

ranging from 3 to 8 years on which the various body system listings would no longer be effective unless extended by the Secretary of Health and Human Services or revised and promulgated again. Effective March 31, 1995, the authority to issue regulations was transferred to the Commissioner of Social Security by section 102 of Public Law 103-296, the Social Security Independence and Program Improvements Act of 1994.

In this final rule, we are extending the dates on which several body system listings will no longer be effective to July 2, 2001. These body systems are:

Cardiovascular System (4.00 and 104.00).

Digestive System (5.00 and 105.00).

Genito-Urinary System (6.00 and 106.00).

We last extended the dates on which these body system listings would no longer be effective in final rules published as follows:

June 5, 1997 (62 FR 30746): Digestive System and Genito-Urinary System.

January 30, 1998 (63 FR 4570):

Cardiovascular System.

We believe that the requirements in these listings are still valid for our program purposes. Specifically, if we find that an individual has an impairment that meets or is medically equivalent in severity to an impairment in the Listings or functionally equivalent to the Listings in SSI claims based on disability filed by individuals under age 18 and also meets the statutory duration requirement, we will find that the individual is disabled at the third step of the sequential evaluation process. We are extending these dates because we do not expect to develop revised listings criteria for these body systems by the expiration dates currently shown in the regulations. However, we are reviewing the listings and we plan to publish proposed and final rules over the course of the next two years.

Regulatory Procedures

Justification for Final Rule

Pursuant to section 702(a)(5) of the Social Security Act, 42 U.S.C. 902(a)(5), as amended by section 102 of Public Law 103-296, SSA follows the Administrative Procedure Act (APA) rulemaking procedures specified in 5 U.S.C. 553 in the development of its regulations. The APA provides exceptions to its notice and public comment procedures when an agency finds there is good cause for dispensing with such procedures on the basis that they are impracticable, unnecessary, or

contrary to the public interest. We have determined that, under 5 U.S.C. 553(b)(B), good cause exists for dispensing with the notice and public comment procedures in this case. Good cause exists because this regulation only extends the date on which these body system listings will no longer be effective. It makes no substantive changes to those listings. The current regulations expressly provide that listings may be extended, as well as revised and promulgated again. Therefore, opportunity for prior comment is unnecessary, and we are issuing this regulation as a final rule.

In addition, we find good cause for dispensing with the 30-day delay in the effective date of a substantive rule provided by 5 U.S.C. 553(d). As explained above, we are not making any substantive changes in these body system listings. However, without an extension of the expiration dates for these listings, we will lack regulatory guidelines for assessing impairments in these body systems at the third step of the sequential evaluation process after the current expiration dates of these listings. In order to ensure that we continue to have regulatory criteria for assessing impairments under these listings, we find that it is in the public interest to make this rule effective upon publication.

Executive Order 12866

We have consulted with the Office of Management and Budget (OMB) and determined that this final rule does not meet the criteria for a significant regulatory action under Executive Order 12866. Thus, it was not subject to OMB review. We have also determined that this final rule meets the plain language requirement of Executive Order 12866 and the President's memorandum of June 1, 1998 (63 FR 31885).

Regulatory Flexibility Act

We certify that this final regulation will not have a significant economic impact on a substantial number of small entities. Therefore, a regulatory flexibility analysis as provided in the Regulatory Flexibility Act, as amended, is not required.

Paperwork Reduction Act

This final regulation imposes no reporting/recordkeeping requirements necessitating clearance by OMB.

(Catalog of Federal Domestic Assistance Program Nos. 96.001, Social Security-Disability Insurance; 96.002, Social Security-Retirement Insurance; 96.004, Social Security-Survivors Insurance; 96.006, Supplemental Security Income)

List of Subjects in 20 CFR Part 404

Administrative practice and procedure, Blind, Disability benefits, Old-Age, Survivors and Disability Insurance, Reporting and recordkeeping requirements, Social Security.

Dated: November 24, 1999.

Kenneth S. Apfel,

Commissioner of Social Security.

For the reasons set forth in the preamble, part 404, subpart P, chapter III of title 20 of the Code of Federal Regulations is amended as set forth below.

PART 404—FEDERAL OLD-AGE, SURVIVORS AND DISABILITY INSURANCE (1950-)

Subpart P—[Amended]

1. The authority citation for subpart P of part 404 continues to read as follows:

Authority: Secs. 202, 205(a), (b), and (d)–(h), 216(i), 221(a) and (i), 222(c), 223, 225, and 702(a)(5) of the Social Security Act (42 U.S.C. 402, 405(a), (b), and (d)–(h), 416(i), 421(a) and (i), 422(c), 423, 425, and 902(a)(5)); sec. 211(b), Pub. L. 104–193, 110 Stat. 2105, 2189.

2. Appendix 1 to subpart P of part 404 is amended by revising items 5, 6, and 7 of the introductory text before Part A to read as follows:

Appendix 1 to Subpart P—Listing of Impairments

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5. Cardiovascular System (4.00 and 104.00):
July 2, 2001.
6. Digestive System (5.00 and 105.00): July 2, 2001.
7. Genito-Urinary System (6.00 and 106.00):
July 2, 2001.
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[FR Doc. 99–31322 Filed 12–2–99; 8:45 am]

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Parts 203 and 205

[Docket Nos. 92N–0297 and 88N–0258]

RIN 0910-AA08

Prescription Drug Marketing Act of 1987; Prescription Drug Amendments of 1992; Policies, Requirements, and Administrative Procedures

AGENCY: Food and Drug Administration, HHS.

ACTION: Final rule.

SUMMARY: The Food and Drug Administration (FDA) is issuing a final

rule to set forth procedures and requirements implementing the Prescription Drug Marketing Act of 1987 (PDMA), as modified by the Prescription Drug Amendments of 1992 (PDA) and the FDA Modernization Act of 1997 (the Modernization Act). The final rule sets forth requirements for the reimportation and wholesale distribution of prescription drugs; the sale, purchase, or trade of, or the offer to sell, purchase, or trade, prescription drugs that were purchased by hospitals or health care entities, or donated to charitable organizations; and the distribution of prescription drug samples. FDA is also amending certain sections of the regulations entitled "Guidelines for State Licensing of Wholesale Prescription Drug Distributors" to make them consistent with this final regulation.

DATES: Submit written comments on the collection of information provisions by February 1, 2000. This regulation is effective December 4, 2000.

ADDRESSES: Submit written comments on the collection of information to the Dockets Management Branch (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20857. All comments should be identified with the docket number found in brackets in the heading of this document.

FOR FURTHER INFORMATION CONTACT:

For information on the PDMA and regulations: Lee D. Korb, Center for Drug Evaluation and Research (HFD-7), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301-594-2041, e-mail address via Internet: "Korbl@CDER.FDA.GOV".

For information on compliance with and enforcement of the regulations: Margaret M. O'Rourke, Center for Drug Evaluation and Research (HFD-330), Food and Drug Administration, 7500 Standish Pl., Rockville, MD 20855, 301-594-0101, e-mail address via Internet: "Oroure@CDER.FDA.GOV".

For information on biologics: Steven F. Falter, Center for Biologics Evaluation and Research (HFM-17), Food and Drug Administration, 1401 Rockville Pike, Rockville, MD 20852, 301-827-6210, e-mail address via Internet: "Falter@CBER.FDA.GOV".

SUPPLEMENTARY INFORMATION:

I. Background

PDMA (Public Law 100-293) was enacted on April 22, 1988, and was modified by the PDA (Public Law 102-353, 106 Stat. 941) on August 26, 1992.

PDMA, as modified by the PDA, amended sections 301, 303, 503, and 801 of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 331, 333, 353, 381) to establish restrictions and requirements relating to various aspects of human prescription drug marketing and distribution. Among other things, PDMA: (1) Banned the sale, purchase, or trade of (or offer to sell, purchase, or trade) drug samples and drug coupons; (2) restricted reimportation of prescription drugs to the manufacturer of the drug product or for emergency medical care; (3) established requirements for drug sample distribution and the storage and handling of drug samples; (4) required wholesale distributors of prescription drugs to be State licensed and required FDA to establish minimum requirements for State licensing schemes; (5) established requirements for wholesale distribution of prescription drugs by unauthorized distributors; (6) prohibited, with certain exceptions, the sale, purchase, or trade (or offer to sell, purchase, or trade) of prescription drugs that were purchased by hospitals or health care entities, or donated or supplied at a reduced price to charities; and (7) established criminal and civil penalties for PDMA violations.

In the **Federal Register** of September 13, 1988 (53 FR 35325), FDA published a proposed rule containing minimum requirements for State licensing of wholesale drug distributors. The final rule on State licensing requirements (part 205 (21 CFR part 205)) was published in the **Federal Register** of September 14, 1990 (55 FR 38012) (hereinafter referred to as the State licensing guideline final rule). The State licensing regulations require that all wholesale distributors be State licensed, establish minimum qualifications for licensees, and set forth minimum requirements for the storage and handling of prescription drugs and for the establishment and maintenance of records of drug distribution by wholesale distributors.

In the **Federal Register** of March 14, 1994 (59 FR 11842), FDA issued a proposed rule to set forth agency policies and requirements for those sections of PDMA not related to State licensing of wholesale distributors (hereinafter referred to as the March 1994 proposal). The March 1994 proposal contained provisions on prescription drug reimportation, wholesale distribution of prescription drugs by unauthorized distributors, the resale of prescription drugs by hospitals, health care entities, and charitable institutions, and distribution of prescription drug samples. The March

1994 proposal called for the submission of comments by May 30, 1994. At the request of certain individuals, the comment period was extended, by notice in the **Federal Register** of July 15, 1994 (59 FR 36107), to August 15, 1994. After careful consideration of the comments, the agency has revised and finalized the March 1994 proposal. A discussion of significant issues, the comments received on the proposal, and the agency's responses to the comments follows.

II. Significant Issues and Revisions to the Proposal

A. Reimportation of Drugs Composed Wholly or Partly of Insulin

On November 21, 1997, the Modernization Act (Public Law 105-115) was enacted. Section 125(a)(2)(D) of the Modernization Act amended section 801(d)(1) of the act to prohibit the reimportation of a drug composed wholly or partly of insulin, except by the manufacturer of the drug or for emergency care. In accordance with the revised statutory requirement, the agency has revised proposed §§ 203.10 and 203.12 (21 CFR 203.10 and 203.12) in the final rule to include insulin-containing drugs.

B. Blood and Blood Components Intended for Transfusion

In the State licensing guideline final rule, FDA excluded from the definition of "wholesale distribution" the sale, purchase, or trade of blood and blood components intended for transfusion (see § 205.3(f)(8)). Thus, persons engaged in the distribution of blood or blood components intended for transfusion are not required to be State licensed wholesale prescription drug distributors or to comply with other part 205 requirements.

Concurrent with the State licensing guideline final rule, FDA published a proposed rule entitled "Applicability to Blood and Blood Components Intended for Transfusion; Guidelines for State Licensing of Wholesale Prescription Drug Distributors" (55 FR 38027) (hereinafter referred to as the September 1990 proposal). In that proposal, FDA: (1) Tentatively concluded that PDMA does not apply to the distribution of blood and blood components intended for transfusion, (2) set forth its rationale for its tentative conclusion, and (3) solicited comments. The agency stated that, if comments persuaded FDA that PDMA should be interpreted as applying to the distribution of blood and blood components intended for transfusion, FDA would amend the State licensing guideline final rule.

Comments received on the proposal supported the exclusion, however, and no action has been taken by the agency to amend part 205.

FDA again tentatively concluded in the March 1994 proposal (59 FR 11842 at 11844) that the restrictions in and the requirements of PDMA do not apply to the distribution of blood and blood components intended for transfusion. Proposed §§ 203.1 and 203.3(v) (21 CFR 203.1 and 203.3(v)) specified that blood and blood components intended for transfusion are outside the scope of PDMA, and do not constitute "prescription drugs" for the purposes of part 203 (21 CFR part 203). In addition, proposed § 203.22(g) specifically excluded the sale, purchase, or trade of, or offer to sell, purchase, or trade blood or blood components intended for transfusion from the sales restrictions in proposed § 203.20. No comments opposing the proposed sections were received.

Based on the rationale set forth in the September 1990 proposal, the agency has made a final determination that blood and blood components intended for transfusion should be excluded from all of the restrictions in and the requirements of PDMA. Accordingly, proposed §§ 203.1, 203.3(v), and 203.22(g) are being finalized, and the September 1990 proposal (Docket No. 88N-0258) is not being adopted.

As discussed in section III.B of this document in conjunction with comments received on the proposed rule, blood and blood components intended for transfusion include whole blood, red blood cells, plasma, fresh frozen plasma, cryoprecipitated AHF, and platelets. Blood derivatives such as Factor IX, Factor IX Complex, and immune globulin, as well as recombinant products regulated as biological products, are not blood or blood components intended for transfusion and, therefore, are subject to the requirements and restrictions of PDMA.

C. Medical Gases

In the March 1994 proposal (59 FR 11842 at 11844), the agency clarified that oxygen, USP (United States Pharmacopeia), is a prescription drug subject to section 503(b) of the act and, therefore, within the scope of PDMA and the proposed regulations. Since the publication of the March 1994 proposal, questions have been raised about the applicability of PDMA to medical gases generally.

FDA advises that all medical gases (i.e., oxygen, USP; nitrogen, NF (National Formulary); nitrous oxide, USP; carbon dioxide, USP; helium USP;

and medical air, USP) are prescription drugs within the scope of PDMA and the State licensing guideline final rule. Therefore, under § 205.4, all persons engaged in the wholesale distribution of medical gases must be State licensed. This includes all air separation plants and units, suppliers, welding firms, durable medical equipment suppliers, and home respiratory care companies that distribute medical gases, except for those entities that exclusively distribute medical gases to patients under a valid prescription (see § 205.3(f)(6)). In addition, distributors of medical gases are subject to all other restrictions and requirements under PDMA and this final rule, including the requirement under § 203.50 to provide a drug origin statement and the requirements for drug sample distribution. The agency notes, however, that because most distributors of medical gases qualify as manufacturers under § 203.3(s), the requirement to provide a drug origin statement will generally not apply to such distributors. In addition, the agency is unaware of the practice of providing samples of medical gases to licensed practitioners. Therefore, the drug sample provisions of PDMA and this final rule should have no practical applicability to the medical gas industry.

D. Revision to Proposed 203.3(e)

In proposed § 203.3(e), the term "bulk drug substance" was defined to mean:

Any drug or drug component furnished in other than finished dosage form that is intended to furnish pharmacological activity or other direct effect in the diagnosis, cure, mitigation, treatment, or prevention of disease, or to affect the structure or function of the body of humans. In § 207.3(a)(4) (21 CFR 207.3(a)(4)), the term is defined to mean:

Any substance that is represented for use in a drug and that, when used in the manufacturing, processing, or packaging of a drug, becomes an active ingredient or a finished dosage form of the drug, but the term does not include intermediates used in the synthesis of such substances. Although the definitions are similar, the agency has decided that it is appropriate to use identical definitions of bulk drug substance throughout the regulations. Accordingly, the final rule adopts the definition of bulk drug substance used in § 207.3(a)(4).

E. Revisions to Proposed § 203.31(d)

For drug samples delivered by representatives, PDMA provides that a manufacturer or distributor is required to conduct a complete and accurate inventory of all drug samples in the possession of representatives at least annually (21 U.S.C. 353(d)(3)(C)). FDA

proposed in § 203.31(d) to require that manufacturers and distributors conduct a "complete and accurate drug sample inventory" at least annually of all drug samples in the possession or control of each manufacturer's and distributor's representatives using "generally accepted inventory practices." In addition, FDA proposed to require that the results of the inventory be "recorded in an inventory record and reconciliation report."

Under proposed § 203.31(d)(1), the inventory record would identify all drug samples by the proprietary or established name, dosage strength, and number of sample units in stock. Under proposed § 203.31(d)(2), the reconciliation report would contain a report of the physical count of the most recently completed prior inventory, a record of each drug sample received since the most recently completed prior inventory, a record of each drug sample distributed since the most recently completed prior inventory, and an explanation for any significant loss. Under proposed § 203.31(d)(3), the inventory would be conducted, and the inventory and reconciliation reports would be prepared by persons other than the representatives being inventoried or supervisors or managers in their department, division, or branch, or in their direct line of supervision or command.

The agency has revised proposed § 203.31(d) in the final rule to clarify certain requirements. The introductory paragraph of § 203.31(d) has been revised to specify that a "physical inventory" of drug samples is required, rather than an inventory. The term "physical inventory" has been added to more clearly distinguish the inventory from the reconciliation process and to clarify that the required inventory consists of a physical count of stock on hand. The proposed requirement that the inventory be conducted "using generally accepted inventory practices" has been deleted in the final rule because the agency has determined that there are no generally recognized standards for conducting a physical count. The final rule has also been revised to clarify that the results of the physical count must be recorded in the inventory record, not in the inventory record and reconciliation report. The proposed requirements for the inventory record remain unchanged.

In contrast to the relatively simple task of conducting a physical count, the reconciliation process involves comparing the latest inventory to the most recent prior inventory and taking into account drug samples acquired and distributed in the interim, to determine

whether sample diversion by a representative has occurred. As discussed by the agency in the March 1994 proposal, Congress' purpose in enacting the inventory requirement was to facilitate detection of diversion activity, and conducting a physical inventory without reconciling that inventory with the most recent prior inventory would not achieve this goal (59 FR 11842 at 11849). Thus, the introductory paragraph of proposed § 203.31(d) has been revised in the final rule to clarify that, in addition to a physical inventory, manufacturers and distributors are required to reconcile the results of the physical inventory with the most recently completed prior physical inventory and to document this process in a reconciliation report.

The agency has revised proposed § 203.31(d)(2)(i) in the final rule to require that the reconciliation report include the inventory record for the most recently completed prior inventory. This is the same as the requirement in proposed § 203.31(d)(2)(i) for a "report of the physical count of the most recently completed prior inventory," but the terminology is clearer and consistent with the terminology used in § 203.31(d)(1).

Proposed § 203.31(d)(2)(iii) has been revised in the final rule to clarify the types of transactions that the agency considers to be "distributions." This clarification is necessary because a representative's stock of drug samples may be affected by various types of dispositions other than distributions to health care practitioners or their designees, and it is necessary that the reconciliation report reflect these different types of dispositions so that an accurate assessment of potential drug diversion activity can be made. Section 203.31(d)(2)(iv), which requires a record of drug sample thefts or significant losses reported by the representative since the most recently completed prior inventory, has been added for the same reason.

Section 203.31(d)(2)(v), which requires a summary record of the information contained in § 203.31(d)(2)(ii) through (d)(2)(iv), has been added in the final rule. The summary record will permit manufacturers and authorized distributors of record and the agency to quickly review the information that is necessary to conduct a reconciliation and thus will help to facilitate checking the accuracy of reconciliations.

Finally, as discussed in section III.E of this document in conjunction with the comments, proposed § 203.31(d)(3) has been substantially revised in the final

rule to eliminate the proposed requirement that the inventory and reconciliation functions be conducted by persons other than the representative or supervisors or managers in the representative's department, division, or branch, or in the representative's direct line of supervision. Instead, manufacturers and authorized distributors are required to take appropriate internal control measures to guard against error and possible fraud in the conduct of the physical inventory and reconciliation, and in the preparation of the inventory record and reconciliation report.

F. Elimination of § 203.31(f)

Proposed § 203.31(f) has been removed from the final rule. The proposed section contained the same requirement for a manufacturer or authorized distributor to notify FDA of any conviction of its representatives as proposed in § 203.37(c) and finalized in the rulemaking.

G. Revisions to Proposed § 203.34

Proposed § 203.34(b), (c), (d), and (g) have been revised and renumbered in the final rule as § 203.34(b)(1) through (b)(4). Proposed § 203.34(d) is being finalized as § 203.34(b)(1) and has been revised to clarify that a manufacturer or authorized distributor must have written policies and procedures detailing its methodology for reconciling sample requests and receipts and for determining if patterns of nonresponse exist that may indicate sample diversion. In addition, written policies and procedures must detail how a manufacturer or authorized distributor will initiate investigations or otherwise respond when patterns of nonreturns of sample receipts are found. Proposed § 203.34(c) is being finalized as § 203.34(b)(2) and has been revised to cover the preparation of the reconciliation report as well as the conduct of the physical inventory. Proposed § 203.34(b) is being finalized as § 203.34(b)(3) and has been revised to require manufacturers and distributors to establish and adhere to written policies describing their administrative systems for conducting random and for-cause audits of sales representatives. The necessity for such audits is discussed in conjunction with comments on proposed § 203.31(d).

H. Charitable Donations of Prescription Drug Samples

In the preamble to the March 1994 proposal (59 FR 11842 at 11853), the agency addressed the practice whereby licensed practitioners donate prescription drug samples to charitable

institutions such as free clinics, nursing homes, and other charitable health care entities for dispensing to patients or for further distribution to other domestic or overseas charities. The agency recognized the importance of this practice to the operations of such institutions and to the goal of providing adequate medical care to patients in need, but also expressed concern that the practice may make enforcement of the sample distribution provisions of PDMA difficult and provide an avenue for drug diversion. The agency tentatively concluded that charitable donations of drug samples is permissible under PDMA, provided that a system of controls is in place to provide accountability and oversight over such donations and to minimize the potential for drug diversion. The agency proposed a system of drug sample donation controls in § 203.39.

Although no comments were submitted concerning the provisions in § 203.39, the agency has determined that some of the proposed requirements are burdensome and unnecessary to ensure accountability and oversight over donated drug samples. Accordingly, the agency has revised the proposed requirements as follows.

Proposed § 203.39(a)(1) and (a)(2), which required that charitable institutions that receive drug sample donations be licensed by the State, if required by State law, and enrolled with FDA, have been eliminated. Regarding the elimination of proposed § 203.39(a)(1), the agency notes that charitable institutions are still required to comply with applicable State law in their operations. However, the agency believes that it is appropriate to defer licensure or other State requirements to the States. Proposed § 203.39(b)(1), which required charitable institutions to provide documentation demonstrating that their agents are authorized to solicit or receive drug sample donations, and proposed § 203.39(b)(2), which required charitable institutions to maintain a list of agents authorized to solicit or receive drug sample donations, have also been eliminated.

Proposed § 203.39(b)(8), which required the donor of a drug sample to prepare a donation record for drug samples delivered by mail or common carrier, has been eliminated. Under § 203.39(e) of the final rule, the charitable institution to which a drug sample is donated must prepare a donation record for the sample regardless of the manner of delivery of the drug sample and must retain the record for at least 3 years. Proposed § 203.39(b)(9) has been revised to require that the donation record contain

only the name, address, and telephone number of the donating licensed practitioner or charitable institution; the manufacturer, brand name, quantity, and lot or control number of the drug sample donated; and the date of the donation.

Proposed § 203.39(b)(11) has been revised to eliminate the proposed requirement that the inventory of donated drug samples in the possession of a charitable institution be conducted using independent inventory personnel. Proposed § 203.39(b)(12), which required that a charitable institution provide written certification to the donating party that it is in compliance with part 203, has been eliminated in the final rule. Finally, proposed § 203.39(c) has been eliminated, but its requirements have been incorporated into the introductory paragraph of § 203.39 such that charitable institutions may donate donated drug samples to other charitable institutions as long as § 203.39 is followed.

I. Charitable Donations of Prescription Drugs Generally

Since the publication of the March 1994 proposal, the agency has received requests that raise questions about whether and how PDMA should be applied to charitable donations of prescription drugs generally, not just drug samples. Nonsample drug products may be donated to charitable institutions from many different sources, including manufacturers, wholesale distributors, retail pharmacies, for profit and nonprofit hospitals and health care entities, other charitable groups, and reverse distributors (i.e., wholesale distributors that handle returns). In addition, FDA is aware that drug salvagers may also be a source of donations.

The donation of nonsample drug products to charitable institutions raises similar concerns about the quality of the drugs being donated and potential drug diversion as the donation of drug samples. Moreover, such donations constitute distribution of a prescription drug to other than a consumer or patient and therefore could be considered "wholesale distribution" under section 503(e)(4)(B) of the act. Although the agency is not establishing controls for nonsample prescription drug donations at this time, the agency is carefully considering the relevant issues and may in the future propose an approach to drug donations that encompasses both prescription drug samples and nonsample prescription drug products.

J. Creation and Maintenance of Required Forms, Reports, Records, and Signatures

Proposed § 203.60 set forth standards for the creation and maintenance of sample request and receipt forms, reports, records, and other documents required under PDMA and part 203. Proposed § 203.60(a) permitted any required document to be created either on paper or on electronic media. Proposed § 203.60(b) permitted any required document created on paper to be maintained on paper or by photographic or electronic imaging, provided the security and authentication requirements in § 203.60(d) were met. Proposed § 203.60(c) permitted required documents created electronically to be stored using computer technologies, provided the requirements in § 203.60(d) were met. Proposed § 203.60(d) provided that required documents and signatures must be created, maintained, or transmitted in a form providing reasonable assurance of being: (1) Resistant to tampering, revision, modification, fraud, unauthorized use, or alteration; (2) preserved in accessible and retrievable fashion; and (3) visible or readily made visible for purposes of review by regulated industry and FDA.

In addition to the requirements in proposed § 203.60, proposed § 203.61 permitted signatures on required forms, reports, and records to be made by means of a writing or marking instrument such as a pen or indelible pencil. The section also permitted signatures to be made by electronic stylus on an electronic pad or by other electronic medium, provided the security requirements in § 203.61(b) were met.

In the **Federal Register** of March 20, 1997 (62 FR 13430), the agency issued final regulations on electronic records and electronic signatures in part 11 (21 CFR part 11). Because of the issuance of those regulations and the applicability of part 11 to part 203 document and signature requirements, the March 1994 proposal has been substantially revised. Under part 11, electronic records, electronic signatures, and handwritten signatures executed to electronic records that meet the requirements of that part may be used to meet requirements to create and maintain records and signatures under the act and agency regulations, unless specifically excepted by future regulations. Therefore, sections of the March 1994 proposal setting forth requirements relating to creation and maintenance of electronic records, electronic signatures,

and handwritten signatures, as those terms are defined in part 11, have been revised or eliminated in the final rule.

Proposed § 203.60(a) has been deleted and replaced in the final rule by revised § 203.60(a)(1), (a)(2), and (a)(3). Revised § 203.60(a)(1) states that electronic records, electronic signatures, and handwritten signatures executed to electronic records may be used in lieu of paper records and handwritten signatures executed on paper to meet any of the record and signature requirements of PDMA or part 203, provided that the requirements of part 11 are met. Although electronic signatures, electronic records, and handwritten signatures executed on electronic records would be permitted to meet PDMA and part 203 records and signature requirements under the provisions of part 11 without further rulemaking in part 203 (see, e.g., § 11.1), this section has been included in the final rule for added clarity. The final rule also defines the terms electronic record, electronic signature, and handwritten signature in revised § 203.3(k), (l), and (p), respectively, to have the same meaning that these terms have in § 11.3(b)(6), (b)(7), and (b)(8).

Revised § 203.60(a)(2) permits combinations of paper records and electronic records, electronic records and handwritten signatures executed on paper, and paper records and electronic signatures or handwritten signatures executed to electronic records to be used to meet PDMA record and signature requirements, provided that the requirements of part 11 are met for the electronic component. In addition, a reasonably secure link must exist between the paper-based and electronic components to ensure that the combined records and signatures are trustworthy and reliable and the signer cannot readily repudiate the signed record as not genuine. A reasonably secure link could consist of a physical link between the electronic and paper-based records (i.e., where the paper-based record(s) and a computer disk containing the electronic record(s) are sealed together in a container and a chain of controlled custody for the sealed container is established) or a technology-based link. The agency is planning to issue in the future further guidance on technology-based links in conjunction with its implementation of part 11.

Revised § 203.60(a)(3) clarifies that the "record and signature requirements" to which § 203.60(a)(1) and (a)(2) refer include drug sample request and receipt forms, reports, records, and any other types of documents and their associated

signatures required by PDMA or part 203.

Because part 11 does not apply to the photographic imaging of paper records, proposed § 203.60(b) has been retained in the final rule. The section has been revised, however, to clarify that electronic scanning of paper records into a computer creates an electronic record that is subject to the requirements of part 11. The security and authentication requirements in proposed § 203.60(d) have been renumbered in the final rule as § 203.60(c) and revised such that the requirements in the section apply only to documents and signatures that are created on paper and that are maintained by photographic imaging or transmitted electronically. Minor revisions have also been made to the security and authentication requirements in revised § 203.60(d)(3).

The requirements for maintenance of documents created by electronic means in proposed § 203.60(c) and the signature requirements in proposed § 203.61 have been superseded by part 11 requirements. Therefore, these sections have been deleted in their entirety in the final rule. Proposed § 203.60(e) and (f) have been renumbered in the final rule as § 203.60(d) and (e).

K. Implementation of the Final Rule

The provisions in the final rule will become effective 1 year after the date of publication of the final rule in the **Federal Register**. The agency is providing this period to give industry sufficient time to implement systems for prescription drug sample distribution and wholesale distribution that are in compliance with the final rule.

III. Comments on the Proposed Rule

A. General Comments

FDA received 56 comments on the March 1994 proposal from prescription drug manufacturers, industry organizations, professional associations and organizations, law enforcement agencies, and others. Although most of the comments addressed only specific provisions of the rule, a few commented generally on the proposed rule, and those comments were mixed. For example, one comment stated that it "supports the controls on prescription drug samples sought through the passage of PDMA and feels that, in general, the proposed rule is a positive step in combating the market in diverted prescription drugs and ensuring consumers that drug products continue to remain safe and effective." Another comment, however, stated that

"finalization of the proposed rule will create unnecessary additional administrative burdens for companies and their sales representatives" and "would not improve significantly the industry's ability to track sample distribution and reduce the possibility of diversion of samples."

A large number of comments addressed the provisions of the proposed rule relating to sample distribution. In fact, comments were received on almost all of the sections of the proposed rule dealing with sample distribution. Most of these comments were critical of the manner in which the agency proposed to implement the sample distribution requirements contained in PDMA. In addition to comments on sample distribution, comments were received on sections of the proposed rule relating to reimportation of prescription drugs, resales of prescription drugs purchased by health care entities, recordkeeping and investigation requirements, and wholesale distribution.

Specific issues raised by the comments and the agency's responses follow.

B. Definitions

Blood component. Proposed § 203.3(d) defined "blood component" as "that part of a single-donor unit of blood separated by physical or mechanical means."

1. One comment requested clarification on whether various plasma products and derivatives, including antihemophilic factor, Factor IX, Factor IX Complex, and immune globulin IV, are considered blood components or drugs. The comment also asked for clarification of whether the agency makes a distinction between human and recombinant products in deciding whether to categorize a blood component preparation as a blood component or drug.

The agency advises that blood components, as defined in § 203.3(d) of the final rule, include red blood cells, plasma, fresh frozen plasma, cryoprecipitated AHF, and platelets. Antihemophilic Factor, Factor IX Complex, and immune globulin products are derivatives of blood, not blood components. Both blood components and blood derivatives are regulated as biologics under the authority of the Public Health Service Act (the PHS Act) and are also drugs under section 201(g)(1) of the act (21 U.S.C. 321(g)(1)). Products manufactured through recombinant technology that mimic blood derivatives or other biological products are also regulated as biologics under the PHS

Act and are drugs under section 201(g)(1) of the act. These products, like blood derivatives, are not blood components.

Distribute. Proposed § 203.3(h) defined "distribute" to mean to sell, offer to sell, deliver, or offer to deliver a drug to a recipient, except that the term "distribute" does not include the providing of a drug sample to a patient by:

- (1) A practitioner licensed to prescribe such drug,
- (2) A health care professional acting at the direction and under the supervision of such a practitioner, or
- (3) The pharmacy of a hospital or of another health care entity that is acting at the direction of such a practitioner and that received such sample in accordance with the act and regulations.

On its own initiative, the agency is revising proposed § 203.3(h) in the final rule to specify that the term "distribute" does not include the delivery of drugs or offer to deliver drugs by a common carrier in the usual course of its business as a common carrier. This revision is necessary to permit common carriers that deliver drug samples, or perform duties incidental to delivery (i.e., delivery verification) for manufacturers or authorized distributors of record, to do so without being required to be authorized distributors of record.¹ Such a requirement would be confusing and inconsistent with language in section 503(d) of the act, which distinguishes between sample distribution and delivery by mail or common carrier. However, comarketers, fulfillment houses, and other entities that perform some or all of the functions associated with sample distribution and promotion that would otherwise be performed by the drug manufacturer are not covered by this exception. Thus, entities that create and maintain required forms, reports, and records; have their own sales forces and representatives; solicit and fill requests for drug samples; or conduct other such activities are engaged in drug sample distribution and must be authorized distributors of record.

Health care entity. Proposed § 203.3(n) defined "health care entity" as "any person that provides diagnostic, medical, surgical or dental treatment, or chronic or rehabilitative care, but does not include any retail pharmacy or any wholesale distributor. A person cannot simultaneously be a 'health care entity'

¹ Under the proposed rule, delivery of drug samples would constitute drug sample distribution. Under section 503(d) of the act, only a manufacturer or authorized distributor of record may distribute drug samples.

and a retail pharmacy or wholesale distributor.”

2. Several comments noted that, under the proposed definition of health care entity, full-service blood centers that currently function both as health care entities and distributors of blood plasma derivatives would not be permitted to continue to operate in both of these capacities. The comments expressed concern that the ability of community health care entities to obtain plasma derivatives would be detrimentally affected if community blood centers were prohibited from distributing them.

One comment explained that plasma derivatives are unique prescription drugs that are largely distributed outside the typical drug distribution network. The comment stated that, historically, blood centers and hospital blood banks have provided plasma processing and distribution services for their local communities. Although the processing has become more complex and is now done largely by for-profit manufacturers, blood centers, hospital blood banks, and transfusion services still act as final distributors of plasma derivatives. The comment said that this arrangement enables the health care providers who receive blood derivatives to use the “expert consultative services” of these entities.

Several comments stated that the same reasons for excluding blood and blood components intended for transfusion from PDMA’s sales restrictions are applicable to blood derivatives. The comments contended that there is no indication in the legislative history that the types of abuses that lead to the restrictions in section 503(c)(3) of the act are present with blood derivatives or that Congress intended the restrictions in section 503(c)(3) of the act to apply to blood derivatives.

The comments suggested ways in which the proposed rule could be amended to allow blood centers to continue to function as wholesale distributors of plasma derivatives. Two comments suggested specifically excluding blood banks, transfusion services, and hospital blood banks from the prohibition against a health care entity simultaneously being a wholesale distributor. Another comment recommended that FDA eliminate entirely the prohibition against a health care entity simultaneously being a wholesale distributor with a clarification in the preamble to the final rule that health care entities engaging in “sham” operations to avoid resale prohibitions remain subject to enforcement of resale prohibitions, even

if licensed as a wholesaler. One comment suggested expanding the definition of “blood” or “blood components” to include plasma derivatives.

The agency declines to revise the definition of health care entity or otherwise revise the proposed rule to permit health care entities to engage in the wholesale distribution of blood derivatives or other prescription drug products. The statutory restrictions in section 503(c)(3)(A) of the act prohibit the sale, purchase, or trade of, or offer to sell, purchase, or trade prescription drugs that are purchased by a public or private hospital or health care entity or donated or supplied at a reduced price to a charitable organization. Because blood derivatives are prescription drugs that are neither blood nor blood components, a hospital or health care entity that purchases these products from a manufacturer or distributor, or a charitable institution that receives these products through a donation or at a reduced price, may not sell or trade these products except as permitted under section 503(c)(3)(B) of the act and § 203.22 of the agency’s regulations.²

The agency is unpersuaded by the comments that blood derivatives should, as a matter of public health policy, be grouped with blood and blood components intended for transfusion as products that Congress did not intend to cover under PDMA generally, or under section 503(c)(3)(A) of the act specifically. In the September 1990 proposal, the agency stated that if PDMA and, in particular, PDMA’s restrictions on the resale of prescription drugs were considered applicable to blood and blood components intended for transfusion, the result would be to seriously impede the present blood distribution system and thereby substantially interfere with, and reduce, the nation’s blood supply. Based largely on this “untenable result,” the agency stated its belief that Congress did not intend to subject blood and blood components to PDMA’s provisions (55 FR 38027).

The comments contend that, as with whole blood and blood components intended for transfusion, the supply of blood derivatives to the public would be impeded if blood banks were not permitted to distribute these products. However, unlike whole blood and blood components, blood derivatives are manufactured in large quantities by manufacturers that are independent of

blood banks and blood centers, are packaged and stored similarly to other pharmaceuticals, and have relatively normal shelf lives. Moreover, blood derivatives need not be matched from a donor to a donee as do whole blood and blood components intended for transfusion. Thus, although in some instances blood derivatives are distributed by blood centers and hospital blood banks, they also are distributed by conventional drug wholesalers. There is no evidence before the agency at this time that a substantial percentage of the nation’s supply of blood derivatives is currently distributed by blood centers, hospital blood banks, or transfusion services, or that the nation’s supply of blood derivatives would be seriously impeded if these entities were prohibited from distributing these products.

Moreover, the comments’ assertion that blood derivatives, like blood and blood components, are not subject to the abuses Congress set out to remedy in PDMA is speculative and unsupported by facts. As discussed previously, blood derivatives are distributed through a normal wholesale distribution system, and they need not be matched to specific patients. Thus, the possibility of diversion of these products exists, and documented instances of diversion of these products have in fact occurred. The fact that blood derivatives were not specifically mentioned by Congress in the legislative history is in itself of little significance.

FDA recognizes that, in addition to selling blood derivatives to community hospitals, blood centers have traditionally provided advice and guidance on how to use the derivatives. The final rule does not prohibit the provision of information by a health care entity to another health care entity, but rather prohibits the selling of prescription drug products, including blood derivatives, that are purchased by a hospital or health care entity. Thus, blood centers or other entities that have traditionally provided information to hospitals or other health care centers are not precluded from doing so under PDMA or the final rule.

3. One comment stated that FDA’s definition of health care entity is “without factual or legal foundation.”

Two comments stated that FDA’s interpretation of section 503(c)(3) of the act as prohibiting a health care entity from simultaneously being a wholesale distributor is contrary to the plain language of the statute and to legislative intent, and places inappropriate restrictions on the legitimate operations of blood centers. These comments interpreted the last sentence in section

² For example, the proposed definition of health care entity would not prevent a hospital, health care entity, or charity from purchasing blood derivatives and administering them to patients under a valid prescription.

503(c)(3)(A) of the act, which states in part that “[f]or purposes of this paragraph, the term ‘entity’ does not include a wholesale distributor of drugs or a retail pharmacy licensed under State law,” as creating an exemption to the sales restrictions in that section for health care entities that are State licensed as wholesale distributors. The comments stated that FDA’s proposed definition of “health care entity” contradicts the clear wording of the statute. The comments also stated that the proposed definition is inconsistent with legislative intent to permit health care entities acting as legitimate wholesalers to engage in wholesale distribution of prescription drugs.

The agency acknowledges that the first clause of the last sentence in section 503(c)(3) of the act could be read to make the restrictions in section 503(c)(3)(A) of the act inapplicable to hospitals or health care entities State licensed as wholesale distributors. However, the agency believes that the statutory language should be read to mean that health care entities subject to the restrictions in section 503(c)(3)(A) of the act cannot simultaneously be wholesale distributors or retail pharmacies. As noted by the agency in the proposed rule (59 FR 11842 at 11845), the former interpretation is inconsistent both with general rules of statutory construction and with legislative intent. If this interpretation were to be given effect, it would mean that a health care entity could circumvent the sales restrictions by obtaining a State wholesale distribution license. Such an interpretation would deprive the sales restrictions of any force or effect. Moreover, Congress expressly enumerated in section 503(c)(3)(B) of the act the circumstances under which drugs purchased by a health care entity may be sold. The agency believes that if Congress had intended to permit sales of prescription drugs purchased by health care entities that are State licensed wholesale distributors, it would have done so under section 503(c)(3)(B) of the act.

Interpreting section 503(c)(3) of the act in the manner suggested by the comments would also be inconsistent with legislative intent as reflected in the congressional findings and legislative history. The statutory restrictions in section 503(c)(3)(A) of the act reflect the congressional finding in section 2(7) of PDMA that the resale of prescription drugs by health care entities at below wholesale prices had helped to fuel the diversion market and constituted an unfair form of competition to legitimate wholesalers and retailers paying prevailing market prices. These same

concerns also were expressed by Congress in the legislative history. (See H. Rept. 100–76, pp. 12–13.) If health care entities were permitted to obtain State wholesale distributor licenses and engage in wholesale distribution of prescription drugs, as suggested by the comments, there would be no way of ensuring that the types of abuses that Congress sought to prevent in section 503(c)(3)(A) of the act would not occur. Neither the requirements applicable to wholesale distributors in section 503(e) of the act nor the State licensing guidelines in part 205 contain requirements to deter a health care entity from reselling prescription drugs, or require or authorize FDA to keep track of the circumstances under which prescription drugs are bought and sold by wholesale distributors. Thus, if health care entities were permitted to be State licensed wholesale distributors, they could purchase drugs for their own use and sell them on the secondary wholesale market with impunity and without the knowledge of the agency or Congress. The agency does not believe that Congress intended such a result.

Licensed practitioner. Proposed § 203.3(o) defined “licensed practitioner” as “any person licensed by State law to prescribe drugs.”

4. One comment recommended that “or authorized” be added after “licensed” in the definition to allow nonphysician practitioners subject to State authorization schemes other than licensing to obtain drug samples.

The agency has decided to follow the suggestion of the comment and revise the definition of “licensed practitioner” in the final rule to include practitioners authorized by State law to prescribe drugs. Congress stated in the legislative history (S. Rept. 100–303, p. 5) that “Drug samples may only be distributed to practitioners licensed or authorized by State law to prescribe such drugs.” Moreover, the use by Congress of the term “licensed practitioner” rather than “physician” in section 503(d)(2)(A) of the act shows congressional intent to allow nonphysician practitioners to obtain drug samples. Because a significant number of these practitioners are subject to different State authorization schemes than licensing, the agency finds that a strict interpretation of the word “license” would be inconsistent with congressional intent.

5. One comment stated that, in some States, advanced practical nurses are licensed to prescribe certain drugs, but are prohibited from obtaining samples of the same drugs. The comment asserted that, under the proposed definition of “licensed practitioner,”

such nonphysician practitioners would be permitted to obtain samples.

In developing the proposed definition of licensed practitioner, the agency was not aware that some States may permit practitioners to prescribe certain drugs, but prohibit them from obtaining samples of those drugs. Because the agency does not wish to interfere with States’ authority to determine who may request and receive drug samples, the agency clarifies that a practitioner who is prohibited by State law from receiving samples of certain types of drugs is not permitted to do so under PDMA even though he or she is licensed or authorized to prescribe those drugs.

Ongoing relationship. Proposed § 203.3(r) defined “ongoing relationship” as an association that exists when a manufacturer and a distributor enter into a written agreement under which the distributor is authorized to sell the manufacturer’s products for a period of time or for a number of shipments, at least one sale is made under that agreement, and the name of the authorized distributor of record is entered on the manufacturer’s list of authorized distributors of record.

6. One comment objected to a requirement for a written agreement between a manufacturer and a distributor. The comment stated that written agreements are not customary in the industry and that such a requirement would be burdensome because distributors distribute for large numbers of vendors. The comment recommended that, for the purposes of proving that an ongoing relationship exists, it should be sufficient to show that sales are made on a continuing basis and that the distributor’s name appears on the manufacturer’s list of authorized distributors.

Another comment objected both to the requirement for a written agreement and to the requirement that a distributor be on the manufacturer’s list of authorized distributors of record. The comment stated that neither of these requirements was previously required by the agency in compliance information provided to industry by the agency. The comment stated that both requirements would make it more difficult for distributors to become authorized distributors of record. In addition, the comment stated that the requirements would give prescription drug manufacturers the ability to deny authorized-distributor-of-record status to distributors with whom they have engaged in ongoing business relationships. The comment stated that by giving drug manufacturers the power to decide to whom PDMA wholesale distribution requirements apply without oversight or review, FDA would be

delegating legislative power to the private sector in violation of separation of powers principles in the U.S. Constitution. The comment recommended that FDA adopt a definition of ongoing relationship that mirrors a definition set forth by the agency in a 1988 compliance letter.

PDMA defines the term "authorized distributors of record" as those distributors with whom a manufacturer has established an ongoing relationship to distribute the manufacturer's products. PDMA does not, however, define what constitutes an "ongoing relationship." In a 1988 letter issued by FDA (see Letter from Daniel L. Michels, Director, Office of Compliance to Regulated Industry, Docket No. 88N-258L, August 1, 1988), the agency made its first attempt to interpret the term in the context of PDMA. FDA stated that "ongoing relationship" may be interpreted to mean a continuing business relationship in which it is intended that the wholesale distributor engage in wholesale distribution of a manufacturer's prescription drug product or products. The agency stated that evidence of such intent could include, but would not be limited to, the existence of a written franchise, license, or other distribution agreement between the manufacturer and wholesale distributor and the existence of ongoing sales by the manufacturer to the distributor.

The agency continues to believe that the term "ongoing relationship" in the context of wholesale distribution infers a continuing business relationship between a distributor and a manufacturer where the intent exists to engage in wholesale distribution. Furthermore, the agency has determined that, to facilitate compliance with and enforcement of the act, it is necessary to have a formalized way of establishing that an ongoing relationship exists. A written agreement in which the manufacturer authorizes the distributor to distribute some or all of its products for a period of time or for a number of shipments will provide a clear and verifiable expression of the parties' intent to engage in a continuing business relationship. The written agreement required by proposed § 203.3(r) (revised as § 203.3(u)) need not rise to the level of a contract or create legally enforceable obligations on the parties. Rather, the agreement need only state that the distributor is authorized to distribute a manufacturer's products for a period of time or for a number of shipments and, if the distributor is not authorized to distribute all of the manufacturer's products, identify those products to

which the authorization extends.³ This latter requirement, although not included in the proposed rule, is consistent with the requirement in proposed § 203.50(c)(1) for manufacturers to maintain a list of authorized distributors that specifies whether distributors are authorized to distribute the manufacturer's full product line or only particular products.

Given the relative ease with which the agreement required by § 20.3(u) can be created, the agency believes that it is highly unlikely that a manufacturer would refuse to enter into a written agreement with a distributor with whom it wishes to have a continuing business relationship. Moreover, it is clearly not the agency's intent in requiring a written agreement to confer additional discretion on manufacturers, but rather to implement the requirement in the act for an ongoing relationship in a manner in which it can be efficiently enforced. This is consistent with the agency's authority under section 701(a) of the act (21 U.S.C. 371(a)) to issue regulations for the efficient enforcement of the act. Accordingly, the agency declines to revise the definition of "ongoing relationship" to eliminate the requirement for a written agreement.

Finally, on its own initiative, the agency has revised the proposed definition of "ongoing relationship" in the final rule to eliminate the requirement that at least one sale be completed under the written agreement and that a distributor be entered on the manufacturer's list of authorized distributors of record. The proposed requirement for a completed sale under the written agreement is unnecessary and, as discussed below, inconsistent with the use of the definition in the context of sample distribution. The proposed requirement that a distributor be entered on the manufacturer's list of authorized distributors of record is unnecessary in light of the requirement, in section 503(e)(1)(B) of the act and revised § 203.50(d) of the final rule, that manufacturers keep an updated list of authorized distributors of record at their corporate offices.

7. Another comment stated that sample fulfillment houses, mailing services, comarketers, and similar entities clearly distribute samples within the meaning of "distribute" in proposed § 203.3(h), but cannot satisfy the requirements for an ongoing relationship in proposed § 203.3(r)

³ The written agreement required under § 203.3(u) to establish an ongoing relationship constitutes a "required record" under revised § 203.60, and must be made available, upon request, to FDA or other Federal, State, or local regulatory or law enforcement officials for review and reproduction.

necessary to be considered authorized distributors of record. The comment recommended that the proposed definition of ongoing relationship be revised to permit these entities to be authorized distributors of record.

The comment raises a valid point. The proposed definition of ongoing relationship is inappropriate for sample distribution, and has been revised in the final rule to specify that an ongoing relationship exists when there is a written agreement between a manufacturer and distributor to distribute, rather than to sell, the manufacturer's products for a period of time or for a number of shipments.

Prescription drug. Proposed § 203.3(v) defined "prescription drug" as any drug required by Federal law to be dispensed only by a prescription, including finished dosage forms, bulk drug substances, and active ingredients subject to section 503(b) of the act.

On its own initiative, the agency has removed "active ingredients" in the final rule. The term "bulk drug substance," as defined under § 203.3(e), is synonymous with "active ingredient."

Wholesale distribution. Proposed § 203.3(y) defined "wholesale distribution" as "distribution of prescription drugs to persons other than a consumer or patient, but does not include: (1) Intracompany sales * * *."

8. One comment objected to the exemption of intracompany sales from wholesale distribution, stating that it "totally gets away from the original intent of the PDMA." The comment said that this provision leaves a gap where diversion can occur between wholesalers and retail outlets owned by them.

The agency disagrees with the comment. Intracompany sales were expressly excluded by Congress from the definition of wholesale distribution in section 503(e)(4)(B) of the act. In addition, both the House and Senate reports referred to the exclusion. (See H. Rept. 100-76, S. Rept. 100-303.) The House report stated:

[i]t is the express intent of the Committee that the scope of [this section] include distribution by chain drug warehouses, wholesale drug warehouses, and all sellers of prescription drugs in wholesale quantities to persons or firms other than the consumer or patient. With respect to section 503(e)(1), intracompany sales, i.e., the distribution between divisions and companies having the same ownership, are excluded. (H. Rept. 100-76, p. 17.)

Thus, as expressed in the language of the act and the legislative history, Congress' intent was to exclude intracompany sales from the requirements for wholesale distribution in section 503(e) of the act. In addition,

the agency advises that § 205.5 contemplates a licensing scheme for business entities with subsidiaries, affiliates, and more than one facility (see § 205.5(b)), and provides that State licensing authorities require each wholesale distributor to supply information on all facilities used by the licensee for the storage, handling, and distribution of prescription drugs (see § 205.5(a)(3)).

C. Reimportation

Proposed § 203.10 stated, in relevant part, that “[n]o prescription drug that was manufactured in a State and exported from the United States may be reimported by anyone other than its manufacturer.”

9. One comment requested that the proposed rule be revised to state that a prescription drug may be reimported by any of a manufacturer’s subsidiary companies or contract manufacturers.

For the reasons discussed in the preamble to the proposed rule (59 FR 11842 at 11844), FDA is adopting the definition of manufacturer set forth in § 201.1 (21 CFR 201.1) of the agency’s regulations for the purposes of part 203. Accordingly, a manufacturer’s subsidiary companies or contract manufacturers may reimport a prescription drug product only if they also qualify as a manufacturer of the drug product under § 201.1.

10. One comment recommended that language be added to the section to include drugs that are sold by a manufacturer for exportation, but never leave the United States. The comment stated that a large proportion of the “export” drugs that are diverted never actually leave the United States.

Because the drugs referred to by the comment are not exported, they cannot be subject to the restriction on reimportation. However, the domestic distribution of such drugs is covered by PDMA and other applicable laws, which should help to reduce the potential for diversion.

D. Sales Restrictions

Proposed § 203.20 prohibited the sale, purchase, or trade of, or offer to sell, purchase, or trade, any prescription drug that was purchased by a public or private hospital or health care entity or donated or supplied at a reduced price to a charitable institution.

1. Section 203.22(e)

Proposed § 203.22(e) provided that § 203.20 does not apply to: “The sale, purchase, or trade of a drug, an offer to sell, purchase, or trade a drug, or the dispensing of a drug under a valid prescription.”

11. A health care organization requested that FDA clarify whether, under this section, its nonprofit affiliates may provide prescription drugs obtained at a nominal cost to patients under a prescription, where the amount charged for the drug varies depending on the patient’s ability to pay.

Section 203.20 does not prohibit a health care entity from obtaining prescription drugs at reduced cost. Rather, it prohibits reselling those drugs except in specified ways. Section 203.22(e) allows the resale of drugs by a health care entity under a valid prescription. The amount of profit derived from such a sale, or the lack thereof, is not addressed by § 203.22(e). Therefore, a health care entity may, subject to other applicable laws, resell prescription drugs to patients under a valid prescription at varying prices.

2. Section 203.22(f)

Proposed § 203.22(f) provided that § 203.20 does not apply to:

The sale, purchase, or trade of a drug or the offer to sell, purchase, or trade a drug by hospitals or health care entities owned or operated by Federal, State, or local governmental units to other hospitals or health care entities owned or operated by Federal, State, or local governmental units.

12. One comment opposed this exclusion. The comment argued that government employees are just as apt to engage in drug diversion activities as are private sector employees. The comment stated that the potential for drug diversion is even greater in the public sector because Federal and State hospitals and health care entities often receive more favorable pricing terms than private hospitals. The comment also stated that the exclusion “appears self serving” and is not supported by the legislative record.

FDA disagrees with this comment. As the agency explained in the preamble to the proposed rule (59 FR 11842 at 11847), any profits from legitimate sales of prescription drugs by government hospitals would accrue to government treasuries. Thus, no financial incentive exists for a government hospital or health care entity, or its representatives acting in an official capacity, to engage in diversion. Given the lack of financial incentive, the amount of profit that could be realized due to the prices at which government hospitals may receive prescription drugs is irrelevant. Moreover, although it is possible that individual employees may steal drugs or obtain them by other criminal methods and sell them, criminal conduct by individual employees was not intended by Congress to be addressed by the sales restrictions. Rather, it was the legal

resale of drugs obtained by hospitals and health care entities, and the potential profit accruing to those entities from such sales, with which Congress was concerned in enacting the sales restrictions.

Finally, the agency disagrees that the exclusion is not supported by the legislative record. As discussed previously and in the proposed rule (59 FR 11842 at 11846 and 11847), the prohibition against sales by hospitals or health care entities was prompted in part because of the temptation for such entities to sell for profit drugs acquired at below wholesale prices. Because no financial incentive exists for government hospitals to profit from sales to other government hospitals, it is unlikely that such sales would result in the kinds of abuses that PDMA sales restrictions were designed to prevent.

In addition, Congress expressly created exclusions permitting, among other things, sales between hospitals or health care entities under common control and emergency sales by hospitals or health care entities to retail pharmacies to allow for the provision of health care to patients. (See H. Rept. 100–76, 13). As discussed in the preamble to the proposal (58 FR 11842 at 11846 and 11847), permitting prescription drug sales between government hospitals and health care entities will help such entities to provide health care services in response to various needs, including the provision of health care to people with low incomes and the distribution of vaccines. Thus, the exception is consistent both with Congress’ general objectives in enacting the sales restrictions and with the rationale supporting other exemptions expressly created by Congress.

3. Sections 203.23 and 203.24

Proposed § 203.23 and 203.24 set forth exemptions to the sales prohibition contained in proposed § 203.20. Proposed § 203.23 provided an exemption for the revocation of a sale and purchase transaction by a hospital, health care entity, or charitable institution because of a mistake in ordering or delivery and the reshipment of the prescription drug to a manufacturer or wholesale distributor for a credit or refund. The section required that the drug be shipped back to the manufacturer or distributor within 10 days and that the reshipment be made under proper conditions for storage, handling, and shipping. In addition, the section required that, if the drug is reshipped to a wholesale distributor, the hospital, health care entity, or charitable institution must provide written notice to the

manufacturer of the revocation and reshipment.

Proposed § 203.24 provided an exemption for the return of a prescription drug purchased by a hospital or health care entity, or acquired at a reduced price by or donated to a charitable institution, to the manufacturer or the wholesale distributor that sold, donated, or supplied the prescription drug. The section required that, if the drug is returned to a wholesale distributor, the hospital, health care entity, charitable institution, or distributor must notify the manufacturer that the drug has been returned. In addition, the hospital, health care entity, or charitable institution must prepare a credit memo for all returns. The returning entity must forward a copy of the memo to the manufacturer and retain a copy for its records. The section also required that returned drugs be kept under proper conditions for storage, handling, and shipping. Finally, the section required that the value of any credit, refund, or exchange not exceed the purchase price or, if a donation, the fair market price of the returned product.

13. One comment said that it generally supported the agency's approach for allowing returns, but questioned the need for § 203.23 and recommended that it be deleted in the final rule. According to the comment, the agency's purpose for calling a return a revocation of acceptance and reshipment was to address concerns that sales provisions in the Uniform Commercial Code (UCC) could make a return a prohibited resale under PDMA. The comment stated that by "expanding on this initial allowance of returned product and proposing § 203.24, FDA has shown that it has overcome UCC concerns and will not view a return as a prohibited resale."

The agency agrees for the most part with the comment. Because proposed §§ 203.23 and 203.24 permit transactions and impose notification and documentation requirements that are similar, and because the situations in which returns would be permitted under § 203.23 would also be permitted by § 203.24, the agency has decided to withdraw proposed § 203.23 and redesignate proposed § 203.24 as new § 203.23 in the final rule. This will simplify the regulation and eliminate potential confusion about whether proposed § 203.23 or § 203.24 applies to a particular return. Under the revised regulation, all prescription drugs returned by a hospital, health care entity, or charitable institution to its supplier will be regarded as "returns" and will be subject to the same

requirements for providing notice to the manufacturer, documenting the return, and maintaining proper storage, handling, and shipping conditions.

On its own initiative, the agency has decided not to include in revised § 203.23 the requirement in proposed § 203.24(a) that a hospital, health care entity, charitable institution, or distributor notify the manufacturer that a prescription drug product has been returned when the return is made to a wholesale distributor. Under revised § 203.23(a) and (b), the hospital, health care entity, or charitable institution is already required to fill out a credit memo documenting the return of a prescription drug and to forward a copy of that memo to the manufacturer. The agency believes that the receipt of the credit memo by the manufacturer should provide sufficient notice to it of the source of a return, and the additional notice that would have been required under proposed § 203.24(a) is not necessary.

14. One comment stated that the concerns addressed by the requirements for notification of the manufacturer and documentation of returns in the proposal is legitimate, but that health care entities should not be "held responsible for helping to police the wholesale drug industry." The comment said that wholesalers should be required to develop mechanisms for documentation and recordkeeping that would achieve the desired goals of the regulation.

The agency believes that the comment misconstrues the purpose of the notice and documentation requirements. As the agency explained in the proposal, the purpose of requiring that a credit memo be forwarded to the manufacturer is to help ensure that any chargebacks or reduced prices will be factored into a credit or refund provided by the manufacturer to prevent windfall profits from the transaction (59 FR 11842 at 11847). There is a potential for such profits to be realized not only by wholesale distributors, but by hospitals, health care entities, and charities. Thus, the agency disagrees that the purpose of providing notice is limited to policing the wholesale drug industry. In addition, the agency believes that the returning hospital, health care entity, or charity is in the best position to provide the information required in the credit memo and, as the party that derives the benefit from any special pricing provided by the manufacturer, should be responsible for ensuring that returns are legitimate.

15. Another comment stated that the resale restrictions were not intended by Congress to cover normal and legitimate

returns of prescription drugs and that FDA is therefore not required or authorized by PDMA to place requirements on returns. The comment said that the provision of notice to a manufacturer when drugs are returned to a wholesale distributor would constitute an unreasonable administrative burden on manufacturers who do not provide a refund or credit in such circumstances.

As discussed in the proposal (59 FR 11842 at 11847), proposed §§ 203.23 and 203.24 were included to address the concern that, subsequent to a completed sale, a return for cash, credit, or other consideration could be viewed as a new and prohibited sales transaction under section 503(c)(3)(A) of the act. Although the agency agrees that Congress did not intend to prohibit legitimate returns of prescription drugs, there is a potential for abuses to occur with returns. The notice and documentation requirements in revised § 203.23(a) and (b) are necessary to help ensure that the returning entity or entities do not profit unfairly by the return and that diversion of returned drugs does not occur. Both of these goals are consistent with Congress' intent in enacting the sales restrictions. (See sec. 2(7), PDMA, H. Rept. 100-76, pp. 12-13.)

16. One comment stated that proposed §§ 203.23 and 203.24 should be clarified so that prescription drugs that are returned to the manufacturer for destruction are exempt from the restrictions in § 203.20, and thus need not adhere to the requirements in proposed §§ 203.23 and 203.24.

The agency declines to provide the clarification sought by the comment. Under § 203.20, the sale, purchase, or trade of a prescription drug purchased by a hospital or health care entity, or donated or supplied at a reduced price to a charitable institution, is prohibited unless the sale, purchase, or trade is exempt from § 203.20 under § 203.22 or revised § 203.23. When a prescription drug that is purchased by a hospital, health care entity, or charity is returned to the manufacturer for destruction and a credit or refund is given for the return, the return constitutes a sale that is prohibited by § 203.20, unless the requirements of § 203.23 are met. Similarly, the agency will consider the provision of destruction services by a manufacturer or distributor at no or reduced cost to the returning entity, relative to the fair market value for such services, to constitute consideration supporting a sale. Thus, returns of prescription drugs for destruction must meet the requirements of § 203.23, unless no credit or refund is given for the return and the returning entity pays

the fair market value for the drugs' destruction.

The conclusion reached above is fully consistent with the policy underlying the requirements in § 203.23. First, drugs that are returned for destruction have the same potential to be diverted as drugs that are returned for redistribution. The threat to the public health from diversion of such drugs could be particularly severe because they are presumably unsuitable for use. Therefore, it is essential that drugs returned for destruction be subject to documentation requirements that provide accountability over the return. Additionally, there may be situations in which a returned drug that is designated for destruction by a hospital, health care entity, or charity may be deemed suitable for sale by the distributor or manufacturer. For example, a drug returned because its outer packaging was damaged may, after examination or testing is conducted by the manufacturer as required by § 205.50(e), prove to be fit for use. Thus, returned drugs must be maintained under proper conditions for storage, handling, and shipping, and written documentation reflecting the maintenance of proper conditions must be provided to help ensure that, if the returned drug is redistributed, it is safe and effective.

17. One comment supported the requirements in proposed §§ 203.23(b) and 203.24(e) (new § 203.23(c)) relating to maintaining proper conditions for storage, handling, and shipping of returned drugs and providing documentation of such conditions. The comment said that wholesalers need the information to carry out their obligations for handling returns under § 205.50(e). The comment recommended that documentation of proper return conditions should be specifically nondelegable.

Section 203.23(c) requires that a drug returned to a manufacturer be stored and handled appropriately, according to its labeled storage requirements, both while it is in the possession of a hospital, health care entity, or charity, and during its return (i.e., during reshipment). Prior to reshipment, only the hospital, health care entity, or charity in physical possession of the drug knows and can document whether the drug has been stored and handled appropriately. However, because a common carrier or other third party may be used to reship the drug, this party may provide documentation that the drug was stored and handled properly during reshipment. Thus, if a returning hospital, health care entity, or charity uses a common carrier or other third party to reship drugs, the third party or

carrier may create the required documentation, and provide the documentation to the manufacturer or distributor on delivery.

The agency clarifies that, regardless of whether a common carrier is used to reship the drug, the returning hospital, health care entity, or charitable institution is responsible for complying with the requirements of § 203.23. Thus, if proper conditions were not maintained during reshipment and/or if written documentation showing that proper conditions were maintained during reshipment was not provided to the manufacturer or wholesale distributor to which the drugs are returned, the requirements of § 203.23 would not be met and the returning hospital, health care entity, or charitable institution would be in violation of § 203.20 of FDA regulations and section 503(c)(3)(A) of the act.

18. Proposed § 203.24(d) required that the value of any credit or refund not exceed the purchase price or fair market price of the returned product. One comment stated that the provision would be burdensome on manufacturers that currently calculate credits or refunds based on the purchase price of the drug as of the date of return. The comment also stated that it would be virtually impossible, without the implementation of a costly, sophisticated system by the manufacturer, to attach a cost to a specific item when it is not known when the item was acquired. The comment recommended that the provision be revised to allow the value of the return to be based on the purchase price of the drug as of the date of the return.

The agency's intent in proposing § 203.24(d) was, as with the notice provisions, to prevent hospitals, health care entities, charities, or distributors from obtaining windfall profits from returns at the expense of manufacturers. Thus, as proposed, the provision would not make manufacturers responsible for ensuring that the amount of a credit, refund, or exchange given for a drug does not exceed the purchase price or, if a donation, the fair market value at the time the donation was made. Instead, the section would make the returning hospital, health care entity, or charitable institution responsible for ensuring that it did not accept a credit, refund, or exchange that exceeds the purchase price or fair market value at the time the drug was purchased or donated. Nevertheless, FDA recognizes that in order to comply with this provision, manufacturers would have to maintain records of the price paid for a drug at the time it was purchased.

Because maintaining such records does not appear to constitute customary industry practice and would impose additional costs and burdens on manufacturers, the agency has revised § 203.23 in the final rule to eliminate the requirement that the value of any credit or refund not exceed the purchase price or fair market price of the returned product.

E. Samples

1. Sample Distribution by Mail or Common Carrier

Proposed § 203.30(a)(2) required that the recipient of a drug sample distributed by mail or common carrier execute "a written receipt, as set forth in paragraph (c) of this section, when the drug sample is delivered." Proposed § 203.30(c) set forth the required contents of the receipt for samples distributed to licensed practitioners, and to designated pharmacies of health care entities. Proposed § 203.30(c) provided:

* * * The receipt is to be on a form designated by the manufacturer or distributor, and is required to contain the following:

(1) If the drug sample is delivered to the licensed practitioner who requested it, the receipt is required to contain the name, address, professional title, and signature of the practitioner or the practitioner's designee who acknowledges delivery of the drug sample; the proprietary or established name and strength of the drug sample, the quantity, and the lot or control number of the drug sample delivered; and the date of the delivery.

(2) If the drug sample is delivered to the pharmacy of a hospital or other health care entity at the request of a licensed practitioner, the receipt is required to contain the name and address of the requesting licensed practitioner, the name and address of the hospital or health care entity pharmacy designated to receive the drug sample; the name, address, professional title, and signature of the person acknowledging delivery of the drug sample; the proprietary or established name and strength of the drug sample, the quantity, and the lot or control number of the drug sample delivered; and the date of the delivery.

19. Several comments stated that not all of the information required to appear on the sample receipt form under proposed § 203.30(c) is necessary to confirm delivery of a sample. One comment stated that the act only requires information sufficient to verify that the sample received matches the sample requested and sent. Another comment asserted that FDA does not have the authority under PDMA to specify the content of the receipt, and that the only information required by PDMA is the signature of the licensed practitioner and any information

necessary to determine the identity of the sample and the recipients.

The agency has determined that, with the exception of the proposed requirement for the lot or control number of the sample (discussed below in conjunction with comments on §§ 203.30 and 203.31), the information requirements in proposed § 203.30(c) are necessary to ensure that samples that are requested are received by the intended recipient and that patterns of nondelivery of drug samples can be identified. Both of these objectives are consistent with legislative intent. (See H. Rept. 100-76 at 15.) The agency therefore declines to eliminate or modify these requirements in the final rule.

The information required under proposed § 203.30(c) mirrors most of the information required to appear on the sample request form under proposed § 203.30(b). This information is the minimum information necessary to identify the type and quantity of drug samples being requested and distributed, the requesting practitioner, and, if applicable, the designated hospital or health care entity to which the drug samples are to be delivered. The only information required by proposed § 203.30 to appear on drug sample receipt forms that is not required to appear on request forms is the name, address, professional title, and signature of the person acknowledging delivery of the drug sample. This information is necessary to establish accountability for receipt of drug samples when samples are delivered to a practitioner's office and the requesting practitioner does not physically receive the drug sample and sign the sample receipt or when samples are delivered to a hospital or health care entity at the request of a practitioner.

20. Several comments objected to the required information because electronic delivery verification systems currently used by delivery services and common carriers cannot accommodate the information. According to the comments, current electronic delivery verification systems are capable of recording some, but not all, of the required information. The comments stated that to capture all of the required information, a manufacturer or authorized distributor of record would have to use a paper system independent of common carriers' delivery verification, such as a business reply mail card. Several comments said that paper systems involve more administrative costs and would result in less compliance by practitioners than electronic delivery verification. One comment stated that, using business reply mail cards, it would take two to

three followup letters to achieve compliance within the 90 to 95 percent range. Another comment said that data may be accessed faster and easier with electronic verification systems than with business reply mail cards, since the data are stored electronically rather than manually. Several comments recommended revising the proposed rule to bring it into conformity with the specific electronic delivery verification system used by the commenter. Other comments recommended that the proposed rule be revised to state that receipts used by common carriers as part of their normal course of business are sufficient.

The agency recognizes that manufacturers and authorized distributors of record may not be able to comply fully with the sample receipt content requirements in proposed § 203.30(c) using commercial carriers' electronic delivery acknowledgment systems. Electronic delivery acknowledgment systems do not appear to be designed to meet the specific informational requirements for sample receipts under § 203.30(c) at the present time. Thus, the use of business reply mail cards or other types of paper systems capable of recording the required information may be necessary. These systems may not be as convenient for health care practitioners receiving samples to use as electronic delivery acknowledgment systems and will probably be more expensive for manufacturers and authorized distributors of record. However, these disadvantages are not in themselves sufficient reason to eliminate the informational requirements in proposed § 203.30(c), where no satisfactory alternatives exist to ensure that congressional objectives for establishing controls on sample distribution are met.

21. Two comments requested that FDA permit the use of combinations of electronic and paper media to create the required receipt form. Under the scenario presented by one of the comments, a receipt would be signed by the practitioner or his designee at the time of delivery, but it would not contain all of the required information. The information not contained on the receipt would be maintained on a separate electronic data base, which would be linked via a "unique number" to the receipt. The other comment requested that the agency permit a signature obtained through a carrier's normal delivery verification to be "added" later to an electronic record containing all of the required information.

As discussed previously, the agency has revised proposed § 203.60 to permit

manufacturers and authorized distributors of record to create and maintain drug sample receipts and other records using combinations of paper-based and electronic media. Under § 203.60(a)(2), combinations of paper records and electronic records may be used provided: (1) The requirements of part 11 are met for the electronic record, and (2) a reasonably secure link between the paper record and electronic record exists to ensure that the combined records are trustworthy and reliable and to ensure that the signer cannot readily repudiate the signed record as not genuine. Neither of the scenarios presented by the comments would ensure that a reasonably secure link exists between the paper-based and electronic records because the individual signing the receipt at the time of the sample delivery would not know the contents of the receipt and thus could not attest that the contents of the receipt are correct. Moreover, under these circumstances, the signer could readily repudiate the signed record as not genuine. Thus, neither of the scenarios would meet the requirements of § 203.60(a)(2).

22. One comment requested clarification of whether the proposed rule would supplant the March 2, 1993, guidance letter recommendations on delivery confirmation of drug samples by common carriers.

Any policy stated in that document, including the policy on delivery verification, is superseded by the policies set forth in the final regulation.

2. Sample Distribution by a Representative or Detailer

a. *Section 203.31(a)(1) and (a)(2)*. Proposed § 203.31(a)(1) required that before a manufacturer or authorized distributor of record distributes a drug sample to a licensed practitioner, it must receive a signed, written request form from the licensed practitioner. Proposed § 203.31(a)(2) required that the recipient sign a receipt form containing the information required under proposed § 203.31(c) when the drug sample is delivered. Proposed § 203.31(a)(3) required that the receipt be returned to the manufacturer or distributor.

23. One comment requested that the proposed rule be revised to clarify that a single form may be used to satisfy the requirements of a request and receipt form.

FDA set forth its policy on the use of one form to satisfy the request and receipt form requirements for samples delivered by a representative in the preamble to the proposed rule (58 FR 11842 at 11849). The agency stated:

A sample request and receipt need not be on separate forms if delivery is by a representative. A single form could be devised and used containing all of the required information, which could be fully completed and executed with a single signature, if the request and delivery are simultaneous, or executed in part with a signature for the request at the time of the request, and executed in part with a second signature acknowledging receipt at the time of the delivery.

The agency wishes to emphasize that, whether one form or separate forms are used, only a licensed practitioner may request a sample and sign the request form. A sample receipt, however, may be signed either by a licensed practitioner or that practitioner's designee.

24. FDA received four comments that objected to any requirement for a receipt for representative-delivered samples. The comments stated that receipts for representative-delivered samples were not required by PDMA and that this requirement goes beyond the scope of the act. Two comments stated that most requests and deliveries take place on the same representative visit. One comment recommended that the rule be revised to cover only those situations where request and delivery of samples do not occur on the same visit. Another comment said that Congress required receipts for samples delivered by mail or common carrier, but not representatives because there are more opportunities for samples to be lost or diverted when the mail is used. The comment recommended that the manufacturer could use the information on the request form to do its own followups with licensed practitioners to see whether samples had been delivered.

Although Congress did not expressly require a receipt for representative-delivered samples in the act, FDA has concluded that additional requirements, including receipts, are necessary to help ensure effective enforcement, increased accountability and oversight of sample distribution, and to provide adequate safeguards against drug sample diversion. All of these goals are consistent with and further the legislative intent in enacting PDMA. Although samples delivered by a representative to a licensed practitioner may be requested and delivered simultaneously, this is not always the case. For example, the delivery of samples by a representative to a hospital or health care entity pharmacy designated by a physician may not occur at the same time a request for such samples is made. When the request for and delivery of a sample by a representative do not occur

simultaneously, the potential for sample diversion and corresponding need for a sample receipt are as great as when samples are delivered by mail or common carrier. When the request for and delivery of a sample do occur simultaneously, the sample request and receipt form may be merged into one form with a single signature (see discussion above).

25. FDA received four comments related to the medium on which the required information for representative-delivered sample receipts may appear. Two comments assumed that proposed § 203.31(a)(2) and (c) required receipts to be in paper form and objected to that requirement. Two comments asked for clarification on whether receipts do, in fact, have to be in paper form or may be electronically created. All four comments assumed that the proposed regulations required that a paper receipt be left with the licensed practitioner even when receipts are electronically created, and objected to this requirement. One comment stated that neither PDMA guidelines nor the proposed regulations require licensed practitioners to keep records of drug samples received, thus a written receipt would serve no purpose.

It appears that the confusion over whether receipts must be written on paper came from the preamble discussion of proposed § 203.31 (59 FR 11842 at 11849). FDA stated that "the agency has tentatively concluded that the requirement for a written receipt should extend to all drug sample deliveries, and that requirement is included in proposed §§ 203.30 and 203.31." Moreover, the word "written" does appear in conjunction with receipts in § 203.30, but not in § 203.31. As discussed in section II.J of this document, request and receipt forms, reports, records, and other documents and signatures required by PDMA and part 203 may be created on paper or on electronic media, provided that records created on electronic media meet the requirements of revised § 203.60 and part 11. In addition, although the final regulations require that a receipt be signed and returned to the manufacturer when a sample is received, they do not require that a receipt be left with the practitioner for his or her records or that practitioners maintain records of samples received.

b. *Section 203.31(c)(2)*. Proposed § 203.31(c)(2) stated that if the drug sample is received by the pharmacy of a hospital or other health care entity at the request of a licensed practitioner, the receipt is required to contain, among other things, the name and address of the hospital or health care entity

pharmacy designated to receive the drug sample.

26. One comment objected to the requirement that the name and address of the hospital or health care entity pharmacy designated to receive the drug sample appear on the receipt. The comment stated that this information is known by the requesting licensed practitioner.

The purpose of the receipt requirement is not to provide information to the licensed practitioner that requests the drug sample, but to provide manufacturers and authorized distributors with documentation that samples that were requested were in fact properly delivered. When a licensed practitioner requests that a drug sample be delivered to a hospital or health care entity pharmacy, it is necessary for the name of the hospital or health care entity pharmacy to appear on the sample receipt so that the person receiving the sample at the pharmacy can verify, through his or her signature on the sample receipt, that the sample was delivered as requested.

c. *Section 203.31(d)(1) and (d)(2)*. Proposed § 203.31(d) required that drug manufacturers and authorized distributors of record conduct an inventory, using generally accepted inventory practices, of drug samples in the possession or control of each of their representatives. The inventory must be conducted at least annually, and the results of the inventory are required to be recorded in an inventory record and reconciliation report. The contents of the inventory record and reconciliation report were set forth in proposed § 203.31(d)(1) and (d)(2). Proposed § 203.31(d)(1) required the identification of each drug sample in a representative's stock by the proprietary or established name and dosage strength, and the number of sample units. Proposed § 203.31(d)(2) required:

- (i) A report of the physical count of the most recently completed prior inventory;
- (ii) A record of each drug sample shipment received since the most recently completed prior inventory, including the sender and date of the shipment, and the proprietary or established name, dosage strength, and number of sample units received;
- (iii) A record of drug sample distributions since the most recently completed inventory showing the name and address of each recipient of each sample unit shipped, the date of the shipment, and the proprietary or established name, dosage strength, lot or control number, and number of sample units shipped; and

(iv) An explanation for any significant loss. As discussed in section II.E of this document, the agency has on its own initiative revised proposed § 203.31(d) to more clearly distinguish between the

inventory and reconciliation functions and to clarify certain required elements of the reconciliation report.

27. Two comments requested clarification of the meaning of the phrase "generally accepted inventory practices." Both comments cited the statement in the preamble of the proposed rule (59 FR 11842 at 11849) that "it is FDA's preliminary view that such an inventory must go beyond a mere physical count, and that meaningful information and data can only be provided if the inventory is conducted utilizing generally accepted inventory practices * * *." The comments said that if generally accepted inventory practice refers to more than a physical count, FDA must clarify what is required.

As discussed in section II.E of this document, the final rule has been revised to eliminate the use of the phrase "generally accepted inventory practices" in conjunction with the inventory requirement.

28. Several comments objected to the requirements in proposed § 203.31(d)(2)(ii) and (d)(2)(iii) because the required information duplicates information contained in sample request forms and corporate distribution records that are already on file. Two comments stated that the reconciliation report should contain a reconciliation of opening and closing inventories against sample allocations received and sample distributions, but not a statement of all individual allocations and distributions. Another comment questioned whether the inclusion of the information required under these sections in a single report is productive or merely an additional clerical burden.

The first comment correctly points out that the information required to be contained in the reconciliation report under revised § 203.31(d)(2)(ii) and (d)(2)(iii) will come from various sources, including drug sample request and receipt forms, distribution records required to be created and maintained under the current good manufacturing practice (CGMP) regulations (see, e.g., 21 CFR 211.196), and other records maintained by the representative or the firm. Nevertheless, the agency believes that the assimilation of information from these multiple records into a single report that concisely identifies and characterizes each type of transaction conducted with drug samples will aid industry in detecting discrepancies in inventory that may be indicative of drug sample diversion activity. In addition, it will permit FDA and other Federal and State government agencies responsible for enforcing PDMA to effectively oversee a company's conduct in

performing its reconciliation and in initiating investigations of potential drug sample record falsifications and significant losses and thefts of drug samples under § 203.37.

29. One comment sought clarification on whether the reconciliation report may consist of several documents that, when taken together, contain all required information.

The reconciliation report for an individual sales representative may consist of several paper documents and/or electronic records. However, all documents or records are to be collected and maintained as a single reconciliation "report."

30. Another comment stated that "PDMA does not require manufacturers to annually compile a report for each sales representative that summarizes in one place all aspects of each sample delivery in minute detail."

Although PDMA does not explicitly require the information under § 203.31(d)(2), it does establish an extensive scheme for monitoring drug sample distributions by a representative that includes requirements for drug sample request forms, an annual inventory, and reporting of significant losses and known thefts of drug samples. As discussed previously, the agency believes that the requirements contained in § 203.31(d)(2)(ii) and (d)(2)(iii), including the requirement for identifying individual transactions conducted with drug samples in revised § 203.31(d)(2)(iii), are necessary to bring potential drug sample diversion activities to the attention of manufacturers and authorized distributors. This objective is consistent with legislative intent in PDMA.

31. Two comments recommended that manufacturers should be permitted to use bar coding that represents the proprietary or established name and dosage strength on the inventory record and reconciliation report instead of actual words. One of the comments said that such coding is "easily translated" into the required information.

The agency advises that it does not object to the use of bar coding that represents required information in the inventory record or reconciliation report provided that the information in such a form can be used by the firm to conduct the reconciliation process and to detect discrepancies in inventory and potential drug diversion. In addition, the bar coding must be capable of being translated into words and the record or report must be capable of being produced in its entirety upon request by FDA or other Federal, State, or local law enforcement authorities.

32. Two comments objected to the requirement in proposed § 203.31(d)(2)(iii) to list the lot or control number in the reconciliation report. One of these comments stated that this requirement would not assist in diversion detection because the batches are so large that significant numbers of representatives in varying geographical areas will receive the same batch. The comment also stated that "existing PDMA records" make it possible to determine every physician called on by representatives who could have received the lot in question. The other comment stated that the requirement would "have little or no effect in assuring a meaningful inventory," but would increase difficulty of conducting inventory and preparing the report.

The requirement in proposed § 203.31(d)(2)(iii) was intended to ensure that a manufacturer or authorized distributor maintains a record enabling it to track the distribution of sample units by lot or control number from a representative to a licensed practitioner. Although the agency agrees that such information would not necessarily enable manufacturers or distributors to pinpoint the representative responsible for distributing a sample unit that has been diverted, it would promote precision in tracking samples and facilitate the location of samples in the event of a recall or other public health emergency. Nevertheless, as discussed below, the agency has determined that manufacturers and authorized distributors of record should be free to choose the types of records used to track the distribution of drug sample lots to licensed practitioners. Therefore, the proposed requirement for inclusion of lot or control numbers in the reconciliation report has been eliminated in the final rule.

d. *Section 203.31(d)(3)*. Proposed § 203.31(d)(3) stated: "The inventory and reconciliation reports shall be conducted and prepared by persons other than the representatives being inventoried or superiors or managers in their department, division, or branch, or in their direct line of supervision or command."

33. Three comments stated that the proposed requirement represents a misinterpretation of PDMA and its legislative history regarding section 303(b)(4)(B)(ii) of the act. The comments stated that this section allows a manufacturer the option of performing an independent audit to protect itself from civil liability for the acts of its representatives, but that FDA has misconstrued the section to mean that

PDMA requires a yearly, independent audit of every representative.

The comments apparently misunderstand the terms "inventory" and "audit." An inventory is an itemized list or catalog of goods or property, usually taken annually. An audit is a formal, periodic examination and checking of accounts or records to verify their correctness. (*Webster's New World Dictionary*, 2d College Ed.) The comments correctly assert that section 303(b)(4)(B)(ii) of the act does not require an annual audit of all representatives. However, proposed § 203.31(d)(3) did not establish an audit requirement, but rather set forth requirements concerning which personnel are to conduct the inventory and reconciliation and prepare the inventory record and reconciliation report. The proposed requirement was therefore intended to implement the requirement in section 503(d)(3)(C) of the act for an annual inventory of drug samples in the possession of a representative, rather than section 303(b)(4)(B)(ii) of the act.

34. Several comments said that the proposed requirement is too costly, and the ends can be achieved through more cost-effective means. Several comments stated that since inventory must be completed onsite, it would be too costly to require personnel other than supervisors or managers within the geographic area of the representative to perform it. On the other hand, the comments said, reconciliation can be performed at a central location, thus it is more susceptible to completion by independent personnel.

Two comments distinguished inventory from reconciliation by stating that the former is relatively simple and can be performed by sales management, while the latter is more complex and should be done by a person independent of sales and marketing. In contrast, another comment recommended allowing representatives to perform the reconciliation, but not the inventory function.

One comment recommended allowing anyone but the representative to perform the inventory or prepare the reconciliation report. Several comments recommended allowing a sales representative's direct supervisor or manager to perform the inventory function because that person is in the best position to assess the performance and cooperation of a representative and to initiate corrective actions. One comment recommended allowing anyone other than a representative or his direct supervisor to perform the inventory. Other comments recommended allowing a

representative's district manager to perform the inventory function.

The objective of the proposed requirement was to guard against errors and possible fraud in the conduct of the physical inventory and reconciliation, and in the preparation of the inventory record and reconciliation report, by the representative or other interested parties. Although the agency continues to believe that this is a legitimate and important objective, the agency agrees that it can be achieved through less burdensome means than by requiring the inventory and reconciliation to be conducted by persons other than the representatives, their superiors or managers, or others in their direct line of supervision or command. Accordingly, the agency has revised the proposed requirement to permit manufacturers and distributors to take "appropriate internal control measures" to guard against error and possible fraud in the conduct of the physical inventory and reconciliation, and in the preparation of the inventory record and reconciliation report.

Under the revised requirement, representatives and their supervisory personnel may conduct the inventory and reconciliation functions and prepare inventory records and reconciliation reports. However, the agency expects that appropriate internal control measures will be taken that include implementation of a security and audit system that is controlled by independent personnel, i.e., personnel other than the representatives, their superiors or managers, or others in their direct line of supervision or command. Under revised § 203.34(b), such a security and audit system must follow a plan that ensures that random audits are conducted on representatives by personnel independent of the sales force. In addition, the plan must ensure that for-cause audits are initiated in response to reports, incidents, or findings identified by the firm as indicating possible drug sample diversion or falsification of sample distribution records. If necessary, the agency will issue additional guidance on audit plans and procedures under revised § 203.34(b).

e. *Section 203.31(d)(4)*. Proposed § 203.31(d)(4) stated: "A manufacturer or authorized distributor of record shall carefully evaluate any apparent discrepancy or significant loss in its inventory and reconciliation, and shall fully investigate any such discrepancy or significant loss that cannot be justified."

35. Two comments stated that the word "apparent" should be changed to "significant". One comment stated that

since manufacturers are permitted, under § 203.37, to determine what constitutes a "significant loss," they should also be allowed to determine which discrepancies merit investigation. Another comment recommended revising "apparent discrepancy" to read "potentially significant discrepancy."

The agency is not requiring manufacturers and distributors to conduct an investigation every time there is an apparent discrepancy in a representative's inventory, but rather that they evaluate all apparent discrepancies. It is only when an apparent discrepancy cannot be justified that an investigation is required. Investigations under these circumstances are reasonable and consistent with the requirement in revised § 203.37(a) to investigate when there is a reason to believe that any person has falsified drug sample records or is diverting drug samples. Accordingly, the agency declines to amend the requirement.

3. Issues Related to Sample Distribution by Mail or Common Carrier or by a Representative or Detailer

a. *Sections 203.30(a)(1) and 203.31(a)(1)*. Proposed §§ 203.30(a)(1) and 203.31(a)(1) required that a licensed practitioner execute and submit a written request to the manufacturer or authorized distributor of record to obtain drug samples.

36. One comment stated that a request form "creates additional paperwork and expense without apparent benefit beyond that obtained by signing a receipt form at the time of delivery of the samples."

In sections 503(d)(2)(A)(i) and (d)(3)(A)(i) of the act, Congress specifically required that a drug sample be distributed only in response to a written request by a licensed practitioner to ensure accountability in the sample distribution process. Sections 203.30 and 203.31 reflect those statutory provisions.

37. Another comment sought clarification on whether the term "written request" includes preprinted forms.

Preprinted drug sample request forms are permissible. However, they must contain all information required by PDMA and the final regulations, and must be signed by a licensed practitioner.

b. *Sections 203.30(a)(3) and 203.31(a)(3)*. Proposed § 203.30(a)(3) required that the recipient of a drug sample delivered by mail or common carrier return the receipt to the manufacturer or distributor from which the drug sample was received. Proposed

§ 203.31(a)(3) required that the receipt for samples distributed by means other than mail or common carrier be returned to the manufacturer or distributor.

38. Two comments requested clarification on whether, if a licensed practitioner fails to return a receipt, he or she is barred from receiving further samples from a manufacturer. Both comments argued that the intent of Congress in enacting PDMA was to detect patterns of nonreturns of receipts. The comments recommended that licensed practitioners should not be barred for isolated failures to return receipts, but rather, where a pattern of nonreturns exists, manufacturers should be required to investigate to see if the samples actually arrived.

The question of whether a licensed practitioner should be barred from receiving further drug samples for failing to return drug sample receipts was not addressed in the proposed rule, and was not addressed directly by Congress. In the legislative history of PDMA (see H. Rept. 100-76, p. 15), Congress stated: "Whether the distributions are made by carrier return receipt or business reply cards, manufacturers or distributors would not be expected to equate each and every delivery and receipt; however, an adequate monitoring system would necessarily need to detect instances where non-return patterns exist." Thus, there is evidence that Congress was not primarily concerned with isolated failures to return drug sample receipts, but with patterns of nonreturns. Moreover, the overall structure of PDMA is not intended to penalize practitioners or prevent them from receiving samples, but rather to ensure that samples are properly distributed to licensed practitioners. Therefore, the agency believes that Congress did not intend for licensed practitioners to be barred from receiving samples for isolated failures to return sample receipts or for isolated instances where receipts are not received for reasons beyond the practitioner's control. However, upon detecting a pattern of nonreturns by a practitioner, a manufacturer or authorized distributor should not distribute further samples until the matter is thoroughly investigated. Such an investigation may, depending on the circumstances, be required under § 203.37, since a pattern of nonreturns may indicate that a representative is falsifying drug sample requests, that other drug diversion activity is occurring, or that a significant loss or theft of drug samples has occurred.

c. *Sections 203.30(b)(1)(ii) and 203.31(b)(1)(ii)*. Proposed § 203.30(b)(1) and (b)(1)(ii) stated: "A written request for a drug sample to be delivered by mail or common carrier to a licensed practitioner is required to contain the following: * * * The practitioner's State license number or Drug Enforcement Administration identification number." Proposed § 203.31(b)(1) and (b)(1)(ii) set out the same requirement for requests for drug samples delivered by means other than mail or common carrier.

39. FDA received 15 comments on these requirements. Many of the comments supported the overall goal of these sections, i.e., to ensure that persons requesting drug samples are licensed practitioners. However, several comments stated that State license numbers are not always assigned to practitioners who are otherwise authorized by State law to prescribe drugs. The comments requested clarification as to what verification is appropriate for practitioners subject to different authorization mechanisms than physicians.

As was discussed in response to the comments on the definition of licensed practitioner, the agency has determined that practitioners authorized by State law to prescribe drugs may request and receive drug samples. Practitioners who are authorized by a State to prescribe drugs and have no State license number may use any number assigned to them by the State that represents that they are authorized to prescribe drugs. The agency is not aware of any State that does not assign some type of number to practitioners that it authorizes to prescribe drugs. However, if such a case arises, the agency will consider how to provide verification at that time.

40. Several comments cited potential problems with the use of DEA numbers for verification. Several comments said that not all licensed practitioners, but only those who prescribe controlled substances, are issued Drug Enforcement Administration (DEA) numbers. Other comments stated that, although DEA numbers can be accessed through a central data base, this practice is discouraged by DEA unless a controlled substance is involved. One comment stated that DEA numbers are often improperly accessed and illegally used to divert drugs and recommended that only State license numbers be used.

The agency has consulted with the DEA on the appropriate use of DEA numbers for identification purposes. DEA policy is that registration numbers assigned by DEA to licensed practitioners are to be used only to obtain scheduled drug products, not for

general identification purposes. Accordingly, the agency has modified the requirement in the final rule to specify that State license or authorization numbers are to be used on sample request forms generally, and DEA numbers are to be used only when a sample of a scheduled drug product is requested.

41. Several comments asked for clarification on whether a manufacturer or authorized distributor would be required under this section to verify the State licensing or DEA number on the request form. One comment stated that the provision of a State license or DEA number, without verification, would not confirm that a practitioner is in fact licensed. Other comments opposed a requirement that the manufacturer or authorized distributor verify the State licensing or DEA number. One comment recommended that the presence of the number on a sample request form be deemed acceptable on its face. Two comments recommended that instead of requiring the manufacturer to verify whether the requesting person is a licensed practitioner, the person requesting samples could be required to attest to being a licensed practitioner on the sample request form, i.e., with the inclusion of a preprinted line next to where his or her signature would go. Three comments recommended that an internal number established by the manufacturer after checking a requesting practitioner's credentials be considered acceptable.

FDA has determined that verification by a manufacturer or authorized distributor of the State license or authorization number, or the DEA number as appropriate, is necessary and has codified the requirement in §§ 203.30(a)(2) and 203.31(a)(2) of the final rule. The agency does not believe that allowing a manufacturer to deem acceptable the number on a request form without verifying its authenticity would offer any assurance that a person requesting samples is in fact licensed or authorized to prescribe drugs. Similarly, an attesting signature on a request form offers little more assurance that a person is in fact licensed or authorized than an unverified license or authorization number. The agency does believe there is merit in the suggestion that, once a practitioner's number is verified by a manufacturer or distributor with a State licensing board or the DEA, an internal number or other tracking system may be devised such that the number does not have to be reverified every time a sample is requested by the same practitioner. However, any list of verified State license or authorization numbers maintained by an authorized

distributor or manufacturer must be updated at least annually to reflect changes in license or DEA status.

42. Several comments stated that it would be difficult for manufacturers to verify State license numbers because there is no national data base that contains all State licensing numbers, State licensing boards do not possess mechanisms to provide wide-scale verification services, and methods of verification vary from State to State.

As discussed in section IV.B of this document, the agency believes that cost-efficient systems for verifying State licensing numbers will be made available to manufacturers and authorized distributors of record in the near future. Until that time, State licensing boards do possess sufficient mechanisms to provide verification that individuals are licensed by them. The agency recognizes that there may be some difficulty associated with verifying State license or authorization numbers. However, State licensing numbers are the only reliable way of proving that a practitioner is actually licensed by a State to prescribe drugs.

43. One comment recommended that FDA require States to adopt uniform methods of assigning licensing numbers.

The power to set prescribing requirements and methods is one that has traditionally been vested in the States. The agency does not wish to interfere with this power by requiring that States adopt uniform methods of assigning State licensing numbers.

44. Several comments recommended that FDA add the American Medical Association's Medical Education (ME) number to the list of permissible verification numbers. The comments stated that the advantages of this number are that it is centrally accessible, it is not subject to change as State license numbers may be, and it includes at least some nonphysician practitioners. Two comments also recommended that use of the Association of Physician's Assistants file number be permissible.

The agency has concluded that where a practitioner has a State license number, that number must be used for verification purposes. As discussed above, nonphysician practitioners who are licensed, or who are not licensed but are authorized by State law to prescribe drugs, may use any number assigned to them by the State that represents that they are authorized to prescribe drugs. The agency does not believe that other types of identification, including numbers assigned to health professionals in connection with membership in professional associations, are reliable means of

proving that a practitioner is licensed or authorized to prescribe drugs.

d. *Sections 203.30(b)(1)(iii) and 203.31(b)(1)(iii)*. Proposed §§ 203.30(b)(1)(iii) and 203.31(b)(1)(iii) required that the proprietary or established name and strength of the drug sample requested appear on the sample request form.

45. Two comments requested that the proposed sections be revised to allow bar coding on the request form that represents the name and strength of the drug sample. Both comments indicated that the bar coding would be translated into words on the form so that the doctor would know what he or she was requesting.

The agency has no objections to allowing bar coding representing information on preprinted sample request forms where that information is also translated into words on the form. However, the bar coding must not cover up or otherwise detract from the ability of practitioners to read the words on the form.

e. *Sections 203.30(b)(1)(v) and 203.31(b)(1)(v)*. Proposed §§ 203.30(b)(1) and 203.31(b)(1) set forth the requirements for contents of written request forms for delivery of samples by mail or common carrier and by representative, respectively. Proposed §§ 203.30(b)(1)(v) and 203.31(b)(1)(v), which are identical, required that the request form contain "the name of the manufacturer and the authorized distributor of record, if the drug sample is requested from an authorized distributor of record."

46. FDA received four comments on these sections. One comment objected to the requirement in § 203.31(b)(1)(v) that the names both of the manufacturer and of the distributor be included on the request form. The comment stated that this requirement is redundant since the manufacturer and authorized distributor of record are responsible for knowing each other, and if a diverted sample is found, the manufacturer will be able to trace the sample to the authorized distributor. Three comments objected to the requirement in both §§ 203.30(b)(1)(v) and 203.31(b)(1)(v). These comments stated that requiring the names both of the manufacturer and of the authorized distributor of record causes additional recordkeeping burdens, serves no useful purpose, and is contrary to the explicit language of section 503(d)(3)(A) of the act.

A distributor may distribute drug samples under section 503 of the act only if it is an authorized distributor of record for the manufacturer of the drug. Thus, the ability of a distributor to distribute samples is directly related to

its relationship with the manufacturer. The agency believes that it is reasonable to require that a sample request form for an authorized distributor of record include the name of the manufacturer that authorizes the distributor to distribute samples. The requirement will help ensure that the parties involved in and responsible for sample distribution can be readily identified by FDA and other government agencies. This purpose is consistent with legislative intent to ensure that distributors of drug samples are authorized distributors of record, and the agency therefore adopts the requirement in the final rule.

f. *Sections 203.30(c)(1) and (c)(2) and 203.31(c)(1) and (c)(2)*. Proposed §§ 203.30(c) and 203.31(c) set forth the requirement that drug sample receipts contain, among other things, the lot or control number of the drug sample delivered.

47. FDA received several comments that objected to the sample lot or control number requirements and recommended that they be eliminated. Two of these comments objected to the requirement for representative delivered samples only, while the remaining comments objected to the requirement for both samples delivered by mail or common carrier and by representative. Several comments argued that, under existing CGMP requirements, the requirement is not necessary because distribution of sample lots is tracked by the manufacturer to the representative, who keeps a record of the practitioners visited and the samples that are distributed. Two comments stated that recording lot numbers on sample receipts is an inefficient way of tracking sample lots to the practitioner level, and that the method of tracking should be left to manufacturers as long as they can provide accurate and timely lot specific records. Other comments argued that lots should only have to be tracked down to the representative level.

The agency believes that the tracking of sample distributions by lot to the level of the licensed practitioner is essential both to maintaining accountability and oversight over sample distribution and to facilitating recalls and, therefore, declines to eliminate the proposed requirements on the ground that samples need only be tracked to the representative level. The agency agrees, however, that recording lot numbers on drug sample receipts and other drug sample distribution records required under part 203 may not be the most efficient method of tracking sample lots and that manufacturers and authorized distributors should be free to use other types of records to accomplish

this purpose. Accordingly, the agency has eliminated the requirement to include lot or control numbers on drug sample receipts in revised §§ 203.30(c)(1) and (c)(2) and 203.31(c)(1) and (c)(2) and on reconciliation reports in revised § 203.31(d)(2)(iii). Moreover, the requirement under proposed § 203.38(b) to include lot or control numbers on all drug sample distribution records has been substantially revised. Under revised § 203.38(b), manufacturers and authorized distributors of record are required to maintain drug sample distribution records containing lot or control numbers that are sufficient to permit tracking of drug sample units to the point of the licensed practitioner. Sample distribution records containing lot or control numbers must be maintained by manufacturers or authorized distributors whether the samples are distributed by the mail or through representatives.

4. Drug Sample Forms

Proposed § 203.33 stated:

A sample request or receipt form may be delivered by mail, common carrier, or private courier or may be transmitted photographically or electronically (i.e., by telephoto, wirephoto, radiophoto, facsimile transmission (FAX), xerography, or electronic data transfer) or by any other system, provided that the method for transmission meets the security requirements set forth in § 203.60(d).

Due to the publication of part 11, which supersedes portions of proposed § 203.60, the security requirements that apply to paper documents transmitted photographically, electronically, or by any other system have been modified and appear under § 203.60(c) in the final rule. Section 203.33 has been revised to refer to this section.

5. Policies and Procedures

Proposed § 203.34 stated:

Each manufacturer or authorized distributor of record that distributes drug samples shall establish, maintain, and adhere to written policies and procedures describing its administrative systems for the following:

- (a) Distributing drug samples by mail or common carrier, including methodology for reconciliation of requests and receipts;
- (b) Distributing drug samples by means other than mail or common carrier including the methodology for their independent sample distribution security and audit system;
- (c) Conducting its inventory of drug samples under § 203.31(d), including an inventory schedule;
- (d) Auditing and detecting falsified or incomplete drug sample records;
- (e) Identifying any significant loss of drug samples and notifying FDA of the loss;
- (f) Monitoring any loss or theft of drug samples; and

(g) Storing drug samples by representatives.

As discussed in section II.G of this document, the requirements in proposed § 203.34 have been renumbered and revised in the final rule. Comments on the proposal are addressed in light of the revisions.

48. One comment stated that PDMA only requires manufacturers to develop adequate audit and security systems to detect and investigate losses and thefts, not to create and adhere to extensive written policies documenting all aspects of the drug sampling process. The comment stated that a manufacturer should not be subject to liability for failing to have a written corporate-wide policy on the subject matter covered by the proposed rule.

The agency believes that the creation of internal policies by a manufacturer or authorized distributor of record to achieve the statutory objectives is important to the attainment of those objectives. PDMA sets forth requirements that manufacturers and authorized distributors of record report significant losses and thefts of samples, that manufacturers' and authorized distributors' representatives be inventoried at least annually, and that drug samples be subject to proper storage conditions. In addition, PDMA's legislative history indicates that Congress intended that manufacturers and authorized distributors have audit and security systems in place to detect losses and thefts, as well as falsified or incomplete drug sample records. (H. Rept. 100-76, p. 20, S. Rept. 100-202, p. 9.) Accordingly, the agency believes that it is authorized to implement specific requirements regarding procedures and systems to accomplish these legislative objectives. However, the agency believes that industry should have the flexibility to develop its own procedures and systems, as long as such procedures and systems are documented and followed.

49. One comment stated that, under PDMA, a manufacturer is already liable for failing to identify and report losses, thefts, or falsification of records, whether it has written policies or not. Thus, according to the comment, written procedures are not necessary to ensure that significant losses of samples are detected.

Section 301(t) of the act subjects manufacturers and authorized distributors to civil and criminal penalties for failure to report significant losses and thefts as required under section 503(d)(3)(D) of the act. While the agency recognizes that this provision provides incentive for a manufacturer or authorized distributor to identify and

investigate potential cases of diversion, it does not ensure that effective written procedures and administrative systems are in place to do so.

50. Another comment requested that the requirement in proposed § 203.34(c) for an inventory schedule be flexible so that a procedure committing to conduct a field force inventory at least yearly would be sufficient.

Administrative procedures adopted by manufacturers and authorized distributors of record must be adequate to ensure compliance with PDMA and agency requirements. With respect to the requirement in revised § 203.34(b)(2) for written policies and procedures describing administrative systems for conducting the annual physical inventory, the administrative procedures must ensure that all representatives are inventoried at least once a year in accordance with the requirements of § 203.31(d) and section 503(d)(3)(C) of the act.

6. Use of Third Parties

a. *Section 203.36(a)*. Proposed § 203.36(a) stated:

Any manufacturer or authorized distributor of record that uses a fulfillment house, shipping or mailing service, or other third party, or engages in a comarketing agreement with another manufacturer or distributor to distribute drug samples or to meet any of the requirements of PDMA, PDA, or this part, remains responsible for creating and maintaining all requests, receipts, forms, reports, and records required under PDMA, PDA, and this part.

51. One comment supported the section as written. Several comments requested clarification on whether the manufacturer or authorized distributor must itself create and maintain forms and records or ensure proper compliance by the third party. Several comments objected to the former interpretation on the ground that it would require so much involvement by the manufacturer or authorized distributor in the day-to-day operations of the third party that it would effectively preclude companies from using third parties.

The agency clarifies that a manufacturer or authorized distributor of record that uses a third party to distribute drug samples or meet any requirements of PDMA or the final rule may have the third party create and maintain required requests, receipts, forms, reports, and records. For example, a shipping company that delivers samples would be permitted to use its own delivery verification receipts and to maintain those receipts for the manufacturer or authorized distributor. However, the manufacturer or authorized distributor is responsible

for ensuring that the third party complies with all requirements under PDMA and the final rule. In the previous example, if all of the information required in § 203.30 is not contained on the shipping company's receipt, the manufacturer or authorized distributor is responsible for compliance, and thus liable for noncompliance, with § 203.30.

Additionally, the agency is aware that some drug manufacturers contract with an "outside" promotional sales force rather than maintaining an "in-house" one. These representatives, known in the industry as "contract representatives," qualify as third parties under this section. Since contract representatives may be paid according to the number of samples distributed, firms using their services should be particularly vigilant concerning the possibilities for sample diversion and sample request and receipt form falsification.

52. One comment requested clarification as to whether, if a manufacturer enters into a comarketing agreement with another manufacturer for the distribution of samples by its representatives, the comarketer would thereby become an authorized distributor of record and would thus be responsible for creating and maintaining its own reports, forms, and records. Another comment contended that comarketers could qualify as manufacturers or authorized distributors of record and recommended that the final rule be revised to make comarketers who are themselves manufacturers or authorized distributors responsible as such for compliance with PDMA.

As the agency explained under the comments on the definition of "ongoing relationship," a comarketer, sample fulfillment house, or other entity that performs sample distribution functions other than delivery or functions that are incidental to delivery is engaged in "distribution" of drug samples and must, under section 503(d) of the act, be an authorized distributor of record. Authorized distributors of record are responsible for complying with all requirements for sample distribution under PDMA and the final rule, including creating and maintaining all required requests, receipts, forms, reports, and records. Thus, if a manufacturer or authorized distributor contracts with a third party which itself becomes an authorized distributor of record, the manufacturer or authorized distributor and the third party are both responsible for compliance with PDMA requirements.

b. *Section 203.36(b)*. Proposed § 203.36(b) stated that a manufacturer or authorized distributor of record that contracts with a third party to maintain some or all of its records shall produce required documents within 48 hours of a request by an authorized representative.

53. Several comments stated that 48 hours is not enough time to produce required documents. Three comments recommended that the section be revised to allow 5 working days for production of records. One comment stated that a manufacturer should be excused from penalty when requested information in the storage of a third party is not produced within 48 hours by reason of "unanticipated events beyond the reasonable control of either the drug manufacturer or the contractor (i.e., a force majeure defense)." The comment stated that, at a minimum, the section should be amended to provide 48 business hours to comply.

In response to the comments, the agency has revised proposed § 203.36(b) to require the production of records maintained by a third party within 2 business days of a request, rather than 48 hours. The agency believes that this period should be sufficient given the fact that most records are maintained electronically and can be quickly and easily retrieved and transmitted to the location where they are requested.

7. Investigation and Notification Requirements

a. *Section 203.37(a)(1) and (a)(2)*.

Proposed § 203.37(a)(1) stated:

A manufacturer or authorized distributor of record that has reason to believe that any person has falsified drug sample requests, receipts, or records shall conduct a full and complete investigation, and shall notify FDA, by telephone or in writing, within 5 working days of becoming aware of a falsification and within 5 working days of the completion of an investigation.

Proposed § 203.37(a)(2) stated: "A manufacturer or authorized distributor of record shall provide FDA with a complete written report, including the reason for and the results of the investigation, not later than 30 days after the date of the initial notification."

The agency, on its own initiative, has reformatted proposed § 203.37(a)(1) and (a)(2) into § 203.37(a)(1), with three subsections. The agency believes that the new format is clearer and easier to understand.

54. FDA received 10 comments on these sections addressing the following issues: (1) The circumstances under which a manufacturer or authorized distributor should be required to investigate, (2) the time period to complete investigation, (3) when and

under what circumstances a manufacturer should be required to give notice to FDA, and (4) the form of the notice and reporting requirements.

Two comments addressed the level of suspicion of falsification that is necessary to trigger the investigation requirement. One comment said that the "reason to believe" language that appears in § 203.37(a)(1) creates a standard that is "vague and difficult to interpret." Another comment stated that "reason to believe needs to be defined so that a manufacturer will not be second guessed." Another comment stated that the proposed rule does not define what constitutes "falsification," and that variances in a representative's reported numbers do not usually give rise to a "reason to believe" that a falsification has occurred, requiring investigation and notice, but rather that a representative has poor work habits. The comment stated that requiring investigation of every variance would be "unrealistic."

Instances of potential falsifications are most likely to come to the attention of manufacturers or authorized distributors through discrepancies that are uncovered during the required annual inventory and reconciliation. However, it is possible that other events or occurrences, some foreseeable and some not, may bring potential falsifications to the attention of a manufacturer or distributor. The agency has determined that the reason to believe standard, while not capable of precise definition, is flexible enough to cover the multiplicity of situations in which potential falsification is brought to light. Moreover, the standard is one that can be applied by manufacturers and authorized distributors using common sense and good judgment. While the agency does not expect manufacturers and authorized distributors to investigate every slight discrepancy, the agency would require investigation under this standard where a pattern of discrepancies exists or where other reliable information indicates that records have been falsified.

55. Another comment said that the circumstance that triggers the investigation requirement should be diversion, not falsification. That comment also stated that the investigation requirement should apply only to a manufacturer's or authorized distributor's employees' misconduct, not to any person.

The drug sample recordkeeping requirements were instituted to help ensure that drug diversion schemes could be detected. The agency believes that patterns of falsification of drug sample requests, receipts, or records,

while not conclusive, are highly probative that drug sample diversion is taking place. Thus, the agency declines to follow the recommendation that knowledge of diversion precede investigation.

The agency recognizes, however, that circumstances other than record falsification may be indicative that drug sample diversion is occurring. Accordingly, the agency has revised proposed § 203.37(a) to require notification, investigation, and reporting where a manufacturer or authorized distributor of record has reason to believe that any person is diverting prescription drug samples.

Finally, the agency believes that the manufacturer or authorized distributor of record is in the best position to detect potential diversion not only by its own employees, but by other persons, such as contract representatives. Accordingly, the agency has determined that manufacturers and authorized distributors must investigate when they have reason to believe that any person has falsified drug sample records or has diverted drug samples.

56. Two comments stated that PDMA statutory requirements did not make falsification of drug sample records reportable to FDA.

Although PDMA did not expressly make falsification of drug sample records reportable to FDA, the agency has determined that such notice is necessary and furthers the legislative intent in PDMA. Persons who falsify drug sample requests, receipts, or records may be criminally prosecuted under sections 301 and 303 of the act, and under Title 18 of the United States Code. Because FDA is responsible for enforcing PDMA, it is necessary that the agency have all pertinent information regarding such potentially criminal conduct. Moreover, Congress did explicitly make significant losses and known thefts reportable to FDA, presumably because such losses and thefts indicate possible sample diversion activity. (See S. Rept. 100-303, p. 6, H. Rept. 100-76, p. 16.) As discussed previously, the agency believes that falsifications of drug sample records are highly probative that drug diversion is taking place. Thus, the agency has determined that it is consistent with congressional intent that the agency be made aware of such falsifications, as well as other activity that is indicative of drug sample diversion, to enable FDA to monitor compliance with PDMA.

57. One comment noted that statements made in the preamble to the proposal (59 FR 11842 at 11851) conflicted with proposed § 203.37(a)(1).

The comment stated that the proposal's preamble indicated that notice would be required to be provided to FDA when an investigation is initiated. However, proposed § 203.37(a)(1) does not require notice until "within 5 working days of becoming aware of a falsification." According to the comment, the notice discussed in the preamble may precede the notice required under the proposed regulation.

The agency acknowledges that the notice discussed in the preamble of the proposal (59 FR 11842 at 11851) is different than the notice that would be required under the proposed regulation. The agency has revised proposed § 203.37(a)(1) and (a)(2) to require that a manufacturer or authorized distributor of record that has reason to believe that any person has falsified drug sample requests, receipts, or records, or is diverting drug samples must notify FDA within 5 working days, immediately initiate an investigation, and submit a written report to FDA within 30 days after the date of the initial notification. Thus, the requirement in proposed § 203.37(a)(1) that a manufacturer or distributor notify FDA within 5 working days of becoming aware of a falsification and within 5 working days of the completion of an investigation has been eliminated. The agency believes that the provision of a single notice to FDA near the time when an investigation is initiated is sufficient.

58. One comment said that firms should be required to provide notice to FDA only in "situations where substantial evidence of apparent attempts to conceal diversion of samples exists." Another comment stated that notice should not be required until a "strong probability" of falsification is indicated by an investigation. Several comments stated that, except for a final written report submitted at the completion of an investigation revealing that falsification has in fact occurred, no notice should be required. One of these comments stated that it would be "improper and unfair" to implicate employees in falsification before all of the facts are known and an informed judgment can be made with respect to responsibility. One comment recommended that a written report should be made available, but not automatically submitted, to FDA.

The agency believes that the manufacturer or authorized distributor, through its own investigation, is in the best position to determine whether falsification has occurred. However, for enforcement purposes, it is necessary that FDA be notified when there is reason to believe that there has been a falsification to ensure that an

investigation is actually undertaken. Moreover, the provision of notice to FDA at the initiation of an investigation will establish a point from which to judge whether the investigation is completed in a timely manner. Thus, the agency disagrees with the recommendation that notice should not be provided to FDA until an investigation is completed and a strong probability of records falsification exists or until records falsification is confirmed. In addition, submission of a final written report to FDA stating the reasons for and the results of an investigation is necessary, even where falsification has not been found, to permit FDA to determine whether the circumstances were adequately investigated and explained.

59. One comment stated that reports of some complex cases could require more than 30 days to complete and requested that the proposed rule be revised to allow for 30 days, except in "unusual circumstances." Another comment recommended allowing completion of the investigation within a "reasonable time," while another recommended that there should be no time restriction for the submission of a final report.

The final rule as revised gives manufacturers 30 days to complete an investigation of possible falsification and to submit a written report. The agency believes that this amount of time is more than adequate in all but the most complex cases. In such cases, a preliminary report may be submitted describing the investigative measures taken, a summary of the findings of the investigation up to that time, the nature of the ongoing investigation, and the reasons the investigation was not completed within the required time.

b. *Section 203.37(b)(1) and (b)(2).*

Proposed § 203.37(b)(1) stated:

A manufacturer or authorized distributor of record that distributes drug samples or a charitable institution that receives donated drug samples from a licensed practitioner shall notify FDA, by telephone or in writing, within 5 working days of becoming aware of any significant loss or known theft of drug samples and within 5 working days of the completion of an investigation into a report of a significant loss or known theft.

Proposed § 203.37(b)(2) stated: "A manufacturer or authorized distributor of record shall provide FDA with a complete written report not later than 30 days after the date of the initial notification."

On its own initiative, the agency has reformatted and revised these sections into a single section, § 203.37(b)(1), with three subsections. The revised section eliminates the requirement in proposed § 203.37(b)(1) for notice to be given to

the agency within 5 days of the completion of an investigation of significant loss or known theft, but otherwise retains and clarifies the requirements in proposed § 203.37(b)(1) and (b)(2).

60. Two comments recommended revision of proposed § 203.37(b)(1) to extend the time a manufacturer or authorized distributor has to notify FDA after becoming aware of a significant loss or theft, with no notification required if subsequent investigation reveals no loss or theft. One of the comments said that it would not be possible to differentiate insignificant accounting mistakes and actual losses within 5 days of learning of an inventory discrepancy and that the requirement would cause too many false alarms.

Unlike falsifications of drug sample records, the agency requires notice of significant losses and known thefts only when a manufacturer or authorized distributor "becomes aware" of such losses or thefts. Thus, the level of certainty under which notice and investigation are required is higher for losses and thefts than it is for falsifications. Consequently, a manufacturer or authorized distributor should have already differentiated insignificant accounting mistakes and actual losses before notice is given to FDA. Thus, the agency believes that 5 working days from the time that a manufacturer or authorized distributor becomes aware of losses or thefts is sufficient to provide notice to FDA of losses or thefts.

61. Two comments recommended allowing 45 days after becoming aware of significant losses during shipment before notice is required, because such apparent losses of drug samples often show up during that time period.

The agency declines to follow the recommendation of the comments. Potential significant losses that occur during shipping must be investigated and reported like other significant losses. When samples thought to be lost or stolen during shipping are later found, a followup report should be made to the agency describing the circumstances of the recovery and the quantity of samples that were recovered.

62. In the preamble to the proposed rule (59 FR 11842 at 11851), the agency stated: "The reporting of any significant loss of drug samples is critical to the success of diversion control. * * * FDA intends this requirement to mean that the agency is to be advised of actual, physical losses, but not insignificant accounting mistakes." FDA stated that it was aware of the difficulty of establishing a threshold for significant

loss and solicited comment on how to distinguish between significant losses and minor accounting or inventory errors. The agency did not propose to establish a tolerance level for sample losses below which no report is required, and stated that each manufacturer or distributor is required to establish its own threshold for determining when inventory not accounted for is significant.

One comment stated that losses may occur in several ways, including losses of shipments in transit, loss by representatives, and unexplained inventory discrepancies. The comment stated that, for shipping losses, it may be appropriate for companies to set a dollar amount above which a single loss is considered significant. This amount would vary by company and would be dependent on the size of the company, number of representatives, and size and value of its total inventory. The comment stated that shipping losses should also be viewed cumulatively over a "fixed, rolling period of time" to determine if there is a pattern of losses that might indicate diversion. Regarding unexplained inventory shortages, the comment stated that each company should be required to establish its own threshold for determining when inventory not accounted for is significant. Inventory discrepancies that can be shown to be caused by math or accounting errors or mistakes that can be reconciled should not be reported. The comment stated that there are three significant loss scenarios that may indicate possible diversion: (1) A single loss that exceeds a company's predefined threshold; (2) the number of loss events over a fixed, rolling period exceeds the company's threshold; or (3) the volume of losses over a fixed, rolling period exceeds the company's threshold.

One comment stated that loss of a certain quantity of one drug sample with a high potential for diversion may be significant, while the loss of the same quantity of another sample with a low potential for diversion may not be significant. Therefore, the comment asserted, no universally applicable threshold can be established and a case-by-case analysis must be employed.

One comment requested that FDA clarify that not all physical losses are significant.

The agency agrees with the first comment that different methods for determining whether a loss is significant may be used depending on the type of loss involved. For single loss events (i.e., "physical" losses) including losses by representatives (except for losses reported as thefts, which must all be

reported and investigated) and losses of drug samples in transit, establishing a predefined threshold based on a set dollar amount or other criteria, such as a fixed number of sample units, may be appropriate. The size of the manufacturer or authorized distributor of record, the number of representatives, and size and value of a firm's total inventory, as well as a firm's past experience with sample losses, are relevant factors in determining the level of the threshold. However, the agency also agrees with the second comment that firms should remain responsive to the individual circumstances surrounding a single loss event, such as the loss of a drug with a particularly high potential for diversion, to determine whether a loss is significant even though the size of the loss does not meet the firm's predefined threshold.

Regarding potentially significant losses that are revealed through unexplained inventory shortages, the agency stated in the preamble to the proposed rule that it does not seek to receive reports concerning minor mathematical errors that are caught and corrected in the normal course of business. The agency stated that firms are required to establish their own threshold for distinguishing between insignificant accounting mistakes and significant losses in inventory shortages based on the firm's past experience in sample distribution and inventory and the level of accuracy of its internal audit and security system. The agency also stated that some manufacturers or distributors might be able to set a "historically validated statistical baseline" for minimal amounts of inventory shrinkage caused by routine accounting errors, mistakes, or losses, and a statistical baseline for the frequency of occurrences (59 FR 11842 at 11851). The views expressed by the second comment regarding discerning significant losses from inventory shortages thus appear to be consistent with those previously set forth by the agency.

63. One comment supported permitting manufacturers and distributors to establish their own thresholds for determining when inventory not accounted for is significant, but said that it was concerned about being second-guessed by the agency in determining what constitutes a significant loss. The comment recommended that FDA clarify within proposed § 203.37 that it would not challenge a manufacturer for following its own definition of significant loss.

The agency declines to revise the proposal to state that it will not

challenge a manufacturer for following its own definition of significant loss. However, the agency advises that a firm can best ensure that no enforcement action will be taken against it for violation of § 203.37(b) where it establishes a system for reporting and investigating significant losses that is consistent with the guidance provided in this notice and in the proposed rule. Additionally, where a manufacturer or distributor is unsure about whether a loss is significant, it should report and investigate the loss as if it were significant.

64. One comment stated that FDA should not give manufacturers or distributors any discretion to define what constitutes significant loss, but rather should define it for them.

As explained previously and in the proposal (59 FR 11842 at 11851), the threshold level of what constitutes a significant loss will necessarily vary depending on such factors as the size of a company and the value of its total inventory, the accuracy of a manufacturer's or distributor's system for tracking sample distribution, and the circumstances surrounding the loss. Thus, the agency declines to codify a definition of significant loss.

65. One comment expressed concern that virtually all losses would have to be reported under the significant loss standard as described by the agency in the proposal and recommended that significant loss be defined as a percentage of total sales or supplies.

The agency believes that it has provided sufficient guidance in the proposed rule and in this notice about how to distinguish between routine losses and significant losses that need to be reported and investigated. Thus, the agency disagrees that all or virtually all losses will have to be reported and investigated and declines to set a threshold based on percentage of total sales or supplies above which a loss will be considered significant.

c. *Section 203.37(d)*. Proposed § 203.37(d) stated: “* * * A manufacturer or authorized distributor of record that distributes drug samples shall inform FDA in writing within 30 days of selecting the individual responsible for responding to a request for information about drug samples of that individual's name, business address, and telephone number.”

66. One comment sought clarification on whether the information required by this section is “for a regulatory agency and PDMA information or information for a potential customer-doctor or patient.”

FDA clarifies that the information required by this section is to facilitate

requests for drug sample information by FDA and Federal, State, and local regulatory and law enforcement officials.

8. Sample Lot or Control Numbers; Labeling of Sample Units

a. *Section 203.38(a)*. Proposed § 203.38(a) stated: “The manufacturer or authorized distributor of record of a drug sample shall include in the labeling of the drug sample and the label of the sample unit an identifying lot or control number that will permit the tracking of the distribution of each drug sample unit.”

67. Two comments stated that the statement “identifying lot or control number that will permit the tracking of the distribution of each drug sample unit” could be interpreted to mean that each drug sample unit would require its own identifying number. The comments requested that the agency clarify that tracking is required only of lots, not of sample units.

FDA clarifies that the section is intended to require only the tracking of sample units by the lot from which they came, and does not require that each sample unit receive its own identifying number.

68. Several comments requested clarification on whether the lot or control number is required to appear only on the external packaging of sample units or on all labeling as defined in 21 CFR part 201, including inserts and circulars. Several comments objected to the latter interpretation on the grounds that such a requirement would be costly and would not aid in the prevention of drug diversion. One comment, for example, stated that package inserts would probably be discarded by individuals engaged in diversion. Several comments stated that inserts are currently not lot-specific and that customizing inserts to lots would be extremely expensive. One comment stated that requiring lot numbers on package inserts would not benefit recall procedures.

The section as proposed would require lot or control numbers to appear both on sample unit labels and on other drug sample labeling. Inserts and circulars are labeling as defined in section 201(m) of the act. However, the agency agrees with the comments that requiring lot or control numbers to appear on package inserts, circulars, or similar labeling is not necessary. The section has been revised to require that the lot or control number appear only on the label of the sample unit itself, and on the outside container or packaging of the sample unit, if any, in

accordance with section 201(k) of the act.

b. *Section 203.38(c)*. Proposed § 203.38(c) stated, in relevant part, that “each sample unit shall bear a label that clearly denotes its status as a drug sample, e.g., ‘sample,’ ‘not for sale,’ ‘professional courtesy package.’”

In the preamble to the proposed rule (59 FR 11842 at 11855), the agency identified “starter packs” as prescription drug products distributed without charge by manufacturers or distributors to pharmacists with the intent that pharmacists place the drugs in stock and sell them at retail. The agency stated that starter packs are intended for sale and therefore do not meet the statutory definition of a drug sample. Since the publication of the proposed regulations, the agency has become aware of the use of the terms “starter,” “starter samples,” and “patient starter pack” to refer to drug sample units. Because the agency does not consider starter packs (as described previously) to be drug samples, the use of the term “starter” on drug sample labeling is inappropriate and should not be used.

69. One comment stated that the proposed requirement goes beyond the intent of Congress in PDMA and that it would not deter diversion because the contents may be removed from the drug package.

Designating a sample unit as a sample is the only way to distinguish drug products manufactured for sale from drug samples. Because Congress prohibited the sale, purchase, or trade of drug samples, or the distribution of samples in a manner that is inconsistent with section 503 of the act, the requirement clearly is consistent with and furthers legislative intent. Although the requirement does not provide a foolproof method of preventing diversion, the requirement will help deter sample diversion by denying diverters a market-ready product.

70. One comment recommended, as an alternative to isolating a manufacturing run of labels, that manufacturers be permitted to use adhesive stickers that could be placed on the outside containers of sample units otherwise labeled for retail.

The agency will not object to the use of stickers provided that a sticker is applied to both the label of the sample unit and the outside container or packaging of the sample unit, if any, in accordance with § 203.38(a). However, to avoid giving diverters a market-ready product, any stickers should be difficult to remove and their removal should be evident. The agency recommends more

durable methods of identifying a sample product, such as overprinting.

71. Several comments opposed the requirement in proposed § 203.38(c) on the grounds that it would entail too much expense.

It is the agency's experience that the packaging of sample units currently used by the majority of manufacturers already identifies the units as samples through the use of terminology such as "not for sale" or "professional use only." Such wording meets the intent of this section. Moreover, as discussed under the previous comment, manufacturers may place an adhesive sticker on the label of a retail unit and on the outside container or package of the unit, if any, designating the retail unit as a sample. Therefore, the agency is unconvinced that this requirement would impose a financial hardship on the majority of manufacturers.

72. One comment objected to the proposed rule as it relates to the distribution of radiopharmaceutical samples. The comment stated that prohibiting manufacturers from supplying radiopharmaceutical samples in retail packages would be unduly burdensome because of the small numbers of such samples that are distributed. The comment recommended that radiopharmaceuticals be exempt from the requirement.

As discussed previously, manufacturers may place an adhesive sticker on the label of a retail unit and on the outside container or package of the unit, if any, designating it as a sample. The agency believes that this is sufficient to address the concerns raised by the comment and declines to create the requested exemption.

73. One comment stated that the increased costs associated with the labeling requirement would affect the ability of manufacturers to provide drugs free of charge to indigent patients.

As discussed in the proposal (59 FR 11842 at 11855), there are some circumstances in which prescription drugs that are provided free of charge will not be considered samples under section 503(c)(1) of the act and § 203.3(i). The example given was of prescription drugs provided at no charge to licensed practitioners for the treatment of indigent patients where the main object is to ensure that patients in need of prescription drugs have access to them (whatever their financial circumstances) and not to promote the drugs. According to information available to the agency, these manufacturer-sponsored indigent patient programs generally include appropriate controls, documentation,

and verification of the distribution and use of these products. Therefore, such drugs would ordinarily not be required to be labeled in accordance with § 203.38(c). Moreover, even where drugs are distributed for a promotional purpose and § 203.38(c) applies, the agency does not believe, for the reasons discussed in response to comment 71, that the labeling requirement will impose a financial burden large enough to affect the ability of manufacturers to provide drugs free of charge to indigent patients.

74. One comment requested a 3-month grace period after the effective date of the regulations in which nonlabeled sample units already in the possession of manufacturers could be used.

As discussed in section II.K of this document, the agency has determined that the provisions in the final rule will not become effective until 1 year after the date of publication of the final rule in the **Federal Register**. Thus, the agency believes that manufacturers and authorized distributors will have ample time from the publication of the final rule to its effective date to come into compliance.

75. One comment recommended that the proposed regulation be rewritten to require that a drug sample label include the terms "sample" or "professional sample" and to allow, in addition to these terms, such terms as "not for sale" or "professional courtesy package."

The wording used in proposed § 203.38(c) was intended to be illustrative only. Any words that clearly designate a sample unit as a sample may be used. As discussed previously, the term "starter" does not designate a sample unit as a sample, and should not be used.

9. Retail Pharmacies and Drug Samples

In the preamble to the proposal (59 FR 11842 at 11853), the agency explained that by limiting the distribution of samples to licensed practitioners and to hospitals or health care entity pharmacies at the request of a licensed practitioner, but not to retail pharmacies, Congress clearly expressed its intent to not allow the distribution of samples to retail pharmacies. Under proposed § 203.40, the presence in a retail pharmacy of any drug sample would have been considered evidence that the drug sample was obtained by the retail pharmacy in violation of section 503(c)(1) of the act.

76. One comment opposed proposed § 203.40, stating that "there is no statutory or evidentiary basis for creating this presumption." The comment also stated that FDA, as a

Federal agency, lacks the authority to shift the burden of proof in an enforcement proceeding.

The agency has decided to withdraw proposed § 203.40 from the final rule. However, the agency continues to interpret the act to prohibit the distribution of drug samples by a manufacturer or distributor to a retail pharmacy and the receipt of a drug sample by a retail pharmacy from any person. Moreover, the agency believes that the presence of drug samples in a retail pharmacy is probative that samples are being sold, purchased, traded, or distributed in violation of the act. Therefore, the agency may investigate the presence of drug samples in a retail pharmacy to determine if other violations warranting enforcement action exist.

77. Three comments objected to the prohibition on the distribution of drug samples to or the receipt of drug samples by retail pharmacies. Two comments stated that the prohibition would prevent pharmacists from providing drug counseling to patients. One comment stated that counseling is important because physicians are not accustomed to counseling patients to whom they give drugs. Another comment asserted that pharmacist-patient counseling improves compliance with drug therapy and reduces overall health care costs. Two comments stated that retail pharmacies should be allowed to store and dispense samples at the direction of a physician because pharmacies are designed for drug storage and physicians' offices are not.

The agency recognizes that proper storage and handling of prescription drugs and adequate counseling in connection with prescription drug use are important concerns. However, the agency believes that both of these goals can and must be accomplished within the system of sample distribution established by Congress in PDMA. As discussed previously, under this system, drug samples may not be distributed to retail pharmacies and retail pharmacies may not receive such samples.

78. One comment objected to the fact that physicians are not permitted to give samples to or to request that samples be sent to a retail pharmacy, although they are expressly permitted to request that samples be sent to hospital or health care entity pharmacies. The comment argued that, except in two States, all pharmacists receive the same type of license regardless of practice setting. The comment also stated that all pharmacists, regardless of practice setting, independently dispense drugs to patients in accordance with a written prescription. The comment

recommended either that all types of pharmacies should be permitted to receive samples at the direction of a licensed practitioner or none should be permitted.

The agency declines to follow the recommendation of the comment. PDMA expressly provided that hospital or health care entity pharmacies may provide drug samples to patients at the direction of a licensed practitioner. Moreover, PDMA provided that manufacturers and authorized distributors of record may distribute drug samples to hospital or health care entity pharmacies at the request of a licensed practitioner. Thus, Congress clearly expressed its intent to allow hospital or health care entity pharmacies to receive and dispense drug samples. No such intent is evident with respect to retail pharmacies.

79. One comment stated that not permitting retail pharmacies to store and to dispense samples at the direction of a physician is inconsistent with agency policy, as expressed in the preamble to the proposal, allowing distribution of prescription drugs through retail pharmacies to indigent patients.

The proposal (59 FR 11842 at 11855) did not address dispensing prescription drugs to indigent patients through retail pharmacies. It discussed the circumstances whereby manufacturers make arrangements to provide prescription drugs to licensed practitioners to prescribe and dispense at no cost or at reduced cost to indigent patients of those practitioners. As previously stated, such drugs will ordinarily not be considered samples. Therefore, a licensed practitioner may direct such drugs to be distributed to and dispensed by a retail pharmacy.

10. Permissible Uses of Drug Samples by Licensed Practitioners

In the preamble to the proposal (59 FR 11842 at 11852), the agency described the permissible uses of drug samples by licensed practitioners by stating:

FDA advises that PDMA and this proposed rule would permit a licensed practitioner to: (1) Dispense the drug sample as set forth in section 503(d)(1) of the act; (2) donate the drug sample to a charitable institution as provided for in proposed § 203.39; (3) return the drug sample to the manufacturer or distributor; or (4) destroy the drug sample.

80. One comment requested that the proposed rule be revised to permit a licensed practitioner to give drug samples to a requesting manufacturer for stability testing and other quality testing. The comment stated that a manufacturer should be allowed to request and retrieve both its own samples and the samples of other

manufacturers for this purpose. According to the comment, allowing manufacturers to retrieve samples for testing would further the purposes of PDMA legislation by ensuring that drug samples in the possession of licensed practitioners are safe and effective. The comment stated that, under the proposed rule, there are no regulatory controls on the handling and storage of drugs in the possession of licensed practitioners. The comment stated that by obtaining and analyzing drug samples that have been stored in practitioners' offices under actual conditions of use, manufacturers will be able to improve packaging design to ensure the stability of drug samples. The comment also stated that allowing manufacturers to obtain and analyze samples "raises minimal, if not nonexistent, risk of samples being diverted into secondary commerce."

As stated in the proposal, the agency's policy is to permit licensed practitioners to return drug samples to the manufacturer or distributor from which they were obtained. Although the agency had originally only considered the scenario in which the licensed practitioner would initiate such returns, the agency clarifies that a request by a manufacturer to a practitioner for return of its own samples for stability testing or other analysis would be permissible.

The agency does not believe, however, that it is permissible under PDMA for licensed practitioners to distribute drug samples to manufacturers or authorized distributors who did not supply them. The agency believes that such distribution would serve no legitimate purpose and would unnecessarily increase the risk of sample diversion. The agency is not persuaded that manufacturers would expend the time and resources necessary to perform stability and quality testing on other manufacturers' samples. Moreover, even if such testing were performed, it is unlikely that the results of such testing would be shared with the manufacturer of the sample. Thus, the sample quality would not be improved by allowing manufacturers to retrieve other manufacturers' samples. Finally, the agency believes that a risk of diversion does exist with such distribution and that the risk is not offset by any appreciable health benefit.

11. Drug Sample Status of Free Distributions

In the preamble to the proposed rule (59 FR 11842 at 11855), the agency stated that because starter packs are intended to be sold, they are not samples and thus the sample distribution requirements do not apply

to them. The agency cautioned, however, that because starter packs provide opportunities for diversion similar to those presented by drug samples, manufacturers and distributors should establish and maintain accounting, audit, and security systems for starter packs to guard against diversion.

81. One comment supported the agency's position on starter packs, stating: "We applaud the FDA for clearing up misunderstandings about the difference between samples and starter packs." Another comment agreed with the agency's position, but stated that the cautionary language used by the agency in connection with starter packs implicitly regulates them as samples. The comment recommended that the proposed regulations be revised to include a definition of starter pack indicating that it is not a sample and to allow manufacturers to decide how to monitor the distribution of starter packs.

As noted previously, the agency has concluded that starter packs do not meet the statutory definition of a drug sample and thus are not subject to PDMA requirements for sample distribution. This determination is consistent with the definition of "drug sample" in the act and final regulations and need not be codified. The agency also clarifies that manufacturers are not required to follow the agency's recommendations for monitoring the distribution of starter packs. However, because of the potential for diversion of these products, the agency continues to recommend that their distribution be monitored in a manner designed to prevent and detect diversion.

82. One comment sought clarification of whether specific distributions of prescription drugs to indigent patients through retail pharmacies would constitute a sample or nonsample transaction. In the scenario presented by the comment, the patient would present a prescription and a "prescription drug card" to the retail pharmacist, who would fill the prescription from a stock bottle and be reimbursed for the cost of the drug and patient counseling services through a "pharmacy benefits company." The comment stated that the manufacturer would have a contract with the pharmacy benefits company to handle all transactions for a drug under the manufacturer's indigent drug program.

The agency advises that the prescription drug dispensed in the scenario presented by the comment would not be considered a sample for purposes of PDMA because the drug product comes from the stock of the

retail pharmacy and is intended to be sold.

83. One comment requested that the agency recognize that drugs distributed to a physician for use by the physician's family are not samples. According to the comment, such drugs should not be considered samples because they are not intended to promote the drug.

The agency believes that distributions of free prescription drugs to a physician for use by his family do constitute samples because they are intended to promote the marketing of a drug. A licensed practitioner is clearly benefitted by the provision of free drugs for personal or family use. The agency believes that the benefit conferred on a practitioner in this manner by a manufacturer or authorized distributor is clearly intended to influence the physician's decisionmaking process about what drugs to prescribe for patients in the future and is therefore intended to promote the sale of the drug.

12. Bid and Commercial Samples

In the preamble to the proposal (59 FR 11842 at 11856), the agency discussed "bid" and "commercial" samples. The agency stated that these include specimens of bulk drug ingredients, precursor specimens, or finished dosage forms that are distributed to a manufacturer in limited quantities for testing and evaluation purposes. As noted by the agency, specimens of bulk drug ingredients may be used by manufacturers to determine whether the bulk drug is compatible with the manufacturer's production equipment or suitable for use in formulating drug products. Finished dosage forms may be used by repackers to determine if they are suitable for use with various packaging materials and equipment. Citing the definition of drug sample in section 503(c)(1) of the act and proposed § 203.3(i), the agency stated that, because of the statutory language and the threat of diversion, persons who distribute bid or commercial samples should follow the requirements for sample distribution set forth in the act and the proposal.

84. One comment asked if the agency intended for manufacturers providing materials for stability trials or for validation studies to follow sample distribution requirements. The comment also sought guidance on which distributions of prescription drugs would be covered by the terms "bid" and "commercial" samples.

The agency clarifies that the terms "bid" and "commercial" samples, as used by the agency in the proposal and in the final rule, refer to distributions of

bulk drug substances or finished dosage forms by a manufacturer or distributor to a manufacturer at no cost for testing and evaluation purposes. Such distributions would include free distributions of bulk drug substances to conduct stability, validation, or characterization studies, or for other purposes related to testing and evaluation of the bulk drug substance. Such distributions would also include the free distribution of a limited quantity of a finished dosage form to a repackager for testing with the repackager's packaging equipment. As discussed in comment 85, the agency has determined that distributions of bid and commercial samples are not subject to requirements for sample distribution under PDMA or the final rule.

85. Several comments objected to subjecting bid and commercial samples to the same requirements as prescription drug samples on the grounds that bid and commercial samples are not intended to promote the sale of a drug and thus are not drug samples. Two comments stated that adhering to drug sample distribution requirements for bid and commercial samples would be burdensome to small companies and drug manufacturers such as repackers that do not have licensed practitioners on their staff. One of these comments stated that the burden would not be offset by any appreciable public health benefit. Several comments stated that the likelihood of diversion of commercial or bid samples is extremely small. Another comment stated that the potential for diversion of bid and commercial samples asserted by the agency is unsupported in either the congressional or administrative record. Several comments recommended applying existing recordkeeping requirements for prescription drugs to bid and commercial samples.

Although bid and commercial samples arguably meet the literal definition of a drug sample under section 503(c)(1) of the act, the agency believes that application of the statutory requirements for drug sample distribution to such drugs would be inconsistent with congressional intent. In PDMA's legislative history, Congress stated that "pharmaceutical manufacturers and distributors have a long-established practice of providing samples of their prescription drugs to physicians and other practitioners licensed to prescribe such drugs who, in turn, provide them to their patients. The ostensible purpose is to acquaint the practitioner with the therapeutic value of the medication and thus encourage the written prescription of the drug." (See H. Rept. 100-76 at p. 12.) Because

bid and commercial samples are not provided to practitioners or their patients, the agency believes that Congress did not intend the drug sample provisions of PDMA to apply to them. Therefore, the agency is no longer recommending that the sample distribution requirements in PDMA and the final rule be followed for bid and commercial samples. However, because the potential for diversion exists, the agency recommends that manufacturers and distributors monitor their bid and commercial sample distribution to prevent and detect diversion.

F. Application of PDMA to Bulk Pharmaceutical Chemicals

In the preamble to the proposal (59 FR 11842 at 11843), the agency concluded that bulk drug substances that are subject to section 503(b) of the act (i.e., prescription) are covered under PDMA.

86. One comment objected to the application of any portion of PDMA, including the sample distribution requirements and wholesale distribution requirements, to bulk pharmaceutical chemicals (BPC's). The comment argued that PDMA was intended by Congress to apply to finished dosage forms only and that the proposed regulations cannot be practically applied to BPC's. The comment stated that the legislative history of PDMA indicates that Congress was concerned with the effects of diversion on consumers and that, since BPC's are not sold to consumers, Congress did not intend for the act to apply to them. The comment also stated that BPC's were not mentioned by Congress in either PDMA or its legislative history and the absence of legislative reference to BPC's indicates that Congress did not even consider including BPC's under PDMA. The comment argued that this reasoning is consistent with the agency's decision to exclude blood and blood components from wholesale distribution requirements in PDMA.

The comment also said that the proposed regulations dealing with wholesale distribution and drug samples cannot be practically applied to BPC's. The comment stated, for example, that the proposed sample regulations would not allow a BPC manufacturer to furnish a finished dosage form manufacturer with BPC samples because a manufacturer is prohibited from distributing drug samples to anyone other than a licensed practitioner or a hospital or health care entity pharmacy designated by a licensed practitioner. The comment said that BPC manufacturers could not comply with wholesale licensing requirements in part 205 because BPC's

are distributed in an entirely different way than other prescription drugs. The comment recommended that if BPC's are to be included under PDMA, the proposed regulations should be revised to "include regulations specific to and appropriate to BPC's that address the problems of diversion and counterfeiting."

The preamble to the proposed regulations (59 FR 11843) discussed the applicability of PDMA not to BPC's, but to bulk drug substances (BDS's). As discussed in section II of this document, the definition of bulk drug substance used in the final rule includes only those substances that become active ingredients when used in the manufacturing, processing, or packaging of a drug. It is the agency's understanding that the term BPC, as used in the comment, includes substances that do not become active ingredients when used in the manufacturing, processing, or packaging of a drug (i.e., substances that are not pharmacologically active, do not furnish direct effect in the diagnosis, cure, mitigation, treatment, or prevention of disease, and do not affect the structure or any function of the body of humans) and thus are not bulk drug substances.

The statutory language of PDMA makes it applicable to all drugs (as defined under section 201(g)(1) of the act) that are subject to section 503(b)(1) of the act. Although components of finished drug products that are not bulk drug substances may meet the statutory definition of a drug under section 201(g)(1)(D) of the act, such materials are not prescription drugs as described under section 503(b)(1) of the act. Accordingly, non-BDS components of finished drug products are not subject to PDMA requirements (e.g., drug sample or wholesale drug distribution). In addition, as discussed under the preceding comment, the drug sample distribution requirements of PDMA do not apply to specimens of BDS's provided to finished dosage form manufacturers for testing and evaluation purposes.

The agency disagrees, however, that PDMA was not intended by Congress to apply to prescription BDS's or that the distribution of prescription BDS's is so different than that of finished dosage forms that the wholesale distribution requirements of PDMA cannot be practically applied to BDS's. As noted previously, the statutory language of PDMA makes it applicable to all drugs subject to section 503(b)(1) of the act. A BDS that is intended to furnish pharmacological activity or other direct effect when it becomes a finished dosage form that is a prescription drug

necessarily falls within the scope of section 503(b)(1) of the act. Thus, on its face PDMA applies to prescription BDS's. Although Congress did not specifically refer to BDS's in the legislative history of PDMA, it also did not specifically refer to finished dosage forms or otherwise indicate that the scope of PDMA is limited to finished dosage forms. Moreover, the agency disagrees with the assertion that because prescription BDS's are not sold to consumers Congress did not intend for PDMA to apply to them. Prescription BDS's are used as components of prescription drug products that are sold to consumers, and clearly any practices that adversely impact upon the quality of prescription BDS's could ultimately harm consumers. Thus, the agency believes that PDMA was intended by Congress to apply to prescription BDS's.

The agency also believes that the wholesale distribution provisions of PDMA should and must be applied to prescription BDS's. Prescription BDS's are distributed from the manufacturer of the BDS to the manufacturer or compounder of the finished dosage form of the drug. That process of distribution may be direct or, as is generally the case for prescription BDS's manufactured by a foreign manufacturer, through one or more brokers/wholesalers. This system of distribution meets the definition of wholesale distribution under section 503(e)(4)(B) of the act. Moreover, because this system of distribution may involve several transfers of the bulk drug substance through numerous parties and facilities over varying periods of time, similar concerns exist with BDS's as with finished dosage forms regarding the personnel and facilities through which BDS's are distributed and the manner in which they are stored and handled.

Accordingly, manufacturers and distributors of prescription BDS's that engage in wholesale distribution of these substances are required, under section 503(e)(2)(A) of the act and part 205, to be State licensed wholesale distributors and to meet other requirements for wholesale distribution of prescription drugs under PDMA and the agency's regulations.

Thus, for prescription BDS's imported into the United States, including BDS's intended for pharmacy compounding, the person responsible for the importation of such BDS is engaged in the wholesale distribution of a prescription drug and must be State licensed in the State into which the prescription BDS is imported and from which distribution of such BDS occurs. In addition, any agent or wholesaler that subsequently distributes the BDS in

interstate commerce must be licensed by the State from which the distribution occurs. For domestically manufactured prescription BDS's, the BDS manufacturer must be licensed by the State where its facilities are located. Agents that subsequently distribute the prescription BDS must be licensed by the State from which the distribution of the BDS occurs.

In addition, any agent or distributor that is not an authorized distributor of record must provide a statement of origin before distributing the BDS. Thus, except for those prescription BDS distributors that have a written agreement with the BDS manufacturer to distribute the manufacturer's products for a period of time or for a number of shipments, prescription BDS distributors must provide a statement of origin showing all prior sales and purchases of the prescription BDS being distributed and the names and addresses of the parties to such transactions. Under § 203.50(c) of the final rule, a manufacturer that subjects a prescription BDS to any additional manufacturing processes to produce a different drug is not required to provide to a purchaser a drug origin statement.

G. Application of PDMA to Radiopharmaceuticals

87. One comment requested that distributions of radiopharmaceuticals be exempt from the definition of wholesale distribution in proposed § 203.3(y) and part 205 such that State licensing and drug origin statement requirements would be inapplicable to these drugs. The comment made the following points about radiopharmaceuticals: (1) Radiopharmaceuticals differ from other prescription drugs in that their radioactive component causes them to lose clinical effectiveness within a few days of manufacture; (2) radiopharmaceuticals are prepared in small quantities, shipped overnight, and used the same day they are received; (3) neither manufacturers nor retailers can have inventory of these drugs for longer than a couple of days; (4) the unique properties of radiopharmaceuticals make many of the storage, handling, and accountability considerations of part 205 inapplicable; (5) regulation by FDA would be inappropriate and was not intended by Congress because it would duplicate existing regulations by several Federal, State, and local agencies; (6) existing regulations cover how radiopharmaceuticals are manufactured, packaged, labeled, stored, shipped, used, and controlled; and (7) radiopharmacies are licensed under State retail pharmacy laws that impose

requirements relating to facilities, security, storage, and recordkeeping.

The agency declines to adopt the exclusions recommended by the comment. The term radioactive drugs, as defined under 21 CFR 310.3(n), encompasses both radioactive and nonradioactive drug products. Radioactive drugs include drug products derived from by-product materials from nuclear reactors (i.e., radionuclide generators), cyclotron-produced products (i.e., Ga-67 Citrate, Tl-201 Chloride, and In-111 Oxide), and positron emission tomography products (e.g., Rubidium-82 and fludeoxyglucose). Nonradioactive reagent kits are also radioactive drugs and are compounded with radioactive substances by radiopharmacies or hospitals to make the final drug product.

As the comment points out, most radioactive drugs have a limited shelf-life which requires that they be distributed in a different manner than many prescription drugs. In addition, certain Federal and various State requirements for shipping, storage, handling, and recordkeeping apply to radioactive drugs. However, as discussed previously in conjunction with medical gases and the comments on bulk drugs, PDMA applies to all prescription drugs. Therefore, unless there is a clear indication in PDMA or its legislative history that Congress did not intend for PDMA to apply to a specific class of drugs, the agency does not believe that it is appropriate to exempt the class from PDMA requirements and restrictions. Except for the factors mentioned above, there is no indication in PDMA or its legislative history that Congress intended that radioactive drugs be treated differently than other types of prescription drug products. The agency does not believe that these factors, by themselves, indicate a clear congressional intent to exempt radioactive drugs from PDMA or to exclude radioactive drugs from specific PDMA requirements.

H. Wholesale Distribution

1. Section 203.50(a) and (a)(6)

Proposed § 203.50(a) and (a)(6) stated:
 * * * Before the completion of any wholesale distribution by a wholesale distributor of a prescription drug for which the seller is not an authorized distributor of record to another wholesale distributor or retail pharmacy, the seller shall provide to the purchaser a statement identifying each prior sale, purchase, or trade of such drug. This identifying statement shall include:
 * * * The business name and address of all parties to each prior transaction involving the drug, starting with the manufacturer * * *.

88. One comment objected to § 203.50(a) and (a)(6) because it would require an unauthorized distributor to provide information about all prior sales, purchases, or trades of the drug, starting with the manufacturer, even in cases where the seller from whom the distributor received the drug was an authorized distributor of record and did not provide any pedigree for the drug. The comment stated that "the proposed regulation would make it impossible, as a practical matter, for authorized distributors to sell into the [prescription] specialty market without providing a pedigree," which was not intended by Congress. The comment recommended revising the proposed rule to require that the drug origin statement (i.e., the "pedigree") only go back to the last authorized distributor of record.

The agency declines to revise the proposal in the manner suggested by the comment. Section 503(e)(1)(A) of the act requires that, prior to completion of a wholesale distribution of a prescription drug by a person who is not the manufacturer or an authorized distributor of the drug, a statement must be provided to the recipient identifying each prior sale, purchase, or trade of the drug, including the date of the transaction and the names and addresses of all parties to the transaction. There is no indication in PDMA that Congress intended that the statement include only those sales, purchases, or trades since the drug was last handled by an authorized distributor. Thus, an unauthorized distributor is required to provide a full drug origin statement in accordance with PDMA and the final rule whether or not it has purchased a prescription drug from an authorized distributor of record. Although the agency encourages authorized distributors to provide a drug origin statement to unauthorized distributors, they are not required to do so under PDMA or the final rule.

89. In the preamble to the proposal (59 FR 11842 at 11856 and 11857), the agency discussed at length its views on the use of coding that represents required information on the drug origin statement. The agency stated that, since the enactment of PDMA, FDA's position has been that the use of coded statements on the drug origin statement that make information unintelligible to purchasers without the intervention of a third party to decipher the code (e.g., "this shipment of drugs came from unauthorized distributor RS47GS2273") does not provide purchasers with the information that Congress intended that they receive. Moreover, the PDA, which amended section 503(e)(1) of the act to

require, among other things, that the drug pedigree contain the "names and addresses of all parties to the transaction," made clear that product source codes may not be used on the drug pedigree as a substitute for required information.

One comment supported the agency's position on the use of coding. The comment stated that the practice of using codes places a large burden on distributors and recommended that the agency go a step further and revise the proposed regulations to prohibit the use of product source codes on drug origin statements.

The agency believes that its position against the use of product source codes as a substitute for the name and address of buyers or sellers in drug origin statements was adequately addressed in the preamble to the proposal and restated here. Accordingly, the agency declines to codify a prohibition on the use of such codes in the final regulation.

2. Section 203.50(b)

The agency has added § 203.50(b) to clarify that the drug origin statement is subject to the revised record retention requirements of § 203.60(d) and must be retained by all wholesale distributors involved in the distribution of the drug product, whether authorized or unauthorized, for 3 years. The agency is providing this clarification in response to numerous inquiries that it has received since the proposed rule was published.

3. Section 203.50(c)

Proposed § 203.50(c) stated: "Each manufacturer shall maintain at the corporate offices a current written list of all authorized distributors of record." Proposed § 203.50(c)(3) stated: "Each manufacturer shall make its list of authorized distributors of record available on request to the public for inspection or copying. A manufacturer may impose reasonable copying charges for such requests from members of the public."

90. One comment recommended that the list of distributors could be maintained at any company site and could be made available via electronic media or within 24 hours to other sites.

The rule does not require company records to be kept at every company site. As long as a company can produce the required information for review and copying by FDA or other Federal, State, or local law enforcement agencies at the site where they are requested within 2 business days, the company may maintain its records at a central location.

91. Several comments objected to the proposed requirement that manufacturers must make their list of authorized distributors of record available to the public. The comments stated that this information is proprietary in nature and should be kept confidential. One comment stated that FDA has acknowledged that this information was considered proprietary in the past.

Other comments stated that providing such information is unduly burdensome on manufacturers. One comment recommended adding a "reasonable hours of inspection and reasonable copying charges" provision to the section. Another comment recommended revising the section to require only that industry respond to individual inquiries about whether a specific wholesaler is an authorized distributor of record.

The requirement that manufacturers maintain a current list of authorized distributors of record appears at section 503(e)(1)(B) of the act. In the legislative history, Congress stated that this list must be made available for public inspection. (See S. Rept. 100-303, p. 7.) Thus, the agency believes that denying public access to lists of authorized distributors maintained by manufacturers would contradict Congress' clearly expressed intent.

In addition, the agency disagrees that a manufacturer's list of authorized distributors constitutes proprietary or confidential information. No provision of PDMA or the act designates such information as proprietary, and the agency is unaware of other laws or regulations that designate such information as proprietary. Moreover, the agency has not previously stated that this information is proprietary. In fact, in a 1988 letter to regulated industry (see Letter from Daniel L. Michels, Director, Office of Compliance to Regulated Industry, Docket No. 88N-258L, August 1, 1988), the agency specifically requested that manufacturers make lists of authorized distributors available at reasonable charge to any requesting person.

Finally, the final rule permits manufacturers to impose reasonable copying charges for requests. Such charges could include clerical time used to create copies, copying costs, and mailing costs, if the requested copies are mailed. Therefore, except for costs associated with creating, updating, and maintaining the authorized distributors lists themselves (a cost that has been evaluated separately by the agency in the "Paperwork Reduction Act of 1995" section under § 203.50(d)), the cost to

comply with revised § 203.50(d)(3) should be reimbursed.

4. Sales to Licensed Practitioners by Retail Pharmacies

In the preamble to the proposal (59 FR 11842 at 11858), the agency stated:

FDA believes that permitting the sale of small quantities of prescription drugs by retail pharmacies to licensed practitioners for office use without the requirement of a State wholesale distributor's license satisfies a legitimate need and is consistent with the intent of the statute. Accordingly, the agency has included language in proposed § 203.3(y) that would exclude the sale of minimal quantities of drugs by retail pharmacies to licensed practitioners for office use from the definition of "wholesale distribution."

In this context, sales of prescription drugs by a retail pharmacy to licensed practitioners for office use will be considered to be minimal if the total annual dollar volume of prescription drugs sold to licensed practitioners does not exceed 5 percent of the dollar volume of that retail pharmacy's annual prescription drug sales.

92. One comment supported the agency's decision to exclude minimal sales of prescription drugs by retail pharmacies from the definition of wholesale distribution and recommended that the 5 percent threshold be codified in the final regulation under § 203.3(y)(11).

The agency believes that its position on what constitutes a minimal amount of prescription drugs for the purposes of revised § 203.3(cc)(10) was adequately explained in the preamble to the proposal and need not be codified.

93. Another comment recommended that the 5 percent threshold be increased to 20 percent and should be based on annual, not monthly or weekly, sales of a retail pharmacy. According to the comment, the 5 percent threshold would disadvantage small, independent pharmacies because a large percentage of their sales is derived from supplying local practitioners with prescription drugs. The comment also said that the 5 percent threshold could be reached easily by a pharmacy that supplies expensive drugs, such as chemotherapy medications, to practitioners.

The distribution of prescription drugs to practitioners for office use constitutes wholesale distribution under section 503(e) of the act and proposed § 203.3(y) (i.e., distribution to other than a consumer or patient). The agency excluded the sale of minimal quantities of drugs by retail pharmacies to licensed practitioners for office use from the definition of wholesale distribution to meet the needs of licensed practitioners who may not purchase enough prescription drugs to go through a wholesale distributor and thus may not

otherwise be able to easily obtain drugs for office use. Thus, the exemption was not created to confer a special benefit on retail pharmacies, but to meet the legitimate needs of licensed practitioners. The agency believes that the 20 percent threshold recommended by the comment is inconsistent with the purpose of the exemption and declines to follow the recommendation. The agency notes that a retail pharmacy is not precluded from making more than 5 percent of its annual sales to licensed practitioners. It must, however, obtain a State wholesale distributor license to do so.

I. Request and Receipt Forms, Reports, and Records

1. Section 203.60(e)(1)

Proposed § 203.60(e)(1) stated: "Any person required to create or maintain reports, lists, or other records under PDMA, PDA, or this part shall retain them for at least 3 years after the date of their creation."

94. One comment objected to the proposed requirement in § 203.60(e)(1), stating that it conflicts with the 2-year retention period requirement under § 205.50(f)(2). The comment said that changing the record retention time in the manner proposed would "require 44 states that adopted FDA's 2-year standard to enact legislative and/or regulatory changes in order to have licensing programs that meet the minimum federal requirements." The comment also said that changing to a 3-year record retention period would serve no apparent public health purpose, citing the agency's rationale behind the 2-year requirement in the preamble to the final rule on State wholesale licensing guidelines. The comment recommended that the proposed section should be revised to require record retention for 2 years for all records kept by prescription drug wholesalers under PDMA.

Section 205.50(f)(1) requires that inventories and records of transactions regarding the receipt and distribution or other disposition of prescription drugs be created and maintained. Section 205.50(f)(2) requires that such records be "made available" to authorized Federal, State, or local law enforcement agencies for a period of 2 years following the disposition of the drugs to which the record relates. Because the requirement under proposed § 203.60(e)(1) that records be retained for 3 years after the creation of the record would apply to records required by § 205.50(f)(1), the requirements could potentially be conflicting. This result

was not anticipated by FDA at the time the proposed rule was issued.

The agency agrees with the comment that it is appropriate to establish one record retention period for all wholesale distribution records required to be created and maintained under PDMA and parts 203 and 205. The agency has determined that because the shelf life of the majority of prescription drug products is longer than the 2-year period specified in § 205.50(f)(2), that period is insufficient to facilitate recalls by manufacturers and to enable the agency to respond to public health emergencies related to prescription drug distribution. Moreover, certain records required to be created and maintained under part 203, such as drug origin statements and written authorization agreements between manufacturers and distributors, are not linked to the disposition of a particular drug product or drug products. Therefore, the agency has decided to adopt the record-retention period specified in proposed § 203.60(e)(1) (renumbered § 203.60(d)), which is 3 years from the time of creation of a record, for all wholesale distribution records required under PDMA, including those wholesale distribution records required under § 205.50(f)(1). Section 205.50(f)(2) has been amended to incorporate the 3-year requirement.

2. Section 203.60(e)(2)

Proposed § 203.60(e)(2) stated: "Any person required to create or maintain reports, or records relating to the distribution of drug samples shall retain them for at least 3 years after the date of their creation or 3 years after the date of expiration of a drug sample for which the record is being kept, whichever is later."

95. Several comments contended that the additional burdens that would result from record retention requirements over 3 years outweigh the possible benefits. One comment stated that the proposed section would require drug sample records to be kept a minimum of 6 years. Two comments stated that it could require record retention for 8 years. One comment stated that "if a practitioner signs a receipt for two different drug samples with different expiration dates, a manufacturer has to go through line by line to see if a record has to be kept." A similar comment stated that the proposed section would require either implementation of a complicated and expensive process for retaining records to make maximum effective use of storage space or storage of all records for the same length of time, taking into account the drug with the longest shelf life plus 3 years.

Two comments stated that section 503(d)(2)(C) and (d)(3)(C) of the act specifically require that records for drug samples be maintained for 3 years and that FDA has no authority to require retention for a longer period.

Several comments recommended that the proposed section be revised to require a maximum record retention period of 3 years. One comment recommended revising the section to require retention for the greater of 3 years from the time of creation or 1 year after the date of expiration. Another comment recommended allowing manufacturers and distributors to decide how to meet PDMA requirements, while still being accountable to provide a complete distribution history.

The agency agrees that the burdens associated with the record-retention requirement in proposed § 203.60(e)(2) may outweigh its benefits. Although the use of the expiration date as a reference point would ensure that the record is kept for the full shelf life of the drug sample, drug sample distribution records may refer to different types of drugs from varying lots that have different expiration dates. Thus, as noted by the comments, requiring a record retention period based on expiration dating would necessitate maintaining different distribution records for different periods of time or maintaining all records for a period that is based on the drug or drugs with the longest shelf life. The agency believes that retention of records relating to drug samples for 3 years from the time of their creation is sufficient to effectuate recalls and to maintain accountability over sample distribution. Accordingly, the agency has eliminated proposed § 203.60(e)(2) in the final rule. Under revised § 203.60(d), all records under PDMA and part 203, including records relating to the distribution of drug samples, must be retained for 3 years from the date of their creation.

3. Section 203.60(e)(3)

On its own initiative, the agency is deleting proposed § 203.60(e)(3) in the final rule. The proposed requirement would have required manufacturers and authorized distributors of record to maintain records of drug sample distribution identifying the drugs distributed, the recipients of the distributions, and all drug samples destroyed or returned to the manufacturer for 3 years. The agency believes that the final rule, as revised, contains adequate recordkeeping provisions to ensure accountability over drug sample distribution.

4. Section 203.60(f)

Proposed § 203.60(f) stated that any person required to create or maintain request and receipt forms, reports, lists, or other records under PDMA, PDA, or part 203 shall make them available upon request, in a form that permits copying or other means of duplication, to FDA or other Federal, State, or local regulatory and law enforcement officials for review and reproduction.

On its own initiative, the agency has revised proposed § 203.60(f) (renumbered § 203.60(e)) to specify that the records must be made available within 2 business days of a request. The agency believes that this constitutes a reasonable period of time to obtain records kept off-site and is consistent with other PDMA record production requirements.

J. Penalties and Rewards

In the preamble to the proposed rule (59 FR 11842 at 11860), the agency stated that "most violations of the act are punishable as misdemeanors." The agency later stated that "most PDMA violations are felonies punishable by a prison term of not more than 10 years, a fine of not more than \$250,000, or both * * *."

96. One comment stated that the two statements made by the agency are conflicting and should be reconciled.

The agency clarifies that the first statement ("most violations of the act are punishable as misdemeanors") refers to the entire act (see sections 303(a)(1) and (a)(2) of the act), not the PDMA provisions. As stated in the preamble to the proposed rule (59 FR 11842 at 11860), most PDMA violations, except for the distribution of a drug sample in violation of section 503(d) of the act and the failure to comply with the drug origin statement requirement in section 503(e)(1)(A) of the act, are felonies.

K. Amendments to 21 CFR Part 205

In the proposal, the agency proposed an amendment to the introductory paragraph of § 205.50(c) that would require that prescription drugs be stored by wholesale distributors at appropriate temperatures and under appropriate conditions in accordance with the labeling requirements of the drugs or with the requirements of USP XXII. The agency also proposed an amendment to § 205.50(c)(1) that would require that, if no storage requirements are established for a prescription drug, the drug must be held at "controlled room temperature" as defined in USP XXII. Current § 205.50(c)(1) states that, if no storage requirements are established for a prescription drug, the drug "may" be

held at controlled room temperature as defined in an official compendium.

97. One comment objected to the proposed changes to § 205.50(c) on the grounds that FDA incorrectly characterized the changes as “technical changes” in the preamble and has given inadequate notice and opportunity to comment on the changes under section 553 of the Administrative Procedures Act (APA). The comment stated that incorporation by reference of USP standards in § 205.50(c) and requiring adherence to USP standards for controlled room temperature in § 205.50(c)(1) would significantly increase the burdens on industry in complying with § 205.50. According to the comment, such “substantive” changes cannot be made unless FDA fully informs interested parties about the elements of the new standard, including any new compliance obligations, and provides an opportunity for comment on the impact of the changes. The comment recommended that “FDA initiate rulemaking proceedings that will adequately apprise interested parties of the issues involved” and forbear from enforcing the proposed changes until the completion of the rulemaking.

The agency agrees that the proposed amendments to § 205.50(c) amount to more than “technical changes” and that they should be the subject of a separate proposal with a more detailed explanation of the associated issues and impacts. Accordingly, the agency has decided to withdraw its proposal of these amendments. Should the agency decide to repropose the amendments in the future, it will do so in a manner that provides sufficient notice and opportunity for comment.

L. Analysis of Impacts in the Proposed Rule

In the section entitled “Analysis of Impacts” in the preamble to the proposal (59 FR 11842 at 11860 and 11861), the agency provided its assessment of the impacts of the proposed rule under Executive Order 12866 and the Regulatory Flexibility Act (Public Law 96–354). The agency stated that the proposed rule is consistent with the principles set out in the Executive Order and is not a significant regulatory action as defined by the Executive Order. The agency explained that most of the requirements in the proposed rule have already been implemented by the regulated industry in response to PDMA’s enactment, FDA’s guidance, and industry trade associations’ recommendations. The agency determined that the regulatory costs of the proposal are due to increased

paperwork requirements. The costs were calculated by multiplying the estimated time necessary to complete the paperwork for each section of the proposal by a standard hourly wage rate. In addition, based on its finding that many of the requirements in the proposed rule have been implemented by regulated industry, including small entities, the agency certified that the proposed rule would not have a significant economic impact on a substantial number of small entities.

98. One comment stated that “FDA’s assessment of all costs and benefits of available regulatory alternatives and selected regulatory approaches does not prove that the proposed rule maximizes net benefits.” The comment stated that the proposed rule will have a “significant negative effect on the industry, health care costs, the environment, and State licensing agencies.” This impact, the comment stated, is not outweighed by benefits in controlling, preventing, or detecting diversion, or by adding significantly to the safety of the consumer. Another comment stated that the proposed rule would add significant costs, including new systems costs, without corresponding benefits.

The agency believes that the final rule is consistent with the principles set forth under Executive Order 12866. The benefits of the final rule, including the public health and safety benefits, have been discussed extensively in the proposal and in this notice. The estimated costs to industry of the final regulation, which are due primarily to additional paperwork costs, are set forth in section IV.B of this document and have been substantially revised from the estimates provided in the proposal. The agency has attempted to accurately represent the benefits and costs of the final regulation, has carefully analyzed them, and believes that the regulatory approaches chosen for the final rule maximize net benefits.

99. One comment stated that the agency’s financial impact estimates are “much too low.” According to the comment, FDA has not considered costs associated with the proposed requirements, including travel and personnel expenses in conjunction with inventorying sales representatives and conducting investigations, increased paperwork in conjunction with comarketing agreements, and administrative and other costs in conjunction with longer record maintenance periods and tracking of bid and commercial samples.

As discussed in section IV.C of this document, the agency has significantly increased its estimates of the reporting

and recordkeeping burdens associated with the final rule under the Paperwork Reduction Act of 1995. In addition, the agency has revised the analysis of impacts section in the final rule to include estimates of nonpaperwork costs of the final rule, such as storage costs associated with retaining records.

100. Two comments disagreed with FDA’s assertion that most of the proposed requirements have been implemented by the industry in response to PDMA’s enactment, FDA’s guidance, and industry trade associations’ recommendations. One of the comments stated that the proposed rule contains items which are a “significant departure” from currently understood requirements. The comment cited the following specific proposed requirements and recommendations: The requirement under proposed § 203.60(e)(2) for retention of drug sample records for 3 years past the expiration date of the drug sample; the requirement under proposed § 203.37(b) for reporting possible falsifications of drug sample records; the requirement under proposed § 203.38(c) for labeling of sample units; the requirements under proposed §§ 203.30 and 203.31 for drug sample receipts; and the agency’s recommendation in the proposal that bid or commercial samples be tracked using PDMA sample controls.

As discussed previously, many of the proposed requirements and recommendations cited by the comment have been deleted or substantially modified in the final rule in response to other comments or on the agency’s initiative. Nevertheless, FDA acknowledges that some of the proposed requirements may not have been implemented by industry at the time the proposal was published and that too much reliance may have been placed by the agency on prior industry implementation in the “Analysis of Impacts” section of the proposal. The agency has significantly revised its analysis of impacts for the final rule.

M. Estimated Annual Reporting and Recordkeeping Burden

101. Several comments stated that the estimated burdens set forth under the “Paperwork Reduction Act of 1980” section of the proposed rule (59 FR 11842 at 11861) were too low. One comment stated that FDA grossly underestimated the annual reporting and recordkeeping burden and that both industry and FDA will be burdened more than anticipated by implementation of many of the regulations. Another comment stated that “the agency’s predicted time estimates to comply with the rule are so

unrealistic as to be arbitrary and capricious.”

One comment cited specific examples of estimates that it considered to be too low. The comment stated that the agency's estimate of 30 minutes to comply with the recordkeeping requirements under proposed § 203.31(d) “grossly understates the time and expense to comply.” The comment stated that the estimate of 30 seconds to comply with §§ 203.30(c) and 203.31(c) takes into account only the time necessary to sign a sample receipt, but not the time necessary for a representative to fill out the receipt with the required information or the time that a representative will have to wait for a practitioner or his or her designee to sign the receipt. The comment stated that the agency's estimate of 30 and 60 minutes to meet the recordkeeping requirements under proposed § 203.37(a) and (b), respectively, may accurately reflect the time necessary to write up the report, but not to initiate and complete a thorough investigation. According to the comment, the estimate of 24 hours to prepare policies and procedures under proposed § 203.34 underestimates the time it will take for a company to research its activities, prepare and revise draft guidance documents, type the material, and obtain management approval. The comment stated that the agency neglected to provide an estimate for the time it will take to comply with proposed § 203.60. Finally, the comment stated that FDA has ignored the burden the proposal will place on the agency.

Based upon the comments, the agency has significantly modified and increased its estimate of the reporting and recordkeeping burdens associated with the final rule under the section of this notice entitled “Paperwork Reduction Act of 1995.” Regarding the absence of a burden estimate for proposed § 203.60, the agency advises that it has included an estimate of the costs associated with the record retention requirement in revised § 203.60 in section IV.B of this document. Finally, the agency expects its administrative costs associated with oversight of the final rule to be minimal. As discussed below, the public has 60 days from the publication of the final rule to comment on the accuracy of FDA's revised burden estimates, and the agency encourages interested parties to do so.

IV. Analysis of Impacts

FDA has examined the impacts of the final rule under Executive Order 12866, the Regulatory Flexibility Act (5 U.S.C. 601–612), and the Unfunded Mandates

Reform Act (Public Law 104–4). Executive Order 12866 directs agencies to assess all costs and benefits of available regulatory alternatives and, when regulation is necessary, to select regulatory approaches that maximize net benefits (including potential economic, environmental, public health and safety, and other advantages; distributive impacts; and equity). The Regulatory Flexibility Act requires an analysis of regulatory options that would minimize any significant economic impact of a rule on small entities unless an agency certifies that a rule will not have a significant economic impact on a substantial number of small entities. The Unfunded Mandates Reform Act requires that agencies prepare an assessment of anticipated costs and benefits before proposing any rule that may result in the expenditure by State, local, and tribal governments, in the aggregate, or by the private sector, of \$100 million (adjusted annually for inflation) in any 1 year. The agency believes that this final rule is consistent with the regulatory philosophy and principles identified in the Executive Order, Regulatory Flexibility Act, and Unfunded Mandates Reform Act.

A. Regulatory Benefits

Through this regulation, the agency is establishing procedures and requirements implementing PDMA. As discussed extensively above and in the preamble of the proposed rule, the requirements in the final rule will, consistent with Congress' intent in enacting PDMA, help to prevent the sale of subpotent, adulterated, counterfeit, or misbranded prescription drugs and drug samples to the American public. For example, the final rule establishes procedural and recordkeeping requirements for drug sample distribution that will help to prevent the diversion and sale of drug samples. The final rule also establishes wholesale distribution requirements that will permit the distribution chain of prescription drugs to be traced, and will make unauthorized wholesale distributors more accountable. In sum, the final rule establishes controls over the distribution of prescription drugs and drug samples that will help to ensure that drugs are safe and effective not only when they leave manufacturers, but when they reach consumers.

B. Regulatory Costs

FDA estimates that the incremental costs that will result from the issuance of this rule will amount to about \$43 million annually. Moreover, industry

will continue to incur an estimated \$39 million in annual costs for those activities initiated shortly after PDMA was enacted into law by Congress 10 years ago. Thus, the total cost of PDMA and this implementing rule is approximately \$82 million. Almost all of the costs are associated with sample distribution, and most are related to paperwork requirements.

1. Cost of Sample Distribution Requirements

a. *Paperwork costs.* The paperwork section of this preamble shows the hourly reporting and recordkeeping burden estimates for all of the sample distribution requirements, including the following: Request and receipt forms, license verification, inventory of representatives, notification of FDA and investigation of losses and falsified information, representative lists and sample storage sites, representative conviction reports, written policies, assignment of individuals responsible for sample information, donation records, and inventory records and reconciliation reports. These costs will be shared by those manufacturers, distributors, and charities subject to the above requirements. These individuals should already possess the necessary professional skills to comply with these paperwork requirements. To determine the paperwork costs for the sample distribution requirements, FDA assumed that sales representatives would complete the majority of the request and receipt forms. In the case of sample distribution by mail or common carrier, the agency assumed that an administrator in the practitioner's office would complete the request and receipt forms. Also, the agency believes that an individual in the office would be authorized to sign the receipt forms for the practitioner. Using 1995 hourly earnings of approximately \$24⁴ (including 40 percent for benefits) for sales representatives and executive, administrative, and managerial positions, the estimated total annual paperwork costs for the sample distribution requirements are \$79 million. Approximately \$36 million of these costs have been incurred annually since PDMA's enactment. The remaining \$43 million are sample paperwork costs that will go into effect as a result of this regulation. These additional costs include: \$22.6 million for receipt recordkeeping, \$2.6 million for license verification, \$2.1 million for establishing written policies and

⁴ *Employment and Earnings*, U.S. Department of Labor, Bureau of Labor Statistics, January 1996, pp. 205 and 206.

procedures for sample distribution, and \$15.6 million for the lot or control number requirements.

b. *Other request and receipt form costs.* Sample request and receipt forms are required under PDMA for samples delivered by mail or common carrier. Under the final rule, FDA is also requiring receipt forms to be used when samples are delivered by representatives. To minimize printing and storage costs, FDA believes companies will primarily use one combination request and receipt form for samples delivered by representatives and separate request and receipt forms for mail delivery. Therefore, a total of three forms will be used, one of which will be new with this rule. The agency estimates that the development and approval of each form may take approximately 2 hours of an administrator's time. Taking into consideration the 2,208 manufacturers and distributors who distribute samples (691 manufacturers of pharmaceutical preparations⁵ plus 25 percent of the 6,069 establishments of wholesale distributors of drugs, drug properties, and druggists' sundries⁶), the total one-time cost of developing these forms is approximately \$318,000 (2 hours x 3 forms x 2,208 x \$24). Of this amount, the one-time cost of developing the additional form attributable to this regulation is approximately \$106,000 (2 hours x 1 form x 2,208 x \$24).

Manufacturers and distributors also incur annual printing costs associated with the distribution of these forms. After evaluating several printing estimates, the agency selected \$0.025 per page as a reasonable printing cost. Based on the paperwork estimates of approximately 32.5 million request and receipt forms for delivery by representatives⁷ and 750,000 receipt forms for mail-delivery (20 percent of 309,807 offices and clinics of doctors of medicine and dentists⁸ x 12 per year), the agency estimates that manufacturers and distributors incur printing costs of approximately \$831,000 annually ((32.5 million + 750,000) x 0.025). FDA does

not include any printing costs for mail-requests, assuming that a paper exchange already occurred in the marketplace for this purpose. In addition, the agency believes that, in most cases, manufacturers and distributors will combine the receipt and request forms when samples are delivered by a representative. Therefore, none of the above printing costs are new to this regulation.

c. *Other license verification costs.* The final rule will require manufacturers and authorized distributors of record to verify with the State that the practitioner to whom samples are distributed is licensed or authorized by law to prescribe the drug product. To evaluate the cost of compliance with this requirement, the agency spoke with a representative of the Board of Physician Quality Assurance in Maryland. FDA found that it costs approximately \$500 to purchase a list of all active practitioners with a license in the State of Maryland. Due to the high cumulative cost for each manufacturer to purchase a list from every State (or from as many States as their distribution reaches), provide it to their distributors, and update it on a regular basis, it is likely that market forces will establish a more efficient process. For example, a third party could easily purchase the information and sell it to manufacturers. Considering the costs for third parties to purchase, manipulate, and disseminate this information, the agency believes that \$500 to \$1,000 would be a reasonable price range for charges by third parties to manufacturers for nationwide data. For the purpose of this analysis, FDA assumes that each of the 691 manufacturers⁹ would pay an average of \$750 each year, yielding total annual costs of approximately \$518,000 to meet the license verification requirement. The agency does not calculate any costs for manufacturers to disseminate this information, but instead assumes that the license numbers would be added to the list of physicians that is currently provided to sales representatives on a yearly basis.

d. *Other sample distribution requirements.* The other requirements of the rule entailed negligible costs, were already part of industry practice, or were attributable to the overall cost of doing business. For example, FDA assumes all charities that receive samples have a licensed practitioner on staff and that the cost of examining drug sample packaging is negligible. The final rule also permits the inventory of samples held by sales representatives to be conducted by the representatives

themselves. Therefore, no travel expenses will be incurred for this purpose. The agency also assumes that most manufacturers and distributors and their representatives are currently following proper storage and handling requirements to prevent the distribution of adulterated samples. In addition, the agency believes that it is already part of company policy for manufacturers and distributors to investigate significant losses and known thefts of samples and common practice to label sample units so they may be tracked in recall situations.

2. Nonsample-Related Costs

To determine the costs associated with the nonsample-related requirements, the agency multiplied the \$24 hourly rate¹⁰ for sales representatives and executive, administrative, and managerial positions by the burden hours estimated under the paperwork section of this preamble. These annual paperwork costs are grouped into the following categories: Reimportation, sales restrictions, and wholesale distribution. To calculate reimportation costs, the agency used the salary data for executive and managerial positions. As few requests for emergency reimportation are expected, the annual paperwork costs for all reimporters to fill out the emergency reimportation application total only \$144. The annual cost of the credit memo and storage documentation required under "Sales Restrictions" is shared by hospitals, healthcare entities, and charities, and is estimated at \$1.3 million. Wholesale distribution requirements, including the drug origin statement and distributor list, are estimated to impose recordkeeping costs of \$258,000 per year on manufacturers and distributors. All of the previous costs were initiated by the enactment of PDMA and will not be significantly affected by the issuance of this rule.

3. Storage Costs for Sample and Nonsample-Related Requirements

The final rule requires that manufacturers and/or distributors retain records for at least 3 years, including the following documents: Drug return memos, request and receipt forms, drug sample inventory records and reconciliation reports, representative lists, and drug origin statements. In 1995, the average expected annual rent for space in commercial buildings equaled \$9.43 per square foot.¹¹ For

⁵ "Drugs Industry Series," 1992 Census of Manufacturers, U.S. Department of Commerce, Economics and Statistics Administration, Bureau of the Census, Table 4, pp. 28C to 12.

⁶ "United States," 1992 Census of Wholesale Trade, U.S. Department of Commerce, Economics and Statistics Administration, Bureau of the Census, Table 1, pp. US to 11.

⁷ Data from IMS, 1996, as presented to FDA on May 27, 1997. Data included an estimated 18.1 million office calls, 8.1 million service calls, and 6.3 million hospital calls made in 1996.

⁸ "Establishment and Firm Size," 1992 Census of Service Industries, U.S. Department of Commerce, Economics and Statistics Administration, Bureau of the Census, Tables 1a and 1b, pp. 1 to 38 and pp. 1 to 51.

⁹ "Drugs Industry Series," Table 4, pp. 28C to 12.

¹⁰ Employment and Earnings, pp. 205 and 206.

¹¹ Dodge, F. W., Dodge Construction Potentials, McGraw-Hill, Inc., 1996.

each of the first 3 years, the agency estimates that an additional 5 square feet of storage space per affected manufacturer and distributor will be needed to accommodate the record retention requirements. After the third year, each subsequent year's records can replace the most previous year's, indicating that no more than 15 square feet of storage space will be necessary. FDA estimates that up to approximately 2,500 manufacturers and distributors will be affected; therefore, average annual storage costs will amount to approximately \$118,000 in year 1, \$236,000 in year 2, and \$354,000 in each year thereafter. Though retention of drug return memos is also required of hospitals and charities, the agency believes these costs are negligible. Some of these storage requirements were initiated by PDMA, but other storage requirements have been added by this regulation. The agency did not separate these storage costs for the purpose of this analysis.

C. Small Business Analysis

The agency has analyzed this rule in accordance with the Regulatory Flexibility Act to determine its effect on small entities.

1. Need for and Objectives of the Rule

As stated previously, PDMA was enacted by Congress to prevent the sale of subpotent, adulterated, counterfeit, or misbranded drugs. Through this regulation, the agency is establishing the procedures and requirements to implement PDMA. The final rule facilitates the goals of PDMA by establishing procedural and recordkeeping requirements for drug sample distribution that will help to prevent the diversion and sale of drug samples. In addition, the final rule establishes wholesale distribution requirements that will permit the distribution chain of prescription drugs to be traced, and will make unauthorized wholesale distributors more accountable.

2. Description and Estimate of the Number of Small Entities

According to the Small Business Administration (SBA), distributors of drugs, drug proprietaries, and druggists' sundries with 100 or fewer employees or manufacturers of pharmaceutical preparations with 750 or fewer employees are considered small entities. The U.S. Census does not disclose data on the number of drug manufacturing firms by employment size, but between 92 percent and 96 percent of drug manufacturing establishments, or approximately 650 establishments, are

small under this definition.¹² Although the number of firms that are small would be less than the number of establishments mentioned above, FDA still concludes that the majority of pharmaceutical preparation manufacturing firms are small entities. In addition, the agency found that 94 percent of the distribution firms, or approximately 4,000 firms, are small.¹³ However, as stated previously, the agency believes that the majority of these do not distribute samples, and thus will not be affected by the rule. According to SBA's definition, general medical and surgical hospitals, and the offices and clinics of dentists and doctors of medicine that are either not-for-profit or have \$5 million or less in revenue are also considered small. Using this definition, FDA determined that approximately 96 percent of the hospitals (or approximately 4,000 hospitals)¹⁴ and 99 percent of the offices and clinics (or approximately 268,000 offices and clinics)¹⁵ are small. In addition, due to their nonprofit status, the agency assumes that the 3,112 charities expected to be affected by this rule (based on a portion of not-for-profit hospitals,¹⁶ doctors' offices, and clinics¹⁷) would be considered small by SBA. As noted in the paperwork section of this regulation, FDA believes that approximately 12 importers will be affected by this rule, and assumes that the majority of them are small.

The agency notes that the great majority of the costs of this rule will be incurred by the manufacturers and distributors that distribute drug samples. The costs will not be evenly distributed, but directly related to the size of each company's sales force. According to Census data, less than 10 percent of the manufacturing companies in the pharmaceutical preparations industry have 90 percent of the industry's sales.¹⁸ Likewise, approximately 1 percent of the firms distributing drugs, drug proprietaries,

and druggists' sundries have 74 percent of the industry's sales.¹⁹ Consequently, the largest firms will incur the majority of the drug sample-related costs of this regulation, and the smallest firms will incur relatively few of these costs. While some small reimporers will be affected by the reimportation restriction, this impact will be moderated because most also import non-U.S. drugs or other products. The cost impact on charities will be minimal.

3. Estimate of the Recordkeeping Burden

The majority of the costs of this regulation are derived from the paperwork requirements. The manufacturers, distributors, and charities involved in the sample distribution process are required to comply with the recordkeeping requirements specified earlier in this analysis. These individuals should already possess the necessary skills to establish written policies and procedures, complete forms and applications, and prepare the required documentation. The paperwork specified by this rule does not require any special professional training or skills to complete and would be of a type already being handled by regulatory affairs professionals who are employed by drug manufacturers and distributors.

4. Analysis of Alternatives

FDA could have implemented the rule as proposed, but instead, the agency took several steps to minimize the economic impact on small entities. Specifically, the agency reduced or eliminated several of the requirements under the proposed rule. Examples of this can be found under the requirements for sample inventory, lot or control numbers, sample unit identification, and sample record retention. Under the proposal, the inventory of drug samples held by sales representatives would be conducted by an executive other than the representative or the immediate supervisor. Comments emphasized the costliness of this requirement, indicating it was time consuming and entailed travel expenses to regional sales offices. In response to these comments, the final rule allows sales representatives and their supervisory personnel to conduct the inventory and reconciliation functions. Also, in response to comments on the proposal, FDA reduced the administrative burden

¹² "Drugs Industry Series," Table 4, pp. 28C to 12.

¹³ "Establishment and Firm Size," 1992 *Census of Wholesale Trade*, U.S. Department of Commerce, Economics and Statistics Administration, Bureau of the Census, Table 7, pp. 1 to 186.

¹⁴ "Establishment and Firm Size," 1992 *Census of Service Industries*, Table a and 4b, pp. 1 to 174 and pp. 1 to 184.

¹⁵ "Establishment and Firm Size," 1992 *Census of Service Industries*, Table 4a and 4b, pp. 1 to 171 and pp. 1 to 183.

¹⁶ *The Statistical Abstract of the United States*, U.S. Department of Commerce, Bureau of the Census, 1996, No. 187, p. 127.

¹⁷ "Establishment and Firm Size," 1992 *Census of Service Industries*, Table 1b, pp. 1 to 51.

¹⁸ "Concentration Ratios in Manufacturing," 1992 *Census of Manufacturers*, U.S. Department of Commerce, Economics and Statistics Administration, Bureau of the Census, Table 3.

¹⁹ "Establishment and Firm Size," 1992 *Census of Wholesale Trade*, Tables 7 and 8, pp. 1 to 186 and pp. 1 to 218.

associated with the donation of prescription drug samples to charity. Furthermore, FDA found it unnecessarily burdensome to require that lot or control numbers appear on drug sample records, receipts, and reconciliation reports, as proposed. Therefore, the final rule adds flexibility by allowing the recording of lot or control numbers on other types of records. Also, in response to comments, the agency is allowing the use of adhesive stickers on retail units to designate a sample unit as a sample. The final rule reduces the drug sample record retention period, which was proposed as 3 years from the sample expiration date. The agency decided that retention of drug sample records for 3 years from the date of their creation is sufficient for recall facilitation and proper accountability over sample distribution.

The agency considered minimizing the impact of this rule by not requiring manufacturers and authorized distributors to verify with the State that the practitioner to whom samples are distributed is licensed or authorized by law to prescribe the drug product. However, under the final rule, this license verification requirement was added in response to comments. The cost of this requirement is estimated at approximately \$3.2 million per year. The agency determined that this requirement is the only reliable way of proving that the practitioner requesting samples is actually licensed by a State to prescribe drugs. The agency does not believe that allowing a manufacturer to deem acceptable a license or authorization number on a request form without verifying its authenticity would offer any such assurance.

The agency considered eliminating the receipt requirement for representative-delivered samples. This would reduce the cost of the final regulation by approximately \$22.6 million per year. However, although Congress did not expressly require a receipt for representative-delivered samples, FDA concluded that this requirement is necessary to help ensure effective enforcement, increased accountability and oversight of sample distribution, and to provide adequate safeguards against drug sample diversion.

5. Response to Comments

Several of the comments indicated that the initial economic analysis understated the impact of the proposed rule. FDA reevaluated and significantly increased the paperwork estimates to more accurately reflect industry's implementation of this final regulation.

For example, the agency increased the estimated time for a manufacturer to conduct an annual inventory and complete a reconciliation report from 30 minutes to 40 hours per manufacturer. The agency also increased the amount of time estimated to generate a sample receipt from 1 minute to 3 and 5 minutes for distribution by mail and representative respectively, and the estimated time to investigate possible significant loss or theft of samples from 1 hour to 24 hours. In addition, the agency identified and estimated the burden associated with requirements other than recordkeeping that were not quantified under the proposed rule. For example, FDA allotted 2 hours for the development of each of the sample request and receipt forms. The annual printing costs associated with these forms have also been assessed. Storage costs have been added as necessitated by the paperwork requirements of this regulation.

D. Conclusion

FDA calculated both the incremental costs of this final rule and the costs initially imposed upon the enactment of PDMA, and determined that there are one-time costs of \$318,000 for developing forms, and total annual costs of approximately \$82 million. Approximately \$39 million of these annual costs have been incurred by industry since the enactment of PDMA by Congress in 1988. An estimated additional \$43 million per year will result from the new requirements in this regulation. This rule is not a significant regulatory action as defined by the Executive Order, and is therefore not subject to review under the Executive Order. This rule does not impose any mandates on State, local, or tribal governments, nor is it a significant regulatory action under the Unfunded Mandates Reform Act. Finally, the agency has analyzed this rule in accordance with the Regulatory Flexibility Act and provided each of the elements required for a final regulatory flexibility analysis.

V. Executive Order 13132: Federalism

FDA has analyzed this final rule in accordance with Executive Order 13132: Federalism. Executive Order 13132 requires Federal agencies to carefully examine actions to determine if they contain policies that have federalism implications or that preempt State law. As defined in the Order, "policies that have federalism implications" refers to regulations, legislative comments or proposed legislation, and other policy statements or actions that have substantial direct effects on the States,

on the relationship between the national government and the States, or on the distribution of power and responsibilities among the various levels of government.

FDA is publishing this final rule to set forth agency policies and requirements and provide administrative procedures, information, and guidance for those sections of PDMA that are not related to State licensing of wholesale prescription drug distributors. Because enforcement of these sections of PDMA is a Federal responsibility, there should be little, if any, impact from this rule on the States, on the relationship between the national government and the States, or on the distribution of power and responsibilities among the various levels of government. In addition, this regulation does not preempt State law.

Accordingly, FDA has determined that this final rule does not contain policies that have federalism implications or that preempt State law.

VI. Paperwork Reduction Act of 1995

This final rule contains information collection provisions that are subject to review by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (44 U.S.C. 3501–3520). The title, description, and respondent description of the information collection provisions 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.

Title: Prescription Drug Marketing Act of 1987; Policies, Requirements, and Administrative Procedures.

Description: The final rule provides for the collection of information from establishments engaged in the reimportation and wholesale distribution of prescription drugs; the sale, purchase, or trade of (or offer to sell, purchase, or trade) prescription drugs by hospitals, health care entities, and charitable institutions; the distribution of prescription drug samples; and the wholesale distribution of prescription drugs.

Description of Respondents:

Businesses, hospitals, health care entities, charitable institutions, and other for-profit and not-for-profit organizations; small businesses or organizations.

Although the March 1994 proposal provided a 60-day comment period under the Paperwork Reduction Act of 1980, and this final rule responds to the comments received, FDA is providing

an additional opportunity for public comment under the Paperwork Reduction Act of 1995, which became effective after the expiration of the comment period and applies to this final rule. Therefore, FDA now 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. Individuals and organizations may submit comments on the information collection provisions of this final rule by February 1, 2000. Comments should be directed to the Dockets Management Branch (address above).

At the close of the 60-day comment period, FDA will review the comments received, revise the information collection provisions as necessary, and

submit these provisions to OMB for review. FDA will publish a notice in the **Federal Register** when the information collection provisions are submitted to OMB, and an opportunity for public comment to OMB will be provided at that time. Prior to the effective date of this final rule, FDA will publish a notice in the **Federal Register** of OMB's decision to approve, modify, or disapprove the information collection provisions. An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.

TABLE 1.—ESTIMATED ANNUAL REPORTING BURDEN¹

21 CFR Section	No. of Respondents	Annual Frequency per Response	Total Annual Responses	Hours per Response	Total Hours
203.11	12	1	12	.5	6
203.30(a)(1) and (b)	61,961	12	743,532	.06	44,612
203.30(a)(3), (a)(4), and (c)	61,961	12	743,532	.06	44,612
203.31(a)(1) and (b)	232,355	135	31,367,925	.04	1,254,717
203.31(a)(3), (a)(4), and (c)	232,355	135	31,367,925	.03	941,038
203.37(a)	25	1	25	6.00	150
203.37(b)	200	1	200	6.00	1,200
203.37(c)	50	1	50	1.00	50
203.37(d)	2,208	1	2,208	.08	177
203.38(a)	2,208	1	2,208	3.00	6,624
203.39(g)	3,221	1	3,221	2.00	6,442
203.50(a)	125	100	12,500	.08	1,000
Total Hours					2,300,628

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

TABLE 2.—ESTIMATED ANNUAL RECORDKEEPING BURDEN¹

21 CFR Section	No. of Recordkeepers	Annual Frequency per Recordkeeping	Total Annual Records	Hours per Recordkeeper	Total Hours
203.23(a) and (b)	31,676	5	158,380	.25	39,595
203.23(c)	31,676	5	158,380	.08	12,670
203.30(a)(2) and 203.31(a)(2)	2,208	100	220,800	.50	110,400
203.31(d)(1) and (d)(2)	2,208	1	2,208	40.00	88,320
203.31(d)(4)	442	1	442	24.00	10,608
203.31(e)	2,208	1	2,208	1.00	2,208
203.34	2,208	1	2,208	40.00	88,320
203.37(a)	25	1	25	18.00	450
203.37(b)	200	1	200	18.00	3,600
203.38(b)	2,208	14,543	32,111,457	.02	642,229
203.39(d)	65	1	65	1.00	65
203.39(e)	3,221	1	3,221	.50	1,610
203.39(f)	3,221	1	3,221	8.00	25,768
203.39(g)	3,221	1	3,221	8.00	25,768
203.50(a)	125	100	12,500	.17	2,125
203.50(b)	125	100	12,500	.50	6,250
203.50(d)	691	1	691	2.00	1,382
Total Hours					1,061,368

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

Section 203.38(c) is exempt from recordkeeping requirements because the information it requires to be placed on drug sample labeling is provided by the agency.

VII. Environmental Impact

The agency has determined under 21 CFR 25.30(h) that this action is of a class of actions that do not individually or cumulatively have a significant effect on the human environment. Therefore,

neither an environmental assessment nor an environmental impact statement is required.

List of Subjects**21 CFR Part 203**

Drugs, Labeling, Manufacturing, Prescription drugs, Reporting and recordkeeping requirements, Warehouses.

21 CFR Part 205

Intergovernmental relations, Prescription drugs, Reporting and recordkeeping requirements, Security measures, Warehouses.

Therefore, under the Federal Food, Drug, and Cosmetic Act and under authority delegated to the Commissioner of Food and Drugs, 21 CFR chapter I is amended as follows:

1. Part 203 is added to read as follows:

PART 203—PRESCRIPTION DRUG MARKETING**Subpart A—General Provisions**

Sec.

- 203.1 Scope.
203.2 Purpose.
203.3 Definitions.

Subpart B—Reimportation

- 203.10 Restrictions on reimportation.
203.11 Applications for reimportation to provide emergency medical care.
203.12 An appeal from an adverse decision by the district office.

Subpart C—Sales Restrictions

- 203.20 Sales restrictions.
203.22 Exclusions.
203.23 Returns.

Subpart D—Samples

- 203.30 Sample distribution by mail or common carrier.
203.31 Sample distribution by means other than mail or common carrier (direct delivery by a representative or detailer).
203.32 Drug sample storage and handling requirements.
203.33 Drug sample forms.
203.34 Policies and procedures; administrative systems.
203.35 Standing requests.
203.36 Fulfillment houses, shipping and mailing services, comarketing agreements, and third-party recordkeeping.
203.37 Investigation and notification requirements.
203.38 Sample lot or control numbers; labeling of sample units.
203.39 Donation of drug samples to charitable institutions.

Subpart E—Wholesale Distribution

- 203.50 Requirements for wholesale distribution of prescription drugs.

Subpart F—Request and Receipt Forms, Reports, and Records

- 203.60 Request and receipt forms, reports, and records.

Subpart G—Rewards

- 203.70 Application for a reward.
Authority: 21 U.S.C. 331, 333, 351, 352, 353, 360, 371, 374, 381.

Subpart A—General Provisions**§ 203.1 Scope.**

This part sets forth procedures and requirements pertaining to the reimportation and wholesale distribution of prescription drugs, including both bulk drug substances and finished dosage forms; the sale, purchase, or trade of (or the offer to sell, purchase, or trade) prescription drugs, including bulk drug substances, that were purchased by hospitals or health care entities, or donated to charitable organizations; and the distribution of prescription drug samples. Blood and blood components intended for transfusion are excluded from the restrictions in and the requirements of the Prescription Drug Marketing Act of 1987 and the Prescription Drug Amendments of 1992.

§ 203.2 Purpose.

The purpose of this part is to implement the Prescription Drug Marketing Act of 1987 and the Prescription Drug Amendments of 1992, except for those sections relating to State licensing of wholesale distributors (see part 205 of this chapter), to protect the public health, and to protect the public against drug diversion by establishing procedures, requirements, and minimum standards for the distribution of prescription drugs and prescription drug samples.

§ 203.3 Definitions.

(a) *The act* means the Federal Food, Drug, and Cosmetic Act, as amended (21 U.S.C. 301 *et seq.*).

(b) *Authorized distributor of record* means a distributor with whom a manufacturer has established an ongoing relationship to distribute such manufacturer's products.

(c) *Blood* means whole blood collected from a single donor and processed either for transfusion or further manufacturing.

(d) *Blood component* means that part of a single-donor unit of blood separated by physical or mechanical means.

(e) *Bulk drug substance* means any substance that is represented for use in

a drug and that, when used in the manufacturing, processing, or packaging of a drug, becomes an active ingredient or a finished dosage form of the drug, but the term does not include intermediates used in the synthesis of such substances.

(f) *Charitable institution or charitable organization* means a nonprofit hospital, health care entity, organization, institution, foundation, association, or corporation that has been granted an exemption under section 501(c)(3) of the Internal Revenue Code of 1954, as amended.

(g) *Common control* means the power to direct or cause the direction of the management and policies of a person or an organization, whether by ownership of stock, voting rights, by contract, or otherwise.

(h) *Distribute* means to sell, offer to sell, deliver, or offer to deliver a drug to a recipient, except that the term "distribute" does not include:

(1) Delivering or offering to deliver a drug by a common carrier in the usual course of business as a common carrier; or

(2) Providing of a drug sample to a patient by:

(i) A practitioner licensed to prescribe such drug;

(ii) A health care professional acting at the direction and under the supervision of such a practitioner; or

(iii) The pharmacy of a hospital or of another health care entity that is acting at the direction of such a practitioner and that received such sample in accordance with the act and regulations.

(i) *Drug sample* means a unit of a prescription drug that is not intended to be sold and is intended to promote the sale of the drug.

(j) *Drug coupon* means a form that may be redeemed, at no cost or at reduced cost, for a drug that is prescribed in accordance with section 503(b) of the act.

(k) *Electronic record* means any combination of text, graphics, data, audio, pictorial, or other information representation in digital form that is created, modified, maintained, archived, retrieved, or distributed by a computer system.

(l) *Electronic signature* means any computer data compilation of any symbol or series of symbols executed, adopted, or authorized by an individual to be the legally binding equivalent of the individual's handwritten signature.

(m) *Emergency medical reasons* include, but are not limited to, transfers of a prescription drug between health care entities or from a health care entity to a retail pharmacy to alleviate a temporary shortage of a prescription

drug arising from delays in or interruption of regular distribution schedules; sales to nearby emergency medical services, i.e., ambulance companies and fire fighting organizations in the same State or same marketing or service area, or nearby licensed practitioners, of drugs for use in the treatment of acutely ill or injured persons; provision of minimal emergency supplies of drugs to nearby nursing homes for use in emergencies or during hours of the day when necessary drugs cannot be obtained; and transfers of prescription drugs by a retail pharmacy to another retail pharmacy to alleviate a temporary shortage; but do not include regular and systematic sales to licensed practitioners of prescription drugs that will be used for routine office procedures.

(n) *FDA* means the U.S. Food and Drug Administration.

(o) *Group purchasing organization* means any entity established, maintained, and operated for the purchase of prescription drugs for distribution exclusively to its members with such membership consisting solely of hospitals and health care entities bound by written contract with the entity.

(p) *Handwritten signature* means the scripted name or legal mark of an individual handwritten by that individual and executed or adopted with the present intention to authenticate a writing in a permanent form. The act of signing with a writing or marking instrument such as a pen or stylus is preserved. The scripted name or legal mark, while conventionally applied to paper, may also be applied to other devices that capture the name or mark.

(q) *Health care entity* means any person that provides diagnostic, medical, surgical, or dental treatment, or chronic or rehabilitative care, but does not include any retail pharmacy or any wholesale distributor. A person cannot simultaneously be a "health care entity" and a retail pharmacy or wholesale distributor.

(r) *Licensed practitioner* means any person licensed or authorized by State law to prescribe drugs.

(s) *Manufacturer* means any person who is a manufacturer as defined by § 201.1 of this chapter.

(t) *Nonprofit affiliate* means any not-for-profit organization that is either associated with or a subsidiary of a charitable organization as defined in section 501(c)(3) of the Internal Revenue Code of 1954.

(u) *Ongoing relationship* means an association that exists when a manufacturer and a distributor enter

into a written agreement under which the distributor is authorized to distribute the manufacturer's products for a period of time or for a number of shipments. If the distributor is not authorized to distribute a manufacturer's entire product line, the agreement must identify the specific drug products that the distributor is authorized to distribute.

(v) *PDA* means the Prescription Drug Amendments of 1992.

(w) *PDMA* means the Prescription Drug Marketing Act of 1987.

(x) *Person* includes any individual, partnership, corporation, or association.

(y) *Prescription drug* means any drug (including any biological product, except for blood and blood components intended for transfusion or biological products that are also medical devices) required by Federal law (including Federal regulation) to be dispensed only by a prescription, including finished dosage forms and bulk drug substances subject to section 503(b) of the act.

(z) *Representative* means an employee or agent of a drug manufacturer or distributor who promotes the sale of prescription drugs to licensed practitioners and who may solicit or receive written requests for the delivery of drug samples. A detailer is a representative.

(aa) *Sample unit* means a packet, card, blister pack, bottle, container, or other single package comprised of one or more dosage units of a prescription drug sample, intended by the manufacturer or distributor to be provided by a licensed practitioner to a patient in an unbroken or unopened condition.

(bb) *Unauthorized distributor* means a distributor who does not have an ongoing relationship with a manufacturer to sell or distribute its products.

(cc) *Wholesale distribution* means distribution of prescription drugs to persons other than a consumer or patient, but does not include:

(1) Intracompany sales;

(2) The purchase or other acquisition by a hospital or other health care entity that is a member of a group purchasing organization of a drug for its own use from the group purchasing organization or from other hospitals or health care entities that are members of such organizations;

(3) The sale, purchase, or trade of a drug or an offer to sell, purchase, or trade a drug by a charitable organization to a nonprofit affiliate of the organization to the extent otherwise permitted by law;

(4) The sale, purchase, or trade of a drug or an offer to sell, purchase, or trade a drug among hospitals or other

health care entities that are under common control;

(5) The sale, purchase, or trade of a drug or an offer to sell, purchase, or trade a drug for emergency medical reasons;

(6) The sale, purchase, or trade of a drug, an offer to sell, purchase, or trade a drug, or the dispensing of a drug under a prescription executed in accordance with section 503(b) of the act;

(7) The distribution of drug samples by manufacturers' and authorized distributors' representatives;

(8) The sale, purchase, or trade of blood or blood components intended for transfusion;

(9) Drug returns, when conducted by a hospital, health care entity, or charitable institution in accordance with § 203.23; or

(10) The sale of minimal quantities of drugs by retail pharmacies to licensed practitioners for office use.

(dd) *Wholesale distributor* means any person engaged in wholesale distribution of prescription drugs, including, but not limited to, manufacturers; repackers; own-label distributors; private-label distributors; jobbers; brokers; warehouses, including manufacturers' and distributors' warehouses, chain drug warehouses, and wholesale drug warehouses; independent wholesale drug traders; and retail pharmacies that conduct wholesale distributions.

Subpart B—Reimportation

§ 203.10 Restrictions on reimportation.

No prescription drug or drug composed wholly or partly of insulin that was manufactured in a State and exported from the United States may be reimported by anyone other than its manufacturer, except that FDA may grant permission to a person other than the manufacturer to reimport a prescription drug or insulin-containing drug if it determines that such reimportation is required for emergency medical care.

§ 203.11 Applications for reimportation to provide emergency medical care.

(a) Applications for reimportation for emergency medical care shall be submitted to the director of the FDA District Office in the district where reimportation is sought (addresses found in § 5.115 of this chapter).

(b) Applications for reimportation to provide emergency medical care shall be reviewed and approved or disapproved by each district office.

§ 203.12 An appeal from an adverse decision by the district office.

An appeal from an adverse decision by the district office involving insulin-containing drugs or prescription human drugs, other than biological products, may be made to the Office of Compliance (HFD-300), Center for Drug Evaluation and Research, Food and Drug Administration, 7520 Standish Pl., Rockville, MD 20855. An appeal from an adverse decision by the district office involving prescription human biological products may be made to the Office of Compliance and Biologics Quality (HFM-600), Center for Biologics Evaluation and Research, Food and Drug Administration, 1401 Rockville Pike, Rockville, MD 20852.

Subpart C—Sales Restrictions**§ 203.20 Sales restrictions.**

Except as provided in § 203.22 or § 203.23, no person may sell, purchase, or trade, or offer to sell, purchase, or trade any prescription drug that was:

- (a) Purchased by a public or private hospital or other health care entity; or
- (b) Donated or supplied at a reduced price to a charitable organization.

§ 203.22 Exclusions.

Section 203.20 does not apply to:

(a) The purchase or other acquisition of a drug for its own use by a hospital or other health care entity that is a member of a group purchasing organization from the group purchasing organization or from other hospitals or health care entities that are members of the organization.

(b) The sale, purchase, or trade of a drug or an offer to sell, purchase, or trade a drug by a charitable organization to a nonprofit affiliate of the organization to the extent otherwise permitted by law.

(c) The sale, purchase, or trade of a drug or an offer to sell, purchase, or trade a drug among hospitals or other health care entities that are under common control.

(d) The sale, purchase, or trade of a drug or an offer to sell, purchase, or trade a drug for emergency medical reasons.

(e) The sale, purchase, or trade of a drug, an offer to sell, purchase, or trade a drug, or the dispensing of a drug under a valid prescription.

(f) The sale, purchase, or trade of a drug or the offer to sell, purchase, or trade a drug by hospitals or health care entities owned or operated by Federal, State, or local governmental units to other hospitals or health care entities owned or operated by Federal, State, or local governmental units.

(g) The sale, purchase, or trade of, or the offer to sell, purchase, or trade blood or blood components intended for transfusion.

§ 203.23 Returns.

The return of a prescription drug purchased by a hospital or health care entity or acquired at a reduced price by or donated to a charitable institution is exempt from the prohibitions in § 203.20, provided that:

(a) The hospital, health care entity, or charitable institution documents the return by filling out a credit memo specifying:

- (1) The name and address of the hospital, health care entity, or charitable institution;
- (2) The name and address of the manufacturer or wholesale distributor from which it was acquired;
- (3) The product name and lot or control number;
- (4) The quantity returned; and
- (5) The date of the return.

(b) The hospital, health care entity, or charitable institution forwards a copy of each credit memo to the manufacturer and retains a copy of each credit memo for its records;

(c) Any drugs returned to a manufacturer or wholesale distributor are kept under proper conditions for storage, handling, and shipping, and written documentation showing that proper conditions were maintained is provided to the manufacturer or wholesale distributor to which the drugs are returned.

Subpart D—Samples**§ 203.30 Sample distribution by mail or common carrier.**

(a) *Requirements for drug sample distribution by mail or common carrier.* A manufacturer or authorized distributor of record may distribute a drug sample to a practitioner licensed to prescribe the drug that is to be sampled or, at the written request of a licensed practitioner, to the pharmacy of a hospital or other health care entity, by mail or common carrier, provided that:

(1) The licensed practitioner executes and submits a written request to the manufacturer or authorized distributor of record, as set forth in paragraph (b) of this section, before the delivery of the drug sample;

(2) The manufacturer or authorized distributor of record verifies with the appropriate State authority that the practitioner requesting the drug sample is licensed or authorized under State law to prescribe the drug product;

(3) The recipient executes a written receipt, as set forth in paragraph (c) of

this section, when the drug sample is delivered; and

(4) The receipt is returned to the manufacturer or distributor from which the drug sample was received.

(b) *Contents of the written request form for delivery of samples by mail or common carrier.*

(1) A written request for a drug sample to be delivered by mail or common carrier to a licensed practitioner is required to contain the following:

(i) The name, address, professional title, and signature of the practitioner making the request;

(ii) The practitioner's State license or authorization number or, where a scheduled drug product is requested, the practitioner's Drug Enforcement Administration number.

(iii) The proprietary or established name and the strength of the drug sample requested;

(iv) The quantity requested;

(v) The name of the manufacturer and the authorized distributor of record, if the drug sample is requested from an authorized distributor of record; and

(vi) The date of the request.

(2) A written request for a drug sample to be delivered by mail or common carrier to the pharmacy of a hospital or other health care entity is required to contain, in addition to all of the information in paragraph (b)(1) of this section, the name and address of the pharmacy of the hospital or other health care entity to which the drug sample is to be delivered.

(c) *Contents of the receipt to be completed upon delivery of a drug sample.* The receipt is to be on a form designated by the manufacturer or distributor, and is required to contain the following:

(1) If the drug sample is delivered to the licensed practitioner who requested it, the receipt is required to contain the name, address, professional title, and signature of the practitioner or the practitioner's designee who acknowledges delivery of the drug sample; the proprietary or established name and strength of the drug sample and the quantity of the drug sample delivered; and the date of the delivery.

(2) If the drug sample is delivered to the pharmacy of a hospital or other health care entity at the request of a licensed practitioner, the receipt is required to contain the name and address of the requesting licensed practitioner; the name and address of the hospital or health care entity pharmacy designated to receive the drug sample; the name, address, professional title, and signature of the person acknowledging delivery of the drug

sample; the proprietary or established name and strength of the drug sample; the quantity of the drug sample delivered; and the date of the delivery.

§ 203.31 Sample distribution by means other than mail or common carrier (direct delivery by a representative or detailer).

(a) *Requirements for drug sample distribution by means other than mail or common carrier.* A manufacturer or authorized distributor of record may distribute by means other than mail or common carrier, by a representative or detailer, a drug sample to a practitioner licensed to prescribe the drug to be sampled or, at the written request of such a licensed practitioner, to the pharmacy of a hospital or other health care entity, provided that:

(1) The manufacturer or authorized distributor of record receives from the licensed practitioner a written request signed by the licensed practitioner before the delivery of the drug sample;

(2) The manufacturer or authorized distributor of record verifies with the appropriate State authority that the practitioner requesting the drug sample is licensed or authorized under State law to prescribe the drug product;

(3) A receipt is signed by the recipient, as set forth in paragraph (c) of this section, when the drug sample is delivered;

(4) The receipt is returned to the manufacturer or distributor; and

(5) The requirements of paragraphs (d) through (e) of this section are met.

(b) *Contents of the written request forms for delivery of samples by a representative.* (1) A written request for delivery of a drug sample by a representative to a licensed practitioner is required to contain the following:

(i) The name, address, professional title, and signature of the practitioner making the request;

(ii) The practitioner's State license or authorization number, or, where a scheduled drug product is requested, the practitioner's Drug Enforcement Administration number;

(iii) The proprietary or established name and the strength of the drug sample requested;

(iv) The quantity requested;

(v) The name of the manufacturer and the authorized distributor of record, if the drug sample is requested from an authorized distributor of record; and

(vi) The date of the request.

(2) A written request for delivery of a drug sample by a representative to the pharmacy of a hospital or other health care entity is required to contain, in addition to all of the information in paragraph (b) of this section, the name and address of the pharmacy of the

hospital or other health care entity to which the drug sample is to be delivered.

(c) *Contents of the receipt to be completed upon delivery of a drug sample.* The receipt is to be on a form designated by the manufacturer or distributor, and is required to contain the following:

(1) If the drug sample is received at the address of the licensed practitioner who requested it, the receipt is required to contain the name, address, professional title, and signature of the practitioner or the practitioner's designee who acknowledges delivery of the drug sample; the proprietary or established name and strength of the drug sample; the quantity of the drug sample delivered; and the date of the delivery.

(2) If the drug sample is received by the pharmacy of a hospital or other health care entity at the request of a licensed practitioner, the receipt is required to contain the name and address of the requesting licensed practitioner; the name and address of the hospital or health care entity pharmacy designated to receive the drug sample; the name, address, professional title, and signature of the person acknowledging delivery of the drug sample; the proprietary or established name and strength of the drug sample; the quantity of the drug sample delivered; and the date of the delivery.

(d) *Inventory and reconciliation of drug samples of manufacturers' and distributors' representatives.* Each drug manufacturer or authorized distributor of record that distributes drug samples by means of representatives shall conduct, at least annually, a complete and accurate physical inventory of all drug samples. All drug samples in the possession or control of each manufacturer's and distributor's representatives are required to be inventoried and the results of the inventory are required to be recorded in an inventory record, as specified in paragraph (d)(1) of this section. In addition, manufacturers and distributors shall reconcile the results of the physical inventory with the most recently completed prior physical inventory and create a report documenting the reconciliation process, as specified in paragraph (d)(2) of this section.

(1) The inventory record is required to identify all drug samples in a representative's stock by the proprietary or established name, dosage strength, and number of units.

(2) The reconciliation report is required to include:

(i) The inventory record for the most recently completed prior inventory;

(ii) A record of each drug sample shipment received since the most recently completed prior inventory, including the sender and date of the shipment, and the proprietary or established name, dosage strength, and number of sample units received;

(iii) A record of drug sample distributions since the most recently completed inventory showing the name and address of each recipient of each sample unit shipped, the date of the shipment, and the proprietary or established name, dosage strength, and number of sample units shipped. For the purposes of this paragraph and paragraph (d)(2)(v) of this section, "distributions" includes distributions to health care practitioners or designated hospital or health care entity pharmacies, transfers or exchanges with other firm representatives, returns to the manufacturer or authorized distributor, destruction of drug samples by a sales representative, and other types of drug sample dispositions. The specific type of distribution must be specified in the record;

(iv) A record of drug sample thefts or significant losses reported by the representative since the most recently completed prior inventory, including the approximate date of the occurrence and the proprietary or established name, dosage strength, and number of sample units stolen or lost; and

(v) A record summarizing the information required by paragraphs (d)(2)(ii) through (d)(2)(iv) of this section. The record must show, for each type of sample unit (i.e., sample units having the same established or proprietary name and dosage strength), the total number of sample units received, distributed, lost, or stolen since the most recently completed prior inventory. For example, a typical entry in this record may read "50 units risperidone (1 mg) returned to manufacturer" or simply "Risperidone (1 mg)/50/returned to manufacturer."

(3) Each drug manufacturer or authorized distributor of record shall take appropriate internal control measures to guard against error and possible fraud in the conduct of the physical inventory and reconciliation, and in the preparation of the inventory record and reconciliation report.

(4) A manufacturer or authorized distributor of record shall carefully evaluate any apparent discrepancy or significant loss revealed through the inventory and reconciliation process and shall fully investigate any such discrepancy or significant loss that cannot be justified.

(e) *Lists of manufacturers' and distributors' representatives.* Each drug manufacturer or authorized distributor of record who distributes drug samples by means of representatives shall maintain a list of the names and addresses of its representatives who distribute drug samples and of the sites where drug samples are stored.

§ 203.32 Drug sample storage and handling requirements.

(a) *Storage and handling conditions.* Manufacturers, authorized distributors of record, and their representatives shall store and handle all drug samples under conditions that will maintain their stability, integrity, and effectiveness and ensure that the drug samples are free of contamination, deterioration, and adulteration.

(b) *Compliance with compendial and labeling requirements.* Manufacturers, authorized distributors of record, and their representatives can generally comply with this section by following the compendial and labeling requirements for storage and handling of a particular prescription drug in handling samples of that drug.

§ 203.33 Drug sample forms.

A sample request or receipt form may be delivered by mail, common carrier, or private courier or may be transmitted photographically or electronically (i.e., by telephoto, wirephoto, radiophoto, facsimile transmission (FAX), xerography, or electronic data transfer) or by any other system, provided that the method for transmission meets the security requirements set forth in § 203.60(c).

§ 203.34 Policies and procedures; administrative systems.

Each manufacturer or authorized distributor of record that distributes drug samples shall establish, maintain, and adhere to written policies and procedures describing its administrative systems for the following:

(a) Distributing drug samples by mail or common carrier, including methodology for reconciliation of requests and receipts;

(b) Distributing drug samples by means other than mail or common carrier including the methodology for:

(1) Reconciling requests and receipts, identifying patterns of nonresponse, and the manufacturer's or distributor's response when such patterns are found;

(2) Conducting the annual physical inventory and preparation of the reconciliation report;

(3) Implementing a sample distribution security and audit system, including conducting random and for-

cause audits of sales representatives by personnel independent of the sales force; and

(4) Storage of drug samples by representatives;

(c) Identifying any significant loss of drug samples and notifying FDA of the loss; and

(d) Monitoring any loss or theft of drug samples.

§ 203.35 Standing requests.

Manufacturers or authorized distributors of record shall not distribute drug samples on the basis of open-ended or standing requests, but shall require separate written requests for each drug sample or group of samples. An arrangement by which a licensed practitioner requests in writing that a specified number of drug samples be delivered over a period of not more than 6 months, with the actual delivery dates for parts of the order to be set by subsequent oral communication or electronic transmission, is not considered to be a standing request.

§ 203.36 Fulfillment houses, shipping and mailing services, comarketing agreements, and third-party recordkeeping.

(a) *Responsibility for creating and maintaining forms, reports, and records.* Any manufacturer or authorized distributor of record that uses a fulfillment house, shipping or mailing service, or other third party, or engages in a comarketing agreement with another manufacturer or distributor to distribute drug samples or to meet any of the requirements of PDMA, PDA, or this part, remains responsible for creating and maintaining all requests, receipts, forms, reports, and records required under PDMA, PDA, and this part.

(b) *Responsibility for producing requested forms, reports, or records.* A manufacturer or authorized distributor of record that contracts with a third party to maintain some or all of its records shall produce requested forms, reports, records, or other required documents within 2 business days of a request by an authorized representative of FDA or another Federal, State, or local regulatory or law enforcement official.

§ 203.37 Investigation and notification requirements.

(a) *Investigation of falsification of drug sample records.* A manufacturer or authorized distributor of record that has reason to believe that any person has falsified drug sample requests, receipts, or records, or is diverting drug samples, shall:

(1) Notify FDA, by telephone or in writing, within 5 working days;

(2) Immediately initiate an investigation; and

(3) Provide FDA with a complete written report, including the reason for and the results of the investigation, not later than 30 days after the date of the initial notification in paragraph (a)(1) of this section.

(b) *Significant loss or known theft of drug samples.* A manufacturer or authorized distributor of record that distributes drug samples or a charitable institution that receives donated drug samples from a licensed practitioner shall:

(1) Notify FDA, by telephone or in writing, within 5 working days of becoming aware of a significant loss or known theft;

(2) Immediately initiate an investigation into the significant loss or known theft; and

(3) Provide FDA with a complete written report, including the reason for and the results of the investigation, not later than 30 days after the date of the initial notification in paragraph (b)(1) of this section.

(c) *Conviction of a representative.*

(1) A manufacturer or authorized distributor of record that distributes drug samples shall notify FDA, by telephone or in writing, within 30 days of becoming aware of the conviction of one or more of its representatives for a violation of section 503(c)(1) of the act or any State law involving the sale, purchase, or trade of a drug sample or the offer to sell, purchase, or trade a drug sample.

(2) A manufacturer or authorized distributor of record shall provide FDA with a complete written report not later than 30 days after the date of the initial notification.

(d) *Selection of individual responsible for drug sample information.* A manufacturer or authorized distributor of record that distributes drug samples shall inform FDA in writing within 30 days of selecting the individual responsible for responding to a request for information about drug samples of that individual's name, business address, and telephone number.

(e) *Whom to notify at FDA.*

Notifications and reports concerning prescription human drugs shall be made to the Division of Prescription Drug Compliance and Surveillance (HFD-330), Office of Compliance, Center for Drug Evaluation and Research, Food and Drug Administration, 7520 Standish Pl., Rockville, MD 20855. Notifications and reports concerning prescription human biological products shall be made to the Division of Inspections and Surveillance (HFM-650), Office of Compliance, Center for Biologics

Evaluation and Research, Food and Drug Administration, 1401 Rockville Pike, Rockville, MD 20852.

§ 203.38 Sample lot or control numbers; labeling of sample units.

(a) *Lot or control number required on drug sample labeling and sample unit label.* The manufacturer or authorized distributor of record of a drug sample shall include on the label of the sample unit and on the outside container or packaging of the sample unit, if any, an identifying lot or control number that will permit the tracking of the distribution of each drug sample unit.

(b) *Records containing lot or control numbers required for all drug samples distributed.* A manufacturer or authorized distributor of record shall maintain for all samples distributed records of drug sample distribution containing lot or control numbers that are sufficient to permit the tracking of sample units to the point of the licensed practitioner.

(c) *Labels of sample units.* Each sample unit shall bear a label that clearly denotes its status as a drug sample, e.g., "sample," "not for sale," "professional courtesy package."

(1) A drug that is labeled as a drug sample is deemed to be a drug sample within the meaning of the act.

(2) A drug product dosage unit that bears an imprint identifying the dosage form as a drug sample is deemed to be a drug sample within the meaning of the act.

(3) Notwithstanding paragraphs (c)(1) and (c)(2) of this section, any article that is a drug sample as defined in section 503(c)(1) of the act and § 203.3(i) that fails to bear the label required in this paragraph (c) is a drug sample.

§ 203.39 Donation of drug samples to charitable institutions.

A charitable institution may receive a drug sample donated by a licensed practitioner or another charitable institution for dispensing to a patient of the charitable institution, or donate a drug sample to another charitable institution for dispensing to its patients, provided that the following requirements are met:

(a) A drug sample donated by a licensed practitioner or donating charitable institution shall be received by a charitable institution in its original, unopened packaging with its labeling intact.

(b) Delivery of a donated drug sample to a recipient charitable institution shall be completed by mail or common carrier, collection by an authorized agent or employee of the recipient charitable institution, or personal

delivery by a licensed practitioner or an agent or employee of the donating charitable institution. Donated drug samples shall be placed by the donor in a sealed carton for delivery to or collection by the recipient charitable institution.

(c) A donated drug sample shall not be dispensed to a patient or be distributed to another charitable institution until it has been examined by a licensed practitioner or registered pharmacist at the recipient charitable institution to confirm that the donation record accurately describes the drug sample delivered and that no drug sample is adulterated or misbranded for any reason, including, but not limited to, the following:

(1) The drug sample is out of date;

(2) The labeling has become mutilated, obscured, or detached from the drug sample packaging;

(3) The drug sample shows evidence of having been stored or shipped under conditions that might adversely affect its stability, integrity, or effectiveness;

(4) The drug sample is for a prescription drug product that has been recalled or is no longer marketed; or

(5) The drug sample is otherwise possibly contaminated, deteriorated, or adulterated.

(d) The recipient charitable institution shall dispose of any drug sample found to be unsuitable by destroying it or by returning it to the manufacturer. The charitable institution shall maintain complete records of the disposition of all destroyed or returned drug samples.

(e) The recipient charitable institution shall prepare at the time of collection or delivery of a drug sample a complete and accurate donation record, a copy of which shall be retained by the recipient charitable institution for at least 3 years, containing the following information:

(1) The name, address, and telephone number of the licensed practitioner (or donating charitable institution);

(2) The manufacturer, brand name, quantity, and lot or control number of the drug sample donated; and

(3) The date of the donation.

(f) Each recipient charitable institution shall maintain complete and accurate records of donation, receipt, inspection, inventory, dispensing, redistribution, destruction, and returns sufficient for complete accountability and auditing of drug sample stocks.

(g) Each recipient charitable institution shall conduct, at least annually, an inventory of prescription drug sample stocks and shall prepare a report reconciling the results of each inventory with the most recent prior inventory. Drug sample inventory discrepancies and reconciliation

problems shall be investigated by the charitable institution and reported to FDA.

(h) A recipient charitable institution shall store drug samples under conditions that will maintain the sample's stability, integrity, and effectiveness, and will ensure that the drug samples will be free of contamination, deterioration, and adulteration.

(i) A charitable institution shall notify FDA within 5 working days of becoming aware of a significant loss or known theft of prescription drug samples.

Subpart E—Wholesale Distribution

§ 203.50 Requirements for wholesale distribution of prescription drugs.

(a) *Identifying statement for sales by unauthorized distributors.* Before the completion of any wholesale distribution by a wholesale distributor of a prescription drug for which the seller is not an authorized distributor of record to another wholesale distributor or retail pharmacy, the seller shall provide to the purchaser a statement identifying each prior sale, purchase, or trade of such drug. This identifying statement shall include:

(1) The proprietary and established name of the drug;

(2) Dosage;

(3) Container size;

(4) Number of containers;

(5) The drug's lot or control number(s);

(6) The business name and address of all parties to each prior transaction involving the drug, starting with the manufacturer; and

(7) The date of each previous transaction.

(b) The drug origin statement is subject to the record retention requirements of § 203.60 and must be retained by all wholesale distributors involved in the distribution of the drug product, whether authorized or unauthorized, for 3 years.

(c) *Identifying statement not required when additional manufacturing processes are completed.* A manufacturer that subjects a drug to any additional manufacturing processes to produce a different drug is not required to provide to a purchaser a statement identifying the previous sales of the component drug or drugs.

(d) *List of authorized distributors of record.* Each manufacturer shall maintain at the corporate offices a current written list of all authorized distributors of record.

(1) Each manufacturer's list of authorized distributors of record shall specify whether each distributor listed

thereon is authorized to distribute the manufacturer's full product line or only particular, specified products.

(2) Each manufacturer shall update its list of authorized distributors of record on a continuing basis.

(3) Each manufacturer shall make its list of authorized distributors of record available on request to the public for inspection or copying. A manufacturer may impose reasonable copying charges for such requests from members of the public.

Subpart F—Request and Receipt Forms, Reports, and Records

§ 203.60 Request and receipt forms, reports, and records.

(a) *Use of electronic records, electronic signatures, and handwritten signatures executed to electronic records.*

(1) Provided the requirements of part 11 of this chapter are met, electronic records, electronic signatures, and handwritten signatures executed to electronic records may be used as an alternative to paper records and handwritten signatures executed on paper to meet any of the record and signature requirements of PDMA, PDA, or this part.

(2) Combinations of paper records and electronic records, electronic records and handwritten signatures executed on paper, or paper records and electronic signatures or handwritten signatures executed to electronic records, may be used to meet any of the record and signature requirements of PDMA, PDA, or this part, provided that:

(i) The requirements of part 11 of this chapter are met for the electronic records, electronic signatures, or handwritten signatures executed to electronic records; and

(ii) A reasonably secure link between the paper-based and electronic components exists such that the combined records and signatures are trustworthy and reliable, and to ensure that the signer cannot readily repudiate the signed records as not genuine.

(3) For the purposes of this paragraph (a), the phrase "record and signature requirements of PDMA, PDA, or this part" includes drug sample request and receipt forms, reports, records, and other documents, and their associated signatures required by PDMA, PDA, and this part.

(b) *Maintenance of request and receipt forms, reports, records, and other documents created on paper.* Request and receipt forms, reports, records, and other documents created on paper may be maintained on paper or by photographic imaging (i.e.,

photocopies or microfiche), provided that the security and authentication requirements described in paragraph (c) of this section are followed. Where a required document is created on paper and electronically scanned into a computer, the resulting record is an electronic record that must meet the requirements of part 11 of this chapter.

(c) *Security and authentication requirements for request and receipt forms, reports, records, and other documents created on paper.* A request or receipt form, report, record, or other document, and any signature appearing thereon, that is created on paper and that is maintained by photographic imaging, or transmitted electronically (i.e., by facsimile) shall be maintained or transmitted in a form that provides reasonable assurance of being:

(1) Resistant to tampering, revision, modification, fraud, unauthorized use, or alteration;

(2) Preserved in accessible and retrievable fashion; and

(3) Available to permit copying for purposes of review, analysis, verification, authentication, and reproduction by the person who executed the form or created the record, by the manufacturer or distributor, and by authorized personnel of FDA and other regulatory and law enforcement agencies.

(d) *Retention of request and receipt forms, reports, lists, records, and other documents.* Any person required to create or maintain reports, lists, or other records under PDMA, PDA, or this part, including records relating to the distribution of drug samples, shall retain them for at least 3 years after the date of their creation.

(e) *Availability of request and receipt forms, reports, lists, and records.* Any person required to create or maintain request and receipt forms, reports, lists, or other records under PDMA, PDA, or this part shall make them available, upon request, in a form that permits copying or other means of duplication, to FDA or other Federal, State, or local regulatory and law enforcement officials for review and reproduction. The records shall be made available within 2 business days of a request.

Subpart G—Rewards

§ 203.70 Application for a reward.

(a) *Reward for providing information leading to the institution of a criminal proceeding against, and conviction of, a person for the sale, purchase, or trade of a drug sample.* A person who provides information leading to the institution of a criminal proceeding against, and conviction of, a person for

the sale, purchase, or trade of a drug sample, or the offer to sell, purchase, or trade a drug sample, in violation of section 503(c)(1) of the act, is entitled to one-half the criminal fine imposed and collected for such violation, but not more than \$125,000.

(b) *Procedure for making application for a reward for providing information leading to the institution of a criminal proceeding against, and conviction of, a person for the sale, purchase, or trade of a drug sample.* A person who provides information leading to the institution of a criminal proceeding against, and conviction of, a person for the sale, purchase, or trade of a drug sample, or the offer to sell, purchase, or trade a drug sample, in violation of section 503(c)(1) of the act, may apply for a reward by making written application to:

(1) Director, Office of Compliance (HFD-300), Center for Drug Evaluation and Research, Food and Drug Administration, 7500 Standish Pl., Rockville, MD 20855; or

(2) Director, Office of Compliance and Biologics Quality (HFM-600), Center for Biologics Evaluation and Research, Food and Drug Administration, 1401 Rockville Pike, Rockville, MD 20852, as appropriate.

PART 205—GUIDELINES FOR STATE LICENSING OF WHOLESALE PRESCRIPTION DRUG DISTRIBUTORS

2. The authority citation for 21 CFR part 205 continues to read as follows:

Authority: 21 U.S.C. 351, 352, 353, 371, 374.

3. Section 205.3 is amended by adding paragraphs (f)(9), (f)(10), and (h) to read as follows:

§ 205.3 Definitions.

* * * * *

(f) * * *

(9) Drug returns, when conducted by a hospital, health care entity, or charitable institution in accordance with § 203.23 of this chapter; or

(10) The sale of minimal quantities of drugs by retail pharmacies to licensed practitioners for office use.

* * * * *

(h) Health care entity means any person that provides diagnostic, medical, surgical, or dental treatment, or chronic or rehabilitative care, but does not include any retail pharmacy or any wholesale distributor. A person cannot simultaneously be a "health care entity" and a retail pharmacy or wholesale distributor.

4. Section 205.50 is amended by revising paragraph (f)(2) to read as follows:

§ 205.50 Minimum requirements for the storage and handling of prescription drugs and for the establishment and maintenance of prescription drug distribution records.

* * * * *

(f) * * *

(2) Inventories and records shall be made available for inspection and photocopying by authorized Federal, State, or local law enforcement agency officials for a period of 3 years after the date of their creation.

Dated: August 3, 1999.

Margaret M. Dotzel,

Acting Associate Commissioner for Policy.

[FR Doc. 99-30954 Filed 11-30-99; 12:38 pm]

BILLING CODE 4160-01-F

DEPARTMENT OF THE TREASURY

Internal Revenue Service

26 CFR Part 1

Determination of Tax Liability

CFR Correction

In Title 26 of the Code of Federal Regulations, part 1 (§§ 1.641 to 1.850), revised as of April 1, 1999, page 293, in § 1.704-1(b)(0), in the table in the first column, under "Section" the first, second, fourth and fifth lines respectively should read, 1.704-1(b)(0), 1.704-1(b)(1), 1.704-1(b)(1)(ii) and 1.704-1(b)(1)(iii).

Also, in the second column, under "Heading" "Maintenance of capital accounts" make the following changes in the second column of the table:

1.704-1(b)(2)(d)(2) should read 1.704-1(b)(2)(iv)(d)(2)

1.704-1(b)(2)(iv)(3) should read

1.704-1(b)(2)(iv)(d)(3)

1.704-1(2)(iv)(e)(1) should read

1.704-1(b)(2)(iv)(e)(1)

1.704-1(b)(2)(e)(2) should read 1.704-1(b)(2)(iv)(e)(2)

[FR Doc. 99-55540 Filed 12-2-99; 8:45 am]

BILLING CODE 1505-01-D

DEPARTMENT OF THE TREASURY

Internal Revenue Service

26 CFR Part 20

[TD 8846]

RIN 1545-AV45

Deductions for Transfers for Public, Charitable, and Religious Uses; In General Marital Deduction; Valuation of Interest Passing to Surviving Spouse

AGENCY: Internal Revenue Service (IRS), Treasury.

ACTION: Final regulations.

SUMMARY: This document contains final regulations relating to the effect of certain administration expenses on the valuation of property that qualifies for either the estate tax marital deduction under section 2056 of the Internal Revenue Code or the estate tax charitable deduction under section 2055. The regulations distinguish between estate transmission expenses, which reduce the value of property for marital and charitable deduction purposes, and estate management expenses, which generally do not reduce the value of property for these purposes.

EFFECTIVE DATES: These regulations are effective on December 3, 1999.

FOR FURTHER INFORMATION CONTACT:

Deborah Ryan, (202) 622-3090 (not a toll-free number).

SUPPLEMENTARY INFORMATION:

Background

On December 16, 1998, the Treasury Department and the IRS published in the **Federal Register** (63 FR 69248) a notice of proposed rulemaking (REG-114663-97) relating to the effect of certain administration expenses on the valuation of property which qualifies for the estate tax marital or charitable deduction. The proposed regulations were issued in response to the decision of the Supreme Court of the United States in *Commissioner v. Estate of Hubert*, 520 U.S. 93 (1997) (1997-2 C.B. 231). Written comments responding to the notice of proposed rulemaking were received, and a public hearing was held on April 21, 1999, at which time oral testimony was presented. This Treasury decision adopts final regulations with respect to the notice of proposed rulemaking. A summary of the principal comments received and revisions made in response to those comments is provided below.

The proposed regulations set forth the substantive provisions as applied to the estate tax marital deduction in § 20.2056(b)-4(a). For the estate tax charitable deduction, the proposed regulations (under § 20.2055-1(d)(6)) merely cross-reference the rules for the marital deduction.

Several commentators suggested that the regulations under section 2055 should contain specific rules relating to the charitable deduction, rather than just a cross-reference. The Treasury and the IRS agree with this suggestion. The final regulations contain rules under § 20.2055-3 specifically addressing the effect of administration expenses on the valuation of property when all or a portion of the interests in property

qualify for the estate tax charitable deduction.

Several commentators stated that the distinction between estate transmission expenses and estate management expenses was not clearly made in the proposed regulations and requested more concrete definitions of each type of expense. In response to these comments, the final regulations characterize estate transmission expenses as those expenses that would not have been incurred except for the decedent's death. Although the amount of these expenses cannot be calculated with any degree of certainty on the date of the decedent's death, they are expenses that are incurred because of the decedent's death. Estate management expenses, on the other hand, are characterized in the final regulations as expenses that would be incurred with respect to the property even if the decedent had not died; that is, expenses incurred in investing, maintaining, and preserving the property. These are expenses that typically would have been incurred with respect to the property by the decedent before death or by the beneficiaries had they received the property on the date of death without any intervening period of administration. In order to be certain that all expenses are classified as either transmission expenses or management expenses, transmission expenses are defined to include all expenses that are not management expenses.

Three commentators stated that the different treatment accorded to estate transmission expenses and estate management expenses under the proposed regulations creates a new federal standard for allocating expenses that may be contrary to the manner in which the expenses must be charged under state law. However, the Treasury and the IRS believe that the allocation of administration expenses based on the distinction between transmission and management expenses provides the most accurate measure of the value of the property which passes to the surviving spouse or to the charity at the moment of the decedent's death for federal estate tax marital and charitable deduction purposes. Transmission expenses that are charged to the property passing to the surviving spouse or to the charity reduce the amount of that property as of the date of the decedent's death because the expenses, as well as the transfer to the surviving spouse or to charity, are a consequence of, and arise as a result of, the decedent's death. In contrast, management expenses do not generally