

# Statement



## Statement of the Pharmaceutical Research and Manufacturers of America

FDA Public Hearing on the  
Prescription Drug Marketing Act Final Rule  
64 Fed. Reg. 67720 (December 3, 1999)

### Pedigree Requirements for Unauthorized Distributors

21 U.S.C. §353(e) (FDCA §503(e))  
21 CFR Part 203 Subpart E

#### Docket Number 92N-0297

Hearing Notice and Request for Comments  
65 Fed. Reg. 56480 (September 19, 2000)

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October 27, 2000

The Pharmaceutical Research and Manufacturers of America (PhRMA) is submitting this set of comments on certain aspects of the 1988 Prescription Drug Marketing Act (PDMA). PhRMA represents the country's leading research-based pharmaceutical and biotechnology companies. PhRMA member companies are devoted to discovering and developing medicines that allow patients to lead longer, healthier, and more productive lives; our members are investing over \$26 billion this year alone in discovering and developing new medicines.

The PDMA is an important piece of consumer legislation passed as a result of Congressional concern that the integrity of the then-existing distribution system for prescription drugs was insufficient to prevent the introduction and eventual resale of substandard, ineffective, or counterfeit drugs.<sup>1</sup>

The PDMA addressed these concerns with various provisions amending the Federal Food, Drug, and Cosmetic Act (FDCA), including: restrictions on the sale and distribution of drug samples (FDCA §§503(c)(1) and 503(d)); restrictions on sales of prescription drugs purchased by hospitals, health care entities, and charitable organizations (FDCA §503(c)); allowing only the original manufacturer to reimport prescription drugs (FDCA §801(d)(1)); **and restrictions on wholesale distributors (FDCA §503(e)).**

The latter provision requires: "Each person who is engaged in the wholesale distribution of a drug . . . and who is not the manufacturer or an authorized distributor of record of such drug shall, before each wholesale distribution . . . provide to the person who receives the drug a **statement (in such form and containing such information**

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<sup>1</sup> Pub. L. No. 100-293, 102 Stat. 95 (1987), 21 USC §§ 331(t), 333(b), 353(c)-(e), and 381.

**as the Secretary may require) identifying each prior sale, purchase, or trade of such drug (including the date of the transaction and the names and addresses of all parties to the transaction)."** FDCA §503(e)(1) (emphasis added).

Noting that the Oversight Subcommittee had held eight days of hearings and had issued three reports on the existing distribution system, the House Energy and Commerce Committee described the purpose of the PDMA in its 1987 report accompanying the bill (H.R. Rep. No. 76, 100<sup>th</sup> Cong., 1<sup>st</sup> Sess. P. 6 (1987)):

American consumers cannot purchase prescription drugs with the certainty that the products are safe and effective. This is not to say that the shelves of the Nation's pharmacies are lined with substandard products, or that there are inadequate controls in the manufacturing process. Rather, the integrity of the distribution system is insufficient to prevent the introduction and eventual retail sale of substandard, ineffective or even counterfeit pharmaceuticals.

Specifically, the existence and method of operation of a wholesale submarket, herein referred to as the "diversion market," prevents effective control over or even routine knowledge of the true sources of merchandise in a significant number of cases. As a result, pharmaceuticals which have been mislabeled, misbranded, improperly stored or shipped, have exceeded their expiration dates, or are bald counterfeits, are injected into the national distribution system for ultimate sale to consumers . . . . The legislation is designed to restore the integrity and control over the pharmaceutical market necessary to eliminate actual and potential health and safety problems before serious consumer injury results.

As recently as October 11 this year, Congressman John Dingell, principal sponsor of the PDMA, took to the floor of the House of Representatives to argue forcefully against the repeal of certain key provisions of this landmark piece of consumer legislation. He specifically noted that "...the PDMA was designed to restore needed integrity and control over the pharmaceutical market, eliminating actual and potential health and safety problems before injury to the consumer could occur." Furthermore, he stated, "...I find nothing today that suggest that the problem with misbranded, adulterated, or even counterfeit drugs has been solved, and if anything, the problem may be getting worse."

With the cautionary words of Congressman Dingell in mind, it is critical that the provisions of the PDMA that require establishment of a chain of custody, or pedigree, be preserved. PhRMA member companies put the safety of patients who need their medicines above all other considerations.

## **A. Compliance with the NDA**

The cornerstone of the development of safe and effective prescription medicines is the original manufacturer's full compliance with an FDA-approved New Drug Application (NDA) and total control of the process from the selection of raw materials, design of the manufacturing process, packaging of the final product, evaluation of the conditions for storage (including the establishment of an expiration date after which the medication should be discarded), and careful selection of the distribution pathway. Compliance with the NDA is the statutory and regulatory touchstone for assuring American patients that the medicines they receive will be of the highest quality.

Pharmaceutical manufacturers ship finished pharmaceuticals in bulk packages to licensed drug wholesalers. The wholesaler insures that the products are stored under the appropriate environmental conditions to prevent product degradation prior to shipment to the various pharmacies that dispense directly to the patient. Some pharmaceuticals such as inhalers and nasal sprays are packaged in their own unit-of-use box with accompanying patient directions. Most pills are packaged in large bottles of varying count depending on customer demand. For example, a large hospital pharmacy may request bottles of 1000 pills (or more) while a neighborhood pharmacy may request smaller bottles. This practice occurs because pharmacies want to control their inventory so that pharmaceutical product dispensed to the consumer is used within the lot expiration date on the label.

Not all pharmaceuticals come in pill or tablet form. There are capsule formulations, liquid formulations for oral administration, freeze-dried powders that must be reconstituted, transdermal patches, powders, creams, and lotions for external use, drops for ocular administration, and liquid concentrates for intravenous formulation. Some timed-release pills are designed to carefully control the release of drug following administration. Every product that is approved by the FDA is individually evaluated for stability and potency over the period from time of release from the manufacturer to the expiration date. Conditions for storage in the manufacturers' original container are specified in the NDA in detail so that the product the consumer receives will be both safe and efficacious when taken as prescribed. The PDMA also required the Secretary of HHS to specify minimal conditions for storage and handling by distributors to preserve product integrity.

## **B. Pedigree Requirement for Unauthorized Wholesalers**

The second critical feature of PDMA, and one of the subjects of the FDA's final rule published last December, is the requirement for secondary wholesalers who are not the wholesaler authorized by the pharmaceutical manufacturer to maintain records of the pharmaceutical's transfer from the manufacturer to the authorized wholesaler and then to any subsequent secondary or unauthorized wholesaler(s). See 64 Federal Register 67720, 67761 (21 C.F.R. Subpart E, §203.50). This record, also commonly termed the pedigree, is in fact required by the PDMA (Section 503(e)(1)). This provision

establishes a legal chain of custody of the pharmaceutical, assuring that it originated from the manufacturer. The provision serves two purposes. First it prevents the introduction of counterfeit medications into the supply chain. Second, it provides the necessary information at all levels of the distribution chain so that in the event of a recall, all the affected pharmaceutical product can successfully be withdrawn from the market. **PhRMA believes that the final rule promulgated by the FDA is an accurate reflection of Congressional intent.**

**C. Response to FDA Questions on Distribution of Prescription Drugs by Unauthorized Wholesalers**

In the notice announcing this hearing, the Food and Drug Administration poses a series of questions (see 65 Federal Register 56480, 56483 (September 19, 2000)). PhRMA does not have first-hand knowledge about the magnitude of the secondary or unauthorized wholesale distribution system within the United States. Because of this, PhRMA is not in a position to respond to several of the questions. However, PhRMA offers responses to the following questions.

- 3. If the act were amended by Congress to delete the requirement for provision of a drug pedigree by unauthorized distributors, would there be an increased risk of distribution of counterfeit, expired, adulterated, misbranded, or otherwise unsuitable drugs to consumers and patients?*

The answer to this question is an unequivocal yes. Without a legally required document assuring traceability back to the original manufacturer, there is no guarantee that the pharmaceutical product is not counterfeit. Furthermore, even in cases where drug product may have originated at the NDA-approved manufacturer, there would not be any history of where the particular lot of pharmaceutical was stored. Exacting storage conditions identified in the NDA must be maintained to assure product quality. Thus, American consumers would be placed at risk of receiving pharmaceuticals that are sub-potent or even have no activity, or are adulterated by dangerous by-products or other contaminants toxic to patients' health.

It is important to consider what type of information the FDA is requesting in the pedigree. This can be found in the final rule (§ 203.50(a)(1-7)). Such information includes the name of the drug, dosage, container size, lot or control number, name of the business selling the drug, and the date of the transaction. All of this information is readily available on the transaction order between the pharmaceutical manufacturer and the authorized wholesaler.

- 6. If actual sales by a manufacturer to a distributor were used by FDA as the only criterion to determine whether an ongoing relationship exists between them (and as a result, whether the distributor is an authorized distributor of record), would it result in more distributors being authorized than if a written authorization agreement is*

*required? What other types of criteria might be used by FDA to make this determination?*

PhRMA believes that it would be wrong for FDA to use simple sales records as the only criterion for an "authorized distributor." This clearly goes against the Congressional intent as outlined in Section 503(e)(4)(A) which states: ". . . the term 'authorized distributors of record' means those distributors with whom a manufacturer has established an ongoing relationship to distribute such manufacturer's products." One or two sales to a secondary distributor does not meet this statutory definition. Pharmaceutical companies establish specific business relationships with wholesale distributors. The definition of "authorized distributors of record" in the final regulations recognizes these relationships in a clear, reasonable, and enforceable way, and thereby implements Congress's intent in the PDMA. That definition should be retained.

\* \* \*

In conclusion, PhRMA believes that this issue cannot be addressed adequately without recognizing the extensive Congressional hearing record that led to passage of the specific provision of the PDMA that is the subject of today's meeting. Consider this passage from the 1986 Congressional report, "**Dangerous Medicine: The Risk To American Consumers From Prescription Drug Diversion And Counterfeiting**" (Committee Print 99-Z, April 1986, p. 20; Report by the Subcommittee on Oversight and Investigations of the Committee on Energy and Commerce, U.S. House of Representatives):

"The realities of the wholesale marketplace have combined to create a system in which a large amount of attractively priced pharmaceuticals are constantly available, some of which are not safe or effective. The physical movement, conditions of storage, and, in some cases, even the origin of much of this merchandise is unknown to the first, second or third level buyer, who in effect plays a form of Russian roulette. This situation cannot be allowed to continue."

PhRMA is concerned that this situation not be allowed to recur; we urge FDA to continue to adhere to the Congressional safeguards established in the PDMA, which are faithfully incorporated in the final PDMA rule.

Respectfully submitted,



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