Contains Nonbinding Recommendations

GUIDANCE FOR INDUSTRY

Prescription Drug Marketing Act (PDMA) Requirements

Questions and Answers

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research
Office of the Commissioner
Office of Regulatory Affairs

November 2006

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I. Introduction

The Prescription Drug Marketing Act of 1987 (PDMA), amended by the Prescription Drug Amendments of 1992 (PDA), requires, among other things, that certain wholesalers provide a statement (also known as a pedigree) prior to each wholesale distribution of prescription drugs. This guidance provides questions and answers relating to the requirements set forth in 21 CFR Parts 203 and 205, and other Parts related to the PDMA.

FDA's guidance documents, including this guidance, do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in Agency guidances means that something is suggested or recommended, but not required.

II. Background

The PDMA excludes manufacturers and authorized distributors of record from the requirement to provide a pedigree prior to each wholesale distribution. The PDMA defines authorized distributor of record as a wholesale distributor that has an ongoing relationship with the manufacturer. The PDMA does not define "ongoing relationship." On December 4, 1999, FDA published in the Federal Register (64 FR 67720) final regulations regarding the PDMA that, among other things, defined "ongoing relationship" (21 CFR § 203.3(u)) and described what information must be included in the pedigree (21 CFR § 203.50). Due to concerns raised at the time, FDA delayed the effective date of

[1] This guidance has been prepared by the Office of Policy in the Office of the Commissioner, the Office of Compliance in the Center for Drug Evaluation and Research (CDER), and the Office of Regulatory Affairs at the Food and Drug Administration, in conjunction with the Agency's Counterfeit Drug Task Force. The Agency may revise this guidance as we receive additional comments and questions.

these two provisions. On June 14, 2006, FDA announced in a Notice in the Federal Register that it would no longer delay the effective date of 21 CFR §§ 203.3(u) and 203.50. (71 Fed. Reg. 34249). The reasons for the agency's decision are described in that Federal Register Notice and its Counterfeit Drug Task Force 2006 Update. After the Federal Register Notice was published, FDA received a number of questions related to implementation of these provisions and the PDMA generally. This guidance is intended to address many of the questions raised.

III. Questions and Answers

A. Authorized Distributor of Record (ADR) Status

1. What information should be in the written agreement between a manufacturer and an ADR?

The written agreement should include:

- A list of the specific products that the wholesale distributor is authorized to distribute or a statement that the wholesale distributor is an ADR for the manufacturer's entire product line. Specific products should be identified by either a) the name, dosage form, and strength of the drug, or b) the NDC number; and
- The period of time the wholesale distributor is granted ADR status or the number of shipments for which the wholesale distributor is an ADR.

2. Would a series of invoices, transactions, or distributions constitute a written agreement?

No. An invoice simply documents drug distributions or transactions. A distribution or transaction is not a written agreement. 21 CFR § 203.3(u) specifically requires a written agreement between a manufacturer and a wholesaler that documents the wholesaler's status as an authorized distributor. FDA recognizes that there may be situations where a wholesaler buys prescription drugs directly from the manufacturer, yet the manufacturer does not make the wholesaler an ADR. In this situation, although the wholesaler is not an ADR, the wholesaler is in a position to create and further provide a pedigree because the wholesaler would have all the information required by 21 CFR § 203.50(a) since they purchased the prescription drugs directly from the manufacturer. In light of the December 1, 2006, implementation of 21 CFR §203.3(u), FDA urges manufacturers to closely examine their business relationships with wholesalers, and if there is an ongoing relationship by virtue of direct, continued sales, enter into a written agreement to grant these wholesalers ADR status. See Addendum Question E at the end of this document.

3. Who should maintain the written agreement? The manufacturer? The wholesaler? Both?

Both. Pursuant to 21 CFR §§ 203.50(b) and 203.60(d), persons required to create or maintain records under PDMA, PDA, or Part 203 of the regulations shall retain them for at least 3 years after the date of their creation. The written agreement falls under this

section. Furthermore, pursuant to 21 CFR §203.60(e), FDA can look to both parties for documentation of the written agreement.

4. If a wholesaler has ADR status, is that wholesaler an ADR for all products that the manufacturer sells?

It depends. The written agreement required pursuant to 21 CFR § 203.3(u) should clearly state whether a wholesaler is an ADR for all products that the manufacturer sells or only for certain products that the manufacturer sells.

5. What information about the ADR does a manufacturer have to make available on the list?

Pursuant to 21 CFR § 203.50(d)(1), a manufacturer shall specify whether each listed distributor is authorized to distribute the manufacturer's full product line or only particular, specified products.

6. How often should manufacturers update their list of ADRs?

Pursuant to 21 CFR § 203.50(d)(2), manufacturers are required to update the list on a continuing basis. Therefore, to keep the list current, manufacturers should maintain lists in a format that allows them to be updated when the ADR status of a distributor changes.

7. Is placing the list of ADRs on the manufacturer's web site adequate to meet the provision of making the list available on request to the public, pursuant to 21 CFR § 203.50(d)?

Yes. We highly encourage manufacturers to post their ADR list on their website in a place and manner that is readily accessible, although they are not required to do so. We note that 21 CFR § 203.50(d) requires the list to be maintained at the manufacturer's corporate offices even when the list is posted on a website.

8. Where can a pharmacist find the list of ADRs?

Pursuant to 21 CFR § 203.50(d)(3), manufacturers are required to make their list of ADRs available to the public upon request. However, we recognize that it may be time consuming to get this information from manufacturers' corporate offices. Therefore, we highly encourage manufacturers to post it on their website in a place and manner that is readily accessible. FDA will monitor the accessibility of these lists and determine whether further measures are needed to make this information more readily available to pharmacies.

9. What information does a manufacturer have to provide to a wholesaler to enable that wholesaler to comply with the PDMA?

Manufacturers are not required under the PDMA to provide any specific information to wholesale customers. However, the information required under 21 CFR § 203.50(a) for a pedigree statement may be included in the invoice or similar document that would typically accompany or be associated with any shipment of prescription drug products from a manufacturer to a wholesale distributor. FDA encourages manufacturers to do

their part to protect public health by furnishing pedigree information to all of their supply chain partners. See Addendum Question E at the end of this document.

10. What information does an ADR have to provide to a non-ADR to enable that non-ADR to comply with the PDMA (e.g., to pass a pedigree that lists all prior transactions back to the manufacturer)?

ADRs are not required to provide a pedigree, whether they obtained the drug directly from a manufacturer, from an ADR, or from a non-ADR. However, to further advance the shared goals of protecting the public health, FDA encourages all parties in the prescription drug supply chain to cooperate fully by providing pedigrees and information to trading partners for each sale, transfer, or trade of prescription drugs. Therefore, when an ADR sells prescription drugs to another ADR or to a non-ADR, the ADR is encouraged to provide pedigree information obtained at the time of the original purchase of the prescription drugs to its wholesale customers. Each wholesale customer of that ADR, in turn, could then provide updated pedigree information with each successive wholesale distribution. See Addendum Question E at the end of this document.

11. If a wholesaler has ADR status for a particular drug product, but it buys that drug from a non-ADR, is the wholesaler still an ADR for that specific quantity of drugs?

Yes. If the specific quantity of drugs purchased from the non-ADR falls within the description contained in the written agreement between that purchasing ADR and the manufacturer, then that purchasing wholesaler would have ADR status for that specific quantity of drugs. However, even though the ADR is not required to provide the pedigree when the product is further distributed, to further advance the shared goals of protecting the public health, FDA encourages all parties in the prescription drug supply chain to cooperate fully by providing pedigree documents and information to trading partners for each sale, transfer, or trade of prescription drugs. See Addendum Question E at the end of this document.

12. What definition is used to determine who is a manufacturer and, thus, exempt from providing a pedigree?

For purposes of the PDMA, “manufacturer” is defined under 21 CFR § 203.3(s), which incorporates the definition from 21 CFR § 201.1.

13. Are contract manufacturers considered “manufacturers” under the PDMA?

Yes. A contract manufacturer falls within the definition of a "manufacturer" under 21 CFR § 203.3(s), which incorporates by reference the definition of "manufacturer" set forth in 21 CFR § 201.1. FDA has received several inquiries regarding the status of an NDA-holder under 21 CFR §§ 203.3(s)/201.1 when that NDA-holder's prescription drugs are made by a contract manufacturer. Unless the NDA-holder has performed the operations necessary to achieve "manufacturer" status under 21 CFR § 201.1, that NDA-

holder is not technically a "manufacturer" of the drugs within the meaning of the 21 CFR § 203.3(s). In such instances, the NDA-holder would therefore not be exempt from the pedigree requirements on the grounds that it was a manufacturer. Thus, for purposes of the PDMA pedigree requirements only, FDA intends to exercise its enforcement discretion as follows: In those instances where a third party contract manufacturer manufactures prescription drugs for an NDA-holder, that NDA-holder may also be regarded as a manufacturer of those drugs for purposes of that NDA-holder's compliance with § 503(e)(1)(A) of the Act, entering into ADR agreements for those prescription drugs, and for purposes of pedigrees created for those prescription drugs. This exercise of enforcement discretion is not intended to relieve the contract manufacturer of its obligations as a manufacturer, including its obligation to register under § 510 of the Act, nor is it intended to require the NDA-holder to file such a registration unless the NDA-holder would otherwise be obligated to do so.

14. Is a repackager or relabeler exempt from providing a pedigree?
No. Relabelers and repackagers are not considered to be manufacturers under 21 CFR § 201.1. Therefore, unless a repackager or relabeler has ADR status with the manufacturer of that product, they are required to provide a pedigree identifying each prior sale, purchase, or trade of the drug. See Addendum Question E at the end of this document.

15. Is a pedigree required if an exclusive distribution agreement exists?
No, so long as the agreement is in writing. By definition, an exclusivity agreement is a written agreement under which the distributor is authorized to distribute the manufacturer's products for a period or time or for a specified volume of products. Accordingly, such a written agreement would satisfy the requirements related to ADR status in 21 C.F.R. 203.3(u). Please note that, in such instances, the wholesale distributor named in the agreement would have to be included in the manufacturer's list of ADRs under 21 CFR § 203.50(d).

B. Pharmacy/End User Responsibilities

16. Do non-ADRs have to provide a pedigree if the customer is a physician's office?
Yes. The Federal Food, Drug, and Cosmetic Act (the Act) requires non-ADRs to provide a pedigree before each wholesale distribution of a drug. Pursuant to 21 CFR § 203.3(cc), wholesale distribution is defined as the distribution of prescription drugs to persons other than a consumer or patient. Although a physician's office is not explicitly mentioned in 21 CFR § 203.50, which discusses pedigree, it is contemplated within the scope of the language set forth in § 503(e)(1)(A) of the Act that a pedigree would be provided because physicians offices are not specifically excluded.

17. Are pharmacies required to provide a pedigree when they transfer drug product between pharmacies?

For transfers other than intra-company transfers, unless the transfer of prescription drug product from one pharmacy to another is for a documented medical emergency (see 21 CFR § 203.3(cc)(5)), or the sale is of minimal quantities of drugs by retail pharmacies to licensed practitioners for office use (see 21 CFR § 203.3(cc)(10)), retail pharmacies that are not ADRs for the prescription drug products sold or transferred to other retail pharmacies will have to provide a pedigree.

18. Does a chain pharmacy warehouse have to provide a pedigree for drugs that it sends to its retail outlets?

No. Pursuant to 21 CFR § 203.33(cc)(1), intra-company sales are excluded from the definition of wholesale distribution. FDA considers intra-company transfers, such as those from a chain pharmacy warehouse to its own retail outlets, to fall within the scope of an intra-company sale.

19. Do pharmacies have to verify the accuracy and authenticity of the pedigree? If so, how should they do this?

No. Pharmacies do not have this express responsibility under the PDMA, but they are encouraged to perform due diligence in verifying the accuracy of the information and integrity of the source of the drug product.

C. Recordkeeping Requirements

20. What are the recordkeeping requirements for pedigree recipients?

Pursuant to 21 CFR § 203.50(b), the pedigree is subject to the record retention requirements in 21 CFR § 203.60, and must be retained by all wholesale distributors involved in the distribution of the drug product, whether ADR or non-ADR, for 3 years. If the pharmacy receiving the pedigree will not itself engage in further distribution of the product to persons other than a consumer or patient, then the pharmacy is not required to maintain that pedigree under 21 CFR § 203.60. However, consistent with the spirit of the PDMA, FDA encourages pharmacies and other end users to retain the pedigree for 3 years. As a result, if there is any question about the source or history of the product, it can be traced back through the drug supply chain.

21. If an ADR obtains drugs from a non-ADR, is the ADR required to maintain the pedigree?

Yes. Although an ADR is not required to provide a pedigree, pursuant to 21 CFR §§ 203.50(b), and 203.60(d), an ADR is required to retain the pedigree for 3 years.

D. PDMA Scope

22. Does PDMA apply to veterinary prescription drugs?

No. PDMA applies only to prescription drugs intended for use by man. However, FDA is aware that many human prescription drugs are sold to veterinarians. Given that the human drugs are subject to section 503(b) of the Federal Food, Drug, and Cosmetic Act,

the pedigree requirements apply to them under section 503(e). Accordingly, wholesale distributors who are not ADRs must provide a pedigree prior to wholesale distribution of human prescription drugs to veterinarians.

23. Is a pedigree required for the distribution of drug samples?
No. Pursuant to 21 CFR § 203.3(cc)(7), the distribution of drug samples by manufacturers and authorized distributor's representatives is exempt from the definition of wholesale distribution, so the pedigree requirement does not apply. However, those distributing drug samples must comply with the separate requirements set forth in 21 USC §§ 353(c) and (d) and 21 CFR Part 203..

24. Is a pedigree required for medical kits that contain prescription drugs, sometimes referred to as convenience kits?
Yes. "Medical kits" that contain devices and prescription drugs are combination products under 21 CFR §3.2(e)(2), which are defined as “two or more separate products packaged together in a single package or as a unit and comprised of a drug and device products, device and biological products, or biological and drug products.” The "medical kits" referred to in the question consist of separable finished devices and drugs that are combined in a kit for ready availability and use together in a medical setting. The drug product in the kit retains its separate form and individual packaging. Although these kits may be assigned to FDA’s Center for Devices and Radiological Health (CDRH) as the lead Center for regulatory review when the primary mode of action of the kit is attributable to its device component, regulations for the drug and the device components continue to apply. Because a prescription drug component of a convenience kit is separable, and in the same form as when distributed independently, it is subject to the same pedigree requirements as when it is independently distributed. The pedigree must contain the drug’s lot or control number(s), pursuant to 21 CFR §203.50(a). We recognize that the convenience kit itself may have a lot or control number that is different than that on the prescription drug component. The outer container of the kit should also list the lot or control number of the prescription drug component so that the integrity of the kit's seal would not have to be compromised to confirm that the drug's lot number is the same as that listed in the pedigree. See Addendum Question E at the end of this document.

25. Does PDMA apply to bulk drug substances?
Yes. The PDMA applies to drugs subject to § 503(b) of the Act (i.e., prescription drugs). Pursuant to 21 CFR § 203.1, the requirements in 21 CFR Part 203 apply to wholesale distribution of bulk drug substances.

E. Returns

26. Is a pedigree required for prescription drugs that are returned from a pharmacy or a physician’s office to a wholesaler?

Pursuant to the definition of wholesale distribution and other relevant provisions under § 503(e) of the Act and 21 CFR Part 203, a pedigree is required for returns from a pharmacy or physician's office to a wholesaler unless that pharmacy or physician's office is an ADR for those prescription drugs. Prescription drugs generally are returned for two reasons: (1) the pharmacy or physician's office ordered too much and returns the drug to the wholesaler or manufacturer from whom they purchased the drugs, or (2) the drug is expired or close to expiring, in which case the product is returned to the wholesaler or manufacturer from which it was purchased, or to a reverse distributor for destruction. Pharmacies and physicians' offices generally are not ADRs, and they would find it extremely difficult to provide a pedigree when they return prescription drugs because they would not have received a pedigree if the drugs were purchased from an ADR.

FDA recognizes the disruption that this could cause to the more than 55,000 pharmacies and the hundreds of thousand physicians' offices in the United States. Therefore, FDA intends to exercise its enforcement discretion to allow pharmacies and physicians' offices to return drugs that are expired, damaged, recalled, or in some other non-saleable condition, without having to provide a pedigree, provided that (1) they return the drugs to the wholesaler or manufacturer from which they purchased the drugs, or to a licensed reverse distributor for destruction, and (2) they maintain for a period of three years records that document each return and the source from which the pharmacy or physician's office originally purchased the drugs. If the returned prescription drugs are in saleable condition and may subsequently be sold, purchased, or traded by the wholesaler or reverse distributor, then that wholesaler or reverse distributor would be required and expected to pass a pedigree if they are not an ADR for those prescription drugs. Any subsequent pedigree should reflect that the drugs were sold, purchased, or traded to the pharmacy or physician's office and subsequently returned. Because the wholesaler to which the drugs are returned originally sold them to the pharmacy or physician's office, the wholesaler would have all the necessary information to provide a pedigree, even without the pedigree from the pharmacy or physician's office**.**

FDA intends to monitor the drug distribution system for abuses or exploitation of this exercise of enforcement discretion.

We note that pursuant to 21 CFR § 203.3(cc)(9), returns by hospitals, health care entities, and charitable institutions are excluded from the definition of wholesale distribution, provided that the returns comply with 21 CFR § 203.23.

F. Shipping/Delivery Arrangements

27. Is a pedigree required if a manufacturer drop ships on behalf of a non-ADR directly to the pharmacy or customer (i.e., ships the product directly to the non-ADR's customer)?

Yes. Pursuant to 21 CFR § 203.50, the non-ADR seller must provide a pedigree to the purchaser.

28. Is a pedigree required if an ADR drop ships on behalf of a non-ADR directly to the pharmacy or customer?
Yes. Pursuant to 21 CFR § 203.50, the non-ADR seller must provide a pedigree to the purchaser.

29. What is the status of third party logistics providers (TPLP or 3PLs) in the context of PDMA? For example, is a TPLP considered to be a distributor or contractor for the manufacturer for whom the TPLP works?
Based on comments that FDA received from a TPLP, TPLPs typically act as distributors for manufacturers. Therefore, unless the TPLP has ADR status with the manufacturer (which should be posted on the manufacturer's website and reflected in a written contract), the TPLP would be required to provide a pedigree prior to each wholesale distribution. Because of the unique ongoing relationship between a TPLP and a manufacturer, most, if not all, TPLPs distributing prescription drugs on behalf of a manufacturer would be able to obtain ADR status from the manufacturer with which they are doing business. Therefore, the TPLP would be listed on any subsequent pedigree because the TPLP was involved in the prior sale, purchase, or trade of the prescription drug. See Addendum Question E at the end of this document.

G. Inventory

30. Is a pedigree required for products already in the supply chain as of December 1, 2006?
It depends. A pedigree would be required for prescription drug products that are sold, purchased, or traded by a non-ADR after December 1, 2006. In order to give wholesalers sufficient time to prepare and deplete stock that would require a pedigree after December 1, FDA provided 6 months' notice that the stay would expire on December 1, 2006. However, FDA recognizes that there may be some situations where a wholesaler has prescription drugs in stock that were purchased while the wholesaler considered itself an ADR, yet the wholesaler clearly will not be an ADR for those drugs under 21 C.F.R. § 202.3(u) after December 1, 2006. FDA intends to exercise its enforcement discretion until April 1, 2007 regarding the pedigree requirement for such drugs, provided that the wholesaler can furnish documentation that the drugs were purchased prior to December 1, 2006, and that it had purchased the same type of drugs from the manufacturer on at least two prior occasions in the previous 24 months. Bills of sale or invoices could be used for this documentation. Wholesalers that cannot meet this criteria with respect to their inventories will be expected to provide a pedigree for those drugs. FDA believes that the combination of the six month notice that the stay would expire, along with additional four months of enforcement discretion, as described above,

provides the wholesalers described above with sufficient time to deplete their pre-December 1, 2006 inventories.

31. If there are two products on a shelf in a pharmacy, with the same lot number, but one was purchased from an ADR and the other was not, how would the pharmacy know which product came from the ADR and which product came from the non-ADR?
Inventory control is a business process. FDA expects firms to be able to identify and differentiate drug products that have been obtained from different sources and maintain appropriate records in compliance with PDMA.

32. Is a pedigree required for inventory acquired through a pharmacy acquisition, merger, or buyout?
No. The purchase of a pharmacy by another pharmacy would not be considered a wholesale distribution, provided that the drugs purchased by the second pharmacy are dispensed or distributed by that pharmacy in the normal practice of retail pharmacy. Therefore, no pedigree would be required. However, the sale, purchase, or trade of those drugs to another pharmacy or wholesale distributor would be considered a wholesale distribution and a pedigree must be provided if that other pharmacy or distributor is not an ADR. If pedigrees are part of the record for the inventory, they must be provided with the sale, purchase, or trade of the product and retained for the appropriate length of time, as required under 21 CFR §§203.50(b) and 203.60(d).

H. Pedigrees

33. What does "date of each previous transaction" refer to in 21 C.F.R. § 203.50(a)(7)?
"Date of each previous transaction" refers to the date of each prior sale, purchase, or trade of the product. See Addendum Question E at the end of this document.

I. Electronic Pedigrees

34. Will electronic pedigrees that conform to the EPCglobal electronic drug pedigree standards be considered PDMA-compliant? At the time of printing, these standards have not been officially adopted or recognized. Therefore, it is premature for FDA to comment on whether they comply with PDMA requirements.

35. Can paper or electronic pedigrees be used?
Section 203.60(a)(2) states that "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 the PDMA." Both paper

and electronic documents and signatures may be used to meet the pedigree requirement of the Act, provided that the requirements of 21 CFR § 203.60 are met.

36. Is RFID the only way to achieve an electronic pedigree?
No. The PDMA and existing regulations do not require any particular technology for pedigrees. Although FDA has stated on several occasions that RFID is the most promising means to achieve an electronic pedigree, electronic pedigree can also be accomplished using bar codes or other track and trace technologies.

J. Compliance/Enforcement

37. Where should a report be sent if there are concerns regarding a pedigree that has been received?
Criminal activity, possible fraud, diversion, counterfeiting, or any other suspicious activity associated with a pedigree should be reported to FDA's Office of Criminal Investigations at rxdrugcops@oci.fda.gov.

38. What are some examples of issues that might raise questions about the pedigree?

- Drugs that are sold below market price
- Unexplained gaps in the pedigree
- Unexplained differences in ordered product vs. shipped product
- Unexplained, unexpected, or unusual changes in supplier chain
- Unusual variety of lot numbers relative to the size of the shipment
- Multiple, unknown wholesalers from various states listed on the pedigree
- Incomplete paperwork, invoices, or other materials that do not match pedigree
- Pattern of discrepancies in ordered vs. shipped product
- Discrepancies in or missing covert/overt anti-counterfeiting measures
- Supplier refuses to provide a wholesale license from the state licensing authority
- Supplier wants payment in cash only
- A non ADR refuses to provide pedigree documentation
- Supplier refuses to divulge source of the prescription drug

39. If a company says that it is an ADR and not required to provide a pedigree, yet the purchaser has reason to believe that the company is not an ADR, what should the purchaser do?
If a purchaser has reason to believe that the wholesaler is not an ADR, FDA recommends that the purchaser contact the manufacturer to determine whether the entity is an ADR for that product. This is an especially important action to take in those instances where unsolicited offers are received from unfamiliar companies that meet some of the above mentioned causes for concern. In addition, report any concerns as suggested in Question 38.

40. Does the PDMA Compliance Policy Guide 160.900 apply to pharmacies and chain pharmacy warehouses?

Yes. CPG 160.900 relates to the PDMA pedigree requirements. Retail pharmacies and chain pharmacy warehouses are included in the definition of wholesale distributors at 21 CFR § 203.3(dd) and are required to comply with the PDMA. Please see Addendum at: http://www.fda.gov/cder/regulatory/PDMA/PDMA_addendum.pdf

ADDENDUM to FDA's *Guidance for Industry: PDMA Pedigree Requirements – Questions and Answers* Related to the Preliminary Injunction ordered 12/5/06 in *RXUSA Wholesalers, Inc. v. HHS*
12.15.06

A. What is affected by the preliminary injunction?

- 21 CFR § 203.50(a). The court order enjoins FDA from implementing 21 CFR § 203.50(a). 21 CFR § 203.50(a)(6), states that information regarding "each prior transaction involving the drug, starting with the manufacture" be included in the pedigree. However, while the preliminary injunction is in effect, pedigrees shall include information regarding prior transactions going back to the manufacturer *or* the last ADR that sold, purchased, or traded the prescription drugs. FDA encourages wholesalers to include information regarding each prior transaction going back to the manufacturer when that information is available.

- 21 CFR § 203.50(a)(1)-(5). The court order also enjoins FDA from implementing the language in 21 CFR § 203.50 that requires pedigrees to include lot and control numbers, dosage, container size, and number of containers. As described in more detail below, however, the preliminary injunction does not affect the statutory requirement that pedigrees contain the dates of all listed transactions and the names and addresses of all parties involved in those transactions. In addition, since the court did not enjoin implementation of 21 CFR § 203.3(u), a written agreement between a manufacturer and a wholesaler may limit ADR status to a particular lot number(s), dosage, or the number or size of the containers of prescription drugs. We also note that, without the lot number on the pedigree, it would be extremely difficult to track the inventory that matches the pedigree if the inventory is further sold, purchased or traded. Therefore, FDA recommends that the lot or control number, dosage, and the number and size of the prescription drug containers be included on the pedigree even though it is not required while the preliminary injunction is in effect.

- Pedigrees for all current and future inventory are affected by the preliminary injunction as long is it remains in effect.

B. What is not affected by the preliminary injunction?

Pedigrees still must be passed by non-authorized distributors of record (non-ADR) prior to each wholesale distribution. In addition, the court does not mention other pedigree-related regulations or other agency-issued documents relating to the pedigree requirement. Accordingly, those regulations and documents, some of which are described below, are not affected by the preliminary injunction.

- 21 CFR § 203.3(u). This regulation, which went into effect on December 1, 2006, defines "ongoing relationship" for the purposes of determining who qualifies as an authorized distributor of record (ADR.) As of December 1, 2006, only those

wholesale distributors who have an ongoing relationship (including a written agreement) with the manufacturer, as that term is defined by this regulation, are exempt from the pedigree requirement.

- Compliance Policy Guide (CPG) 160.900, which issued in November 2006, remains in effect until December 1, 2007. The CPG describes how FDA intends to prioritize its enforcement efforts regarding the pedigree requirements in the first year after the effective date of 21 CFR §§ 203.3(u) and 203.50. However, FDA will not enforce 203.50(a) as long as the preliminary injunction remains in effect.

- All other definitions in 21 CFR Part 203 that relate to the pedigree requirement, including but not limited to, the definitions of manufacturer and wholesale distribution, have been in effect since December 2000 and remain in effect despite the injunction.

- The names and addresses of all parties to the transaction and the date of the transactions are required by the statute and must be included in the pedigree.

- 21 CFR § 203.50(b). This regulation, which went into effect on December 1, 2006, requires all wholesale distributors (both ADRs and non-ADRs) involved in the distribution of a prescription drug to retain a copy of the pedigree for three years. Accordingly, all wholesale distributors that provide or receive pedigrees after December 1, 2006, must retain copies of the pedigrees for three years.

- 21 CFR § 203.50(c). This regulation, which also went into effect on December 1, 2006, provides that a manufacturer that subjects a drug to additional manufacturing processes is not required to provide a pedigree identifying previous sales of the drug or its components.

- 21 CFR § 203.50(d). This regulation also went into effect on December 1, 2006, and requires manufacturers to maintain a current written list of all ADRs, to specify whether each ADR is authorized to distribute all of the manufacturer's drug products or only particular products, to update its list of ADRs on a continuing basis, and to make its list of ADRs available for public inspection or copying. Accordingly, as of December 1, 2006, all manufacturers should have available for public inspection a current list of ADRs that indicates which drug products the ADR is authorized to distribute.

- 21 CFR § 203.60. This regulation sets forth certain requirements with respect to the use of electronic records and signatures, record retention, and the availability of records for review and reproduction by FDA and other federal, state, and local regulatory and law enforcement officials. This regulation has been in effect since December 2000 and remains in effect despite the injunction.

C. Since the court's order only applies to 21 CFR § 203.50(a), does this mean that the statutory requirement that non-ADRs provide pedigrees that include "each prior sale, purchase, or trade" of the drugs is still in effect?

- Yes. The court order does not enjoin FDA from enforcing the statute. The court order affects only the regulations at 21 CFR § 203.50(a). It has been FDA's long-standing position, consistent with the language of the PDMA and its legislative history, that, 21 CFR § 203.50 notwithstanding, the statute itself requires non-ADRs to provide pedigrees that documents each prior transaction going back to the manufacturer. FDA recognizes, however, that confusion regarding the pedigree requirement could cause disruptions or delays in the nation's drug distribution system. Accordingly, as long as the court order remains in effect, FDA intends to exercise enforcement discretion, as described below. To this end, FDA does not intend to enforce the statute insofar as it requires pedigrees to contain information regarding each transaction going back to the manufacturer. Rather, FDA intends to permit non-ADRs to provide pedigrees that include information regarding transactions going back to the manufacturer *or* the last ADR that handled the prescription drugs. FDA, however, encourages all wholesalers to provide complete pedigrees documenting each prior transaction involving the prescription drug when that information is available.

D. How will FDA apply the court's order outside of the Eastern District of New York (EDNY) and to wholesale distributors that are not plaintiffs in the lawsuit?

- FDA believes that limiting application of the preliminary injunction to either the named plaintiffs or the EDNY could lead to confusion and possible disruptions or delays in the nation's drug distribution system and could provide undue advantage to certain wholesale distributors. Accordingly, to the extent that it could be argued that the injunction should be limited in scope, FDA intends to exercise enforcement discretion in a manner that is consistent with the court's opinion. To this end, as long as the court's order is in effect, FDA does not intend to initiate any enforcement actions against any wholesalers solely for (1) failing to include lot numbers, dosage, container size, or number of containers on a pedigree; or (2) failing to provide a pedigree that goes back to the manufacturer so long as the pedigree otherwise identifies the last authorized distributor of record that handled the drugs.

E. How does the court's order impact what FDA said in the Guidance to Industry: PDMA Pedigree Requirements – Questions and Answers (http://www.fda.gov/cder/regulatory/PDMA/PDMA_qa.pdf)?

- To the extent that Questions 2, 9, 10, 11, 14, 24, 29, and 33 refer to 21 CFR § 203.50(a), as long as the preliminary injunction is in effect, such references are limited to the scope of the court's order. For example, if the question states that a pedigree include information about each prior transaction going back to the

manufacturer, then the answer would be limited to including information going back to the manufacturer *or* the last ADR that handled the drugs.