparation, propagation, compounding, or processing of an animal feed (including a Type B and Type C medicated feed) bearing or containing an animal drug * * *.''

The proposed rule would amend § 207.20(a) to clarify that the exemptions are under section 510(g) of the act or subpart B (''Exemptions'') of part 207. The agency is making this change because the proposed rule would place all exemptions in subpart B of part 207 and would remove all exemptions from subpart D.

The proposal would also revise § 207.20(a) so that the language requiring owners and operators to register their establishments and to list drugs, whether or not the output of the establishment or any particular drug so listed enters interstate commerce, would apply only to domestic firms. FDA is proposing this change because the agency has no intent to require foreign establishments to list drugs that do not enter interstate commerce by being imported or offered for import into the United States.

The proposal would also make two minor amendments to § 207.20(a). The proposed rule would delete the phrase ''at this time'' because the phrase is unnecessary. The proposal would also move the parenthetical language referring to Type B and Type C medicated feed so that it refers accurately to animal feeds bearing or containing an animal drug rather than to animal feeds generally and revise the parenthetical language so that it refers to Type B ''or'' Type C medicated feed. This would eliminate any misconception that the product be both a Type B and Type C medicated feed.

Additionally, FDA notes that § 207.20(a), as currently written, permits a company to submit listing information on behalf of a parent, subsidiary, and/or affiliate company for all establishments when operations are conducted at more than one establishment and there exists joint ownership and control among all the establishments. FDA interprets this provision, and similar provisions at §§ 607.20(a) and 807.20(a), as including foreign establishments so long as operations are conducted at more than one establishment and there exists joint ownership and control among all the establishments.

The proposed rule would also add ''abbreviated new drug applications'' and ''abbreviated new animal drug applications'' to the list of marketing applications in § 207.20(c). FDA is proposing these actions because such applications, which were created by the Drug Price Competition and Patent Term Restoration Act and the Generic Animal Drug and Patent Term Restoration Act, are marketing applications that require a registered establishment. These applications were inadvertently omitted from previous rulemakings amending part 207. (The agency notes that, in the **Federal Register** of July 31, 1998 (63 FR 40858), it published a proposed rule that would eliminate establishment and product licenses and implement biologics licenses.)

5. Section 207.21—Times for Registration and Drug Listing

Section 207.21 currently describes when establishments should register and submit listing information and states that an owner or operator of an establishment that has just begun manufacturing or processing drugs should register within 5 days after submitting a new drug application, new animal drug application, medicated feed application, antibiotic application, or an establishment license application to manufacture a biological product. (The agency notes that, in the **Federal Register** of July 31, 1998 (63 FR 40858), it published a proposed rule that would eliminate establishment and product licenses and implement biologics licenses.)

The proposed rule would add ''abbreviated new drug applications'' and ''abbreviated new animal drug applications'' to the list of marketing applications in § 207.21. As stated earlier, these applications were inadvertently omitted from previous rulemakings amending part 207.

6. Section 207.25—Information Required in Registration and Drug Listing

Section 207.25(b)(2) currently requires the numbers for various marketing applications to be included in the drug listing information submitted to the agency. For example, if a new drug application were assigned number 20–570, the application number that would be included in the drug listing information would be NDA 20–570.

The proposed rule would add abbreviated new animal drug applications to the list of marketing applications in § 207.25. As stated earlier, this action is necessary because abbreviated new animal drug applications were inadvertently omitted from previous rulemakings amending part 207.

7. Section 207.37—Inspection of Registrations and Drug Listings

Section 207.37(a) currently states where copies of registration forms filed by establishments are available for inspection. In general, the forms are available at the Center for Drug Evaluation and Research and at FDA district offices.

The proposed rule would amend § 207.37(a) to update the addresses in the Center for Drug Evaluation and Research and would state that copies of registration forms submitted by foreign establishments are available for inspection at the Office of Compliance in the Center for Drug Evaluation and Research. Copies of forms submitted by domestic establishments would continue to be available for inspection at FDA district offices and at the Office of Compliance in the Center for Drug Evaluation and Research.

The proposal would also update the addresses in § 207.37(b).

8. Section 207.40—Drug Listing Requirements for Foreign Drug Establishments

Section 207.40 currently requires foreign drug establishments to comply with drug listing requirements and prohibits the importation of drugs that are not listed (except for investigational drugs). It also requires foreign establishments to submit drug listing information in English and to provide the name and address of the

establishment and the person responsible for submitting the drug listing information.

Proposed § 207.40(a) would revise the existing language to require foreign establishments whose drugs are imported or offered for import into the United States to comply with the establishment registration and listing requirements in subpart C (''Procedures for domestic drug establishments''), unless exempt under subpart B (''Exemptions''). The proposal would expressly require foreign establishments to register as required by section 510(i)(1) of the act.

Proposed § 207.40(b) would prohibit the importation of drugs from unregistered foreign establishments, in addition to prohibiting the importation of unlisted drugs. This action is consistent with several provisions of the act. Section 301(p) of the act (21 U.S.C. 331(p)) considers a foreign establishment's failure to register or to submit listing information to be a prohibited act. Section 501(a)(2)(B) of the act (21 U.S.C. 351(a)(2)(B)) considers a drug to be adulterated if the methods used in or the facilities or controls used for the drug's manufacture, processing, packing, or holding do not conform to current good manufacturing practice (CGMP). Additionally, under section 801(a) of the act (21 U.S.C. 381(a)), FDA may refuse to admit into the United States drugs that appear to be: (1) Manufactured, processed, or packed under insanitary conditions; (2) forbidden or restricted in sale in the country in which they are produced or from which they are exported; or (3) adulterated, misbranded, or in violation of section 505 of the act (21 U.S.C. 355). Here, if a foreign establishment fails to register (thereby engaging in a prohibited act), it is likely that FDA has not inspected the establishment. As a result, FDA would be unable to determine whether that foreign establishment meets CGMP. Consequently, drugs from such unregistered establishments would appear to be adulterated under section 801(a)(3) of the act. Therefore, to enforce sections 301(p), 501(a), and 801(a) of the act effectively, in conjunction with section 510(i) of the act as it pertains to foreign establishment registration, the agency is proposing to amend § 207.40(b) to prohibit the importation of drugs that are not manufactured, prepared, propagated, compounded, or processed at a registered foreign establishment.

Moreover, this interpretation is consistent with the purpose of the registration provision as originally enacted in 1962. While the FDAMA legislative history is virtually silent on the purpose of foreign registration, the Drug Amendments of 1962 make clear the connection between registration and factory inspection. The Drug Amendments amended the act to include, among other things, a registration provision requiring domestic drug establishments to register and authorizing foreign establishments to register, and a ''current good manufacturing practice'' provision which now appears at section 501(a)(2)(B) of the act. According to the Senate Report accompanying the amendments, the purpose of the registration provision is

> to assist the [FDA] to identify and inspect all places where drugs are being made, and to take appropriate action * * * against those who fail to register * * * The committee believes that drugs should not be on the market unless the [FDA] knows who is making them, and where they are being made, and is able to inspect the facilities in which they are being made. This will help to stop illicit and substandard manufacturers who do not follow the methods or establish the controls called for by good manufacturing practice. The registration system * * * is thus a facet of * * * the provisions on quality manufacturing controls * * *.''

S. Rept. 87–1744 (1962), reprinted in 1962 U.S.C.C.A.N., 2884, 2888–89. Therefore, the agency believes that the act supports a prohibition on importation of drugs manufactured by unregistered establishments.

FDA acknowledges that section 502(o) of the act (21 U.S.C. 352(o)) considers a drug to be misbranded if the drug was manufactured, prepared, propagated, compounded, or processed in an establishment that is not registered in any State and that FDAMA did not amend section 502(o) of the act to include language describing a similar restriction on drugs from unregistered foreign establishments. Nevertheless, as explained above, FDA has sufficient legal authority to prohibit the importation of drugs from unregistered foreign establishments, as a regulation for the efficient enforcement of the act under section 701(a) of the act (21 U.S.C. 371(a)), and such a prohibition would give foreign establishments, like their domestic counterparts, an incentive to register.

Proposed § 207.40(b) would also require foreign establishments to submit registration and listing information, including labels and labeling, in English. This would be consistent with the existing provision which requires that listing information be submitted in the English language.

Section 207.40(c) currently requires every foreign drug establishment to submit, as part of its drug listing, the establishment's name and address and the name of the individual responsible for submitting the listing information. It also directs the foreign establishment to report any changes at specified intervals.

The proposed rule would revise § 207.40(c) to require each foreign establishment to submit the name, address, and phone number of its United States agent as part of the establishment's initial and updated registration information. As stated earlier, FDA interprets section 510(i) of the act as allowing for only one United States agent for each foreign establishment and providing a foreign establishment the discretion to choose either an individual person or entity to serve as its United States agent. Some establishments may prefer to select a company or firm as the United States agent rather than depend on a single person, and so proposed § 207.40(c) would allow an entity to be the United States agent.

Proposed § 207.40(c) would also require a foreign establishment to report changes in the United States agent's name, address, or phone number to FDA within 5 days of the change and would require each foreign establishment to designate only one United States agent. In drafting this provision, FDA considered allowing such changes to be reported either by the foreign establishment or by the United States agent because, on rare occasions, the agency has contacted individuals whom establishments had identified as their agent or representative only to find that the individual had terminated its relationship with the establishment or was unaware that the establishment had designated the individual as its representative. Although the proposal would permit only establishments to report changes in the United States agent's name, address, or phone number, the agency invites comments as to whether the rule should permit the United States agent to report such changes as well.

Additionally, proposed § 207.40(c) would require the United States agent to reside or maintain a place of business in the United States, and, upon request from FDA, to assist FDA in communications with the foreign drug establishment, to respond to questions about the establishment's products that are imported or offered for import into the United States, and to assist FDA in scheduling inspections of the foreign drug establishment. For example, in the event of a product recall, the agency might ask the United States agent about the product's distribution in the United

States in order to facilitate the recall (although, in many instances, FDA will either have information on the imported product's distribution or be able to acquire such information from other government agencies so as to reduce the need to contact the United States agent on such matters). The agency is proposing these requirements because its experience indicates that communications with foreign establishments are much better and problems or concerns are resolved much faster when the agency can work with a person residing or maintaining a place of business in the United States.

FDA considered, but did not propose, a requirement that the United States agent possess sufficient knowledge of English to facilitate communications between FDA and the foreign establishment. The agency chose to omit such a requirement, in part, because the United States agent, by virtue of residing or maintaining a place of business in the United States, should be able to communicate in English or may be assumed to have sufficient knowledge of English. Should this assumption prove to be incorrect, FDA may revise the rule to require the United States agent to be able to communicate in English.

The proposal would also consider information or documents provided by FDA to the United States agent to be equivalent to providing the same information or documents to the foreign drug establishment. This provision would apply when the agency is unable to contact the foreign manufacturer directly or expeditiously, including (but not limited to) situations where FDA has been unsuccessful in contacting the foreign establishment directly because the establishment has moved, when FDA correspondence sent directly to the foreign establishment has been returned to the agency because the local postal authorities cannot locate the foreign establishment, or in emergencies. This proposed provision, however, suggests that foreign establishments should select their United States agent carefully. FDA is aware that some foreign establishments have multiple distributors in the United States, but sometimes select one distributor as the establishment's representative or agent. This may present a problem if FDA, under proposed § 207.40(c), sought to provide certain documents or information to a distributor-agent concerning products that might have been supplied to or actions taken by a different distributor. For example, foreign establishment ''A'' might have three distributors in the United States (distributors ''B,'' ''C,'' and ''D'') and have selected distributor B as its United States agent. If FDA, under proposed § 207.40(c), were to contact distributor B, in its capacity as the United States agent, about problems associated with a particular import, such contact might inadvertently present business concerns for the foreign establishment because distributor B might be unaware of other distributors in the United States or other products shipped to the United States, or FDA might be unaware that the information concerned a product that had not been shipped to distributor B. Distributor B also might not relay the information from FDA to the foreign establishment if the failure to relay the information would confer a competitive advantage to itself.

Contact between FDA and a United States agent might also present issues involving trade secrets or confidential commercial information. For example, section 301(j) of the act, with few exceptions, prohibits the agency from disclosing trade secrets. Yet there may be instances where the agency needs to discuss information which may involve trade secrets or confidential commercial information. If the agency is unable to contact the foreign manufacturer, it may not be permitted to discuss the information with the United States agent, even if a public health emergency exists.

Thus, FDA advises foreign establishments to choose their United States agents carefully in order to avoid any conflict of interest or confidentiality problems.

B. Proposed Changes to Part 607 (Human Blood and Blood Products)

1. Section 607.3—Definitions

a. *Definition of ''commercial distribution''.* Section 607.3(e) currently defines ''commercial distribution,'' in part, as ''any distribution of a blood product except pursuant to the investigational use provisions of part 312 of this chapter * * *.''

The proposal would add a new sentence to § 607.3(e) to state that, for foreign establishments, commercial distribution does not include distribution of any blood or blood product that is neither imported nor offered for import into the United States. This change is necessary because FDA does not intend to require foreign establishments to register or to list blood products that are not imported to or offered for import into the United States, consistent with the language of section 510(i)(1) of the act.

b. *Definition of ''United States agent''.* The proposed rule would define ''United States agent,'' in a new § 607.3(j), as ''any person residing or maintaining a place of business in the United States whom a foreign establishment designates as its agent.'' This definition, and FDA's interpretation of the definition, would be identical to those in proposed § 207.3(a)(11).

2. Section 607.7—Establishment Registration and Product Listing of Blood Banks and Other Firms Manufacturing Human Blood and Blood Products

Section 607.7(b) and (c) currently provide an address for the Center for Biologics Evaluation and Research from which registration forms may be obtained and to which they may be sent.

The proposed rule would amend § 607.7(b) and (c) to update the address.

3. Section 607.20—Who Must Register and Submit a Blood Product List

Section 607.20(a) currently states, in part, that an owner or operator of an establishment that engages in the manufacture of blood products must register and submit a list of every blood product in commercial distribution, ''whether or not the output of such blood product establishment or any particular blood product so listed enters interstate commerce.''

The proposal would revise § 607.20(a) so that the language requiring owners and operators to register their establishments and to list blood products whether or not the output of the establishment or any particular blood product so listed enters interstate commerce applies only to domestic firms. This change is consistent with proposed § 607.3(e).

4. Section 607.22—How and Where to Register Establishments and List Blood Products

Section 607.22 currently describes which forms should be used for registration and listing purposes and provides an address from which the forms may be obtained. Section 607.22(b) further states that listing information may be submitted on computer tapes.

The proposed rule would update FDA's addresses in § 607.22(a). The proposal would also amend § 607.22(b) to delete the language concerning tapes for computer input and the submission of proposed formats for FDA review and approval. FDA is proposing to delete this provision because it has never been used.

5. Section 607.25—Information Required for Establishment Registration and Blood Product Listing

Section 607.25(a), in describing FDA Form FD–2830, uses the words ''post office ZIP code.''

The proposal would revise § 607.25(a) to refer to a post office code. This change reflects the fact that many foreign countries do not use the term ''ZIP'' code.

6. Section 607.26—Amendments to Establishment Registration

Section 607.26 requires changes in individual ownership, ''corporate or partnership structure location or blood-product handling activity'' to be reported. This provision was intended to require, among other things, firms to report changes in corporate or partnership structure as well as changes in location, but was occasionally misinterpreted as applying solely to changes in location.

Consequently, the proposal would revise this language to read as ''Changes in individual ownership, corporate or partnership structure, location, or blood-product handling activity'' to clarify that changes in corporate or partnership structure or location or blood-product handling activity are to be reported.

7. Section 607.31—Additional Blood Product Listing Information

Section 607.31 describes additional information that FDA may require by letter, but states that the Commissioner will perform various actions, such as making a request or a finding, before requiring the additional information.

The proposal would substitute the ''Director of the Center for Biologics Evaluation and Research'' for the ''Commissioner'' throughout § 607.31(a) because the center director, rather than the Commissioner, performs those functions.

The proposal would also delete the text in § 607.31(b) pertaining to the voluntary reporting of information on the quantity of blood product distributed. FDA is proposing to delete the text in paragraph (b) because the form specified in the rule, Form FD–2831 (Blood Establishment Resource Summary), is obsolete, and the provision has not been used.

8. Section 607.35—Notification of Registrant; Blood Product Establishment Registration Number and NDC Labeler Code

Section 607.35(a) currently states that the Commissioner will provide a validated copy of form FD–2830 to the location shown for the registering establishment.

The proposal would amend § 607.35(a) to state that a copy will also be sent to the reporting official if that official is at another address. This would accommodate those employees or representatives who submit registration and listing information for an establishment but are not located at that establishment.

The proposal would also substitute the ''Director of the Center for Biologics Evaluation and Research'' for the ''Commissioner'' because the center director, rather than the Commissioner, performs that function.

9. Section 607.37—Inspection of Establishment Registrations and Blood Product Listings

Section 607.37 currently lists addresses where filed forms are available for inspection or where requests for information regarding blood establishment registration and listing should be sent.

The proposal would update the addresses.

10. Section 607.40—Establishment Registration and Blood Product Listing Requirements for Foreign Blood Product Establishments

Currently, § 607.40, entitled ''Blood product listing requirements for foreign blood product establishments,'' requires such establishments to comply with blood product listing requirements and prohibits the importation of most nonlisted blood products. The provision also requires foreign blood product establishments to submit listing information in English and, as part of their listing, to submit the name and address of the establishment and the name of the individual responsible for submitting the product listing information.

Proposed § 607.40(a) would require foreign establishments to comply with establishment registration requirements in addition to blood product listing requirements. To complement this change, the proposal would revise the title to § 607.40 to read as ''Establishment registration and blood product listing requirements for foreign blood product establishments.''

Proposed § 607.40(b) would enable FDA to prohibit the importation of blood products from unregistered foreign establishments, in addition to prohibiting the importation of unlisted blood products. This prohibition would be similar to proposed § 207.40(b) because blood and blood products are ''drugs'' within the meaning of section 201(g) of the act. As stated earlier, the prohibition is consistent with sections 301(p), 501(a), and 801(a) of the act because, if a foreign establishment fails to register, FDA will be unable to determine, through an establishment inspection, whether that foreign establishment meets CGMP. Consequently, blood and blood products from those establishments would appear to be adulterated under section 801(a)(3) of the act. Therefore, to enforce sections 301(p), 501(a), and 801(a) of the act effectively, in conjunction with section 510(i) of the act as it pertains to foreign establishment registration, proposed § 607.40(b) would prohibit the importation of blood products that are not manufactured, prepared, propagated, compounded, or processed at a registered foreign establishment.

Proposed § 607.40(b) would also add establishment registration information to types of information that must be submitted in the English language.

Proposed § 607.40(c) would require foreign blood product establishments to submit the name and address of the establishment and the name of the individual responsible for submitting the establishment registration and product listing information as part of the establishment registration and blood product listing. Proposed § 607.40(c) would also require foreign establishments to report any changes in their registration or listing information.

Proposed § 607.40(d) would require each foreign blood product establishment to submit the name, address, and phone number of its United States agent as part of its initial and updated registration information. Each foreign blood product establishment would be permitted to designate only one United States agent. Similar to proposed § 207.40(c), proposed § 607.40(d) would require the United States agent to reside or maintain a place of business in the United States, and, upon request from FDA, assist FDA in communications with the foreign establishment, respond to questions concerning imported products, and assist FDA in scheduling inspections. Proposed § 607.40(d) would also enable FDA, when it is unable to contact the foreign manufacturer directly or expeditiously, to provide information or documents to the United States agent and for that act to be considered equivalent to providing the same information or documents to the foreign establishment. Changes to the United States agent's name, address, or phone number would, under proposed § 607.40(d), be reported to FDA within 5 days of the change.

11. Section 607.65—Exemptions for Blood Product Establishments

Section 607.65 lists several classes of persons who are exempt from registration and blood product listing under part 607. These exemptions, which currently pertain only to domestic establishments, reflect the statutory exemptions in section 510(g) of the act or represent a finding by the agency that registration of such persons is not necessary for the protection of the public health. For example, § 607.65(c) exempts persons who manufacture blood products solely for use in research, teaching, or analysis. This exemption is consistent with section 510(g)(3) of the act. Section 607.65(d) exempts carriers who receive, carry, hold, or deliver blood products in their usual course of business, while § 607.65(e) exempts persons who engage solely in the manufacture of in vitro diagnostic blood products and reagents that are not subject to licensing under section 351 of the Public Health Service Act (42 U.S.C. 262). FDA created the exemption in § 607.65(d) because registering these persons was not necessary to protect the public health, whereas the exemption in § 607.65(e) exists because nonlicensed, in vitro diagnostic establishments are subject to registration under part 807 instead of part 607.

The proposed rule would amend § 607.65 so that paragraphs (c), (d), and (e) would apply to both foreign and domestic persons or establishments. Foreign persons or establishments would not be included in the remaining exemptions in § 607.65 because those exemptions depend on compliance with Federal, State, or local laws in the United States and its territories and because FDA has insufficient information to make a finding, under section 510(g)(5) of the act, that registration by such foreign establishments is not necessary to protect the public health. For example, § 607.65(a) pertains to pharmacies operating under applicable local laws, while § 607.65(b) pertains to practitioners licensed by law. Notwithstanding the proposed rule's limitation of these exemptions to pharmacies and practitioners in the United States and its territories, few foreign pharmacies or foreign practitioners are expected to be importing or offering for import blood and blood products into the United States, so they would not be subject to the foreign establishment registration requirement. As with the similar requirement in proposed § 207.10, those that do import or offer to import such products to the United States should register to allow FDA to carry out its oversight responsibilities in this area. Similarly, § 607.65(f) (transfusion services that are part of a facility approved for Medicare reimbursement) and § 607.65(g) (clinical laboratories approved for Medicare reimbursement) both involve establishments approved for Medicare reimbursement; the agency does not anticipate that many foreign establishments are approved for Medicare reimbursement. Consequently, FDA is not proposing to extend these exemptions to foreign establishments and does not anticipate that many foreign transfusion services or clinical laboratories will be subject to the statutory registration requirement.

C. Proposed Changes to Part 807 (Devices)

1. Section 807.3—Definitions

a. *Definition of ''commercial distribution''.* Section 807.3(b) currently defines ''commercial distribution,'' in part, as ''any distribution of a device intended for human use which is held or offered for sale * * *.''

Similar to the proposed changes to §§ 207.3 and 607.3, the proposed rule would create a new § 807.3(b)(4) to state that, for foreign establishments, commercial distribution does not include distribution of a device that is neither imported nor offered for import into the United States.

b. *Definition of ''United States agent''.* Currently, § 807.3(r) defines a ''U.S.-designated agent'' as a person, residing in the United States, who is ''designated and authorized by the owner or operator of a foreign manufacturer who exports devices into the United States'' and who is responsible for submitting medical device reports and annual certifications, acting as the official correspondent, and submitting registration and listing information and premarket notifications. In the **Federal Register** of July 23, 1996 (61 FR 38345), FDA stayed the effective date for this and other provisions in part 807 (and elsewhere) that mention a U.S.-designated agent.

The proposed rule would revise § 807.3(r) to define a ''United States agent'' as ''any person residing or maintaining a place of business in the United States whom a foreign establishment designates as its agent.'' As stated earlier, FDA interprets the statutory requirement of a United States agent as allowing for only one United States agent for each foreign establishment and providing a foreign establishment the discretion to choose either an individual person or entity to serve as its United States agent.

Additionally, unlike the existing provision, proposed § 807.3(r) would not prescribe any duties for the United States agent. Proposed § 807.40 would describe the United States agent's responsibilities and is discussed later in this document.

2. Section 807.20—Who Must Register and Submit a Device List

Section 807.20(a) currently requires an ''owner or operator of an establishment not exempt under section 510(g) of the act'' or subpart D of part 807 who is engaged in the manufacture, preparation, propagation, compounding, assembly, or processing of a device intended for human use to register and to submit listing information. It also states that an owner or operator shall register and list devices ''whether or not the output of the establishments or any particular device so listed enters interstate commerce.'' Section 807.20 also lists persons who are subject to the registration and listing requirements; one paragraph, at § 807.20(a)(6), refers to persons who act as the ''U.S.-designated agent.''

The proposal would amend § 807.20(a) to clarify that an owner or operator ''shall'' register and list (unless it is otherwise exempt from such requirements). The proposal would also clarify that the language requiring owners and operators to register their establishments and to list devices, even if the devices do not enter interstate commerce, applies only to domestic firms. FDA is proposing this change because the agency has no intent to require foreign establishments to list devices that are not imported or offered for import into the United States, consistent with the language in section 510(i)(1) of the act.

The proposal would also amend the heading of subpart B, ''Procedures for Domestic Device Establishments,'' to remove the word ''domestic.'' This would reflect the fact that the act's registration and listing requirements now apply both to domestic establishments and to foreign establishments whose devices are imported or offered for import into the United States.

The proposal would also delete § 807.20(a)(6) pertaining to persons acting as the U.S.-designated agent. This deletion would complement changes to §§ 807.3 and 807.40 (discussed below) which would give a foreign establishment discretion in defining most responsibilities of its United States agent.

3. Section 807.25—Information Required or Requested for Establishment Registration and Device Listing

Section 807.25 currently states that FDA Forms FD–2891 and 2891(a) are the approved forms for establishment registration and device listing and that the required information includes ''post office ZIP Code.''

The proposal would change this to read as ''post office code'' because the term ''ZIP Code'' is not used in many foreign countries.

4. Section 807.40—Establishment Registration and Device Listing for U.S. Agents of Foreign Establishments

Currently, § 807.40 requires foreign device manufacturers who export devices to the United States to designate a person as a ''U.S.-designated agent.'' The U.S.-designated agent is responsible for duties such as submitting medical device reports, submitting annual certifications, acting as the manufacturer's official correspondent, and submitting registration and listing information and premarket notifications. The rule also directs foreign manufacturers to provide a statement of authorization for the U.S.-designated agent to FDA. However, in the **Federal Register** of July 23, 1996 (61 FR 38345), FDA stayed the effective date of this provision.

The proposal would delete the existing language in § 807.40 entirely and replace it with general descriptions of the foreign establishment's obligations and the United States agent's role. The proposal would also use the term ''foreign establishment,'' rather than ''foreign manufacturer,'' and revise the heading of § 807.40 to be more consistent with section 510 of the act.

Proposed § 807.40(a) would require any foreign establishment engaged in the manufacture, preparation, propagation, compounding, or processing of a device that is imported or offered for import into the United States to register and list its devices in conformance with subpart B (''Procedures for Device Establishments''). This would have foreign establishments comply with the same procedures as domestic establishments.

The proposal would also require the official correspondent for the foreign establishment to facilitate communication between the establishment's management and FDA. This change complements the requirement for an official correspondent in § 807.25(d).

Proposed § 807.40(b) would require each registered foreign establishment to submit the name, address, and phone number of its United States agent as part of its registration information. Under the proposal, each foreign establishment would be able to designate only one United States agent. The proposal would also require the agent to reside or maintain a place of business in the United States, but would allow (rather than require) a foreign establishment to designate its United States agent as its official correspondent. Designating the United States agent as the official correspondent may be more efficient than having a separate United States agent and an official correspondent, but the proposed rule would give foreign establishments flexibility in deciding how to allocate their resources in this area and what the United States agent's responsibilities would be.

FDA notes that electronic product manufacturers, under § 1005.25 (21 CFR 1005.25), must designate a permanent resident of the United States as the manufacturer's agent upon whom service of process may be made for and on behalf of the manufacturer as provided in section 360(d) of the Radiation Control for Health and Safety Act of 1968. Manufacturers of products that are both medical devices and electronic products, therefore, may wish to consider whether their agents, under § 1005.25, can also serve as their United States agent under proposed § 807.40 and perform the duties expected of a United States agent.

Like proposed §§ 207.40 and 607.40, proposed § 807.40(b) also would require the United States agent, upon request from FDA, to assist the agency in communications with the foreign establishment, to respond to questions regarding devices imported or offered for import, and to assist FDA in scheduling inspections of the foreign establishment. Proposed § 807.40(b) would also enable FDA, when it is unable to contact the foreign manufacturer directly or expeditiously, to provide information or documents to the United States agent and for that act to be considered equivalent to providing the same information or documents to the foreign establishment, and would further require a foreign establishment to report to FDA changes in the United States agent's name, address, or phone number within 5 days of the change.

Proposed § 807.40(c), like proposed §§ 207.40(b) and 607.40(b), would prohibit the importation of devices that have not been listed or manufactured, prepared, propagated, compounded, or processed at a registered foreign establishment. This provision is consistent with the act in several respects. Under section 502(o) of the act, a device that is not included in a list is misbranded, and section 801(a)(3) of the act authorizes FDA to refuse admission of misbranded articles. Additionally, prohibiting imports from unregistered foreign establishments is consistent with sections 301(p), 501(h), and 801(a) of the act because, if a foreign establishment fails to register, FDA will be unable to determine whether that foreign establishment meets the requirements of the CGMP/quality systems regulation. (Section 501(h) of the act considers a device to be adulterated if the device and the methods used in, or the facilities or controls used for, the device's manufacture, packing, storage, or installation are not in conformity with CGMP.) Consequently, to enforce sections 301(p), 501(h), and 801(a) of the act effectively, in conjunction with section 510(i) of the act as it pertains to foreign establishment registration, proposed § 807.40(c) would prohibit the importation of devices that are not manufactured, prepared, propagated, compounded, or processed at a registered foreign establishment. Such a requirement is therefore authorized under section 701(a) of the act for the efficient enforcement of the act.

D. Other Rules Affecting Establishment Registration and Listing

The proposed rule would also revise the authority citations for parts 207 and 807 to be consistent with other regulations published by the agency in the **Federal Register** of May 13, 1998 (63 FR 26690) and May 14, 1998 (63 FR 26744). The former would amend various FDA regulations to delete references to the certification of insulin and to section 506 of the act (which was repealed by FDAMA), while the latter would require establishment registration and listing for manufacturers of human cellular and tissue-based products.

The proposal would also add sections 201, 801, and 903 of the act (21 U.S.C. 393) to the authority citation for parts 207, 607, and 807. Section 201 of the act contains definitions, such as the definition of a ''State,'' and some definitions are relevant to these regulations. Section 801 of the act provides authority over imports, whereas section 903 of the act establishes, among other things, FDA's mission and interagency collaboration obligations.

The proposal would further revise the authority citation for part 607 by deleting the citation for 42 U.S.C. 216, and adding 42 U.S.C. 264 and 271. The former provision concerns regulatory authority relating to commissioned corps members and is therefore

inapplicable to part 607, whereas the latter provisions provide authority to issue regulations to control communicable disease and establish penalties for violation of quarantine laws.

E. Registration Schedules

Because part 207 applies to human drugs, animal drugs, and some biologics, FDA intends to develop a staggered schedule for foreign establishment registration. In general, the registration schedule would be similar in concept to § 207.21 whereby firms whose name began with a particular letter of the alphabet would register within a specific month. For example, a firm whose name began with the letter ''a'' or ''b'' might be requested to register by January, whereas a firm whose name began with the letter ''c'' might be requested to register by February. The precise dates, however, may depend upon the date on which FDA publishes a final rule in the **Federal Register**. Therefore, FDA intends to announce the schedule for foreign establishment registration for firms subject to part 207 in the preamble to the final rule.

Comparatively fewer foreign manufacturers are subject to the registration requirements in parts 607 and 807. Consequently, the agency does not intend to develop any special registration schedules for parts 607 and 807.

III. Analysis of Impacts

FDA has examined the impacts of the proposed rule under Executive Order 12866 and the Regulatory Flexibility Act (5 U.S.C. 601–612). 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 proposed rule is consistent with the principles set out in the Executive Order. In addition, the proposed rule is a significant regulatory action as defined in Executive Order 12866.

The Regulatory Flexibility Act requires agencies to analyze regulatory options that would minimize any significant economic impact of a rule on small entities. FDA believes that the proposed rule will not have a significant economic impact on a substantial number of small entities, but has conducted an initial regulatory flexibility analysis to ensure that impacts on small entities were assessed and to alert any potentially impacted small entities to the opportunity to submit comments to FDA.

The proposed rule would require foreign establishments that import or offer for import human drugs, animal drugs, biologics, blood, blood products, and devices into the United States to register and to identify a United States agent. Before FDAMA amended section 510 of the act to require foreign establishment registration, many foreign establishments voluntarily registered their establishments, but all foreign establishments that imported or offered for import drugs, blood and blood products, and devices into the United States were required to list their products. The registration and listing activities used forms prepared by FDA. (FDA plans to revise these forms in the future to provide for the identification of a United States agent by foreign establishments.)

Because foreign establishments were (and still are) required to list their products, FDA can estimate the number of foreign establishments that would be required to register under the proposed rule. However, because all of these establishments are outside the United States, FDA is unable to estimate accurately the number of foreign establishments that would be considered small entities and the extent to which these foreign establishments conduct business in the United States.

Nevertheless, FDA is able to estimate the proposed rule's economic impact by using time and cost estimates for registration. FDA estimates the costs associated with establishment registration are small, ranging from $20 per hour for device establishments, $25 per hour for blood and blood product establishments, and $100 per hour for drug establishments. These costs are based on information obtained primarily from domestic establishments, and FDA is assuming that the average costs for foreign establishments will be similar. FDA also estimates that completing an establishment registration form will range from 15 minutes to 1 hour (depending on the form used). These estimates are derived from the estimated registration costs for domestic establishments and foreign establishments that voluntarily registered before FDAMA's enactment. Thus, the proposed rule, if finalized, should not have a significant economic impact on a substantial number of small entities.

The agency examined, but rejected, alternatives to the proposed rule. The registration information required by FDA in the proposal is minimal, consisting largely of the establishment's address, names of owners or responsible officials, and additional identifying information on the establishment (such as type of establishment, types of products at the establishment, type of ownership). Similarly, identification of the United States agent would require minimal information (name, address, phone number). An alternative that required less information from foreign establishments would not provide sufficient information to identify the foreign establishment's location, a responsible person at the foreign establishment, or the type of establishment, thereby complicating any effort to locate or contact the foreign establishment or to determine whether the foreign establishment complied with the appropriate statutory and regulatory requirements. An alternative that required less frequent reporting by foreign establishments was rejected because it would increase the likelihood that the information possessed by FDA would be incorrect or obsolete and hinder the conduct of regulatory actions involving foreign establishments.

The Unfunded Mandates Reform Act (Pub. L. 104–114) requires that agencies prepare an assessment of anticipated costs and benefits before proposing any rule that may result in an expenditure in any 1 year by State, local, and tribal governments, in the aggregate, or by the private sector, of $100 million or more (adjusted annually for inflation). FDA estimates that the reporting costs for industry under the proposed rule would total $809,820. This estimate is based on annual projections of 4,160.5 hours for drug industry reports, 108.5 hours for blood and blood product reports, and 15,664 hours for device reports, multiplied by hourly industry costs of $100, $20, and $25 per report respectively. The estimated recordkeeping cost to industry is $810,000, based on an estimated 32,400 records at $25 per hour. Thus, because the total expenditures under the proposal will not result in a 1-year expenditure of $100 million or more, FDA is not required to perform a cost-benefit analysis under the Unfunded Mandates Reform Act.

IV. Environmental Impact

The agency has determined, under 21 CFR 25.30(h), 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.

V. Paperwork Reduction Act of 1995

This proposed rule contains information collection provisions that are subject to public comment and review by OMB under the Paperwork Reduction Act of 1995 (44 U.S.C. 3501–3520). The title, description, and respondent description for the information collection requirements are shown below with an estimate of the annual reporting and recordkeeping burden. Included in the estimate is the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing each collection of information.

FDA invites comments on: (1) Whether the proposed collection of information is necessary for the proper performance of FDA's functions, including whether the information will have practical utility; (2) the accuracy of FDA's estimate of the burden of the proposed collection of information, including the validity of the methodology and assumptions used; (3) ways to enhance the quality, utility, and clarity of the information to be collected; and (4) ways to minimize the burden of the collection of information on respondents, including through the use of automated collection techniques, when appropriate, and other forms of information technology.

Title: Foreign Establishment Registration and Listing.

Description: The proposed rule would require foreign establishments that import or offer to import human drugs, animal drugs, biologics, blood products, and devices into the United States to register and to name a United States agent. This information is required by section 510(i)(1) of the act, as amended by section 417 of FDAMA.

Although section 510(i)(2) of the act also requires foreign establishments to list their products at FDA, the proposed rule does not include such a requirement because FDA's existing regulations already require foreign manufacturers to submit such lists, and the agency has already obtained OMB approval for the information collection burden associated with product listing for parts 207 and 607 (for part 207, the OMB approval number is 0910–0045 and expires on April 30, 2001; for part 607, the OMB approval number is 0910–0052 and expires on April 30, 2000). Through this notice, FDA is also seeking approval for the device listing requirements insofar as they will be applied to foreign establishments.

Description of Respondents: Persons and businesses, including small businesses.

FDA estimates the burden of this collection of information as follows:

TABLE 1.—Estimated Annual Reporting Burden[1]

21 CFR Section	No. of Respondents	No. of Responses per Respondent	Total Annual Responses	Hours per Response	Total Hours
207.21(a)	2,463	1	2,463	0.5	1,231.5
207.22(a) and 207.40	5,630	1	5,630	0.5	2,815
207.25(b)	53	4.8	228	0.5	114
607.22(a) and 607.40	98	1	98	1	98
607.26	1	1	1	0.5	0.5
607.31	1	1	1	10	10
807.22(a) and 807.40	7,200	1	7,200	0.25	1,800
807.22(b)	27,720	1	27,720	0.5	13,860
807.31(e)	7	1	7	0.5	4
Total					19,933

[1]There are no capital costs or operating and maintenance costs associated with this collection of information.

TABLE 2.—Estimated Annual Recordkeeping Burden[1]

21 CFR Section	No. of Recordkeepers	No. of Records per Recordkeeper	Total Annual Records	Hours per Record	Total Hours
807.31	6,480	10	64,800	0.5	32,400
Total					32,400

[1]There are no capital costs or operating and maintenance costs associated with this collection of information.

In general, FDA based the above estimates on the number of foreign establishments that currently list drugs, blood products, or devices (as required by existing FDA regulations) and on comparable burden hour estimates for registration by domestic establishments. Accordingly, FDA's estimate of 30 minutes for each initial drug report (§ 207.22), 1 hour for each initial biologic report (§ 607.22), 45 minutes for each device report (§ 807.22), and 30 minutes for each additional report submitted (§ 807.31) is consistent with current practices.

For proposed §§ 207.21(a) and 207.25(b), the agency estimated the number of respondents submitting ANDA's or ANADA's from the number of establishments submitting listing information. For proposed § 207.21(a), FDA's drug listing records indicate that there are 2,410 firms submitting ANDA's and 53 firms submitting ANADA's, for a total of 2,463 respondents. The proposed rule would amend § 207.25(b) to include ANADA's, and FDA records indicate that 228 ANADA's were submitted; consequently, the total number of respondents is 53, with a total of 228 annual responses. The estimated total annual responses and hours per response are consistent with existing figures for other establishments subject to §§ 207.21 and 207.25.

For proposed §§ 607.26 and 607.31, FDA's experience reveals that only one establishment has reported information under these provisions in recent years. Therefore, the agency assigned an estimate of one respondent for each provision. The agency estimated the burden hours for these provisions by examining their complexity. Because proposed § 607.26 would require reporting changes in individual

ownership, corporate or partnership structure, location, or blood-product handling activity, the agency assigned 30 minutes as the reporting burden. In contrast, § 607.31 authorizes the agency to request additional information by letter. FDA has made no requests in recent years, but has assigned 10 hours as a reporting burden for this provision.

The estimated recordkeeping burden for proposed § 807.31 is based on FDA's experience with foreign device establishments. FDA's experience indicates that there are approximately 9 owners or operators for every 10 foreign device establishments. Consequently, the estimated number of recordkeepers is 6,480 (7,200 x 0.9 = 6,480), and the average frequency and average burden per record, based on comparable figures for domestic establishments, are 10 and 30 minutes respectively. This results in a total recordkeeping burden of 32,400 hours (6,480 recordkeepers x 10 records per recordkeeper x 0.5 hours per record = 32,400 hours).

In compliance with section 3507(d) of the Paperwork Reduction Act of 1995 (44 U.S.C. 3507(d)), the agency has submitted the information collection requirements of this proposed rule to OMB for review. Interested persons are requested to send comments regarding information collection by June 14, 1999, to the Office of Information and Regulatory Affairs, OMB, New Executive Office Bldg., 725 17th St. NW., Washington, DC 20503, Attn: Wendy Taylor, Desk Officer for FDA.

List of Subjects

21 CFR Part 207

Drugs, Reporting and recordkeeping requirements.

21 CFR Part 607

Blood.

21 CFR Part 807

Confidential business information, Imports, Medical devices, Reporting and recordkeeping requirements.

Therefore, under the Federal Food, Drug, and Cosmetic Act and under authority delegated to the Commissioner of Food and Drugs, it is proposed that 21 CFR parts 207, 607, and 807 be amended as follows:

PART 207—REGISTRATION OF PRODUCERS OF DRUGS AND LISTING OF DRUGS IN COMMERCIAL DISTRIBUTION

1. The authority citation for part 21 CFR part 207 is revised to read as follows:

Authority: 21 U.S.C. 321, 331, 351, 352, 355, 360, 360b, 371, 374, 381, 393; 42 U.S.C. 262, 264, 271.

2. Section 207.3 is amended by revising paragraph (a)(5) and by adding paragraph (a)(11) to read as follows:

§ 207.3 Definitions.

(a) * * *

(5) *Commercial distribution* means any distribution of a human drug except for investigational use under part 312 of this chapter, and any distribution of an animal drug or animal feed bearing or containing an animal drug for noninvestigational uses, but the term does not include internal or interplant transfer of a bulk drug substance between registered establishments within the same parent, subsidiary, and/or affiliate company. For foreign establishments, the term ''commercial distribution'' shall have the same meaning except that the term shall not include distribution of any drug that is neither imported nor offered for import into the United States.

* * * * *

(11) *United States agent* means a person residing or maintaining a place of business in the United States whom a foreign establishment designates as its agent.

* * * * *

3. Section 207.7 is amended by revising paragraph (a) to read as follows:

§ 207.7 Establishment registration and product listing for human blood and blood products and for medical devices.

(a) Owners and operators of human blood and blood product establishments shall register and list their products with the Center for Biologics Evaluation and Research (HFM–375), Food and Drug Administration, 1401 Rockville Pike, suite 200N, Rockville, MD 20852–1448, on Form FDA–2830 (Blood Establishment Registration and Product Listing), in accordance with part 607 of this chapter. Such owners and operators who also manufacture or process other drug products at the same establishment shall, in addition, register and list all such other drug products with the Drug Listing Branch in accordance with this part.

* * * * *

4. Section 207.10 is amended by revising the section heading and the introductory text to read as follows:

§ 207.10 Exemptions for establishments.

The following classes of persons are exempt from registration and drug listing in accordance with this part under section 510(g)(1), (g)(2), and (g)(3) of the act, or because FDA has found, under section 510(g)(5), that their registration is not necessary for the protection of the public health. The exemptions in paragraphs (a) and (b) of this section are limited to pharmacies, hospitals, clinics, and public health agencies located in any State as defined in section 201(a)(1) of the act.

* * * * *

5. Section 207.20 is amended by revising paragraphs (a) and (c) to read as follows:

§ 207.20 Who must register and submit a drug list.

(a) Owners or operators of all drug establishments, not exempt under section 510(g) of the act or subpart B of this part 207, that engage in the manufacture, preparation, propagation, compounding, or processing of a drug or drugs shall register and submit a list of every drug in commercial distribution (except that listing information may be submitted by the parent, subsidiary, and/or affiliate company for all establishments when operations are conducted at more than one establishment and there exists joint ownership and control among all the establishments). Drug listing is not required for the manufacturing, preparation, propagation, compounding, or processing of an animal feed bearing or containing an animal drug (i.e., a Type B or Type C medicated feed), nor is drug listing required for establishments engaged in drug product salvaging. Drug products manufactured, prepared, propagated, compounded, or processed in any State as defined in section 201(a)(1) of the act must be listed whether or not the output of such establishments or any particular drug so listed enters interstate commerce. No owner or operator may register an establishment if any part of the establishment is registered by any other owner or operator.

* * * * *

(c) Before beginning manufacture or processing of a drug subject to one of the following applications, an owner or operator of an establishment is required to register before the agency approves it: A new drug application, an abbreviated new drug application, a new animal drug application, an abbreviated new animal drug application, a medicated feed application, or a biologics license application.

* * * * *

§ 207.21 [Amended]

6. Section 207.21 *Times for registration and drug listing* is amended in the second sentence of paragraph (a) by adding the phrase ''abbreviated new drug application,'' after the phrase ''new drug application,'' and by adding the

phrase ''abbreviated new animal drug application,'' after the phrase ''new animal drug application,''.

§ 207.25 [Amended]

7. Section 207.25 *Information required in registration and drug listing* is amended in paragraph (b)(2) by adding the phrase ''abbreviated new animal drug application number,'' after the phrase ''new animal drug application number,''.

8. Section 207.37 is amended by revising the introductory text of paragraph (a) and by revising paragraph (b) to read as follows:

§ 207.37 Inspection of registrations and drug listings.

(a) A copy of the Form FDA–2656 (Registration of Drug Establishment) filed by the registrant will be available for inspection in accordance with section 510(f) of the act, at the Division of Labeling and Non-Prescription Drug Compliance (HFD–310), Office of Compliance, Center for Drug Evaluation and Research, Food and Drug Administration, 7520 Standish Pl., Rockville, MD 20855. In addition, copies of these forms for establishments located within a particular geographic area are available for inspection at FDA district offices responsible for that geographical area. Copies of forms submitted by foreign drug establishments are available for inspection at the Foreign Inspection Team (HFD–322), Office of Compliance, Center for Drug Evaluation and Research, Food and Drug Administration, 7520 Standish Pl., Rockville, MD 20855. Upon request and receipt of a stamped, self-addressed envelope, the Division of Labeling and Non-Prescription Drug Compliance, the Foreign Inspection Team, or the appropriate FDA district office will verify registration numbers or provide the location of a registered establishment.

* * * * *

(b) Requests for information about registrations and drug listings of an establishment should be directed to the Information Management Team (HFD–095), Office of Information Technology, Center for Drug Evaluation and Research, Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857 or, with respect to the information described in paragraph (a) of this section, to the FDA district office responsible for the geographic area in which the establishment is located.

9. Section 207.40 is revised to read as follows:

§ 207.40 Establishment registration and drug listing requirements for foreign drug establishments.

(a) Foreign drug establishments whose drugs are imported or offered for import into the United States shall comply with the establishment registration and drug listing requirements in subpart C of this part, unless exempt under subpart B of this part.

(b) No drug, unless it is listed as required in subpart C of this part and manufactured, prepared, propagated, compounded, or processed at a registered foreign drug establishment, may be imported or offered for import into the United States except a drug imported or offered for import under the investigational use provisions in part 312 of this chapter. Foreign drug establishments shall submit all listing information, including labels and labeling, and registration information in the English language.

(c) Each foreign drug establishment required to register under paragraph (a) of this section shall submit the name, address, and phone number of its United States agent as part of its initial and updated registration information in accordance with subpart C of this part. Each foreign drug establishment shall designate only one United States agent.

(1) The United States agent shall reside or maintain a place of business in the United States.

(2) Upon request from FDA, the United States agent shall assist FDA in communications with the foreign drug establishment, respond to questions concerning the foreign drug establishment's products that are imported or offered for import into the United States, and assist FDA in scheduling inspections of the foreign drug establishment. If the agency is unable to contact the foreign drug establishment directly or expeditiously, FDA may provide information or documents to the United States agent, and such an action shall be considered to be equivalent to providing the same information or documents to the foreign drug establishment.

(3) The foreign drug establishment shall report changes in the United States agent's name, address, or phone number to FDA within 5 days of the change.

PART 607—ESTABLISHMENT REGISTRATION AND PRODUCT LISTING FOR MANUFACTURERS OF HUMAN BLOOD AND BLOOD PRODUCTS

10. The authority citation for 21 CFR part 607 is revised to read as follows:

Authority: 21 U.S.C. 321, 331, 351, 352, 355, 360, 371, 374, 381, 393; 42 U.S.C. 262, 264, 271.

11. Section 607.3 is amended by revising paragraph (e) and by adding paragraph (j) to read as follows:

§ 607.3 Definitions.

* * * * *

(e) *Commercial distribution* means any distribution of a blood product except pursuant to the investigational use provisions of part 312 of this chapter, but does not include internal or interplant transfer of a bulk product substance between registered establishments within the same parent, subsidiary, and/or affiliate company. For foreign establishments, the term ''commercial distribution'' shall have the same meaning except that the term shall not include distribution of any blood or blood product that is neither imported nor offered for import into the United States.

* * * * *

(j) *United States agent* means a person residing or maintaining a place of business in the United States whom a foreign establishment designates as its agent.

12. Section 607.7 is amended by revising paragraphs (b) and (c) to read as follows:

§ 607.7 Establishment registration and product listing of blood banks and other firms manufacturing human blood and blood products.

* * * * *

(b) Forms for registration of an establishment are obtainable on request from the Center for Biologics Evaluation and Research (HFM–375), Food and Drug Administration, 1401 Rockville Pike, suite 200N, Rockville, MD 20852–1448, or at any of the Food and Drug Administration district offices.

(c) The completed form should be mailed to the Center for Biologics Evaluation and Research (HFM–375), Food and Drug Administration, 1401 Rockville Pike, suite 200N, Rockville, MD 20852–1448.

13. Section 607.20 is amended by revising paragraph (a) to read as follows:

§ 607.20 Who must register and submit a blood product list.

(a) Owners or operators of all establishments, not exempt under section 510(g) of the act or subpart D of this part 607, that engage in the manufacture of blood products shall register and submit a list of every blood product in commercial distribution (except that listing information may be submitted by the parent, subsidiary, and/or affiliate company for all establishments when operations are conducted at more than one establishment and there exists joint

ownership and control among all the establishments). Blood products manufactured, prepared, propagated, compounded, or processed in any State as defined in section 201(a)(1) of the act must be listed whether or not the output of such blood product establishment or any particular blood product so listed enters interstate commerce.

* * * * *

14. Section 607.22 is revised to read as follows:

§ 607.22 How and where to register establishments and list blood products.

(a) The first registration of an establishment shall be on Form FD–2830 (Blood Establishment Registration and Product Listing) obtainable on request from the Center for Biologics Evaluation and Research (HFM–375), Food and Drug Administration, 1401 Rockville Pike, suite 200N, Rockville, MD 20852–1448, or from Food and Drug Administration district offices. Subsequent annual registration shall also be accomplished on Form FD–2830 which will be furnished by the Food and Drug Administration before November 15 of each year to establishments whose product registration for that year was validated pursuant to § 607.35. The completed form shall be mailed to the above address before December 31 of that year.

(b) The first list of blood products and subsequent June and December updatings shall be on Form FD–2830, obtainable upon request as described in paragraph (a) of this section.

§ 607.25 [Amended]

15. Section 607.25 *Information required for establishment registration and blood product listing* is amended in the second sentence of paragraph (a) by removing the word ''ZIP''.

16. Section 607.26 is amended by revising the first sentence to read as follows:

§ 607.26 Amendments to establishment registration.

Changes in individual ownership, corporate or partnership structure, location, or blood-product handling activity shall be submitted on Form FD–2830 (Blood Establishment Registration and Product Listing) as an amendment to registration within 5 days of such changes. * * *

17. Section 607.31 is amended by revising paragraph (a) and by removing and reserving paragraph (b) to read as follows:

§ 607.31 Additional blood product listing information.

(a) In addition to the information routinely required by §§ 607.25 and 607.30, the Director of the Center for Biologics Evaluation and Research may require submission of the following information by letter or by **Federal Register** notice:

(1) For a particular blood product so listed, upon request made by the Director of the Center for Biologics Evaluation and Research for good cause, a copy of all advertisements.

(2) For a particular blood product so listed, upon a finding by the Director of the Center for Biologics Evaluation and Research that it is necessary to carry out the purposes of the act, a quantitative listing of all ingredients.

(3) For each registrant, upon a finding by the Director of the Center for Biologics Evaluation and Research that it is necessary to carry out the purposes of the act, a list of each listed blood product containing a particular ingredient.

(b) [Reserved]

18. Section 607.35 is amended by revising paragraph (a) to read as follows:

§ 607.35 Notification of registrant; blood product establishment registration number and NDC Labeler Code

(a) The Director of the Center for Biologics Evaluation and Research will provide to the registrant a validated copy of Form FD–2830 (Blood Establishment Registration and Product Listing) as evidence of registration. This validated copy will be sent to the location shown for the registering establishment, and a copy will be sent to the reporting official if at another address. A permanent registration number will be assigned to each blood product establishment registered in accordance with the regulations of this subpart.

* * * * *

19. Section 607.37 is amended by revising the introductory text of paragraph (a) and by revising paragraph (b) to read as follows:

§ 607.37 Inspection of establishment registrations and blood product listings.

(a) A copy of the Form FD–2830 (Blood Establishment Registration and Product Listing) filed by the registrant will be available for inspection pursuant to section 510(f) of the act, at the Office of Communication, Training and Manufacturers' Assistance (HFM–40), Center for Biologics Evaluation and Research, Food and Drug Administration, 1401 Rockville Pike, suite 200N, Rockville, MD 20852–1448. In addition, for domestic firms, the same information will be available for inspection at each of the Food and Drug Administration district offices for firms within the geographical area of such district office. Upon request and receipt of a self-addressed stamped envelope, verification of registration number, or location of registered establishment will be provided. The following information submitted pursuant to the blood product listing requirements is illustrative of the type of information that will be available for public disclosure when it is compiled:

* * * * *

(b) Requests for information regarding blood establishment registrations and blood product listings should be directed to the Office of Communication, Training and Manufacturers' Assistance (HFM–40), Center for Biologics Evaluation and Research, Food and Drug Administration, 1401 Rockville Pike, suite 200N, Rockville, MD 20852–1448.

20. Section 607.40 is revised to read as follows:

§ 607.40 Establishment registration and blood product listing requirements for foreign blood product establishments.

(a) Every foreign establishment shall comply with the establishment registration and blood product listing requirements contained in subpart B of this part, unless exempt under subpart D of this part.

(b) No blood product may be imported or offered for import into the United States except a blood product imported or offered for import pursuant to the investigational use provisions of part 312 of this chapter, unless it is the subject of a blood product listing as required under subpart B of this part and is manufactured, prepared, propagated, compounded, or processed at a registered foreign establishment. The establishment registration and blood product listing information shall be in the English language.

(c) Each foreign establishment required to register under paragraph (a) of this section shall, as part of the establishment registration and blood product listing, submit the name and address of the establishment and the name of the individual responsible for submitting establishment registration and blood product listing information. Any changes in this information shall be reported to the Food and Drug Administration at the intervals specified for updating establishment registration information in § 607.26 and blood product listing information in § 607.30(a).

(d) Each foreign establishment required to register under paragraph (a) of this section shall submit the name, address, and phone number of its United States agent as part of its initial and updated registration information in

accordance with subpart B of this part. Each foreign establishment shall designate only one United States agent.

(1) The United States agent shall reside or maintain a place of business in the United States.

(2) Upon request from FDA, the United States agent shall assist FDA in communications with the foreign establishment, respond to questions concerning the foreign establishment's products that are imported or offered for import into the United States, and assist FDA in scheduling inspections of the foreign establishment. If the agency is unable to contact the foreign establishment directly or expeditiously, FDA may provide information or documents to the United States agent, and such an action shall be considered to be equivalent to providing the same information or documents to the foreign establishment.

(3) The foreign establishment shall report changes in the United States agent's name, address, or phone number to FDA within 5 days of the change.

21. Section 607.65 is amended by revising the introductory text to read as follows:

§ 607.65 Exemptions for blood product establishments.

The following classes of persons are exempt from registration and blood product listing in accordance with this part 607 under the provisions of section 510(g)(1), (g)(2), and (g)(3) of the act, or because the Commissioner has found, under section 510(g)(4), that such registration is not necessary for the protection of the public health. The exemptions in paragraphs (a), (b), (f), and (g) of this section are limited to those classes of persons located in any State as defined in section 201(a)(1) of the act.

* * * * *

PART 807—ESTABLISHMENT REGISTRATION AND DEVICE LISTING FOR MANUFACTURERS AND DISTRIBUTORS OF DEVICES

22. The authority citation for 21 CFR part 807 is revised to read as follows:

Authority: 21 U.S.C. 321, 331, 351, 352, 360, 360c, 360e, 360i, 360j, 371, 374, 381, 393; 42 U.S.C. 264, 271.

23. Section 807.3 is amended by revising paragraphs (b) and (r) to read as follows:

§ 807.3 Definitions.

* * * * *

(b) *Commercial distribution* means any distribution of a device intended for human use which is held or offered for sale but does not include the following:

(1) Internal or interplant transfer of a device between establishments within the same parent, subsidiary, and/or affiliate company;

(2) Any distribution of a device intended for human use which has in effect an approved exemption for investigational use pursuant to section 520(g) of the act and part 812 of this chapter;

(3) Any distribution of a device, before the effective date of part 812 of this chapter, that was not introduced or delivered for introduction into interstate commerce for commercial distribution before May 28, 1976, and that is classified into class III under section 513(f) of the act: *Provided,* That the device is intended solely for investigational use, and under section 501(f)(2)(A) of the act the device is not required to have an approved premarket approval application as provided in section 515 of the act; or

(4) For foreign establishments, the distribution of any device that is neither imported nor offered for import into the United States.

* * * * *

(r) *United States agent* means a person residing or maintaining a place of business in the United States whom a foreign establishment designates as its agent.

* * * * *

24. The heading to subpart B ''Procedures for Domestic Device Establishments'' is revised to read as follows:

Subpart B—Procedures for Device Establishments

25. Section 807.20 is amended by revising paragraph (a) to read as follows:

§ 807.20 Who must register and submit a device list.

(a) An owner or operator of an establishment not exempt under section 510(g) of the act or subpart D of this part who is engaged in the manufacture, preparation, propagation, compounding, assembly, or processing of a device intended for human use shall register and submit listing information for those devices in commercial distribution, except that listing information may be submitted by the parent, subsidiary, or affiliate company for all the domestic or foreign establishments under the control of one of these organizations when operations are conducted at more than one establishment and there exists joint ownership and control among all the establishments. The term ''device'' includes all in vitro diagnostic products and in vitro diagnostic biological products not subject to licensing under section 351 of the Public Health Service Act. An owner or operator of an establishment located in any State as defined in section 201(a)(1) of the act shall register its name, places of business, and all establishments and list the devices whether or not the output of the establishments or any particular device so listed enters interstate commerce. The registration and listing requirements shall pertain to any person who:

(1) Initiates or develops specifications for a device that is to be manufactured by a second party for commercial distribution by the person initiating specifications;

(2) Manufactures for commercial distribution a device either for itself or for another person. However, a person who only manufactures devices according to another person's specifications, for commercial distribution by the person initiating specifications, is not required to list those devices;

(3) Repackages or relabels a device;

(4) Acts as an initial importer; or

(5) Manufactures components or accessories which are ready to be used for any intended health-related purpose and are packaged or labeled for commercial distribution for such health-related purpose, e.g., blood filters, hemodialysis tubing, or devices which of necessity must be further processed by a licensed practitioner or other qualified person to meet the needs of a particular patient, e.g., a manufacturer of ophthalmic lens blanks.

* * * * *

§ 807.25 [Amended]

26. Section 807.25 *Information required or requested for establishment registration and device listing* is amended in the last sentence of paragraph (a) by removing the word ''ZIP''.

27. Section 807.40 is revised to read as follows:

§ 807.40 Establishment registration and device listing for foreign establishments importing or offering for import devices into the United States.

(a) Any establishment within any foreign country engaged in the manufacture, preparation, propagation, compounding, or processing of a device that is imported or offered for import into the United States shall register and list such devices in conformance with the requirements in subpart B of this part. The official correspondent for the foreign establishment shall facilitate communication between the foreign establishment's management and

representatives of the Food and Drug Administration.

(b) Each foreign establishment required to register under paragraph (a) of this section shall submit the name, address, and phone number of its United States agent as part of its initial and updated registration information in accordance with subpart B of this part. Each foreign establishment shall designate only one United States agent and may designate the United States agent to act as its official correspondent.

(1) The United States agent shall reside or maintain a place of business in the United States.

(2) Upon request from FDA, the United States agent shall assist FDA in communications with the foreign establishment, respond to questions concerning the foreign establishment's products that are imported or offered for import into the United States, and assist FDA in scheduling inspections of the foreign establishment. If the agency is unable to contact the foreign establishment directly or expeditiously, FDA may provide information or documents to the United States agent, and such an action shall be considered to be equivalent to providing the same information or documents to the foreign establishment.

(3) The foreign establishment shall report changes in the United States agent's name, address, or phone number to FDA within 5 days of the change.

(c) No device may be imported or offered for import into the United States except a device imported or offered for import pursuant to the investigational use provisions of part 812 of this chapter, unless it is the subject of a device listing as required under subpart B of this part and is manufactured, prepared, propagated, compounded, or processed at a registered foreign establishment. The establishment registration and device listing information shall be in the English language.

Dated: January 26, 1999.

William K. Hubbard,

Acting Deputy Commissioner for Policy.

[FR Doc. 99–12040 Filed 5–13–99; 8:45 am]

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 640

[Docket No. 98N–0608]

Revision of Requirements Applicable to Albumin (Human), Plasma Protein Fraction (Human), and Immune Globulin (Human); Companion Document to Direct Final Rule

AGENCY: Food and Drug Administration, HHS.

ACTION: Proposed rule.

SUMMARY: The Food and Drug Administration (FDA) is proposing to amend the biologics regulations by removing, revising, or updating specific regulations applicable to blood derivative products to be more consistent with current practices and to remove unnecessary or outdated requirements. FDA is taking this action as part of the agency's ''Blood Initiative'' in which FDA is reviewing and revising, when appropriate, its regulations, policies, guidance, and procedures related to blood products, including blood derivatives. This proposed rule is a companion document to the direct final rule published elsewhere in this issue of the **Federal Register**. FDA is taking this action because the proposed changes are noncontroversial and FDA anticipates that it will receive no significant adverse comment.

DATES: Submit written comments on or before July 28, 1999. If FDA receives any significant adverse comment regarding this rule, FDA will publish a document withdrawing the direct final rule within 30 days after the comment period ends. FDA then and will proceed to respond to the comments under this proposed rule using the usual notice and comment procedures. Any parties interested in commenting on this document should do so at this time.

If FDA receives no significant adverse comments within the specified comment period, the agency intends to publish a document confirming the effective date of the final rule in the **Federal Register** within 30 days after the comment period on the direct final rule ends. The direct final rule will be effective September 27, 1999.

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

FOR FURTHER INFORMATION CONTACT: Sharon A. Carayiannis, 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

This proposed rule is a companion to the direct final rule published in the final rules section of this issue of the **Federal Register**. This companion proposed rule will provide the procedural framework to finalize the rule in the event that the direct final rule receives any adverse comment and is withdrawn. The comment period for this companion proposed rule runs concurrently with the comment period for the direct final rule. Any comments received under this companion rule will also be considered as comments regarding the direct final rule. FDA is publishing the direct final rule because the rule contains noncontroversial changes, and FDA anticipates that it will receive no significant adverse comment.

A significant comment is defined as a comment that explains why the rule would be inappropriate, including challenges to the rule's underlying premise or approach, or would be ineffective or unacceptable without a change. In determining whether a significant adverse comment is sufficient to terminate a direct final rulemaking, FDA will consider whether the comment raises an issue serious enough to warrant a substantive response in a notice-and-comment process. Comments that are frivolous, insubstantial, or outside the scope of the rule will not be considered significant or adverse under this procedure. A comment recommending a rule change in addition to the rule would not be considered a significant adverse comment, unless the comment states why the rule would be ineffective without additional change. In addition, if a significant adverse comment applies to an amendment, paragraph, or section of this rule and that provision can be severed from the remainder of the rule, FDA may adopt as final those provisions of the rule that are not subjects of significant adverse comments.

If no significant adverse comment is received in response to the direct final rule, no further action will be taken related to this proposed rule. Instead, FDA will publish a confirmation document within 30 days after the comment period ends confirming that the direct final rule will go into effect on September 27, 1999. Additional information about FDA's direct rulemaking procedures is set forth in a guidance published in the **Federal**